

**Abstracts**  
of the  
**Annual Meeting**  
of the  
**Iuliu Hațieganu University of Medicine and Pharmacy**  
**Cluj-Napoca**  
**2-5 December 2014**

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### CONTENTS

#### MEDICINE

##### Medical Sciences

- Heart rate variability in coronary heart disease  
LUCIAN DANIEL RUSU, LAURA POANTĂ, MIHAI LUCIAN RUSU.....S131
- Prognostic factors of response to endoscopic treatment in painful chronic  
pancreatitis - retrospective observational study  
ALINA MÂNDRUȚIU, ALINA TANȚĂU, MARCEL TANȚĂU.....S132
- The efficiency and the safety of the biologic treatment in elderly patients with  
multiple comorbidities and Crohn's disease. Case report  
ALINA MÂNDRUȚIU, IOANA VIȘOVAN, LIDIA CIOBANU, MIHAELA LASZLO,  
ALINA TANȚĂU.....S133
- Total shoulder arthroplasty for a giant-cell tumor of the bone  
ALINA POPA, ALEXANDRINA NICU, MONICA BORDA, LÁSZLÓ IRSAY,  
RODICA UNGUR, IOAN ONAC, VIORELA CIORTEA.....S134
- Utility of modified stop bang questionnaire for the assessment of the risk and the level  
of knowledge on obstructive sleep apnea syndrome of participants in driving schools  
ANDREEA CODRUTA COMAN, CRISTINA BORZAN, DOINA ADINA TODEA.....S135
- Challenges of chronic cough in respiratory practice  
DOINA ADINA TODEA, ANDREEA CODRUTA COMAN.....S136
- Multiple trauma patient following road traffic accident rehabilitation -  
Case presentation  
ELENA CLAUDIA MICU, LASZLO IRSAY, VIORELA CIORTEA, RODICA UNGUR,  
IOAN ONAC, MONICA BORDA.....S137

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Ethical aspects of smoking cessation among the population from  
Transylvania region - stop smoking cessation program  
DOINA ADINA TODA, ANDREEA CODRUTA COMAN.....S138

Osteoporosis in patients with total hip arthroplasty  
VIORELA CIORTEA, RODICA UNGUR, LASZLO IRSAY, ALINA POPA, DELIA POPA,  
CLAUDIA MICU, IOAN ONAC, MONICA BORDA.....S139

Occupational stress in irritable bowel syndrome  
STEFAN-LUCIAN POPA, DAN LUCIAN DUMITRASCU.....S140

Differences in the surface ECG aspect depending on the type of flutter  
(clockwise or counterclockwise)  
RADU ROSU, OLIVIA SECATUREANU, LUCIAN MURESAN, GABRIEL CISMARU,  
MIHAI PUIU, GABRIEL Gusetu, DANA POP, LAURA MADA, CATALIN PESTREA,  
DUMITRU ZDRENGHEA.....S141

Anthropometric and morbidity assessment on late preterm newborn infants with  
intrauterine growth restriction  
MONICA G. HĂȘMĂȘANU, MELINDA I. BAIZAT, SORANA D. BOLBOACĂ,  
TUDOR C. DRUGAN, MELINDA MATYAS, GABRIELA ZAHARIE.....S142

*PONI* in patients with non-alcoholic steatohepatitis  
MIRCEA VASILE MILACIU, ȘTEFAN CRISTIAN VESA, DOREL SÂMPELEAN,  
IOANA PARA, MARIA-SÎNZIANA MOLDOVAN, LORENA CIUMĂRNEAN.....S143

Clinical and paraclinical aspects of the diabetic foot – a 5-year study  
VASILE NEGREAN, TEODORA ALEXESCU, MIRCEA VASILE MILACIU.....S144

Is pulmonary sarcoidosis a difficult diagnosis?  
DANIELA NICOARA, DOINA TODA.....S145

Tuberculosis - lung cancer association, a diagnostic challenge?  
DOINA TODA, DANIELA NICOARA.....S146

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Hemophagocytic syndrome related to chronic B and C hepatitis in autoimmune diseases: A case series  
 PAULINA VELE, LAURA DAMIAN, SIAO-PIN SIMON, NADIA RADICS,  
 SIMONA REDNIC.....S147

Associations between adherence, attitude towards pain medication and quality of life in patients with chronic rheumatic diseases  
 LINDA GHIB, SONIA IURIAN, MARIA-MAGDALENA TĂMAȘ, ADINA POPA,  
 SIMONA REDNIC.....S148

The value of cardiac MRI in the differential diagnosis between infectious myocarditis and myocardial fibrosis in patients with systemic sclerosis  
 GABRIEL CISMARU, ROXANA MATUZ, LUCIAN MUREȘAN, GABRIEL GUȘETU,  
 PAUL PUIE, MIRELA CEBANU, RADU ROȘU, DUMITRU ZDRENGHEA,  
 DANA POP.....S148

Fascicular ventricular tachycardia in a student, treated by ablation  
 GABRIEL CISMARU, PAUL PUIE, LUCIAN MURESAN, RADU ROSU,  
 ROXANA MATUZ, ANDREI CISMARU, MIHAI PUIU, GABRIEL Gusetu,  
 DUMITRU ZDRENGHEA, DANA POP.....S150

The importance of nutrition in HIV patients  
 FLAVIA-IOANA MANOLE, DOINA MIERE, FLOAREA MOCEAN.....S151

Ventricular tachycardia ablation in the Cardiology Department - Rehabilitation Hospital Cluj-Napoca  
 CISMARU GABRIEL, LUCIAN MURESAN, RADU ROSU, MIHAI PUIU,  
 MARIUS ANDRONACHE, PAUL PUIE, ROXANA MATUZ, ANDREI CISMARU,  
 GABRIEL Gusetu, DANA POP, DUMITRU ZDRENGHEA.....S152

Relationship between fall risk factors, bone mineral density and fragility fractures in postmenopausal women  
 ILEANA MONICA BORDA, RODICA UNGUR, LASZLO IRSAY, IOAN ONAC,  
 ALINA POPA, ELENA CLAUDIA MICU, VIORELA CIORTEA.....S153

Quality of life in children with liver diseases  
 TUDOR L. POP, ANTONIA FARCASIU, ALINA GRAMA, ANA ȘTEFĂNESCU.....S154

# - Clujul

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Supplement No. 3, Vol. 87, 2014; B+ category Journal; CNCSIS code 253, no. 94  
p-ISSN 1222-2119, e-ISSN 2066-8872

The importance of allegiance for producing the placebo effect  
SEBASTIAN-MIHAI ARMEAN, KRISZTINA-AGOTA MATYAS,  
IOANA-VALENTINA MICLUTIA, ANCA-DANA BUZOIANU.....S155

Non-invasive assessment of fibrosis in children with liver diseases  
TUDOR L. POP, ANA ȘTEFĂNESCU, ALINA GRAMA, ANCA MANIU,  
HORIA ȘTEFĂNESCU.....S156

Alagille syndrome as a cause for neonatal cholestasis  
ALINA GRAMA, SIMONA CĂINAP, SIMONA OPRÎȚA, OTILIA FUFUZAN,  
TUDOR L. POP.....S157

Opportunistic inaugural infections in patients living with HIV/AIDS in the  
Regional Center Cluj  
IRINA FILIPESCU, ROXANA IUBU, CRISTIAN MARCU, MIRELA FLONTA,  
MIHAELA LUPSE, CORINA ITU.....S158

Can mood stabilizers improve the antidepressant therapy?  
KRISZTINA-AGOTA MATYAS, SEBASTIAN-MIHAI ARMEAN, OANA TUDORACHE,  
IOANA-VALENTINA MICLUTIA, ANCA-DANA BUZOIANU.....S159

The *VKORC1 -1693G>A* polymorphism is not associated with atrial fibrillation  
STEFAN CRISTIAN VESA, ADRIAN PAVEL TRIFA, SORIN CRISAN,  
ANCA DANA BUZOIANU.....S160

Body Integrity Identity Disorder - an ethical dilemma  
BIANCA-IASMINA DRAGOMIR, ALEXANDRA CAMPEAN.....S161

The study of oxidative stress in preterm newborns with respiratory distress  
syndrome  
MELINDA MATYAS, LIGIA BLAGA, MONICA HASMASANU,  
GABRIELA ZAHARIE.....S162

“Old” and “new” markers in early neonatal sepsis – diagnostic value  
GABRIELA ZAHARIE, MONICA HASMASANU, SORANA BOLBOACA,  
LIGIA BLAGA, T. ZAHARIE, MELINDA MATYAS.....S163

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Cardiac involvement in scleroderma patients  
 I. R. DOBROTĂ, L. MUREŞAN, A. PETCU, S. REDNIC.....S164

Prognostic factors for outcome of patients with *Clostridium Difficile* infection  
 TEODORA IACOB, IOANA CUCUIANU, OVIDIU IONESCU, IONEL CIUTICA,  
 MIHAELA LUPSE.....S165

### Basic Sciences

Epidemiological implications and nosocomial risks associated with  
 systemic infections  
 IRINA BRUMBOIU, VALENTINA TZANEVA, DANIELA PETRUŞ.....S166

Quercetin associated with chronic moderate exercise protects the endothelial  
 function in the rat model of type 1 diabetes  
 IRINA C. CHIŞ, ANDREI COSERIU, BIANCA AZAMFIREI, REMUS MOLDOVAN,  
 SIMONA CLICHICI.....S167

Publishing time-frame evaluation for doctoral students in the United Kingdom  
 ANDRADA ELENA URDA-CÎMPEAN, ANDREI ACHIMAŞ-CADARIU,  
 TUDOR C. DRUGAN.....S168

Efficiency of photodynamic therapy on WM35 melanoma with new synthetic  
 porphyrins: role of chemical structure, intracellular targeting and antioxidant defense  
 IOANA BALDEA, DIANA ELENA OLTEANU, POMPEI BOLFA, RODICA MARIA ION,  
 NICOLETA DECEA, MIHAI CENARIU, MANUELA BANCUI,  
 ALINA VIORICA SESARMAN, ADRIANA GABRIELA FILIP.....S169

The combined therapy with resveratrol and hypothermia prevents apoptosis  
 and improves oxidative stress in a neonatal rat model of hypoxic-ischemic  
 encephalopathy  
 A. M. TOADER, V. GRIGORIAN, M. POPESCU, A. G. FILIP, F. TABARAN, O. GRAD,  
 A. MUREŞAN.....S170

Assessment of health related quality of life concept in patients with premalignant  
 and malignant cervix pathology  
 MIHAELA IANCU, TUDOR C. DRUGAN, PATRICIU ACHIMAŞ-CADARIU,  
 ANDREI ACHIMAŞ-CADARIU.....S171

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Celiac disease concealed by allergic manifestations (case report)  
GABRIEL SAMASCA, CARMEN ABRUDAN, GENEL SUR, DIANA DELEANU.....S172

Modulation of UVB-induced oxidative stress and apoptosis with a vegetal extract  
with antioxidant capacities via BAX- $\alpha$  and NF- $\kappa$ B cytosolic factors in hacat human  
keratinocytes cell line  
HANA PETRA DECEAN, REMUS IOAN ORASAN, PIROSKA VIRAG.....S173

The therapeutic modulation of essential hypertension in connection with the genetic  
polymorphism of the renin-angiotensin-aldosterone system (RAAS)  
OANA MOCAN, LUCIA-MARIA PROCOPCIUC.....S174

The status of quality management training among Romanian dentists  
MARIUS-IONUȚ UNGUREANU, SIMONA-ELENA ZAVROȚCHI,  
MARA PAULA TIMOFE, FLOAREA MOCEAN.....S175

Injury surveillance in Romania. JAMIE project  
DIANA RUS, FLORIN JURCHIS, ERIKA ANDRADA BARAGAN,  
RAZVAN MIRCEA CHERECHES, CATALIN BABA, FLOAREA MOCEAN.....S176

Assessment of the clinical laboratories performance and quality management from  
the clients' perspective  
MARIUS-IONUȚ UNGUREANU, FLOAREA MOCEAN.....S177

Treatment with non-steroidal anti-inflammatory drugs (NSAIDS) in ankylosing  
spondylitis. What is the reality of their effectiveness in current practice?  
RUXANDRA ELENA SCHIOTIS, PILAR FONT, ALEJANDRO ESCUDERO,  
EDUARDO COLLANTES, ANCA DANA BUZOIANU AND THE REGISPONSER  
STUDY GROUP.....S178

The evaluation of therapy with proton pump inhibitors in patients admitted to a non  
ICU gastroenterology department  
MARIA NEAG, CORINA BOCSAN, ANCA DANA BUZOIANU, ADINA POPA,  
REMUS CAMPEAN, PETRU ADRIAN MIRCEA.....S179

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NMR spectroscopy - a modern metabolomic technique used in the diagnosis and management of metabolic genetic diseases; our experience of Romanian patients with urea cycle disorders, alkaptonuria or galactosemia  
 ROMANA VULTURAR, ALINA NICOLESCU, PAULA AVRAM,  
 CĂLIN DELEANU.....S180

Stakeholders involved in physical activity services delivery for youth and adolescents at a local level. The case study of two university centers  
 PETRU SANDU, FLOAREA MOCEAN.....S181

The influences of built environment on the physical activity of youth and adolescents. A literature review  
 PETRU SANDU, FLOAREA MOCEAN.....S182

### Surgical Sciences

Proinflammatory cytokines - a possible diagnostic method in endometriosis  
 ANDREI MALUȚAN, NICOLAE COSTIN, RAZVAN CIORTEA, CARMEN BUCURI,  
 MARIA RADA, DAN MIHU.....S183

New possibilities of stem cells utilization for the treatment of articular cartilage focal defects  
 HOREA BENEĂ, GHEORGHE TOMOAIĂ.....S184

Tibio-tarsal joint biomechanics analysis through finite element modeling  
 DORU-ALEXANDRU TOFAN, CIPRIAN BARDAS, ARTUR MARTIN,  
 GHEORGHE TOMOAIĂ.....S185

Neovascular glaucoma after central retinal artery obstruction and chronic hypoxia of the head.  
 CRISTINA NICULA, RALUCA POPESCU.....S186

A case of Harada disease  
 CATALIN CARAUS, ADRIAN MOROTI.....S187

# - Clujul

## Medical - Journal of Medicine and Pharmacy

Supplement No. 3, Vol. 87, 2014; B+ category Journal; CNCSIS code 253, no. 94  
p-ISSN 1222-2119, e-ISSN 2066-8872

Correlation between the differences of macular thickness and the differences of retinal nerve fiber layer, measured with *Stratus OCT*, in the diagnosis of Primary Open-Angle Glaucoma (POAG)  
RALUCA MARIA LASCA, OMAR ZAHAF, CRISTINA STAN, ANA BANC,  
HARRIETTA ANCA CIPLEA, SORINA DEMEA, HOREA DEMEA.....S188

Evaluation of inflammatory markers in pregnant women at risk for the prediction of preeclampsia  
MIHAELA OANCEA, DAN MIHU, RAZVAN CIORTEA, DARIA GROZA,  
SEPTIMIU CIUCHINA, HAJNALKA HUDACSKO, CRISTIAN-IOAN IUHAS.....S189

The results of the selective ultrasound screening program of the neonatal hip  
DANA VASILESCU, DAN VASILESCU, SORIN DUDEA, DAN COSMA,  
ANDREI CORBU.....S190

The surgical hip dislocation for anatomical reduction of the slipped capital femoral epiphysis in children and adolescents - preliminary results and review of the literature  
DAN COSMA, DANA VASILESCU, ANDREI CORBU.....S191

Mechanical complications of acute myocardial infarction: between agony to ecstasy. Report of two surgically treated cases  
DAN BINDEA, BOGDAN VASILIU, SILVIU SALOMIE, CATALIN TRIFAN,  
ALEXANDRU OPREA, SIGISMUND PAPP, STANCA ASZALOS, ADRIAN STEF,  
TRAIAN SCRIDON, ADRIAN MOLNAR, CAMELIA OBER, RUXANDRA BEYER,  
CALIN HOMORODEAN.....S192

Native valve infectious endocarditis: surgical treatment in the experience of the cardiovascular surgery clinic at the "Niculae Stăncioiu" Heart Institute in Cluj-Napoca  
ADRIAN MOLNAR, IOAN MUREȘAN, DIANA SĂCUI, CATALIN TRIFAN,  
TRAIAN SCRIDON.....S193

Congenital optic nerve pit: A case report  
ANA BANC, CRISTINA STAN.....S194

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## Medical - Journal of Medicine and Pharmacy

Supplement No. 3, Vol. 87, 2014; B+ category Journal; CNCSIS code 253, no. 94  
p-ISSN 1222-2119, e-ISSN 2066-8872

Dedifferentiated liposarcoma of the spermatic cord  
 TRAIAN ONIU, MIHAI SUCIU, CORNEL LUNGOCI, IOAN SIMON,  
 VALERIAN LUCAN, VALENTIN MUNTEAN.....S195

Gastric outlet obstruction: a late sequelae of acid ingestion in children  
 ANCA BUDUȘAN, ALEXANDRU PÂRVAN, ALEXANDRA PAL.....S196

Anomalous right hepatic artery reconstruction during duodenopancreatectomy for  
 pancreatic head adenocarcinoma  
 RAZVAN SCURTU, RALUCA APOSTU, CEZAR POP, CONSTANTIN CIUCE.....S197

A rare case of Buschke-Lowenstein tumor with scumous cell carcinoma:  
 A case report  
 CRISTINA GIURGIU, CRISTINA MUNTEAN, GABRIEL PETRE, RAZVAN SIMESCU,  
 VALENTIN MUNTEAN.....S198

Multidisciplinary and individualized approach of hyperthermic intraperitoneal  
 chemotherapy  
 CORNELIU LUNGOCI, DANIEL MOGA, DORIN PETREUS, NICOLETA STROIA,  
 ROZICA MOGA, TRAIAN DORIN ONIU, AUREL ION MIRONIUC.....S199

Necrotizing fasciitis in the perineal and gluteal areas  
 IOAN SIMON, OVIDIU FABIAN, DARIUS SALCERIU,  
 MAXIMILIAN MUNTEAN, TRAIAN ONIU.....S200

Compartment syndrome of the leg  
 VALENTIN MUNTEAN, DARIUS SALCERIU, OVIDIU FABIAN, TRAIAN ONIU,  
 RAZVAN SIMESCU, GABRIEL PETRE, COSMIN RADU.....S201

Ten tips for safe and effective surgery of thyroid cancer  
 VALENTIN MUNTEAN, RAZVAN SIMESCU, GABRIEL PETRE, COSMIN RADU,  
 OVIDIU FABIAN.....S202

# - Clujul

## Medical - Journal of Medicine and Pharmacy

Supplement No. 3, Vol. 87, 2014; B+ category Journal; CNCSIS code 253, no. 94  
p-ISSN 1222-2119, e-ISSN 2066-8872

### PHARMACY

- Simultaneous quantification of biogenic amines by liquid chromatography with fluorescence detection  
MARIA ILIEȘ, ALINA UIFĂLEAN, CODRUȚA HEGHEȘ, CRISTINA IUGA,  
FELICIA LOGHIN.....S203
- Stability evaluation of the growth hormone by SDS-PAGE  
RAUL NICOARĂ, ELENA DINTE, ALINA UIFĂLEAN, MARIA ILIEȘ,  
CODRUȚA HEGHEȘ, CRISTINA IUGA.....S204
- Synthesis of iron oxide nanocubes and manganese ferrites nanospheres for magnetic hyperthermia applications  
CRISTIAN IACOVITA, RARES STIUFIUC, ADRIAN FLOREA, ALINA DUTU,  
GABRIELA STIUFIUC, SEVER MICAN, TEODORA RADU, ROMULUS TETEAN,  
CONSTANTIN M. LUCACIU.....S205
- Preliminary phytochemical studies on some indigenous species belonging to Cucurbitaceae family  
IRINA IELCIU, LAVINIA RUS, RAMONA PĂLTINEAN, LAURIAN VLASE,  
GIANINA CRIȘAN.....S206
- Morphological and histo-anatomical differences between two indigenous corydalis species: *Corydalis cava* L. and *Corydalis solida* L.  
RAMONA PĂLTINEAN, IRINA IELCIU, ALINA POPA, GIANINA CRIȘAN.....S207
- B-cyclodextrin/polyethyleneimine film modified glassy carbon electrodes for the detection of some pharmaceuticals  
LUMINIȚA FRITEA, MIHAELA TERTIȘ, CECILIA CRISTEA,  
ROBERT SÂNDULESCU.....S208
- Nanostructured polymeric films for biosensor design  
ANDREEA CERNAT, ALAN LE GOFF, ROBERT SÂNDULESCU,  
SERGE COSNIER.....S209

### Editorial board

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p-ISSN 1222-2119, e-ISSN 2066-8872

- 
- Nanomaterials-based sensors for acetaminophen and dopamine detection  
MIHAELA TERTIȘ, LUMINIȚA FRITEA, ROBERT SĂNDULESCU,  
CECILIA CRISTEA.....S210
- Nanostructured platforms with different types of polymers for biosensors  
development  
CECILIA CRISTEA, MIHAELA TERTIȘ, LUMINIȚA FRITEA, ANCA FLOREA,  
OANA HOSU, ROBERT SĂNDULESCU.....S211
- Antineoplastic drug detection by molecular imprinting sensor based on  
electropolymerization of microporous-metal-organic framework  
ANCA FLOREA, CECILIA CRISTEA, ROBERT SĂNDULESCU, FRANCIS VOCANSON,  
NICOLE JAFFREZIC-RENAULT.....S212
- Immunosensor based on magnetic nanoparticles for selective detection  
of acetaminophen  
OANA-ALEXANDRA HOSU, MIHAELA TERTIȘ, CECILIA CRISTEA,  
ROBERT SĂNDULESCU.....S213
- Chiral calix[6]arene derivative as chiral selector for the enantioseparation  
of warfarin  
IOANA TIUCA, ANAMARIA ANTAL, EDE BODOKI, RADU OPREAN.....S214
- Impact of experimental variables over enantio recognition in the development of  
MIP-based chiral electrochemical sensors  
BOGDAN-CEZAR IACOB, VICTOR MATEICIUC, EDE BODOKI,  
RADU OPREAN.....S215
- In vivo/in vitro evaluation of the antioxidant and anti-inflammatory potential of  
some 2'-phenil-2,5'-bisthiazoles  
CATALIN ARANICIU, ALINA ELENA PARVU, OVIDIU ONIGA, DANIELA BENEDEC,  
SMARANDA ONIGA, MARIANA PALAGE.....S216
- Antioxidant activity evaluation of some chromenyl-thiosemicarbazones and  
chromenyl-thiadiazolines  
IOANA IONUT, BOGLARKA SORBAN, BRINDUSA TIPERCIUC, DANIELA BENEDEC,  
ILIOARA ONIGA, OVIDIU ONIGA.....S217

# - Clujul

## Medical - Journal of Medicine and Pharmacy

Supplement No. 3, Vol. 87, 2014; B+ category Journal; CNCSIS code 253, no. 94  
p-ISSN 1222-2119, e-ISSN 2066-8872

Synthesis and antimicrobial screening of some new hybrid chromonyl-heterocyclic compounds

CRISTINA MARIANA NASTASĂ, BRÎNDUȘA TIPERCIUC, LAURIAN VLASE,  
ADRIAN PÎRNĂU, MIHAELA DUMA, OVIDIU ONIGA.....S218

Synthesis, characterization and evaluation of anti-inflammatory activity of some new pyridyl-thiazolo[3,2-b][1,2,4]triazole derivatives

ALEXANDRA TOMA, DENISA LEONTE, LAURIAN VLASE, CRISTINA MOGOȘAN,  
VALENTIN ZAHARIA.....S219

Synthesis of l- $\alpha$ -amino acids with thiazole structure by enzymatic dynamic kinetic resolution

DENISA LEONTE, CSABA PAIZS, FLORIN DAN IRIMIE,  
VALENTIN ZAHARIA.....S220

Design, synthesis and biological evaluation of new neurotensin analogues containing the 2-arylthiazole moiety

DENISA LEONTE, EMMANUELLE RÉMOND, ADELINÉ RENÉ, CÉLINE M'KADMI,  
JEAN MARTINEZ, VALENTIN ZAHARIA, FLORINE CAVELIER.....S221

Synthesis and characterization of a series of novel phenothiazinyl-aryl-amides and thioamides

ADRIANA GROZAV, BALAZS BREM, EMESE GAL, LUIZA GAINA,  
CASTELIA CRISTEA, VALENTIN ZAHARIA.....S222

Pain management in the elderly patient: community and nursing home

DANIELA P. PRIMEJDIE, MARIUS TRAIAN BOJIȚĂ, CORNELIA REVNIC,  
ADINA POPA.....S223

The assessment of potential drug interactions in community pharmacy patients receiving cardiovascular drugs

CORINA BRICIU, LAURIAN VLASE, DIANA E. DUMITRAS, ADINA POPA.....S224

Evaluation of antibiotic use in a thoracic surgery department

LAVINIA ALEXANDRA DRĂGAN, DIANA ELENA DUMITRAȘ, ADINA POPA.....S225

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p-ISSN 1222-2119, e-ISSN 2066-8872

- 
- Off-label use of antibiotics in neonates  
PATRICIA TARCEA BIZO, ADINA POPA.....S226
- Comparative phytochemical characterization, antioxidant and antibacterial  
properties of mentha viridis and mentha longifolia  
DANIELA BENEDEC, DANIELA HANGANU, LAURIAN VLASE, ILIOARA ONIGA,  
IULIA POPICA, AUGUSTIN MOT, GRIGORE DAMIAN,  
RADU SILAGHI-DUMITRESCU.....S227
- Phytochemical, antioxidant and hepatoprotective evaluation of Rosmarinus  
officinalis L. hydroalcoholic extract  
DANIELA HANGANU, NELI-KINGA OLAH, BOGDAN SEVASTRE,  
RAMONA FLAVIA BRINZAN, SONIA SOCACI, OANA RAITA, CONSTANTIN BELE,  
ILIOARA ONIGA, DANIELA BENEDEC.....S228
- Pharmacognostical research on Heracleum sphondylium L. (Apiaceae) from Romania  
DANIELA BENEDEC, ANDREEA DRĂGUŞ, VLASE LAURIAN, DANIELA HANGANU,  
ANCA TOIU, ILIOARA ONIGA.....S229
- Romanian code of the pharmaceutical ethics – a new conception  
OFELIA CRIŞAN, SPERANŢA IACOB.....S230
- Decision analysis of the use of antibiotics in Romania  
ANAMARIA BOBOIA, LAURA SILVIA FLOREA, CONSTANTIN POLINICENCU....S231
- Comparative study between the sales of H2 antagonists and proton pump inhibitors  
LAVINIA ALEXANDRA FEHER, ANAMARIA BOBOIA,  
CONSTANTIN POLINICENCU.....S232
- The influence of duloxetine on the atomoxetine pharmacokinetics  
IOANA TODOR, CORINA BRICIU, MARIA NEAG, DANA MUNTEAN,  
CORINA BOCŞAN, ANCA BUZOIANU, MARCELA ACHIM, ADINA POPA,  
ANA-MARIA GHELDIU, LAURIAN VLASE .....S233
- Formulation optimization of quercetin-loaded liposomes through a D-optimal  
experimental design  
LUCIA RUXANDRA TEFAS, DANA-MARIA MUNTEAN, ALINA SILVIA PORFIRE,  
LAURIAN VLASE, MARCELA ACHIM, IOAN TOMUŢĂ.....S234

# - Clujul

## Medical - Journal of Medicine and Pharmacy

Supplement No. 3, Vol. 87, 2014; B+ category Journal; CNCSIS code 253, no. 94  
p-ISSN 1222-2119, e-ISSN 2066-8872

Nirs and chemometric analysis of gallic acid in dry rose petal extracts  
and oral tablets  
ALEXANDRU GĂVAN, ANCA TOIU, MIRCEA TĂMAȘ, IOAN TOMUȚĂ.....S235

Pharmacokinetics and bioavailability of Celecoxib from immediate release solid  
dosage formulations  
DIANA POP, TAUSIF MONIF, ADRIANA MARCOVICI, SANDEEP BHARDWAJ,  
LAURIAN VLASE.....S236

The effects of bupropion on the pharmacokinetics and pharmacodynamics of  
neбиволol and its active metabolite  
ANA-MARIA GHELDIU, CORINA BRICIU, MARIA NEAG, DANA MUNTEAN,  
CORINA BOCSAN, ANCA BUZOIANU, IOAN TOMUȚĂ, ADINA POPA,  
LAURIAN VLASE.....S237

The pharmacokinetic study of zopiclone after single-dose administration in rats  
MARIA-BIANCA ABRUDAN, DANA MUNTEAN, CORINA BRICIU,  
ANA-MARIA GHELDIU, LAURIAN VLASE.....S238

Development and characterization of enoxaparin sodium polymeric microparticles  
for oral administration and colonic absorption  
DANA HALES, ANNE SAPIN-MINET, MAXIME CASTERAN, IOAN TOMUȚĂ,  
MARCELA ACHIM, LAURIAN VLASE, PHILIPPE MAINCENT.....S239

The influence of dissolution conditions on the release of ketoprofen from extended  
release tablets  
ANDRA REZNEK, KOVACS MELINDA, TIBOR CASIAN, IOAN TOMUȚĂ.....S240

Phenotypic differences in neбиволol metabolism and bioavailability after  
administration of a single dose in healthy volunteers  
CORINA BRICIU, MARIA NEAG, DANA MUNTEAN, CORINA BOCSAN,  
ANCA BUZOIANU, ANA-MARIA GHELDIU, MARCELA ACHIM,  
ADINA POPA, LAURIAN VLASE .....S241

The formulation of freeze dried orodispersible tablets containing a natural polymer  
SONIA IURIAN, RAMONA PĂLTINEAN, CRISTINA IUGA, CĂTĂLINA BOGDAN,  
IOAN TOMUȚĂ, GIANINA CRIȘAN, MIRELA MOLDOVAN,  
SORIN E. LEUCUȚA.....S242

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Development of high-throughput NIR-chemometric methods for the pharmaceutical  
 characterization of ketoprofen extended release tablets  
 TIBOR CASIAN, ANDRA REZNEK, ANDREEA LOREDANA VONICA – GLIGOR,  
 IOAN TOMUTA.....S243

In vitro evaluation of the estrogenic/anti-estrogenic potential of binary mixtures of  
 selected food additives and cosmetic preservatives  
 ANCA POP, TUDOR DRUGAN, FELICIA LOGHIN, ARNO C. GUTLEB,  
 JULIEN CHERFAN, BÉLA KISS.....S244

Evaluation of in vitro activation of estrogen-dependent gene transcription by  
 norfluoxetine  
 DIANA LUPU, ANCA POP, BELA KISS, FELICIA LOGHIN.....S245

The study of the oxidative metabolism of estrone in rat liver microsomes under the  
 influence of genistein and bisphenol A  
 DANIELA-SAVETA POPA, LAURIAN VLASE, ANA-MARIA GHELDIU,  
 FELICIA LOGHIN.....S246

### DENTISTRY

Biocompatibility study of a graphene composite with gold nanoparticles (AUNPS)  
 and hydroxyapatite (HA) on human osteoblasts  
 LIANA CRISAN, OLGA SORITAU, ALEXANDRU BIRIS, MIHAELA BACIUȚ,  
 GRIGORE BACIUȚ, BOGDAN CRISAN.....S247

Comparative evaluation of the behavior of dental materials used in endodontic  
 surgery  
 ANDREEA I. GULIE KUI, GHEORGHE ZSOLT NICULA, CODRUTA POPESCU,  
 LIANA LASCU, MINDRA BADEA.....S248

Regeneration methods of the peripheral sensitive and motor nervous structures of the  
 maxillofacial region  
 ANDREEA MAGDAS, GRIGORE BACIUȚ, DAFIN MURESANU,  
 MIHAELA BACIUȚ.....S249

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## Medical - Journal of Medicine and Pharmacy

Supplement No. 3, Vol. 87, 2014; B+ category Journal; CNCSIS code 253, no. 94  
p-ISSN 1222-2119, e-ISSN 2066-8872

Osseointegration assessment of Ti-Al-Nb alloy implants using EDX  
GABRIEL ARMENCEA, CRISTIAN BERCE, HORATIU ROTARU, ADRIANA VULPOI,  
DAN LEORDEAN, CAMELIA-AUGUSTA JULA, SIMION BRAN,  
LUCIA HURUBEANU, MIHAELA BACIUT, GRIGORE BACIUT,  
RADU SEPTIMIU CAMPAN.....S250

Study on oral lichenoid lesions and oral lichen planus prevalence in patients with  
silver amalgam fillings  
DOINA ROTARU, DIANA BERECHET.....S251

Host Modulatory Therapy (HMT) in a rat model of periodontitis  
CARINA CULIC, ALINA ELENA PARVU, SANDU FLORIN ALB, CAMELIA ALB,  
ANGELA POP.....S252

Imaging and histopathological evaluation of experimentally induced periapical  
lesions in rats  
ANTONELA BERAR, ANDREEA KUI, CORINA MORARU,  
ALEXANDRU FARCASANU, FLAVIU TURCU, LIANA LASCU, SIMION SIMON,  
RADU SEPTIMIU CAMPAN.....S253

Odontogenic maxillary sinusitis  
DANIELA POPA, ALEXANDRU PRECUP, MARIANA CONSTANTINIUC,  
RADU SEPTIMIU CÂMPIAN.....S254

Comparison between clinical examination, computerized axiography,  
ultrasonography and mri in assessing the temporo-mandibular joint status  
DANIEL TALMACEANU, SMARANDA BUDURU, ROXANA STANILA,  
HORATIU ROTARU, GRIGORE BACIUT.....S255

The influence of smoking on oral health  
MINODORA MOGA, ONDINE LUCACIU, ARIN SAVA, ARANKA ILEA,  
DAN BUHATEL, ADINA SIRBU, CLAUDIA FEURDEAN, ANCA IONEL,  
DUMITRU TRITEAN, RADU SEPTIMIU CAMPAN.....S256

Mini-implants in orthodontics  
ADINA SIRBU, RADU CAMPAN, ONDINE LUCACIU, MINODORA MOGA,  
ANCA IONEL, BOUHDID LAMIAE.....S257

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Diagnostic wax up construction: harmonization between the patient expectation and aesthetic of the final restoration in oral anterior zone rehabilitation  
 WILLI ANDREI URICIUC, MONICA RUS, ARIN SAVA,  
 RADU SEPTIMIU CAMPIAN.....S258

Comparative radiologic evaluation of the endodontic filling for three different sealers  
 RADU CHISNOIU, OVIDIU PASTRAV, MARIOARA MOLDOVAN, DOINA PRODAN,  
 STANCA BOBOIA, ADA DELEAN, ANDREA CHISNOIU.....S259

Periodontal disease induced in Wistar rats - experimental study  
 ANCA IONEL, ONDINE LUCACIU, MINODORA MOGA, ARANKA ILEA,  
 DAN BUHATEL, CLAUDIA FEURDEAN, ARIN SAVA, ADINA SARBU,  
 MIHAI TIRIAC, MIRCEA MURESAN, FLAVIU TABARAN, CORNEL CATOI,  
 CRISTIAN BERCE, SEPTIMIU TOADER, RADU SEPTIMIU CAMPIAN.....S260

Lingual retainer or orthodontic treatment in periodontal disease  
 CLAUDIA FEURDEAN, LUCACIU ONDINE, ADINA ȘIRBU, ARIN SAVA,  
 DAN BUHĂȚEL, ARANKA ILEA, MINODORA MOGA, ANCA IONEL,  
 RADU SEPTIMIU CÂMPIAN.....S261

Interaction of stem cells derived from maxillary and mandibular bone with salts from culture medium  
 ARANKA ILEA, OLGA SORIȚĂU, PIROSKA VIRAG, ADRIANA VULPOI,  
 SIMION ȘIMON, BIANCA BOȘCA, EMOKE PALL, DAN BUHĂȚEL, ARIN SAVA,  
 CLAUDIA FEURDEAN, MINODORA MOGA, ANCA IONEL, MIHAI ȚIRIAC,  
 RADU SEPTIMIU CÂMPIAN.....S262

The suitability of introducing a new type of dental implant  
 AVRAM MANEA, GRIGORE BACIUT, SIMION BRAN, MIHAELA BACIUT,  
 HORATIU COLOSI, DUMITRU POP.....S263

Clinical approach of impacted lower third molars  
 ARIN SAVA, ANAMARIA SAVU, ONDINE LUCACIU, RADU CAMPIAN.....S264

Assessment of the naso-pharyngeal space in cephalometric analysis  
 DIANA BERECHET, LIGIA VAIDA.....S265

# - Clujul

## Medical - Journal of Medicine and Pharmacy

Supplement No. 3, Vol. 87, 2014; B+ category Journal; CNCSIS code 253, no. 94  
p-ISSN 1222-2119, e-ISSN 2066-8872

Biocompatibility initial tests on a new type of dental material  
MEDA-ROMANA SIMU, RALUCA CICEO-LUCACEL, OANA PONTA,  
MICHAELA MESAROȘ, TEODORA RADU, CRISTINA BORZAN.....S266

Bioceramic materials used in endodontics - literature review  
MARIUS BUD, STEFAN JITARU, LUCIA TIMIS, SANDA CAMPEAN,  
ADA DELEAN.....S267

Laser applications in soft tissue remodeling  
IOANA ROXANA BORDEA, BOGDAN CRIȘAN, ONDINE LUCACIU,  
MIHAELA BĂCIUȚ, RADU SEPTIMIU CÂMPIAN.....S268

Minimal invasive alternatives in the prosthetic restoration of posterior teeth  
DAN BUHĂȚEL, ONDINE LUCACIU, ARANKA ILEA, CLAUDIA FEURDEAN,  
ANCA IONEL, MINODORA MOGA, ARIN SAVA, ADINA SARBU,  
MIHAELA MURESAN, MIHAI TIRIAC, MIRCEA MURESAN,  
RADU SEPTIMIU CÂMPIAN.....S269

Computer assisted analysis in a simulated self inflicted bite-mark  
ALEXANDRU-VICTOR BURDE, SORANA BACIU, DIANA DUDEA,  
RADU-SEPTIMIU CÂMPIAN.....S270

The contribution of occlusal forces to non-carious lesions formation  
ANA ISPAS, RODICA HOLONEC, GABRIEL FODOR, TITUS CRISAN,  
MARIANA CONSTANTINIUC.....S271

Evaluation of color changes in composite resins after the use of bleaching agents  
OVIDIU PĂSTRĂV, MIHAELA PĂSTRĂV, RADU CHISNOIU, ADA DELEAN,  
MĂRIOARA MOLDOVAN, LAURA SILAGHI-DUMITRESCU.....S272

Microleakage and interfacial micromorphology of dental restorations made with  
new experimental giomers  
IOANA HODISAN, GABRIEL FURTOS, CRISTINA PREJMEREAN, TINCA BURUIANA,  
DOINA PRODAN, LOREDANA COLCERIU, IOAN PETEAN,  
MARIA TOMOAI-A-COTISEL.....S273

Evaluation of the status of the orthodontic patient in Cluj-Napoca  
ANCA LABUNET, ANA MIHAILESCU, CRISTIAN OLTEANU.....S274

### Editorial board

Radu Oprean (Cluj-Napoca)  
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**HEART RATE VARIABILITY IN CORONARY HEART DISEASE****LUCIAN DANIEL RUSU, LAURA POANTĂ, MIHAI LUCIAN RUSU****Dept of Semiology and Internal Medicine, 2nd Medical Clinic, “Iuliu Hațieganu” University of Medicine and Pharmacy, Cluj-Napoca, Romania**

---

**Introduction.** Coronary heart disease (CHD) was the most frequent cause of death in 2012 and its prevention is essential. Heart rate variability (HRV) reflects the autonomic system balance and is a prognosis factor.

**Material and methods.** We analyzed the HRV in 140 patients (98 males), mean aged 58 years, with stable effort angina; we considered 120 healthy matched age subjects as controls. We excluded those who had other severe diseases. We assessed the CHD by clinical and laboratory data (ECG, effort test), echocardiography, coronarography; blood tests. ECG was used to for revealing left ventricle hypertrophy, the presence of arrhythmias and ischemia. Holter recording for 24 hours was performed and analyzed for HRV. Echocardiography role was to establish the ejection fraction and the parameters for diastolic dysfunction: E-wave, A-wave, deceleration time and isovolumetric relaxation time. We analyzed the data in Epiinfo 6 and we compared the results by T student and ANOVA tests and other additional statistical tests.

**Results.** There were significant statistical differences between groups regarding E/A, ER, IVRT and some HRV values. HRV proved to be reduced in patients with CHD, although not by much, the basal HR was higher in those with CHD and the more ischemic episodes the less was the HRV on 24h recording; systolic and diastolic functions had a tendency to drop in relation with some HRV parameters.

**Discussion and conclusion.** Data from other studies has showed a concordance between HRV and ischemic episodes throughout a one-day recording even if it is silent ischemia. In patients with angina pectoris there was a clear tendency to have the diastolic and systolic function impaired, related to some HRV parameters changes. Assessing the HRV may be useful for an early diagnose of the CHD, initiating and monitoring the treatment and indicate a prognosis for this disease although this applies only to some HRV parameters.

Lucian Daniel Rusu  
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## PROGNOSTIC FACTORS OF RESPONSE TO ENDOSCOPIC TREATMENT IN PAINFUL CHRONIC PANCREATITIS - RETROSPECTIVE OBSERVATIONAL STUDY

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---

The goal of the endoscopic treatment of painful chronic pancreatitis is to drain the pancreatic duct, reduce the frequency and severity of pain, resolve local complications.

**Material.** All patients with painful chronic pancreatitis in last 5 years at a single tertiary referral endoscopy center were identified from hospital database. The inclusion criteria: the pancreatic pain and dilated pancreatic duct. Demographics data, the clinical history, the endoscopic procedures and the follow-up were collected from the medical charts and analyzed.

**Results.** 132 patients. The pancreatography showed: minimal changes of the pancreatic ducts - 10 patients, pancreatic duct stones - 30 patients, pancreatic pseudocyst - 24 patients, chronic pancreatitis related biliary strictures 29 patients; 375 procedures were performed. The sphincterotomy was sufficient in 25 patients, 2 patients needed ESWL. Pancreatic stone extractions were performed in 39 patients; pancreatic plastic stenting in 49 patients and 34 patients required many long term stenting. The pseudocyst was drained by transpapillary procedure (11 patients), transmural (9 patients) and EUS (4 patients); 10 patients developed a biliary stricture. The biliary decompression was performed by CBD plasticstenting (22 patients), multiple plastic stents (8 patients), SEMS (2 patients). In 90.16% cases the procedures was successful, in 9.8% it failed. Mean follow up after treatment was 24 months. About 90% patients had substantial improvement of symptoms. Pain disappeared completely in 56% of cases. The pseudocysts were successfully drained and did not reappear during follow-up in 95% cases. Success of endotherapy in chronic pancreatitis with minimal changes was 94.12% vs. 89.8% in patients with pancreatic duct strictures.

**Conclusion.** We consider that in painful chronic pancreatitis the minimal endoscopic treatment is sufficient. Due to the increased risk of complications and higher costs, additional endoscopic treatment and surgical intervention should be reserved for cases with no response to the minimal endoscopic treatment.

Alina Mandrutiu

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## THE EFFICIENCY AND THE SAFETY OF THE BIOLOGIC TREATMENT IN ELDERLY PATIENTS WITH MULTIPLE COMORBIDITIES AND CROHN'S DISEASE. CASE REPORT

ALINA MÂNDRUȚIU<sup>1</sup>, IOANA VIȘOVAN<sup>1</sup>, LIDIA CIOBANU<sup>2,3</sup>, MIHAELA LASZLO<sup>1</sup>,  
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---

In patients with inflammatory bowel disease, the biologic treatment may have multiple side effects.

Case report: 77 years old female, ex-smoker, with Crohn's disease, A3L1B1 since 2010, treated with Salofalk without any clinical improvement.

In Jan. 2011 she presented in our clinic for inferior abdominal pain, multiple diarrhea stools with mucus, asthenia, deep back bone pain.

This patient has a multiple severe pathology: ischemic heart disease, arterial hypertension, paroxysmal atrial fibrillation with a ischemic stroke; severe chronic obstructive pulmonary disease, chronic respiratory insufficiency; surgically induced menopause at the age of 38 years; severe osteoporosis since 2001 with several vertebral compression and right femoral neck fracture.

During the disease activity, the patient presented erythematous papules and vesicles in posterior thorax, upper limbs, cervical area, interpreted like Sweet syndrome with good response to cortisol and metronidazole.

Initially she was administered budesonide and azathioprine, but considering the frequent relapses and the worsening of osteoporosis due to corticosteroid therapy, in July 2012 the biological treatment with Adalimumab was initiated, with maintenance dose 40 mg every 2 weeks. The evolution was favorable, without side effects, with clinical remission. In November 2013 the patient presented a new clinical and biological relapse, with the appearance of two inflammatory stenoses with deep ulcers in proximal and terminal ileum. The dose of Adalimumab was increased to 40 mg a week until May 2014. Until now complete clinical and biological remission was obtained with partial imaging response, with the persistence of the active lesions and the two inflammatory stenosis, reason why the biological treatment will be continued 40 mg every 2 weeks.

**Conclusions.** By presenting this case, we argue that in conditions of a careful, accurate and close monitoring, the Adalimumab is a safe and effective treatment in older patients with multiple severe comorbidities.

Alina Mandrutiu

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## TOTAL SHOULDER ARTHROPLASTY FOR A GIANT-CELL TUMOR OF THE BONE

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RODICA UNGUR<sup>1,2</sup>, IOAN ONAC<sup>1,2</sup>, VIORELA CIORTEA<sup>1,2</sup>

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---

Total shoulder arthroplasty is a standard operative treatment for a variety of disorders of the glenohumeral joint. Successful outcome of total shoulder arthroplasty depends on a well-designed and a well-executed physical therapy program. The rehabilitation program needs to observe a logical sequence: tissue healing, joint mobility and muscle strength.

We present the case of a 25 year old female who presented in September 2013 for rehabilitation after undergoing total shoulder arthroplasty for a giant-cell bone tumor localized in the proximal region of the right humerus. In our hospital, she underwent the current Neer protocol for postoperative total shoulder arthroplasty rehabilitation, which is widely used and is based on the basic science of soft tissue and bone healing. The functional outcome was good as range of motion and strength of the upper right limb improved.

When a well-performed surgical procedure is supplemented by a well-designed and frequently monitored therapy program, an excellent outcome of shoulder replacement should be expected.

Viorela Ciorteza

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## UTILITY OF MODIFIED STOP BANG QUESTIONNAIRE FOR THE ASSESSMENT OF THE RISK AND THE LEVEL OF KNOWLEDGE ON OBSTRUCTIVE SLEEP APNEA SYNDROME OF PARTICIPANTS IN DRIVING SCHOOLS

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---

**Introduction.** Comorbidities and risk of road accidents by up to 7 times, due to undiagnosed and untreated obstructive sleep apnea syndrome (OSAS) draws the attention of the Health Services.

**Material and methods.** We conducted an observational descriptive study, using as a tool the Modified Stop Bang questionnaire, which was validated and applied to a number of 293 people registered at three driving schools from Cluj-Napoca area.

**Results.** 88.22% were aged between 18 and 50 years, 73.79% were male. 50% were normal weight, 40.22% were overweight, and 8.80% had obesity of I and II degree. The analysis of the risk factors in the emergence of OSAS reveals that nearly half of the respondents stated that they had the neck circumference greater than 40 cm, more than two-fifths of them claimed that they snored moderately, hard and very hard. More than half of the total of 98 subjects, who invoked moderate, hard and very hard felt sleepiness and fatigue during the day, had a high body mass index, were overweight or obese of I and II degree. Over a fifth of the respondents with the neck circumference is greater than 40 cm, confirmed the presence of daytime sleepiness and fatigue. Only 4.71% of the respondents stated that they had been tested for OSAS. There is a statistically significant correlation between the presence of risk factors for OSA, daytime sleepiness and the respondents' need for knowledge and diagnosis for disease ( $p < 0.01$ ,  $p < 0.001$ ).

**Conclusions.** The Modified Stop Bang questionnaire can be used both as a screening method of OSAS and also as a method of informing the population in the process of obtaining a driving license on the OSAS. It is necessary the implementation in Health Services of some information systems on the population about OSAS, moreover the OSAS investigation should be compulsory in the medical record of the drivers' enrollment in the driving school. A law should be passed in this respect.

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## CHALLENGES OF CHRONIC COUGH IN RESPIRATORY PRACTICE

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**Introduction.** In pneumologist clinical practice cough is a real challenge. Beside of classical causes of cough, epidemiological and physiological studies suggest an association between gastroesophageal reflux disease (GERD) and chronic cough. Gastroesophageal reflux induced cough (GERC) is a common cause of chronic cough and accounts for 5-41% of chronic cough. The purpose of this study was to assess the relationship between chronic cough and GERD, and to monitor the response of respiratory symptoms after 8 weeks of acid suppressive therapy.

**Material and method.** 174 consecutive patients, nonsmokers, immunocompetent, with chronic cough undiagnosed at least 6 weeks and clinical symptoms specific for GERD (heartburn and regurgitations) were prospectively recruited into this study between 2012-2013. They were assessed by history, physical examination, chest radiograph, spirometry, reversibility to nebulized salbutamol, skin prick tests to common allergens and esophageal endoscopy. A clinical diagnosis was made and the patient had an 8-week trial of appropriate therapy with proton pump inhibitors (Omeprazole 20 mg o.d.) and prokinetic agents (Metoclopramide 30 mg tid).

**Results.** In 78.16% cases reflux preceded respiratory symptoms. After treatment 65 patients (74.71%) classified as responders (improvement of cough), in 44 cases (25.28%) respiratory symptoms persisted unchanged, none of patients had aggravation of cough. After supplementary investigations a final diagnosis was established in non responders patients.

**Conclusion.** GERD is a common disorder related with chronic cough. A therapeutic benefit for acid-suppressive therapy in chronic cough patients cannot be dismissed, because it may be useful for differential diagnosis of chronic cough.

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## **MULTIPLE TRAUMA PATIENT FOLLOWING ROAD TRAFFIC ACCIDENT REHABILITATION - CASE PRESENTATION**

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Currently there is an increased number of patients presenting to rehab clinics, in order to recover the locomotor deficits after various orthopaedic interventions, such as devices implantation for strengthening purposes, or osteoarticular reconstruction. Most common causes are involution processes, due to age (especially osteoarthritis and osteoporosis and its fractures) and posttraumatic pathology (road traffic accidents).

In order to provide the best quality of care for an orthopaedic patient there is a requirement for a multidisciplinary approach and involving the most qualified staff. Both drug and kineto-therapy have to be adapted accordingly. The osteosynthesis materials used currently are chosen so that they are well tolerated by the human body and at the same time have less contraindications regarding the various diagnostic and treatment options available in the medical field, for the use of various diagnostic and treatment options available in the medical field.

A 22-year-old man was admitted at the Cluj Napoca Rehabilitation Clinic, following a road traffic accident in February 2014, in Italy. He was in induced coma for 2 months considering the severity of the injuries. 5 months following the accident (July 2014), he is discharged from the surgical ward in Italy and brought back home in Romania and admitted to the rehab unit in Cluj, aiming for full recovery using specialized rehabilitation treatment and procedures.

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## ETHICAL ASPECTS OF SMOKING CESSATION AMONG THE POPULATION FROM TRANSYLVANIA REGION - STOP SMOKING CESSATION PROGRAM

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**Introduction.** In the context of current medicine, we will comprehensively present the ethical aspects of the approach of persons addicted to tobacco use. We will present the clinical experience data of ethical counseling and therapy for smoking cessation, based on the National Smoking Cessation Program.

**Material and methods.** A retrospective descriptive observational study was performed in the period 2009-2013 in 392 patients representing all persons who voluntarily presented to the Service of Counseling for smoking cessation.

**Results.** 52.07% were male. 94.81% were aged between 20 and 59 years. According to the data obtained, male sex, adult age and the status of married person with children represent the prototype of the smoking patient who wishes to receive counseling for smoking cessation. Among the reasons reported by the subjects regarding smoking cessation, the concern for health was ranked first (40.04%), followed by financial reasons (21.37%), the wish to be free of nicotine dependence (11.20%), and the influence of the entourage (10.17%). The study shows the fact that persons who during counseling were found to have a moderate and high nicotine dependence using the Fagestrom test quantification were also those who were more subjectively aware of the severity of their status in relation to tobacco use ( $p < 0.0001$ ). The evaluation of the results six months after the initiation of counseling reveals the fact that more than half of the subjects included in the study 54.98% were non-smokers, with significant statistic regarding the ethical considerations of smoking cessation ( $p < 0.005$ ).

**Conclusion.** The aim of the medical intervention was the restoration of the patient's autonomy in making decisions about smoking cessation, as well as a change in the patient's lifestyle. In the patients' change of attitude, the principles of autonomy and non-maleficence represented a strong motivation, the patients benefiting from the implementation of a National Smoking Cessation Program.

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**OSTEOPOROSIS IN PATIENTS WITH TOTAL HIP ARTHROPLASTY****VIORELA CIORTEA<sup>1,2</sup>, RODICA UNGUR<sup>1,2</sup>, LASZLO IRSAY<sup>1,2</sup>, ALINA POPA<sup>2</sup>, DELIA POPA<sup>2</sup>,  
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**Introduction.** The postoperative evolution of patients with hip arthroplasty depends on a series of factors, bone mineral density (BMD) demonstrating its influence on the functional rehabilitation of the replaced hip. Osteoporosis associated with hip endoprosthesis may be involved in some postoperative complications and may become a serious problem in the case of the intervention for the revision of the endoprosthesis; thus, the knowledge of BMD values allows to choose the adequate type of prosthesis, as well as to initiate optimal drug and rehabilitation treatment.

The objective of the study is to evidence the role of bone mineral density (BMD) in the rehabilitation of patients with total hip arthroplasty.

**Material and method.** The study, a representative sample analysis, was carried out at the Department of Medical Rehabilitation of the "Iuliu Hațieganu" UMPH Cluj-Napoca, in the period June-December 2009. The study inclusion criteria were met by a number of 58 patients aged between 30-83 years with uni- and bilateral cemented and uncemented total hip endoprostheses. A standard study protocol was elaborated, which included the measurement of BMD in the spine and both hips, using dual X-ray absorptiometry (DXA), with the Lunar Prodigy Advance osteodensitometer, the software for orthopedic prostheses being available. The patients were clinically evaluated using two scales: the Oxford Hip Score and the Quality of Life Questionnaire of the European Foundation of Osteoporosis QUALEFFO-4.

**Results.** The two scores were significantly correlated ( $p < 0.005$ ) with the diagnosis made based on DXA examination and with the type of hip endoprosthesis (cemented or uncemented); they were higher in the case of low BMD (osteopenia/osteoporosis) and cemented endoprostheses.

**Conclusions.** Low periprosthetic BMD values delay the rehabilitation of patients with total hip endoprostheses.

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## OCCUPATIONAL STRESS IN IRRITABLE BOWEL SYNDROME

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**Introduction.** Irritable bowel syndrome (IBS) is a functional disorder which affects about 20% of the population and is the result of interaction of genetic predisposition and environmental factors. The aim of this study is to highlight the possible correlation between occupational stress and the occurrence of IBS.

**Methods.** Two groups of IBS patients and healthy controls were investigated. Stress was assessed by the standard questionnaires. Stress was also estimated by the measurement of serum IL-6, salivary cortisol.

**Results.** Occupational stress is encountered in higher proportion in IBS as compared to the matched control group. Salivary cortisol levels were not higher in IBS patients as compared to the healthy controls. Serum IL-6 levels tended to be higher in patients relative to controls. The biological markers of stress are correlated with the severity of the symptoms measured with the severity symptoms score, also with sleep disorders.

**Conclusions.** Occupational stress, assessed by specific questionnaires, was related with the presence of IBS and high levels of IL-6. No relation between salivary cortisol and the presence of IBS was found.

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**DIFFERENCES IN THE SURFACE ECG ASPECT DEPENDING ON THE TYPE OF FLUTTER (CLOCKWISE OR COUNTERCLOCKWISE)****RADU ROSU, OLIVIA SECATUREANU, LUCIAN MURESAN, GABRIEL CISMARU, MIHAI PUIU, GABRIEL Gusetu, DANA POP, LAURA MADA, CATALIN PESTREA, DUMITRU ZDRENGHEA****Department of Cardiology, The Rehabilitation Hospital, University of Medicine and Pharmacy, Cluj-Napoca, Romania**

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**Introduction.** Atrial flutter is a rhythm disturbance caused by a re-entry circuit, located mostly at the level of the right atrium, the left atrium being passively activated. Before radiofrequency ablation, a careful intracardiac mapping and entrainment mapping are mandatory for determining the nature of the reentry circuit and certifying its cavo-tricuspid isthmus dependency. The aim of the study was to evaluate differences in the surface ECG aspect depending on the type of atrial flutter: clockwise or counterclockwise.

**Material and methods.** The study included patients who underwent a radiofrequency ablation procedure for a typical atrial flutter between 2010 and 2013 in the Electrophysiology Department of The Rehabilitation Hospital, Cluj-Napoca, Romania. The flutter rotation sequence (clockwise or counterclockwise) was assessed by analyzing the depolarization sequence of the right atrium. The aspect of the F waves in leads DII, DIII, aVF, aVL, V1 and V6 on the surface ECG was then analyzed. We determined sensibility (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) for each aspect.

**Results.** Among the 387 patients, 152 (39,27%) had clockwise atrial flutter 112 cases had positive F waves in inferior leads and negative in V1 (73,68%), Se=0,89; Sp=0,98; PPV=0,94; NPV=0,97. There were 235 cases (60,73%) of counterclockwise atrial flutter: 196 cases had negative F waves in inferior leads and positive in V1 (83,40%), Se=0,80; Sp=0,98; PPV=0,87; NPV=0,96.

**Conclusion.** The surface ECG is an important diagnostic tool in the diagnosis of atrial flutter, having an important role in determining the rotation sequence of the macro-reentry circuit in the case of a typical atrial flutter. The most useful leads for determining the macro-reentry rotation sequence are DII, DIII, aVF, V1, V6±aVL.

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## ANTHROPOMETRIC AND MORBIDITY ASSESSMENT ON LATE PRETERM NEWBORN INFANTS WITH INTRAUTERINE GROWTH RESTRICTION

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**Aim.** The aim of this study was to evaluate anthropometric data and morbidity on IUGR late preterm infants compared with without non-IUGR infants on a population of Romania in a third level maternity.

**Material and methods.** An observational retrospective study was carried out in the Emergency County Hospital of Cluj-Napoca on infants admitted to the Neonatal Ward at 1st Gynecology Clinic, from January 2012 to June 2014. The infants included in the study were those classified as late preterm infants (born at gestational age >34 and <37 weeks). The cases were represented by infants with IUGR defined as infants with birth weight for gestational age below the 10th percentile. For each case included in the study a matched healthy control in terms of gestational age and gender was identified in a ratio of 1:1.

**Results.** Twenty six cases and an equal number of controls accomplished the inclusion and exclusion criteria and were investigated. The investigated sample comprised for each group 16 girls and 10 boys, the percentage of girls being significantly higher ( $p=0.016$ ). The birth weight mean of infants with IUGR was significantly lower compared to non-IUGR infants (IUGR:  $1738\pm 331$ g; non-IUGR:  $2576\pm 209$ ;  $p<0.001$ ) but no significant difference was observed between groups for neonatal ponderal index (IUGR:  $2.00\pm 0.35$ g; non-IUGR:  $2.15\pm 0.22$ ;  $p=0.105$ ). The hospitalization proved longer for IUGR infants compared to controls (IUGR:  $16.73\pm 9.04$ g; non-IUGR:  $8.77\pm 8.00$ ;  $p=0.002$ ). The analysis of co-morbidities revealed no significant difference between groups for respiratory distress, hemorrhage, hyperbilirubinemia, hypocalcemia, enterocolitis and heart failure ( $p>0.31$ ). The percentage of cases with hypoglycemia was significantly higher in IUGR group compared to controls (IUGR: 42%; non-IUGR: 8%;  $p<0.001$ ). A significantly higher percentage of infants in non-IUGR group had trauma compared to IUGR group (non-IUGR: 46%, IUGR: 8%,  $p<0.001$ ).

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**PON1 IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS****MIRCEA VASILE MILACIU<sup>1</sup>, ȘTEFAN CRISTIAN VESA<sup>2</sup>, DOREL SÂMPELEAN<sup>3</sup>, IOANA PARA<sup>3</sup>, MARIA-ȘINZIANA MOLDOVAN<sup>4</sup>, LORENA CIUMĂRNEAN<sup>3</sup>**<sup>1</sup>4th Medical Dept., Cluj-Napoca, Romania<sup>2</sup>Department 2 - Functional Sciences, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania<sup>3</sup>Department 5 - Internal Medicine, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania<sup>4</sup>Heart Institute „Niculaie Stăncioiu”, Cluj-Napoca, Romania

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**Introduction.** Non-alcoholic steatohepatitis (NASH) is a disease with an increasing incidence worldwide, which is important to study because of the possible evolution to hepatic fibrosis and cirrhosis. Human serum paraoxonase 1 (PON1) is an enzyme excreted by the liver, primarily associated with high density lipoproteins (HDL). Very few studies have evaluated the possible association of NASH with low levels of PON1 activity or with a certain expression of the PON1 gene. The aim of this study was to identify variations in PON1 activity and PON1 gene polymorphisms in patients with NASH.

**Material and methods.** We studied a group of 17 patients with non-alcoholic steatohepatitis, diagnosed by elevated aminotransferases, with ultrasonographic hepatic steatosis, with negative markers for hepatic viral infection, in which alcohol consumption and any other disease that might influence PON1 were excluded, compared to a group of 17 patients without NASH or any other pathology known to have an influence on PON1. In each patient, we dosed the serum activities of PON1 (paraoxonase, arylesterase and lactonase). Using the PCR-RFLP method, we determined the PON1 gene polymorphisms L55M, Q192R, C-108T, A832G and A162G. Statistical analysis was performed using the statistical software SPSS version 20.0.

**Results.** We did not observe statistically significant differences between the NASH group and the control group regarding the serum activities of PON1. L55M polymorphisms presented the greatest variability between groups, the heterozygous variant Im being present in 41.2% of the patients in the NASH group and only in 17.6% of the patients in the control group, with a p-value close to the statistical significance level ( $p=0.088$ ).

**Conclusions.** PON1 genotype seems to influence the status of patients with non-alcoholic steatohepatitis. Studies on large groups of patients are needed to confirm a possible role of PON1 polymorphisms in the prediction and/or evolution of NASH.

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## CLINICAL AND PARACLINICAL ASPECTS OF THE DIABETIC FOOT – A 5-YEAR STUDY

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**Introduction.** Diabetes mellitus is an important health problem worldwide. Diabetic foot is one of the most important complications of diabetes mellitus, both in terms of severity and financial costs incurred. We performed a study aimed at evaluating clinical, biochemical and imaging aspects in a group of patients admitted to the CF Clinical Hospital Cluj in the last 5 years.

**Material and method.** This was a retrospective analytical study that included a group of 43 diabetic patients with diabetic foot admitted to the CF Clinical Hospital Cluj-Napoca –Medical and Surgical Clinic IV– in the period 2009-2014. We analyzed anamnestic, clinical, biochemical and imaging data, the last consisting of foot X-ray and Doppler ultrasound of the lower limbs.

**Results.** 81% of the patients were male and 72% of the patients were smokers or ex-smokers, the highest prevalence of diabetic foot being found in the 60-69 age group. A worrying aspect was the fact that 65% of the patients needed amputations at different limb levels or even bilaterally. The majority of the patients had long-duration diabetes, with an unsatisfactory control of glycemic values, identified based on HbA1c levels. 88% of the patients included in the study were overweight or obese and the majority had at least one of the other complications of diabetes mellitus. We noted a close association between the clinical aspects suggestive of arteriopathic foot and vascular changes detectable using Doppler ultrasound. A plane X-ray of the foot provided very few elements for supporting the diagnosis.

**Conclusions.** In our study, we found that the majority of the patients with diabetic foot were men, smokers or ex-smokers, in the 60-69 age group, with long-duration diabetes, with multiple comorbidities, and 65% of the patients needed amputations. Strict protocols for the diagnosis, follow-up and treatment of diabetic foot should be implemented in order to limit the severe consequences of this complication of diabetes mellitus.

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## IS PULMONARY SARCOIDOSIS A DIFFICULT DIAGNOSIS?

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**Introduction.** Sarcoidosis is a multisystem granulomatous disease of unknown etiology that occurs most commonly in young people and is often asymptomatic.

**Material and method.** Patient of 55 years shows intermittent dry cough, unorganized chest pain, progressive dyspnea, profuse sweating, impaired exercise tolerance.

**Results.** Lung imaging highlights hilum and mediastinal lymphadenopathy, pulmonary fibrosis associated with bilateral honeycomb, which would correspond to a stage II/III of the disease.

**Discussion.** The diagnostic challenge came from the fact that the two bronchoscopies with lavage and Angiotensin-Converting Enzyme were within physiological limits. We required mediastinoscopy with lymph node biopsy that showed non-caseating granulomas typical composed of epithelioid cells, multinucleated giant cells and asteroid body. Also, given the important association of adenopathies and fibrotic changes, it is very difficult to stick to a clear stage of the disease. Furthermore, here is questioning whether there might be present a connecting tissue disease, considering the radiological appearance and the presence of positive blood antinuclear antibody.

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## TUBERCULOSIS - LUNG CANCER ASSOCIATION, A DIAGNOSTIC CHALLENGE?

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**Introduction.** Secondary pulmonary tuberculosis is one of the most prevalent infectious pathologies in developing countries and in our country. Lung cancer is the most common cause of cancer deaths in women and men. According to recent studies, people with tuberculosis have a 11 times greater risk of developing lung cancer.

**Material and methods.** Patient, 44 years old, accusing difficult coughing, fever, marked weight loss, fatigue, starting two months ago. X ray is suggestive of bilateral upper lobe cavitory infiltrative secondary pulmonary tuberculosis and cultures for Mycobacterium tuberculosis were positive, DOTS therapy is initiated. The patient's condition deteriorates gradually, developing acute respiratory failure with hypoxemia. Imaging and bronchoscopy show right primitive bronchial tumor with total right lung atelectasis.

**Results.** Histopathological diagnosis proves to be difficult due to the lack of atypical cells in bronchial aspirate or tissue biopsy. A third bronchoscopy with tissue sampling is needed to determine positive diagnosis of squamous cell lung carcinoma with marked necrosis.

**Discussion.** The association of lung cancer and tuberculosis is a dual one, with unfavorable prognosis. Mycobacterium tuberculosis is an important pathogen in patients with lung cancer. On the other hand, tuberculosis can sometimes be misinterpreted as cancer. A differential diagnosis must be performed correctly, but the clinician should not lose sight of association of the two diseases for early initiation of an appropriate therapy in both cases.

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## HEMOPHAGOCYTIC SYNDROME RELATED TO CHRONIC B AND C HEPATITIS IN AUTOIMMUNE DISEASES: A CASE SERIES

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**Background.** Hemophagocytic syndrome (HPS) is a rare, life threatening disease. The aim was to identify the cases of HBV and HCV infections in the patients with macrophage activation syndrome (MAF).

**Methods.** We reviewed the charts of patients with autoimmune diseases between 2000 and 2014 from a tertiary referral center in order to identify the cases of MAF associated HBV and HCV infection diagnosed using the Ravelli criteria.

**Results.** Three patients were diagnosed with HPS and hepatitis virus, two with HBV and one with HCV. All patients were males, mean age 32.33 years and all had fever, rash, arthralgias/arthritis, splenomegaly, leucopenia, thrombocytopenia, ferritinemia, high reactive protein C, hypertriglyceridemia, hypocoesterolemia, hyposodemia, low erythrocyte sedimentation rate. Also, all three patients had hypo-complementemia, Two patients had an infectious trigger and in a patient was the interferon.

Cytopenias, ferritinemia and transaminitis are common in HPS, determined by TNF alpha, IFN gamma and consumption by hemophagocytosis, but also common in viral hepatic infection. In those cases the diagnosis can be delayed. We suggest to use hypertriglyceridemia or hyposodemia, which are common in HPS, but rare in viral hepatitis for an early diagnosis. Interferons are the mainstay of treatment regimens in hepatitis infection but is also an immunomodulating agent implicated in HPS, therefore it may have a potential role in immune stimulation. Also iron overload may modulate the course of viral infection, because iron may interact directly with cell-mediated immune pathways. Recent data suggest that HPS is associated with lobular hepatitis and severe bile duct injury. Two patients had cholestasis one patient had transaminitis, which could be explained by the chronic evolution of hepatitis.

**Conclusion.** HPS is rarely associated with HBV and HCV. A high index of suspicion is necessary to identify these patients due to some common features.

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## ASSOCIATIONS BETWEEN ADHERENCE, ATTITUDE TOWARDS PAIN MEDICATION AND QUALITY OF LIFE IN PATIENTS WITH CHRONIC RHEUMATIC DISEASES

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**Introduction.** Certain convictions about pain medication seem to influence adherence to treatment. Understanding the reasons why adherence to treatment is low could contribute to a better management of the disease.

**Objectives.** This study aims to investigate the attitude towards pain medication and the associations between treatment adherence, attitude towards medication and quality of life in a group of patients with chronic rheumatic diseases.

**Material and methods.** We conducted this cross sectional study in the in patient Rheumatology Clinic from Cluj. Inclusion criteria were pain over 10 mm on a visual analogue scale (VAS) and chronic pain medication treatment. Adherence (Morisky-8), pain medication and quality of life (SF 36) questionnaires were applied to all patients. Three adherence categories were set based on the Morisky 8 questionnaire results: low adherence (LA) <6, moderate adherence (MA) 6-7 and high adherence 8 (HA).

**Results.** Preliminary data were obtained from 36 patients (23F, 13M), mean age 56 years old. Patients with rheumatoid arthritis 18 (48.6%), spondylarthritis 8 (22.9%), osteoarthritis 3 (2.9%), gout 4 (11.4%), systemic sclerosis 1 (2.9%), systemic vasculitis 1 (2.9%) and fibromyalgia 1 (2.9%) were included. According to the Morisky 8 questionnaire 13 (36.1%) had LA, 16 (44.4%) MA and 7 (19.4%) HA. Among patients with low income (below 600 RON) 47% had LA. Although patients with LA had lower scores on physical function and social domains, there were no statistically significant differences for the different domains of the SF 36 questionnaire. Patients with LA had greater fear of addiction and mistrust in doctors and a lower perceived need for pain medication.

**Conclusion.** Adherence to treatment is influenced by the patients' attitude towards medication and social factors. This preliminary study validates the need for further investigation of treatment adherence and attitude towards treatment and their relationship with quality of life.

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## THE VALUE OF CARDIAC MRI IN THE DIFFERENTIAL DIAGNOSIS BETWEEN INFECTIOUS MYOCARDITIS AND MYOCARDIAL FIBROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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**Introduction.** Myocardial involvement in systemic sclerosis (SSc) is generally the result of a primary fibrotic process. It can be also caused by infectious myocarditis and differentiating these 2 forms of myocardial involvement is important, since the therapeutic approaches are different.

**Material and methods.** We present the case of a 32 year-old female patient with a 3 year history of SSc who presented with dyspnea on exertion, orthopnea and dry cough, which appeared a few days after flu-like symptoms. Physical exam revealed bilateral crepitant rales and peripheral edema. ECG showed frequent premature ventricular contractions and echo demonstrated a moderately reduced ejection fraction (EF) of 40%, compared to her last examination of 60%. The diagnosis of heart failure (HF) was established and treatment with diuretics, aldosterone antagonists, ACE inhibitors and nitrates was started. Three days later, the patient developed three episodes of ventricular fibrillation, which were successfully resuscitated. Control echocardiography showed an EF of 15%.

**Results.** A Cardiac magnetic resonance imaging (CMRI) was performed, which showed myocardial inflammation and extensive endocardial fibrosis. This pattern of extensive endocardial rather than epicardial fibrosis was in favor of a primary myocardial involvement. Infective myocarditis was excluded based on negative serum markers. Immunosuppressive treatment with dexamethasone, methotrexate and cyclophosphamide was initiated and an ICD was implanted. Despite an increase in the EF% to 23% in the following days, the patient developed multiple organ failure and died 2 weeks later.

**Conclusion.** CMRI has the ability to suggest the specific etiology of myocarditis: a focal pattern of fibrosis is usually found in infectious myocarditis, while a more diffuse pattern is present in primary myocardial involvement. Cardiac MRI is a valuable tool for establishing the diagnosis of myocarditis and identifying the underlying cause.

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## FASCICULAR VENTRICULAR TACHYCARDIA IN A STUDENT, TREATED BY ABLATION

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**Introduction.** Idiopathic left ventricular posterior fascicular tachycardia (LVPFT) typically occurs in young adults and mainly affects males. The most frequent clinical presentation is paroxysmal episodes of palpitations, rarely syncope. Most episodes occur at rest, but exercise, and emotional stress can act as triggers. Radiofrequency ablation is ideal for definitive treatment of arrhythmia.

**Material and methods.** A 24 years old medical student presented in the emergency department after an emotional stress with sustained palpitations lasting 10 hours, without hemodynamic instability. ECG showed right bundle branch block) tachycardia with an appearance illustrative for LVPFT. Intravenously (I.V.) adenosine and beta-blockers were not effective for conversion. After i.v administrated Amiodarone, ventricular captures and fusions confirmed VT, subsequently yielding conversion to sinus rhythm. Laboratory values were normal. Echocardiography revealed normal left ventricle and ejection fraction of 60%. Verapamil was administrated at discharge, but because of hypotension and psychological effects, discontinuation of antiarrhythmic was desired.

**Results.** We performed electrophysiological study with three-dimensional electroanatomical mapping system using CARTO 3 (Biosens Webster). The mechanism of arrhythmia was identified as a reentry circuit using posterior inferior fascicle of the left ventricle. The radiofrequency applications effectuated at the Purkinje fibers of the posterior fascicle interrupted his tachycardia and made it non-inducible at programmed stimulation before and after administration of Isoprenaline.

**Conclusion.** LVPFT is a rare rhythm disorder, which does not respond to i.v. Adenosine and Beta-blockers. The diagnosis is clarified by the electrophysiological study. Catheter ablation is recommended when symptoms are severe or pharmaological treatment is ineffective or poorly tolerated.

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## THE IMPORTANCE OF NUTRITION IN HIV PATIENTS

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**Introduction.** We all know how important nutrition is for keeping our health and to reduce the chances of developing various chronic conditions. For a proper functioning the body needs energy, protein, vitamins and minerals, all of which are provided through food. The lack of any of the key nutrients can weaken the body and the ability to fight various infections. The importance of diet in people with HIV has been demonstrated, so that through optimal nutrition, the body can fight and cope with the chronic viral infection.

**Objectives.** To determine the importance of nutritional support to patients diagnosed with HIV, according to body mass index, triglyceride levels, serum cholesterol and HDL values and LDL cholesterol; also evidence the presence of anemia, oral stomatitis and oral candidiasis.

**Material and methods.** The study was conducted in the Infectious Diseases Hospital of Cluj-Napoca, by accessing patient discharge records from the period 23.02.2013-23.04.2013, where the study group has revealed a number of 13 cases. The inclusion of patients in this study was based on HIV-positive diagnosis. We also collected general data on each patient, such as age, gender and urban/rural origin. Calculations and data presentation were achieved using Microsoft Excel.

**Results.** There is a high percentage of people in rural areas who have shown changes of values in the lipid panel. Body mass index also shows an increase in patients living in villages as compared to those who live in urban areas. The urban/rural distribution for conditions of the oral cavity has shown a high incidence of oral candidiasis in rural areas and a high incidence of aphthous stomatitis in urban areas.

**Conclusions.** A healthy and balanced diet should be one of the main objectives in the counseling and care of HIV-positive patients. An effective program of nutritional care and support will improve the quality of life in people living with HIV.

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## VENTRICULAR TACHYCARDIA ABLATION IN THE CARDIOLOGY DEPARTMENT - REHABILITATION HOSPITAL CLUJ-NAPOCA

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**Introduction.** There are 3 treatment options for ventricular tachycardia (VT), although many patients require a combination: ICD implant, antiarrhythmic medications, or catheter ablation. While ICD is like having an ambulance crew 24 hours a day near the patient, catheter ablation targets the origin of the VT and aims to stop the mechanism of the arrhythmia. We aim to describe the types of ventricular tachycardia that were addressed to our cardiology department for treatment by catheter ablation.

**Material and method.** All ventricular tachycardias that were addressed for ablation in our electrophysiology center from Rehabilitation Hospital Cluj-Napoca between 2010 and 2014 were analyzed.

**Results.** Between November 2010 and June 2014, 24 cases of VT were attempted for ablation in conventional or three-dimensional system: 1 case of polymorphic electrical storm, 1 case of multiple ventricular tachycardias in a patient with left ventricular non-compactation, 2 cases TV in patients with arrhythmogenic right ventricular dysplasia, 1 case of hypertrophic cardiomyopathy, 1 case of branch-to-branch reentrant VT, 1 case of idiopathic left ventricular fascicular VT, 1 case of TV epicardial substrate without endocardial scar, 1 case of RVOT-VT and 15 cases of ischemic TV. We had no VT on congenital heart disease.

**Conclusions.** Interventional treatment of ventricular tachycardia include both internal defibrillator implantation and catheter ablation. There are types of VT that can be addressed for catheter ablation either as single procedure or in conjunction with ICD implantation.

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## RELATIONSHIP BETWEEN FALL RISK FACTORS, BONE MINERAL DENSITY AND FRAGILITY FRACTURES IN POSTMENOPAUSAL WOMEN

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**Introduction.** Fracture risk is determined by both bone health and fall risk. Evidence suggests that postmenopausal women with reduced bone mineral density may have greater risk of falling than age-matched healthy women. The aim of this pilot study was to compare quadriceps strength, balance and functional mobility in decreased bone mineral density patients with and without fragility fractures.

**Material and methods.** 52 postmenopausal women, diagnosed with osteoporosis or osteopenia by dual-energy x-ray absorptiometry, participated in this observational cross-sectional study. Quadriceps strength (isokinetic dynamometry), balance (Berg scale) and functional mobility (Timed Up and Go test) were assessed. Fragility fractures were anamnesticly or radiographically identified. Performance was compared between the 2 groups (with and without fractures).

**Results.** Fragility fractures were identified in 19 patients (37%). Patients with fragility fracture history performed significantly worse than the others for all measured parameters ( $p < 0.05$ ).

**Conclusion.** Impairments in balance, muscle strength or functional mobility increase the risk of fragility fractures in postmenopausal women with reduced bone mineral density. Therefore, in order to avoid fractures in this population, attention should be paid not only in restoring bone mass, but also in fall risk factors assessment and their adapted correction by comprehensive rehabilitation programs.

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## QUALITY OF LIFE IN CHILDREN WITH LIVER DISEASES

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**Introduction.** Liver diseases could have a negative impact on the life of children. The evaluation of health related quality of life (HRQOL) could be an instrument to analyze the disease evolution. Symptoms, complications, diet or medication could influence negatively the life of liver patients.

**Material and methods.** We have studied the HRQOL in children aged 2 to 18 years, with liver diseases, using PedsQL-4.0-Core Questionnaire. During their follow-up visit, 51 patients completed the questionnaire (for children aged 2-4 years the parents filled up the answers). The questionnaire assessed four dimensions of HRQOL: physical, emotional, social and school functioning. Higher scores indicate better HRQOL.

**Results.** The liver diseases in our patients (27 males, 24 females) were: Wilson’s disease (12 patients), Hepatitis B (12 patients), Hepatitis C (4 patients), liver transplantation (11 patients), autoimmune hepatitis (4 patients), portal hypertension (6 patients) and other in 2 patients. The HRQOL mean score was similar in both sexes ( $p=0.4030$ ), and was lower in liver transplanted patients and higher in Wilson disease and autoimmune hepatitis patients ( $p=0.0145$ ). The HRQOL score was higher in older patients ( $p=0.0019$ ), due to higher scores for social and school functioning ( $p=0.1069$  and  $p=0.0000$ ). There was no significant difference for physical ( $p=0.0721$ ), emotional ( $p=0.3288$ ) and social ( $p=0.2658$ ) functioning related to diagnosis. The score for physical and scholar functioning were lower for liver transplanted patients compared to other patients, but only for school activity the difference were significant ( $p=0.0003$ ).

**Conclusions.** There is no difference in HRQOL function to the sex. Older patients have a better HRQOL scores probably due to their more successful way to adapt to the disease, mainly in social and school life. Liver transplantation could have a greater impact on life quality compared to other diseases (due to physical impact and school problems).

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**THE IMPORTANCE OF ALLEGIANCE FOR PRODUCING THE PLACEBO EFFECT****SEBASTIAN-MIHAI ARMEAN<sup>1</sup>, KRISZTINA-AGOTA MATYAS<sup>1</sup>,  
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Placebo is mentioned in the Psalm CXIV “Placebo Domino in regione vivorum [...]”. At first, the connotation was depreciative - medieval physicians only “pleased” the untreatable patients, but by 1885 it was considered a “necessary deception”. Before World War II, physicians thought that placebo only brought comfort to the patient without having any impact on pathophysiology. It was also considered that the use of medical rituals was more effective and, in some cases, even necessary for unintelligent, neurotic, or inadequate patients. Numerous definitions of placebo and the placebo effect have been proposed. The mechanisms of action have been intensely studied and interesting theories have emerged. It is well-known that the effects of the drugs are influenced by the clinical setting and that the complexity of human mind and the social context make the patient highly suggestible to (auto)suggestion.

Five clinical cases from our medical practice are compared to the data from medical literature. These cases are: woman, 58 years old, psychiatric inpatient complaining of “paralyzed bowels and muscles” after undergoing a surgical intervention for an abdominal hernia; man, 68 y.o., psychiatric inpatient complaining of insomnia, with medically treated hypertension; woman, 64 y.o., neurological inpatient complaining of severe back pains that were neurologically uncommon, but impaired her walking and caused sleep disturbances and were not alleviated by a complex and combined analgesic pharmacotherapy; woman, 72 y.o., known for doctor shopping, who came at the Neurology Emergency Department at 1:00 a.m. for headache, foot burns, and abnormal gait; woman, 49 y.o., schizophrenic inpatient at a Chronic Psychiatric Disorders Department, often complaining of headaches.

The patients were placebo-responders. There was a decrease in the placebo effect in some patients, if chronically used and a spectacular amelioration of the symptoms when there was a high rate of allegiance.

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## NON-INVASIVE ASSESSMENT OF FIBROSIS IN CHILDREN WITH LIVER DISEASES

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**Introduction.** Liver biopsy is recognized as gold-standard for liver fibrosis staging, but it has many limits (invasively method, sampling errors, and major risks). There is an increasing preoccupation for using non-invasive methods for evaluation of the liver fibrosis. In practice, mainly in adults, the most used and validated methods are FibroTest/ActiTest and the evaluation of the liver stiffness by FibroScan.

**Material and methods.** We have analyzed the liver fibrosis in 30 patients (age from 6 months to 25 years old) with liver diseases: chronic hepatitis B or C, Wilson diseases, autoimmune hepatitis, neonatal of familial cholestasis, glycogenosis and cirrhosis. We have used for 33 times both FibroTest/ActiTest-Biopredictive and FibroScan-Echosens. We have analyzed the relationship between the fibrosis staging obtained by both methods.

**Results.** Fibrotest scores were between 0.05 and 0.97, and the patients were grouped in F0 (9 patients), F0-F1 (4 patients), F1 (4 patients), F1-F2 (9 patients), F2 (one patient), F3 (3 patients), F4 (3 patients). FibroScan measurements were between 2.8 kPa and 75 kPa and the patients were grouped in F0 (14 patients), F1 (9 patients), F2 (one patient), F3 (3 patients) and F4 (6 patients). There is a very good relationship between the both measurements ( $p=0.0012$ ,  $r=0.5385$ ). In 5 cases FibroScan results were with more than two stages higher than FibroTest (one case of cirrhosis and 4 cases with elevated transaminases). Inversely, FibroTest resulted in a staging with two stages more than FibroScan in 3 cases (all of them also with high activity results – A3).

**Conclusion.** FibroTest and FibroScan are useful non-invasive tools for liver fibrosis assessment that are in concordance and can be used alone or together with good results, if we respect the indications and limitations for each one. More extensive studies are needed in order to assess the utility in liver fibrosis in children.

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**ALAGILLE SYNDROME AS A CAUSE FOR NEONATAL CHOLESTASIS****ALINA GRAMA<sup>1</sup>, SIMONA CĂINAP<sup>1</sup>, SIMONA OPRIȚA<sup>2</sup>, OTILIA FUFEZAN<sup>3</sup>, TUDOR L. POP<sup>1</sup>****<sup>1</sup>2nd Pediatric Dept., “Iuliu Hațieganu” University of Medicine and Pharmacy, Cluj-Napoca, Romania****<sup>2</sup>“Niculae Stăncioiu” Heart Institute Cluj-Napoca, Romania****<sup>3</sup>3rd Pediatric Dept., “Iuliu Hațieganu” University of Medicine and Pharmacy, Cluj-Napoca, Romania**

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Alagille syndrome (syndromic paucity of interlobular bile ducts), also known as arteriohepatic dysplasia, is a multisystem autosomal dominant disorder defined clinically by the association of at least three of the following features: chronic cholestasis, congenital heart disease, “butterfly-like” vertebrae, posterior embryotoxon and triangular face. Genetically is characterized by mutations in the Jagged 1 gene. Other features have been described involving kidney, vascular anomalies, ear, pancreas, intestine, growth retardation, mental retardation. It is one of the most common inherited disorders that cause chronic liver disease in children.

We report a case of Alagille syndrome in a 1-year-old boy who presented with a history of progressive jaundice since neonatal period, generalized pruritus, renal tubular acidosis, recurrent otitis media, failing to thrive and characteristic facial appearance. He was also found to have stenosis of the peripheral pulmonary artery, butterfly vertebrae and micro-cystic lesions of the kidney. The treatment is mostly symptomatic (nutritional support, fat-soluble vitamin supplementation, Ursodeoxycholic acid) and he will probably need a liver transplant in the future. The patient has to be followed in a cautious way due to high risk of complications.

A liver transplant may be the last resort for patients with chronic liver failure, intractable portal hypertension and impaired quality of life with severe growth failure and refractory pruritus. Evaluation for liver transplantation in patients with Alagille syndrome is a complex process because of the multitude of clinical manifestations of the disease as well as its inherent multi-organ involvement.

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## OPPORTUNISTIC INAUGURAL INFECTIONS IN PATIENTS LIVING WITH HIV/AIDS IN THE REGIONAL CENTER CLUJ

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**Introduction.** In the world there are 34 million persons living with HIV, in Romania there are 12603 persons living with HIV, half of them in the southern part of the country. In the regional center Cluj there are 371 patients with HIV infection, 288 on antiviral therapy.

**Material and method.** This is a retrospective study, performed analyzing the medical records of newly diagnosed patients during a follow-up period of 66 months, between January 2009 and June 2014. The registered parameters were: CD4 cell count, inaugural opportunistic infections and other defining clinical conditions for AIDS, present at the moment of diagnosis.

**Results.** There were 173 newly diagnosed patients during the follow-up period: 18 in 2009, 13 in 2010, 41 in 2011, 42 in 2012, 30 in 2013, 29 in 2014; 50 patients (29%) had a CD4 cell count over 500 cells/cmm, 71 (41%) had a CD4 count between 200-500 cells/cmm and 52 patients (30%) had a CD4 count below 200 cells/cmm. There were 111 asymptomatic patients at the moment of diagnosis. The major opportunistic infections were: Pneumocystis jirovecii pneumonia in 10 patients, CMV retinitis in 2 patients, cerebral toxoplasmosis in 8 patients, extrapulmonary and pulmonary tuberculosis in 12 patients, cerebral cryptococcosis in 4 patients and candidiasis in 11 patients. Wasting syndrome was present in 51% of the newly diagnosed cases.

**Conclusion.** During the follow-up period the number of HIV infected patients increased. Moreover in the last year the number of symptomatic patients was high due to reduce awareness for screening at risk population. The most frequent opportunistic infections at the moment of the diagnosis were: pulmonary and extrapulmonary tuberculosis and candidiasis.

Wasting syndrome is the most frequent clinical defining AIDS condition associated with the opportunistic infections in newly diagnosed patients.

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**CAN MOOD STABILIZERS IMPROVE THE ANTIDEPRESSANT THERAPY?****KRISZTINA-AGOTA MATYAS<sup>1</sup>, SEBASTIAN-MIHAI ARMEAN<sup>1</sup>, OANA TUDORACHE<sup>2</sup>,  
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Major depression is associated with irritability and personality disorders. Up to two thirds of patients suffering from major depressive disorder may present a suboptimal response to the first line of antidepressant treatment, and up to a half of them do not even respond to the second line of treatment. There is no specific medication approved for controlling irritability, aggressiveness or personality disorders, and symptomatic treatment includes most of the time a mood stabilizer, but there is more of empirical evidence, although there are some certified studies. In psychiatry, mood stabilizers can be prescribed as an adjuvant pharmacotherapy in major depression without a specific indication from the producer. There are no clear evaluations of the dose-effect correlations, or of the plasma level concentrations and effect. There is little knowledge regarding the pharmaco-therapeutic approach of irritability. If we consider irritability as a symptom of depression, alleviating this symptom may improve the antidepressant pharmacotherapy. By determining plasma level concentrations of mood stabilizers, we may evaluate the patient's adherence to the treatment, monitor the risk of adverse events, adjust the dose. Our aim is to evaluate the efficiency and safety of mood stabilizer treatment as adjuvant pharmacotherapy for major depression. The role of irritability in the outcome and long-term evolution of major depression must be clarified. Management of irritability as a factor for improving the antidepressant response to drugs must be further investigated. Evidence based medical strategy for treating irritability as a symptom of major depression has to be established. Development of new strategies to increase the therapeutic response in patients with drug-resistant depression may include adjuvant therapy with mood stabilizers.

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## THE *VKORC1* -1693G>A POLYMORPHISM IS NOT ASSOCIATED WITH ATRIAL FIBRILLATION

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**Introduction.** Vitamin K epoxide reductase (VKOR) is an enzyme implicated in the process of recycling of vitamin K. Several studies showed that proteins that are dependent of vitamin K might be implicated in atherosclerosis. The gene that is responsible for VKOR exhibits several polymorphisms which determine an altered vitamin K metabolism. The VKORC -1639G>A polymorphism was described by several studies as associated with atherosclerosis due to increased calcification. The aim of our study was to determine a potential association between VKORC1 -1639 G>A polymorphism and AF.

**Material and methods.** The study included 46 patients (24 (52.2%) women and 22 (47.8%) men) diagnosed with AF and 72 controls (43 (59.7%) women and 29 (40.3%) men) without AF, coronary heart diseases, heart failure or diabetes mellitus. Patients and controls were selected from those hospitalized to the internal medicine department of the Municipal Clinical Hospital, Cluj-Napoca. Clinical and demographic data were recorded for each patient. Genetic analysis was performed in order to determine the genotype for the VKORC1 gene.

**Results.** The GG genotype of the VKORC1 -1693G>A polymorphism was found in 21 (29.2%) controls and in 16 (34.8%) patients. The GA genotype of the VKORC1 -1693G>A polymorphism was found in 30 (41.7%) controls and in 16 (34.8%) patients. The AA genotype of the VKORC1 -1693G>A polymorphism was found in 21 (29.2%) controls and in 7 (15.2%) patients. We did not find a difference in genotypes frequency between the two groups (p=0.22).

**Conclusion.** The VKORC1 -1693G>A polymorphism does not seem to be associated with atrial fibrillation.

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## BODY INTEGRITY IDENTITY DISORDER - AN ETHICAL DILEMMA

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**Introduction.** Body Identity Integrity Disorder (BIID) describes the extremely rare phenomenon of subjects who desire the amputation of one or more healthy limbs or who desire a paralysis. The etiology and pathogenesis of this disturbance has yet to be elucidated, turning it into a controversial phenomenon debated by psychiatrists, neurologists, psychologists and psychotherapists. It was subsequently considered to be an obsessive-compulsion disorder, an identity disorder like transsexuality, or a neurological conflict between a person’s anatomy and body image, which could stem from damage to a part of the brain that constructs the body image in map-like form.

**Methods.** We evaluated available scientific articles from 1977 to 2013 describing this disorder, using Pubmed, EMBASE, EBSCO and the library of the University of Medicine and Pharmacy “Iuliu Hațieganu” Cluj-Napoca.

**Results.** BIID is a controversial disorder, recent researche suggesting both psychological and neurological bases.

**Conclusions.** A clear definition of the diagnostic criteria and nosological framing are necessary for BIID in order to be properly evaluated and approached. Therapies are empirical and controversial. Important ethical issues are involved in the efforts of life quality improvement of these patients.

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## THE STUDY OF OXIDATIVE STRESS IN PRETERM NEWBORNS WITH RESPIRATORY DISTRESS SYNDROME

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**Aim.** The diseases of newborns which involve oxidative stress are: respiratory distress (RDS), bronchopulmonary dysplasia, retinopathy and necrotizing enterocolitis. The aim of the study was to evaluate the oxidative stress through the lipid peroxidation at preterm newborns with RDS.

**Material and methods.** We conducted a prospective, non-randomized study. The study group was represented by sixty preterm newborns with RDS. The control group included 20 healthy late preterm newborns. For all patients the family's consent was obtained. The study of the oxidative stress was performed by the measurement of malondialdehyde (MDA) by Satoh's method. For each newborn we determined the MDA on the first and third day of life. For the control was carried out one determination on the first day of life. The statistical analysis was done using the SPSS program.

**Results.** The RDS was present in mild form in 35% newborns, medium form in 42% and severe form in 23%. Seven newborns presented neonatal septicemia. Cerebral hemorrhage was present in 12 newborns of the study group. In 13 preterm the RDS was treated by mechanical ventilation. The MDA was higher in the neonates with the above circumstances. On the first day of life the MDA value was higher than on third day at the control. Also the MDA was significantly higher in the study group than in controls.

**Conclusion.** The RDS at preterm is a significant risk factor for oxidative stress. The association of other diseases to RDS will increase the oxidative stress.

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**“OLD” AND “NEW” MARKERS IN EARLY NEONATAL SEPSIS – DIAGNOSTIC VALUE****GABRIELA ZAHARIE<sup>1</sup>, MONICA HASMASANU<sup>1</sup>, SORANA BOLBOACA<sup>2</sup>, LIGIA BLAGA<sup>1</sup>, T. ZAHARIE<sup>3</sup>, MELINDA MATYAS<sup>1</sup>**<sup>1</sup>Department of Neonatology, University of Medicine and Pharmacy Cluj-Napoca, Romania<sup>2</sup>Department of Informatics and Biostatistics, University of Medicine and Pharmacy Cluj-Napoca, Romania<sup>3</sup>Department of Pathology, Regional Institut of Gastro-Enterology and Hepatology, Romania

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**Background and Aim.** To evaluate the diagnostic value of TLR-2 (Toll-like Receptors), TLR-4, IL-6 (interleukine -6), TNF- $\alpha$  (tumor necrosis factor -  $\alpha$ ) and CRP in the diagnosis of early neonatal sepsis in the premature babies with premature rupture of the membranes.

**Material and methods.** Diagnosis of sepsis was performed according to the International Sepsis Definitions Criteria. The study group included newborns with signs and symptoms suggestive for systemic infection, requiring full sepsis evaluation and antibiotic treatment, and the control group was represented by healthy newborns. We determined in the I-st day TLR-2, TLR-4, IL-6, TNF- $\alpha$  and CRP and in the III-th day the same without TLR. We used latex agglutination test for CRP, Elisa technique for TNF- $\alpha$  and IL-6 and flow cytometry for TLR. Statistical analysis was done with “Statistica VI”.

**Results.** The sepsis group presented in the I-st day: TNF- $\alpha$  (pg/ml)=14.7[5.0-24.3]; IL6 (pg/ml)=153.7[82.3-225.1]; CRP (mg%)=0.83[0.54-1.12]; and the expression(%) of TLR2=42.5 [29.5-55.4]; and TLR4=2.2[1.26-3.15]. TNF-  $\alpha$  correlates significantly and negative with TLR2. TLR2 correlates significantly and positive with TLR4. In the 3-rd day: TNF- $\alpha$  (pg/ml)=10.1[5.1-15.1]; IL6(pg/ml)=46.5[16.3-76.7]; CRP (mg%)=1.2[0.6-1.81]. Control group presented: TLR2(%)=5.69 (p=0.00006) and TLR4(%)=0.67(p=0.037). In the first day TNF- $\alpha$  and IL6 were higher in study group vs. control group but no statistical differences were found.

**Conclusions.** TLR-2 and TLR-4 could be confirmed as markers the neonatal sepsis. IL-6 and TNF- $\alpha$  are considered to be markers of early neonatal sepsis. CRP could not be considered as a marker for early neonatal sepsis.

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## CARDIAC INVOLVEMENT IN SCLERODERMA PATIENTS

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**Introduction.** Systemic sclerosis (SSc) is a connective tissue disease characterized by widespread vascular lesions and fibrosis of the skin and internal organs. Myocardial involvement has been estimated to occur in almost all patients with SSc. The cardiac involvement implies a poor prognostic. Therefore, we assessed cardiac involvement in a group of patients with SSc from our clinic.

**Material and methods.** In our study we included 30 patients with SSc (mean age 49±12 years, 27 female, 3 male, 14 limited SSc, 16 diffuse SSc). All patients were investigated by transthoracic Doppler echocardiography. We assessed: E/A, E' lateral, E/E', left ventricular ejection fraction (LVEF), contractility, valvulopathies and pericardial effusion. Sixteen of the patients were evaluated after one year.

**Results.** At first assessment 37% patients had left diastolic dysfunction, all patients had normal LVEF, 7% patients had pericardial effusion, 9 patients had a valvulopathy, all patients had normal cardiac contractility. Left diastolic dysfunction was not associated with disease duration (9.18±7.4 vs 7.05±3.5, p>0.05). At the second assessment 3 patients developed left diastolic dysfunction, 4 patients developed pericardial effusion and 2 patients had abnormal contractility. Two patients had a LVEF below the cut-off (<50%) at the second assessment and there was a decrease in left systolic function statistical significant (p<0.05). There was an increase of E' marker between first and second assessment not statistical significant (0.13±0.04 vs 0.12±0.04) and an increase in E/E' marker (5.66±2.01 vs 6.91±2.05, p<0.05) statistical significant.

**Conclusions.** There was a high percent of left diastolic dysfunction in our group. Our data may suggest that there is an evolution of myocardial fibrosis which can explain the increase in the left diastolic dysfunction. We also found a decrease in the left ventricular systolic function even though only 2 patients had a LVEF below the cut-off.

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## PROGNOSTIC FACTORS FOR OUTCOME OF PATIENTS WITH CLOSTRIDIUM DIFFICILE INFECTION

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**Introduction.** One of the most challenging aspects of Clostridium difficile infection (CDI) is its propensity to recur. Recurrent CDI (rCDI) is a cause of high morbidity, and its economic impact is substantial. A precise understanding of who is likely to recur is an important clinical question (if there are modifiable exposures/ underlying diseases that increase this risk, knowing what the clinicians could avoid).

**Aim.** The aim of the study was to evaluate age and comorbidities as prognostic factors for the outcome of patients with CDI.

**Method.** We conducted a single center retrospective cohort analysis among patients hospitalized with a CDI episode at the University Hospital of Infectious Diseases Cluj Napoca, during a period of 42 months (01.01.2011–30.06.2014). We analyzed the first episode of diarrhea for all included adult patients and we compared age and the number of comorbidities for patients with no-recurrence, recurrence or death.

**Results.** There were 336 patients included with 415 episodes of CDI (1.23 episodes of CDI/patient). The demographic characteristics of our patients were: M:F 151:185, average age 56 years (min 18, max 94). The outcome was: death in 25 patients (7%), recurrence in 58 patients (17%) and recovery in 253 patients (76%). The average age was 78 years for patients with poor outcome, 69 years for patients with recurrences and 65 years for patients with good outcome. 72% of patients who died, 64% of those with recurrences and 63% of patients who were cured had more than three associated comorbidities.

**Conclusions.** Recurrence after CDI and risk of death are important problems. Most patients are severely ill with many comorbidities. Increased age may predict recurrence and mortality. It may identify patients who would benefit from enhanced treatment of an initial CDI episode. There is a need for better comorbidities surveillance and treatment with a good interdisciplinary collaboration for a limitation of an unfavorable evolution.

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## EPIDEMIOLOGICAL IMPLICATIONS AND NOSOCOMIAL RISKS ASSOCIATED WITH SYSTEMIC INFECTIONS

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**Introduction.** Sepsis is a severe invasive infectious pathology which is often associated with nosocomial dissemination, and also with certain community particular phenomena. In this context, the objective of this study was to highlight the epidemiological characteristics of the cases that present a septicemic infectious process.

**Material and methods.** A cross-sectional study was performed for identification of the descriptive epidemiological characteristics regarding hospitalized cases with septicemia, in the period 2009-2013. The database was made in Excel, and the statistics were calculated with EpiInfo package 7/2012.

**Results.** The invasive septicemic pathology affected especially women (54%), aged between 61 and 80 years (39.7%) from urban areas (76.7%). In 74% of the cases, the patients presented with chronic pathology and 78.3% of them required hospitalization for more than a week. The gateways most frequently were respiratory (26.7%), urinary (25.7%) and digestive tracts (17.3%). Bacterial aetiology was identified in 73.7% of cases, with predominant isolation of Staphylococcus (12.7%), Klebsiella (11.3%) and Enterobacter (7.7%). Polymicrobial aetiology was identified in 8.3% of the cases with sepsis. The profile of sensitivity to the tested antibiotics, outlined the following resistance patterns: Carbapenems for the strains of Acinetobacter, Enterococcus and Pseudomonas and Vancomycin for the strains of Enterococcus, Pseudomonas and Staphylococcus.

**Conclusion.** The aetiological causes of septicemia are related to strains with multidrug resistance which can be easily disseminated to other members of community. The septicemic infectious process occurs in population at high risk which can be identified by appropriate epidemiological investigation, distinguishing also the nosocomial risks and the necessity to impose appropriate anti-epidemic measures.

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**QUERCETIN ASSOCIATED WITH CHRONIC MODERATE EXERCISE PROTECTS THE ENDOTHELIAL FUNCTION IN THE RAT MODEL OF TYPE 1 DIABETES**

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**Background.** Endothelial dysfunction is an important factor in the pathogenesis of cardiovascular complications of diabetes. Quercetin is a natural flavonoid that has a variety of pharmacological effects including the reduction of oxidative stress and improvement of the endothelial cell function. Chronic moderate exercise can ameliorate oxidative stress-mediated diabetic vascular endothelial dysfunction.

**Objectives.** The aim of the present study was to investigate the synergistic protective effects of Quercetin and moderate exercise on endothelial function in the rat thoracic aorta after streptozotocin (STZ)-induced diabetes.

**Material and methods.** Diabetes was induced by a single intraperitoneal injection of STZ. The rats in the Quercetin-treated groups were given Quercetin (20 mg/kg body weight) orally daily for 4 weeks, starting 4 days prior STZ injection. The rats were subjected to a swimming training program (1 hour/day, 5 days/week, 4 weeks). At the end of the study, all animals were sacrificed and the thoracic aorta was dissected. We examined aortic endothelial cell function indirectly by determining the NO bioavailability and various biomarkers of oxidative stress (malondialdehyde, MDA and protein carbonyl, PC levels) and antioxidant enzymes activity (superoxide dismutase, SOD, and catalase, CAT).

**Results.** Chronic moderate exercise improved NO bioavailability, lowered oxidative stress (MDA and PC levels) and increased SOD and CAT activity in aortic tissue of the STZ-diabetic rat. Oral supplementation of Quercetin to diabetic trained rats restored NO bioavailability, significantly brought back lipid peroxidation and protein carbonilation markers and increased SOD and CAT activity to near normalcy in the thoracic aorta.

**Conclusion.** These findings suggest that Quercetin treatment in association with chronic moderate exercise protects vascular endothelial function in diabetic rats.

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## PUBLISHING TIME-FRAME EVALUATION FOR DOCTORAL STUDENTS IN THE UNITED KINGDOM

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**Introduction.** The growing pressure to publish is currently felt by novice and more experienced scientists alike. Doctoral students are considered to produce a significant number of publications within a university. In the UK the traditional PhD, still the most common doctorate, is being challenged by several doctoral degrees. The PhD by publication focuses on the publication of books, book chapters, refereed journal papers, other media. The time lag between the completion of a research and its publication in a biomedical scientific journal is generally 6-12 months (longer in some fields). This study aimed to calculate the time between completion and publication of scientific research and to evaluate if the PhD theses format (monograph or publication-based) can influence this time.

**Material and methods.** We assessed a sample of 30 free full-text medical PhD theses from UK universities completed in the period 2005-2013, which had minimum 2 original publications by the end of the doctoral studies. Oral presentations, conference proceedings and posters were excluded. The time between 2 consecutive publications of the same thesis was considered the time between completion and publication for the second publication.

**Results.** For all theses (prospective and retrospective) the mean time between completion and publication was 13.88 months (95% CI [9.06–18.70]) and the median time was 9.15 months. The median time between completion and publication for the prospective publication-based format (6.61 months) proved significantly smaller than the median time for the traditional format (11.68 months). Analyzing only the text of the theses created limitations. The publication time might have been influenced by different factors, which we had no means to assess or exclude.

**Conclusion.** The time between completion and publication could help doctoral students organize their research better with a more realistic publishing plan. Future studies should evaluate a larger sample of theses from several medical faculties in the UK.

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## EFFICIENCY OF PHOTODYNAMIC THERAPY ON WM35 MELANOMA WITH NEW SYNTHETIC PORPHYRINS: ROLE OF CHEMICAL STRUCTURE, INTRACELLULAR TARGETING AND ANTIOXIDANT DEFENSE

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**Introduction.** Photodynamic therapy (PDT) could be an adjuvant therapy in melanoma, an aggressive cancer that arises from melanocytes. Several reports showed encouraging results of the efficacy of PDT in melanoma on experimental models and in clinical trials.

**Material and methods.** We studied the efficacy of two new, synthetic porphyrins: meso-5,10,15,20-tetrakis (4-hydroxyphenyl) porphyrin (THOPP) and meso-5-(4-hydroxyphenyl)-10, 15, 20- tris (4-methoxyphenyl) porphyrin (THOMPP) as photosensitizers for PDT, compared to FDA approved delta aminolevulinic acid (ALA) against a melanoma cell line, WM35, in vitro.

**Results.** Both porphyrins were efficient as photosensitisers, as opposed to ALA, without dark toxicity. The efficiency depended on the intracellular localization and the molecule structure. THOPP, the most efficient porphyrin localized mostly in mitochondria, while THOMPP predominantly localized in lysosomes; both porphyrins showed melanosomal localization. The symmetric THOPP molecule was able to generate increased oxidative stress damage and apoptosis. THOPP also induced a low activation of the defense mechanisms like antioxidant enzyme SOD (superoxide dismutase), NFkB (nuclear transcription factor kB) activation and MITF (microphthalmia transcription factor). The lower efficiency of the asymmetric molecule, THOMPP was probably due to a diminished photoactivation, which led to a lower ROS induced damage. Also, the THOMPP lysosomal localization allowed the activation of the defense mechanisms. Both porphyrins increased pigmentation, with THOPP having a greater effect. Melanogenesis provided no tumor protection, probably due to ROS production and melanosomal localization.

**Conclusion.** Both porphyrins were effective photosensitizers for PDT in melanoma cells.

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## THE COMBINED THERAPY WITH RESVERATROL AND HYPOTHERMIA PREVENTS APOPTOSIS AND IMPROVES OXIDATIVE STRESS IN A NEONATAL RAT MODEL OF HYPOXIC-ISCHEMIC ENCEPHALOPATHY

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**Introduction.** Perinatal hypoxic events are major causes for neonatal mortality and neurological morbidity resulting in central nervous system injury through hypoxia and ischemia. Hypoxia and ischemia produce severe brain damage following a typical pattern, defined by selective vulnerability of the brain regions and oxidative stress implication.

**Aims.** The main objective of this study was to test the possible protective effect of resveratrol as pretreatment and hypothermia in hypoxic-ischemic encephalopathy at newborn rats. The changes in terms of histology and apoptosis were determined in different brain regions so as to assess the local damages induced by hypoxic ischemia and oxidative stress parameters were evaluated as well.

**Materials and methods.** The experiment was performed on 32 newborn Wistar rats pretreated with resveratrol in a dose of 20 mg/kg/day for seven days. At the end of this period the animals were exposed to hypobaric hypoxia (9% O<sub>2</sub> for 90 minutes) and ischemia (by ligation of the right carotid artery). In order to test the effect of combined therapy of resveratrol with hypothermia, several animals were exposed after hypoxic-ischemic injury to whole body hypothermia (with 4OC) for 3 h.

**Results.** In global hypoxic-ischemic encephalopathy resveratrol, at a dose of 20 mg/kg/day as premedication offers neuroprotection by reducing the number of cells expressing apoptosis in CA1, CA2, CA3 and Dentate Gyrus of the hippocampus and cerebral cortex under the conditions of conjugation with post-injury hypothermia. In terms of oxidative stress, antioxidant enzyme defense expressed by SOD and CAT was increased.

**Conclusion.** The results of this study prove that resveratrol offers neuroprotection in hypoxic ischemic brain injuries, but the protection is conditioned in most of the brain regions by the conjugation of the protective therapy with post-injury hypothermia treatment.

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## ASSESSMENT OF HEALTH RELATED QUALITY OF LIFE CONCEPT IN PATIENTS WITH PREMALIGNANT AND MALIGNANT CERVIX PATHOLOGY

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**Introduction.** Health-related quality of life (HRQOL) has become increasingly important in medical research and is considered a dynamic, multidimensional and subjective concept. There is no universal instrument for evaluating all the HRQOL facets by populations or pathologies, the choice of certain measurement instruments being based on the objectives and outcomes of the research. The aim of this study was to test the factorial structure and reliability of health related quality of life scale using EORTC QLQ-C30 instrument for the Romanian population of patients with pre-malignant and malignant cervical pathology.

**Materials and methods.** Data from a convenience sample consisted of 102 women of reproductive age, treated at "Prof. Dr. Ion Chiricuta" Institute of Oncology (IOCN), Cluj-Napoca, during 2007-2012, for premalignant and malignant pathology of the cervix, namely high grade dysplasia and microinvasive carcinoma, by conservative surgery (cervical conization) were analyzed by confirmatory factor analysis (CFA). Several alternative measurement models were tested for statistical model fit to the sample data. The fit of models was analyzed by  $\chi^2$  goodness-of-fit test and descriptive goodness-of-fit indices.

**Results.** Two models showed an acceptable fit to data ( Second order CFA model: Satorra-Bentler scaled  $\chi^2=214.65$ ,  $df=163$ ,  $p=0.004$ ,  $RMSEA=0.056$ , 90% CI  $RMSEA [0.04-0.07]$ ,  $TLI=0.90$ ,  $CFI=0.91$ ,  $AGFI=0.96$ , Second order model with multiple indicators and multiple causes: Satorra-Bentler scaled  $\chi^2=212.88$ ;  $df=161$ ,  $p=0.0038$ ,  $RMSEA=0.056$ , 90% CI  $RMSEA [0.038-0.072]$ ,  $TLI=0.83$   $CFI=0.86$ ,  $AGFI=0.91$ ) and a good reliability (coefficient  $\omega$  at level 1  $>0.70$ , coefficient  $\omega$  at level 2  $>0.80$ ).

**Conclusion.** Confirmatory factor analysis brought two measurement HRQOL models in patients with the studied pathology. Between the two models, the model with multiple indicators and multiple causes is more plausible when evaluating HRQOL, as it involves assessing the patients' symptoms.

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## CELIAC DISEASE CONCEALED BY ALLERGIC MANIFESTATIONS (CASE REPORT)

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It is known that celiac disease may manifest under different masks. We present a pediatric patient whose manifestations of celiac disease were masked by allergic skin manifestations. The patient came to our medical service for the appearance of erythematous pruriginous macules especially on the legs. The clinical investigation suggested malabsorption syndrome because the child was weak, with weight less than percentile 5th, with a larger abdomen, pale skin and mucous membranes. Besides allergy tests, we asked the laboratory to determine specific markers for celiac disease. Laboratory tests showed total IgE=168 IU/ml (VN <10 IU/ml), IgA antitissue transglutaminase antibodies (ELISA)=63 U/ml (VN = <10 U/ml), IgA antiendomysium antibodies (immunofluorescence) = positive. According to the American Association of Family Physicians „autoimmunity in celiac disease involves plasma cells that produce IgA and IgG directed against a variety of antigens, including trans glutaminase, endomysium, gliadin and to a lesser extent or without involvement of IgE-mediated immune response”. Allergy and celiac disease are two different entities but medical practice proves that the presence of one should not exclude the presence of another.

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**MODULATION OF UVB-INDUCED OXIDATIVE STRESS AND APOPTOSIS WITH A VEGETAL EXTRACT WITH ANTIOXIDANT CAPACITIES VIA BAX- $\alpha$  AND NF-K $\beta$  CYTOSOLIC FACTORS IN HACAT HUMAN KERATINOCYTES CELL LINE****HANA PETRA DECEAN<sup>1</sup>, REMUS IOAN ORASAN<sup>1</sup>, PIROSKA VIRAG<sup>2</sup>****<sup>1</sup>Department of Physiology ,”Iuliu Hațieganu” University of Medicine and Pharmacy Cluj-Napoca, Romania****<sup>3</sup>”Ioan Chiricuta” Oncology Institute, Cluj Napoca, Romania**

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In the present study we showed that the UVB-induced ROS and subsequent apoptosis production in the human keratinocyte cell line (HaCat) could be contra balanced by a vegetal extract with antioxidant capacities.

**Materials and Methods.** The VV extract total polyphenolic content (TPC) was determined with Folin-Ciocalteu method and the most important biologically active compounds were evidenced by high-performance liquid chromatography (HPLC). The antioxidant activity was measured by 2,2-diphenyl-1-picryl-hydrazyl (DPPH) radical assay and Trolox-equivalent antioxidant capacity with ABTS test. A UVB dose below its IC50 value on HaCaT cells (217 mJ/cm<sup>2</sup>), was chosen for testing in the present study (100 mJ/cm<sup>2</sup>). The level of ROS was evaluated with CM-H2DCFDA assay, while apoptosis, Bax- $\alpha$  and NF-k $\beta$  p65 proteins with ELISA and confirmed by western-blot.

**Results.** For the VV extract the TPC was standardized as 3 mg GAEq/ml of which 2.02 mg/ml catechins, 1.073 mg/ml proanthocyanidine and 3.17  $\mu$ g/ml antocyanidine. HPLC analysis detected peaks for epigallocatechin and epicatechin, catechin hydrate, procyanidin B and gallic acid. Antioxidant activity showed 0.072 $\pm$ 0.002 mM/mM DPPH and 52.89 $\pm$ 0.02 mM Trolox equivalent. The UVB irradiation-induced ROS occurred at their highest levels at 1-2 h (p<0.0001 and p<0.001, respectively, as compared to control), while apoptosis later (at 4 h) after the exposure of the skin cells (p<0.0001 vs. control). The most significant changes in Bax- $\alpha$  protein was produced at 4 h (p<0.05), while the NF-kB values increased linearly in time.

**Conclusions.** The VV extract exerted beneficial effects on the UVB-induced ROS and apoptosis, reducing ROS production and protecting cells from apoptosis.

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## THE THERAPEUTIC MODULATION OF ESSENTIAL HYPERTENSION IN CONNECTION WITH THE GENETIC POLYMORPHISM OF THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM (RAAS)

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**Introduction.** uncontrolled essential hypertension (HTA) determines left ventricular hypertrophy (LVH). The increased size of the LV's muscle is caused by the reaction of the myocytes to mechanical, neuro-hormonal and genetic stimuli with reserved prognosis and increased mortality without any treatment.

**Objectives.** the analysis of the therapeutic response and of the adaptive modifications in essential HTA and the connection between the first and the genetic polymorphism of RAAS.

**Materials and Methods.** in the case of patients with HTA the intima-media thickness (IMT) was determined, a morphologic parameter of the vascular injury, a good foreteller of the coronary events and of the cerebral vascular accidents respectively. Ultrasound was used in order to identify LVH and arterial Doppler ultrasound to measure IMT. The arterial stiffness was measured by the velocity of the pulse wave. Mutations which are related to the RAAS: renin (REN, chr1q32), angiotensinogen (AGT, chr1q4243), the angiotensin II receptor type 1 (AGTR1, chr3q2125), the angiotensin-converting enzyme (ACE, chr17q23) and aldosterone (CYP11B2, chr8q22).

**Results.** describe the efficacy of the therapy with ACE inhibitors and with antagonists of the angiotensin II receptor, in the case of patients with HTA and high activity of the plasma renin, as well as in patients with normal or low plasma renin activity. This type of therapy is used as first line therapy by patients with HTA and heart failure, myocardial postinfarction, diabetic nephropathy, atrial fibrillation or metabolic syndrome. These observations leave no question about the importance of the RAAS. At present no conclusive information was obtained to find a connection between RAAS gene variants and therapeutic response.

**Conclusion.** Hypertension represents a major cardio-vascular risk factor, ACEI and ARBs are recommended as first line therapy for essential HTA because they improve the cardio-vascular prognosis.

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## THE STATUS OF QUALITY MANAGEMENT TRAINING AMONG ROMANIAN DENTISTS

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**Introduction.** Quality management concepts and practice begin to impact to a higher extent the manner in which dental care is provided to patient. However, the potential of quality management is not fully exploited that. In order to achieve that, one pre-requisite is a good understanding of quality management, through appropriate training. The aim of the present study was to assess the degree to which Romanian dentists are exposed to and benefit from quality management training.

**Methods.** Written questionnaires were distributed to a statistically significant sample of Romanian dentists. The questionnaire assessed the dentists' attitudes, knowledge and practice of quality management.

**Results.** Of the 115 participants, only 33.1% had been exposed to quality management knowledge during their studies. In only 5.95% of the cases dentists had attended such courses after they started practicing dentistry.

**Conclusion.** Our results show that there is an increasing need to provide quality management training for dentists, in order to ensure that their practice is guided not only by the principle of evidence-based medicine, but also by the principle of evidence-based management.

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## INJURY SURVEILLANCE IN ROMANIA. JAMIE PROJECT

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**Introduction.** The scope of the research is to present an overall view on what type of data are collected and the characteristics of patients with injuries, including external risk factors, treated in an emergency department (ED).

**Materials and Methods.** Injury data were collected in Romania as part of the EU-Injury Database Project and Joint Action for Monitoring Injuries in Europe Project (JAMIE). Part of the JAMIE Project data was used to explore the characteristics of injuries treated in a large ED. Data were collected for a period of twelve months, between July 2013 and July 2014 from the ED of Mures County Emergency Hospital, a total of 4114 cases.

**Results.** There were 4114 patients with an injury admitted to the ED during the 12 months data collection period. The sample population represents 80% of the total number of injuries treated in the ED during this period. The elderly (65+) represent the highest proportion of the population who had suffered an injury (n=909, 22.1%) followed by children aged 0 to 17 (n=614, 14.92%) and adults aged 25-34 (n=588, 14.3%). The male to female ratio was 1.8:1, with 2665 males (64.8%) suffering an injury, compared with 1449 females (35.2%); the difference was kept also when the data was stratified by age. The majority of injuries happened at home (45.7%) followed by transport area: public highway, street or road (31.01%), and during unpaid work (39.1%) followed by leisure or play (25.2%). Falls account for almost half of all injuries (n=1951, 47.4%). 92.2% (n=3786) of the patients required some type of treatment, out of which 1360 (35.8%) patients were hospitalized.

**Conclusion.** Injury surveillance provides an improved understanding of the prevalence and risk factors associated with injuries. The data can be used for health communication, development of injury prevention on different levels, and evidence-informed policy making.

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## ASSESSMENT OF THE CLINICAL LABORATORIES PERFORMANCE AND QUALITY MANAGEMENT FROM THE CLIENTS' PERSPECTIVE

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**Introduction.** The introduction of quality management systems and standards regarding the accreditation of laboratories (ISO/IEC 17025) brought challenging requests and tasks, essential for quality improvement as well as their accreditation maintenance. The information on the Romanian healthcare system regarding laboratory services is almost totally lacking. As a consequence, the proposed project aims to fill a knowledge gap in the field of quality management and client satisfaction in the Romanian healthcare system.

**Methods.** A descriptive cross sectional study will be conducted among 300 respondents aged 18 years and above who attend a laboratory in Cluj-Napoca. The study setting will include three laboratories in Cluj-Napoca. In order to achieve the mentioned objectives, we will use exit interview structured questionnaires, that will contain satisfaction indicators which are related to socio-demographic characteristics of the patients and different dimensions of monitoring laboratory services such as waiting time, availability of requested laboratory tests, availability of space, privacy, respect, courtesy, confidentiality.

**Results.** Data is in the process of being collected and analyzed.

**Conclusion.** Due to the fact that Romania is lacking data regarding the clients' satisfaction of laboratory services and this issue has become an emergent health management concern, the data obtained in the project will be valuable for designing customized interventions to increase clients' satisfaction and overall quality of the laboratory services. By implementing this study, we will get a clearer view upon the aspect of clients' satisfaction towards laboratory services at the local level and will get more information so that future healthcare programs can be developed.

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## TREATMENT WITH NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) IN ANKYLOSING SPONDYLITIS. WHAT IS THE REALITY OF THEIR EFFECTIVENESS IN CURRENT PRACTICE?

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**Introduction.** The only classes of drugs that have proven effective in controlling disease manifestations are non steroidal anti-inflammatory drugs (NSAIDs) and the newer anti-TNF-alpha biological agents. Long influence on disease activity radiological progression and patients' functionality following the administration of NSAIDs is not well known and characterized. Moreover, the majority of the information was obtained from the patients included in clinical trials and less evidence about their effectiveness on real patients from clinical practice.

**Material and methods.** All patients belong to Spanish Register of Spondyloarthropaties - REGISPONSER. Of all patients with AS we have selected for this study only those who met the modified New York criteria for AS. Patients with AS had to fulfill in addition the following three inclusion criteria: a) a follow-up period since inclusion visit in REGISPONSER of at least three years b) continuous treatment only with NSAIDs at recommended dosage during 3 years. Disease parameters were assessed annually in the same session for all patients and included metrological measures, registers of the C-reactive protein (CRP) level (mg/l), erythrocyte sedimentation rate (ESR), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Radiological Index (BASRI) and Ankylosing Spondylitis Disease Activity Index (ASDAS)

**Results.** Table.1 Baseline clinical characteristics of the treatment group. Table 2. Clinical, radiologic and biochemical parameters at baseline compared with follow-up.

**Conclusion.** Continuous treatment with NSAIDs does not control disease activity, reflected in the maintenance of BASDAI and ASDAS scores at high values. NSAIDs do not inhibit radiographic progression of the disease, which, in conjunction with high activity leads to progressive deterioration of the functional status of patients with SA.

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## THE EVALUATION OF THERAPY WITH PROTON PUMP INHIBITORS IN PATIENTS ADMITTED TO A NON ICU GASTROENTEROLOGY DEPARTMENT

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**Introduction.** There is increasing evidence indicating that proton pump inhibitors (PPIs) are used improperly. This contributes, on the one hand, to the increase of the cost of health care services, and on the other hand, it impairs the safety and quality of patients' lives. The aim of this study was to identify whether PPIs are used according to the current clinical guidelines in a non ICU ward.

**Material and methods.** The research is based on the assessment of the therapeutic schemes of 98 patients which were hospitalized in a non-ICU ward, summarizing 236 days of treatment with PPIs. PPI administration was analyzed in related to indication, dose, route of administration and drug interactions. We also tried to determine if there was a potential cost of PPI therapy which could, potentially, be saved.

**Results.** We found that PPIs were unnecessarily administered in 8.05% of days, having inadequate doses in 21.61% of days, there have been interactions for 1.69% of days, and route of administration was inadequate for 10.17% of days.

**Conclusion.** By comparing the total cost with the potential total cost, the first was found as significantly higher. A solution for improving PPI therapy might be to include a clinical pharmacologist as part of the medical team and follow minimal prescribing rules.

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**NMR SPECTROSCOPY - A MODERN METABOLOMIC TECHNIQUE USED IN THE DIAGNOSIS AND MANAGEMENT OF METABOLIC GENETIC DISEASES; OUR EXPERIENCE OF ROMANIAN PATIENTS WITH UREA CYCLE DISORDERS, ALKAPTONURIA OR GALACTOSEMIA**

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The emerging field of metabolomics, in which a large number of small-molecule metabolites are detected quantitatively in a single step, promises immense potential for early-diagnosis, monitoring, and understanding the pathogenesis of many diseases. The clinical/ biochemical findings in some inborn errors of metabolism (IEM) are often nonspecific; an early differential diagnosis made in a single urinary sample provides an important advantage. We present the spectrum of metabolites of urine from one patient with neurological signs suspected for an inborn error of metabolism, being first interpreted as encephalitis. Beside the clinical presentation, the fast results given by urinary NMR-spectrum showing a high concentration of orotic acid indicates the presence of an urea cycle disorder. Beside this, we present our results and the utility of this method for rapid diagnosis and monitoring steps for galactosemia and alkaptonuria. The level of excretion of the metabolites in these three IEM has been well within the range of NMR detection.

In the critical care setting, IEM that were not diagnosed through the neonatal screening should be considered as cause of acute neurologic, hepatic/ renal decline, rapid diagnosis being essential. We demonstrate the effective use of NMR-spectroscopic-profiles of urine in differential diagnosis or management in urea cycle diseases, organic acidurias or other IEM.

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## STAKEHOLDERS INVOLVED IN PHYSICAL ACTIVITY SERVICES DELIVERY FOR YOUTH AND ADOLESCENTS AT A LOCAL LEVEL. THE CASE STUDY OF TWO UNIVERSITY CENTERS

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**Introduction.** The levels of physical activity of youth and adolescents are influenced by factors related to the built environment, community and family influences. The goal of this research was to identify the stakeholders involved in the delivery of physical activity services to youth and adolescents at local level.

**Material and methods.** Document analysis was conducted for exploring the national legislative framework, as well as the websites of the local public, private and civil society institutions with responsibilities and activities in delivering physical activity related services to youth and adolescents in two University Centers in Romania, Cluj-Napoca and Iasi respectively.

**Results.** Stakeholders involved in physical activity services delivery are from the public, private and civil-society sectors from the sport, education, and public health domains. The legal attributes and the activities of these stakeholders differ between sectors and domains, but are very similar between Centers (i.e. Cluj-Napoca and Iasi). The differences in the delivery of services by the civil society stakeholders in the two Centers of research are given by different human and financial resources as well as by the levels of communication and collaboration between these institutions and the public institutions, which are specific to each of the two centers.

**Conclusion.** Public, private and civil society stakeholders from the sport, education and health-related domains are delivering physical activity related services to youth and adolescents, according to the national legislation and to local arrangements (e.g. resources, public-civil society communication and collaboration). These aspects should be considered when tailoring intervention for increasing the attitudes and behavior of youth and adolescents towards physical activity.

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## THE INFLUENCES OF BUILT ENVIRONMENT ON THE PHYSICAL ACTIVITY OF YOUTH AND ADOLESCENTS. A LITERATURE REVIEW

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**Introduction.** Physical activity is a complex behavior influenced by a large array of factors, from personal traits and attitudes to community services and environmental design. The purpose of the research was: Exploring the current knowledge regarding the influences of the built environment on the physical activity attitudes, perceptions and levels in the youth and adolescents population.

**Material and methods.** We conducted a literature review of articles published between 2000 and 2014 in the following databases: Medline, Scopus, Google Scholar, EbscoHost and Web of Knowledge as well as conducting manual searches of the reference lists of retrieved studies. Inclusion criteria were: peer-reviewed article, published in English, in the time-frame 2000-2014. The following keyword combinations were used: environment, built environment, determinant, influence, physical activity, levels, attitudes, perceptions, youth, and adolescents.

**Results.** There is a clear association between the built environments characteristics, namely the availability and accessibility of recreational physical activity facilities (infrastructure) and the physical activity related attitudes, perceptions and levels in youth and adolescents. Both subjective (in terms of perception of availability and access) and objective measurements of sport infrastructure are positively associated with physical activity in these population sub-groups.

**Conclusion.** Built environment, more specifically the recreational physical activity opportunities have an influence on the physical activity of youth and adolescents. These aspects have to be considered when tailoring interventions that target the personal influences on physical activity, without looking into the (lack of) opportunities to support or, by contrary, limit the adoption of this health enhancing behavior.

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## PROINFLAMMATORY CYTOKINES - A POSSIBLE DIAGNOSTIC METHOD IN ENDOMETRIOSIS

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**Introduction.** The aim of the study was to investigate the serum pro-inflammatory cytokine profile in patients with diagnosed endometriosis.

**Material and methods.** The study included 160 women, who were divided in two study groups (Group 1 – endometriosis; Group 2 – healthy women). We evaluated the serum levels of interleukin (IL)-1 $\beta$ , IL-5, IL-6, IL-7, IL-12, and of tumor necrosis factor (TNF)- $\alpha$  with the use of Human Multiplex Cytokine Panels.

**Results.** The serum level of IL-1 $\beta$ , IL-6 and TNF- $\alpha$  is significantly higher in women with endometriosis compared to women free of disease from the control group (mean 10.777, 183.027, and 131.326 respectively, compared to 3.039, 70.043, and 75.285 respectively;  $p=0.002$ ,  $p<0.001$ , and  $p=0.015$ , respectively). No significant differences in the serum levels of IL-5 and IL-12 was observed between the studied groups and IL-7 had a very low detection rate.

**Conclusions.** Women with elevated levels of the key pro-inflammatory cytokines, i.e. IL-1  $\beta$ , IL-6 and TNF- $\alpha$  also had endometriosis more frequently. At the same time, IL-1 $\beta$  and IL-6 could be used as a non-surgical diagnostic test for endometriosis.

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## NEW POSSIBILITIES OF STEM CELLS UTILIZATION FOR THE TREATMENT OF ARTICULAR CARTILAGE FOCAL DEFECTS

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**Introduction.** Although a few procedures for cartilage repair are currently in use, the problems arise from their low efficacy, technical difficulty or increased costs. In this context, more and more ground is gained by the biological procedures utilizing mesenchymal stem cells (MSC), growth factors, with or without scaffold insertion.

**Material and methods.** We propose a preclinical experimental comparative in-vivo study on ovine model. On 15 sheep knees we perform full-thickness chondral defects. In six cases we apply bone marrow aspirate concentrate from the iliac crest (BMAC) and in the other six, adipose derived stem cells from fat tissue aspirate (ADSC) and platelet rich plasma (PRP), embedded in a matrix. Three sheep will be left untreated, as controls. At three months we will perform a macro and microscopic examination, without animal sacrifice.

**Results.** We shall investigate whether the results will support our hypothesis that under the influence of local factors, the MSC implanted at the site of an articular chondral defect will be directed towards the chondrocyte line and thus providing local healing with a hyaline-like tissue. We will comparatively evaluate the following criteria: clinical aspect, complications, specific scores for macroscopic morphologic evaluation (Niederaurer, Fortier, ICRS), qualitative histological analysis and ICRS-II-2010 quantitative parameters, immunohistochemical determination of collagen I/II.

**Conclusion.** The present study will bring concrete scientific benefits, deriving from the promise of these stem cells therapies, which represent a real hope for the future not only in the treatment of articular cartilage focal defects, but also in osteoarthritis, non-unions or bone and joint infections.

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## TIBIO-TARSAL JOINT BIOMECHANICS ANALYSIS THROUGH FINITE ELEMENT MODELING

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**Introduction.** The purpose of this paper is to analyze the behavior of the human tibio-tarsal joint during static loading. The tibio-tarsal joint represents the transition area between the verticality of the calf and the foot. Along with the subtalar and transverse tarsal joints, it represents a crucial component of the ankle.

**Material and methods.** A Finite Element Model (FEM) of the human tibia, fibula and talus was created, taking into consideration the anatomical characteristics of an average weight male adult. In order to analyze the behavior of the tibio-tarsal joint during static loading, the fore mentioned components were rendered in vertical position, and the relations between components were defined. The biomechanical properties (Young's Modulus, Density and Poisson's Ratio) of the human cortical bone were applied with regard to current literature and research. The resulting assembly was subjected to a uniformly distributed pressure of 0.625 kg/ccm. Displacement, von Mises Stress and Strain were the selected output parameters. The software used to obtain the respective results was SolidWorks® 2014.

**Results.** Analysis of the Finite Element Model revealed a concentration of forces at the base of the medial and lateral malleoli. Strain analysis shows compression forces on the medial cortex of the tibial malleolus and lateral cortex of the perroneal malleolus, with compression forces on the opposing cortexes of both malleoli. A tendency of compression is also noted in the postero-medial aspect of the tibial diaphysis.

**Conclusions.** Understanding the biomechanical behavior of the tibio-tarsal joint during static as well as dynamic loading is essential in order to formulate objective treatment solutions in case of ankle trauma and fracture.

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**NEOVASCULAR GLAUCOMA AFTER CENTRAL RETINAL ARTERY OBSTRUCTION  
AND CHRONIC HYPOXIA OF THE HEAD.**

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We present the case of a patient hospitalized in emergency at our clinic with the diagnosis of central retinal artery obstruction. During the hospitalization, after complementary examination, we found out the bilateral stenosis of the internal carotide artery. At three weeks after the vascular obstruction, he developed neovascular glaucoma. We began the local treatment with antiglaucomatous drugs but the intraocular pressure did not decrease. So trabeculectomy was performed with a good result. We present also the data of the follow-up of the patient. The links between the central retinal artery obstruction and the appearance of the neovascular glaucoma are discussed.

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## A CASE OF HARADA DISEASE

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We present the case of a woman with an abrupt decrease of visual acuity (hand moving) and bilateral retinal detachment. Under treatment the clinical evolution was unexpectedly well with improvement in visual acuity (5/5) and re-attachment of both retinae, with a long period of clinical remission.

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**CORRELATION BETWEEN THE DIFFERENCES OF MACULAR THICKNESS AND THE DIFFERENCES OF RETINAL NERVE FIBER LAYER, MEASURED WITH STRATUS OCT, IN THE DIAGNOSIS OF PRIMARY OPEN-ANGLE GLAUCOMA (POAG)**

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**Introduction.** This study tests the existence of a correlation between the differences of macular thickness (MT) and the differences of the corresponding retinal nerve fiber layer (RNFL) thickness, measured by optical coherence tomography (OCT).

**Material and methods.** The study group (23 subjects) with POAG (various stages) was compared to a control group (10 subjects) without POAG or other pathology. For all subjects we calculated the differences of thickness between 4 macular areas and the differences between RNFL thickness corresponding to the macular areas, measured with Stratus OCT (Zeiss). We determined the correlation between these differences within each group. We set, for the control group, the physiological ranges of the differences of nerve fibers corresponding (DRNFLcorresp) to the differences of macular thickness (DMT). Data were tested using t test, Kruskal Wallis test, Spearman and Pearson correlation coefficient.

**Results and Discussion.** In pre-perimetric glaucoma group, the maximum DMT (DMTmax) was not significantly different ( $p=0.733$ ), compared to controls, meaning that macula has little or no modification; maximum DRNFL (DRNFLmax) was significantly higher ( $p=0.004$ ), compared to controls, meaning RNFL is affected. Correlation DMT-DRNFLcorresp was weakly negative (Pearson= -0.381), different from controls, which shows a weak positive trend (Pearson=0.225). In POAG with localized perimetric defect, DMTmax was significantly higher ( $p=0.049$ ) compared to controls, meaning that macula is modified; DRNFLmax was significantly higher ( $p=0.004$ ), compared to controls, meaning that RNFL is also affected; but there is no correlation between DMT -DRNFLcorresp (Pearson= -0.024).

**Conclusion.** We established "normal" intervals of DRNFL corresponding to different DMT, allowing individualized analysis for each patient, based on the thickness of macula and nerve fiber layer. Values outside these ranges can be observed in pre-perimetric and localized perimetric defect glaucoma groups.

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## EVALUATION OF INFLAMMATORY MARKERS IN PREGNANT WOMEN AT RISK FOR THE PREDICTION OF PREECLAMPSIA

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**Introduction.** A low degree of inflammation has been associated with complications in pregnancies, including preeclampsia (PE). The aim of our study was to determine the serum values of high-sensitivity C Reactive Protein (hs-CRP) and Interleukin -6 (IL-6) in the first and second trimesters of pregnancy in pregnant women with risk factors for the development of PE, and to evaluate their relevance for the prediction of this disorder.

**Material and methods.** We performed a prospective longitudinal study on 120 pregnant women, which were divided based on the pregnancy evolution, into two groups: group I- 26 pregnant women who developed preeclampsia and group II- 94 pregnant women with physiological evolution of pregnancy. Our study has shown an increase in serum levels of hs-CRP and IL-6 in the first and second trimester of pregnancy in patients from group I, significant values being revealed only in the second trimester of pregnancy. The predictive power of the selected inflammatory markers is significant only for values of hs CRP in the second trimester of pregnancy, and the association with IL-6 increases the prediction. In conclusion, increased values of hs- CRP and IL-6 in the second trimester of pregnancy are associated with higher risk for preeclampsia, but the study is providing only a modest efficiency of the prediction capacity.

**Results.** Our study detected increased hs-CRP values in the first and second trimesters of pregnancy in pregnant women who subsequently developed PE, a significant increase of hs-CRP being evidenced in the second trimester. We also found an increase of serum IL-6 levels in PE compared to normal pregnancy, with more significantly increased values in the second trimester.

**Conclusion.** Our data suggest the presence of a generalized inflammatory response in patients with PE as early as the first trimester of pregnancy.

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## THE RESULTS OF THE SELECTIVE ULTRASOUND SCREENING PROGRAM OF THE NEONATAL HIP

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**Introduction.** Due to the increased incidence of developmental dysplasia of the hip (DDS) in our geographic area, this pathology represents a public health priority because of its frequency, possibility of secondary prevention and successful treatment. The aim of this study was to explore the results of introduction of a selective ultrasound (US) screening program in our hospital.

**Material and methods.** In 2000 we started a selective US screening program of clinically unstable hips and "at risk" hips. The hips were examined clinically by a senior pediatric orthopedic surgeon at 4–6 weeks after birth and those abnormal were referred for US examination to an experienced radiologist. If the US hip measurements were abnormal, the hips were classified as dysplastic and treated immediately using hip abduction devices. If the US examination showed normal angles after 6 weeks of treatment the child was seen clinically again at the age of 6 months, together with those with normal initial US examination. In order to evaluate the efficiency of the program, we studied the rate of surgery for DDH during the years 2004, 2009 and 2013 in our hospital.

**Results.** During the year of 2004, 286 operations were carried out in our service. Of them 32 operations were performed for DDH (11.18%) in children under the age of 8 years. 18 operations were pelvic and/or femoral osteotomies. In 2009, 40 operations out of 389 (10.28%) were done for DDH and only 11 were pelvic and/or femoral osteotomies. In 2013, 15 pelvic and/or femoral osteotomies out of 270 operations were done for DDH.

**Conclusion.** In the period analyzed by our study, an increase in the number of operations in our service was observed concomitantly with the reduction of major interventions for DDH. At the same time, it contributes to the decrease of the hospitalization time and of the cost of treatment. We assume this result as a consequence of the US program started in our county.

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## THE SURGICAL HIP DISLOCATION FOR ANATOMICAL REDUCTION OF THE SLIPPED CAPITAL FEMORAL EPIPHYSIS IN CHILDREN AND ADOLESCENTS - PRELIMINARY RESULTS AND REVIEW OF THE LITERATURE

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**Introduction.** The optimal treatment of slipped capital femoral epiphysis (SCFE) in children still remains a controversial issue. Anatomic reduction of the proximal femoral epiphysis using the surgical dislocation of the hip while preserving a retinacular flap, has been recently described as an efficient and safe treatment method. The purpose of this study was to evaluate the first results of the cases treated in our service during 2013-2014.

**Material and methods.** Five hips of 5 patients diagnosed with SCFE were surgically treated in our service during 2013-2014, by performing surgical dislocation of the hip according to Ganz. The medium age at the time of intervention was 15.7 years. All patients were male, with a minimum follow up time of 6 months.

**Results.** In all patients we performed a subcapital reduction osteotomy of the femoral head after the surgical dislocation of the hip and the development of an extended retinacular flap in order to preserve the vascularization of the femoral head. The mean operating time was 131 minutes and the mean blood loss was 364 ml. The mean preoperative slip angle was 40.2° on the AP view and 50.65° on the lateral view. The mean postoperative values of the slip angle were 7.2° on the AP view and 9.45° on the lateral view. The mean hip flexion amplitude improved from 74.7° preoperatively to 115.4° postoperatively. Rehabilitation started at 6 weeks after operation and the patients were followed up periodically to the end of growth. Femoral head AVN, delay of union and infection have been absent at the time of the last postoperative control.

**Conclusion.** Taking into consideration the high complexity of this procedure, our preliminary clinical and radiological result have been according to the current literature data. This surgical technique, used for the first time in our country to our knowledge, can reestablish the normal anatomical configuration of the proximal femur and it can also reduce the risk of secondary arthritis.

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**MECHANICAL COMPLICATIONS OF ACUTE MYOCARDIAL INFARCTION:  
BETWEEN AGONY TO ECSTASY. REPORT OF TWO SURGICALLY TREATED CASES**

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Mechanical complications of acute myocardial infarction (ventricular free wall rupture, ventricular septal rupture, acute mitral regurgitation, left ventricular aneurysm) are true “challenges” for heart surgeon and this surgery is associated with high perioperative mortality.

This paper aims to present two interesting cases:

a) The case of a patient late diagnosed with chronic pericardial collection with compression of the right ventricle (pseudoaneurysm rupture?), left ventricle aneurysm, chronic fibrous pericarditis on the right heart, patient who underwent to surgery but with negative result

b) The second case presented is of a patient operated in emergency for postinfarction ventricular septal rupture using exclusion technique. Initially the evolution was slowly favorable, due to the presence of residual shunts and associated symptomatology, but in the end the result was excellent.

These two cases described, between agony to ecstasy, two serious complications of acute myocardial infarction leaving free space on surgical questions: If/Where? How? Why

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**NATIVE VALVE INFECTIOUS ENDOCARDITIS: SURGICAL TREATMENT IN THE EXPERIENCE OF THE CARDIOVASCULAR SURGERY CLINIC AT THE “NICULAE STĂNCIOIU” HEART INSTITUTE IN CLUJ-NAPOCA**

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**Introduction.** The introduction of Duke’s criteria and the perfection of imaging methods has led to the diagnosis of infectious endocarditis (IE) earlier and more accurately.

**Material and method.** We undertook a retrospective, descriptive study, spanning over a period of five years (January 1st, 2007 to December 31st, 2012), on 100 patients who underwent surgery for native valve infectious endocarditis in our clinic.

**Results.** The overall mortality was 5% well between the limits presented in literature, being high (30%) in patients with emergency surgery (and in patients with prosthetic valve IE (50%).

**Conclusion.** Choosing the exact therapeutic approach and the timing of surgery is still a matter of debate and requires a close collaboration between the cardiologist, the infectionist and the cardiac surgeon.

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## CONGENITAL OPTIC NERVE PIT: A CASE REPORT

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**Introduction.** Optic pit is a rare congenital optic nerve defect that appears as a round depression that differs in color from the surrounding optic nerve fibers. It is usually a single lesion located in the temporal quadrant of the optic nerve head; more often it is unilateral.

**Case report.** A 63-year old patient presented to a routine ophthalmological examination; his visual acuity was 100% in both eyes with adequate optical correction. The dilated fundus examination evidenced in both eyes optic nerve excavations suggestive for glaucoma and two gray depressions suggestive for optic pit in the temporal quadrant of the left optic nerve. The intraocular pressures ranged between 17 and 20 mmHg in both eyes. The visual field test revealed no defects for the right eye and blind spot enlargement for the left eye. Optical coherence tomography showed normal thickness of retinal nerve fibers for the right eye and localized decrease of retinal nerve fibers thickness corresponding to the two gray depressions in the left eye.

**Discussion.** The criteria that sustain the diagnosis of glaucoma are borderline. The presence of the two optic pits in the left eye contributes to the visual field and optical coherence tomography defects that may be superimposed to the defects caused by glaucoma.

**Conclusion.** The double unilateral congenital optic nerve pit is a rare condition that may alter the visual field - although the patient is asymptomatic, and may determine difficulties of differential diagnosis of glaucoma.

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## DEDIFFERENTIATED LIPOSARCOMA OF THE SPERMATIC CORD

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**Introduction.** Spermatic cord liposarcomas (SCL) are very rare paratesticular tumors with fewer than 200 cases reported in literature and case series not exceeding 82 patients in two decades. We present here the clinical features of a case of SCL.

**Material and methods.** The clinical data and treatment of a case of SCL was retrospectively reviewed in combination with related literature.

**Results.** The 61-year-old obese patient was initially misdiagnosed as an incarcerated inguinal hernia. Surgical preoperative examination and CT-scan oriented the diagnosis towards a solid tumor of the spermatic cord. Some infracentimetric para-aortic nodes were also noted but were considered insignificant. The patient underwent tumor resection by left inguinal orchiectomy. Postoperative pathology confirmed the case to be a low grade (G1) but dedifferentiated SCL. Based on pathology and preoperative imaging the case was staged pT2N0 M0. Adjuvant radiotherapy was also performed. Neither recurrence nor metastasis was found during the 6-month follow-up.

**Conclusion.** SCL is a rare medical condition with no specific clinical and imaging features. The dedifferentiated type is common. While radical orchiectomy with wide local excision is the recommended treatment, the decision for retroperitoneal lymphadenectomy and adjuvant radiotherapy is difficult. Beside the margin status, tumor grade and local relapse, we suggest considering dedifferentiation among the criteria for radiotherapy. One should be aware that regardless of initial therapy, the risk of local recurrence always necessitates long-term follow-up.

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## GASTRIC OUTLET OBSTRUCTION: A LATE SEQUELAE OF ACID INGESTION IN CHILDREN

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**Introduction.** Corrosive stomach injury without esophageal involvement is a rare entity in children. Usually they present esophageal lesions due to corrosive ingestion and gastric involvement is not suspected until complications are clinically revealed. A few cases are reported in literature, none in our country until now. Acids are commonly available in household items such as toilet cleaners (sulfuric acid) which makes them easily accessible to the kids, thus resulting in high incidence of accidental ingestion by neglected children.

**Material and methods.** We present the case of a 1.3 year old boy who was referred to our hospital with complaint of hematemesis after accidental ingestion of corrosive acid. Oropharyngeal, abdominal and chest examination revealed no abnormality and patient was managed conservatively and discharged after 14 days. After another 7 days he started complaining of vomiting, dehydration and weight loss and upper GI endoscopy revealed complete obstruction of the pylorus, due to a large scar. After preoperative preparation, the patient underwent laparotomy and omega loop gastrojejunostomy and Brown entero-enterostomy. Postoperative period remained uneventful and patient was discharged after 8 days; he was asymptomatic and gaining weight for the last 11 months.

**Discussion.** Due to contact burns, concentrated acids are usually vomited and thereby producing a little damage to esophagus and stomach. Gastric injuries usually follow ingestion of dilute acids due to pylorospasm induced by the presence of acid in stomach. Clinical signs develop after a latent period of 3-6 weeks.

**Conclusion.** A pyloric and gastric outlet may develop after corrosive ingestion and we recommend upper GI endoscopic evaluation in all children with positive history even in the absence of clinical signs, with the aim of satisfactory recovery by early surgical intervention.

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## ANOMALOUS RIGHT HEPATIC ARTERY RECONSTRUCTION DURING DUODENOPANCREATECTOMY FOR PANCREATIC HEAD ADENOCARCINOMA

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**Introduction.** The arterial anatomy supplying the liver is highly variable. One of the most common variants is a completely replaced right hepatic artery which is seen in about 11% of the population and may pose technical and oncologic challenges during pancreatoduodenectomy (PD) for pancreatic adenocarcinoma (PA) as a result of its proximity to the head of the pancreas. Despite the fact that arterial resection and reconstruction can improve the resectability in pancreatic malignancies, few reports on this topic have been published.

**Material and methods.** We report the case of a 60 years old female patient with PA with portal vein compression and with anatomic absence of the common HA. Computed tomography revealed a left hepatic artery derived from the left gastric artery while the right hepatic artery origin was the gastroduodenal artery, and passing right through the tumor. A PD was performed with vascular reconstruction of the right hepatic artery by arterial end to end anastomosis between the right hepatic artery stump, in the hepatic hilum, with the terminal gastric branches of the left gastric artery, associated with portal resection and end to end venous reconstruction. The pancreatic stump was anastomosed into the stomach.

**Results.** An R0 resection was achieved. The postoperative course was uneventful, with patent right hepatic arterial and portal flow as shown by a computed tomography performed 6 months after the intervention.

**Conclusion.** Complete surgical resection (R0) combined with main vascular resection could be safely performed in selected patients and may be the only alternative in those with vascular anatomic anomalies.

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## A RARE CASE OF BUSCHKE-LOWENSTEIN TUMOR WITH SQUAMOUS CELL CARCINOMA: A CASE REPORT

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**Introduction.** Giant condyloma acuminatum, also known as Buschke-Lowenstein tumor (BLT), is a rare sexually transmitted disease of the ano-genital region. Malignant transformation occurs in 40-60% of cases and it is important to identify it in order to establish the proper treatment. Complete surgical excision is the treatment of choice and often wide wounds are necessary to reach clear margins and prevent recurrence.

**Case Presentation:** We present the case of a 42-year-old woman consulting for a large exophytic mass that originated 21 years ago, involving the entire ano-genital region and extending superficially in the anal canal, until the level of the dentate line. The treatment consisted of complete surgical excision with clear resection margins, reconstructive surgery with a bilateral pediculated vertical rectus abdominis myocutaneous (VRAM) flap and a temporary colostomy, with good functional results. The histopathological result showed the presence of a moderately differentiated squamous cell carcinoma. The necessity of further adjuvant treatment is still being discussed.

**Conclusion.** The Buschke-Lowenstein tumor presents as a slow growing, cauliflower-like mass, locally aggressive and destructive, with a great potential of malignant transformation and a great tendency of recurrence. Given the rarity of the disease, there are no standard protocols regarding treatment. Wide perineal excision with histopathological margins control remains the best surgical choice. A more radical approach (abdominoperineal resection) is indicated only in patients with extensive lesions and deep tumor invasion. In order to prevent recurrences, in cases associated with squamous cell carcinoma, adjuvant chemo-radiation therapy is indicated following the protocols used for anal canal squamous cell carcinoma.

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## MULTIDISCIPLINARY AND INDIVIDUALIZED APPROACH OF HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY

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**Background/Aims.** Hyperthermic Intraperitoneal Chemotherapy is an option for selected patients, but there is a lack of standardization. The studies related to the peritoneal surface area and the circulated solutions are coming from Peritoneal Dialysis; there is only one multidisciplinary approach model. We want to update those approaches based on Three-Dimensional Reconstructions and Cyber-Physical Systems paradigm.

**Materials/Methods.** The Three-Dimensional Reconstruction involves: images acquiring, specific software programs, segmentation method and computational resources. Regarding Cyber-Physical Systems, the architectural design and the implementation on embedded platform is a co-design problem: the cyber part (embedded control systems, networks) and the physical part influence each other. There are specific challenges related to: peritoneal cavity reconstruction, equipment architecture.

**Results.** Our proposals are: 64-slice multi-detector row computed tomographic images (3-5 mm slice length) acquisitions method; Mimics software; manual segmentation method. The essential blocks of the equipment are: dedicated safety controller, top controller, family of heat and flow controllers; all connected to a common bus and having defined a hierarchy at the superior level. The development platform is structured on the open-source toolset (Java Messaging).

**Conclusions.** The expected result resides in treatment efficacy and patient safety.

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## NECROTIZING FASCIITIS IN THE PERINEAL AND GLUTEAL AREAS

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We present the clinical observation of a patient diagnosed with necrotizing fasciitis, localized in the perineal and gluteal region.

Patient aged 72 (with a history of coccygeal fistula surgery) was operated for a left voluminous gluteal abscess. We practiced the incision, evacuation, lavage, drainage of the abscess. Postoperative evolution was unfavorable, with sepsis, purulent fluid externalizing and necrotic tissue from the incision. Surgical reintervention was performed, and we practiced debridement of necrotic areas with wound healing by secondary intent. The patient was given broad spectrum antibiotic therapy, electrolytic and volemic treatment, symptomatic treatment, daily toilet and lavage of the wound, with favorable evolution, without acute events. About two months after the first surgery the patient returns for surgery (secondary suture). We practiced debridement, secondary suture. At seven days postoperatively in the surgical wound, a dehiscence was noticed, for which reintervention was needed and secondary suturing was performed, with favorable evolution.

The case draws our attention to this polymicrobial necrotizing infections with severe and rapidly progressive evolution, affecting the superficial fascia and subcutaneous adipose tissue, with secondary involvement of the skin, accompanied by general, toxic severe manifestations, which can ultimately determine the patient's death.

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## COMPARTMENT SYNDROME OF THE LEG

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We present the clinical observation of a patient with a rare complication, consecutive to prolonged operators immobilization. Patient (28 years) underwent surgery for locally advanced sigmoid cancer perforated with generalized peritonitis, left ureterohydronephrosis; we practiced subtotal colectomy, ileostomy, left ureterostomy; subsequently followed by adjuvant chemotherapy Xelox (8 cycles). The re-intervention for reintegration of the rectum into the digestive transit revealed a peritoneal carcinomatosis, which required a change of operative strategy; ileorectal anastomosis was performed, and peritonectomy and resection of carcinomatosis nodules from mesentery, peritoneum visceral, intraperitoneal chemohyperthermia with Oxaliplatin. During surgery (over 6 hours) the patient was immobilized in Lloyd-Davis position. Immediate postoperative evolution was complicated by a minor compartment syndrome in the left leg and significantly at the right leg, which slowly evolved favorably under conservative treatment.

The case draws our attention to these forgotten complications due to prolonged compression of muscle mass during long operations.

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## TEN TIPS FOR SAFE AND EFFECTIVE SURGERY OF THYROID CANCER

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**Introduction.** For surgeons who treat differentiated thyroid cancer the injury of the recurrent laryngeal nerve and postoperative hypoparathyroidism remain the uppermost subjects of concern. In our experience, surgery can be performed in a safe and effective way in most of the patients.

**Material and methods.** First of all, it is mandatory to perform thorough clinical, ENT, laboratory and imaging examinations and ultrasound guided FNAC of tumor and suspicious lymph nodes. Before surgery it is useful to review the patient data with the pathologist, radiologist and oncologist and to discuss with the patient the options of treatment.

We start surgery with the central compartment, progressing from the less involved/most accessible anatomical landmarks toward less obvious anatomy. In difficult cases we first perform thyroid lobectomy on the less involved side, preserving the recurrent laryngeal nerve and the two ipsilateral parathyroid glands. Then we proceed in the same way with the lobectomy on the tumor side. In simple cases we start with the tumor side.

When obviously invaded by the tumor, the recurrent laryngeal nerve should be sacrificed during dissection. The recurrent laryngeal nerve should be preserved by all means, at least in one side. When bilaterally damaged during tumor resection and/or without signal on neuromonitoring, tracheostomy is mandatory.

R0 resection should be the goal of resection in all but very few tumors. As planned/needed, we perform "en-block" resection of the thyroid lobe and nearby structures involved by the tumor with frozen sections so as to single out resection margins free of tumor.

We perform central neck dissection in all cancer patients. For the parathyroid glands with obvious vascular compromise we do immediate re-implant. Selective lateral neck dissection is performed when indicated.

**Conclusion.** A safe and effective surgery can be performed in all but a few exceptional cases.

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## SIMULTANEOUS QUANTIFICATION OF BIOGENIC AMINES BY LIQUID CHROMATOGRAPHY WITH FLUORESCENCE DETECTION

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**Introduction.** Biogenic amines: serotonin (ST), noradrenaline (NA), adrenaline (AD) and dopamine (DA) occupy key positions in the neurological functioning. Since they have the potential to serve as theranostic biomarkers, the development of a validated analytical instrument method for their quantification is extremely useful in clinical practice. The aim of this study was the optimization of simultaneous derivatization of biogenic amines using a mixture of reagents and the subsequent separation and quantification of their fluorescent derivatives in a single run analysis by high performance liquid chromatography (HPLC) with fluorescence detection (FLD).

**Material and methods.** We optimized the reagents ratios in order to obtain stable fluorescent derivatives. Separation was accomplished using a C18 chromatographic column (4.6x150 mm, 3.5 μm) protected by a precolumn (4.6x20 mm, 3.5 μm), at 30°C column temperature. Mobile phase A consisted of 100% acetonitrile, while mobile phase B was a 10 mM acetate buffer (1 mM heptan-1-sulfonic acid sodium salt, pH=5.30). Gradient steps were programmed as follows: 32% A (0 min) to 52% A (20 min), end run at 60 min; 0.80 mL/min flow rate. Fluorescence was monitored at  $\lambda_{ex}=345$  nm/ $\lambda_{em}=480$  nm.

**Results.** Optimal conditions for the simultaneous derivatization of the amines were the following: methanol used as solvent, two step derivatization (benzylamine/room temperature; 1,2-diphenylethylenediamine/50°C), ice cooling to quench the reaction. The simultaneous derivatization allows the quantification of the amines at concentrations of ng/mL. The method was pre-validated according to accuracy profile with good results.

**Conclusion.** A HPLC-FLD method was elaborated, optimized and pre-validated. It allows the simultaneous quantification of biogenic amines. This method will be validated according to bioanalytical method validation guidelines and applied for the quantification of ST, NA, AD and DA in biofluids.

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## STABILITY EVALUATION OF THE GROWTH HORMONE BY SDS-PAGE

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**Introduction.** The Growth Hormone (GH) is a hormone with proteic structure involved in growth stimulation, cell reproduction and regeneration. Clinical studies indicate a more rapid re-epithelization following its topical administration in patients presenting burnt wounds.

The objective of this study was the assessment of GH stability in the preformulation stage of a topical medication and the identification of the optimal conditions for its conservation and validity.

**Material and methods.** Stability studies were conducted both under accelerated conditions (25°C±2°C, relative humidity 60%±5%) and long-term stability studies (5°C±3°C). Samples were analyzed using sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) on a discontinuous gel (5-15%). The voltage applied for the separation of the proteic bands was 200V. Gels were stained using silver staining protocol. High performance liquid chromatography was used to highlight the oxidation and deamidation products formed.

**Results.** Assessment of stability was achieved by monitoring the occurrence of additional bands with molecular weight <22kDa corresponding to degradation products formed. It was found that GH is stable for up to 8 days after its reconstitution in a 0.4% NaHCO<sub>3</sub> solution at 25°C±2°C. While maintaining the solutions at 5°C±3°C the stability increased considerably.

**Conclusion.** Preliminary results of stability studies performed on GH indicate the need to preserve topical preparations at 5°C±3°C in order to assess the comparative stability and establish their validity.

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## SYNTHESIS OF IRON OXIDE NANOCUBES AND MANGANESE FERRITES NANOSPHERES FOR MAGNETIC HYPERTHERMIA APPLICATIONS

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**Introduction.** The heating ability of magnetic nanoparticles (MNPs) under an alternating magnetic field has led to the development of a novel therapeutic concept for cancer treatment. Therefore, the synthesis of magnetic nanoparticles with enhanced magnetic properties and efficient heat induction represents a major goal in this research field. Here we report two approaches based on solvothermal reduction method to prepare magnetic nanoparticles by using polyethylene glycol as reducing agent.

**Materials and methods.** For the preparation of iron oxide MNPs, FeCl<sub>3</sub>·6H<sub>2</sub>O (0.675 g) and NaAc (1.8 g) were mixed and dissolved in 60 ml PEG 200, while for the preparation of manganese ferrites, Fe(acac)<sub>3</sub> (0.635g) and Mn(acac)<sub>2</sub> (0.225 g) were mixed and dissolved in a mixture of PEG 200 (4 ml) and diphenyl ether (10 ml). Both solutions were stirred thoroughly then transferred in sealed glass bottles and heated at 240°C for 6h and 24h respectively. The obtained black precipitates were washed several times with ethanol.

**Results.** Transmission electron microscopy (TEM) images reveal that iron oxide MNPs have roughly cubic shape (mean edge length of 125 nm), while the manganese ferrites display a spherical shape (mean diameter around 20 nm). According to X-ray powder diffraction (XRD) measurements the manganese ferrites exhibit a pure phase spinel ferrites. Instead, the iron oxide nanoparticles are composed of two phases: magnetite-Fe<sub>3</sub>O<sub>4</sub> and hematite Fe<sub>2</sub>O<sub>3</sub>. Both types of magnetic nanoparticles are superparamagnetic at room temperature. The specific absorption rate (SAR) values recorded on cube-shape MNPs in a.c. magnetic field of different frequencies and strengths reach several hundreds of W/g higher than those given by manganese ferrites.

**Conclusion.** By applying the solvothermal reduction method we have been able to synthesize cube-shaped iron oxide MNPs and spherical shaped manganese ferrites with good hyperthermia performance.

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## PRELIMINARY PHYTOCHEMICAL STUDIES ON SOME INDIGENOUS SPECIES BELONGING TO CUCURBITACEAE FAMILY

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**Introduction.** *Bryonia alba* L. and *Echinocystis lobata* (Michx.) Torr. & A.Gray (Cucurbitaceae) are climbing plants, spontaneous in the Romanian flora, which can be found throughout the whole country and are known for their analgesic, antipyretic, anti-inflammatory, antibacterial, anti-rheumatic, laxative-purgative and smooth muscle relaxant properties. The main objective of this study consists in the study of the polyphenolic profile, total hydroxycinnamic acid derivatives and total flavonoidic content of the extracts obtained from different vegetative organs of the two species.

**Materials and methods.** The vegetal material was harvested from the spontaneous flora of Cluj county. The vegetal extracts were obtained by ultrasonication in 500 alcohol. The polyphenolic content was determined by Folin-Ciocalteu method. The hydroxycinnamic acid derivatives content was determined by a method similar to the one described in the European Pharmacopoeia, 8th edition, in the *Fraxini folium* monography, with some improvements. Total flavonoidic content was determined using a spectrophotometric UV-VIS, as described in the Romanian Pharmacopoeia, 10th edition, in the *Cynarae folium* monography. Polyphenols and flavonoids were identified and quantified by an LC-MS method.

**Results.** A medium content of polyphenolic compounds was highlighted in all the analyzed extracts. The profile of these compounds varied depending on the nature of the vegetative organ from which the extract was obtained. The *Echinocystis lobata* (Michx.) Torr. & A.Gray species was characterized by a higher content of polyphenols compared with the *Bryonia alba* L. species.

**Conclusion.** The scientific literature provides insufficient data on the two species, our study being a first step towards the determination of a more detailed biochemical fingerprint of the polyphenolic content of *Bryonia alba* L. and *Echinocystis lobata* (Michx.) Torr. & A.Gray.

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## MORPHOLOGICAL AND HISTO-ANATOMICAL DIFFERENCES BETWEEN TWO INDIGENOUS CORYDALIS SPECIES: CORYDALIS CAVA L. AND CORYDALIS SOLIDA L.

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**Introduction.** *Corydalis* genus (family Fumariaceae) comprises 11 taxons, which are found especially in Central and Western Europe. In Romania, 5 species and 4 subspecies of this genus vegetate. The vegetal medicinal product, *Corydalis* tuber represents the tuberous roots and the tubers of *Corydalis cava* L. and *Corydalis solida* L. Scientific literature states the presence of aporphine, protopine and protoberberine alkaloids also in the aerial parts of the species belonging to *Corydalis* genus. Bulbocapnine and corydaline have sedative, antispasmodic, tranquilizing and depurative effects. The Identification of the morphological and histo-anatomical differences between the two species, *Corydalis cava* L. ssp. *cava* and *Corydalis solida* f. *densiflora*, was performed in order to establish the identity of the two species.

**Material and methods.** The vegetal material was harvested from the spontaneous flora of Cluj county and preserved in 70c ethanol. Morphologic and micromorphologic characterisation was performed with a Motic-K-500L stereomicroscope, equipped with a MoticamPro 205A digital camera. Study of the histo-anatomic characters was performed by analyzing with an Olympus CX 31 optical microscope specimens obtained both by classical and by histological technique.

**Results.** Macroscopic characters required for a correct identification of the species and the microscopic characters of the studied organs were identified.

**Conclusions.** The results obtained are important criteria for the macroscopic and microscopic identification of the two species.

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## B-CYCLODEXTRIN/POLYETHYLENEIMINE FILM MODIFIED GLASSY CARBON ELECTRODES FOR THE DETECTION OF SOME PHARMACEUTICALS

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**Introduction.** Ascorbic acid (AA), uric acid (UA) and dopamine (DA) play an important role in bioelectrochemistry, neurochemistry and clinical diagnostic. Cyclodextrins (CDs) as electrode modifiers are used in order to enhance the sensitivity and the selectivity in pharmaceutical and biomedical analysis.

**Material and methods.** The electrochemical behavior of AA and UA at glassy carbon electrodes (GCEs) modified with  $\beta$ -cyclodextrin ( $\beta$ -CD) entrapped in polyethyleneimine (PEI) film has been investigated using square wave voltammetry.

**Results.** The oxidation peak potential of AA shifted to more negative values with over 0.3 V, while in the case of UA the negative potential shift was about 0.15 V, compared to the bare GCE. The peak potentials recorded for samples containing both analytes, at  $\beta$ -CD/PEI/GCEs were separated by 0.4 V, allowing their simultaneous detection. FTIR measurements, Raman spectra and microscopic investigations confirmed the formation of inclusion complexes between  $\beta$ -CD and the two analytes. The modified electrodes were successfully applied for the determination of AA in two pharmaceutical formulations with a detection limit of 0.22  $\mu$ M and for the quantification of AA and UA in real samples with good recoveries.

For DA detection, several GCEs were modified with reduced graphenes and  $\beta$ -CD in PEI in order to obtain an enzyme biosensor with tyrosinase. The deposition technique and the number of graphenes layers were optimized by using square wave voltammetry and electrochemical impedance spectroscopy. After the tyrosinase immobilization, the biosensor tested by chronoamperometry for dopamine detection showed a detection limit of 10.42  $\mu$ M, in the range 30–2500  $\mu$ M and a sensitivity of 0.073  $\mu$ A/ $\mu$ M.

**Conclusions.** A sensor and a biosensor based on GCEs modified with  $\beta$ -CD entrapped in polymeric film were elaborated and were successfully applied for the determination of AA, UA and DA in pharmaceutical products and biological samples.

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## NANOSTRUCTURED POLYMERIC FILMS FOR BIOSENSOR DESIGN

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**Objectives.** Nanostructuring of polymeric films by nanospheric lithography is an easy and inexpensive way to improve the performances of biosensors in order to detect biomedical compounds.

**Material and methods.** The polymeric pattern was created by electrochemical polymerization of the functionalized monomer of pyrrole by cyclic voltammetry onto the polystyrene nanospheres (100 or 900 nm diameter), previously deposited on the electrode surface. The nanospheres were removed by soaking the electrodes in tetrahydrofuran. The structure was investigated by laser microscopy, SEM and fluorescent characterization via streptavidin-RPE. Biomolecules such as Polyphenol oxidase and Glucoseoxidase conjugated with biotin and histidine groups, were immobilized by coordination of the biotin groups on the polymerized polypyrrole.

**Results.** The enzyme binding was demonstrated by amperometric measurement of glucose and catechol and showed an improvement in the performances of the biosensors fabricated on the structured platforms in comparison with those on the flat polymeric films, due to the increase of the active surface.

**Conclusions.** Well-defined two-dimensional honeycomb structures of polymer were obtained and the resulting stable films were used for the immobilization of enzymes. This approach offers potential applications such as engineering of porous materials for the coupling of antibodies and DNA fragments for the design of immunosensors.

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## NANOMATERIALS-BASED SENSORS FOR ACETAMINOPHEN AND DOPAMINE DETECTION

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**Introduction.** The development of electrochemical sensors has attracted a great interest due to their high sensitivity and selectivity. By including an enzyme in the sensors they also gain high specificity. Various nanomaterials have been successfully applied for the immobilization of bioelements and among these, carbon nanotubes (CNTs) and graphenes have gained special attention in the last years.

**Material and methods.** For the first analyte a sensor based on glassy carbon electrodes (GCE) modified with CNT and HRP entrapped in polymeric films was used. The biorecognition elements were immobilized onto the electrode and the experimental protocols were optimized. Several immobilization methods were also tested. For the dopamine detection the layer by layer technique on the surface of GCE was chosen for the reduced graphene oxide deposition on the electrode surface before the enzyme immobilization. The number of the graphene layer deposited on the electrode was optimized using SWV and EIS.

**Results.** The dopamine detection was possible in the presence of tyrosinase in the range of 30 to 2500  $\mu\text{M}$  using amperometry. The sensitivity of enzyme sensor was  $0.073 \mu\text{A } \mu\text{M}^{-1}$  and the detection limit  $10.42 \mu\text{M}$ . The acetaminophen detection on GCE modified with CNT and HRP entrapped in PEI film was performed in the ranges of 4 to 80  $\mu\text{M}$  and 20 to 160  $\mu\text{M}$  with detection limits of 1.36 and 8.09  $\mu\text{M}$ .

**Conclusions.** The combination of different types of nanomaterials and polymers as immobilization platform with different bioreceptors reveals enhanced the electroanalytical performances of the sensors in the pharmaceutical analysis. The obtained sensors present good sensitivity and selectivity for the detection of acetaminophen and dopamine. Good recoveries and RSD between 1.67% and 3.27% were obtained after real samples analysis.

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## NANOSTRUCTURED PLATFORMS WITH DIFFERENT TYPES OF POLYMERS FOR BIOSENSORS DEVELOPMENT

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**Introduction.** Different types of electrochemical bio/immunosensors are reported based on conductive polymers and nanoelements like carbon nanotubes, graphenes, cyclodextrines. Two model molecules were detected with those biosensors and an innovative way to obtain an immunosensor for MUC 4 detection was investigated. MUC4 is a tumor marker with elevated levels in various types of cancer such as pancreatic, lung, breast or ovarian cancer and their sensitive detection can play an important role in the early diagnosis of cancer and during follow-up therapy.

**Material and methods.** The first example consisted of a biosensor based on GCE modified with CNT and HRP entrapped in polymeric films and was used for acetaminophen detection. A second example used dopamine as target molecule and the determination was made by using a tyrosinase biosensor based on GCE modified with graphenes and  $\beta$ -CD entrapped in polyethyleneimine film. The layer by layer technique was chosen for the reduced graphene oxide deposition on the electrode surface before the enzyme immobilization.

The immunosensor for MUC4 detection used polyanthranilic acid and CNT as platforms for the antibody and antigen immobilization on graphite SPSs

**Results.** The amperometry allowed the estimation of the current response which was linear with dopamine concentration in the range of 30 to 2500  $\mu$ M. The sensitivity of enzyme sensor was 0.073  $\mu$ A  $\mu$ M<sup>-1</sup> and the detection limit 10.42  $\mu$ M. In the case of the acetaminophen biosensors based on GCE modified with CNT and HRP entrapped in PEI film, the detection limits were between 1.36 and 8.09  $\mu$ M and the biosensors were applied in the ranges of 4 to 80  $\mu$ M and 20 to 160  $\mu$ M.

**Conclusions.** The potential of different types of nanocomposites based on the combination of CNT/graphene/CD and polymers as immobilization platform for innovative devices was studied. The obtained electrochemical sensors were applied for the drug analysis and cancer biomarkers detection.

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## ANTINEOPLASTIC DRUG DETECTION BY MOLECULAR IMPRINTING SENSOR BASED ON ELECTROPOLYMERIZATION OF MICROPOROUS-METAL-ORGANIC FRAMEWORK

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**Introduction.** The analysis of drugs is important in the monitoring of the patients under treatment, as well as in the quality control in pharmaceutical industry. Monitoring of drug concentration in the serum allows the selection of the appropriate dose for individual patient. Therefore, fast and reliable sensors for drug detection are of high importance. Molecularly imprinted polymers are promising materials continually being used in sensor fields as biomimetic elements. An increasing interest has been given to microporous metal-organic frameworks as highly sensitive and selective platforms for the detection of analytes. Gemcitabine is a pyrimidine analogue used for the treatment of non-small cell lung cancer, pancreatic cancer, and breast cancer and, associated with cisplatin, in relapses of ovarian cancer.

**Material and methods.** In the present study, a selective electrochemical sensor was developed for the detection of gemcitabine based on molecularly imprinting microporous-metal-organic framework. Gemcitabine molecules were imprinted in a polythioaniline-gold nanoparticles film to create specific places in the polymer network for selective stereo chemical recognition. The molecularly imprinted sensor was characterized by linear sweep voltammetry.

**Results.** The sensitivity of the sensor could be enhanced by an increase in the electrochemical conductivity through the use of gold nanoparticles. A linear response was obtained in the range of  $3.8 \times 10^{-15}$  to  $3.8 \times 10^{-10}$  M with a limit of detection of  $3.8 \times 10^{-18}$  M. The applicability of the sensor was further verified on real drug samples.

**Conclusions.** A sensitive and selective sensor was developed for the detection of gemcitabine based on molecularly imprinted polymers, showing promising results for real samples analysis.

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## IMMUNOSENSOR BASED ON MAGNETIC NANOPARTICLES FOR SELECTIVE DETECTION OF ACETAMINOPHEN

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**Introduction.** Immunosensors are high sensitive biosensors that are based on the interaction between an antigen and its complementary antibody. In the electrochemical immunosensors, one of the immunoagents is immobilized on a solid carrier, capturing/binding the analyte to form an immunocomplex. As an ideal platform candidate, magnetic beads (MBs) allow for quick and efficient purification and concentration from crude samples, thereby eliminating the need for most of the pretreatment steps, as well as the matrix effect from the samples. Additionally, MBs can provide a low detection limit since they have large surface area to immobilize biomolecules and can allow a simple manipulation by reducing the complexity and time required for sensing application.

**Material and methods.** The first example consisted in a biosensor based on GCE modified with carbon nanotubes and the aim of the study was to develop an electrochemical immunosensor based on acetaminophen antibody as a molecular recognition element for the detection of acetaminophen. For this purpose, magnetic nanoparticles modified with Protein G were incubated with acetaminophen antibody in order to bind the biocomponent within the amidic bond. The unoccupied active sites were then blocked with Albumin from bovine serum (BSA) and the sandwich type assay was incubated with acetaminophen. Electrochemical impedance spectroscopy (EIS) measurements were carried out in the presence of the redox probe ferri/ferrocyanide which showed variations in charge transfer resistance after each incubation step, then proving the MBs surface modification. The optimized acetaminophen immunosensor was tested using EIS and differential pulse voltammetry (DPV).

**Conclusions.** An electrochemical immunosensor based on magnetic beads modified with protein G, antiacetaminophen antibody and bovine serum albumin was elaborated and optimized for the selective and sensitive detection of acetaminophen using EIS and DPV determination.

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## CHIRAL CALIX[6]ARENE DERIVATIVE AS CHIRAL SELECTOR FOR THE ENANTIOSEPARATION OF WARFARIN

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**Introduction.** Calixarenes represent a versatile class of compounds which offer good perspectives in host-guest type complex research. They act by forming a cavity inside their macrocycle and form non-covalent interactions with the guest molecules, from which hydrogen bonds are the most important. Water soluble calixarenes are preferred to be used as chiral selectors in capillary electrophoresis, due to the fact that they are easier to be added to the background electrolyte than to be fixed on a stationary phase.

Warfarin is the most used anticoagulant worldwide, being used in the prevention and treatment of venous thrombosis, post-myocardial infarction or heart failure. The enantiomers of warfarin show different anticoagulant activity, the (S)-(-)-warfarin being more active than the (R)-antipode.

**Material and methods.** For the present study, we synthesized a p-tert-butyl-calix[6]arene, derived in the endo position with an L-alanine group, in a three stage reaction. The peptidation agent used was 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (HATU). The products of reaction in every synthetic stage were characterized by ATR-FT-IR spectroscopy.

The obtained chiral water soluble calix[6]arene derivative was employed in the development of chiral separation of warfarin, as part of the running buffer.

**Results.** The chiral method was optimized considering the nature of the buffer, concentration, pH and the concentration of the chiral selector. Also, a dual selector system was taken in consideration.

**Conclusions.** The obtained calix[6]arene derivative showed good retention towards warfarin. However, the high UV absorbance of the chiral selector lead us to considering, in perspective, developing a separation method using chiral calix[6]arene based stationary phases.

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## IMPACT OF EXPERIMENTAL VARIABLES OVER ENANTIORECOGNITION IN THE DEVELOPMENT OF MIP-BASED CHIRAL ELECTROCHEMICAL SENSORS

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**Introduction.** Despite the massive advancements in molecularly imprinted polymers (MIPs) technology, MIP-based electrochemical sensors are very scarce and the vast majority of them deals with the analysis of chiral amino-acids or other small molecules. However, chiral molecules of pharmaceutical interest rarely resembles with the amino-acids on which the chiral capability is demonstrated in literature. Therefore, it was envisaged the study of functional monomer's nature and the position of stereogenic center in molecule, in the enantiodiscrimination of amino-acids and chiral pharmaceutical molecules.

**Materials and methods.** It was investigated several functional monomers with acidic character, as well as others with basic character, both electrically conductive as well as insulating. The MIP-films were deposited on the surface of a carbon paste electrode by the electropolymerization of functional monomers in the presence of a template by using cyclic voltammetry in 100 mM phosphate buffer solution.

**Results.** The efficiency of the chiral recognition of the obtained polymers was assessed by differential pulse voltammetry. After the preconcentration in a diluted solution of amino-acid, only the template enantiomer generated an oxidation peak.

**Conclusion.** The obtained results demonstrate the versatility with which MIP-modified sensors can be achieved for the chiral analysis of amino acids, with absolute enantioselective capacity, and also the different situation in the case of molecules in which the chiral center is inside the molecule.

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## IN VIVO/IN VITRO EVALUATION OF THE ANTIOXIDANT AND ANTI-INFLAMMATORY POTENTIAL OF SOME 2'-PHENIL-2,5'-BISTHIAZOLES

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**Introduction.** The continuing struggle to obtain the optimum NSAID characterized by excellent efficacy and a good safety profile has led to the concept of preferential inhibitor of COX-2. Also, current research suggests that the preferential COX-2 inhibition must be associated with other anti-inflammatory mechanisms such as direct antioxidant capacity or selective inhibition of iNOS. To that effect we evaluated a series of bisthiazoles derivatives in order to determine their direct in vitro antioxidant potential and their in vivo anti-inflammatory activity.

**Materials and methods.** All bisthiazoles evaluated were obtained by our research group, as described in our previous works. The in vitro direct antioxidant capacity was determined by using the DPPH radical scavenging method. The in vivo anti-inflammatory activity was assessed in an induced acute inflammation experimental model on rats. The parameters evaluated were: the acute phase bone marrow response, the phagocytic capacity, seric NO levels and the serum oxidative stress status.

**Results.** Most of the tested substances showed a direct antioxidant effect only at high concentrations. When considering the anti-inflammatory activity results revealed a great variation between compounds. Some of the tested compounds had a similar activity to that of the meloxicam standard used.

**Conclusions.** The active molecules improve in vivo serum oxidative stress and other tested parameters in a manner independent of the in vitro direct antioxidant activity. This suggests that the good anti-inflammatory activity showed is due to a specific pharmacological mechanism such as COX inhibition and /or selective iNOS inhibition.

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## ANTIOXIDANT ACTIVITY EVALUATION OF SOME CHROMENYL-THIOSEMICARBAZONES AND CHROMENYL-THIADIAZOLINES

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**Introduction.** It has been proven that Schiff bases and thiadiazolines present good antioxidant activities. On the other hand, several studies present the broad range of biological activities, including antioxidant, of compounds bearing chromenyl moieties.

**Material and methods.** 20 compounds - 10 chromenyl-thiosemicarbazones and 10 chromenyl-thiadiazolines - were investigated for their antioxidant capacities. Their synthesis and structures were previously reported. The free radical scavenging activities of these compounds were measured in terms of hydrogen donating or radical scavenging ability using the stable DPPH radical method.

1 mg/mL stock solutions in DMSO were prepared which were then diluted to various concentrations. To these solutions methanolic DPPH was added at different concentrations. After 30 min of incubation at 40°C in a thermostatic bath, the decrease in the absorbance was measured at 517 nm and the DPPH scavenging abilities (I%) were then calculated. Afterwards, a curve of % DPPH scavenging capacity versus concentration was plotted and IC<sub>50</sub> values were calculated. The results obtained were compared to that of butylated hydroxytoluene (BHT) as a positive control.

**Results.** All chromenyl-thiosemicarbazones presented excellent antioxidant activities, IC<sub>50</sub> values ranging between 7 and 11 µg/mL. Meanwhile, chromenyl-thiadiazoline derivatives showed no significant antioxidant potential.

**Conclusion.** The results obtained revealed that the cyclisation of chromenyl-thiosemicarbazone derivatives to corresponding thiadiazolines leads to the disappearance of the antioxidant effect.

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## SYNTHESIS AND ANTIMICROBIAL SCREENING OF SOME NEW HYBRID CHROMONYL-HETEROCYCLIC COMPOUNDS

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**Introduction.** Chromone and thiazolidinedione scaffolds are important pharmacophores found in many compounds with medicinal significance: tyrosine and protein kinase C inhibitors, antibacterial, antifungal, antiviral and anticancer agents. The presence of these two active fragments inside one molecule may lead to a synergistic activity, enhancing the effect of each scaffold or may lead to new biological properties. Based on these facts, we report here the synthesis and the antimicrobial screening of some new chromonyl-thiazolidinedione derivatives.

**Material and methods.** The compounds were obtained by the condensation of 2,4-thiazolidinedione with 3-formyl-chromones, followed by the reaction with several halogenated ketones, in order to obtain N-derivatives. The new molecules were isolated and their purity was verified by TLC.

**Results.** The combined use of <sup>1</sup>H NMR, <sup>13</sup>C NMR, mass spectral data and elemental analysis confirmed the structures of the new molecules. The antimicrobial screening was done by the agar diffusion method. The test was conducted on several Gram-positive (*Listeria monocytogenes*, *Staphylococcus aureus*, *Bacillus cereus*) and Gram-negative (*Escherichia coli*, *Salmonella typhi*) bacterial strains and also on one fungal strain of *Candida albicans*. Reference antibacterial and antifungal drugs were used for the evaluation of the compounds' potential, assessed as growth inhibition diameter.

**Conclusions.** The newly synthesized N-substituted 5-chromonyl-thiazolidinediones expressed good antimicrobial activity.

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## SYNTHESIS, CHARACTERIZATION AND EVALUATION OF ANTI-INFLAMMATORY ACTIVITY OF SOME NEW PYRIDYL-THIAZOLO[3,2-B][1,2,4]TRIAZOLE DERIVATIVES

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**Introduction.** Heterocyclic chemistry is rapidly evolving in synthesizing new molecules with different pharmacological properties. These bioactive molecules include polyheterocyclic azolic compounds such as thiazolo[3,2-b][1,2,4]triazole derivatives with antimicrobial and anti-inflammatory activities. Taking into consideration all this data, as well as the biological potential of the pyridine ring, our aim was the synthesis, characterization and evaluation of anti-inflammatory activity of some new pyridyl-thiazolo[3,2-b][1,2,4]triazole compounds.

**Material and methods.** Condensation of 3/4-pyridyl-mercapto-1,2,4-triazoles with different  $\alpha$ -halogenocarbonyl compounds afforded the corresponding thiazolo-triazoles with or without isolation of iminothioether intermediates. The anti-inflammatory activity was evaluated using the carrageenan-induced rat paw edema assay.

**Results.** Fourteen iminothioethers and fourteen corresponding thiazolo-triazoles containing 3/4-pyridine moiety were obtained. We highlighted the influence of the nature of reaction partners and the influence of reaction conditions (temperature, catalyst) on the synthesis of thiazolo-triazole compounds. The results of quantitative elementary analysis and the results of spectral analysis (IR, <sup>1</sup>H RMN, <sup>13</sup>C RMN, MS) confirmed the structure of all synthesized compounds. Three of the tested compounds showed significant anti-inflammatory activity, comparable with diclofenac.

**Conclusions.** New polyheterocyclic azolic compounds containing 3/4-pyridine moiety were synthesized. Three of the synthesized compounds presented significant anti-inflammatory activity.

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## SYNTHESIS OF L- $\alpha$ -AMINO ACIDS WITH THIAZOLE STRUCTURE BY ENZYMATIC DYNAMIC KINETIC RESOLUTION

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**Introduction.** As a continuation of our concerns regarding the development of enzymatic procedures for the preparation of optically active heterocyclic compounds with biological potential, we report the chemoenzymatic synthesis of L- $\alpha$ -amino acids bearing the thiazole core, starting from their racemic N-acetyl derivatives.

**Material and methods.** The cyclization of racemic N-acetyl amino acids afforded the corresponding oxazol-5(4H)-ones, which were used as substrates in the enzymatic enantioselective ring opening using alcohols as nucleophiles, in a dynamic kinetic resolution process (DKR). The chemical hydrolysis at the ester group followed by the enantioselective hydrolysis of the amide group, mediated by Acylase I, afforded the corresponding thiazolic L- $\alpha$ -amino acids.

**Results.** Lipase B from *Candida antarctica* (CaL-B) proved to be the most efficient biocatalyst for the DKR of thiazole-derived oxazol-5(4H)-ones, in the presence of a racemisation catalyst. Due to the L-specificity of Acylase I, the enantiomeric excess of the final products was increased to more than 99%. The optimized chemoenzymatic procedure was applied at preparative scale, affording the thiazole-derived L- $\alpha$ -amino acids of high enantiopurity, with 55-58% global yields.

**Conclusions.** A series of thiazole based L- $\alpha$ -amino acids of high enantiopurity were obtained by combining two chemoenzymatic steps: CaL-B catalyzed DKR of oxazol-5(4H)-ones followed by Acylase I catalyzed enantioselective hydrolysis of the amide group.

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## DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF NEW NEUROTENSIN ANALOGUES CONTAINING THE 2-ARYLTHIAZOLE MOIETY

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**Introduction.** In the continuation of our previous research concerning the synthesis of N-Boc-L-(2-arylthiazol-4-yl)alanines by (+)-hydroxypinanone induced diastereoselective alkylation, our aim was to obtain a group of oligopeptides containing thiazole-derived amino acids and to evaluate their biological activity. Being aware of the multiple pharmacological effects of the neurotransmitter neurotensin and its potential applications in the creation of new analgesics with improved functions and better metabolic stability, we opted for the design, synthesis and biological evaluation of new neurotensin analogues containing the 2-arylthiazole moiety.

**Material and methods.** A series of thiazole-derived L-amino acids were obtained by (+)-2-hydroxy-3-pinanone induced diastereoselective alkylation, starting from glycine tert-butyl ester, (+)-2-hydroxy-3-pinanone and 2-aryl-4-iodomethylthiazoles. The obtained N-Boc amino acids were integrated in the peptide sequence of neurotensin, by solution-phase peptide synthesis. We opted for a convergent strategy based on the condensation of two peptide segments which was possible without racemisation at a proline residue. The obtained oligopeptides were evaluated for their affinity to neurotensin receptors.

**Results.** Spectral analyses MS, <sup>1</sup>H NMR and <sup>13</sup>C NMR confirmed the structures of the obtained thiazole-derived L-amino acids and neurotensin analogues. Some of the tested oligopeptides presented a high affinity and selectivity for the neurotensin receptors involved in the antinociceptive effect.

**Conclusions.** The stereoselective synthesis of thiazole-derived L-amino acids followed by solution-phase peptide synthesis via convergent condensation allowed us to obtain new neurotensin peptide analogues with potential applications in the treatment of pain by non-opioid mechanism.

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## SYNTHESIS AND CHARACTERIZATION OF A SERIES OF NOVEL PHENOTHIAZINYL-ARYL-AMIDES AND THIOAMIDES

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**Introduction.** Phenothiazine is a pharmacophore unit with major applications emerged as neuroleptic drugs used in clinical therapy [1]. More recently an increased interest was directed at its antimicrobial, anti-inflammatory and antitumour properties [2,3]. In this work we describe the chemical synthesis and structural characterization of a series of new phenothiazinyl-amides and thioamides with potential biological activity.

**Material and methods.** A series of N-phenothiazinyl-aryl-amides was obtained by the condensation of 3-amino-10-methyl-10H-phenothiazine with aroyl-chlorides (benzoyl-, p-nitro- benzoyl-, p-bromo-benzoyl- and 1-naftoyl- respectively). New N-phenothiazinyl-aryl-thioamides were further obtained by the treatment of the corresponding amides with the Lawesson reagent.

**Results.** The reaction conditions for the synthesis of new N-phenothiazinyl-aryl-amides and their corresponding thioamides were optimized using both conventional and microwaves assisted procedures. The structural assignment was based on modern spectroscopic techniques (high resolution <sup>1</sup>H-, <sup>13</sup>C-NMR and mass spectrometry).

**Conclusion.** We developed a reliable synthetic procedure for obtaining N-phenothiazinyl-aryl-amides and thioamides. These new compounds may be further investigated as potential biologically active molecules as well as precursors in the synthesis of new functionalized heterocyclic compounds.

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## PAIN MANAGEMENT IN THE ELDERLY PATIENT: COMMUNITY AND NURSING HOME

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**Introduction.** Persistent pain is a frequent and difficult to control geriatric syndrome. The objective of this study was to characterize the analgesic therapies provided to two groups of elderly patients, cared for in two different environments: community and nursing home.

**Material and methods.** The analysis included the medications recommended for various pain indications, during one-month interval. We analyzed the reimbursed prescriptions delivered from two community pharmacies and the information available on the medication charts of the nursing home residents. For data interpretation, we used the nationally adopted guidelines referring to pain management.

**Results.** 345 prescriptions delivered to the elderly (34.36% of the total of 1004) and 91 medication charts were included in the analysis. The community- dwelling elderly had a mean age of  $74.8 \pm 6.24$  years and received a daily mean of  $3.22 \pm 1.80$  medications. In the institutionalized group, the mean age was  $80.81 \pm 6.84$  years and they received on average  $7.93 \pm 2.48$  medications/day. The main pain-associated indication was osteoarthritis with 34 (56.66%) diagnoses recorded on the prescriptions and 31 (88.57%) nursing home cases. Nonsteroidal anti-inflammatory drugs (NSAIDs) were the most frequent analgesics for both populations: 34 prescriptions (9.85% of total) and 31 nursing-home residents (34.06%). On 24 prescriptions (71% of total), the NSAIDs were recommended for a maximum of 20 days/month, while 21 (23%) of the institutionalized elderly had an untreated pain-associated indication. Opioids and adjuvant analgesics for neuropathic pain were rarely used (less than 5% of both data sets).

**Conclusion.** Both populations presented a high use of NSAIDs, which was associated with potential serious safety concerns. Underuse of acetaminophen and potential underdosing of analgesics were also common. Pain management in this population requires a cautious and individualized approach.

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## THE ASSESSMENT OF POTENTIAL DRUG INTERACTIONS IN COMMUNITY PHARMACY PATIENTS RECEIVING CARDIOVASCULAR DRUGS

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**Introduction.** Drug interactions may be associated with important clinical consequences as they can diminish or enhance a drug effect in patients receiving multi-drug therapy. Cardiovascular drug interactions are an important factor affecting the development of adverse drug reactions. The objective of the study was to evaluate the nature, type and prevalence of potential drug interactions that involve cardiovascular drugs.

**Material and methods.** This observational study included 232 patients and was undertaken at a community pharmacy in Cluj-Napoca during a 3-month period. Eligible patients were considered adults that received 2 or more drugs and at least one was a cardiovascular drug. Patient demographics were collected in addition to information about prescription medication and self-medication use currently and in the last month. The data were collected during an interview and contained information about the use of drugs, herbal products and nutritional supplements. MicroMedex®2.0 software was used to screen potential drug interactions and to classify them according to severity, onset and drug interaction mechanism.

**Results.** Of a total of 232 enrolled patients, at least one interacting drug combination involving cardiovascular drugs was identified in 218 (93.96%) patients. A total of 974 drug interactions were identified and the majority of interactions were moderate severity (79.16%), delayed onset (47.74%) and pharmacodynamic in nature (69.20%). There were 542 (55.65%) drug interactions that included only prescription medication and 432 (44.35%) consisted of interactions that involved self-medication. Cardiovascular drug classes most commonly involved in potential drug interactions were beta-blockers, angiotensin-converting enzyme inhibitors and thiazide diuretics.

**Conclusion.** Pharmacists have the responsibility to promote rational use of drugs and to contribute to the detection and prevention of clinically significant drug interactions.

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**EVALUATION OF ANTIBIOTIC USE IN A THORACIC SURGERY DEPARTMENT****LAVINIA ALEXANDRA DRĂGAN<sup>1</sup>, DIANA ELENA DUMITRAȘ<sup>2</sup>, ADINA POPA<sup>1</sup>****<sup>1</sup>Clinical Pharmacy Department, Faculty of Pharmacy, University of Medicine and Pharmacy "Iuliu Hațieganu", Cluj-Napoca, Romania****<sup>2</sup>Economic Sciences Department, University of Agricultural Science and Veterinary Medicine, Cluj-Napoca, Romania**

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**Introduction.** To evaluate the appropriateness of antibiotics use in relation to diagnosis and the impact of pharmacist recommendations in a thoracic surgery department in an academic hospital in Cluj-Napoca.

**Material and methods.** Between April and June 2013, antibiotic prescriptions of hospitalized patients were prospectively evaluated. Therapeutic guidelines and literature were used for the evaluation of antibiotics treatment. The appropriateness antibiotics use was verified, according to 3 main criteria: appropriate indication (type of treatment, diagnosis), dose and duration of treatment. Descriptive statistics and multiple logistic regression analysis were performed.

**Results.** 220 prescriptions were evaluated. The most frequently prescribed antibiotics were ceftriaxone (50.81%), ciprofloxacin (18.82%) and clindamycin (17.74%). Diagnoses for which antibiotics were prescribed include: pleural empyema, haemopneumothorax, pneumothorax, pneumoniae, pleuresis, lung abscess, lung tumor. Antibiotic use was inappropriate in 82.73% of prescriptions. Inadequate antibiotic use was 88.82% in surgical prophylaxis and 69.12% in curative treatment of infections. Antibiotic prescriptions for curative treatment were found to be more appropriate than those for prophylaxis (OR=0.28 p<0.05 CI=0.13-0.57) but the inappropriate use was not influenced by age and sex. Inappropriate antibiotic use was significantly higher for elderly patients in the prophylactic treatment (OR=1.03 p<0.05 CI=1.00-1.07). Rational use of antibiotics was higher in the curative treatment of lung tumors surgery than in prophylaxis (OR=0.02 p<0.05 CI=0.001-0.547). The specialists accepted the recommendations of the clinical pharmacist in 57.27% cases.

**Conclusions.** The results of study suggest the need and the role of the clinical pharmacist in the hospital. The implementation of antibiotic guidelines in hospitals and the involvement of the clinical pharmacist may ensure rational antibiotic therapy.

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## OFF-LABEL USE OF ANTIBIOTICS IN NEONATES

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**Introduction.** A number of studies have shown that many of the drugs prescribed to neonates and infants are prescribed off-label. The most often prescribed off-label drugs are antibiotics, especially meropenem. The Summary of Product Characteristics (SPC) approves its use to children above 2 months of age. The objective of this study was to evaluate the off-label use of meropenem in a neonatology unit in a tertiary university hospital in Romania.

**Material and methods.** A retrospective evaluation of the use of antibiotics issued based on antibiotic formularies in a neonatology unit was made. International guidelines and SPC were used for the evaluation.

**Results.** A total of 47 patients were involved in this study. For these patients a total of 88 antibiotic prescriptions formularies were issued. The mean age of the patients was 22.01 days with a minimum of one day and a maximum of 126 days. The mean weight of the patients was 2.53 kg. Of the total prescriptions 55 (62.5%) were for meropenem. 33 (70.2%) of all patients were treated with meropenem, for 8 of this patients vancomycin was used in association. Of the 55 prescriptions 50 were prescribed off-label to patients with less than 2 months of age. Of the 33 patients treated with meropenem in 9 cases (27.27%) the dose was too high according to guidelines.

**Conclusion.** Most of the neonatology patients are treated off-label with meropenem. More studies are needed to optimize the use of antibiotics in neonates to ensure an optimal treatment in this age group.

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## COMPARATIVE PHYTOCHEMICAL CHARACTERIZATION, ANTIOXIDANT AND ANTIBACTERIAL PROPERTIES OF MENTHA VIRIDIS AND MENTHA LONGIFOLIA

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**Introduction.** This study was designed to characterize the phenolic composition of *Mentha viridis* and *Mentha longifolia* from the Apuseni Mountains and to examine in vitro antioxidant and antimicrobial activities, for a better characterization and exploitation of these medicinal plants.

**Material and methods.** The hydroxybenzoic acids content was spectrophotometrically determined. The identification and quantification of polyphenolic compounds were made by HPLC/MS. The antioxidant activity was evaluated using the DPPH bleaching method, TEAC assay, hemoglobin ascorbate peroxidase activity inhibition (HAPX) assay, and an EPR method. The antimicrobial tests were performed using the disk diffusion assay.

**Results.** The extract of *M. viridis* contains a larger amount of polyphenols compounds (total polyphenols, flavonoids and caffeic acid derivatives) than the extract of *M. longifolia*. In the *M. viridis* extract, the phenolic profile showed the presence of some phenolic acids, while in the extract of *M. longifolia*, the flavonoids predominated. Using the DPPH assay, the two samples showed a high radical scavenging activity with similar IC<sub>50</sub> (DPPH) values (around 30 µg/mL). According to TEAC, HAPX and RES results, the *M. longifolia* extract was significantly higher in antioxidant capacity than *M. viridis*. The studied extracts of *Mentha* were active against at least one or two microorganisms.

**Conclusions.** The comparative study showed significant differences, both qualitative and especially quantitative, between the two species of *Mentha*. This study suggests that the leaves of *M. viridis* and *M. longifolia* may be considered a potential source of polyphenols with bioactive properties and it may be concluded that these species could be pharmaceutically exploited for antioxidant properties.

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## PHYTOCHEMICAL, ANTIOXIDANT AND HEPATOPROTECTIVE EVALUATION OF ROSMARINUS OFFICINALIS L. HYDROALCOHOLIC EXTRACT

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**Introduction.** The use of fresh vegetal products is the new trend in phytotherapy. The interest in obtaining and characterizing bioactive extracts from plant is increasing. This paper presents a phytochemical and pharmacological study on *Rosmarinus officinalis* L. (rosemary) extract, obtained by cold extraction from fresh shoots, according to Eur. Ph. This plant has been widely studied due to the potent antioxidant activities associated to some of its components; among them phenolic diterpenes, rosmarinic acid have attracted more attention, although other compounds (essential oil, polyphenols) also present in rosemary.

**Material and methods.** The phytochemical analysis of this hydroalcoholic extract was performed using chromatographic (TLC, GC-MS, HPLC-DAD, HPLC-MS) and spectral methods. The antioxidant potential was evaluated by DPPH, FRAP, EPR and SNPAC (Silver Nanoparticules Antioxidant Capacity) methods. The hepatic protective activity of extract (300 mg/kg body weight) was performed on CCl<sub>4</sub> hepatitis rat model by assessing the levels of plasma total protein, albumin, AST, ALT and GGT. Additionally routine hematology was performed.

**Results.** The initial screening indicates the borneol, bornyl acetate, rosmarinic acid and luteoline-7-O-glucoside. The total polyphenolic content was expressed in rosmarinic acid and the flavonoid content was expressed in luteoline. By GC-MS analysis was identified 33 terpenes, mainly 1,8-cineole, d-limonene and  $\alpha$ -pinene. The rosmarinic acid was quantified by HPLC analysis. An increased antioxidant effect was evidenced. The hepatotoxicity was reflected by the elevated levels of AST, ALT, GGT ( $p < 0.01$ ) and decreasing of albumin and A/G ratio. The extract administration prevented the rise of serum AST and ALT ( $p < 0.01$ ), increased A/G ratio ( $p < 0.05$ ) and improved the hematological parameters.

**Conclusions.** The phytocomplex of rosemary extract, rich in terpenes and polyphenols, provides a significant antioxidant and hepatoprotective activity.

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## PHARMACOGNOSTICAL RESEARCH ON HERACLEUM SPHONDYLIIUM L. (APIACEAE) FROM ROMANIA

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**Introduction.** Heracleum sphondylium L. (Apiaceae), commonly known as popular hogweed, is used in folk medicine for its tonic, aphrodisiac, vasodilator properties, in the treatment of digestive disorders or for local applications in rheumatic diseases. Because the scientific data on this species are few, the aim of this study was to analyze this medicinal plant in order to obtain some pharmacognostical information.

**Material and methods.** In order to obtain a pharmacognostic characterization of Heracleum sphondylium, we proposed qualitative and quantitative analysis of polyphenolic compounds, as well as antioxidant and antimicrobial potential evaluation. Alcoholic extracts of roots, stems, leaves, flowers and fruits of hogweed harvested from the spontaneous flora of Romania were used as samples. For identification and quantification of polyphenolic compounds chromatographic (TLC, HPLC-MS) and spectrophotometric methods were employed. Antioxidant activity was determined by using the stable radical DPPH and the antimicrobial activity was evaluated by means of diffusimetric method.

**Results.** Certain phenolic acids (chlorogenic, p-coumaric, ferulic acid), flavonoid glycosides (rutin, isoquercitrin, quercitrin), flavonoid aglycons (quercetol, luteolin) have been identified, in various levels in different plant organs. Rutin is the major flavonoid in all extracts, in large quantities in flowers methanolic extracts. The largest amounts of total polyphenols were found in leaves and flowers extracts, which are the most active in terms of antioxidant properties and antimicrobial activity on *Staphylococcus aureus*.

**Conclusions.** The obtained results allow completing the scientific data on native species Heracleum sphondylium, in order to use it for a more accurate and proper treatment.

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## ROMANIAN CODE OF PHARMACEUTICAL ETHICS – A NEW CONCEPTION

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**Introduction.** Romanian researchers and practitioners in the pharmaceutical field are increasingly concerned with ethical issues in the pharmaceutical activity. The aim of this paper is to present a new conception on the code of pharmaceutical ethics. Our objectives were to present the reflection process and the most relevant new provisions for this code.

**Material and methods.** Official European documents and national codes of ethics were investigated using the interpretation and the comparative methods.

**Results.** The current code of ethics refers especially to community pharmacists. However, the practice as a pharmacist also includes working in research, industry, wholesale, hospital pharmacy, education, laboratory or administration. In any of these fields, the pharmacist can have an impact on safe and effective delivery of professional services. Therefore, our project includes general principles and specific principles for each professional field. The general principles express essential values and standards for the profession and set the foundation of the code: protecting life and patients' rights, professional independence and integrity, commitment to the development of the profession, collaboration with other health professionals. New specific principles refer to the obligation to comply with the highest standards of quality and ethics in research, teaching, communicating and publishing, pharmacovigilance, visits by medical sales representative, brokering medicinal products, pharmacy advertising, laboratory work, supervision and inspection. The project of the new pharmaceutical code of ethics was submitted to the Romanian College of Pharmacists, the financier of the research.

**Conclusions.** The professional ethics of Romanian pharmacists can be optimized through the development of the code of conduct. The mission of the College of Pharmacists is to ensure that a new code of ethics, reflecting the evolution of the profession, is adopted, known and respected in practice.

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## DECISION ANALYSIS OF THE USE OF ANTIBIOTICS IN ROMANIA

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**Introduction.** While in most countries of Europe, bacterial resistance to antibiotics has decreased, Romania is facing a real increase of the cases of antibiotic resistance. The most important reason of emergence of antibiotics resistance is their irrational use. The aim and objectives of the research have been analyzing the profile of the antibiotics consumers in Romania, causes and risks of the irrational use of antibiotics, the way of their purchasing from community pharmacies in the country, and the proposal of correct and efficient methods of informing the population on the risks of an irrational antibiotics consumption.

**Material and methods.** An instrumental marketing research was conducted, based on a survey using a questionnaire distributed to 976 people, the selection being achieved in all counties in Romania.

**Results.** The results have highlighted the main causes of irrational use of antibiotics: their administration in conditions that don't require such a treatment, population's inability to clearly and accurately correlate the antibiotic with the conditions to be treated, insufficient counseling provided by physicians and pharmacists regarding posology and risks of antibiotics consumption, and getting antibiotics from community pharmacies without presenting a medical prescription. In order to educate the population, an original, interactive and suggestive booklet has been accomplished, to correctly inform patients about antibiotics and treated diseases, so that they understand the risk involved in the irrational use of antibiotics.

**Conclusions.** The study results have indicated a series of problems related to antibiotic use in Romania. It is very important to be aware of the risks associated with an irrational consumption of antibiotics, which is the main factor in the emergence of bacterial resistance. One proposed solution has aimed at educating the public through elaboration and dissemination of the quality informative materials to patients.

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## COMPARATIVE STUDY BETWEEN THE SALES OF H2 ANTAGONISTS AND PROTON PUMP INHIBITORS

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**Introduction.** Gastric ulcer is a frequent affection that occurs on a national level. Because of that reason, at present there is, on the Romanian pharmaceutical market, a large number of antiulcer medications. The purpose and objectives of this research were the analysis of the products' sales containing active substances from the following classes: Proton Pump Inhibitors (PPIs) and H2 Antagonists, their comparison and the highlighting of the best selling medications from the two pharmacological classes.

**Material and methods.** There have been analyzed the quantitative sales of the products containing active substances on a two years-long period of time in the interval 1.10.2012-1.10.2014. The necessary data for the study have been collected from Romanian community pharmacies, using pharmaceutical management programs, while the used methods were: the retrospective analysis, the sampling method, the comparison method and the descriptive method.

**Results.** The obtained results showed that from the entire quantity of medications released in the analyzed pharmacies (13955 units), PPIs represents 81.64%, while the H2 Antagonists represents only 18.35%. The best selling active substance from the PPIs class, was Omeprazolium (6074 units, 53.31%) and the best selling active substance from H2 Antagonists was Ranitidinum (2005 units, 78.25%). The results of the study highlighted the releasing from pharmacies of a considerable quantity from the two pharmacological classes, explained by the fact that these medications are affordable for patients because in pharmacies there are available cheaper generic products, made in Romania.

**Conclusions.** The results of the research indicated that the active substances from the Proton Pump Inhibitors class are sales leaders and the medicines that contain Omeprazolium are released in the biggest quantities from the analyzed community pharmacies.

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## THE INFLUENCE OF DULOXETINE ON THE ATOMOXETINE PHARMACOKINETICS

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**Objective.** To evaluate the possible pharmacokinetic interaction between atomoxetine, a compound metabolized by CYP2D6 enzyme and an inhibitor of this enzyme, duloxetine, after a co-administration of these two substances.

**Material and methods.** An open-label, single-center, non-randomized clinical trial which included 23 healthy volunteers, was assessed. A single dose of atomoxetine 25 mg was administrated alone or in combination with duloxetine 30 mg to 23 subjects, in a two-treated study design: reference period (I) and test period (II). Between the two periods, the volunteers received an oral daily dose of 30 mg duloxetine, for 6 days. Atomoxetine and 4-hydroxyatomoxetine (active metabolite) plasma concentrations were determined during 48-hour period, following drug administration. The pharmacokinetic parameters of both compounds were determined using a non-compartmental method, and the results from each period were compared to evaluate a statistically significant difference.

**Results.** During the two treatment periods, the maximum plasma concentrations (C<sub>max</sub>) were 224.81±94.29 ng/ml (I) vs. 233.69±67.29 ng/ml (II) for unchanged atomoxetine; and 660.95±295.83 ng/ml (I) vs. 596.50±271.27 ng/ml (II) for 4-hydroxyatomoxetine. The total areas under the curve from time zero to infinity (AUC<sub>∞</sub>) increased from 1544.14±1679.42 hr\*ng/ml (I) to 2034.95±2200.67 hr\*ng/ml (II) for atomoxetine and decreased from 4854.06±906.95 (I) to 4889.93±980.63 (II) for the active metabolite.

**Conclusions.** The co-administration of atomoxetine and duloxetine significantly modifies atomoxetine pharmacokinetics.

**Acknowledgments.** This work was supported by CNCS Romania – project PN-II-ID PCE-2011-3-0731. PhD student Todor Ioana acknowledges financial support from a POSDRU grant, no. 159/1.5/S/136893 grant with title: "Parteneriat strategic pentru creșterea calității cercetării științifice din universitățile medicale prin acordarea de burse doctorale și postdoctorale – DocMed.Net\_2.0".

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## FORMULATION OPTIMIZATION OF QUERCETIN-LOADED LIPOSOMES THROUGH A D-OPTIMAL EXPERIMENTAL DESIGN

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**Introduction.** This study aimed at investigating the influence of formulation factors on the physico-chemical properties of quercetin-loaded liposomes and optimizing the preparation conditions.

**Material and methods.** An experimental design with three factors and three levels was used. The variables were Dipalmitoylphosphatidylcholine (DPPC) concentration, DPPC-Cholesterol (CHOL) molar ratio and quercetin (QU) concentration. The responses were the mean diameter, polydispersity index (PdI) and drug encapsulation efficiency. All samples were prepared according to the experimental design matrix consisting of 17 experiments. The QU-liposomes were obtained by a film hydration method. The size and PdI were determined using Dynamic Light Scattering. The entrapment efficiency was calculated based on data obtained from HPLC-UV quantitative analysis.

**Results.** Results showed that DPPC concentration and DPPC: CHOL ratio had a strong influence on liposome size and PdI. Higher DPPC concentrations led to larger particles and PdI values, but further increase of DPPC concentration produced a reduction in size and lower PdI. Increasing the lipid ratio caused a decrease in size, but a somewhat higher PdI. QU concentration only slightly influenced particle size and PdI. Higher QU concentrations led to smaller liposomes. The degree of QU loading depended on the factors assessed. Increasing DPPC concentration and lipid ratio significantly enhanced QU entrapment. However, higher QU concentrations had a negative effect on drug retention. Based on this, an optimized formulation was determined, prepared and analyzed.

**Conclusions.** The overall results showed that DPPC concentration and lipid ratio were the main factors influencing particle size, while entrapment efficiency was predominantly affected by QU concentration.

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## NIRS AND CHEMOMETRIC ANALYSIS OF GALLIC ACID IN DRY ROSE PETAL EXTRACTS AND ORAL TABLETS

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**Introduction.** NIRS is a fast and non-destructive technique requiring no sample preparation and in association with chemometrics it may lead to precise results. The aim of this study was to demonstrate that the active content of dry rose petals extract and the oral tablets obtained from it can be quantified through Near Infrared Spectrophotometry (NIRS) and chemometrics.

**Material and methods.** Formulations with four different concentrations were prepared through pulverisation of alcoholic extracts on a solid isomalt support, then the mixtures were compressed into tablets. The content in gallic acid was determined in all four samples using the method described in the European Pharmacopeia and the results were compared with those obtained by pre-processing the NIR spectral data.

**Results.** For oral tablets, the best results for the NIR data pre-processing were obtained by analyzing it at three selected spectral ranges: 10000-7400 cm<sup>-1</sup>, 7100-5600 cm<sup>-1</sup> and 5275-4000 cm<sup>-1</sup>, using a number of six partial least-squares (PLS). Using only the standard normal variate (SNV) as a method of pre-processing we obtained a coefficient of correlation (R<sup>2</sup>) of 0.9912 and a recovery of 100.09%.

The best results regarding the extract were obtained by pre-processing the data at the full spectral range of 10000-4000 cm<sup>-1</sup>, using five PLS. The combined methods of first derivate and standard normal variate (FD+SNV) proved to deliver the best results, R<sup>2</sup> of 0.9914 and a recovery of 100.19%.

**Conclusions.** These results prove that dry rose petal extracts and oral tablets can be analyzed and characterized using NIRS in association with chemometrics.

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## PHARMACOKINETICS AND BIOAVAILABILITY OF CELECOXIB FROM IMMEDIATE RELEASE SOLID DOSAGE FORMULATIONS

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**Introduction.** The objective of this study was to evaluate the pharmacokinetics of Celecoxib and to assess the average bioequivalence of two immediate release formulations of 200 mg celecoxib capsules, in 48 healthy adult volunteers.

**Material and methods.** The relative bioavailability of the test (newly developed formulation, 200 mg) product with respect to the reference product already marketed was determined in a single dose, randomized, crossover study. The noncompartmental analysis was used for calculation of main pharmacokinetic parameters of celecoxib.

**Results.** The mean values for C<sub>max</sub> were 516.0(±242.8) ng/mL for test and 559.9(±248.3) ng/mL for reference product, while T<sub>max</sub> values were 2.7(±2.5) hours and 2.3(±1.1) hours, respectively. The mean values for the AUC<sub>0-t</sub> were 4764.8(±1540.0) ng/mL.hr for test and 4993.3(±1709.1) ng/mL.hr for reference product, while AUC<sub>0-∞</sub> values were 4922.8(±1563.2) ng/mL.hr for test and 5160.0(±1748.8) ng/mL.hr for reference product. The 90% confidence intervals for test/reference mean ratios of the plasma pharmacokinetic variables C<sub>max</sub>, AUC<sub>0-t</sub> and AUC<sub>0-∞</sub> for celecoxib lie within the conventional bioequivalence range of 80-125% (Schuirmann test). The difference between T<sub>max</sub> of the test and reference products was statistically non-significant (The Wilcoxon's Signed Rank Test) for Celecoxib.

**Conclusions.** The newly developed product is therefore bioequivalent to the reference product with respect to the rate and extent of celecoxib pharmacokinetics.

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## THE EFFECTS OF BUPROPION ON THE PHARMACOKINETICS AND PHARMACODYNAMICS OF NEBIVOLOL AND ITS ACTIVE METABOLITE

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**Objectives.** To evaluate the pharmacokinetic interaction between nebivolol and its active metabolite, and bupropion in healthy volunteers.

**Material and methods.** 18 healthy subjects were enrolled in an open clinical trial, non-randomized, consisting of two periods. During the first period (Reference) the volunteers received 5 mg nebivolol single dose, and during the 2nd period (Test) 5 mg nebivolol and 300 mg bupropion, after a 6 days pre-treatment with bupropion. The non-compartmental analysis was used to determine the pharmacokinetic parameters of nebivolol and hydroxi-nebivolol. Pharmacodynamic parameters (systolic and diastolic blood pressure, heart rate) were assessed after each administration of nebivolol. The data obtained were compared to determine the existence of statistically significant differences.

**Results.** Bupropion increased the exposure of unchanged nebivolol and its active metabolite. The AUC<sub>0-t</sub>, AUC<sub>0-∞</sub> and C<sub>max</sub> values for nebivolol were significantly different before and after bupropion multiple-dose treatment (AUC<sub>0-t</sub>: 10.38±10.53 vs 72.49±46.20 ng\*h/mL; AUC<sub>0-∞</sub>: 12.10±11.02 vs 87.29±57.49 ng\*h/mL; C<sub>max</sub>: 1.67±0.69 vs 3.80±1.70 ng/ml). A similar increase regarding these pharmacokinetic parameters was recorded for its metabolite when the two treatment periods were compared. Analysis of variance (ANOVA) showed no statistically significant difference between the pharmacodynamic parameters of nebivolol monitored during the two periods.

**Conclusions.** Bupropion significantly influences the pharmacokinetics of nebivolol and hydroxy-nebivolol in healthy volunteers but it did not have a significant effect on nebivolol pharmacodynamics.

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## THE PHARMACOKINETIC STUDY OF ZOPICLONE AFTER SINGLE-DOSE ADMINISTRATION IN RATS

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**Introduction.** A pharmacokinetic study of zopiclone was carried out, as a starting point for the evaluation of its pharmacokinetic drug-drug interactions. The aim of the study was to assess the pharmacokinetic parameters of zopiclone after a single dose administered to rats and to evaluate its bioavailability by two different routes of administration: intraperitoneal and subcutaneous.

**Material and methods.** The study included 10 white male Wistar rats, divided in two groups. Each rat was cannulated by surgery before being connected at BASi Culex® ABC. A single dose of 1070 µg/kg body-weight zopiclone was administered either by intraperitoneal or subcutaneous route. The non-compartmental analysis was used to determine the pharmacokinetic parameters of zopiclone.

**Results.** The non-compartmental analysis revealed a plasma maximal concentration of 528 ng/mL for the intraperitoneal route and 5 times lower for the subcutaneous route (110 ng/mL). The time to reach plasma concentration varied from 15 minutes (the intraperitoneal route) to 1 hour for the subcutaneous route. The elimination rate constant had values closed to 0.31 h<sup>-1</sup> and the half-life of zopiclone was around 2 hours. The relative bioavailability of zopiclone after a subcutaneous dose was 38% compared to intraperitoneal route. Analysis of variance (ANOVA) was used to compare the pharmacokinetic parameters obtained after intraperitoneal and subcutaneous routes. The results showed statistically significant differences for the plasma maximal concentration, the time to reach plasma maximal concentration, the area under the curve, the apparent clearance and for the apparent distribution volume, respectively.

**Conclusions.** The pharmacokinetics of zopiclone after single dose administration in rats, by either intraperitoneal or subcutaneous route was assessed. The findings from this pilot study will be further considered in the study of pharmacokinetic drug-drug interactions of zopiclone.

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## DEVELOPMENT AND CHARACTERIZATION OF ENOXAPARIN SODIUM POLYMERIC MICROPARTICLES FOR ORAL ADMINISTRATION AND COLONIC ABSORPTION

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**Introduction.** The purpose of this research was to develop a microparticulate polymeric system for the oral delivery and colonic absorption of enoxaparin sodium, in an attempt to develop a colonic targeted dosage form allowing maximum 10% drug release in the gastric environment and providing the release of enoxaparin directly in the inflamed tissue.

**Material and methods.** Microparticles were prepared by using water/oil/water double emulsion technique followed by solvent evaporation. In order to increase the entrapment efficiency and to retard enoxaparin release, several parameters, as alginate concentration in the inner phase, polymer concentration (Eudragit® FS or Eudragit® RS) in the organic phase or the ratios between the two polymers, were improved. The microparticles were characterized in terms of morphology, size, encapsulation efficiency and the controlled release was assessed by in vitro release studies over a period of 24 hours.

**Results.** The results showed that increasing sodium alginate percentage determined an increase in particle's size, reduced the encapsulation efficiency of enoxaparin and accelerated enoxaparin release. Regarding the influence of the two polymers, reducing polymer concentration in the organic phase led to a smaller size of microparticles, to a lower entrapment efficiency and to an important retardation of enoxaparin release, so that the formulation prepared with Eudragit® FS allowed a maximum release of 3% in gastric simulated environment and achieved our objective of delaying the release. In what concerns the combined use of the polymers, increasing the ratio between Eudragit® FS and Eudragit® RS led to reductions in: size (244 to 108 μm), entrapment efficiency (50 to 38%) and enoxaparin release (77 to 14%).

**Conclusions.** The developed microparticles were satisfactory in terms of size, encapsulation efficiency and one formulation based on Eudragit® FS exhibited controlled release, promising for the oral delivery of heparin to the colon.

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## THE INFLUENCE OF DISSOLUTION CONDITIONS ON THE RELEASE OF KETOPROFEN FROM EXTENDED RELEASE TABLETS

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**Introduction.** The objective of this research was to study the influence of dissolution conditions (type of device, stirring rate, and dissolution medium) upon the release of ketoprofen from hydrophilic matrix extended release tablets.

**Material and methods.** The dissolution profile of ketoprofen from Profenid LP 200 mg was compared with an optimized formulation using the similarity factor ( $f_2$ ). The similarity of the dissolution profiles of the two products was evaluated in two different devices (palette/basket), using different stirring rate (50/100 rpm) and different pH of the dissolution medium (5.4, 6.8, 7.4).

**Results.** In accordance with the obtained results at pH 7.4, neither the stirring rate nor the device type influenced the release of ketoprofen. At pH 6.8 at 50 rpm the dissolution profiles were similar regardless of the device or the formulation used, but a stirring rate of 100 rpm led to an increase of the percentage of released ketoprofen after a 12 hour period in the case of palettes device. At pH 5.4 the dissolution profiles showed differences regarding the type of device, the stirring rate and the formulation used. A pH of 7.4 smoothed the differences between the formulations and the hydrodynamic conditions, ensuring the similarity of the dissolution profiles. A pH of 6.8 led to a decrease of the percentage of the released ketoprofen compared to pH 7.4 and highlighted the differences between the hydrodynamic conditions. At pH 5.4 the differences between the dissolution profiles were the most prominent.

**Conclusions.** This type of dissolution study makes possible to highlight the differences between extended release formulations.

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## PHENOTYPIC DIFFERENCES IN NEBIVOLOL METABOLISM AND BIOAVAILABILITY AFTER ADMINISTRATION OF A SINGLE DOSE IN HEALTHY VOLUNTEERS

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**Introduction.** Nebivolol (NEB), a third-generation  $\beta$ -blocker, is subject to extensive first-pass metabolism and produces active  $\beta$ -blocking hydroxylated metabolites, like 4-OH-nebivolol (HNEB). It is primarily a substrate of CYP2D6, a metabolic pathway that is under polymorphic genetic regulation. The objective of this study was to evaluate the interphenotype bioavailability and metabolism of nebivolol.

**Material and methods.** Forty-three healthy volunteers were included in this open-label, non-randomized clinical trial and each volunteer received a single dose of 5 mg nebivolol. Non-compartmental pharmacokinetic analysis was performed to determine the pharmacokinetic parameters of nebivolol and its metabolite. The phenotypic distribution was assessed based on the AUC metabolic ratio of NEB/HNEB and statistical analysis.

**Results.** The AUC metabolic ratio of NEB/HNEB was not characterized by a normal distribution. The unique distribution underlined the existence of two groups and the 43 healthy volunteers were classified as follows: poor metabolizers (PMs)=3, extensive metabolizers (EMs)=40. The sum of NEB and HNEB concentrations were different between the two groups. The drug exposure to nebivolol was greater for PMs in comparison to EMs.

**Conclusions.** The study highlighted the existence of interphenotype differences regarding nebivolol metabolism. Furthermore, the bioavailability was different between the phenotype groups, suggesting the polymorphic metabolism in this case may be of clinical significance.

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## THE FORMULATION OF FREEZE DRIED ORODISPERSIBLE TABLETS CONTAINING A NATURAL POLYMER

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**Introduction.** The aim of this study was the formulation and in vitro characterization of freeze dried orodispersible tablets with meloxicam, using *Trigonella foenum graecum* seed mucilage (TSM) as a binder.

**Material and methods.** Suspensions of meloxicam in 0.5, 0.75, 1, 1.25, 1.5% TSM dispersions containing 5% mannitol were prepared. Differential scanning calorimetry was used to determine the glass transition temperature (T<sub>g</sub>) and crystallisation event of the 1% TSM formulation in its frozen state, before freeze drying. 0,5 ml of each stock suspension were poured in tablet moulds, annealed and then freeze dried at -20°C, for 40 h. The tablet characterization consisted of uniformity of weight, disintegration time, mechanical properties, wetting time, water absorption ratio and pore size measurement.

**Results.** The suspension's glass transition temperature was -27°C. Annealing at -8°C was required to avoid matrix collapse and to increase freeze drying temperature. The disintegration times ranged between 4s for 0.5% TSM tablets and 46.5s for 1.5% TSM tablets. The hardness increased with the TSM rate, from 6.5 to 24.13N. The wetting times were between 1s and 201.66s, correlated with water absorption ratios of 158.32% for 0.5% TSM tablets, to 369.78% for 1.5% TSM tablets. The structure with the highest number of pores corresponds to 1% TSM content and the largest pores were found in 0.5% TSM tablets, with a medium surface of 3283.41 μm<sup>2</sup>.

**Conclusions.** The fenugreek seed mucilage can be successfully used as a binder in highly porous fast disintegrating oral dosage forms.

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## DEVELOPMENT OF HIGH-THROUGHPUT NIR-CHEMOMETRIC METHODS FOR THE PHARMACEUTICAL CHARACTERIZATION OF KETOPROFEN EXTENDED RELEASE TABLETS

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**Introduction.** The aim of this study was to develop and validate NIR-chemometric methods for direct quantification of ketoprofen and lactose in powder blends for tableting, and also ketoprofen, lactose and the kinetics of release from extended release inert matrix tablets.

**Material and methods.** Calibration samples were prepared according to an experimental design with 2 variables and five levels, including 26 formulations. The in vitro release was carried out in phosphate buffer (pH=7.4), using a dissolution testing device equipped with baskets, at 100 rpm.

**Results.** The calibration algorithm for ketoprofen was obtained using as pretreatment method FD+MSC (PLS=7, RMSECV=1.46) for powder blends, respectively SNV (PLS=14, RMSECV=3.94) and SD (PLS=10, RMSECV=5.26) for tablets in the 10000-6098 cm<sup>-1</sup>; 5454-4596 cm<sup>-1</sup> spectral ranges. In case of lactose the calibration algorithm was obtained using as pretreatment method SLS (PLS=7, RMSECV=1.79) for powder blends, respectively SNV (PLS=3, RMSECV=6.79) and FD+SNV (PLS=4, RMSECV=6.45) for tablets, in the 10000-4200 cm<sup>-1</sup> spectral range. For kinetic release characterization the Peppas equation parameters were determined and correlated with the NIR-spectra of the tablets, in order to develop a NIR-chemometric method for direct estimation of the kinetic release.

**Conclusions.** According to the experimental data obtained the calibration algorithms allowed to validate the methods with satisfactory accuracy, reproducibility and linearity. NIR-spectroscopy can be applied for the pharmaceutical characterization of extended release tablets.

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## IN VITRO EVALUATION OF THE ESTROGENIC/ANTI-ESTROGENIC POTENTIAL OF BINARY MIXTURES OF SELECTED FOOD ADDITIVES AND COSMETIC PRESERVATIVES

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**Introduction.** Butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), propyl gallate (PG) and parabens (PB) are extensively used as antioxidants/conservatives. The in vitro evaluation of the individual compounds on an estrogen responsive cell line (T47DKBluc) indicated BP and PG to have dual effects (estrogenic (E)/anti-estrogenic (AE)). BHA was discovered to have only AE effects, while BHT did not have any effect. To date, many of the studies regarding EDCs were focused on risk assessment of individual compounds. In reality, humans are exposed to complex mixtures of potential EDCs. The objective of this study was to investigate the E/AE potential of binary mixtures of the selected compounds and the predictability of the combined effect of mixtures based on data from the individual toxicity studies and by using an additive model.

**Material and methods.** T47DKBluc cells were exposed to binary mixtures (+/- estradiol) for 24 hours before lysis and luminometric analysis. The experimental values were compared to those estimated by the additive, but also with those estimated for the individual compounds.

**Results.** In case of a binary mixture of a moderate/strong E compound (BP, PG) and a very weak E or non-E one (BHA, BHT) the effect of the mixture could be predicted both by the additive model or based on the dose-response curve from the individual testing of the E effect, of the compound with the strong E effect. The same prediction could be made in case of a binary mixture of a moderate/strong antiE (BP, PG, BHA) compound and a very weak anti-E one (BHT).

In case of binary mixtures between two moderate/relatively strong estrogenic or AE compounds a much better correlation was obtained by using the addition model.

**Conclusions.** The study confirms the possibility to predict the effect of binary mixtures of E/AE compounds by using either the addition model or the estimation based on the individual dose-response curve of the more potent component of the mixture.

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## EVALUATION OF IN VITRO ACTIVATION OF ESTROGEN-DEPENDENT GENE TRANSCRIPTION BY NORFLUOXETINE

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**Introduction.** Fluoxetine, a selective serotonin reuptake inhibitor (SSRI), has been linked to reproductive and endocrine toxicity in aquatic organisms, rodents and humans. This compound is metabolized in vivo to norfluoxetine, an active molecule with longer half-life for which data on endocrine effects are absent. Consequently, this study aimed at assessing the capacity of norfluoxetine to induce estrogen-dependent gene transcription in vitro.

**Material and methods.** The capacity of norfluoxetine to activate gene transcription was assessed using a reporter gene assay in T47Dkb-luc breast carcinoma cells. These cells express nuclear estrogen receptors that can activate the transcription of the luciferase-coding reporter gene upon binding of ER agonists. If the transfected reporter gene is expressed, the resulting luciferase enzyme can then convert its substrate, luciferin, into a luminescent product. Light emission was monitored for norfluoxetine at concentrations between 0.3–30  $\mu\text{M}$ , alone or in binary mixtures with 30 pM estradiol. Cellular viability was assessed using a resazurin-based assay.

**Results.** Norfluoxetine had a maximum luciferase induction between 10 and 20  $\mu\text{M}$ . Concentrations above 30  $\mu\text{M}$  could not be tested due to the cytotoxicity of the compound. Compared to 30 pM estradiol, this induction represents 17% of the maximum effect of E2. In binary mixtures with 30 pM E2, norfluoxetine caused a significant increase in luciferase activity at lower concentrations.

**Conclusions.** Norfluoxetine can activate gene transcription in vitro, as shown by luciferase induction in T47Dkb-luc cells. This suggests an agonistic effect of norfluoxetine on nuclear estrogen receptors. The increase in luciferase activity observed in the case of binary mixtures with estradiol suggests a potential synergy between the two compounds.

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## THE STUDY OF THE OXIDATIVE METABOLISM OF ESTRONE IN RAT LIVER MICROSOMES UNDER THE INFLUENCE OF GENISTEIN AND BISPHENOL A

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**Introduction.** The aim of this study was to determine the degree of inhibition induced by genistein (G) and/or bisphenol A (BPA) on the formation of 2 hydroxyestrone (2-OH-E) and 16 $\alpha$ -hydroxyestrone (16 $\alpha$ -OH-E) in rat liver microsomes, the 2-OH-E/16 $\alpha$ -OH-E ratio being a biomarker of breast cancer risk.

**Methods.** The rat liver microsomes were separated by differential centrifugation. The quantification of estrone metabolites, 2-OH-E and 16 $\alpha$ -OH-E, was performed by a LC-MS/MS method. The influence of genistein (100  $\mu$ M) and/or bisphenol A (100  $\mu$ M) on the rate of formation of 2-OH-E and 16 $\alpha$ -OH-E was determined using a microsomal preparation marked with different concentrations of substrate (100-800  $\mu$ M). A NADPH generating system was used. After different incubation times (0-30 min) at 37°C, the reactions were stopped with acetonitrile and centrifugation. The supernatant was analyzed by LC-MS/MS chromatography.

**Results.** The formation of 2-OH-E was significantly inhibited by genistein (46.9 $\pm$ 8.4%), and by bisphenol A (57.8 $\pm$ 4.7%), the inhibition being more intensely induced by their association (71.2 $\pm$ 8.2%). Genistein showed a minor inhibitory effect on the formation of 16 $\alpha$ -OH-E (8.7 $\pm$ 23.3%) and induced a reduction of the inhibitory potential of bisphenol A (48.0 $\pm$ 8.5%) in the case of their association (31.9 $\pm$ 21.9%). The different inhibitory degree of the two estrone metabolic pathways caused a reduction of the 2-OH-E/16 $\alpha$ -OH-E ratio, which was mild in the presence of BPA, significant in the presence of G, and much higher in the presence of the association.

**Conclusions.** The inhibitory potential of the tested xenoestrogens on the oxidative metabolism of estrone and the additive effect of the association on the diminution of the 2-OH-E/16 $\alpha$ -OH-E ratio were highlighted.

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## BIOCOMPATIBILITY STUDY OF A GRAPHENE COMPOSITE WITH GOLD NANOPARTICLES (AUNPS) AND HYDROXYAPATITE (HA) ON HUMAN OSTEOBLASTS

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**Introduction.** This study aimed to investigate the biocompatibility degree of different substrates made of graphene composites, gold nanoparticles and hydroxyapatite using bone derived cells.

**Material and methods.** Graphenes were obtained using method of catalytic decomposition of acetylene on the catalyst Au/HAP using inductive heating. We used nanostructured hydroxyapatite nanoparticles which were coated with 1% gold nanoparticles and finally obtained six variants of composites. Six kinds of substrates were tested for biocompatibility on primary culture of human osteoblasts. The cytocompatibility study was performed using fluorescein diacetate assay for assessment of viability and proliferation of osteoblasts cultivated in presence of HA, Au/HA and Au/HA@graphene composites as colloidal suspensions or as substrates. Experiments were carried out to determine cell proliferation at 24, 48 hours and 7 days in case of exposure to the composite as a suspension and at 24, 96 hours and 19 days in case of exposure to 2 composite concentration as a substrate. To assess the effects of composite substrate on osteoblasts behavior an immunocytochemical analysis for phosphatase alkaline, osteopontin and actin F fibers organization was performed after 19 days of cultivation.

**Results.** The most favorable composites for cell adhesion and proliferation were HA,Au/HA and Au/HA composites with 1.6% and 3.15% concentration of graphenes. Immunocytochemical staining performed after 19 days of osteoblasts cultivation on substrates showed that the graphene composites induced low expression of alkaline phosphatase compared to control group and HA and Au/HA substrates.

**Conclusions.** The rate of proliferation of osteoblasts exposed to composite as a colloidal suspension was greater than controls at 24 hours using concentrations of 30 and 60 µg /ml in case of Au/HA, and Au/HA graphene composites with low concentration of graphenes.

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## COMPARATIVE EVALUATION OF THE BEHAVIOR OF DENTAL MATERIALS USED IN ENDODONTIC SURGERY

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**Introduction.** Every root end filling material should have an excellent apical sealing ability. The aim of this in vitro study was to assess dye microleakage and sealing ability of four materials: a polycarboxilate cement (Adhesor Carbofine®), a glass ionomer cement (Kavitan Plus®), a composite resin (Core-It®) and a MTA based cement (MTA Fillapex®).

**Materials and methods.** Forty, extracted, human teeth with single, straight root canals were selected for this in vitro experimental study. The teeth were randomly divided into four study groups and one control group. The root canals were instrumented and filled with gutta percha and AH26 sealer. We removed 3 mm from the root-end and then we prepared 3 mm deep cavities inside the root canal. Subsequently, the root end cavities were filled with each material. For determination of dye leakage we used methylene blue dye. Then, in order to evaluate the sealing ability of each material, we used scanning electron microscopy (SEM). Data were analyzed using Kolgorov-Smirnov Z test. One-way analysis of variance (ANOVA) followed by a Tukey test were used to determine the statistical difference between groups, with  $p < 0.05$  set as significant. All the four sealers produced apical leakage to a certain extent.

**Results.** The teeth in the control group showed maximum penetration. There was no statistically significant difference between the five experimental groups. For SEM evaluation, the results showed that there was a statistically significant difference between the control group and the Adhesor Carbofine group.

**Conclusion.** MTA based cement provides leakage results comparable to other commonly used root-end filling materials such as composite resin.

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## REGENERATION METHODS OF THE PERIPHERAL SENSITIVE AND MOTOR NERVOUS STRUCTURES OF THE MAXILLOFACIAL REGION

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**Introduction.** The peripheral nervous system (PNS) features an intrinsic capacity for self-regeneration and repair, in contrast to the central nervous system (CNS) which, for the most part, is incapable of self regeneration and repair. Neuroregeneration of PNS differs from the CNS by means of functional mechanisms, growth and speed.

**Material and methods.** The success of tissue engineering is limited because of the limited knowledge of the regeneration environment.

In order to regenerate, a nervous fiber needs passive structures, which allow cells to express themselves, by forming extracellular matrix, and active elements with neurotrophic, neuroprotective and neuroplasticity role. The active elements are divided into intrinsic ones, secreted by the injured axon, and extrinsic ones, obtained through pharmaceutical input.

A peptide complex extracted from pig brain, known as hydrolyzed cerebrolysine, is part of these active intrinsic elements. They are biologically active molecules used in interneuron communication. They easily bypass the hematoencephalic barrier and act directly on the neurons, the neurotrophic effect manifesting itself through cellular differentiation and growth. They also promote neurogenesis, an essential element in posttraumatic regeneration.

**Results.** It is the sole peptide complex with proven neurotrophic activity, similar to the neural growth factor.

Few studies are known regarding the effect of this protein complex on PNS, meaning the posttraumatic regeneration of nervous structures.

**Conclusions.** The trend in research is towards the response of the nervous fiber within the regeneration programme of the peripheral nervous fiber; this fiber can be influenced by the cerebrolysine complex, which stimulates neurogenesis, through an increase in protein growth at the site of lesion.

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## OSSEOINTEGRATION ASSESSMENT OF TI-AL-NB ALLOY IMPLANTS USING EDX

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**Introduction.** The objectives of the study were to test the osseointegration of Titanium–Aluminum–Niobium (Ti6Al7Nb) alloy. While the osseointegration evaluation of various implants has been standardized by ISO-10993, some methods that are most commonly used in physics and chemistry have been neglected for their potential in preclinical research use. Energy dispersive X-ray analysis (EDX) is a spectroscopic assay used to determine the elemental concentration of various chemical components and it relies on the interaction between an X-ray source and a sample. Thus, all the identified chemical elements from the sample are represented on an X-ray emission spectrum. The present study aims to identify the possibility of using EDX analysis to assess the biological integration of a new Titanium-Aluminum-Niobium alloy in the bone tissue of an animal model.

**Material and methods.** The Ti6Al7Nb implants were manufactured using a selective laser melting technology and had a total porosity of 25%. Thus, 10 rabbits were used in this study which received intrafemoral implants. The samples were harvested 3 months after implantation and analyzed using EDX.

**Results.** EDX analysis have shown the presence of new chemical elements on the surface of the Ti6Al7Nb implants, such as N, C, O, S, Mg, Na and most importantly Ca and P. The Ca/P ratio has also been calculated to determine the presence of hydroxyapatite on the intraosseous implants.

**Conclusion.** The presence of Ca and P at the implant surface shows the biocompatibility and osseinduction of the Ti6Al7Nb alloy; EDX analysis proves to be a simple and reliable test for implant osseointegration.

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## STUDY ON ORAL LICHENOID LESIONS AND ORAL LICHEN PLANUS PREVALENCE IN PATIENTS WITH SILVER AMALGAM FILLINGS

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**Introduction.** Oral lichenoid lesions were first associated with silver amalgam fillings in 1979. Since then, a variety of studies were subsequently carried out whose results constitute the pros and cons of using dental amalgam as a restorative material.

**Material and methods.** From a total of 10.910 patients that were consulted between 2007 and 2013 for various dental problems, 58 patients were diagnosed with amalgam associated oral lichenoid reactions or oral lichenoid lesions (OLLs) and 38 patients were diagnosed with oral lichen planus (OLP) and silver amalgam restorations.

The diagnosis was set based on characteristic clinical manifestations of the oral mucosa, localized most commonly unilateral, in intimate contact or close proximity to silver amalgam fillings; in some cases with uncertain diagnosis a histopathological examination was performed.

To compare independent samples Student's t test was used. To establish links between two numerical variables we used Pearson correlation coefficient (r). For statistical analysis we used the following software programs: SPSS 10.0 for Windows, EPIINFO 2000 and EXCEL.

**Results.** Of the 10910 cases examined clinically, 10736 patients had silver amalgam fillings. 58 patients had amalgam associated OLLs diagnosis (0.54%); 101 patients had OLP with amalgam restorations only (0.94%). In our study the prevalence of OLLs and OLP in patients with silver amalgam fillings is 1.48%.

**Conclusions.** An accurate diagnosis is always of utmost importance, especially in the context of OLP and OLLs management.

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## HOST MODULATORY THERAPY(HMT) IN A RAT MODEL OF PERIODONTITITS

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**Background and aims.** Currently, the fundamental treatment of periodontitis is aimed to reduce the pathogenic microbiota and to modulate the host immune and inflammatory responses (Lu, et al., 2013; Cochran, 2008; Lee et al., 2013; Taubman et al., 2005). Because of the similarity of structure of inducible nitric oxide synthase (iNOS) and cytochrome P-450, cimetidine may block the inflammation-generated production of nitric oxide (NO) catalyzed by iNOS. We aimed to evaluate the effect of low-dose cimetidine (CIM) on nitro-oxidative stress in a model of periodontitis in rats.

**Methods.** A rat model of ligature-induced periodontitis was used. After two weeks, the periodontitis groups were treated with cimetidine, aminoguanidine, N-nitro- L-arginine methyl ester and trolox for one week. On day 21, blood was drawn and the serum analyzed for measurement of total nitrites and nitrates, total oxidative status, total antioxidant response, and oxidative stress index.

**Results.** Cimetidine had an inhibitory effect on the synthesis of nitric oxide ( $p=0.001$ ), total oxidative status ( $p=0.01$ ) and oxidative stress index ( $p=0.01$ ). Total antioxidant reactivity was increased by cimetidine ( $p=0.01$ ). The effects of cimetidine were almost like those of aminoguanidine, NG-nitro-L-arginine methyl ester, and trolox.

**Conclusions.** The present study provided evidence for the hypothesis that low-dose CIM has anti-inflammatory activity in a model of periodontitis in rats by reducing nitro-oxidativestress. Our findings suggest that CIM may be a useful adjunctive HMT in conditions associated with periodontitis.

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## IMAGING AND HISTOPATHOLOGICAL EVALUATION OF EXPERIMENTALLY INDUCED PERIAPICAL LESIONS IN RATS

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**Introduction.** The periapical lesions (PL) entail an inflammatory state in response to prolonged irritation of periapical tissues by bacteria from the infected root canals as a result of caries, trauma. The aim of this experimental study was to induce PL in rat molars. The periapical status of the involved teeth was assessed by using digital radiographs, magnetic resonance imaging and histopathological findings.

**Material and methods.** 40 adult Wistar rats were divided into four experimental groups. The right first mandibular molars were opened by coronal access. The molars were left open to the oral environment for 7 days in Group 1, 14 days Group 2, 30 days Group 3, and 60 days Group 4, in order to induce PL. Before the end of experimental period, MRI using a scanner 7 Tesla was performed in each animal before and after intravenous contrast agent administration. Pre and post contrast MRI protocols were performed. At the end of experimental period, the animals were sacrificed. The digital x-ray were taken to detect the periapical bone resorption. The periapical structures were analyzed on radiographic images by two observers using five point rating scale. The histological samples from periapical region were prepared and examined.

**Results.** PLs were visible radiographically after 14 days and their sizes increased significantly until day 30. It was observed that on x-ray images the apices of the molars were surrounded by radiolucent sites of different sizes starting with the second experimental period. PL were also visible on MR images and appear in hyper-signal on T1 sequences. The agreement between observers was statistically significant regarding the visibility of periapical lesions on the radiographic images ( $p < 0,05$ ).

**Conclusion.** The digital radiographs did not detect PL in the initial stages, but when the histological samples were examined, the area of inflammation was observed in all groups. The qualitative changes on MR images appear earlier than in digital radiographs.

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## ODONTOGENIC MAXILLARY SINUSITIS

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**Introduction.** The maxillary sinuses are situated in a topographic region where there is a great variety of anatomical structures. There are morphofunctional connections to the neighboring regions and close anatomic relationship, therefore the signs and symptoms evidenced in pathology may be identical or similar to those of neighboring regions diseases. Because of this fact it is necessary to study the case carefully and in detail, using clinical examination and also laboratory investigations to determine the exact diagnosis and to distinguish from other disorders.

Maxillary Sinusitis is an inflammation of the lining of the maxillary sinus, without bony walls involvement.

The interest in this subject derives from the multitude of clinical pathology often involving the removal of the causative tooth and bone, leading to prosthetic difficulties.

**Material and methods.** The source of information for this paper consisted of the observation sheets of the Oro-Maxillofacial Surgery Clinic from where the parameters were extracted, on which we performed the study of odontogenic maxillary sinusitis.

**Results.** Casework analysis according to the causes of the disease led to the finding that most often the chronic maxillary sinusitis occurred because of the dental factor (periapical pathology), followed in second place by oro-antral communications.

**Conclusion.** Odontogenic maxillary sinusitis is frequently encountered in adults between 25 and 50 years, when patients have the most dental events. It does not occur in infants and is rarely encountered in children and young people because, although it is the only sinus present in the newborn, its development starts only after the age of 12-13 years, and its final shape is reached only after the eruption of the upper molars.

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## COMPARISON BETWEEN CLINICAL EXAMINATION, COMPUTERIZED AXIOGRAPHY, ULTRASONOGRAPHY AND MRI IN ASSESSING THE TEMPORO-MANDIBULAR JOINT STATUS

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**Objective.** Temporomandibular disorder is a complex pathology which can manifest upon every component of the masticatory system, namely teeth, periodontium, muscles and TMJ. In order to obtain a positive diagnosis it is necessary to perform different examinations. The purpose of this study is to assess the relationship between the clinical findings and the results provided by the MRI (which is the golden standard) and axiography and ultrasonography (which are investigations more accessible for the patients).

**Material and Methods.** We have taken into study 16 patients diagnosed with temporomandibular disorders after the clinical examination (muscles, TMJ, occlusion). After the clinical examination another 3 examinations were performed: axiography, ultrasonography, MRI. All examinations were performed by two different clinicians to compare the results.

**Results.** In most of the cases the clinical findings were supported by the paraclinical examinations, but in some situations the initial diagnosis was completely changed.

**Conclusion.** The MRI remains the most important investigation for a precise diagnosis but ultrasound is an investigation tool of TMJ which seems interesting to further be taken into account. All the investigations offer an objective means of assessing the initial status and the progress of the treatment project.

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## THE INFLUENCE OF SMOKING ON ORAL HEALTH

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**Introduction.** Cigarette smoking is one of the most significant risk factors for multiple diseases, including periodontal disease.

The aim of this study was the assessment of oral and periodontal changes and socioeconomic inequalities in smoking patients. Further, specific goals of this study were health promotion in smokers.

**Material and methods.** We designed an observational study with two groups of smoking patients. The difference between those groups were the socioeconomic condition and the level of education. The relationship between tobacco smoking, oral hygiene, gingival and periodontal health were examined in both groups. The following clinical variables were recorded for patients from both groups: CPITN scores, OHI-S scores, probing attachment level, loss of attachment. In addition, the subjects reported in a questionnaire their tobacco habits, oral hygiene habits, dietary habits for evaluating the level of oral health education for those patients.

**Results.** The values of OHI-S index and CPITN index recorded in the patients from the first group were higher. Women in both groups had a better hygiene than men. The socioeconomic status had an inverse relationship with tooth loss and conservative therapy, but a direct relation with worsening of the periodontal condition.

**Conclusion.** The adverse effect of smoking on the initiation and progression of periodontal disease is highlighted in this study. There is a correlation between oral health and the quality of life for those patients.

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## MINI-IMPLANTS IN ORTHODONTICS

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**Introduction.** In many orthodontic cases moving teeth in a desired position is an important key to achieve the best treatment results. Skeletal anchorage provided by orthodontic mini-implants has attracted great attention in recent years because of its minimal surgical invasiveness and because it is not relied on patient cooperation. Mini-implants provide reliable three-dimensional anchorage and predictable treatment outcome which in orthodontics is an important factor. Miniscrews are easily placed and removed and can be loaded immediately following insertion. Mini-implants may be immediately loaded, they require adequate primary stability followed by a consolidating period of secondary stabilization.

**Material and methods.** In order to evaluate the acceptance of mini-implants we designed a questionnaire for 23 subjects. We also evaluated the angle of insertion and the quality of cortical bone using traditional radiographs.

**Results.** For the side effect felt after implant placement 30% reported irritation inside the mouth, 22% aphthous ulcers, 48% reported no side effects. Reinserting mini-implants increased stability. To achieve the best primary stability, an insertion angle is advisable.

**Conclusion.** We achieved best anchorage results during orthodontic treatment. Almost all patients were satisfied with the treatment and would recommend the procedure to a friend.

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## DIAGNOSTIC WAX UP CONSTRUCTION: HARMONIZATION BETWEEN THE PATIENT EXPECTATION AND AESTHETIC OF THE FINAL RESTORATION IN ORAL ANTERIOR ZONE REHABILITATION

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**Introduction.** Oral rehabilitation of the anterior area involve the harmonization between the patient expectation and the aesthetics limits of the final restoration.

**Purpose.** The simulation with diagnostic wax-up construction, will help the patient to validate the volume and the shape of the final restoration.

**Materials and Methods.** Diagnostic construction was made on the master model, the same model that is used for the final reconstruction. The diagnostic construction performed in white wax on elastic polypropylene structure provided the detachment from the model and the insertion in oral cavity without damage. The management of the space dedicated to the resistance structure and for the aesthetic component was provided by the silicon index that keep the features of he diagnostic wax up.

**Results and discussion.** The patients that benefit of the final restoration simulation with diagnostic wax up construction adjusted their initial expectation to the limits of aesthetic possibilities. The patients that benefited from the transitory reconstruction adjusted their initial expectation to the social environment opinion.

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## COMPARATIVE RADIOLOGIC EVALUATION OF THE ENDODONTIC FILLING FOR THREE DIFFERENT SEALERS

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Cone beam computed tomography (CBCT), this 3-dimensional diagnostic imaging technique, has become an important tool for both diagnosis and treatment planning, being able to support endodontic treatments and also providing useful information regarding the quality of the endodontic filling. This paper aims to evaluate the sealing capacity of three endodontic materials using conventional 2D digital radiography (Rx) and CBCT.

**Materials and method.** sixty single-rooted freshly extracted human teeth were cleaned and prepared using ProTaper up to F3 instrument. The teeth were randomly divided into three groups (n=20) and filled with gutta-percha and sealer using the lateral condensation technique in the apical third and gutta-percha injection in the coronal two thirds. In the first group RealSeal, in the second AH Plus and in the third group a new hydroxyapatite based material (HA) were used. Conventional Rx and CBCT were taken for each filled tooth. The sealing ability of each material was evaluated by a radiographic scale (0-4) indicating the density of the endodontic obturation, presence and dimension of voids, the adaptation of gutta-percha to the canal outline. All data were analyzed using the one way Anova statistic test.

**Results.** RealSeal had better sealing ability compared to AH Plus and the new HA material. The average scores for RealSeal were lower than for AH Plus on Rx and CBCT evaluations ( $p < 0,05$ ). Although the new HA material obtained lower scores than AH Plus the differences were not statistically significant (Rx  $p = 0.058$ ; CBCT  $p = 0.48$ ). The CBCT provided more accurate data (higher scores) for all materials, but the results were not significant comparing to Rx evaluation ( $p = 0.62$ ).

**Conclusions.** The new HA material has a medium sealing capacity, lower than RealSeal and better than AH Plus. The CBCT is a useful instrument but the results are similar with the conventional 2D Rx when used for the quality of the endodontic filling evaluation.

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## PERIODONTAL DISEASE INDUCED IN WISTAR RATS - EXPERIMENTAL STUDY

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**Introduction.** Animal models have contributed to the generation of new knowledge in biological sciences, including periodontology. Periodontitis is a highly prevalent, chronic immunoinflammatory disease of the periodontium that results in progressive loss of gingival tissue, the periodontal ligament, and adjacent supporting alveolar bone with significant impact on human health.

The aim of the present research was to develop an experimental model for the induction of periodontal disease in Wistar rats to study the systemic implications of periodontitis. We also aimed to assess the efficiency of local and general therapeutic modalities against this disease.

**Materials and methods.** Ten male adult Wistar rats obtained from Laboratory animal facility - Centre for Experimental Medicine, "Iuliu Hațieganu" University of Medicine and Pharmacy, average weight 180-200 g, were included in this study. Ligatures in "8" with 4/0 nonresorbable sterile silk thread were placed in the inferior frontal group under general anesthesia. After 14 days the animals were euthanized and samples representing the cephalic extremity were stored in formalin and prepared for histological processing. In an attempt to detect possible systemic alterations related to periodontitis, body weight and white blood cell counts of animals were recorded.

**Results.** Periodontal disease induction by ligature placement caused a significant inflammation of periodontal tissue and alveolar bone loss, observed at 14th day.

Histopathological analysis showed a progressive mononuclear cell infiltration and an increase in the osteoclast numbers was evident.

**Conclusions.** The development of experimental animal models for periodontal disease are essential for the understanding of the etiopathogenesis and evolution of these diseases in the human species and represents a necessary step before performing clinical trials on the proposal and testing of new materials and methods of treatment.

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**LINGUAL RETAINER OR ORTHODONTIC TREATMENT IN PERIODONTAL DISEASE****CLAUDIA FEURDEAN, LUCACIU ONDINE, ADINA SÎRBU, ARIN SAVA, DAN BUHĂȚEL,  
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**Introduction.** The number of patients with periodontal disease has increased in the last years. Planning the treatment of this patients is of paramount importance for the final outcome. The treatment includes different stages: the etiopathic, the surgical and the orthopedic one. The aim of our research was to assess functional rehabilitation using the immobilization of the affected teeth versus orthodontic treatment, in the last treatment stage.

**Material and method.** The material included 20 patients (10 female and 10 male) diagnosed with periodontal disease. All the patients underwent the etiopathic and surgery stage of the periodontal treatment. 10 patients were treated with lingual retainer made of composite materials (LRC), we named this subjects study group 1. The other ten were treated with orthodontic treatment (OT), we referred these subjects as study group 2. Patients from both groups were examined at 6 and 12 months. We evaluated patients retainer and periodontal status.

**Results.** Patients with LRC: teeth were in a stable position without mobility, plaque index had a high level, gingivitis and 2 of LRC were fractured.

Patients with OT: teeth alignment, occlusal rehabilitation and the teeth were well maintained without plaque or gingivitis.

**Conclusion.** Patients with OT have a better periodontal status and a better long time prognosis than the patients with LRC.

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## INTERACTION OF STEM CELLS DERIVED FROM MAXILLARY AND MANDIBULAR BONE WITH SALTS FROM CULTURE MEDIUM

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**Introduction.** Growing stem cells require specific culture media from each cell cultures in part. Between culture medium and synthesis products of stem cells there may exist unexpected chemical reactions.

**Material and methods.** In this study we used two human bone fragments: interradicular mandibular bone and tuberosity bone. Isolation of stem cells derived from bone was performed by explants method. The culture medium used was DMEM / F-12 (Dulbecco's modified Eagle's medium/Nutrient mixture F-12). Cell cultures were maintained at a humidity of 99%, a temperature of 37 °C and 5% CO<sub>2</sub>. Stem cells derived from bone were evaluated by optical inverted microscopy (Zeiss) and scanning electron microscopy FEI Quanta 3D FEG 200/600 system with EDAX qualitative and quantitative elemental analysis. The study was approved by the Ethics Committee from University of Medicine and Pharmacy "Iuliu Hațieganu" Cluj-Napoca, no. 343 / 02.10.2014. Patients have expressed their informed consent to participate in the study.

**Results.** Primary stem cell cultures derived from bone occurred at day 7 (from tuberosity origin) and day 11 (from interradicular origin), after isolation. In optical microscopy, while stem cells were developing, we observed spherical or oval formations, with varying sizes, pearly white formation with hyperchromic center and amorphous appearance. At scanning electron microscopy and EDAX qualitative and quantitative elemental analysis, these formations were NaCl crystals precipitated around some organic structure. These precipitated NaCl salts increased numerically within the development of bone stem cells and limited stem cell conglomeration towards confluence.

**Conclusion.** Stem cells derived from maxillary and mandibular bone favor precipitation of NaCl salts in culture medium that arrest the cell confluence.

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## THE SUITABILITY OF INTRODUCING A NEW TYPE OF DENTAL IMPLANT

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**Introduction.** The aim of our study was to review published results regarding the survival rates of dental implants as well as the quality of the surrounding bone. This review of published data served to evaluate the suitability of a new and original dental implant, designed to increase its survival rate and maintain the health of surrounding tissues.

**Materials and Methods.** A systematic review of PubMed indexed literature was conducted in November 2014, to identify studies focusing on dental implants survival rates and bone levels surrounding dental implants. The articles were selected regardless of study design, but using specific inclusion criteria. Data on marginal bone loss and implant survival were collected from all included articles. Median survival rates (%) and median marginal bone loss (mm) were calculated at 1, 2, 3, 5 and 10 years.

**Results.** Forty-nine studies (19 retrospective and 30 prospective studies) were included in the analysis out of a total of 808 search results. The total number of included patients was 5646, with 12271 endosseous dental implants. The median survival rate after 1 year was 96.95% (22 studies), after 2 years 96.94% (9), 3 years 96.40% (6), 5 years 95.42% (18) and 10 years 93.50% (6). The median marginal bone loss was 0.72 mm after the first year (26 studies) and 0.87 mm, 1.29 mm and 1.43 mm respectively, after the 2nd, 3rd and 5th year, based on 14, 7 and 7 studies, respectively.

**Conclusion.** Given the need to increase success rates of dental implants and to maintain the health of surrounding tissues, a new type of dental implant, that could improve these parameters, could be suitable. Perspectives: We intend to develop and test a dental implant designed with a three-dimensional buffering system that limits non-physiological masticatory forces transmitted to the peri-implant bone. By reproducing natural tooth mobility, such an implant could also be used as an abutment in prosthesis supported by both implants and teeth.

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## CLINICAL APPROACH OF IMPACTED LOWER THIRD MOLARS

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**Introduction.** Lower third molars are the permanent teeth that have the highest risk for impaction, and extraction of impacted third molars is one of the most frequent surgical procedures carried out by oral surgeons worldwide, both in private practice and in hospital settings.

**Materials and Methods.** A group of 60 practitioners of dental medicine were included in the study: 29 general dental practitioners, 15 oral and maxillofacial surgeons (specialized surgeons and surgeons in training) and 16 dental practitioners in training for non-surgical specialties.

The subjects were evaluated using a questionnaire that covered aspects as symptomatic and asymptomatic impaction, alternative procedures, radiological assessment, associated medication, patient information, surgical technique and post-operator control.

**Results and Discussion.** Dental practitioners in Cluj-Napoca prefer a non-surgical attitude towards impaction on lower third molars and investigate the risk and the need of removal.

Prophylactic removal was considered appropriate when a partially impacted lower third molar, on a young patient, was in question.

Medical opinions and strategies vary in a wide range, as they are influenced by objective parameters (type of impaction and patient's age) and subjective parameters (professional training, practical experience of the practitioner and patient preferences), particularly in asymptomatic cases.

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**ASSESSMENT OF THE NASO-PHARYNGEAL SPACE IN CEPHALOMETRIC ANALYSIS****DIANA BERECHET<sup>1</sup>, LIGIA VAIDA<sup>2</sup>****<sup>1</sup>Department of Conservative Odontology, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania****<sup>2</sup>Department of Dental Medicine, University of Oradea, Romania**

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**Introduction.** The cephalometric analysis represents a routine paraclinical examination in every orthodontic case, therefore it is very useful in the evaluation of the size of the adenoid vegetations. The aim of this study is to assess the adenoid tissue from the naso-pharyngeal space using cephalometry.

**Material and methods.** The measurements obtained with cephalometric analysis are necessary to detect patients who require an ENT treatment before orthodontic treatment. For the purpose of this study, 25 mouth breathing orthodontic patients were taken into consideration, aged between 6 to 12 years. The dimension of the naso-pharyngeal space was measured on the cephalometric radiographs and was compared to Ricketts' analysis according to patients' age. The measurements were applied to the following points: PSN-ad1- the distance between PSN point and ad1 in millimeters, PSN-ad2 – the distance between PSN and ad2 in millimeters, PSN-ad1-ad2-PSN – the naso-pharyngeal area in millimeters.

**Results.** 14 cases (56%) were diagnosed with severe adenoidal hypertrophy, 9 (36%) cases had moderate adenoidal hypertrophy, and 2 (8%) cases had mild adenoidal hypertrophy.

**Conclusions.** Cephalometric analysis is very helpful in assessing the size and shape of adenoid vegetations. The success of therapy of malocclusions in mouth breathing patients and especially the stability of treatment outcome are highly correlated with an adequate etiological treatment (adenoidectomy, re-education of nasal breathing) that should precede and/or follow the orthodontic treatment.

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## BIOCOMPATIBILITY INITIAL TESTS ON A NEW TYPE OF DENTAL MATERIAL

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**Introduction.** Because of several biological disadvantages of some dental materials we thought of a new type of material with a good biocompatibility and antibacterial properties.

**Material and methods.** In our research we tested an innovative material obtained as a homogeneous glass, enriched with silver, for its antibacterial properties. The constituent particles were characterized using scanning electron microscopy and by means of X-ray photoelectron spectroscopy. Then in vitro tests on a human fibroblast cell line were performed. The cells were incubated with the proposed new material.

**Results.** Cell viability tests and optical microscopy images showed that the HFL1 cells remained viable after 48 hours incubation with the obtained samples.

**Conclusion.** These results support our initial hypothesis that the proposed material is a biomaterial and could enter in the structure of a new material for dentistry.

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**BIOCERAMIC MATERIALS USED IN ENDODONTICS - LITERATURE REVIEW****MARIUS BUD, STEFAN JITARU, LUCIA TIMIS, SANDA CAMPEAN, ADA DELEAN****Department of Conservative Odontology, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania**

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**Introduction.** Bioceramics are ceramics obtained by chemical processes generally through hydration, in situ and in vivo. Bioceramics opened new directions to replace and regenerate lost tissues (tooth enamel, dentin, cementum or bone). The first bioceramic successfully used in endodontics was a calcium silicate cement, MTA (Mineral Trioxide Aggregate) developed based on Portland cement in the Loma Linda University - California in the early 90's as a retrograde filling material for closure of perforations. Bioceramics including MTA cement are the subject of numerous in vivo and in vitro scientific researches. The purpose of our analysis was to perform a review of the literature published to date about the main types of bioceramic used in endodontics.

**Material and methods.** Analysis of the literature published to date in the bioceramics used in endodontics was performed by examining articles published in international indexed databases. We selected both articles referring to studies in vivo and in vitro that addressed to cytotoxicity, microleakage and microbiological analysis of these materials.

**Results.** MTA shows a similar composition, physical and chemical properties to Portland cement, which did not contain bismuth oxide to confer radio-opacity. MTA adhesion to dentin is superior to that of cements and sealers (non MTA ) widely used in endodontics in humidity conditions. Antibacterial action of bioceramics is effective but does not cover the full spectrum of bacteria involved in endodontic pathology. Success rate reported after direct pulp capping with MTA exceeds the success of using calcium hydroxide.

**Conclusion.** Bioceramics is a new class of materials with proved advantages in endodontic treatment.

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## LASER APPLICATIONS IN SOFT TISSUE REMODELING

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**Introduction.** The use of laser therapy in soft tissue remodeling as an adjuvant to conventional surgery has become an increasingly debated topic due to the large number of benefits it provides. Gingival hyperplasia may occur due to a number of causes, among which we mention the one caused by irritation, microbial inflammation and drug induced. Gingivectomy was originally used as a treatment option in periodontal diseases. Nowadays, it is mainly used for cosmetic and aesthetic purposes in soft tissue remodeling.

**Material and methods.** Diode lasers ( $\lambda = 980$  nm) are mainly used for soft tissue therapy. We used this wavelength to remodel the soft tissue in the studied clinical cases.

**Results.** This study examined the many ways of using diode lasers ( $\lambda = 980$  nm) in the selected group of patients which required soft tissue remodeling. Clinical cases are presented for the use of laser in gingivectomy, gingival hyperplasia, root planning. Using diode lasers helped solving soft tissue problems such as: aesthetic gingival recontouring, soft tissue crown lengthening, exposure of soft tissue impacted teeth, removal of inflamed and hypertrophic tissue, frenectomies, tissue removal at the site for miniscrew.

**Conclusions.** Due to the multiple advantages of diode lasers, soft tissue manipulation has become easier and the recovery time after therapy has become considerably shorter. Using these type of lasers has become very promising due to the fact that it increases both patient and physician satisfaction.

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## MINIMAL INVASIVE ALTERNATIVES IN THE PROSTHETIC RESTORATION OF POSTERIOR TEETH

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**Introduction.** Dental prostheses used for posterior teeth have to fulfill biofunctional, biomechanical and prophylactic principles. Biofunctional and biomechanical conditions narrow the possibilities of preserving tooth substance. Therefore, the practitioner is forced to choose prosthetic solutions to restore teeth integrity. Modern prosthetic dentistry brings minimally invasive methods in posterior teeth treatment.

**Objectives.** In this study we aim to restore posterior teeth with minimal dental structure sacrifice.

**Materials and methods.** This current study evaluates 20 dental prostheses constructed in the dental laboratory, after minimal invasive preparation.

**Results. Conclusions.** Accuracy of the fabrication, marginal integrity, marginal closure, the possibility of control on the marginal periodontal structures are essential factors that may interfere with the therapeutical algorithm in manufacturing dental prostheses.

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## COMPUTER ASSISTED ANALYSIS IN A SIMULATED SELF INFLICTED BITE-MARK

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**Introduction.** Human bite-mark identification is an interdisciplinary field based on the transfer of methodology and knowledge between dental medicine, forensic medicine and criminology and it is used mainly in legal investigations. This article combines different comparative methods - analyzing photographs of bite marks, overlays of a suspected biter's dentition using image perception software- in a simulated case of self inflicted bite-mark.

**Materials and methods.** Visual examination of the lesion was first conducted by one examiner who determined, based on the morphological appearance and topography of the lesion, that it was a human bite-mark. Following the standard procedure set by the American Board of Forensic Odontology (ABFO) the double swab technique was used for a potential DNA profiling of the aggressor and subsequently digital photography of the bite-mark was performed and analyzed using digital comparison (Adobe Photoshop™ CS 3). Silicone impression material in combination with an individualized tray was used to obtain the impression of the bite-mark and type IV dental stone was used to obtain the cast. Alginate and type III stone was used to obtain study plaster casts of the upper and lower jaws of the suspect. Overlays of the bite-mark were obtained through 3 methods (manual tracing, silicone index and computer assisted generation) and were superimposed. Metric analysis of the subjects' casts was digitally performed. Comparative examination was performed manually and digitally.

**Results.** The injury was consistent with an adult, human bite. There were significant concordance features between the pattern of the injury and the spatial alignment and dimension of the suspect's teeth. Based on the topography of the lesion and comparative examination, the bite-mark was self-inflicted.

**Conclusion.** Digital imaging methods substantially improve the conservation, analysis and comparison of data in bite-mark pattern recognition.

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## THE CONTRIBUTION OF OCCLUSAL FORCES TO NON-CARIOUS LESIONS FORMATION

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**Introduction.** Non-cariou cervical lesions are formed by the loss of tooth structure in the cervical third of the crown that is unrelated to dental caries.

For many decades, non-cariou cervical lesions were attributed to the effects of abrasion and erosion mainly because of toothbrush trauma and abrasive toothpaste. However, though the above may be involved, more recent studies have shown the existence of a biomechanical theory for the formation of these lesions and as a result the term abfraction was coined.

The purpose of this study was to assess the potential relationships between the type of lesion and the abfraction which appeared after the application of occlusal loading.

**Material and Methods.** The study was carried out on extracted teeth which were put under axial (functional) and para-axial (non-functional) loading of 50N-250N. An axial load was applied on the buccal cusp tip, whereas the para-axial load was applied obliquely on the long axis of the tooth.

**Results.** The results indicated a significant relationship between the occlusal loads and the abfraction. Thus, the teeth that were moderately axially loaded did not show any cervical lesions, while the teeth that were non-functionally overloaded showed abfraction.

**Conclusion.** Oblique loading on simulated non-cariou cervical lesions resulted in greater stress concentration as compared to that of the vertical loading. Thus, the change of the axis led to lesion appearance in the cervical area.

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## EVALUATION OF COLOR CHANGES IN COMPOSITE RESINS AFTER THE USE OF BLEACHING AGENTS

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**Introduction.** Tooth bleaching is often used in dental offices in order to achieve the esthetic aspect that patients desire.

The study examined the chromatic and structural changes which occurred on the surface of test tubes made of four studied diacrylic resin composites which, after having been colored with coffee and commercial cherry juice underwent bleaching by using two experimental jellies produced by the research team from the Institute of Chemical Research “Raluca Ripan” (ICCRR) of Cluj-Napoca (one with 15% hydrogen peroxide –GA, and the other one with 15% peroxidase – GAP).

**Materials and Methods.** The differences in color which occurred in the studied composites were subsequently correlated with their chemical structure. The four resins were: Restacryl (a composite from ICCRR Cluj-Napoca), Tetric Evo Ceram (Ivoclar Vivadent), Filtek Supreme (3M ESPE), Premise (Kerr).

The chromatic changes were analyzed by studies of spectrophotometry UV-VIS, while the structural ones, which occurred following the application of bleaching jellies, were shown through images of electron microscopy.

**Results.** Modifications of color occurred in all composites in accordance with the bleaching jellies, regardless of the various pigments and type of bleaching agent used.

The electron microscopy images showed a certain degree of bleaching of the composite resins, but also a less wanted effect- structural changes of the resins.

**Conclusions.** 1. The bleaching agents used in this study (GA and GAP) led to chromatic changes of the studied composite resins. 2. On the microscopic level the present study demonstrated that following the bleaching process some fissures are produced in the resin, a fact that determines the appearance of roughness and the liberation of some inorganic components from the composite resin, thus leading to diminished hardness of the material used for the dental restoration

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## MICROLEAKAGE AND INTERFACIAL MICROMORPHOLOGY OF DENTAL RESTORATIONS MADE WITH NEW EXPERIMENTAL GIOMERS

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**Introduction.** The aim of this study was to develop two experimental total etch adhesive systems (A1, A2) and two experimental light-cure giomers (G1, G2) and to evaluate the marginal integrity and the interface tooth restoration in comparison with commercial product.

**Material and methods.** Seventy box-type Class V standardized cavities were prepared on premolar teeth on the facial and oral surfaces of each tooth, with coronal margins in enamel and apical margins in dentin. The preparations were divided randomly into five equal groups (n=14) and restored with: group I (control): Beautiful II and FL-Bond II; group II: A1 and G1; group III: A1 and G2; group IV: A2 and G1; group V: A2 and G2. The teeth were thermocycled, then immersed in 2% methyl blue solution for 24 h. The specimens were sectioned bucco-lingually into slices of 1 mm and the resulted sections were examined for microleakage using a stereomicroscope. Microleakage was evaluated using a score method, a quantitative analysis and one way variance analyses (ANOVA), and Tukey's test (p<0.05). Giomer-adhesive-tooth interfaces were also evaluated using SEM and AFM.

**Results.** Microleakage and sealing of group IV and V were comparable with the control group both in the enamel and dentin margin. The group II and III showed microleakage higher than the control group. SEM and AFM investigations evidenced a good giomer-adhesive-tooth interface and dentin seal for group IV and V.

**Conclusion.** A2 adhesive system could be used for dental clinical application and the new monomer bis-GMA-G1 could be a promising monomer for obtaining new giomer material with clinical application.

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## EVALUATION OF THE STATUS OF THE ORTHODONTIC PATIENT IN CLUJ-NAPOCA

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**Introduction.** The purpose of this study is to evaluate the status of the orthodontic patient treated in Cluj-Napoca through a questionnaire-based survey.

**Material and methods.** 130 questionnaires were applied over a period of six months to patients undergoing orthodontic treatment aged between 12 and 43 years. The main areas investigated were hygiene, self evaluated facial aspect before, during and after orthodontic treatment, overall quality of life, satisfaction on information offered by the orthodontist before during and after treatment.

**Results.** The patients' hygiene is insufficient, 61% of patients are more confident in their appearance after starting orthodontic treatment, most patients are satisfied with information offered by the orthodontist.

**Conclusion.** Thorough recommendation should be given to the patient before treatment regarding hygiene measures, data of this research should be helpful in encouraging patients to undergo orthodontic treatment.

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