

## REVIEW

# Research Progress of Anti-tumor Active Ingredients in Dandelion

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### ABSTRACT

As a traditional Chinese herb, dandelion, containing complicated active ingredients which includes polysaccharide, flavonoid, terpene, pigment, phytosterol, coumarin, organic acid and etc, plays significant roles in various physiological activities in organisms. The active ingredients generally interfere in signal transduction of cancer cells, regulate cell cycle and apoptotic protein expression, inhibit cancer cells proliferation and migration and etc, which effectively restrains tumor development and deterioration. This article summarizes the anti-tumor mechanism of five active ingredients in dandelion through paper reading which provides thoughts and references for anti-tumor research.

## 1. Introduction

Radiation in physics, various chemical carcinogens and biological factors could cause tumorigenesis<sup>[1-3]</sup>. 9.6 million people around the world were estimated to have died from cancers in 2018 according to WHO and 1 out of 6 deaths is due to cancer, globally. New cancer cases rose to 18.1 million in 2018 based on WHO data statistics. Anti-cancer research remains hot topic for decades, besides surgery, radiation, immunotherapy, hormone therapy, stem cell transplant, precision medicine and targeted therapy, chemotherapy is a traditional and major method which uses drugs to kill cancer cells, whereas the correlated disadvantages decreased the therapeutic effect<sup>[4-9]</sup>. Traditional Chinese herbs are being used

to cure various diseases for thousand years in China, nowadays, effective ingredients extracted from herbs are being more and more popular in drug research, development and clinical trials<sup>[10-24]</sup>.

Dandelion, perennial plant, belongs to taraxacum genus of asteraceae family, also known as Yellow flower, Huanghua DeDing, Milk grass and etc, in China<sup>[25]</sup>. There are more than 300 species and 2000 subspecies of taraxacum, globally, and among those 70 species are discovered in China<sup>[26,27]</sup>. Dandelion tastes bitter, sweet, cold and return to the liver and stomach due to traditional Chinese medicinal literature. Dandelion harboring multiple active ingredients includes polysaccharide, flavone, terpene, pigment, phytosterol, coumarin, organic acid and etc<sup>[28,29]</sup>. Active ingredients of dandelion function mainly in anti-tumors,

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antioxidation, boosting immunity and bacteriostatic [30]. In this paper we reviewed several active ingredients with anti-tumor effect in dandelion and aimed to provide new thoughts and references in anti-neoplastic research, treatment and antineoplastic agents development.

## 2. Active Ingredient in Dandelion

Dandelion possesses abundant of protein (18.8%), amino acid, carbohydrate vitamins and etc, and besides concentrations of calcium [31], phosphorus and iron elements are higher than common fruits and vegetables [28,32,33]. Dandelion contains various active ingredients, for instance, taraxacin, taraxasterol, saponin, caffeic acid, chlorogenic acid, flavonoid, polysaccharide, volatile oil, choline, inositol and etc [28,32,34]. In addition to the illustrated active ingredients above, the whole dandelion herb harbors amaroid, resin, synanthrin, pectin and etc [35,36].  $\beta$ -sitosterol, stigmasterol, linoleic acid were identified in dandelion root, and xanthophyll, phylloquinone,  $\gamma$ -aminobutyric acid, sulfonyl amino acids, ornithine acid in dandelion leaf, and capretin, sarcohediol, lutein in dandelion blossom, and  $\beta$ -sitosterol, folate in pollen [28,29,37]. A total of 66 trace elements have been detected in dandelion and among those Cd, Cu, Zn, Fe, Mn and Mo essential trace elements are higher in contents [38] (Chinese paper with DOI: 10.3969/j.issn.1006-0111.2002.04.026). Dandelions contain up to 14.7  $\mu\text{g}/100\text{ g}$  of selenium which is considered a rare anti-tumor active substance in human body (Chinese paper with DOI: 10.3969/j.issn.1008-1445.2015.01.009). Dandelions, as a scarce selenium-rich plant in nature, has high nutritional and medical value, and is a veritable plant for both medicine and food [39,40]. Dandelions as a traditional herb is widely used to treat inflammation, constipation, stomach diseases, scald, tumor prevention and treatment, etc, in China, and those may correlate to the contained active ingredients [28,41-43].

## 3. Anti-tumor Active Ingredients in Dandelion

### 3.1 Dandelion Polysaccharide

Dandelion polysaccharide is one of the active component extracted from the whole dandelion grass and mainly gathering in root [44-46]. Dandelion polysaccharide functions in anti-tumor, boosting immunity, decreasing blood sugar and lipid, antioxidant and anti-aging [44,45,47-51]. Clinical trials have proved good effect of dandelion polysaccharide on anti-tumor [52,53]. Dandelion polysaccharide could induce melanoma cells and leukemia cells (Jurkat) apoptosis through caspase-8 and cause no harm to normal

cells [54,55].

### 3.2 Triterpenoid

Triterpenoids are widely distributed in plant kingdom and composed of 30 carbon atoms, polymerized to form six isoprene units [56]. Through promoting cell apoptosis, intervening cell signaling transduction and regulating cell apoptosis-related protein expression, triterpenoids realize anti-tumor effect [57-60]. Taraxerol and taraxeryl acetate both exhibit gastric cancer cell line AGS growth suppression, but taraxerol shows more significant in cell cycle arrest and apoptosis of AGS cell lines [61,62]. When taraxerol concentration reached 300  $\mu\text{mol}/\text{L}$  and action time achieved 72 hours, AGS cell line growth inhibition rate attained 99.1%. Taraxerol inhibited cell cycle at G<sub>2</sub>/M stage, thereby inhibiting AGS cells growth [62]. Shi segmented rat urine that were fed with dandelion extract with semi-prepared HPLC and divided into 11 subsections. The urine subsections were applied to MTT testing, and potential active sections were analyzed through UPLC-MS, and lupeol and taraxerol were detected in the subsections (Chinese paper with DOI:10.3724/sp.j.1123.2013.11010).

### 3.3 $\beta$ -sitosterol

Phytosterols are kinds of active ingredients in plant cell membrane which are structurally similar with animal sterol, such as cholesterol. Dandelion  $\beta$ -sitosterol belongs to phytosterols and plays significant roles in antagonizing cancers [63]. Previous studies had proved sitosterol inhibited lung cancer A549 and NCI-H460 cells growth through a dose-dependent manner and blocked cell cycle in G<sub>2</sub>/M phase [64-66]. Western Blot results showed expressions of tumor suppressive protein P53 and pro-apoptotic protein Bax increased along with  $\beta$ -sitosterol concentration, whereas expression of anti-apoptotic protein Bcl-2 decreased gradually (Chinese paper with DOI: 10.3969/j.issn.1673-4130.2016.07.001). Tumor cells experienced some morphological changes, such as density reduction, nuclear shrinkage and apoptotic body emerging after Dandelion  $\beta$ -sitosterol treatment [64].

### 3.4 Flavonoid

Flavonoid generally refers to a series of compounds formed by interconnecting two phenolic hydroxyl benzene rings through a central three-carbon chain, and its basic parent nucleus is 2-phenylchromogenic ketone [67,68]. Flavonoids are a large class of secondary metabolites having a structure based on or similar to flavone which are secreted by plant and fungus [69]. Flavonoid, harboring various physiological activities, attracts much

more attention, globally. Anti-cancer mechanism of flavonoids includes inhibiting the proliferation of cancer cells and inducing apoptosis, inhibiting cancer cells migration, inhibiting VEGF activation and thus inhibiting neovascularization<sup>[70-73]</sup>. Dandelion flavone suppressed esophageal cancer cell line TE-1 growth, and low concentration of flavone in the dandelion extract could not produce cell growth inhibition, but when dandelion flavone concentration reached to 80 µg/mL, inhibition rate of TE-1 growth attaining maximum that was 54.2% (A Chinese maser thesis with DOI: CNKI: CDMD:2.1016.215206). Anti-tumor effect of dandelion flavone was significant in cellular level *in vitro*, but not in human trails and animal model. The reason might be that dandelion flavone could not enter the circulatory system completely cause of dual barrier of small intestine and liver, leading to low bioavailability of flavonoids (a Chinese paper with DOI: 10.3969/j.issn.1007-8517.2009.22.001).

### 3.5 Organic Acid Compounds

The most common organic acids are carboxylic acids and widely distributed in animal, plant, and microbial sources, whose acidity is derived from the carboxyl group (-COOH)<sup>[74-76]</sup>. Dandelion organic acids mainly include chlorogenic acid, caffeic acid, ferulic acid, and etc<sup>[68,77]</sup>. Gallic acid can inhibit gastric cancer cells metastasis and invasive growth<sup>[78,79]</sup>. Studies have shown that chlorogenic acid has an inhibitory effect on human nasopharyngeal carcinoma cell line CNE-1 by activating tumor suppressor genes P27 and P16 and inhibiting the expression of cyclin D1 (a Chinese paper with DOI:10.7652/jdyxb201406022). Yoon found that chicory acid may play an important role in inducing apoptosis which worked as a novel TRAIL sensitizer for cancer cells<sup>[80]</sup>.

### 4. Pharmacological Research of Dandelion

Modern pharmacological studies have shown that 50% ethanol reflux extracts of dandelion dry plants can induce breast cancer cells arresting at G<sub>2</sub>/M stage and cell apoptosis through endoplasmic reticulum stress<sup>[52,81]</sup>. Researches proved that dandelion dried herbs decocted extracts exhibited anti-tumor properties and reduced liver cancer cell line Hep G2 survival rate about 26%, whereas tumor necrosis factor (TNF-α) and interleukin (IL-1α) increased significantly<sup>[58]</sup>. Dandelion whole grass decoction extraction had significant inhibitory effects on the proliferation of hepatocellular carcinoma cells and colorectal cancer Lovo cells *in vitro*, with inhibition rates of 23.34% and 30.33%, respectively, suggesting that they may have certain application value in cancer treatment (A Chinese

paper with DOI: 10.3969/j.issn.1004-2113.2005.04.010).

Dandelion whole herb decoction extract has a broad spectrum of bacteriostasis, including staphylococcus, streptococcus pneumoniae, beta hemolytic streptococcus, enterococcus, E. coli, klebsiella pneumoniae, sewer enterobacter, citrate coli, pseudomonas aeruginosa, h. influenzae, Branhamellacatarrhalis, and etc<sup>[48, 82, 83]</sup> (A Chinese paper with DOI: CNKI:SUN:ZWZX.0.2009-11-015). Dandelion extract had been used to treat skin diseases, clinically<sup>[84,85]</sup>. Modern pharmacological studies have shown that dandelion extract has certain effects on the gastrointestinal tract, mainly between the stomach and duodenum<sup>[32,70,86]</sup>. Previous studies demonstrated that dandelion extract could inhibit Helicobacter pylori (Hp) infection and then reduced gastric pain (A Chinese paper with DOI: 10.3969/j.issn.1000-7369.2011.06.078). Dandelion extracts had significant inhibitory effect on gastric acid secretion induced by histamine, penta-peptide and Carbamyl choline<sup>[62,87]</sup>. Dandelion had vital effect in gastric ulcer mucosal inflammation and erosion treatment<sup>[87]</sup>.

Dandelion extract improves T-lymphocyte activity and enhances macrophage phagocytosis index while dandelion polysaccharide promotes spleen and thymus growth and development which strengthens immune function in mice<sup>[88]</sup>. Dandelion extract could suppress glucosidase activity and reduce blood glucose in mice, therefore improving its immune function (A Chinese paper with DOI: 10.15889/j.issn.1002-1302.2016.08.005). Besides, dandelion extract holds strong oxygen radical scavenging activity and anti-inflammatory activity<sup>[44,50,89-91]</sup>.

### 5. Conclusion

Dandelion, as a kind of traditional Chinese medicine, has little toxic and side effects and high medicinal value which is widely used clinically in China (plenty of research papers in Chinese). The medicinal effect of dandelion may be due to the contained active ingredients. Dandelion possesses anti-cancer effect and the mechanism mainly includes interfering cell signal transduction, regulating expression of apoptosis-related proteins, suppressing carcinoma cells proliferation and migration, inhibition of angiogenesis, and so on<sup>[47,52,73,92,93]</sup>. To date, researches mainly focus on anti-cancer effect of dandelion whole grass extract which contains polysaccharides, flavones, organic acids, triterpenes, sterols and other active components<sup>[28,41,94,95]</sup>. However, the specific active components of extracts from different parts of dandelion have hardly been investigated. Therefore, it is great value to analyze and separate the anti-cancer active components of extracts from various parts of dandelion. Researches and developing of drugs has stepped into a new stage. Dandelion, as a

natural drug, has a good research prospect, and development and utilization of dandelion active ingredient is of great scientific significance for anti-tumor research.

### Conflict of Interests

The authors declare no conflict of interests.

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