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Parsley: a review of ethnopharmacology, phytochemistry and biological activities

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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 "Petroseli-

num hortense".

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, gastro-protective, 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.

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

INTRODUCTION

Petroselinum crispum (mill.) Nym.ex A.W. Hill and in some region *Petroselinum hortense* 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 hortense". 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 med-

icine, *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, dysmenorrhoea, kidney stones, prostatitis, halitosis, anaemia, hypertension, hyperuricaemia, constipation, odontalgia, 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 hortense*.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 ⁶	Food flavor
Morocco	Leaf ¹⁰⁻¹³	Arterial hypertension, diabetes, cardiac disease, renal disease, lumbago, high blood pressure, eczema, and nose bleed Amenorrhoea, dysmenorrhoea, kidney stones
Spain	Leaf ¹⁴	Prostatitis, diabetes, halitosis, abortion, anaemia, hypertension, hyperuricaemia, constipation, odontalgia, 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 <i>Petroselinum hortense</i> ²⁰ Leaf ²³
Luteolin	Flavonoid	Cell suspension cultures of <i>Petroselinum hortense</i> ²⁰
Chrysoeriol	Flavonoid	Cell suspension cultures of <i>Petroselinum hortense</i> ²⁰
Quercetin	Flavonoid	Cell suspension cultures of <i>Petroselinum hortense</i> ²⁰
Isorhamnetin	Flavonoid	Cell suspension cultures of <i>Petroselinum hortense</i> ²⁰
Apiose	Hydrocarbon	Cell suspension cultures of <i>Petroselinum hortense</i> ²⁰ Seed, stem and leaf of <i>Petroselinum crispum</i> 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	Flavone glycoside	Aerial part/methanol extract ²²
7-O-β-D-glucopyranoside	Flavone glycoside	Aerial part/methanol extract ²²
Kaempferol	Flavone glycoside	Aerial part/methanol extract ²²
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 p-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
p-1,3,8-Menthatriene	Essential oil/ monoterpene hydrocarbon	Leaf/essential oil ²⁸
		Plant, callus and cell extracted volatile oil ²⁹
cis-Hex-3-en-1-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-(p-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 ₂ O extract ³³
Crispanone	Sesquiterpene	Seed/Et ₂ O extract ³³
1-methyl-4-(methylethenyl)-2,3-dioxabicyclo [2.2.2]Oct-5-ene	Oxygenated derivative of monoterpenes	Leaf/Et ₂ O 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 hortense* (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-tetra-methoxy-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-1-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 monoterpenes 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, 1-methyl-4-(methylethenyl)-2,3-dioxabicyclo [2.2.2]oct-5-ene and 4-methyl-7-(methylethenyl)-3,8-dioxatricyclo [5.1.0²⁻⁴] 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 (CCl₄) 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 CaCl₂-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 Aqueous extract from *Petroselinum hortense* seeds demonstrated laxative activity in rat by significant absorption of sodium and water and also enhancing Na-KCl₂ 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 leaves 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- <i>in vitro</i>	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- <i>in vitro</i>	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- <i>in vitro</i>	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- <i>in vitro</i>	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 screening 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- <i>in vivo</i>	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, CCl ₄ 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 CCl ₄ received animals showed both protective and deteriorative activity: both inducing and suppressing of the oxidative action of CCl ₄	Flavonoids
Brain protective- <i>in vivo</i>	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- <i>in vivo</i>	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)

Pharmacologic al activity	Plant part	Plant extract	Method	Result	Active constituent
Antidiabetic, hepato-protective <i>-in vivo</i>	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 <i>-in vivo</i>	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 β -cells occurred by extract	-
Antidiabetic, heart damage <i>-in vivo</i>	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 <i>-in vivo</i>	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 <i>-in vivo</i>	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 <i>-in vitro</i>	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 <i>-in vitro</i>	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 <i>-in vitro</i>	Seeds ⁴⁵	Essential oil	Effect of parsley essential oil in different concentrations (0.01-100 μ g/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 μ g/mL)	-
Peptic ulcer protection <i>-in vivo</i>	Leaf ⁴⁶	Ethanol extract	Pyloric ligation-induced hyper secretion and ulcer, stress induced- ulcer using hypothermic restraint, indomethacin-induced ulcer and cytotoxic agents (80% ethanol, 0.2 M NaOH and 25% NaCl) -induced ulcer on rats	Significant suppression of gastric secretion in concentrations of 1 and 2 g/kg; significant protection on stress- induced ulcer and indomethacin- induced ulcer; replenishment of gastric wall mucus and non-protein sulfhydryl contents in cytotoxic agents-induced ulcer	Tannins, flavonoids and triterpenes

Table 3 Pharmacological activities of parsley (continued)

Pharmacologic al activity	Plant part	Plant extract	Method	Result	Active constituent
Estrogenic function <i>-in vitro</i>	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 μ M, respectively that are equal to soybean isoflavone	Flavone glycosides particularly, 6"-acetylapiin and the aglycones; apigenin, diosmetin and kaempferol
Uterine tonic <i>-in vivo</i>	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 <i>-in vitro</i>	Leaf ⁷	Hot and cold water extract	100 ,150, 200, 250 mg/mL of parsley extract on <i>Pseudomonas aeruginosa</i> , <i>Staph aureus</i> and <i>Staph pyogenes</i> isolated from patient with burn infection	Antibacterial activity; higher inhibition zone in hot water extract	-
Antimicrobial <i>-in vitro</i>	Leaf and stem ³⁶	Methanol and water extract	Effect on bacterial cell damage and Bacterial growth inhibition on <i>Bacillus subtilis</i> and <i>Escherichia coli</i>	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 <i>-in vitro</i>	Leaf ⁵³	Photoactive furocoumarins extract	Antimicrobial assay on human pathogens bacteria and spoilage microorganisms by media-modified method and also, DNA repair-deficient <i>Escherichia coli</i> using photobiological method	Inhibitory activity on <i>Escherichia coli</i> O157:H7, DNA repair-deficient <i>E. coli</i> , <i>Listeria monocytogenes</i> , and also the spoilage microorganisms <i>Erwinia carotovora</i> , and <i>Listeria innocua</i> ; no inhibitory activity on <i>Pseudomonas fragi</i>	Psoralen, 8-methoxypsoralen, 5-methoxypsoralen, oxypeucedanin and isopimpinellin
Antimicrobial <i>-in vitro</i>	Leaf ⁵²	Ethanol extract	Antibacterial assay on <i>Lactobacillus plantarum</i> and <i>Leuconostoc mesenteroides</i> using culture media assay	inhibitory activity on both <i>Lactobacillus plantarum</i> and <i>Leuconostoc mesenteroides</i>	-
Antimicrobial <i>-in vitro</i>	Aerial part ⁵⁴	Essential oil	Effect on the growth of <i>Listeria innocua</i> , <i>Serratia marcescens</i> and <i>Pseudomonas fluorescens</i> by disc diffusion method	No antibacterial activity against <i>Listeria innocua</i> , <i>Serratia marcescens</i> and <i>Pseudomonas fluorescens</i>	-
Antimicrobial <i>-in vitro</i>	Leaf ⁵⁵	Methanol extract	Effect 37 μ g/ml of extract on the growth of <i>Bacillus subtilis</i> , <i>Escherichia coli</i> , <i>Micrococcus luteus</i> , <i>Pseudomonas aeruginosa</i> , <i>Staphylococcus epidermidis</i> , <i>S.aureus</i> , <i>Candida albicans</i> , <i>Saccharomyces cerevisiae</i> and <i>Aspergillus niger</i> using agar diffusion method	inhibitory activity on <i>B. subtilis</i> , <i>P. aeruginosa</i> , <i>S. epidermidis</i> , <i>S. aureus</i> and <i>S. cerevisiae</i> .	Coumarins
Anti- platelet <i>-in vitro</i>	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 <i>-in vitro</i>	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)

Pharmacologic activity	Plant part	Plant extract	Method	Result	Active constituent
Anti-platelet - <i>in vitro</i> , ex vivo and <i>in vivo</i>	Leaf ⁵¹	Aqueous extract	Effect of parsley extract on thrombin-, ADP-, collagen- and epinephrine-induced aggregation (<i>in vitro</i>) subsequent to pre-incubation of platelets with the extract and also on bleeding time of rat and <i>ex vivo</i> aggregation after oral treatment with extract (3 g/kg)	dose dependent inhibition on all model of <i>in vitro</i> aggregation; significant inhibition on <i>ex vivo</i> platelet aggregation in rats and significant delay in bleeding time	Polyphenols
Cardiovascular activity - <i>in vivo</i>	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 - <i>in vitro</i> and <i>in vivo</i>	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 - <i>in vitro</i> and <i>in vivo</i>	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 (<i>in vitro</i>); (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 decrease 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 condition	-
Cytotoxic - <i>in vitro</i>	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 - <i>in vivo</i>	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; lessened 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 apigenin and apigenin were responsible for this activity.²² *Pseudomonas crispum* oil demonstrated significant protective activity against zearalenone-induced reproductive tox-

icity and significantly improved testosterone level, sperm count and sperm motility and inhibited germ cells chromosomal aberrations.⁴⁸ Aqueous 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 abortifacient. 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-diabetic, 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 uterine 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.

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