

ARTICLE

PHARMACOLOGICAL EFFECT OF SEVEN MEDICINAL PLANTS AS A TRADITIONAL PREPARATION

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ABSTRACT

Medicinal plants have been utilized as a part of essentially all societies as a wellspring of medicine. Affirmation of the security, quality, and adequacy of therapeutic plants and natural products has now turned into a key issue in industrialized and in developing nations. Medicinal plant species are known for producing beneficial active compounds or secondary metabolites with many therapeutic values, for centuries. Traditional medicines or folk medicines in worldwide are the synthesis of the therapeutic experience of generations of practicing physicians of indigenous systems of medicine. Recently, Herbal products are increasingly used, mainly in human illnesses. This review investigates the available studies on the pharmacological effects of some medicinal plants (*Silybum marianum*, *Taraxacum officinale*, *Fumaria officinalis*, *Cynara scolymus*, *Cichorium intybus*, *Echium amoenum* and *Viola odorata*) on different human diseases. The present article incorporated a detailed interpretation of the seven medicinal plants, emphasizing its therapeutic uses, pharmacological properties such as anti-hyperlipidemic, anti-hepatitis, anti-obesity and antioxidant activities, and mechanism of action based on preclinical and clinical studies, safety issues along with the current research potential of the medicinal plants.

INTRODUCTION

Plants are among the main natural bio-factories on Earth, and are capable of producing many valuable and unique biochemical compounds. Medicinal plant species are known for producing beneficial active compounds or secondary metabolites with many therapeutic values, for centuries. Recently, the huge demand for the plant secondary metabolites to support various health and pharmaceutical purposes has put tremendous pressure on the planet's already depleting natural resources [1]. The modern pharmacological therapy is costly and associated with multiple side effects resulting in patient non-compliance. Thus there is a need to explore alternative therapies particularly from herbal sources as these are cost effective and possess minimal side effects. Plant secondary compounds are usually classified according to their biosynthetic pathways. Three large molecule families are generally considered: phenolics, terpenes and steroids, and alkaloids. A good example of a widespread metabolite family is given by phenolics: because these molecules are involved in lignin synthesis, they are common to all higher plants. For many of the medicinal plants of current interest, a primary focus of research to date has been in the areas of phytochemistry, pharmacognosy, and horticulture. In the area of phyto chemistry, medicinal plants have been characterized for their possible bioactive compounds, which have been separated and subjected to detailed structural analysis. Research in the pharmacognosy of medicinal plants has also involved assays of bio-activity, identification of potential modes of action, and target sites for active phytomedicinal compounds [2]. Traditional medicines or folk medicines in worldwide are the synthesis of the therapeutic experience of generations of practicing physicians of indigenous systems of medicine. In different traditional medicinal systems plants are the primary component to treat a diseases and subsequently so many plants, fruit, vegetable are used to keep the body healthy. The decision was based on two foundations; first, lack of access of a great number of people (up to 80% in some counties) to primary healthcare and second, dissatisfaction from the outcomes of treatments by modern medicine, especially in relation to chronic diseases and the side effects of chemical drugs [3]. Till date, numerous medicinal plants have been reported to be effective in different diseases, however plenty of research is still needed to be done. This article focuses on the various plants that could be effective in the treatment of illnesses.

Characteristics of seven medicinal plants

Silybum marianum, commonly known as 'milk thistle' (Family: Asteraceae/Compositae) is one of the oldest and thoroughly researched plants in the treatment of liver diseases. The plant itself grows as a stout thistle in rocky soils with large purple flowering heads. The leaves are characterized by milky veins, from which the plant derives its name [4].

Taraxacum officinale, the common dandelion (Often simply called "dandelion"), is a flowering herbaceous perennial plant of the family Asteraceae (Compositae). With a long history of traditional use in the treatment of hepatobiliary problems, its root has been shown to have sesquiterpene lactones, triterpenes, carbohydrates, fatty acids (myristic), carotenoids (lutein), flavonoids (apigenin and luteolin), minerals, taraxalisin, coumarins, and cichoriin. Aesculin has been reported from the leaf [5].

Fumaria officinalis (common fumitory, drug fumitory or earth smoke) is a herbaceous annual flowering plant in the poppy family Papaveraceae It is the most common species of the genus *Fumaria* in Western and Central Europe [6].

KEY WORDS

Medicinal plants; Anti-hyperlipidemic activity; Antioxidant activities; Anti-hepatitis Activity; Anti-cholesterol activity; Anti-obesity activity

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Cynara scolymus (artichoke) from Apiaceae family, a species of perennial thistle and with a Mediterranean origin, is traditionally used for the treatment of digestive disorders, moderate hyperlipidemia, and liver and bile diseases. The leaf extract of *C. scolymus* has been used for its hepatoprotective effects. Leaves contain several polyphenolic compounds flavonoids and sesquiterpenes (cynarin, luteolin, isochlorogenic acid, chlorogenic acid, caffeic acid and quinic acid [7].

Cichorium intybus is a perennial plant with blue or white flowers is easy to grow and can be used for many medicinal purposes. *Cichorium* means field and *intybus* are partly derived from the Greek "to cut," because of the leaves, and partly from the Latin *tubus* to indicate the hollow stem [8].

Echium amoenum (Borage) is a wild annual herb that belongs to Boraginaceae family which grows in large parts of Europe, Mediterranean region, and also in parts of Iran. The flowers and the leaves of borage are known as a traditional remedy and possesses antioxidant, analgesic, antibacterial, anxiolytic, antidepressant, and immunomodulatory properties. It is a rich source of anthocyanins including cyanidin and delphinidin [9].

Viola odorata commonly known as sweet violet in English, belongs to the family Violaceae. It is called Banafsha in Indo-Pakistan. The plant is native to Asia, North Africa and Europe. Its history as a medicinal herb dates back as far as 500 BC, where it was known to be used to relieve pain due to cancer. *Viola odorata* contains alkaloid, glycoside, saponins, methyl silylate, mucilage and vitamin C [10].

Anti- hyperlipidemic activity

The extract from roasted chicory (*Cichorium intybus*) root (chicory root extract), which contains inulin-type fructans, has favorable effects including anti-hyperglycemic and anti-dyslipidemic effects and the improvement of bowel movement [11].

It has been reported that hydroalcoholic extract of *Echium amoenum* has hypoglycemic effect on diabetic rats and leads to valuable changes in blood lipid profiles as well as lipoprotein levels [12]. *Viola odorata* leaf extract caused a reduction in total cholesterol and triglyceride levels in tyloxapol-induced dyslipidemia model, the plant extract caused significant decrease in total cholesterol, LDL-C and atherogenic index and prevented the increase in average body weight [10].

Cynara scolymus extract can be conducive to the reduction in phosphatidate phosphor hydrolase activity and liver triglyceride. *C. scolymus* has benefits for controlling of hyperlipidemia, oxidative stress in hyperlipidemic regimes, and abnormalities in lipid profiles [13].

Abd El Azeem et al., (2016) suggested that leaf extract of *Cynara scolymus* could be helpful in decreasing the incidence of several fatty liver disease through a reduction in TC, LDL and TG and an increase in HDL level. In addition, it appears to exert these effects through suppressing lipogenesis in the liver and promoting lipolysis in white adipose tissue [14].

The water extract of *C. intybus* showed an antioxidant effect on low density lipoprotein (LDL) and inhibitory effects on the production of thiobarbituric acid reactive substance and the degradation of fatty acids in LDL. Chicory root aqueous extract decreased cholesterol absorption by 30% in the jejunum and by 41% in the perfused ileum [Table 1] [8].

Anti-hepatitis activity

The extracts of milk thistle became a favored medicine for hepato biliary diseases in 16th century and the drug was revived again in 1960 in central Europe [4, 15]. In Silymarin, amongst the flavonoids, which have proven anti oxidative, antiviral or anti carcinogenic properties like glycyrrhizin, phyllanthin, silybin, picnoside and baicalein, can serve as primary compounds for further development as hepato protective drugs [4].

Even though silymarin does not affect viral replication it may have beneficial role in viral hepatitis by its inhibitory action on inflammatory and cytotoxic cascade of events induced by the viral infection. Also, it can improve the regeneration process and normalize the liver enzymes by its action on protein synthesis [16]. So it can use to treat alcoholic liver disease, acute and chronic viral hepatitis and toxin-induced liver diseases.

Among the many therapeutic properties that have been traditionally ascribed to the artichoke, the liver-protecting action is not certainly the least important, to the extent that its use was recommended to patients affected by hepatitis, jaundice, cirrhosis and liver steatosis. Cynarin and caffeoylquinic acids are thought to be the substances that are chiefly responsible for the protective action against such hepatotoxic agents as carbon tetrachloride [14].

The folkloric use of chicory as hepato protectant has been well documented. Ethanolic extract of chicory given orally at doses of 6, 18, and 54 mg/kg BW per day showed a significant hepato protective effect by reducing the liver enzymes (aspartate transaminase [AST] and alanine transaminase [ALT]). The results were highly significant at the dose of 54 mg/kg BW per day [Table 1] [8].

Anti-oxidant activity

Free radicals induced oxidative stress is now believed to be a fundamental mechanism underlying a number of human cardiovascular, neurologic and other disorders. Antioxidants are our crucial defense against free radical induced damage, and are critical for maintaining optimum health and wellbeing. Antioxidant properties of *Silybum marianum*, Free radicals, including the superoxide radical, hydroxyl radical (.OH), hydrogen peroxide (H₂O₂), and lipid peroxide radicals have been implicated in liver diseases. These reactive oxygen species (ROS) are produced as a normal consequence of biochemical processes in the body and as a result of increased exposure to xenobiotics [17]. The cyto protective effects of *silymarin* are mainly attributable to its antioxidant and free radical scavenging properties. *Silymarin* can also interact directly with cell membrane components to prevent any abnormalities in the content of lipid fraction responsible for maintaining normal fluidity [18].

The pharmacological rationale for the use of *silymarin* relates to its antioxidant action, selective inhibition of leukotriene formation by Kupffer cells as well as its antiapoptotic action. *Silymarin* is found in the entire plant but it is concentrated in the fruit and seeds. Silymarin acts as an antioxidant by reducing free radical production and lipid peroxidation, has anti-fibrotic activity and may act as a toxin blockade agent by inhibiting binding of toxins to the hepatocyte cell membrane receptors [17].

The artichoke leaf extract induces the concentration- dependent inhibition of induced oxidative stress in human neutrophils. Cynarin, caffeic acid, chlorogenic acid and luteolin have been found to be the active ingredients that play the major role in the antioxidant protective activity. The antiradical properties of aqueous and alcoholic artichoke extracts, as well as their capability of inhibiting lipid peroxidation, were recently confirmed [8].

Chicory has promising potential to be considered as a natural substance for ameliorating oxidative stress and hepatic injury induced by nitrosamine (sodium nitrite, 0.05% in DW) compounds. Red chicory was also studied for its polyphenol content and the antioxidant activity by using the synthetic 2, 2-diphenyl-1-(2, 4, 6-trinitrophenyl) hydrazyl radical scavenging activity. Total phenolic content is correlated with antioxidant activity in both the synthetic radical scavenging activity and the enzyme-catalyzed reactions (xanthine oxidase, myeloperoxidase, and diaphorase). A high level of anthocyanins, present in the seeds of *C. intybus*, might exert a direct scavenging effect against reactive oxygen species (ROS) formation due to antioxidant activity [8]. The antioxidant activity of violet flavonoids results from the combination of their iron chelating activity and their ability to scavenge the aging-inducing free radicals. Flavonoids can inhibit oxidases such as lipooxygenase (LO), cyclooxygenase (CO), mieloperoxidase (MPO), NADPH oxidase and xanthine oxidase (XO), thus preventing the in vivo formation of reactive oxygen species and organic hydro peroxide. Additionally, it has been found that flavonoids inhibit enzymes indirectly involved in oxidative processes, such as the A2 phospholipase and stimulate other enzymes with well-known antioxidant properties, such as catalase and superoxide dismutase (SOD). These are the mechanisms through which flavonoids interfere with the propagation of free radicals and also their formation [19]. *E. amoenum* (Boraginaceae) is known as a traditional remedy for depression and possesses antioxidant activity because of the presence of anthocyanin [Table 1] [9].

Anti-obesity activity

Obesity, a pathological condition characterized by excessive accumulation of body lipids, is by far the most prevalent metabolic disease affecting hundreds of millions of people worldwide. The leading cause of this excessive lipid accumulation is a chronic positive energy balance combined with energy partitioning toward lipids [20]. The number of people with obesity and obesity related diseases, such as diabetes mellitus, hypertension, coronary artery disease, and cancers, has increased at an alarming rate all over the world [21]. Consequently, the idea of developing anti-obesity drugs with no undesirable side effect has become a hot topic. Herbal medicine has been looked at as a complementary treatment [22].

Recent studies had shown that the *Cynara scolymus* L. leaf extract (CLE) is effective on visceral fat levels and hepatic lipid accumulation in mice with high fat diet-induced obesity. In addition [21, 22]. It has been found that the hydroalcoholic extract of Iranian *Echium amoenum* has hypoglycemic effects and can be used to prevent weight loss due to diabetes. These effects might be due to the presence of compounds such as flavonoids and saponins and some of the plant's antioxidant properties [Table 1] [12].

Other activities

It has been reported that chicory has anti-diabetic activity. The effect of methanolic extract of *C. intybus* (CME) on glucose transport and adipocyte differentiation in 3T3-L1 cells was studied by radiolabelled glucose uptake and lipid accumulation assays, respectively. CME exhibited a significant increase in glucose uptake with a dose-dependent response. It also inhibited the differentiation of preadipocytes [8].

Viola odorata leaves extract, which tested positive for alkaloids, saponins, tannins, phenolics, coumarins and flavonoids, caused a dose-dependent (0.1-1.0 mg/kg) decrease in mean arterial blood pressure in anaesthetized rats [10].

The anti-cancer activity of *Viola odorata* has been documented. Cycloviolacin O2 (CyO2), a cyclotide from *Viola odorata* (Violaceae) has antitumor effects and causes cell death by membrane permeabilization [23]. *Echium amoenum* induce antidepressant effective in part by increasing level CSF serotonin and dopamine [24]. Silymarin treatment produced significant reduction in daily and fasting blood glucose, daily glucosuria, glycosylated haemoglobin values, malondialdehyde values and a drop in insulin requirement and fasting insulinaemia [25].

Taraxacum officinale is a rich source of a variety of vitamins and minerals, including beta carotene, nonprovitamin 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. *Taraxacum officinale* might possess blood sugar modulating activity [26]. *Taraxacum officinale* also can restore experimentally-induced suppressed immune function in animals by enhancing cell-mediated, humoral, and non-specific immunity [27]. Evidence also suggests *Taraxacum officinale* influences nitric oxide production [28].

Phytochemical effects of *Fumaria officinalis* related to several alkaloids such as adlumidicine, copticine, fumariline, perfumine, protopine, fumaranine, fumaritine, paprafumicin and paprarine [29]. Extracts of *Fumaria officinalis* have been traditionally used for treatment of some skin diseases (rashes or conjunctivitis), rheumatism, stomach ache, abdominal cramps, fever, diarrhea, syphilis and leprosy. *Fumaria* extracts also possessed strong antihypertensive, diuretic, hepato protective and laxative effects, mainly because of the isoquinoline alkaloids [30]. Herbal medicinal study of *Fumaria* has shown that it used for the treatment of diabetes mellitus, hypertension diseases and cardiac disorders [31]. It also has anti-bactericidal activity against the Gram-positive organisms like *Staphylococcus* and *Bacillus anthracis*.

A few compounds found in the *Cynara scolymus* (artichoke) exhibited a significant hypo glycemizing activity. Chlorogenic acid was identified by Arion and collaborators as a powerful and specific glucose-6-phosphate-translocase inhibitor. This enzyme is essential for the formation of endogenous glucose during the gluconeogenesis process, as well as for the glycolytic process. Artichoke leaf extracts was proved to have anti carcinogenic, anti-oxidative, anti-inflammatory, antibacterial, anti HIV, bile expelling, and urinate activities as well as the ability to inhibit cholesterol biosynthesis and LDL oxidation [Table 1] [32].

Future direction

Considering therapeutic potential of these seven medicinal plants in terms of their efficacy and adaptability is such that combination of them as one organic product can be noticed in future, since obesity, hyperlipidemia and fatty liver are becoming more epidemic around the world especially in developing countries as an organic product by using local knowledge can reduce many problems associated with the use of chemical drugs and their side effects to a large extent.

Table 1: Seven medicinal plants with evidence of their activities

Plant	Plant part used	Bioactive compounds	Screened activity
<i>Silybum marianum</i>	seeds	silymarin	Anti-hepatit, antioxidative, antiviral or anticarcinogenic [4]
<i>Taraxacum officinale</i>	Roots and leaves	sesquiterpene lactones, triterpenes, carbohydrates, fatty acids (myristic), carotenoids (lutein), flavonoids (apigenin and luteolin), minerals, taraxalisin, coumarins, and cichoriin	Anti-bacterial, anti-inflammatory, anti-hepatitis and appetizer [26, 28]
<i>Fumaria officinalis</i>	Leaves, flowers and stems	adlumidicine, copticine, fumariline, perfumine, protopine, paprafumicin and paprarine	Amphicholeratic, appetizer, antihypertensive, diuretic, hepatoprotective and laxative effects and anti-diabetic [30]
<i>Cynara scolymus</i>	Leaves	cynarin, luteolin, cynaroside, scolmoside; phenolic acids such as caffeic, coumaric, hydroxycinnamic, ferulic, caffeoylquinic acid derivatives	Anti-hepatitis, anti-cholesterol, anti-carcinogenic, antioxidative, anti-inflammatory, antibacterial, anti HIV [32]
<i>Cichorium intybus</i>	Roots and leaves	thiobarbituric acid, inulin-type fructans, phenol, flavonoid, tocochromanol (tocopherol and tocotrienol)	Anti-hyperglycemic, anti-dyslipidemic, anti-oxidative, anti-cholesterol, and anti-diabetic [8]
<i>Echium amoenum</i>	Leaves and flowers	phenolic compounds like rosmarinic acid, cyanidin, and delphinidin	Anti-obesity, anti-hyperlipidemic, anti-cholesterol, antibacterial, anti-diabetic, anti-oxidative and anti-depressant [25]
<i>Viola odorata</i>	Leaves and flowers	alkaloid, glycoside, saponins, methyl silylate, mucilage and vitamin C, Cycloviolacin O2 (CyO2)	Anti-hyperlipidemic, anti-cholesterol, anti-depressant, anti-blood pressure, anti-cancer and anti-tumor [23]

CONFLICT OF INTEREST

There is no conflict of interest.

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