JTCM 中医杂志 Journal of Traditional Chinese Medicine

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J Tradit Chin Med 2013 December 15; 33(6): 815-826
ISSN 0255-2922

REVIEW

Parsley: a review of ethnopharmacology, phytochemistry and biological activities

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Accepted: August 12, 2013

Abstract

OBJECTIVE: To summarize comprehensive information concerning ethnomedicinal uses, phytochemistry, and pharmacological activities of parsley.

METHODS: Databases including PubMed, Scopus, Google Scholar, and Web of Science were searched for studies focusing on the ethnomedicinal use, phytochemical compounds and biological and pharmacological activities of parsley. Data were collected from 1966 to 2013. The search terms were: "Parsley" or "Petroselinum crispum" or "Petroselinum hortence".

RESULTS: Parsley has been used as carminative, gastro tonic, diuretic, antiseptic of urinary tract, anti-urolithiasis, anti-dote and anti-inflammatory and for the treatment of amenorrhea, dysmenorrhea, gastrointestinal disorder, hypertension, cardiac disease, urinary disease, otitis, sniffle, diabetes and also various dermal disease in traditional and folklore medicines. Phenolic compounds and flavonoids particularly apigenin, apiin and 6"-Acetylapiin; essential oil mainly myristicin and apiol; and also coumarins are the active compounds identified in Petroselinum crispum. Wide range of pharmacological activity including antioxidant, hepatoprotective, brain protective, anti-diabetic, analgesic, spasmolytic, immunosuppressant, anti-platelet, gastroprotective, cytoprotective, laxative, estrogenic, diuretic, hypotensive, antibacterial and antifungal activities have been exhibited for this plant in modern medicine.

CONCLUSION: It is expectant that this study resulted in improvement the tendencies toward Petroselinum crispum as a useful and important medicinal plant with wide range of proven medicinal activity.

Key word: Petroselinum; Jafari; Medicine, traditional; Pharmacological processes; Chemistry

INTRODUCTION

Petroselinum crispum (mill.) Nym.ex A.W. Hill and in some region Petroselinum hortence Hoffm. From the

family Umbeliferae, are commonly known as parsley. The origin of parsley is from Mediterranean region, but today is cultivated wherever of the world. Parsley is biennial and glabrous. Its height is 60 to 100 cm, numerous stems grow from one root. Roots are thin or thick fusiform to tuberous and vertical. The leaves are tripinnate and ovate. Inflorescences are long pedicled, terminal, with yellowish umbels. The involucre possesses one or two bracts. The petals are splayed with a curved tip. The style thickening is very developed. The fruit is orbicular ovate and greenish-gray, with 2.5 mm length.[1] Moreover than its widely use as a green vegetable and garnish, it is used for different medicinal purposes in traditional and folklore medicine of different countries. Various compounds from different phytochemical categories have been identified in Parsley. Also, different pharmacological activities have been attributed to this plant. The present review summarizes comprehensive information concerning ethnomedicinal uses, phytochemistry, and pharmacological activities of parsley. For this purpose, databases including PubMed, Scopus, Google Scholar, and Web of Science were searched for studies focusing on the ethnomedicinal use, phytochemical compounds and biological and pharmacological activities of parsley. Data were collected from 1966 to 2013 (up to June). The search terms were: "Parsley" or "Petroselinum crispum" or "Petroselinum hortence". There was no language restriction. The reference list from retrieved articles was also reviewed for additional applicable studies. All published studies as well as abstracts presented at meetings were evaluated. *In vitro*, *in vivo* and human studies were separated and the data from each was extracted in individual tables.

Ethnomedicinal uses

Ethnomedicinal uses of parsley in different countries have been shown in Table 1. In traditional Iranian medicine, Petroselinum crispum seeds have been claimed to be antimicrobial, antiseptic, astringent, gastrotonic, antidote, antispasmodic, carminative, digestive and sedative and is used for gastrointestinal disorder, inflammation, halitosis, kidney stone, and amenorrhoea.[2-6] Leaves also are employed as food flavor and antitussive and used for gastrointestinal disorder, exanthema, dermatitis, alphosis, macula, headcool, sniffle, vision performance, hemorrhoid, kidney stone, diuretic and otitis.[4-6] The leaves also possess anticoagulant and abortifacient activity and are useful in skin disease, hypertension, hyperlipidemia, hepatotoxic, diabetes, cardiac disease, renal disease, lumbago, eczema, nose bleed, amenorrhoea, dysmenorrhea, kidney stones, prostatitis, halitosis, anaemia, hypertension, hyperuricaemia, constipation, odontalgy, pain, baldness, urinary tract disease, fluid retention and urinary tract infections in ethnomedicine of other countries.[7-16] The seeds showed diuretic and carminative activity and are useful in gastritis.[17,18]

Phytochemical constituents

Table 2 shows the structure and phytochemical category of compounds isolated from different parts of parsley.

Flavonoids

Flavonoids are dominant compounds of this plant.[19] Flavonoids including Apigenin, luteolin, chrysoeriol, quercetin and isorhamnetin were detected in cell suspension cultures of Petroselinum hortence.[20] Flavonoids apigenin, cosmosiin, oxypeucedanin hydrate and apiin were detected from aqueous extract of Petroselinum crispum leaves.[21] 6"-Acetylapiin, a flavone glycoside, and petroside, its monoterpene glucoside, were isolated for the first time from methanol extract of Petroselinum crispum aerial part. Myristicin, apiol, cnidilin, isoimperatorin, diosmetin, 7-O-β-D-glucopyran-

Table 1 Ethnomedicinal uses of Petroselinum crispum

Region	Plant part (s) used	Traditional uses and ethnobotanical reports
Iran	Seeds[2-6]	Antimicrobial, antiseptic, antispasmodic and sedative, gastrointestinal disorder and carminative, digestive, astringent, gastrotonic, inflammation, antidote, halitosis, kidney stone and amenorrhoea
	Leaf [4-6]	Food flavor, exanthema, alphosis, macula, headcool, sniffle, otitis, antitussive, diuretic, kidney stone, hemorrhoid, gastrointestinal disorder, vision performance and dermatitis
Iraq	Leaf [7]	Skin disease
Turkey	Leaf [8,9]	Anticoagulant, hypertension, hyperlipidemia, hepatotoxic and diabetes
	Seeds[17]	Diuretic
China	Leaf[36]	Food flavor
Morocco	Leaf [10-13]	Arterial hypertension, diabetes, cardiac disease, renal disease, lumbago, high blood pressure, eczema, and nose bleed Amenorrhoea, dysmenorrhea, kidney stones
Spain	Leaf [14]	Prostatitis, diabetes , halitosis, abortion, anaemia , hypertension, hyperuricaemia, constipation, odontalgy, pain, baldness
Italy	Aerial part[15]	Abortifacient
Peru	Seeds[18]	Carminative and gastritis
Serbia	Leaf [16]	Urinary tract disease, fluid retention and urinary tract infections

Table 2 Phytochemical constituents of parsley

Compound	Chemical category	Part/extract
Apigenin	Flavonoid	Leaf/aqueous extract[21]
		Cell suspension cultures of Petroselinum hortense[20]
		Leaf[23]
Luteolin	Flavonoid	Cell suspension cultures of Petroselinum hortense[20]
Chrysoeriol	Flavonoid	Cell suspension cultures of Petroselinum hortense[20]
Quercetin	Flavonoid	Cell suspension cultures of Petroselinum hortense[20]
Isorhamnetin	Flavonoid	Cell suspension cultures of Petroselinum hortense[20]
Apiose	Hydrocarbon	Cell suspension cultures of Petroselinum hortense[20]
		Seed, stem and leaf of Petroselinum crispum[24]
Petroside	Hydrocarbon	Aerial part/methanol extract[22]
Cosmosiin	Flavonoid glycoside	leaf/aqueous extract[21]
Oxypeucedanin hydrate	Flavonoid	leaf/aqueous extract[21]
Apiin	Flavonoid glycoside	leaf/aqueous extract[21]
6"-Acetylapiin	Flavone glycoside	Aerial part/methanol extract[22]
Cnidilin	Flavonoid	Aerial part/methanol extract[22]
Diosmetin 7-O-β-D-glucopyranoside	Flavone glycoside	Aerial part/methanol extract[22]
Kaempferol 3-O-β-D-glucopyranoside	Flavone glycoside	Aerial part/methanol extract[22]
Kaempferol	Flavonoid	Leaf[23]
Myristicin	Essential oil/ phenylpropene	Aerial part/methanol extract[22]
		Seed/essential oil[26]
Apiol	Essential oil/ phenylpropanoid	Aerial part/methanol extract[22]
		Seed/essential oil[26]
		Plant, callus and cell extracted volatile oil[29]
α-Pinene	Essential oil/ sesquiterpene hydrocarbon	Seed/essential oil[26]
		Leaf/essential oil[28]
Sabinene	Essential oil/ monoterpene hydrocarbon	Seed/essential oil[26]
		Leaf/essential oil[28]
β-Pinene	Essential oil/ monoterpene hydrocarbon	Seed/essential oil[26]
		Leaf/essential oil[28]
ρ-Cymene	Essential oil/ monoterpene hydrocarbon	Seed/essential oil[26]
		Leaf/essential oil[28]
Limonene	Essential oil/ monoterpene hydrocarbon	Seed/essential oil[26]
		Leaf/essential oil[28]
β-Phellandrene	Essential oil/ monoterpene hydrocarbon	Seed/essential oil[26]
		Plant, callus and cell extracted volatile oil[29]
		Leaf/essential oil[28]
γ-Terpinene	Essential oil/ monoterpene hydrocarbon	Seed/essential oil[26]
		Leaf/ essential oil[28]
Elemicin	Essential oil/ phenylpropene	Seed/essential oil[26]
		Leaf/essential oil[28]
1-Allyl-2,3,4, 5-tetramethoxy-benzene	Essential oil/ phenylpropene	Seed/essential oil[26]
Carotol	Essential oil/ alcohol sesquiterpene	Seed/essential oil[26]
Eugenol	Essential oil/ phenylpropene	Seed/essential oil[27]
β-Elemene	Essential oil/ sesquiterpene hydrocarbon	Leaf/essential oil[28]
β-Caryophyllene	Essential oil/ sesquiterpene hydrocarbon	Leaf/essential oil[28]

Table 2 Phytochemical constituents of parsley (continued)

Compound	Chemical category	Part/extract
Phenylacetaldehyde	Essential oil/ aldehyde	Leaf/essential oil[28]
γ-Elemene	Essential oil/ sesquiterpene hydrocarbon	Leaf/essential oil[28]
α-Terpineol	Essential oil/ Monoterpene alcohol	Leaf/essential oil[28]
α-Thujene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil[28]
Toluene	Essential oil/ aromatic compound	Leaf/essential oil[28]
Camphene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil[28]
Hexanal	Essential oil/ aldehyde	Leaf/essential oil[28]
3-Carene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil[28]
m- and/or ρ-Xylene	Essential oil/ aromatic compound	Leaf/essential oil[28]
Myrcene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil[28]
α-Phellandrene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil[28]
α-Terpinene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil[28]
2-Pentylfuran	Essential oil/ether	Leaf/essential oil[28]
cis-β-Ocimene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil[28]
trans-β-ocimene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil[28]
α-Terpinolene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil[28]
ρ-1,3,8-Menthatriene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil[28]
		Plant, callus and cell extracted volatile oil[29]
cis-Hex-3-en-l-ol	Essential oil/ alcohol	Leaf/essential oil[28]
4-isopropenyl-1-Methylbenzene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil[28]
α-Cubebene	Essential oil/ sesquiterpene hydrocarbon	Leaf/essential oil[28]
Benzaldehyde	Essential oil/ aldehyde	Leaf/essential oil[28]
α-Copaene	Essential oil/ sesquiterpene hydrocarbon	Leaf/essential oil[28]
Cryptone	Essential oil/ ketone compound	Leaf/essential oil[28]
β-Bisabolene	Essential oil/ sesquiterpene hydrocarbon	Leaf/essential oil[28]
α-Elemene	Essential oil/ sesquiterpene hydrocarbon	Leaf/essential oil[28]
2-(ρ-Tolyl) propan-2-ol	Essential oil/ monoterpene alcohol	Leaf/essential oil[28]
δ-Cadinol	Essential oil/ sesquiterpene alcohol	Leaf/essential oil[28]
Nonanal	Essential oil/ aldehyde	Plant, callus and cell extracted volatile oil[29]
Decanal	Essential oil/ monoterpene aldehyde	Plant, callus and cell extracted volatile oil[29]
Oxypeucedanin	Furanocoumarin	Leaf and root[30]
Psoralen	Furanocoumarin	Leaf and root[30]
8-Methoxypsoralen	Furanocoumarin	Leaf and root[30]
5-Methoxypsoralen	Furanocoumarin	Leaf and root[30]
Imperatorin	Furanocoumarin	Leaf and root[30]
Isoimperatorin	Furanocoumarin	Aerial part/methanol extract[22]
		Leaf and root[30]
β-Carotene	Carotenoid	leaf and stem acetone extract[31]
Lutein	Carotenoid	leaf and stem acetone extract[31]
Violaxanthin	Carotenoid	leaf and stem acetone extract[31]
Neoxanthin	Carotenoid	leaf and stem acetone extract[31]
Ascorbic acid	Vitamin	Aerial part[32]
Crispane	Sesquiterpene	Seed/Et_2O extract[33]
Crispanone	Sesquiterpene	Seed/Et_2O extract[33]
l-methyl-4-(methylethenyl)-2,3-dioxabicyclo [2.2.2]Oct-5-ene	Oxygenated derivative of monoterpens	Leaf/Et_2O extract[34]

oside and kaempferol 3-O-β- D-glucopyranoside were also detected in this extract.[22] Moreover, Gadi *et al* [23] detected kaempferol and apigenin are in Petroselinum crispum leaf.

Carbohydrates

D-glucose and apiose have been detected in cell suspension cultures of Petroselinum hortence (Kreuzaler 1973). Apiose is a sugar detected in seed, stem, and leaf of Petroselinum crispum.[24] These sugars mostly contribute in the structure of flavonoid glycosides.

Essential oil components

Seeds of Petroselinum crispum produced high amount of essential oil. Root and leaf also possess the essential oil.[25] Myristicin and apiol are the two main components of Petroselinum crispum essential oil which are responsible for its antioxidant activity.[26] α-pinene, sabinene, β-pinene, ρ-cymene, limonene, β-phellandrene, γ-terpinene, myristicin, elemicin, 1-allyl-2,3,4,5-tetramethoxy-benzene, carotol, eugenol and apiol were identified in Petroselinum crispum seed essential oil.[26,27] Leaf essential oil contained β-elemene, β-caryophyllene, phenylacetaldehyde, γ-elemene, α-terpineol, α-pinene, α-thujene, toluene, camphene, hexanal, β-pinene, sabinene, 3-carene, m- and/or ρ-xylene, myrcene, α-phellandrene, β-phellandrene, α-terpinene, limonene, 2-pentylfuran, cis-β-ocimene, γ-terpinene, trans-β-ocimene, ρ-cymene, α-terpinolene, ρ-1,3, 8-menthatriene, cis-Hex-3-en-l-ol, 4-isopropenyl-1-methylbenzene, α-cubebene, benzaldehyde, α-copaene, cryptone, β-bisabolene, α-elemene, 2-(ρ-Tolyl) propan-2-ol, δ-cadinol and elemicin.[28] Analysis of volatile oil from Petroselinum crispum plant, callus and cell culture showed that monoterpenes were the main constituent. ρ-1,3,8-menthatriene was high abundant compound among monoterepenes followed by β-phellandrene and apiol. Moreover, aldehydes (nonanal and decanal) and also fatty acids (Free and bound) were found in the volatile oil.[29]

Coumarins

Oxypeucedanin is the major furocoumarin of Petroselinum crispum and is responsible for contact photodermatitis induced by this plant. Psoralen, isopimpinellin, 8-methoxypsoralen, 5-methoxypsoralen and imperatorin are other furocoumarins isolated from its leaf and root.[30]

Miscellaneous compounds

Carotenoids including β-carotene, lutein, violaxanthin and neoxanthin were detected in Petroselinum crispum leaf and stem.[31] Moreover, ascorbic acid is identified in Petroselinum crispum.[32] Ethanol extract of Petroselinum crispum seed have crispane and crispanone.[33] Moreover, l-methyl-4-(methylethenyl)-2,3-dioxabicyclo [2.2.2]oct-5-ene and 4-methyl-7-(methylethenyl)-3,8-dioxatricyclo [$5.1.0^{2-4}$] octane were isolated from leaves.[34]

Pharmacological activities

Table 3 shows pharmacological effects of Petroselinum crispum in detail.

Antioxidant activity

Adding Petroselinum crispum leaves to the diet of 14 people for one week caused significant increase in antioxidant enzymes compared with their levels in the basic diet received group. Apigenin was demonstrated to be the main compound responsible for this activity Petroselinum crispum.[35] Different extracts from Petroselinum crispum leaves and stems exhibited antioxidant properties in various *in vitro* models.[36-39] The essential oil from seed showed *in vitro* antioxidant activity. Apiol and myristicin were two components responsible for its antioxidant activity.[26]

Antidiabetic activity

Various extract from Petroselinum crispum leaves enhanced the liver and blood antioxidant function in normal mice. On the other hand in carbon tetrachloride (CCl(4)) induced oxidative stress mice, the extracts showed both protective and deteriorative activity on liver and blood antioxidant function.[37] Petroselinum crispum leaves decreased blood glucose level and demonstrated hepatoprotective activity in diabetic rats via antioxidant activity.[9,40] Yanardağ *et al* reported that the antihyperglycemic activity of Petroselinum crispum is not due to improvement and regeneration of secretory granules and β-cells of pancreas islets.[41] Furthermore, Petroselinum crispum improves hyperglycemia- induced heart and aorta oxidative damage via its antioxidant activity in the heart and aorta tissue.[42] However, it did not showed significant effect on non-enzymatic glycosylation of skin proteins in diabetic rats.[43]

Analgesic and spasmolytic activity

Petroselinum crispum seed hydroalcoholic extract revealed analgesic activity in mice.[2] It also reduced KCl- and $CaCl_2$-induced contractions on rat isolated ileum dose dependently via blocking voltage-gated calcium channels.[3] Different extracts from aerial parts demonstrated antispasmodic activity on spontaneous and acetylcholine- induced contractions of rat isolated ileum.[44]

Immunomodulating activity

Essential oil from Petroselinum crispum seed suppressed humoral and cellular immune response via inhibiting splenocytes and macrophages function.[45]

Gastrointestinal activity

Ethanol extract from Petroselinum crispum leaves executed beneficial effects on different models of peptic ulcer in rats via its anti-secretory and cytoprotective activity.[46] Aqeoues extract from Petroselinum hortence seeds demonstrated laxative activity in rat by significant absorption of sodium and water and also enhancing Na-KCl_2 transporter activity in the colon.[47]

Table 3 Pharmacological activities of parsley

Pharmacological activity	Plant part	Plant extract	Method	Result	Active constituent
Antioxidant-clinical trial	Leaf [35]	Plant material	Randomized crossover clinical trial on 7 men and 7 women added leafs in their daily diet for one week	↑ Erythrocyte glutathione reductase (GR) and superoxide dismutase (SOD) compared with those in the basic diet received group	Apigenin
Antioxidant-*in vitro*	Leaf and stem[36]	Methanol and water extract	(a) DPPH radical-scavenging activity, (b) reducing power of ferric-ferricyanide complex, (c) ferrous ion-chelating activities, (d) hydroxyl radical-scavenging activity, (e) iron-induced linoleic acid oxidation model	(a) DPPH radical-scavenging activity, (b) significant reducing power, (c) higher ion- chelating activity than EDTA, (d) higher hydroxyl radical activity than ascorbic acid of all extracts except all extracts except stem water extract, (e) inhibition of lipid peroxidation inhibition especially by methanol extracts	-
Antioxidant -*in vitro*	Leaf and root[37]	Methanol extract	(a) lipid peroxidation activity, (b) hydroxyl radical activity, (c) DPPH radical scavenging activity of fractions	(a) Dose dependent inhibition of lipid peroxidation, (b) dose dependently hydroxyl radical scavenging, DPPH radical scavenging; (c) ethyl acetate fraction showed the highest activity	
Antioxidant *-in vitro*	Leaf [38]	(a) Methanol extract and (b) water extract	(a) Non-specific free radical scavenging activity via chemiluminescence method, (b) determination of malondialdehyde production in isolated brains from young male wistar albino rats	(a) Dose- dependent free radical scavenging activity, (b) inhibition of lipid peroxidation (membrane protection activity)	
Antioxidant *-in vitro*	Seeds[26]	Essential oil	(a) β-carotene bleaching assay, (b) ferrous ion chelating assay, (c) DPPH free radical scavenging assay, (d) fractionation of the essential oil and screeninig of components with antioxidant activity using DPPH free radical scavenging method	(a) EC50 of the essential oil dissolved in methanol in bleaching test was 5.12 mg/mL which was much less than the standard agents (BHT and α-tocopherol), (b) no inhibition on metal chelating, (c) EC50 of the essential oil in DPPH radical scavenging activity was 80.21 mg/mL and was very less than standards, (d) only ethyl acetate/methanol fraction demonstrated free radical scavenging activity	Myristicin and apiol
Antioxidant and hepato -protection *-in vivo*	Leaf [37]	Aqueous, ether, chloroform, ethylacetate, and n-butanol extract	(a) Measurement of lipid peroxidation, glutathione peroxidase, peroxidase, catalase, and xanthine oxidase, (b) glutathione reductase and reduced glutathione in liver homogenate and blood of mice after 5 days, CCl4 induced liver damage in mice	(a) Enhancing activities on measured antioxidant enzymes and reduced lipid peroxidation in liver homogenate and blood sample of mice, (b) the extracts in CCl4 received animals showed both protective and deteriorative activity: both inducing and suppressing of the oxidative action of CCl4	Flavonoids
Brain protective *-in vivo*	Leaf [39]	Ethanol extract	Measurement of superoxide dismutase, catalase, glutathione peroxidase and also lipid peroxidation in mitochondrial fraction of various regions of the mouse brain in mice brain of D-galactose-induced oxidative stress	Significant increase of antioxidant enzymes and decrease of lipid peroxidation level	
Antidiabetic, hepato-protective *-in vivo*	leaf [9]	Aqueous extract	STZ- induced diabetic rats, parsley extract at 2 g/kg administrated for 28 days	No change in body weight; significant decrease in blood glucose level, serum ALP and ALT compared with control; hepatocytes were improved and degenerative changes were reduced	Flavonoids and ascorbic acid

Table 3 Pharmacological activities of parsley (continued)

Pharmacological activity	Plant part	Plant extract	Method	Result	Active constituent
Antidiabetic, hepato -protective *-in vivo*	leaf [40]	Aqueous extract	STZ- induced diabetic rats, parsley extract at 2 g/kg for 28 days	Significant decrease in blood glucose, serum ALP, sialic acid, uric acid, potassium and sodium levels, liver lipid peroxidation and non-enzymatic glycosylation and increase in liver glutathione; no effect in body weight	Flavonoids, phenolic compounds and ascorbic acid
Antidiabetic *-in vivo*	leaf [41]	Aqueous extract	STZ- induced diabetic rats, 2 g/kg parsley extract for 28 days	Significant decrease in blood glucose; no increase in number of secretory granules and cells in islets of pancreas; morphologic changes of the pancreas tissue were not different from control; no regeneration of -cells occurred by extract	-
Antidiabetic, heart damage *-in vivo*	leaf [42]	Aqueous extract	STZ- induced diabetic rats, 2 g/kg parsley extract for 28 days administrated, blood glucose, lipid peroxidation and glutathione activity of aorta and heart tissue were measured.	Significant decrease in blood glucose and lipid peroxidation activity in aorta and heart tissue; increase of glutathione level in the aorta and heart tissue	Flavonoids
Antidiabetic, skin damage *-in vivo*	leaf [43]	Aqueous extract	STZ- induced diabetic rats, 2 g/kg parsley extract for 28 days	Significant decrease in blood glucose; no effect on lipid peroxidation and non enzymatic glycosylation of skin tissue	-
Analgesic *-in vivo*	Seed[2]	Hydroalcoholic extract	300, 600, 800 mg/100 g Parsley extract administrated in 2.5% formalin induced paw licking test and 150, 300, 600 mg/100 g parsley extract administrated in 1% acetic acid (intraperitoneal injection)-induced writhing test on male swiss mice	significant analgesic action on formalin induced paw licking test; no significant activity on writhing test	-
Spasmolytic *-in vitro*	Aerial part[44]	Aqueous and ethanol extracts	Spontaneous and acetylcholine-induced contractions on rat isolated ileum	Dose dependently reduction in spontaneous and acetylcholine-induced ileum contraction; ethanol extract had higher activity	-
Spasmolytic *-in vitro*	Seed[3]	80% ethanol extract	Contraction induced by 60 mM KCl, parsley added before and after contraction and also induced by $CaCl_2$ on Wistar rat isolated ileum	dose dependently reduction in KCl- induced contraction; inhibition of KCl contraction and dose dependently reduction in $CaCl_2$-induced contraction; blocking of voltage-gated calcium channels	-
Immunosuppressant *-in vitro*	Seeds[45]	Essential oil	Effect of parsley essential oil in different concentrations (0.01-100 μg/mL) on proliferation of splenocytes by using methyl tetrazolium (MTT) method; nitrite (NO) levels of the cells measured using the diazotization method.	Suppression of splenocytes proliferation, PHA-stimulated splenocytes and NO by all plant concentrations (0.01-100 μg/mL)	-
Peptic ulcer protection *-in vivo*	Leaf [46]	Ethanol extract	Pyloric ligation-induced hyper secretion and ulcer , stress induced- ulcer using hypothermic restraint, indomethacin-induced ulcer and cytodestructive agents (80% ethanol, 0.2 M NaOH and 25% NaCl) -induced ulcer on rats	Siginificant suppression of gastric secretion in concentrations of 1 and 2 g/kg; siginificant protection on stress- induced ulcer and indomethacin- induced ulcer; replenishment of gastric wall mucus and non-protein sulfhydryl contents in cytodestructive agents-induced ulcer	Tannins, flavonoids and triterpenes

Table 3 Pharmacological activities of parsley (continued)

Pharmacological activity	Plant part	Plant extract	Method	Result	Active constituent
Estrogenic function *-in vitro*	Aerial part[22]	Methanol extract	Proliferation of the estrogen-sensitive breast cancer cell line (MCF-7) was assayed and bioassay-guided separation performed for detection of the active compounds	Significant proliferative activity on MCF-7 cell which was equal to isoflavone glycosides from soybean; removing the glycoside moieties of the components resulted in increasing of Estrogenic activities: the EC50 values of apigenin, diosmetin, kaempferol were 1.0, 2.9, and 0.56 μM, respectively that are equel to soybean isoflavone	Flavone glycosides particularly, 6"-acetylapiin and the aglycones; apigenin, diosmetin and kaempferol
Uterine tonic *-in vivo*	Aerial part[22]	Methanol extract	7 days oral administration of the extract in ovariectomized mice.	Significant regeneration in the uterus weight of the ovariectomized mice	Apiin, and apigenin
Antimicrobial *-in vitro*	Leaf[7]	Hot and cold water extract	100 ,150, 200, 250 mg/mL of parsley extract on Pseudomonas aeruginosa, Staph aureus and Staph pyogenes isolated from patient with burn infection	Antibacterial activity; higher inhibition zone in hot water extract	-
Antimicrobial *-in vitro*	Leaf and stem[36]	Methanol and water extract	Effect on bacterial cell damage and Bacterial growth inhibition on Bacillus subtilis and Escherichia coli	Leaf extracts showed higher cell damage on both bacteria with higher activity with methanol extract; stem extracts showed higher action on the inhibition of the growth of both bacteria	Furocoumarins and furanocoumarins
Antimicrobial *-in vitro*	Leaf[53]	Photoactive furocoumarins extract	Antimicrobial assay on human pathogens bacteria and spoilage microorganisms by media-modified method and also, DNA repair-deficient Escherichia coli using photobiological method	Inhibitory activity on Escherichia coli O157:H7, DNA repair-deficient E. coli , Listeria monocytogenes, and also the spoilage microorganisms Erwinia carotovora, and Listeria innocua; no inhibitory activity on Pseudomonas fragi	Psoralen, 8-methoxypsoralen, 5-methoxypsoralen, oxypeucedanin and isopimpinellin
Antimicrobial *-in vitro*	Leaf[52]	Ethanol extract	Antibacterial assay on Lactobacillus plantarum and Leuconostoc mesenteroides using culture media assay	inhibitory activity on both Lactobacillus plantarum and Leuconostoc mesenteroides	-
Antimicrobial *-in vitro*	Aerial part[54]	Essential oil	Effect on the growth of Listeria innocua, Serratia marcescens and Pseudomonas fluorescens by disc diffusion method	No antibacterial activity against Listeria innocua, Serratia marcescens and Pseudomonas fluorescens	-
Antimicrobial *-in vitro*	Leaf[55]	Methanol extract	Effect 37 μg/ml of extract on the growth of Bacillus subtilis, Escherichia coli, Micrococcus luteus, Pseudomonas aeruginosa, Staphylococcus epidermidis, S.aureus , Candida albicans, Saccharomyces cerevisiae and Aspergillus niger using agar diffusion method	inhibitory activity on B. subtilis, P. aeruginosa, S. epidermidis, S. aureus and S. cerevisiae.	Coumarins
Anti- platelet *-in vitro*	Leaf[21]	Aqueous extract	Inhibitory effect of extract and isolated flavonoids on clotting formation and ADP- induced platelet aggregation	No inhibitory effect on clotting activity, while strong antiplatelet aggregation was demonstrated	Apigenin and cosmosiin
Anti-platelet *-in vitro*	Leaf[23]	Aglycone flavonoids	Effect of pre-incubation of the parsley components on human platelet adhesion to a collagen-coated surface under physiologic flow situation and human platelet thrombin-, ADP- and collagen- induced aggregation	Decreased adhesion of human platelets to collagen surface and also inhibited platelet aggregation in all models dose dependently; the higher inhibition was demonstrated in collagen induced aggregation	Aglycone flavonoids; kaempferol and apigenin

Table 3 Pharmacological activities of parsley (continued)

Pharmacological activity	Plant part	Plant extract	Method	Result	Active constituent
Anti-platelet *-in vitro*, ex vivo and *in vivo*	Leaf [51]	Aqueous extract	Effect of parsley extract on thrombin-, ADP-, collagen- and epinephrine-induced aggregation (*in vitro*) subsequent to pre-incubation of platelets with the extract and also on bleeding time of rat and *ex vivo* aggregation after oral treatment with extract (3 g/kg)	dose dependent inhibition on all model of *in vitro* aggregation; significant inhibition on *ex vivo* platelet aggregation in rats and significant delay in bleeding time	Polyphenols
Cardiovascular activity *-in vivo*	Leaf [50]	Aqueous and ethanol extracts	Effect on mean blood pressure which recorded from the carotid artery in anaesthetized rats and concomitant with muscarinic receptor antagonist (atropine 1 mg/kg). Effect on rate and amplitude of contraction of atria on isolated rat atria and in pre-administration of atropine (1 mg/kg).	Aqueous extract showed less activity on mean blood pressure than ethanol; ethanol extract showed stronger inhibitory action on rate and amplitude of the contraction, which blocked by muscarinic antagonist agent	-
Laxative *-in vitro* and *in vivo*	Seed[47]	Water extract	(a) Effect on the activity of kidney Na+-K+ and colonocyte Na+-K+ ATPase activity in homogenate of crude rat colon and effect of 20% w/v parsley extract on movements of rat colon luminal water in the presence and (b) absence of sodium buffer and also concomitant with furosemide by perfusion method	(a) Inhibition of both kidney Na+-K+ ATPase and colonocyte Na+-K+ATPase activity; (b) inhibition of absorption of sodium and water in the luminal which enhanced by adding furosemide	Essential oil
Diuretic *-in vitro* and *in vivo*	Seed[49]	Aqueous extract	(a) Effect on urine volume of rats which received the extract 20 %w/v compared with control; (b) Inhibitory effect of extract on kidney homogenate Na+-K+ ATPase activity (*in vitro*); (c) effect of extract on urine flow using kidney perfusion method in following condition was assayed: extract with sodium free buffer, extract with potassium free buffer, extract with amiloride and extract with furosemide	(a) Significant increase in urine volume; (b) significant decreas in activity of kidney cortex and medulla Na+-K+ ATPase compared with control; (c) significant increase in kidney urine flow rate compared with control; diuretic action of extract was enhanced with amiloride and furosemide and also in sodium free condition, which was not observed in potassium free codition	-
Cytotoxic *-in vitro*	Aerial part[57]	Hot water extract	Effect on viability of CV1-P fibroblast cells and SH-SY5Y neuroblastoma cells	No significant activity on the growth of fibroblast cells and neuroblastoma cells	-
Protection of reproductive system *-in vivo*	Seed[48]	Isolated oil	Effect on Zearalenone (nonsteroidal estrogenic mycotoxin)- induced testis toxicity assayed by determination of testosterone level and also sperm abnormality and germ cells chromosomal analysis	improved significantly reduction in testosterone level and sperm count and sperm motility; lessoned significantly germ cells chromosomal aberrations induced by Zearalenone	-

Note: STZ: streptozotocin; ALP: alkaline phosphatase; ALT: Alanine aminotransferase; ADP: Adenosine diphosphate.

Effects on genitourinary system

Methanol extract from pseudomonas crispum aerial part showed proliferative activity in estrogen-sensitive breast cancer cell line (MCF-7) equal to isoflavone glycosides from soybean. This estrogenic activity was related to flavone glycosides; 6"-acetylapiin and also aglicones; apigenin, diosmetin, and kaempferol. Furthermore, oral administration of the extract regenerated the uterus weight in ovariectomized mice and apiin and apigenin were responsible for this activity.[22] seudomonas crispum oil demonstrated significant protective activity against zearalenone -induced reproductive toxicity and significantly improved testosterone level, sperm count and sperm motility and inhibited germ cells chromosomal aberrations.[48] Aqeoues extract of pseudomonas hortense seeds exhibited diuretic effect and inhibited Na^+-K^+ ATPase activity in kidney cortex and medulla.[49]

Cardiovascular activity

Pseudomonas crispum leaves decreased mean blood pressure which recorded from the carotid artery in anaesthetized rats. This effect was attenuated with muscarinic receptor antagonist. It also decreased rate and am-

plitude of contraction on isolated rat atria which weakened by muscarinic antagonist. These data indicate hypotensive and negative inotropic and chronotropic activity of pseudomonas crispum.[50] pseudomonas crispum leaves demonstrated strong antiplatelet aggregation effect. Aglycone flavonoids; keampferol, apigenin and cosmosiin are responsible compounds for this activity. However, it did not exert inhibition on clotting activity *in vitro*.[21,23,51]

Antimicrobial and cytotoxic activity

Pseudomonas crispum leaves and stems possess antibacterial activity on B. subtilis and E. coli.[36] Hot and cold water extract from pseudomonas crispum leaves demonstrated antibacterial activity against pseudomonas aeruginosa, S. aureus and S. pyogenes isolated from patient with burn infection.[7] Ethanol extract of pseudomonas crispum leaves inhibited the growth of Lactobacillus plantarum and Leuconostoc mesenteroides.[52] The furocoumarins isolated extract from pseudomonas crispum leaves demonstrated inhibitory activity against E. coli, L. monocytogenes, Erwinia carotovora, and Listeria innocua and no inhibition against Pseudomonas fragi. Psoralen, 8-methoxypsoralen, 5-methoxypsoralen, oxypeucedanin and isopimpinellin were among the responsible antimicrobial furocoumarins.[53] Essential oil from aerial part of Petroselinum crispum had no antibacterial activity against Listeria innocua, Serratia marcescens and Pseudomonas fluorescens.[54] Methanol extract of Petroselinum crispum leaves demonstrated antimicrobial activity on B. subtilis, Petroselinum aeruginosa, S. epidermidis, S.aureus and S. cerevisiae *in vitro*. Coumarins are responsible components for this property.[55]

Toxicity and tolerability

In ethnomedicine, it has been claimed that parsley is abortificient. Acute toxicity of pseudomonas crispum was evaluated in rat and no toxicological effect was observed.[46] Photodermatitis has been reported in pigs exposed to pseudomonas crispum.[56] Furocoumarins particularly oxypeucedanin are responsible for its contact photodermatitis activity.[30]

CONCLUSION

Parsley is a medicinal plant with various proven pharmacological properties including antioxidant, hepatoprotective, neuroprotective, anti-diabeic, analgesic, spasmolytic, immunosuppressant, anti-coagulant, anti-ulcer, laxative, estrogenic, diuretic, hypotensive, antibacterial and antifungal activities.

Beneficial effects of pseudomonas crispum on gastrointestinal tract which claimed in ethnomedicine of various nations, proved via spasmolytic, analgesic, gastroprotective, anti secretive and laxative mechanisms in modern scientific investigations. Moreover, the useful activity of pseudomonas crispum on urinary tract disease was proved via diuretic activity. Its antiseptic property on urinary tract could be due to antimicrobial activity. Ethnomedicinal use of pseudomonas crispum on amenorrhea and dysmenorrhea can be related to its anti-platelet, anti-coagulant, spasmolytic, analgesic and also estrogenic activity. Furthermore, the abortive property could be due to estrogenic and utrerine tonic activity. Efficacious uses of pseudomonas crispum in cardiac disease and hypertension were proved which may be related to its hypotensive, anti-platelet and negative inotropic and chronotropic mechanism. Useful effect on hemorrhoids in ethnomedicine may be due to its immunomodulatory, anti-inflammatory and antioxidant mechanisms. Efficacious folklore uses of pseudomonas crispum on liver disease and diabetes were confirmed by several modern studies. Beneficial activity of pseudomonas crispum on Headcool, otitis, sniffle and flu may be related to its antimicrobial and immunomodulatory activity. Pharmacological studies in order to evaluation and confirmation of other unproved ethnomedicinal effects of parsley especially antiurolithiasis and antitussive activity and beneficial effects on exanthema, eczema and various dermal disease and also visuality are recommended. Because of the reports about abortive properties of parsley, It should not be administered during pregnancy.

Phenolic compounds particularly flavonoids (such as apigenin, apiin and 6"-Acetylapiin), essential oil components (mainly Myristicin and apiol), coumarins and furocoumarins are the active components isolated and detected in Petroselinum crispum. Various bioactive compounds have been isolated and identified in Petroselinum crispum, whereas many active compounds responsible for ethnomedicinal uses or proved pharmacological activities have not been completely evaluated. Therefore, new investigations are proposed to isolate, identify, and obtain the Petroselinum crispum active compounds in order to explore novel natural component for rectifying the stalemate on the way of modern medicine. Overall, it is expectant that this study resulted in improvement the tendencies toward Petroselinum crispum as a useful and important medicinal plant with wide range of proven medicinal activity.

ACKNOWLEDGEMENTS

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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