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Gundelia: A Systematic Review of Medicinal and Molecular Perspective

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Abstract: Gundelia (*Gundelia tournefortii* L.) is a member of the Asteraceae (Compositae) family which grows in the semi-desert areas of Iran, Jordan, Palestine, Syria, Iraq, Syria, Azerbaijan, Armenia, Anatolia and other countries. Traditionally, *G. tournefortii* (L.) is used for treatment of liver diseases, diabetes, chest pain, heart stroke, gastric pain, vitiligo, diarrhea and bronchitis. It is also reported to have hypoglycaemic, laxative, sedative, anti-inflammatory, anti-parasite, antiseptic and emetic effects. It has enhanced gingivas and removed water from patients having spleenomegaly. Compounds found in gundelia proved to have several pharmacological effects, e.g. antibacterial, anti-inflammatory, hepatoprotective, antioxidant, antiplatelet and hypolipemic activities. The observed pharmacological properties indicated a close association of these effects with infectious diseases, digestive disorders, high blood pressure and cancer. In traditional medicine, this plant has been prescribed in many disorders; therefore, clinical trials on the compounds of gundelia seem essential. This study gives an overview of traditional uses of gundelia, irrespective of pharmacological studies on its effects.

Key words: Medicinal plants, liver diseases, antibacterial, anti-inflammatory, antioxidant, antiplatelet, hypolipemic

INTRODUCTION

Medicinal plants are amply used in folk medicine in different parts of the world and are considered as pivotal in human health care. There has been a renewed interest in medicinal plants in recent years, culminating in the discovery of new biologically active molecules by the pharmaceutical industry and the use of plant crude extracts for self-medication in general. A detailed study of plants employed in local health traditions as well as their pharmacological assessment and taxonomical relatives can be conducive to the development of invaluable plant drugs for many hard-to-cure diseases such as cancer (Shirzad *et al*., 2011; Azadmehr *et al*., 2011), atherosclerosis (Asgari *et al*., 2012; Rafieian-Kopaei *et al*., 2011) or diabetes (Asgary *et al*., 2011).

One of important medicinal plants easily found in nature and used in local health traditions is Gundelia. In this study, we investigated, in detail, traditional and pharmacological properties of this plant.

Botanical specifications, geographic distribution and ecology: *Gundelia tournefortii* L. [Asteraceae (Compositae)], grows in the semi-desert areas of many countries including Iran, Syria, Iraq, Azerbaijan, Jordan, Palestine, Armenia and Turkey (Karis *et al*., 2001; Coruh *et al*., 2007; Cakilcioglu and Khatun, 2011; Matthaus and Ozcan, 2011). In folk medicine, Gundelia species have utilities as herbal medicine. Recently two new well-defined localities of Gundelia, i.e., *G. tournefortii* and *Gundelia rosea* have been suggested in Armenia, with different distribution areas, different flower shapes and different pollinators (Vitek and Jarvis, 2007). In Flora Iranica, only *G. tournefortii* is addressed. A look at the Iranian collections results in this supposition that all collections from the Flora Iranica could, in reality, belong to *G. rosea* (Rechinger, 1989). In the Flora of Turkey (Kupicha, 1984) only *G. tournefortii* is recognized for its flower color as "white, yellow, green, maroon or red" and the hairiness as "smooth or arachnoid". Both species grow widely in Turkey. However, *G. rosea* is more observed in regions near Iranand Armenia. In Flora Armenii (Avetisian, 1995) *G. rosea* is considered as a synonym of *G. tournefortii*. In addition to fruit characters, the color of the corolla is considered as the main distinguishing character: "bright to light yellow inside, rusty brown or sometimes purple" for *G. tournefortii* versus "bright to light pink inside, never yellow, deep purple outside, never rusty brown" for *G. rosea*. Nothing is mentioned about the hairiness of the leaves (Vitek and Jarvis, 2007).

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Gundelia is common name of *G. tourenfortii* and tumbleweed, akub (kuub or aqub) and kanger, respectively, are English, Arabic and Kurdish equivalents for this plant. *G. tourenfortii*, locally known as "kangar" in Iran, is found as a wild herb growing during late winter and early spring on the hills of western, northwestern, south and southeastern parts of Iran (Vivian, 1996; Jamshidzadeh *et al*., 2005; Duke, 2008; Haghi *et al*., 2011; Mosaddegh *et al*., 2012).

In Jordan and the Mediterranean areas including Palestine and Syria, this plant is locally known as akub (Halabi *et al*., 2005). Also *G. tournefortii* var. armata Freynet Sint. is known as "kenger" in Arat Mountain (Akan *et al*., 2008). But in Maden and Ankara of Turkey *G. tournefortii* var. tournefortii is known as "kenger" (Cakilcioglu *et al*., 2011).

G. tournefortii, as hemicryptophytes, have a thick perennial rootstock from which new seasonal growth occurs. *G. tourneforti*, as one of the naturally growing plants, is a perennial spiny herb of Irano-turanian origin (Lev-Yadun and Abbo, 1999; Halabi *et al*., 2005; Karabulut *et al*., 2006). After the autumn rains and during the winter to late spring, depending on the rainfall and temperature of the season, the plants develop a new rosette. Spine is specific feature of the lobed and mostly smooth leaves that have either a red, yellow, or purple central vein (Lev-Yadun and Abbo, 1999; Halabi *et al*., 2005). The rosette diameter may reach 50-60 cm. At elevations of 2000 m above sea level, sometimes covered by snow during the winter, *G. tournefortii* plants gradually develop their rosette. From March to April, the plants develop a central stem that holds about a dozen inflorescence branches. In case of large specimens, the height of total plant accompanied by this branched inflorescence, may amount to 50 cm. In the end of inflorescence branches is a compound spiny ovoid head with a diameter of 4-8 cm (Aburjai *et al*., 2001; Gnanadesigan *et al*., 2011). In maturation, the above ground parts of the plant dry and late spring to early summer, they become separated from the root and disseminate their fruits (Lev-Yadun and Abbo, 1999; Halabi *et al*., 2005). Before dying, they detach from the root and are pushed around by the wind, disseminating seeds for the following year's harvest (Yavuz *et al*., 2011).

G. tournefortii grows well in different localities. The plant, is not able to grow in shade, but prefers sandy and loamy or acid, neutral and alkaline, drained and moist soils (Hedrick, 1972; Jeffrey, 2007; Matthaus and Ozcan, 2011).

Non-clinical popular application: The stems, flowers, leaves, seeds and of *G. tournefortii* could be used as food (Hedrick, 1972; Coruh *et al*., 2007; Sarper *et al*., 2009). The young leaves are used in soup (Aburjai *et al*., 2001; Matthaus and Ozcan, 2011). In western and central Anatolia of Turkey *G. tournefortii* is used as roasted, salad and pickled. For example, its fruits are treated with vinegar, or lemon with salt and used as a garnish (Dogan *et al*., 2004). In Haymana District of Ankara, stem spiny part and stem of fresh plant are pounded and the juice obtained is applied on swelled part on neck (Sarper *et al*., 2009). The plant is also collected and dried for winter fodder (Lev-Yadun and Abbo, 1999). In the Middle East, undeveloped flower buds are locally available just like artichoke hearts (Hedrick, 1972; Halabi *et al*., 2005; Duke, 2008). The oil-rich ripe nuts are considered as a kind of tasty dish. Thick stems, flower buds, leaves and roots may be consumed as food while toasted seeds are consumed as kenger coffee (Duke, 2008). In the Palestinian traditional culture and ethnobotany, its roots are used as vegetables and consumed as fried in olive oil especially in an omelette. *G. tournefortii* inflorescence and leaves are an ingredient of akoob in which the inflorescence, young stems and leaves are fried by olive oil, then accompanied with meat chops, boiled and after it gets well done and a boiled yogurt suspension is introduced, the mixture will be left to boil (Ali-Shtayeh *et al*., 2008). Mature tumbleweed hay is sometimes used for feeding camels (Bailey and Danin, 1981; Kamalak *et al*., 2005). When young heads are still at ground level, they are eaten as a fresh or cooked artichoke-like vegetable by several ethnicities in the Palestine, Israel and surrounding countries (Lev-Yadun and Abbo, 1999; Duke, 2008).

In Jordan, *G. tournefortii* is available especially in north and in certain stores in Amman. In Syria, *G. tournefortii* is sold in the Hamadia Sook of Damascus and other cities. The stalk of *G. tournefortii* is used in different parts of Iran as an occasional food in different forms and also as a folk remedy. According to the Persian traditional medicine, the stalk of the plant ishepatoprotective and blood purifier (Jamshidzadeh *et al*., 2005; Haghi *et al*., 2011). In Kurdistan, Iran, *G. tournefortii* straw is used in preparing dung cakes.

In northeast Lebanon, *G. tournifortii* is considered a nutritious food. It is not eaten during summer and autumn and the main edible part is the stalk and consumed specially if freshly gathered, usually eaten cooked (Jeambey *et al*., 2009). Lebanese propose its latex for burning off warts, drying up sores and as an emetic and snakebite cure (Duke, 2008).

The results of a study indicated that *G. tournefortii* could accumulate phytoremediation of the soils polluted with metals (Chehregani *et al*., 2009). In addition, *G. tournefortii* had high potential for accumulating

arsenic, perhaps very effective for removing contamination from soils (Shahraki *et al*., 2008).

Phytochemical compounds: The nutritive values of *G. tournefortii* were evaluated by chemical composition *in vitro*, e.g. gas production and *in situ*, e.g. dry matter degradation (Kamalak *et al*., 2005; Haghi *et al*., 2011). All known phytochemical compositions of *G. tournefortii* are shown in Table 1. In addition, a selection of some important phytochemical compounds is shown in Fig. 1.

In a study tumbleweeds harvested at the proper stage of maturity offered considerable potential for ruminants during winter. There were also significant differences between chemical compositions of tumbleweed hays harvested at different stages of maturity (Kamalak *et al*., 2005).

Comparing chemical analysis of the oil of tumbleweed seeds and sunflower seeds indicated that oil, saponification number and unsaponifiable matter percents of tumbleweed are higher but its protein, ash and saponifiable matter percents are lower (Sharaf *et al*., 2004). Karabulut *et al*. (2006) concluded that chemical compounds of tumbleweed hay were better and crude protein concentration of tumbleweed was higher, compared to the others. However, crude fiber concentration of tumbleweed hay was lower. Tumbleweed hay was rich in phosphorus and iron in contrast to alfalfa hay and wheat straw.

Therapeutic uses in traditional medicine and pharmacopoeia of various countries: The use of *G. tournefortii* probably dates back to ancient times. As

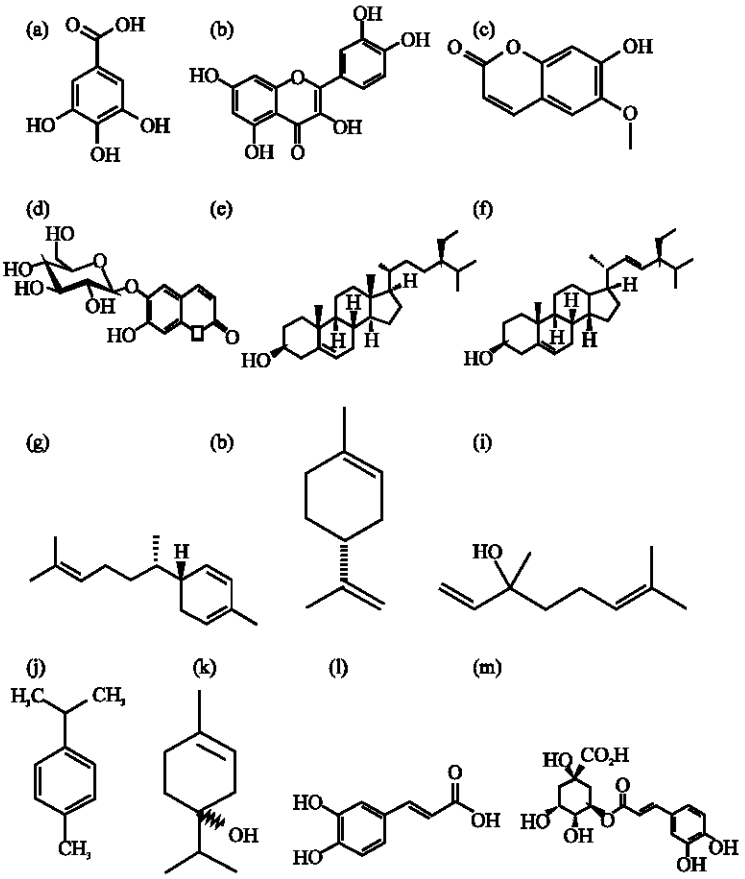

Fig. 1(a-m): Important phytochemical compounds of *Gundelia tournefortii*, (a) Gallic acid (C7H6O5), (b) Quercetin (C15H10O7), (c) Scopoletin (C10H8O4), (d) Aesculin (C15H16O9), (e) β-Sitosterol (C29H50O), (f) Stigmasterol (C29H48O), (g) Zingiberene (C15H24), (h) Limonene (C10H16), (I) Linalool (C10H18O), (j) Cymene, or p-cymene (C10H14), (k) Terpinen-4-ol (C10H18O), (l) Caffeic acid (C9H8O4) and (m) Chlorogenic acids (C16H18O9), (Galvez *et al*., 1994; Olthof *et al*., 2001; Clifford *et al*., 2003; Fahlbusch *et al*., 2005; Sultan *et al*., 2005; Matsuoka *et al*., 2008; Davis *et al*., 2009; Panda *et al*., 2009)

Table 1: Phytochemical compositions of tumbleweed (Haghi *et al.*, 2011; Halabi *et al.*, 2005; Erciyes *et al.*, 1989; Matthaus and Ozcan, 2011; Karabulut *et al.*, 2006)

Compounds	Type and %	Isolated organs	Location	Methods
Scopoletin	Coumarins	Aerial parts	Jordan	GC-MS
Isoscopoletin	Coumarins	Aerial parts	Jordan	GC-MS
Esculin	Coumarins	Aerial parts	Jordan	GC-MS
3-δ-Carene	Monoterpenoids-<.05%	Aerial parts	Jordan	TIC chromatograms
2,4-Nonadienal	Alcohols-0.23%	Aerial parts	Jordan	TIC chromatograms
p-Cymene	Monoterpenoids-0.57%	Aerial parts	Jordan	TIC chromatograms
Limonene	Monoterpenoids-0.88%	Aerial parts	Jordan	TIC chromatograms
β-Terpinene	Monoterpenoids-0.17%	Aerial parts	Jordan	TIC chromatograms
α-Terpinolene	Monoterpenoids-0.08%	Aerial parts	Jordan	TIC chromatograms
Linalool	Monoterpenoids-1.40%	Aerial parts	Jordan	TIC chromatograms
Terpinen-4-ol	Essential oils-0.40%	Aerial parts	Jordan	TIC chromatograms
α-Terpineol	Monoterpenoids-1.25%	Aerial parts	Jordan	TIC chromatograms
Cuminal	Essential oils-2.73%	Aerial parts	Jordan	TIC chromatograms
Linalool acetate	Essential oils-0.47%	Aerial parts	Jordan	TIC chromatograms
Trans-Anethole	Phenylpropenes-0.47%	Aerial parts	Jordan	TIC chromatograms
Safrole	Phenylpropenes-0.40%	Aerial parts	Jordan	TIC chromatograms
Carvacrol	Monoterpenoids-3.19%	Aerial parts	Jordan	TIC chromatograms
α-Terpinyl acetate	Monoterpenoids-36.21%	Aerial parts	Jordan	TIC chromatograms
Eugenol	Monoterpenoids-6.70%	Aerial parts	Jordan	TIC chromatograms
α-Copaene	Sesquiterpenes-0.22	Aerial parts	Jordan	TIC chromatograms
Methyl eugenol	Monoterpenoids-12.57%	Aerial parts	Jordan	TIC chromatograms
β-Caryophyllene	Monoterpenoids-5.94%	Aerial parts	Jordan	TIC chromatograms
α-Humulene	Sesquiterpenes-1.65%	Aerial parts	Jordan	TIC chromatograms
α-Curcumene	Sesquiterpenes-3.10%	Aerial parts	Jordan	TIC chromatograms
Zingiberene	Monoterpenoids-3.10%	Aerial parts	Jordan	TIC chromatograms
α-Farnesene	Sesquiterpenes-2.59%	Aerial parts	Jordan	TIC chromatograms
β-Bisabolene	Sesquiterpenes-0.19%	Aerial parts	Jordan	TIC chromatograms
β-Sesquiphellandrene	Monoterpenes-2.54%	Aerial parts	Jordan	TIC chromatograms
Caryophellene oxide	Sesquiterpenes-1.26%	Aerial parts	Jordan	TIC chromatograms
Crude protein	11.2%	Aerial parts	Turkey	Solvent extraction
Crude fiber	31.3%	Aerial parts	Turkey	Solvent extraction
Crude ash	11.3%	Aerial parts	Turkey	Solvent extraction
Caffeic acid	Phenolic compounds	Aerial parts	Iran	HPLC
Neochlorogenic acid (3-COA)	Phenolic compounds	Aerial parts	Iran	HPLC
Cryptochlorogenic acid (4-CQA)	Phenolic compounds	Aerial parts	Iran	HPLC
Chlorogenic acid (5-CQA)	Phenolic compounds	Aerial parts	Iran	HPLC
Neochlorogenic Acid (NCGA)	Phenolic compounds	Aerial parts	Iran	HPLC
Cryptochlorogenic acid (CCGA)	Phenolic compounds	Aerial parts	Iran	HPLC
β-sitosterol	Sterols	Aerial parts	Jordan	GC-MS
Stigmasterol	Sterols	Aerial parts	Jordan	GC-MS
5-Avenasterol	Sterols-9.82%	Aerial parts	Turkey	HPLC
Campesterol	Sterols-6.02%	Aerial parts	Turkey	HPLC
7-stigmasterol	Sterols-3.68%	Aerial parts	Turkey	HPLC
7-avenasterol	Sterols-2.63%	Aerial parts	Turkey	HPLC
Cholesterol	Sterols-1.78%	Aerial parts	Turkey	HPLC
7-Campesterol	Sterols-0.75%	Aerial parts	Turkey	HPLC
24-methylencholesterol	Sterols-0.72%	Aerial parts	Turkey	HPLC
Molluscicidal	Saponins	Root	Iran	HPLC
linoleic	Fatty acids-62.04%	Seed	Turkey	Solvent extraction
Oleic	Fatty acids-23.43%	Seed	Turkey	Solvent extraction
Palmitic	Fatty acids-12.08%	Seed	Turkey	Solvent extraction
Stearic	Fatty acids-2.45%	Seed	Turkey	Solvent extraction
Stigma sterol	Sterols-18.52%	Flower bud	Turkey	HPLC
α-tocopherol	Tocopherols-48.9 mg/100 g	Flower bud	Turkey	HPLC
β-tocopherol	Tocopherols-1.1 mg/100 g	Flower bud	Turkey	HPLC
β-tocotrienol	Tocopherols-1.0 mg/100 g	Flower bud	Turkey	HPLC
α-tocotrienol	Tocopherols-0.4 mg/100 g	Flower bud	Turkey	HPLC
δ-tocotrienol	Tocopherols-0.1 mg/100 g	Flower bud	Turkey	HPLC
p8	Tocopherols-0.4 mg/100 g	Flower bud	Turkey	HPLC
β-sitosterol	Sterols-51.76%	Flower bud	Turkey	HPLC
Arachidic	Fatty acids-0.3%	Flower bud	Turkey	GC
Linolenic	Fatty acids-0.1%	Flower bud	Turkey	GC
Ca	Minerals	Flower bud	Turkey	Solvent extraction
K	Minerals	Flower bud	Turkey	Solvent extraction
P	Minerals	Flower bud	Turkey	Solvent extraction
Mg	Minerals	Flower bud	Turkey	Solvent extraction

Table 1: Continue

Compounds	Type and %	Isolated organs	Location	Methods
Na	Minerals	Flower bud	Turkey	Solvent extraction
Crude oil	11.35% to 39.17%	Flower bud	Turkey	Solvent extraction
Crude oil	16.2%	Flower bud	Turkey	Solvent extraction
Crude protein	12.6%	Flower bud	Turkey	Solvent extraction
Crude fiber	27.2%	Flower bud	Turkey	Solvent extraction
Crude ash	8.7%	Flower bud	Turkey	Solvent extraction
Stearic	Fatty acids-2.5%	Flower bud	Turkey	GC
Palmitic	Fatty acids-8.1%	Flower bud	Turkey	GC
Oleic	Fatty acids-28.5%	Flower bud	Turkey	GC
Linoleic	Fatty acids-57.8%	Flower bud	Turkey	GC

an occasional food, this plant or its extract has been used for prevention and treatment of liver diseases (Jamshidzadeh *et al*., 2005). In addition, it could relieve pain and inflammation (Oryan *et al*., 2011). Ethnobotanical survey of herbal remedies traditionally used in Kohgiluyeh va Boyer-Ahmad, Iran showed that root of *G. tournefortii* has antiparasitic effect for digestive system orally (Mosaddegh *et al*., 2012).

G. tournifortii is used among Jordanian Bedouins for the treatment of chest pain and heart stroke (Halabi *et al*., 2005) and to treat diabetes by the tribal people (Jarald *et al*., 2008). Traditionally, *G. tournefortii* is believed, in Lebanon, to have hypoglycemic and laxative properties (Khalil, 1995; Jeambey *et al*., 2009). In turkey, it is proposed to enhance gingivas and used as an appetizer (Cakilcioglu and Khatun, 2011). Its stem is used for treatment in case of gastric pain, diarrhea, bronchitis, inflammations and kidney. In addition, stem spiny part and stem of fresh plant are used as mumps (Sarper *et al*., 2009). The dry seeds of this plant are also known, in Eastern Anatolia folk medicine, to be effective for the treatment of vitiligo disease. Fresh seeds are effective diuretics and used in pickles (Coruh *et al*., 2007; Matthaus and Ozcan, 2011). In addition, this plant is used in folk medicine to remove water from patients with splenomegaly (Sezik *et al*., 2001; Halabi *et al*., 2005). In Duke's handbook of medicinal plants of the Bible, some of activities such as antiseptic, bactericide and emetic have been mentioned for *G. tournefortii*; it could also act as an inhibitor of multidrug resistance and a vulnerary agent.

Pharmacological effects

Antibacterial activity: Drug resistance to human pathogenic microorganisms has been recently reported from different parts of the world. Thus, the increasing incidence of multidrug resistant strains of microorganisms with reduced susceptibility to antibiotics highlights the need for seeking for new sources of antimicrobial agents (Sieradzki *et al*., 1999; Obeidat, 2011).

According to some of studies (Aburjai *et al*., 2001; Darwish and Aburjai, 2010) methanol extracts of the whole plant material of *G. tournefortii* acted as antibacterial against multi drug resistant *Escherichia coli* and *Pseudomonas aeruginosa*. These studies showed that when combined with penicillin G and erythromycin gundelia, full growth of standard strain of *P. aeruginosa* was possible while the growth of a resistant strain isolated from hospitalized patients was inhibited (Halabi *et al*., 2005).

Methanolic extract of *G. tournefortii* in combination with seven different antibiotics was investigated to monitor the synergic activities against *P. aeruginosa*, including a resistant strain. Their results showed that the effects of some compounds on the resistant and the standard strains varied significantly probably because of structural changes. Nearly all the plant parts combined with penicillin G and erythromycin helped full growth of the standard strain, while the combination with *G. tournefortii* and *Lepidium satium* L. inhibited its growth (Aburjai *et al*., 2001).

In another study, the inhibitory effects of methanol extracts of some Jordanian plants, such as *G. tournefortii* and their combinations with different antibiotics on the resistance of *Staphylococcus aureus* have been surveyed. Assessment of antibiotic resistant inhibitors of some plant materials showed that cephaloxin compounds accompanied with the plant materials against the resistant strain improved the antimicrobial activity. The antibacterial activity of gentamycin and chloramphenicol, when mixed with *G. tournifortii* methanol extract, was significantly improved against strains of *Staphylococcus aureus* (Darwish *et al*., 2002).

In a study of nineteen plants in Jordan, known for their antimicrobial property in folk medicine, it was indicated that extract of *G. tournefortii* L. generally enhanced activity against resistant strain. It also enhanced activity of clarithromycin against the resistant strain of *E. coli* (Darwish and Aburjai, 2010).

Study of phytocompounds and antibacterial effects of four medicinal plants' essence in Lorestan, Iran showed that essence of *G. tournefortii* leaves has bacteriostatic effect on *Staphylococcus* epidermis. Essence of leaves

has effect in concentration of 30 μ mL^{-1}, indicating bacteriostatic effect on Gram-positive cocci (Talei *et al*., 2007). In addition, a study on twenty native Iranian plants against 10 clinical isolates of *H. pylori* found that sixteen had good anti *H. pylori* activity. Majority of the plant extracts used in this study such as *G. tournefortii* had considerable in vitro activity against clinical isolates of *H. pylori* (Nariman *et al*., 2009).

However, the results of recent studies demonstrated that only root extracts of *G. tournefortii*, rather than the whole plant parts, are responsible for antimicrobial properties (Obeidat, 2011).

Inflammatory activity: Anti-inflammatory and antinociceptive effects of aerial parts of *G. tournefortii* on NMRI male mice indicated that the total extract with 0.3, 0.6, 1.2 and 2.4 g kg^{-1} doses had significant antinociceptive and anti-inflammatory effects. The most effective dose of extract was obtained at 2.4 g kg^{-1} and LD50 was obtained at 6.28 g kg^{-1} of animal weight. Finally the total extract significantly reduced the nociception and inflammation (Oryan *et al*., 2011).

Hepatoprotective activity: The effects of the hydroalcoholic extract of *G. tourenfortii*, in various concentrations, on carbon tetrachloride (CCl_4)-induced hepatotoxicity in rats showed that its extract could protect the liver against CCl_4-induced damages with doses of 200 and 300 mg kg^{-1}. Regarding *in vitro* studies, extract with concentrations of 0.2-0.8 mg mL^{-1} protected the cells against CCl4-induced cytotoxicity and its maximum protective effect was about 0.5 mg mL^{-1}, but concentrations of 1.0 mg mL^{-1} and higher increased the CCl4-induced cytotoxicity. The results confirmed the traditional beliefs on hepatoprotective effects of *G. tourenfortii*, however, it is possible that its extract with concentrations above 300 mg kg^{-1} have side effects on the liver and its toxic effect be higher than its protective effect (Jamshidzadeh *et al*., 2005; Kumar *et al*., 2011).

Antiplatelet activity: In phytochemical and antiplatelet investigation of *G. tournifortii*, the antiplatelet activity of the crude extracts, pure isolated compounds and the volatile oil of *G. tournifortii* on human platelet-rich plasma aggregation induced by arachidonic acid and adenosine-5-diphosphate was mentioned. The chloroform extract of *G. tournifortii* had a mild inhibitory effect on platelet aggregation induced by adenosine-5-diphosphate and arachidonic acid. The degree of aggregation inhibition induced by arachidonic acid was a bit higher than that induced by adenosine-5-diphosphate (Halabi *et al*., 2005).

Hypolipemic activity: Given the review of the literature, the list of the medicinal plants found in the local flora and used mainly by the inhabitants of remote areas and those plants recommended by the herbalists for their hypoglycemic activity is quite long, one of which is *G. tournifortii* (Hamdan and Afifi, 2004).

Study of hypolipemic effect of *G. tournifortii* oil and clofibrate on lipid profile of rats showed that gundelia oil could be considered a hypolipemic agent, enhancing nutritional and physiological status in rats and lowering atherogenic indices and liver Tc, but its effect is still less considerable than the effect of the hypolipemic clofibrate compound (Sharaf *et al*., 2004). In study of Mavi *et al*. (2011) inhibition of iron-fructose-phosphate-induced lipid peroxidation by ethanol extracts of 10 edible plants including *G. tournefortii* was examined in two different lipid systems (lecithin liposome and linoleic acid emulsion). Oxidation of lecithin liposomes was measured by Thiobarbituric Acid Reactive Substances (TBARS) and oxidation of linoleic acid emulsions by the Fe (II)-thiocyanate. In this study, *G. tournefortii* extract in both lipid systems inhibited iron-fructose phosphate-induced lipid peroxidation.

In study of Asgary *et al*. (2008, 2009) effect of *G. tournefortii* on some cardiovascular risk factors in animal model was investigated. Results of this study showed that *G. tourenfortii* decreased the cholesterol, LDL-cholesterol, triglyceride, VLDL-Cholesterol, apolipoprotein B, oxidized LDL and factor VII. It also increased the level of HDL-Cholesterol and apolipoprotein when compared to diet with high cholesterol.

Mechanisms of action: Regarding *in vitro* and animal studies, several pharmacological properties have been offered for *Gundelia tournefortii*, most of which are attributable to polyphenolic and flavonoid compounds. Plant phenols and polyphenols are effective in preventing various pathological conditions (Losso *et al*., 2007; Haghi *et al*., 2011). According to some reports, plant phenols contribute to important activities including antiviral, antitumoral, antibiotic and antioxidant activities (Apak *et al*., 2007). Phenolic compounds affect remarkably various detoxification enzymes, such as glutathione-S-transferases, playing a major role in phase II systems (Coruh *et al*., 2007). Phenolic compounds have cytoprotective and hepatoprotective effects against CCl4. They are expected to take part in inhibition of cytochrome P450, leading to CCl_4 metabolism to reactive free radicals. Antioxidant effects of these compounds scavenge free radicals which lead to cell damage and induction or degeneration of the liver cells (Jamshidzadeh *et al*., 2005). Antioxidants counteract chemically active products of

metabolism which could damage the body (Losso *et al*., 2007; Kazemi *et al*., 2010; Rafieian-Kopaei *et al*., 2012).

The total phenolic content and antioxidant activity of the *G. tournefortii* have been previously reported (Alali *et al*., 2007; Coruh *et al*., 2007; Tawaha *et al*., 2007). Kaempferol and Quercetin are representative flavonoids; with preventive affect on Interleukin four (IL-4) syntheses (Kawai *et al*., 2007). High antioxidant activities are attributed to Gallic acid and Quercetin, typical flavonoids of Gundelia tournefortii. These materials inhibit glutathione-S-transferase activity. The seed extracts were also more influential glutathione-S-transferases inhibitors, with an IC50 of 97.5 l mg mL^{-1} (Coruh *et al*., 2007).

Flavonoids' antioxidant activities are exerted in different ways, including (Bombardelli and Morazzoni, 1993; Niki and Noguchi, 2000; Apak *et al*., 2007) radical scavenging activity toward either reactive species or lipid peroxidizing radicals; inhibition of production of reactive species through metal chelation; and interaction with other antioxidants, localization and mobility of the antioxidant at the microenvironment.

Chlorogenic acid is an important constituent of *G. tournefortii*, identified to be a scavenger for reactive species of nitrogen and oxygen and an inhibitor against the formation of conjugated diene from the linoleic acid oxidation (Nakatani *et al*., 2000; Haghi *et al*., 2011). *G. tournefortii*, due to chlorogenic acid, decreases atherosclerosis, reducing lipid, lipoproteins and lipid peroxidation (Hamdan and Afifi, 2004).

G. tournefortii seeds have tocopherols, fatty acids and sterols. a-tocopherol (48.9 mg/100 g) and g-tocopherol (1.1 mg/100 g) are main tocopherols in this plant (Matthaus and Ozcan, 2011). Tocopherols are natural antioxidants, mainly involved in biological activity. The main function of tocopherols is to protect polyunsaturated fatty acids against peroxidation (Matthaus and Ozcan, 2011). Phytosterols such as β-sitosterol may be applied to treat hypercholesterolemia (Matsuoka *et al*., 2008). They also inhibit absorption of cholesterol in the intestine and decreases serum cholesterol levels. Stigmasterol is a strong antioxidant and has hypoglycemic and thyroid inhibiting features (Panda *et al*., 2009).

Dosage and side effects: Consumption for traditional uses is in general once or twice a day in the form of stalks in salad, pickled or roasted. *G. tourenfortii* extract with concentrations higher than 300 mg kg^{-1} may be more threatening to the liver, with toxic effect higher than protective effect against CCl_4. *G. tourenfortii* extract was more toxic in vitro compared to *in vivo* which possibly results from the limitation of the entry of the compounds in the extract into hepatocytes *in vivo* in contrast to the exposed isolated hepatocytes (Jamshidzadeh *et al*., 2005; Kumar *et al*., 2011). The green plant of *G. tournefortii* is considered a danger to livestock especially cattle and sheep, causing many deaths in Australia due to hydrocyanic acids (Sharaf *et al*., 2004). In the case of gundelia's high consumption, it has only emetic effect.

CONCLUSION

In animal and human experiments, *G. tournefortii* had several pharmacological effects. Considering its very valuable pharmacological features in traditional medicine and frequent use, *G. tournefortii* could be applied in treating infectious diseases, digestive disorders, cancer and high blood pressure. What should be kept in mind is that the use of *G. tournefortii* as a drug for prevention and treatment of diseases requires complementary clinical trials.

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