Dandelion: Phytochemistry and clinical potential

Tabasum Fatima, Omar Bashir, Bazila Naseer and Syed Zameer Hussain

Abstract

*Taraxacum officinale* (dandelion), a member of the Asteraceae family, commonly found in the temperate zone of the Northern hemisphere, is a herb that grows to a height of about 12 inches, producing spatula-like leaves and yellow flowers that bloom year round. Dandelion is used in many traditional and modern herbal medical systems, as particularly has been documented in Asia, Europe, and North America. Dandelion is grown commercially in the United States and Europe, the leaves and roots are used in herbal medicine. It is commonly used as a food. Sesquiterpene lactones impart a bitter taste to the plant, which is especially notable in the leaf but also in the root particularly when spring-harvested. Preclinical research on dandelion has revealed numerous properties, including its actions as an inflammation modulator, diuretic, digestive stimulant, insulin stimulant, demulcent, prebiotic, immunomodulator, antiangiogenic, and anti-neoplastic. Dandelion root and leaf could protect against oxidative stress linked atherosclerosis and decrease the atherogenic index. Dandelion offers a compelling profile of bioactive components with potential anti-diabetic properties. *Taraxacum officinale* has been used in folk medicine in the treatment of hepatic and several diseases such as breast and uterus cancers. Dandelion extract has a potent inhibitory activity against HIV-1 replication and reverse transcriptase (RT) activity. Several flavonoids including caffeic acid, chlorogenic acid, luteolin, and luteolin 7-glucoside have been isolated from the dandelion. *Taraxacum officinale* leaves are rich in fiber, potassium, iron, calcium, magnesium, phosphorus, vitamins A and C, the B vitamins thiamine and riboflavin, and protein. The aim of this review is to evaluate the properties of dandelion with exploration of its diverse biological activities.

Keywords: Dandelion, diuretic, oxidative stress, sesquiterpene, type 2 diabetes

Introduction

History of using herbs to treat diseases and health gain has been common in human societies. Large numbers of drugs are being isolated and extracted from herbs. The medicinal plants and herbs are the sources of secondary metabolites and essential oils of therapeutic importance. The important advantages against the therapeutic use of medicinal plants in various ailments and disorders are their safety besides being economical, effective and easily available. *Taraxacum officinale*, commonly called Dandelion, is a herbaceous perennial belonging to family Asteraceae (Compositae) (Damyo et al., 1984) [8]. This herb usually has deeply toothed hairless leaves, 5–30cm long and 1–10cm wide. It grows 3–35cm in height, forming a rosette of leaves at ground level. It has single, golden yellow flowers on straight leafless hollow stems, which emerge from the centre of the rosette. Each flower consists of a collection of florets. Dandelion plants have tap roots, tapering from 2 to 3cm wide and at least 15cm in length. Roots are fleshy and brittle, and area dark brown color on the outside and white on the inside. It was native to Europe but now can be found throughout the northern temperate zones (Ali et al., 1989) [2]. Dandelion is a rich source of vitamins and minerals and is particularly high in vitamins A and C and iron, carrying more iron and calcium than spinach (Ali et al., 1989) [2]. The concerned plant is being consumed in the Kashmir valley from times immemorial as source of vegetable and for the lactating mothers as a source of minerals especially calcium. It is used for treatment of jaundice and disorders of the liver, gallbladder and other various hepatic ailments (You et al., 2010; Ahmed et al., 2013.) [26, 1]. The folk medicines of China, India, and Russia have recognized dandelion’s effect as a liver tonic. Traditional Chinese medicine combines dandelion with other herbs to treat hepatitis (Modaresi, 2012) [22]. Conventionally, root and herb from *Taraxacum officinale* (TO) has been reported to be used for the treatment of various ailments, including liver and gallbladder disorders. It is used to enhance the immune response to upper respiratory tract infections, bronchitis and pneumonia, and as a topical compress to treat mastitis, anemia and inflammation (Blumental et al. 2000) [18].

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Abstract

*Taraxacum officinale* (dandelion), a member of the Asteraceae family, commonly found in the temperate zone of the Northern hemisphere, is a herb that grows to a height of about 12 inches, producing spatula-like leaves and yellow flowers that bloom year round. Dandelion is used in many traditional and modern herbal medical systems, as particularly has been documented in Asia, Europe, and North America. Dandelion is grown commercially in the United States and Europe, the leaves and roots are used in herbal medicine. It is commonly used as a food. Sesquiterpene lactones impart a bitter taste to the plant, which is especially notable in the leaf but also in the root particularly when spring-harvested. Preclinical research on dandelion has revealed numerous properties, including its actions as an inflammation modulator, diuretic, digestive stimulant, insulin stimulant, demulcent, prebiotic, immunomodulator, antiangiogenic, and anti-neoplastic. Dandelion root and leaf could protect against oxidative stress linked atherosclerosis and decrease the atherogenic index. Dandelion offers a compelling profile of bioactive components with potential anti-diabetic properties. *Taraxacum officinale* has been used in folk medicine in the treatment of hepatic and several diseases such as breast and uterus cancers. Dandelion extract has a potent inhibitory activity against HIV-1 replication and reverse transcriptase (RT) activity. Several flavonoids including caffeic acid, chlorogenic acid, luteolin, and luteolin 7-glucoside have been isolated from the dandelion. *Taraxacum officinale* leaves are rich in fiber, potassium, iron, calcium, magnesium, phosphorus, vitamins A and C, the B vitamins thiamine and riboflavin, and protein. The aim of this review is to evaluate the properties of dandelion with exploration of its diverse biological activities.

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Wolbis et al., 1993 [34] carried out an analysis in which he mentioned and isolated various polyphenolic compounds from T. officinale plant extracts thereby showing that the plant is rich in various antioxidants and can have a direct effect of these phytochemicals on health of an organism. Cinnamic acid, coumarins and flavonoids and other phytochemicals bearing important medicinal and therapeutic importance have been isolated from different tissue of T. officinale plant by various analytical methods by Williams et al., 1996 [33]. Budzianowski et al., 1997 [35] has isolated a large number of Coumarins and caffeïльн tartaric acid from the leaves of T. officinale. Modern pharmacological research suggests this plant has broad-spectrum antibacterial (Woods-Panzarú et al., 2009) [36], anti-fungal (Odintsova et al., 2010) [37], antiviral, anti-diabetic, choleretic, antihypertensive, anti-inflammatory (Koh et al., 2010) [38], hepatoprotective, diuretic, and tumor apoptosis-inducing properties (Schutz et al., 2006) [39]. Virus cell-based fluorescence assay using pseudotype particles is an efficient and cost-effective screening system that has been used for primary screening of novel agents against HIV-1 (Lindsten et al., 2001) [32]. Pseudotyped viruses produced in this system can mimic most stages of the HIV-1 life cycle, including viral protein production, assembly, release, maturation, entry, integration and replication without producing replication-competent viruses. This approach has the potential to identify inhibitors against multiple viral and cellular functions essential for HIV. The results suggested that T. officinale extract has a potent inhibitory activity against HIV-1 replication and RT activity.

Chemical Composition
Among the most important compounds in dandelion are sesquiterpene lactones also known as bitter elements principally taraxacin and taraxacerin (Leung et al., 1996) [40], (believed to have anti-inflammatory and anticancer effects). Other related compounds include beta-amyrin, taraxasterol, and taraxerol, as well as free sterols (sitosterin, stigmastin, and phytosterin), phenylpropanoids (believed to have inflammationmodulating effects), triterpenoid saponins and polysaccharides (primarily fructosans and inulin), smaller amounts of pectin, resin (complexcarbohydrates). Three flavonoid glycosides – luteolin7-glucoside and two luteolin 7-diglucosides – have been isolated from its flowers and leaves. Hydroxycinnamic acids, choric acid, monocaffeyltartaric acid, and chlorogenic acid are found throughout the plant, and the coumarins, chiorriin, and aesculin have been identified in theleaf extracts (Williams et al., 1996) [33]. Dandelion leaves are a rich source of a variety of vitamins and minerals, including beta carotene, non-provitamin A carotenoids, xanthophylls, chlorophyll, vitamins C and D, many of the B-complex vitamins, choline, iron, silicon, magnesium, sodium, potassium, zinc, manganese, copper, and phosphorous.

Pharmacology
Dandelion leaf and root have both been studied for their effects on digestion, mostly as bitter digestive stimulants. Dandelion root has been investigated for demulcent, prebiotic, hypoglycemic, and immune-modulating effects. Dandelion leaf has also been investigated as a diuretic and inflammation modulator.

Demulcent and Prebiotic Activity
Dandelion roots have a distinct demulcent action and prebiotic properties due to their content of inulin. Sesquiterpenelactones impart a bitter taste to the plant, which is especially notable in the leaf but also in the root (particularly when spring-harvested). These compounds also likely explain the increase in bile production seen in animal studies with dandelion, with the studies themselves lending support to the traditional use of dandelion as a bitter digestive stimulant. One study showed that sesquiterpenelactones contributed to the inflammation-modulating properties of dandelion root. Other studies showed that crude extracts of both root and flower modulated inflammation, and some evidence suggests that phenylpropanoids might be key to this activity. Ethanol extracts of the dried aerial parts have been shown in rodent studies to reduce inflammation and inhibit angiogenesis, though which constituents were responsible for these effects were not investigated. For most clinical uses, dandelion has not been scrutinized rigorously according to modern scientific methods. Traditionally, the leaf is regarded as a useful bitter and moderately potent diuretic. The German Commission E approves the use of dandelion as a diuretic and also for use in anorexia, dyspepsia, and biliary abnormalities (Ali et al., 1989) [1].

Gastrointestinal Complaints
The use of dandelion leaf for indigestion or other atomic gastrointestinal complaints is also largely unverified by modern studies. However, a case series of 24 patients with nonspecific, chronic colitis treated with a formula consisting of dandelion (specifically, T. officinal), St John’s wort (Hypericum perforatum), lemon balm (Melissa officinalis), calendula (Calendula officinalis), and fennel (Foeniculum vulgare) demonstrated remarkable symptomatic improvement in terms of stool normalization and pain reduction (Racz-Kotilla et al., 1974) [31].

Anti-diabetic properties of dandelion and its components
The bioactive components in dandelion have demonstrated a series of anti-diabetic effects, which are due to the pharmacological actions of components such as sesquiterpene lactones, triterpenes/phytosterols (taraxasterol), phensols, flavonoids, and phenolic acids (Schützet al., 2006) [40]. The main factor in T2D is the dysregulation of insulin secretion and insulin sensitivity that leadsto increased blood sugar levels (hyperglycemia) and T2D, which can later cause the development of vascular diseases (Resnick et al., 2002) [26]. As T2D is both an epidemiophenomenon and a huge economic and social burden, many countries are becoming more reliant on anti-diabetic medicines (Onal et al., 2005) [24]. The root of dandelion contains inulin which includes fructooligosaccharides (FOS). FOS is a complex carbohydrate; its intake benefits bifido-bacteria, which eliminate pathogens in the gastrointestinal tract. As a result of mineral absorption, FOS stimulates the immune system, and thereby suppresses normal cell growth. This complex carbohydrate can help to normalize blood sugar levels. The plant extract reduces hyperglycemia when used in high levels of water extract. Chlorogenic acid (CGA) has been a potential compound for preventing obesity and inflammation. It also impacts on insulin secretion and sensitivity, making it an attractive option for use as a future
anti-diabetic drug.

**Action mechanisms of dandelion in Type -2 diabetes (T2D)**

T2D impacts many biological systems that influence the proper function of lipid metabolism, glucose metabolism, and insulin regulation. Glucotoxicity is the main energy source for most organs of the body and insufficient release of insulin by the β-cells to control glucose levels leads to metabolic disorders. Therefore, a possible explanation for the effects and mechanisms of dandelion on T2D could be its interaction with factors involved in the metabolic syndrome (lipid metabolism, glucose metabolism, protein metabolism, α- and β-cells dysfunction) (Grundy et al., 2004) [10]. The mechanisms by which plant-derived compounds manifest their anti-diabetic properties are (Mir et al., 2015) [21]:

1. Inhibition of renal glucose reabsorption.
2. Reduction of the activity of carbohydrate enzymes (α-amylase with β-galactosidase and α-glucosidase).
3. Reduction of dietary blood sugar (which stimulates hepatic glycolysis and glycogenesis).
4. Inhibition of potassium channel flow.

**Anti-inflammatory action**

Seo et al. (2005) [31] showed that dandelion leaf extract has anti-inflammatory properties, which may protect against cholecystokinin-induced acute pancreatitis in rats. Cholecystokinin is known to exert trophic effects in several species. *Taraxacum officinale* has been used to cure liver and gallbladder disorders, which is attributable to its content of terpenoid and bitter steroid components such as taraxacandin taraxacerin. Koo et al. (2004) [31] found that *Taraxacum officinale* induces apoptosis of human hepatoma (HepG2) cells through tumor necrosis factor α (TNF-α) and interleukin (IL) 1α secretion, implying anti-inflammatory effects within the central nervous system.

**Anti-oxidative properties**

It has also been shown that glucose may generate ROS in β-cells, implying that glucose-induced oxidative stress is a mechanism of glucose toxicity (Robertson et al., 2007) [20]. The process of ROS formation involves autoxidation, oxidative phosphorylation, glycosylation, and glucosamine pathways (Robertson et al., 2004) [29]. Excess ROS production requires anti-oxidant defense, which is provided by dandelion extract, as is known from several studies conducted both in vitro and in vivo (You et al., 2010) [30]. Flowers from dandelion are potential antioxidantrates, exerting their effect by way of their rich content of phenolic components including flavonoids, coumaric acid, and ascorbic acid. Their leaf extracts are effective hydroxyn donors, hydrogen peroxide scavengers, and reducing agents. Several studies have demonstrated the antioxidative effect of dandelion. According to Hagymasi et al. (2000) [31], extracts from dandelion and root are hydrogen-donating, ROS formation-inhibiting, and radical-scavenging. In another recent study of dandelion flower extracts, ethyl acetate fraction scavenged ROS by preventing DNA from ROS-induced damage. The prevention of oxidative stress was due to the presence of bioactive components including luteolin and luteolin7-O-glucoside.

**Action of dandelion on digestion, glycolysis, and Krebs cycle**

Mitochondria plays another critical role in the onset of insulin resistance as they are the site at which the Krebs cycle and fatty acid oxidation take place. Their dysfunction may cause the accumulation of fat in muscle tissue and subsequently the decrease of adenosine triphosphate (ATP) in membrane transport. Bioactive components in dandelion may be able to regulate these pathways, possibly via inhibition of certain enzymes that digest carbohydrates (Prabhakar et al., 2008) [25]. The pathways involved are the glycolytic cycle and Krebs cycle, in addition to other pathways involved in the release of insulin from β-cells. Cholegogenic acid and dandelion acid (CRA) may activate glucokinase in glycolysis, which catalyzes the phosphorylation of glucose to glucose-6-phosphate (G6P) (Coman et al., 2012) [7]. Glycolysis is a metabolic pathway in which a 6-carbon glucose molecule is oxidized to result in two pyruvic acid molecules. This glycolytic pathway mainly produces energy in tissues that remain in low-oxygenated blood cells. The catalytic reactions involve the actions of several enzymes, including phosphofructokinase, hexokinase, and pyruvate kinase. Bioactive components from medicinal plants such as dandelion are known to regulate enzymes such as hexokinase, glucokinase, and phosphofructokinase. These enzymes are involved in the processes of glycolysis and the Krebs cycle. Studies have shown that plants rich in CGA can improve the functional activities of these crucial enzymes (phosphofructokinase, hexokinase, and pyruvate kinase).

**Hepatoprotective Effects**

**Antioxidant Effect**

Oxidative stress is a common feature observed in a wide spectrum of chronic liver diseases including viral hepatitis, alcoholic, and nonalcoholic steatohepatitis. Oxidative stress leads to deleterious processes in the liver and produces liver diseases. Therefore, restoring antioxidants is essential to maintain homeostasis. One method of restoring antioxidants is suggested to consume natural compounds with antioxidant capacity (Casas-Grajales et al., 2015) [4]. Dandelion, a natural antioxidant compound has been empirically used due to its health-promoting properties as an anti-carcinogenic, anti-inflammatory, and anti-oxidant (You et al., 2010) [30]. Ethanol extract of *Taraxacum officinale* leaves and root extract significantly attenuated marker enzymes of liver toxicity, aspartate and alanine transaminases (AST and ALT), lipid peroxidation, and oxidative stress induced by acetaminophen in mice. The *Taraxacum officinale* extract has shown to possess the free radical quenching activities. This protective effects of *Taraxacum officinale* have been suggested due to the presence of phenolic compounds in the extract (Colle et al., 2012) [6]. In a recent study, ethanol and n-hexane *Taraxacum officinale* leaves extract significantly decreased the liver marker enzymes, superoxide dismutase (SOD), catalase, lipid peroxidation and glutathione peroxidase (GPx) in rats intoxicated with CCl4. The efficacy of *Taraxacum officinale* ethanolic leaves extract was found to be more effective as compared with n-hexane extract and silymarin against CCl4-induced hepatoxicity and oxidative stress in rats (Ahmed et al., 2013) [1]. In CCl4 induced oxidative stress model *Taraxacum officinale* extract reversed the glutathione (GSH) depletion, up-regulation of Nuclear factor-kb (NF-kB) and increased expression of regulatory inflammatory mediators, such as inducible nitric oxide synthase (iNOS), cyclooxygenase (COX)-2, Tumor necrosis factor-α (TNF-α) and interleukin (IL)-1α (Koh et al., 2010) [12]. These results suggest that
Taraxacum officinale have a hepatoprotective effect by modulating inflammatory responses and ameliorating oxidative stress. Alcohol is a leading cause of liver disease and is associated with significant morbidity and mortality. Alcohol induced liver diseases represents a spectrum of liver pathology ranging from fatty change to fibrosis to cirrhosis (Dugum and McCullough, 2015) [9]. The protective effects of Taraxacum officinale root against alcholic liver damage were investigated In vitro in HepG2/2E1 cells. In this study, ROS was generated by the administration of ethanol, this was consequent to decrease in cell viability by less than 40%. However, cells were simultaneously treated with ethanol and Taraxacum officinale hot water root extract, did not induce cytotoxicity as compare to ethanol alone treated HepG2/2E1 cells (You et al., 2010) [30].

Antifibrotic Effects
Hepatic fibrosis is common sequel following chronic liver injury and reversal of fibrosis prior it attains the cirrhotic stage would be a clear therapeutic strategy (Lee et al., 2015). Taraxacum officinale extract has been evaluated against the drug and chemical induced hepatic fibrosis in experimental animals and came out with promising results. The study suggested that administration of Taraxacum officinale promote the complete regression of fibrosis and the enchantment of hepatic regenerative capabilities.

Anticancer Activity
Hepatocellular carcinoma (HCC) is one of the most common malignancies, which accounts for 90% of primary liver cancer. HCC usually presents with poor outcomes due to the high rates of tumor recurrence and widespread metastasis (Mao and Wang, 2015) [19]. Recent results pointed out that natural products, in particular those present in Taraxacumroot extract, have great potential as non-toxic and effective alternatives to conventional modes of chemotherapy available today. Dandelion has been said to induce cytotoxicity in Hep G2 cells and decreases its viability below 40% (You et al., 2010) [30]. Taraxacum officinale extract significantly induced the secretion of TNF-α and IL-1 α and apoptosis of Hep G2 cells (Koo et al., 2004) [31]. These strategies are clearly implicated in anticancer efficacy of dandelion. In a very recent study it was found that relevant cytotoxic effect in T. lacustrumextract over HeLa and HepG2 cell lines (Mingarro et al., 2015) [20]. However, studies regarding the usefulness of Taraxacum officinale against liver carcinoma experimental models are scanty or not available in literature. Hence, further studies are warranted in animal models to prove the promising anti-cancer efficacies of Taraxacum officinale observed in vitro cancer cell line models i.e., Hep G2 and HeLa.

Inhibitory effect on HIV-1 replication and reverse transcriptase activity
Human immunodeficiency virus type 1 (HIV-1) is the causative agent of acquired immunodeficiency syndrome (AIDS). This disease represents a huge concern for globalpublic health. Currently, there is no effective vaccinefor HIV-1 (Cohen et al., 2007) [3] thus, prevention and antiviral drugs arethe only option to decrease morbidity and mortality inHIV-1-infected individuals. Several classes of antiretroviraldrugs have been developed targeting viral proteinasat different stages of the HIV-1 life cycle or host factors. Virus cell-based fluorescence assay using pseudo typeparticles is an efficient and cost-effective screening systemand has been used for primary screening of novelagents against HIV-19 (Lindsten et al., 2001) [17]. Pseudo typed viruses produced in this system can mimic most stages of the HIV-1 life cycle, including viral protein production, assembly, release, maturation, entry, integration and replication without producing replication-competent viruses. This approach has the potential to identify inhibitors against multiple viral and cellular functions essential for HIV replication (Kremb et al., 2010) [14]. The level of HIV-1 replication has been assessed by the expression of reporter genes represented by the percentage of GFP-positive cells. Reverse transcriptase assay kit was used to detect inhibitory effect on RT enzyme activity of dandelion. These results suggest that dandelion extract has a potent inhibitory activity against HIV-1 replication and RT activity.

Conclusion
The findings from literature overwhelmingly revealed that Taraxacum officinale (dandelion) is widely used in traditional and natural medicine systems worldwide. Taraxacum officinale (dandelion) has a significant antioxidant capacity as the leaves are rich in vitamin C, flavonoids and carotenoids. It can be a readily available source of minerals and antioxidants in human diet. Physico-chemical and sensory qualities of dandelion recommend to use its leaves as fresh salad, flowers and roots in acidic dairy or cheese for the content in carotenoids, chlorophyll and fiber that raise the nutritional value and appearance of products. Some promising research has been done with underlying reasons to screen different parts of this herbal plant for their anti-diabetic effect, hepatoprotective effects, antitumor effect, antileishmanial and anticancer effects. Dandelion has been credited to be safe with GRAS status. Since, there are currently insufficient data from well-conducted clinical trials so, extensive invitro, in-vivo, and clinical research is required to investigate further the pharmacological, physiological, and biochemical mechanisms underlying the health promoting effects of dandelion to promote its usage for therapeutic purposes.

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