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Origanum majorana L. -Phyto-pharmacological review

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Origanum majorana L. (Family Lamiaceae) is a frost tender perennial undershrub, native to Cyperus and naturalised in Mediterranean regions, particularly found in temperate regions of the Himalayas. Its usage for flavour and aroma dates back to ancient times. Traditionally, the leaves of marjoram are used for its medicinal properties to cure insomnia, gastritis, asthma and nervousness. Now-a-days, it is in great demand to be used in aromatherapy. Although various bioactive constituents are reported in aerial parts of the herb, but isolation of volatile oil and identification of its constituents has been the area of focus of the researchers. This article is compilation of traditional uses, phytochemical and pharmacological knowledge of the herb.

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Introduction

Origanum L. is one out of 200 genera in the family Lamiaceae (mint family) of 3500 species spread all over the world. Most of the species are aromatic and they grow wild in the Mediterranean basin[1-4]. The genus consists of over 44 species, 6 subspecies, 3 botanical varieties and 18 naturally occurring hybrids and includes several types of oregano as well as sweet marjoram (*O. majorana* L.) and dittany of Crete (*O. dictamnus* L.)[5]. The name '*Oregano*' has originated from Greek words *óros*' means mountains and *'ganos'* means light/joy and thus commonly known as 'joy of mountains' due to their beauty and abundance on the Mediterranean mountain sides.

The genus is characterized by large morphological and chemical diversity. Forty nine taxa divided into 10 sections, belong to this genus are locally distributed around the Mediterranean. In particular, 3 taxa are restricted to Morocco and Spain, 2 occurs in Algeria and Tunisia, 3 are endemic to Cyrenaica, 9 are restricted to Greece and Asia minor, 21 are found in Turkey, Cyprus, Syria and Lebanon and are locally distributed in Israel, Jordan and Sinai Peninsula. The morphological variations within the genus results in the distinction of 10 sections, consisting of 49 taxa (species, sub-species and varieties)[6-8].

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O*riganum majorana* L.*,* formerly known as *Majorana hortensis* Moench is a tender perennial herb of '*Origanum*' genus[9]. It is commonly known as sweet marjoram and native to Cyperus, Antolia (Turkey) and naturalised in parts of Mediterranean region especially Egypt[10]**.** It is cultivated all over the world in different parts of India, France, Hungry and United States for its flavour and fragrance. Marjoram was initially used by Hippocrates as an antiseptic agent. It is a well-liked home remedy for chest infection, cough, sore throat, rheumatic pain, nervous disorders, cardiovascular diseases, epilepsy, insomnia, skin care, flatulence and stomach disorders[11-13]. In different parts of the India, it is known by various names: Hindi – *Marwa*; Bengali – *Murru*; Tamil – *Marru, Maruvu*; Kannada – *Maruga*; Malyalam – *Maruvanu* ; Kumaun – *Bantulsi*; Deccan – *Murwa*.

Sweet marjoram being native to Asia, was found in Europe as favourite of the Greeks and Romans[14]. It is commonly grown in India and distributed widely in temperate regions of the Himalayas from Kashmir to Sikkim at altitudes from 500-1200 m.

Cultivation, collection and propagation

Marjoram is mainly cultivated for its aromatic leaves (both green and dry) for culinary purpose. Though, it's a perennial herb, it is treated as an annual under cultivation. It generally requires dry, warm, well-drained fertile garden loamy soil. Sometimes it can even thrive on chalk. It grows well under wide pH

ranges from acidic, neutral to basic soils. It requires nearly full sun and can be grown in semi-shade (light wood land) or no shade, being drought tolerant. Sweet marjoram dries out rather quickly. It requires well-drained soil and frequent watering. Sweet marjoram, being a frost-tender herb should be grown outdoors as an annual and replanted in the spring. It is propagated by seeds and cutting. Seeds are sown in the plains in October and in the hills from March to the middle of June[15]. Seeds can be sown in pots initially and then transplanted in the field 20-25 cm part in rows, spaced 30 cm apart. At higher elevation, sometimes propagation is done by cutting. The crop is harvested in three to four months. The tops are cut at the time of flowering and dried in shade. Volatile oil content of the leaves is maximum when the plant is harvested before seed formation. It flowers from June to September and the seeds ripen from August to September. The flowers are hermaphrodite and are pollinated by bees[15].

Morphology

Origanum majorana L. is a bushy half hardy perennial sub shrub that grows as annual. It is cold sensitive, frost tender aromatic herb that grows up-to 30-60 cm height. It has descending multi-branched reddish square stems that spill over to create a mound. The stems are straight having weak, hairy, round and green with red speckles[16]. Leaves are smooth, simple, petiolate and ovate to oblong-ovate, grey green in colour arranged opposite to each other on a square stem. The texture is extremely smooth due to presence of numerous hairs. They are 0.5-1.5 cm long and 0.2-0.8 cm wide, with obtuse apex, entire margin, symmetrical but tapering base and reticulate venation[16]. Marjoram have tiny, two lipped, tubular, white or pale pink flowers with grey green bracts that bloom in spike like clusters from mid to late summers (June to September). They are less than 0.3 cm long and arranged in burr-like, 1.3 cm long heads. Flowers are hermaphrodite in nature[17]. Seeds are minute, oval, dark and brown in colour that ripens from August to September. It has sub–cylindrical, longitudinally wrinkled tap roots with transverse fissures; 0.2-0.6 mm in diameter. The outer surface of root is dark brown while light brown internally with several long rootlets and root scars are also present. Fractures being long, irregular and fibrous having aromatic odour and non-bitter[18] (Plate 1).

Microscopy

Diacytic type stomata are present in leaves, uniformly distributed with presence of veins, vein islet and vein terminations at the surface. Polygonal cells are present on upper epidermis while numerous covering trichomes on outer. The covering trichomes are multicellular, uniserrate, pointed and thin walled. Leaf shows cuticularized epidermis consisting layers of compactly arranged chollenchyma followed by vascular bundles whereas; the mesophyll exhibited only palisade cells and spongy parenchyma. Collenchyma tissue consists of thick walled round parenchyma cells and xylem fibers[16]. Stem of the herb is circular in transverse section consisting of a thick

Plate 1—Aerial parts of *Origanum majorana* L.

cuticle. The epidermis is composed of single layer rectangular cells and 5-6 layers of closely packed polygonal parenchyma cells form the cortex. Phloem fibres and phloem parenchyma are clearly distinguished. Two cell thick medullary rays along with xylem vessels, xylem parenchyma and prominent parenchymatous pith is present at the centre. Root section is circular in outline consisting of 2-3 layers of rectangular cork cells with 6-7 layers of closely packed parenchyma forming cortex. Xylem elements consist of xylem vessels and xylem parenchyma. The medullary rays are composed of 2 cell thick rectangular cells. Phloem present outer to the xylem and pith absent[18].

Phytochemistry

Sweet marjoram is characterized by a strong, spicy and pleasant odour and flavour[19]. Analysis of herb reported presence of especially volatile oil as major constituents, due to its aromatic nature. Various phytochemical tests revealed the presence of terpenoids, flavonoids and tannins in ethanol extract whereas saponins and carbohydrates were present in stem and root water extract, respectively. Alkaloids, glycosides and proteins were absent in both of the extracts (root and stem)[18]. Essential oil from *O. majorana* contains terpinen-4-ol (31.15 %), cis-sabinene hydrate (15.76 %), p-cymene (6.83 %), sabinene (6.91 %), trans-sabinene hydrate (3.86 %) and α-terpineol (3.71 %) as the main constituent[20]. The most prominent components of *O. majorana*[20] were carvacrol (65 %) and thymol (4 %). Fig. 1 shows structures of terpinen-4-ol, trans-sabinene hydrate, cis-sabinene hydrate, α-terpineol, p-cymene, thymol, sabinene and carvacrol, respectively.

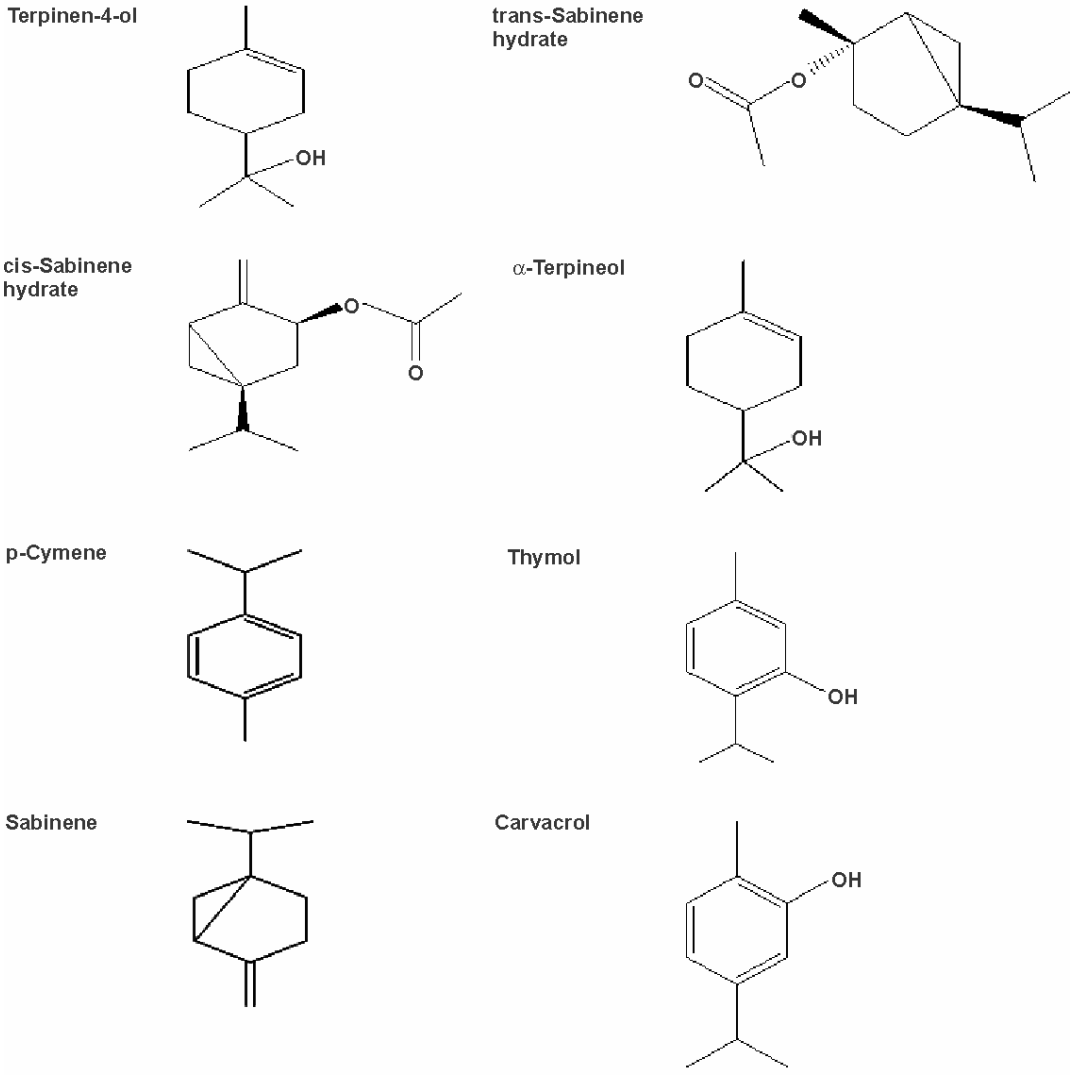

Fig. 1—Major phytoconstituents reported in *Origanum majorana* L. essential oil

The oil obtained from the aerial parts of the plant is reported to contain monoterpenoids, sesquiterpenoids[10,20], terpenic esters i.e. linalyl-acetate, terpenyl-acetate, geranyl-acetate[21], phenol-methyl ethers i.e. *trans*-anethole[20], tri-terpenoids, oleanolic acid and ursolic acid[9,21]. Gallic acid, caffeic acid, p-coumaric acid, ferulic acid, apigenin, trans-2 hydro cinnamic acid are the phenolic compounds obtained through ultrasonically assisted extraction technique from water, 60 % methanol, 60 % acetone, and ethyl acetate/water extract[23]. Cavaciol and thymol are the phenols present in the oil. The plant is rich in polyphenols such as arbutin, 6-O-4-hydroxybenzoyl arbutin, and 2-hydroxy-3-(3,4- dihydroxyphenyl) propionic acid, isolated as moderate antioxidants[24] .

Catechin, rutin (quercetin 3-o-rhamnose glycoside), quercetin and eriodictyol are the flavonoids reported in different extracts of water, 60 % methanol, 60 % acetone and ethyl acetate[26]. Amentoflavone is a flavonoid which has been determined by reversed phase HPLC in two different varieties of *O. majorana* L. Luteolin-7- diglucoside, apigenin-7-glucoside, and diosmetin-7-glucuronide, 6-hydroxyluteolin and 6-hydroxyapigenin glycosides, arbutin, methylarbutin are present as flavonoid glycosides in marjoram[22]. Aqueous and methanol extracts from sweet marjoram contain multiple compounds e.g. phenolic derivatives (phenolic acids, flavonoids as apigenin, luteolin, quercitin and their glycosides as rutin or isovitexin[25]. β-Sitosterol is reported in the aerial parts of the plant[22]. Linolenic, linoleic and oleic acid are the fatty acids present in its leaves[26]. Vitamin A and C are reported in the leaves and floral parts of marjoram herb[26]. Caffeic acid, carnosic acid, carnosol, labiatic acid and rosmarinic acid are various types of tannins found in aerial parts of the herb[27].

Traditional uses

Marjoram was initially used by Hippocrates as an antiseptic agent. It was introduced in the middle ages in Europe and Greece. To the ancient Greeks, it was ‘amarakos’, a symbol of love, honour and happiness. Aristotle reported it as an anti-poison. In the old Egypt, marjoram was used to disinfect and preserve food and its oil was massaged on the forehead and in the hairs. Dioscorides named it as “sampsouchon”. The people of Europe used to rub the leaves of the herb on oak pieces of furniture and floors to get fragrant glow over it. Traditionally, the leaves of marjoram are employed to cure diabetes, insomnia, catarrh, asthma and nervousness[28]. Dried marjoram, its volatile oil and the extracts have been applied in the flavouring of various foods, particularly soups, sauces, meat, fish, canned foods, liqueurs, vermouths and bitters[29,30]. Herb of sweet marjoram has been included in the formulations of patented shashlik sauces[31]. As a medicinal plant, it has been traditionally used as stimulant and in tonic preparations. From the earliest time marjoram has been used as an aromatic adjunct[30] and reported to be useful in asthma, hysteria and paralysis[32]. Marjoram has been traditionally used for the treatment of gastrointestinal disturbances, cough and bronchial diseases. It is used in mouthwashes for oral hygiene and also applied topically to relieve symptoms of common cold, such as nasal congestion[33]. An infusion made from the fresh plant was used to relieve nervous headaches by virtue of camphouraceous constituent present in the oil and externally applied in bags as a hot fomentation to painful swellings and rheumatism, as likewise for colic. The sweet marjoram has also been successfully employed externally for healing scirrhous carcinoma of the breast[34]. It is a home remedy for chest infection, cough, sore throat, rheumatic pain, nervous disorders, cardiovascular diseases, epilepsy, insomnia, skin care, flatulence and stomach disorders[11-13]. The leaves of the plant are used fresh or dried and highly esteemed as a condiment for seasoning food, garnishing salads and in flavouring vinegars, they are also used in poultry seasoning. Dried flowering tops are used for sachets and potpourris. The aromatic seeds were used in confectionery and French confitures. The oil of marjoram has been used since ages in external application for sprains, bruises, stiff and paralytic limbs and toothache and as hot fomentation in acute diarrhoea[32]. In aromatherapy, essential oil made from marjoram bolsters the mind and spirit and relieves the feeling of grief and loneliness. It is used for easing sore muscles and swollen joints while stimulating peristaltic movement of the digestive system for bad appetite as well for menstrual cramps.

Pharmacological activities and uses

Antioxidant

The ethanol extract of the leaves of marjoram showed antioxidant and free radical-scavenging activity using colorimetric assays. The extract exhibited a marked inhibitory effect in 1,1-diphenyl-2-picrylhydrazyl (DPPH) scavenging assay[35]. The

ethanol extracts of both stem and root has shown *in vitro* antioxidant activity, respectively using spectrophotometric method by DPPH, H_2O_2 free radical scavenging, metal chelating and ferric reducing power assay. Both the extracts showed potent antioxidant activity in all models. The IC_{50} values were found comparable with ascorbic acid and the reducing ability of root ethanol extract was found to be high compared to stem ethanol extract[36]. The ethyl-alcohol, n-hexane and aqueous extracts obtained from leaves and flowering tops of two marjoram herbs from Hungary and Egypt showed antioxidant activity *in vitro* by spectrophotometric and chemiluminometric methods using DPPH and Rancimat method. The Egyptian herb and its aqueous extract was better antioxidant compared to Hungarian ones[17].

Anti-anxiety

The extract of leaves has shown anti-anxiety effects on rats in open maze model at intraperitoneal dose of 200 mg/kg b.w. The effect was dose dependent and comparable to diazepam[37].

Anticonvulsant

Different extracts of leaves have shown anticonvulsant effect on rats using the Pentylenetetrazole (PTZ) and maximal electroshock (MES) test at two different doses of 250 and 500 mg/kg, i.p. each. The chloroform extract exhibited maximum reduction in the duration of seizures, compared to the control group[38].

Antidiabetic

Methanol extract of the leaves showed antidiabetic activity in streptozotocin-induced mice through various *in vitro* and *in vivo* assays. *O. majorana* has shown significant effects on *in vitro* inhibition of Advanced Glycation End product formation. The effect was more than the standard antiglycation agent, aminoguanidine[39].

Anti-gout

The ethanol extracts of both stem and root showed anti-gout activity in potassium oxonate induced Swiss albino rats at oral dose of stem (200 mg/kg b.w.) and root (400 mg/kg b.w.) extracts, respectively. The effect was dose dependent and found significant in decreasing uric acid, creatinine, ESR, MDA and increasing reduced glutathione level[36].

Anti-mutagenic activity

The ethanol extract of the aerial parts of marjoram has shown anti-mutagenic effect against cyclophosphamide induced mutation in mice at the minimum effective dose 125 mg/kg. The effect of marjoram extract was found to protect any changes in RNA, DNA and protein contents in the liver and testes of treated mice as compared with the control[40].

Antiulcer

The hydrodistilled volatile oil and methanol extract of the leaves showed ulcer healing properties in streptozotocin-nicotinamide induced diabetic rats at three different doses (100, 200 and 400 mg/kg, p.o.). The effect was dose dependent and more effective than glibenclamide and comparable to ranitidine[17].

Antibacterial

The essential oils (EOs) derived from leaves showed antibacterial effect on various bacteria (*Bacillus cereus*, *Escherichia coli*, *Staphylococcus coagulase*, *Enterobacter* spp., *Proteus* spp., *Acinetobacter* spp., *Klebsiella* spp. and *Pseudomonas* spp.) in agar diffusion assay and using *S. aureus, E. coli, K. pneumoniae* and *Pseudomonas* spp. by using dilution techniques of Kirby-Bauer method[41-46]. The ethanol and water extract of *O. majorana* L. have shown antimicrobial activity against Gram positive and Gram negative bacteria and its possible food applications by minimum inhibition concentration estimation. Ethanol extract had high inhibition effect against bacteria comparable to water extract[47].

Antifungal

The EOs obtained from the marjoram leaves have shown antifungal activity against *Aspergillus flavus* and *A. parasiticus,* by observing their growth and/or mycelial inhibition through comparison with the standard dish (without oil)[46-48]. Various extracts of the leaves namely, n-hexane, aqueous ethanol, ethanol ammonia extracts showed *in vitro* antifungal effect against six *Candida* sp. yeast strains by the disk-diffusion method. The n-hexane extract had shown highest antifungal activity[44].

Anti-protozoal

The volatile oil and various extracts of the leaves namely, n-hexane, aqueous ethanol, ethanolic ammonia extracts have shown *in vitro* anti-protozoal effect against single protozoan species *Pentatrichomonas hominis* by the disk-diffusion method[44].

Insecticidal

The EO of leaves showed insecticidal activity against fourth instars of *Spodoptera littoralis* and

adults of *Aphis fabae* L. and *Aspergillus* spp. by topical application assay and residual film assay[48,49].

Antiovicidal activity

The EO showed ovicidal and adulticidal activities against insecticide-susceptible and pyrethroid/ malathion-resistant *Pediculus humanus capitis* obtained from human head lice. The EO and its constituents particularly linalool, (-)-terpinene-4-ol and r-terpineol were found useful as fumigants with contact action in the control of *P. h. capitis* adults and eggs[50].

Conclusion

Flavours and fragrances have been part of our daily life since ages. Medicinal and aromatic plants are increasing in demand in several fields such as agro-alimentary, cosmetic, perfumery and pharmacy. *Origanum* species are rich in aromatic constituents and widely known for its taxonomic value and essential oils. Despite its economic importance, genetic variability and potential, *Origanum* is one of the underutilized genus. The present review enlightens the rich history of its use in traditional medicine all over the world along with its botanical description, phytochemistry, pharmacology explored so far. Phenols and flavonoids present in the essential oil of the herb may be responsible for its diverse pharmacological activities. The summarized information may prove to be useful tool for researchers to carry out further study and explore other scientific aspects of the herb.

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