



# New prospects in oncotherapy: bioactive compounds from *Taraxacum officinale*

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## Abstract

Cancer remains one of the most significant global health challenges, requiring continuous exploration of novel therapeutic agents. Traditional medicine has long used *Taraxacum officinale* H.Wigg, commonly known as dandelion, for its diverse pharmacological properties. Recent studies have highlighted its potential anticancer effects attributed to a rich phytochemical profile containing flavonoids, terpenoids, phenolic acids, polysaccharides, and sterols. This review systematically examines the available scientific literature regarding *Taraxacum officinale*, focusing on its ethnomedical application, phytochemical composition, and anticancer mechanism demonstrated *in vitro* and *in vivo* models. Key bioactive compounds, such as taraxasterol, chlorogenic acid, chicoric acid, and taraxinic acid, have been identified as promising agents capable of inhibiting tumor cell proliferation and modulating oncogenic pathways. Additionally, the plant's safety profile and toxicological assessments are discussed to evaluate its therapeutic viability. Given its multi-target biological activity and low toxicity, *Taraxacum officinale* holds significant potential for integration into oncotherapy as an adjuvant treatment. However, further preclinical and clinical investigations remain essential to validate its efficacy and mechanism of action, paving the way for the development of cost-effective, plant-based cancer therapeutics.

**Keywords:** *Taraxacum officinale* H.Wigg, cancer therapy, phytochemicals, bioactive compounds

## Introduction

Cancer is one of the most devastating diseases worldwide, ranking second only to cardiovascular diseases in terms of mortality. It is characterized by the uncontrolled proliferation of malignant cells in the body. According to a recent report, cancer was responsible for approximately 10 million deaths worldwide in 2020 [1]. In Romania, cancer is the second leading cause of death after cardiovascular diseases, accounting for nearly 19% of all fatalities, with over 95,000 new cases and nearly 54,000 deaths reported annually for about 19% of all deaths [2].

In recent decades, research on plant-derived bioactive compounds has played a pivotal role in the discovery of novel therapeutic agents with anticancer

potential. To date, more than 35,000 plant species have been examined for their possible applications in oncology [3] and it is estimated that over 60% of anticancer drugs currently in use are derived from natural sources, including plants and animals [4].

Advanced technological methods such as virtual screening, molecular modeling, natural product databases, high-resolution analytical methods, and bio-analysis under laboratory conditions and biological assays — both *in vitro* and *in vivo* — are increasingly employed in the drug discovery process [5,6].

Among the many medicinal plants explored, *Taraxacum officinale* H.Wigg (*T.officinale*) has recently gained significant attention due to its complex phytochemical profile and promising

DOI: 10.15386/mpr-2875

Manuscript received: 04.03.2025

Received in revised form: 25.06.2025

Accepted: 26.06.2025

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anticancer activity. This review aims to establish a clear connection between the plant's bioactive constituents and their antitumor mechanism of action, as demonstrated in *in vitro* and *in vivo* studies. The plant secretes a milky white latex and can reach a height of up to 60 cm.

*T. officinale*, commonly known as dandelion, is a plant commonly used in traditional herbal medicine, belonging to the *Asteraceae* family. Its scientific name comes from Greek, where “taraxos” means disorder and “akos” remedy, while the term “officinale” indicates its medicinal relevance [7]. It forms a basal rosette of deeply lobed dark green leaves, and its robust taproot can grow 15–45 cm in length. The inflorescence-bearing stalks arise from the center of the rosette and produce bright yellow hermaphroditic flowers [8,9]. Phytochemical investigations have revealed that *T. officinale* is rich in flavonoids (e.g., luteolin, quercetin glycosides), phenolic acids (chicoric, chlorogenic, and caffeic acids), terpenoids (taraxasterol, taraxerol), sesquiterpene lactones (taraxinic acid  $\beta$ -D-glucopyranosyl ester), and phytosterols ( $\beta$ -sitosterol, cycloartenol) [10]. These compounds are distributed throughout various parts of the plant—roots, leaves, and flowers—and are considered responsible for its diverse biological activities.

*T. officinale* has been reported to exhibit a broad spectrum of pharmacological effects, including antidiabetic, antioxidant, hepatoprotective, diuretic, anti-inflammatory, neuroprotective, antidepressant, antimicrobial, and immunostimulant properties [11–18]. In addition, recent studies have demonstrated its anticarcinogenic activity against several types of malignant tumors, such as colorectal, liver, and gastric cancers [12].

Given the increasing scientific interest in this plant's therapeutic efficacy, phytochemical complexity, and pharmacological properties, a comprehensive and systematic review of available studies on its anticarcinogenic activity is warranted.

A 2021 review emphasized the therapeutic potential of *T. officinale*, highlighting its hepatoprotective, immunomodulatory, antiviral, antifungal, antibacterial, antioxidant, and anticancer effects [7]. However, more recent studies have indicated a more explicit antitumor potential for the plant and its active constituents, though without a detailed analysis of the underlying mechanisms [13,14,19]. Given the increasing scientific interest in this plant's therapeutic efficacy, phytochemical complexity, and pharmacological proprieties, a comprehensive and systematic review of the available studies exploring its anticarcinogenic action is warranted.

This paper aims to synthesize current scientific evidence concerning the ethnomedical relevance, phytochemical composition, anticancer potential, and safety profile of *T. officinale*. Attention will also be given to identifying bioactive substances and understanding the mechanism by which they act. Such an approach may contribute to the development of natural, low-toxicity, and cost-effective anticancer therapies.

### Traditional uses and ethnomedicinal applications of *T. officinale*

The different parts of *T. officinale*—including the roots, leaves, flowers, latex, aerial parts, and seeds—have been widely used in traditional medicine systems across different cultures. Traditionally, dandelion has been employed to manage and treat a broad spectrum of health conditions, including liver disorders, digestive issues, skin ailments, inflammation, and infections. The therapeutic versatility of *T. officinale* is attributed to its diverse phytochemical composition, which has made it a staple remedy in folk medicine.

Table I presents evidence-based correlations between plant part, extract type, pharmacological action, treated condition, and clinical indications, with supporting references from the scientific literature.

**Table I.** Traditional medical uses and pharmacological effects of *T. officinale*.

No.	Plant part	Extract type	Pharmacological action	Treated condition	Symptoms / Indications	References
1	Whole plant	Aqueous extract	Diuretic, anti-inflammatory	Kidney/liver disorders, rheumatism	Edema, joint pain	[7,11]
2	Leaves	Aqueous extract	Antidiabetic, antioxidant	Type 2 Diabetes	Hyperglycemia, oxidative stress	[15,21]
3	Root	Aqueous extract	Appetite stimulant, hepatoprotective	Appetite loss, liver support	Lack of appetite, hepatic dysfunction	[16,22]
4	Flowers	Alcoholic extract	Antioxidant, digestive aid	Digestive discomfort	Constipation, bloating	[17,21]
5	Aerial parts	Aqueous extract	Antioxidant, anti-ulcerogenic	Gastrointestinal disorders	Ulcers, stomach pain	[22,24]
6	Aerial parts	Alcoholic extract	Antiproliferative, anti-inflammatory	Support in tumor management	Inflammation, cell proliferation	[18,19]

### Phytochemical and nutritional profile of *T. officinale*

*T. officinale* is a chemically and nutritionally rich medicinal plant characterized by a wide range of bioactive secondary metabolites and essential nutrients. Its major phytochemical constituents belong to distinct structural classes, including sesquiterpene lactones, triterpenoids, flavonoids, phenolic acids, sterols, alkaloids, and carbohydrates. These compounds are unevenly distributed across different parts of the plant, reflecting functional specialization related to ecological adaptation and therapeutic relevance. A summary of the distribution of major compound classes across different plant parts is presented in table II, providing an organized overview of representative phytochemicals and relevant references. The table highlights the spatial distribution of key phytochemicals, includes supporting literature references, and summarizes their reported bioactivities.

The following sections describe the key chemical classes and representative compounds in greater detail, highlighting their specific localization within the plant and their potential pharmacological significance:

- flavonoids, such as luteolin-7-glucoside, apigenin-7-glucoside, quercetin, and their derivatives, are primarily found in the leaves and flowers. These compounds are well known for their strong antioxidant capacity and have been associated with anti-inflammatory and antiproliferative effects, contributing to the plant's chemopreventive potential.

- phenolic acids, including caffeic acid, chicoric acid, chlorogenic acid, and moncaffeoyltartaric acid, are abundant in the roots, flowers, and aerial parts. These compounds play important roles as free radical scavengers and modulators of cellular signaling pathways, supporting immunomodulatory and anticancer activity.

- sterols, such as  $\beta$ -sitosterol, stigmasterol, and cycloartenol acetate, are mainly detected in the aerial parts and latex. These lipophilic molecules contribute to membrane stability and have been implicated in anti-inflammatory and cholesterol-lowering effects, with emerging evidence suggesting anticancer potential through modulation of cell proliferation and apoptosis.

- alkaloids, though less extensively characterized in *T. officinale*, include isobornyl thiocyanate, which has been identified in leaf and whole-plant extracts. Alkaloids in general are known for their pharmacological versatility, and while their specific activity in dandelion remains underexplored, they may contribute to its therapeutic properties.

- carbohydrates, especially inulin - a fructan polysaccharide reaching concentrations of up to 40% in roots during autumn - represent a significant nutritional and functional component. Inulin acts as a prebiotic, promoting gut microbiota health, and is also widely used in the food industry for its texturizing and metabolic benefits. Other sugars, including fructose, serve as storage carbohydrates and energy sources, particularly in the roots.

**Table II.** Phytochemical constituents identified in different parts of *T. officinale*, categorized by compound class and representative bioactive molecules.

No.	Plant product	Compound class	Main bioactive compounds	Reported Bioactivity	References
1	Leaves	Flavonoids	Luteolin, Quercetin Glycosides	Antioxidant, anti-inflammatory, antiproliferative	[20,21]
		Terpenoids	Taraxasterol, Taraxacin	Anti-inflammatory, cytotoxic	
		Phenolic Acids	Caffeoylquinic Acids	Antioxidant, hepatoprotective	
		Alkaloids	Isobornyl Thiocyanate	Potential antimicrobial	
2	Root	Phenolic Acids	Chicoric Acid, Caffeic Acid, Ferulic Acid	Antioxidant, immunomodulatory	[21,22]
		Terpenoids	Taraxinic Acid $\beta$ -D-glucopyranosyl ester, Ixerin D	Cytotoxic, anti-inflammatory	
		Sugars	Inulin	Prebiotic, metabolic modulator	
3	Flowers	Flavonoids	Luteolin-7-glucoside	Antioxidant, anti-inflammatory	[21,24]
		Terpenoids	Tricosane	Unknown	
		Phenolic Acids	Chicoric Acid, Moncaffeoyltartaric Acid	Antioxidant, immunomodulatory	
4	Latex	Sesquiterpene Lactones	Taraxinic Acid $\beta$ -D-glucopyranosyl ester	Anti-inflammatory, cytotoxic	[22-24]
		Triterpenoids	Lupeol Acetate, $\beta$ -Amyrin Acetate	Antiproliferative, anti-inflammatory	
5	Aerial parts	Terpenoids	Phytol, Lupeol, Taraxasteryl Acetate	Antioxidant, anti-inflammatory	[22-24]
		Sterols	$\beta$ -Sitosterol, Cycloartenol Acetate	Anti-inflammatory, cholesterol-lowering	
6	Whole plant	Alkaloids	Isobornyl Thiocyanate	Potential antimicrobial	[23-25]
		Flavonoids	Luteolin, Quercetin	Antioxidant, chemopreventive	
		Terpenoids	Saponins	Immunomodulatory, antitumor	
		Phenolic Acids	Moncaffeoyltartaric Acid, Chicoric Acid, Chlorogenic Acid	Antioxidant, anti-inflammatory	

Beyond its phytochemical diversity, *T. officinale* exhibits a valuable nutritional profile, comprising essential vitamins (A, C, E, K), minerals, proteins, fiber, and unsaturated fatty acids. The aerial parts and leaves, in particular, are nutritionally dense and may contribute to the plant's overall health-promoting potential. This complex combination of nutrients and bioactive compounds supports the broad therapeutic applications of *T. officinale* in natural medicine, functional foods, and pharmaceutical development, emphasizing the need for further mechanistic and clinical investigations [22,24,25].

### Anticancer activity of *T. officinale* extracts

Various parts of *T. officinale*, including leaves, roots, stems, flowers, and the whole plant, have demonstrated anticancer activity in both *in vitro* and *in vivo* models. These effects are attributed to different extract types (aqueous, ethanolic, methanolic, non-polar) and are mediated through mechanisms such as apoptosis induction, inhibition of cell proliferation, mitochondrial dysfunction, immune

modulation, and gene expression regulation.

*T. officinale* extracts have been widely investigated for their anticancer potential across various cell lines and experimental models. A schematic summary of the major extract types, target cancer cell lines, and proposed mechanisms of action is presented in table III.

### Aqueous extracts

Aqueous extracts, in particular, have demonstrated broad-spectrum cytotoxicity. One study reported antitumor effects against 14 cancer cell lines, including HeLa, MCF-7, SK-BR-3, MDA-MB-231 (breast), Ishikawa and AN3 Ca (endometrial), NIH: OVCAR-3 and SKOV-3 (ovarian), EJ28 and RT112 (bladder), SW620 (colon), PANC-1 (pancreatic), HuH-7 (hepatocellular), and A549 (lung), with IC<sub>50</sub> values ranging from 12 to 160 mg/mL. The extract induced apoptosis, inhibited migration, and caused mitochondrial dysfunction in ovarian cancer cells, while sparing normal fibroblasts (NHDF-C), suggesting cancer cell specificity [39,40].

**Table III.** Anticancer activity of *T. officinale* extracts.

Extract type	Plant part	Cancer cell lines / models	Concentration / IC <sub>50</sub>	Mechanism of action	References
Aqueous	Leaves, roots, whole plant	HeLa, MCF-7, SK-BR-3, MDA-MB-231, Ishikawa, AN3 Ca, NIH:OVCAR-3, SKOV-3, EJ28, RT112, SW620, PANC-1, HuH-7, A549	12–160 mg/mL	Apoptosis, inhibition of migration, mitochondrial dysfunction; cancer-cell selectivity	[26,27]
Aqueous polysaccharides	Whole plant	HepG2	2000 µg/mL (52% inhibition)	Direct cytotoxicity	[28]
Aqueous (cytokine-mediated)	Leaves	MCF-7/AZ, LNCaP C4-2B, Calu-6, HCT-116, SNU-601, HepG2	200 µg/mL (40–50% viability loss)	Immune-mediated cytotoxicity via TNF-α and IL-1α	[29-31]
<i>In vivo</i> (aqueous root)	Roots	DMBA-induced breast cancer (rat model)	Not specified	CA15-3 reduction; modulation of <i>Pdk1</i> , <i>Akt1</i> , <i>Pik3r1</i> , <i>ErbB2</i> ; decreased <i>Bcl2</i> expression	[30,31]
Methanolic	Roots	Huh7	Not specified	Apoptosis via JNK pathway (MKK7-TIPRL inhibition)	[32]
Ethanolic	Flowers	SK-OV-3	Not specified	Cell cycle arrest (S, G2/M); ↑ <i>p53</i> , <i>Bax</i> ; ↓ <i>BCL-2</i>	[33]
Ethanolic	Leaves	Cervical carcinoma stem cells	Not specified	↑ <i>RARβ2</i> , ↓ <i>Sox2</i> , impaired self-renewal	[34]
Ethanolic	Leaves	MCF-7 cells	Not specified	inducing apoptosis with lower toxicity toward normal hepatic (WRL-68) cells	[35]
Non-polar (methylene chloride)	Leaves, stems	SGT (oral squamous cancer), HL-60 leukemia	71–540 µg/mL	Strong cytotoxicity; higher potency in stems than leaves	[36,37]
Silver nanoparticles (TOL-AgNPs)	Leaves	HepG2, other models	200 µg/mL (up to 95% inhibition)	Enhanced cytotoxicity through nanoformulation	[38-40]
Root extracts (lncRNA modulation)	Roots	Gastric cancer cells	Not specified	Downregulation of <i>lncRNA CCAT1</i> ; reduced migration and invasion; sparing of normal gastric cells	[39]
Fruit extracts (neuroprotection)	Fruits	Rat brain tissue (ex vivo)	Not applicable	Antioxidant activity; inhibition of lipid peroxidation and free radical generation	[13]

In addition, aqueous polysaccharide fractions inhibited HepG2 hepatocellular carcinoma cell proliferation by 52% at 2000 µg/mL [41]. Another aqueous extract demonstrated 40–50% cell viability reduction in MCF-7/AZ, LNCaP C4-2B, Calu-6, HCT-116, SNU-601, and HepG2 lines after 48 hours at 200 µg/mL. This response was associated with increased levels of pro-inflammatory cytokines TNF- $\alpha$  and IL-1 $\alpha$ , indicating a potential immune-mediated mechanism. Similarly, an aqueous leaf extract from *T. officinale* was shown to induce cytotoxicity in HepG2 cells through the upregulation of TNF- $\alpha$  and IL-1 $\alpha$ , further supporting the role of cytokine-mediated pathways in its anticancer effects [42–44].

Further support for the antitumor potential of *T. officinale* comes from *in vivo* studies. In a rat model of DMBA-induced breast cancer, aqueous root extract significantly reduced serum CA15-3 levels and modulated key oncogenes such as *Pdk1*, *Akt1*, *Pik3r1*, and *ErbB2*. Histological examination revealed decreased epithelial proliferation and downregulation of *Bcl2* [45,46].

### Organic solvent extracts

Extracts prepared using methanolic and ethanolic solvents have also shown strong cytotoxic properties. A methanolic root extract induced apoptosis in Huh7 hepatocarcinoma cells via activation of the JNK pathway, mediated by inhibition of the MKK7-TIPRL signaling axis [47]. An ethanolic flower extract suppressed proliferation in SK-OV-3 ovarian cancer cells by inducing cell cycle arrest in S and G2/M phases. This was accompanied by upregulation of p53 and Bax and downregulation of BCL-2, indicating involvement of intrinsic apoptotic pathways [48]. Similarly, an ethanolic leaf extract increased RAR $\beta$ 2 expression and suppressed Sox2, impairing the self-renewal capacity of cervical carcinoma stem cells [49]. Furthermore, the ethanolic extract of *T. officinale* leaves exhibited significant cytotoxic activity against human breast cancer (MCF-7) cells, while showing lower toxicity toward normal hepatic (WRL-68) cells, which suggests a selective anticancer potential and highlights the importance of extraction method and plant part in evaluating the bioactivity of the plant [50]. Alcoholic extracts of *T. officinale* leaves demonstrated significant antiproliferative and antioxidant activities against human HL-60 leukemia cells, inducing apoptosis effectively [40]. These findings suggest the potential of leaf-derived alcoholic extracts in targeting leukemia cell growth through mechanisms involving oxidative stress modulation and programmed cell death.

### Non-polar extracts and nanoformulations

Non-polar fractions, particularly methylene chloride extracts, have shown potent cytotoxic effects. A study reported that methylene chloride extracts from *T. officinale*

leaves inhibited 97% of oral squamous cancer (SGT) cells at 200 µg/mL - surpassing the efficacy of methanolic and aqueous counterparts [51]. Moreover, stem-derived extracts exhibited greater cytotoxicity against HL-60 leukemia cells ( $IC_{50}$  = 71 µg/mL) compared to leaf-derived ones ( $IC_{50}$  = 540 µg/mL), suggesting differences in phytochemical composition [52].

Innovative formulations such as silver nanoparticles synthesized using aqueous leaf extracts (TOL-AgNPs) demonstrated enhanced cytotoxicity, achieving 95% inhibition of HepG2 cell proliferation at 200 µg/mL [53,54]. Similar nanoparticle systems also showed activity in other cancer models, highlighting the influence of delivery strategy on therapeutic efficacy [55].

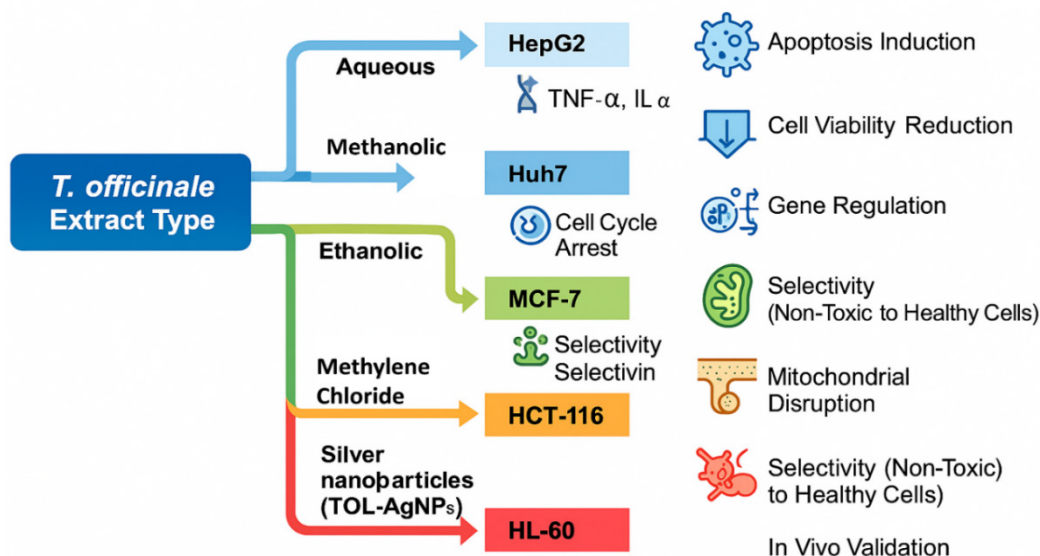
### Additional anticancer and protective effects

Beyond cytotoxicity and apoptosis, *T. officinale* extracts have also demonstrated effects on cancer cell migration and gene regulation. For instance, root extracts downregulated long non-coding RNA *CCAT1*, impairing the migration and invasion of gastric cancer cells while sparing normal gastric epithelium [56]. Moreover, fruit-derived extracts exhibited neuroprotective and antioxidant effects by inhibiting lipid peroxidation and free radical generation in rat brain tissue [13]. In an *in vivo* investigation, Modaresi and Resalatpour [32] evaluated the hematological effects of a hydroalcoholic extract of *T. officinale* in mice. The extract was administered intraperitoneally over a 20-day period, and its impact was assessed on several blood parameters, including red and white blood cell counts, hemoglobin concentration, and platelet numbers. While the study did not explore anticancer or cytokine-mediated mechanisms, it demonstrated that *T. officinale* extract may exert immunomodulatory effects by increasing white blood cell (WBC) and lymphocyte counts, suggesting a potential role in enhancing hematopoietic function [41,47].

These findings, derived from both *in vitro* and *in vivo* studies, highlight the complex and multifaceted anticancer potential of *T. officinale*. To provide a clearer overview of the main extract types, tested cancer cell lines and mechanisms of action, a schematic representation is provided in figure 1.

The diagram summarizes key findings from various studies, illustrating the relationship between extract types (aqueous, ethanolic, methanolic, silver nanoparticles, etc.), the targeted cancer cell lines (e.g., HepG2, MCF-7, SK-OV-3, HL-60), and the biological mechanisms involved. Reported actions include induction of apoptosis, inhibition of cell proliferation, gene expression modulation (e.g., p53, Bax, Bcl-2, RAR $\beta$ 2), immune response activation, and selective toxicity toward malignant cells. The figure was created by the author based on data compiled from references [13,39–58].





**Figure 1.** Overview of anticancer activities of *T. officinale* extracts.

As illustrated, aqueous and methanolic extracts were the most frequently studied, with significant activity observed against a variety of tumor cell lines. Moreover, specific extracts were shown to modulate genes and signaling pathways involved in apoptosis and cell cycle regulation, supporting the potential therapeutic relevance of *T. officinale* in oncology research.

Collectively, these findings suggest that *T. officinale* possesses multifaceted anticancer potential, modulated by extract type, plant part, and delivery system. Further studies are warranted to isolate active constituents and validate their mechanisms in clinical settings.

### Anticancer activity of bioactive compounds isolated from *T. officinale*

Taraxasterols, the main bioactive compounds in *T. officinale*, are involved in inhibiting cell proliferation and limiting tumor invasion, particularly in colon and breast cancer. Specifically, taraxasterol demonstrated a significant ability to block hepatocellular carcinoma cell multiplication by arresting the cell cycle in the G0/G1 phase, activating Hint1 and Bax (pro-apoptotic factors), reducing Bcl2 (anti-apoptotic factor) and cyclin D1 expression, and promoting demethylation in the Hint1 promoter region [25]. Furthermore, studies showed that taraxasterol inhibits papillary thyroid cancer cell migration and prevents epithelial-mesenchymal transition (EMT) induced by TGF- $\beta$  by decreasing the expression of matrix metalloproteinases MMP-2 and MMP-9 and blocking the Wnt/ $\beta$ -catenin signaling pathway, which plays a crucial

role in cancer progression [42].

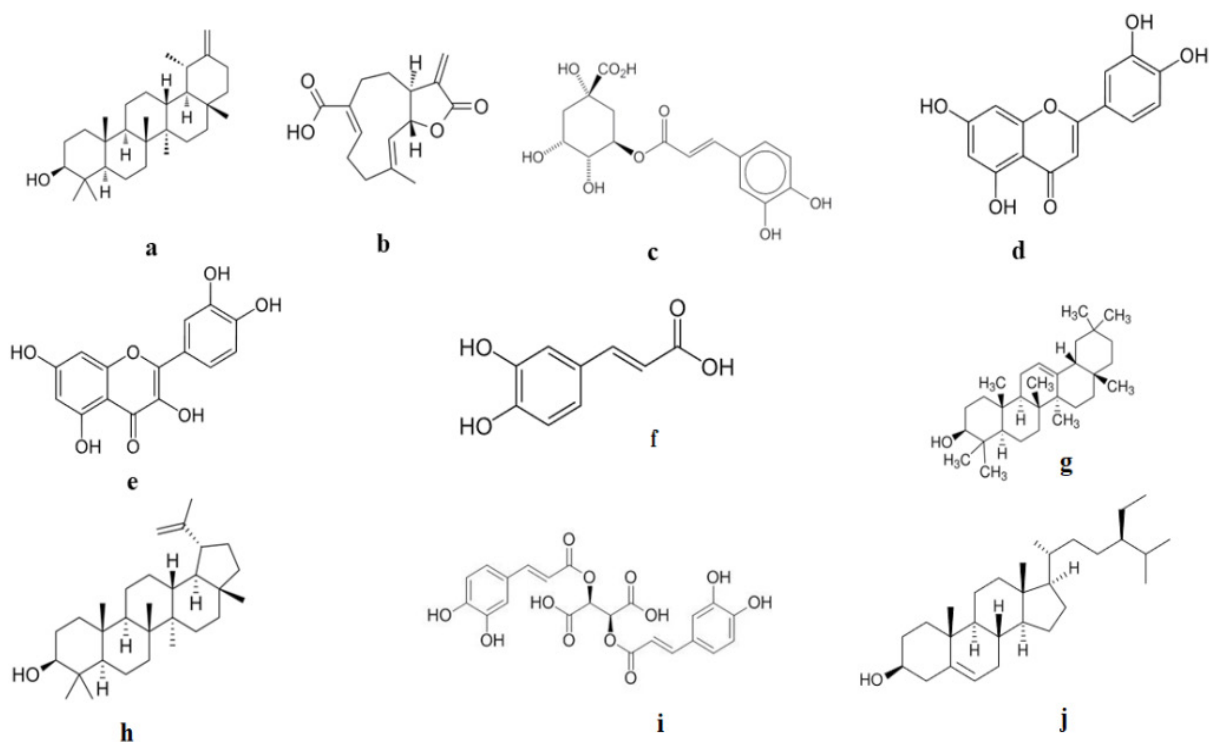
In addition, taraxinic acid exhibited antiproliferative activity against human HL-60 leukemia cells, promoting cellular differentiation and reducing *c-Myc* oncogene expression. This compound also stimulated cyclin-dependent kinase inhibitors p21<sup>CIP1</sup> and p27<sup>KIP1</sup>, suggesting potential therapeutic applications in leukemia treatment [26].

$\beta$ -sitosterol, a phytosterol present in *T. officinale*, has also shown promise, as it reduced the expression of the nuclear antigen of proliferating cells and inhibited the multiplication of cervical carcinoma cells (CaSki and HeLa). This inhibitory effect was associated with increased p53 mRNA levels and reduced HPV *E6* transcription, which is implicated in cervical cancer progression [43].

Similarly, chlorogenic acid inhibited hepatocellular carcinoma (HepG2) cell proliferation through ERK1/2 pathway inactivation and induced apoptosis in osteosarcoma cell lines (U2OS, Saos-2, MG-63 OS) via the same signaling pathway [44].

Moreover, chicoric acid reduced gastric cancer cell viability (SGC7901, MGC803) in a dose-dependent manner (5–100  $\mu$ M) through AMPK activation and autophagy induction [45].

Among the secondary metabolites, flavonoids such as luteolin and quercetin have demonstrated strong antioxidant, anti-inflammatory, and anticancer properties. These compounds are particularly abundant in the leaves and flowers, correlating with their traditional use in treating inflammatory conditions, liver disorders, and skin diseases [31].



**Figure 2.** Chemical structures of selected bioactive compounds from *T. officinale* with reported anticancer activity, including taraxasterol (a), taraxinic acid (b), chlorogenic acid (c), luteolin (d), quercetin (e), caffeic acid (f),  $\beta$ -amyrin (g), lupeol (h), chicoric acid (i),  $\beta$ -sitosterol (j).

Phenolic acids like caffeic acid, chlorogenic acid, and chicoric acid, found mainly in the root and leaves, contribute significantly to the plant's hepatoprotective, immunomodulatory, and antidiabetic effects. Their well-documented antioxidant activity not only supports cellular protection, but also the plant's use in glycemic control, by its capacity to inhibit  $\alpha$ -glucosidase enzymes [46].

In the same context, terpenoids such as taraxasterol,  $\beta$ -amyrin, and lupeol, commonly found in the aerial parts and roots, have been reported to exhibit anti-inflammatory, anticancer, and analgesic effects. These compounds help rationalize the use of *T. officinale* in managing rheumatism, tumor growth, and digestive disorders [47,59].

Moreover, the selective cytotoxicity of compounds like taraxasterol, as observed in molecular docking and *in vitro* studies, supports the growing interest in *T. officinale* as a source of antitumor agents. Their ability to bind with high affinity to oncological targets such as the A2B adenosine receptor, apelin receptor, and  $\beta$ 2-adrenoceptor further validates this potential [48,49].

The chemical structures of key anticancer compounds isolated from *T. officinale* are illustrated in figure 2, highlighting their structural diversity and potential mechanisms of action.

## Conclusions

The reviewed studies clearly demonstrate that *T. officinale* exerts its anticancer effects through multiple, well-documented mechanisms, including inhibition of cell proliferation, induction of apoptosis, disruption of mitochondrial function, modulation of inflammatory mediators, and regulation of key signaling pathways such as PI3K/Akt, JNK, and ERK1/2. These effects have been observed across a wide range of tumor cell lines, including breast (MCF-7), liver (HepG2, Huh7), ovarian (SK-OV-3), cervical (HeLa), and gastric cancer models, *both in vitro* and *in vivo*.

Specific bioactive compounds such as taraxasterol, taraxinic acid  $\beta$ -D-glucopyranosyl ester, chicoric acid, and chlorogenic acid have shown selective cytotoxicity toward cancer cells, with minimal effects on normal cell lines like NHDF-C and GES-1. Their ability to induce apoptosis and modulate the expression of pro- and anti-apoptotic genes (e.g., Bax, Bcl-2, p53) highlights their therapeutic relevance.

Furthermore, aqueous and ethanolic extracts from various plant parts (leaves, roots, flowers, latex) have demonstrated concentration-dependent effects, with  $IC_{50}$  values ranging from 12 to 200  $\mu$ g/mL depending on the model used.

In addition to its antitumor potential, *T. officinale* exhibits a broad pharmacological profile, including antioxidant, anti-inflammatory, hepatoprotective, and immunomodulatory activities—properties that could support conventional oncologic therapies and reduce treatment-related toxicities.

Despite these promising results, the clinical translation of *T. officinale*-based therapies remains limited by the lack of standardized extracts, variable bioavailability, and the absence of comprehensive human trials. Rigorous preclinical studies and well-controlled clinical investigations are urgently needed to validate its efficacy, safety, and pharmacokinetics.

In conclusion, *T. officinale* represents a promising candidate for integrative oncological approaches, combining low toxicity with multi-target antitumor mechanisms. Its bioactive compounds and extracts may offer cost-effective, plant-based alternatives or adjuvants to current cancer therapies.

### List of Abbreviations

- **DM** – Diabetes Mellitus
- **IC50** – Half maximal inhibitory concentration
- **AgNPs** – Silver nanoparticles
- **SK-OV-3** – Human ovarian cancer cell line
- **HL-60** – Human promyelocytic leukemia cell line
- **RAW 364.7** – Mouse macrophage cell line
- **SGT** – Oral squamous cancer cells
- **NHDF-C** – Normal Human Dermal Fibroblasts-

Classic

- **HepG2** – Human hepatocellular carcinoma cells
- **MCF-7** – Human breast cancer cell line
- **SK-BR-3** – Human breast cancer cell line
- **MDA-MB-231** – Human breast cancer cell line
- **AN3 Ca** – Human endometrial cancer cell line
- **OVCAR-3** – Human ovarian cancer cell line
- **RT112** – Human bladder carcinoma cell line
- **SW620** – Human colon cancer cell line
- **PANC-1** – Human pancreatic carcinoma cell line
- **HuH-7** – Human hepatocellular carcinoma cell

line

- **A549** – Human lung carcinoma cell line
- **LNCaP C4-2B** – Prostate cancer cell line
- **Calu-6** – Human lung carcinoma cell line
- **HCT-116** – Human colorectal carcinoma cell line
- **SNU-601** – Human gastric carcinoma cell line
- **TNF- $\alpha$**  – Tumor Necrosis Factor alpha
- **IL-1 $\alpha$**  – Interleukin 1 alpha
- **PI3K** – Phosphoinositide 3-kinase
- **Akt1** – Protein Kinase B alpha
- **MAP3K1** – Mitogen-activated protein kinase

kinase kinase 1

• **ErbB2** – Receptor tyrosine-protein kinase erbB-2 (HER2/neu)

• **TRAIL** – Tumor necrosis factor-related apoptosis-inducing ligand

• **JNK** – c-Jun N-terminal kinase

• **MKK7** – Mitogen-activated protein kinase kinase

7

• **TIPRL** – TOR signaling pathway regulator

• **lncRNA** – Long non-coding RNA

• **CCAT1** – Colon cancer associated transcript 1

• **EMT** – Epithelial-mesenchymal transition

• **MMP-2** – Matrix metalloproteinase 2

• **MMP-9** – Matrix metalloproteinase 9

• **SNP** – Sodium nitroprusside

• **AMPK** – AMP-activated protein kinase

• **Nrf2** – Nuclear factor erythroid 2-related factor 2

• **ERK1/2** – Extracellular signal-regulated kinases

1 and 2

• **Bax** – BCL2 Associated X, apoptosis regulator

• **Bcl-2** – B-cell lymphoma 2 protein

• **HPV** – Human papillomavirus

• **DPPH** – 2,2-diphenyl-1-picrylhydrazyl (radical scavenging assay)

• **ROS** – Reactive Oxygen Species

• **DMBA** – 7,12-Dimethylbenzanthracene

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