Int J Pharma Res Health Sci. 2017; 5 (4): 1717-23
DOI:10.21276/ijprhs.2017.04.01
B Tripathy *et* al.
CODEN (USA)-IJPRUR, e-ISSN: 2348-6465

PHS Scientific House
PHARMAHEALTHSCIENCES

International Journal of Pharma Research and Health Sciences

Available online at www.pharmahealthsciences.net

Review Article

An Updated Review on Traditional Uses, Taxonomy, Phytochemistry, Pharmacology and Toxicology of *Origanum majorana*

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ARTICLE INFO

Received: 14 Jul 2017
Accepted: 02 Aug 2017

ABSTRACT

Origanum majorana or Majorana hortensis is known as Marwa in India. It is an evergreen and pleasant smelling herbaceous plant grows up to the height of 30 to 60 cm. belonging to the mint family (Lamiaceae). Commonly known as Sweet marjoram. This perennial herb has small leaves with hair on either side. It is commonly grown in India and distributed widely in temperate regions of the Himalayas from Kashmir to Sikkim at altitudes from 500-1200m. Marjoram has many uses with numerous health benefits. Digestive benefits (Increasing the efficiency of digestion by increasing digestive enzymes and saliva, improving appetite, relieving nausea, eliminating flatulence, preventing intestinal infections, relieving diarrhea and constipation). Marjoram is a great antiseptic, antibacterial, antifungal, and antiviral agent and used in a variety of common illnesses (Food poisoning, Staph infection, Tetanous infection in wounds, Typhoid, Malaria, Influenza, Common cold, Mumps, Measles). Another benefit of marjoram is the enhancement of the cardiovascular and circulatory system (Lowering the blood pressure, greatly reducing the risk of hypertension, preventing the buildup of cholesterol).Anti-inflammatory effects like (Asthma, Muscle spasms, Sinus headaches, Migraines, Fever, Body aches). Topical application for (Painful joints, Sore muscles, Sprains, Back aches, Toothaches.), Emotional and neurological benefits like (Relieving insomnia, Reducing stress, Calming anxiety, Minimizing emotional reactions, Increasing control of sexual desire). The herb contains important phyto constituents like tannins, glycosides, terpenes, flavonoids, linalool and cavacrol. In this review report we collected information related to taxonomy, monographs, distribution, morphology, phytochemistry, traditional uses and pharmacological studies of Origanum majorana plant in details.

Keywords: *Origanum majorana*, medicinal uses, phyto-chemistry, Pharmacology.

1. INTRODUCTION

Origanum majorana Syn. Majorana hortensis (M.), is a bushy half-hardy perennial sub-shrub, growing to a height of 1 to 2 feet, with descending, multibranched stems, the stems

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taking root as they touch the ground. [1] Leaves are simple, opposite and stalked, elliptic, 10 to 13 millimeters long, exuding a fragrance when bruised. The well dried leaves of the herb used in medicinal products. It has fragrant, sharp, bitter, camphor like and spicy flavored herb. Flowers are small, purple or white, few too many, arranged in spikelets. Inflorescences with enlarged overlapping bracts. [2] Marjoram is one of the most common medicinal and aromatic species and as described by Wagner et al. (2004) in most Lamiaceae species, we have observed epidermal trichomes in leaves and stems, leaf has a typical dorsiventral structure and with hair on either side. It is endemic to the Island of Cyprus, but is cultivated worldwide as a culinary herb. It is especially important in the cuisines of Western Europe and the Mediterranean. It is frost- sensitive perennial that is usually grown as an annual in temperate climates. The green tree has white flowers and has branched heads which from a distance look like knots. [3, 4]

Fig 1: ***Origanum majorana***

Taxonomy

Kingdom: Plantae
Subkingdom: Viridiplantae
Infrakingdom: Streptophyta
Superdivision: Embryophyta
Division: Tracheophyta
Sub-division: Spermatophytina
Class: Magnoliopsida
Super-order: Asteridae
Order: Lamiales
Famil: Lamiaceae
Subfamily: Nepetoideae
Tribe: Mentheae
Genus: *Origanum* L.
Species: *Origanum majorana L* .

Monographs

English –Marjoram, Sweet marjoram, Sanskrit- Ajanmasurabhi, marwa, Hindi – Murwa, Sathra, Odiya- Maruwa, Bengali – Murru, Telugu – Maruvamu, Tamil – Marru,Maruvu, Marikojhundhu, Chutanaccu, Kuvalamayam, Marathi – Marwa, Mijirikamy, Kannada – Maruga, Malyalam- Maruvanu, Kumaun- Bantulsi , Urdu- Marwa, marzanjosh, Deccan- Murwa , Saudi Arabia- Doash, Portuguese – Manjerona, Mangerona, Manjarona, Spanish – Dulce mejorana, French –Marjolaine, German- Majoran, Italy- Maggiorana

2. PHYTOCHEMISTRY

- *Majorana hortensis* is peculiarized with the aid of powerful, aromatic and amusing fragrance quality. Investigation on marjoram herb recorded the extremely existence of volatile oil as chief phyto constituents due to its fragrant character [5].
- Different qualitative phytochemical tests exhibited for the presence of flavonoids, tannins, glycosides, cardiac glycosides, sterols, terpenoids in ethanol extract of leaves, root and stem whereas saponin and carbohyderate present in aqueous extract respectively. Alkaloids, glycosides and proteins were absent in ethanol and aqueous extract of root and stem part [6].
- *O. majorana* contains essential oils like terpinen-4-ol, cis- sabinene hydrate, p- cymene and α- terpineol as primary constituents and the utmost eminent constituents of this herb are carvacrol and thymol (phenols) present in oil [7].
- From the existing record it was revealed that the areal part of the plant comprise monoterpenoids, sesquiterpenoid [8, 9], linalyl acetate, terpenyl acetate, granyl acetate 18(terpene ester),phenol-methyl ethers i.e trans-anethole 10 tri-terpenoids, oleanolic acid and ursolic acid [3,10].
- Gallic acid, caffeic acid, p- coumaric acid, ferulic acid, apigenin, trans-2-hydro cinnamic acid are the phenolic compounds are generally available in water, methanol, acetone and ethaylacetate/ water extract. [11]
- The plant having huge amount of arbutin, 6-o-4-hydroxybenzoyl arbutin, and 2-hydroxy-3-(3,4-dihydroxyphenyl) propionic acid (polyphenols) Catechin, rutin (quercetin-3-o-rhamnose glycoside), quercetine and eriodictyyol are the flavonoids reported in different solvents extract. [9]
- Amentoflavone is a flavonoid which has been determined by reverse phase HPLC in two different varities of *O. majorana* L. Luteolin-7-diglycoside, 6-hydroxyluteolin and 6-hydroxyapigenin glycosides, arbutin, methylarbutin are present as flavonoid glycoside in *majorana*. [12]
- Aqueous and methanol extract from sweet majoram contains multiple compounds e.g. phenolic derivatives (phenolic acids, flavonoids as apigenin, luteolin, quercitin and their glycosides as rutin or isovitexin. [13]
- *β*- Sitosterol is reported in the aerial parts of the plant.[14] Caffeic acid, carnosic acid,carnosol, labiatic acid and rosmarinic acid are various types of tannins found in aerial parts of the herb. [15] Linolenic, linoleic and oleic acid are the fatty acids present in its leaves.Vitamin A and C are isolated from the leaves and floral parts of marjoram herb. [16]
- Plant yields the compounds eugenol, used as flavoring agents. Nutritive analysis of dried leaves per 100 g yields : (Principle) energy 271 cal, carbohydrates 60.56

g, total fat 7.04 g, cholesterol 0 mg, dietary fiber 40.3 g; (Vitamins) folate 274 µg, niacin 0.902 mg, pantothenic acid 0.209 mg, pyridoxine 1.190 mg, riboflavin 0.316 mg, thiamin 0.289 mg, vitamin A 8058 IU, vitamin C 51.4 mg, vitamin E 1.69 mg, vitamin K 621.7 µg; (Electrolytes) sodium 77 mg, potassium 1522 mg; (Minerals) calcium 1990 mg, copper 1.133 mg, iron 82.71 mg, magnesium 346 mg, manganese 5.433 mg, zinc 3.60 mg; (Phytonutrients) carotene-ß 4806 µg, cryptoxanthin-ß 70 µg, lutein-zeaxanthin 1895 µg. [17]

Traditional uses

Marjoram (*Origanum majorana*) is an aromatic herb in the mint family which originated in Egypt and Arabia. It is also widely referred to as *Oregano.* Marjoram was initially used by Hippocrates as an antiseptic agent. To the ancient Greeks, it was names as 'Amarakos', a symbol of love, honour and happiness. Aristotle reported it as anti-poison. In the old Egypt, Marjoram was used to disinfect and preserve food and its oil was messaged on the forehead and in the hair. Traditionally, the leaves of marjoram are employed to cure diabetes, insomnia, catarrh, asthma and nervousness.[18] Today, it is commonly found in the Mediterranean region or grown in gardens around the world. In its varied forms of: marjoram essential oil, fresh or dried marjoram leaves, or marjoram powder (ground up marjoram), it has many uses. As a culinary additive, it is commonly used to flavor soups, sauces, salads, and meat dishes. [19] Cosmetically, marjoram is used in skin cream, body lotion, shaving gel, and bath soaps. Whether used as an essential oil, powder, fresh leaves, or dried leaves, marjoram has many uses with numerous health benefits. It increases the efficiency of digestion by increasing digestive enzymes and saliva, improving appetite, relieving nausea, eliminating flatulence, preventing intestinal infections, relieving diarrhea and constipation, gallstones, intestinal gas, and stomach cramps[20,21]. Marjoram is a great antiseptic, antibacterial, antifungal, and antiviral agent and used in a variety of common illnesses like food poisoning, staph infection, tetanus infection in wounds, typhoid, malaria, influenza, common cold, mumps, measles[22]. Another use of marjoram is enhancement of the cardiovascular and circulatory system lowering the blood pressure, greatly reducing the risk of hypertension, preventing the buildup of cholesterol. It also having anti-inflammatory effects like asthma, muscle spasms, sinus headaches, migraines, fever, body aches. It is used for topical application in painful joints, sore muscles, sprains, back aches, toothache. [21] Emotional and neurological uses of *Origanum majorana* are relieving insomnia, reducing stress, calming anxiety, minimizing emotional reactions, increasing control of sexual desire. [23] Some women use marjoram tea for relieving symptoms of menopause, treating mood swings related to menstrual periods, starting menstruation, and promoting the flow of breast milk. [24]

3. PHARMACOLOGICAL ACTIVITIES

Antiseptic and Antidote

Antiseptic(s) are antimicrobial substances that are applied to living tissue/skin to reduce the possibility of infection, sepsis, or putrefaction. In ancient time Hippocrates introduced marjoram herb's antiseptic activity because it contains lot of phenolic constituents which act against microbial infections. Essential oils like terpinen-4-ol, cis- sabinene hydrate, p- cymene and α- terpineol, carvacrol and thymol (phenols) are eminent constituents may responsible for antiseptic activity. Aristotle reported that turtles that ate a snake immediate had to eat oregano not to die, thus became oregano also taken by men as anti-poison. [18]

Antioxidants

The ethanol extract of the eaves of marjoram shows antioxidant and free radical scavenging activity using colorimetric assays. The extract exhibited a marked effects in DPPH (1, 1-diphenyl-2-picrylhydrazyl) scavenging assay. 27The 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 ion reducing power assay. Both the extracts showed potent antioxidant activity in all models. The IC50 values were found comparable with ascorbic acid and the reducing ability of root ethanol extract.25 The ethyl-alcohol, n-hexane and aqueous extracts obtained from leaves and flowering tops of two marjoram Hungary and Egypt showed antioxidant activity in vitro by Spectrophotometric and Chemilaminometric method methods using DPPH and Rancimat methods. [26]

Ethanol extracts (stem and root) of *Origanum majorana* showed strong antioxidant activity , reducing power ability, free radical scavenging activity and metal chelating ability when compared to standards such as ascorbic acid which may be due to presence of flavonids, phenols, tannins(phenolic compounds) and triterpenoids. [27]

Anticonvulsant activity

O. majorana possess significant anticonvulsant activity in Pentylenetetrazole (PTZ) and Maximal electroshock (MES) induced seizures at 500 mg/kg dose. The most popular and widely used animal seizure models are the traditional MES and PTZ test. The MES test is considered to be a predictor of likely therapeutic efficacy against generalized tonic-clonic seizures. By contrast PTZ test represents a valid model for human generalized myoclonic seizures and also generalized seizures of petit mal (Loscher et al,1998). Thus, our results suggest the *O. majorana* extracts may be effective against human generalized myoclonic seizures and also absence ones. PTZ a chemoconvulsant is reported to induce seizures by depressing chloride channel function by binding to picrotoxin site on the Gamma amino butyric acid (GABA) receptor complex (Kulkarni et al, 1993). It has been indicated that PTZ induced seizures can be prevented by drugs that enhance GABAA receptormediated inhibitory

neurotransmission (Rogawski et al, 1995; Macdonald et al, 1995). Preliminary phytochemical analysis performed in this study showed that terpenoids, steriods and flavonoids are the major components of *O. majorana* extracts.

Different extracts of leaves have shown anticonvulsant effect on rats using the Pentylene tetrazole (PTZ) and maximal electroshock (MES) test at two different doses of 250 and 500 mg/kg i.p. each. The chloroform extract exhibited maximum in the duration of seizures compared to the control group. [28, 29]

Anti-anxiety

The extract of leaves has shown anti-anxiety effects on rats in open maze model in intraperitoneal dose of 200 mg/kg b.w The effects was dose dependent and comparable to diazepam. [30]

Antimicrobial activity

The methanol extract showed considerable activity against Aspergillus niger, Fusarium solani and Bacillus subtilis. The methanol extract was more active than the standard nystatin against Aspergillus niger. A more recent work conducted by Farooqi and Sreeramu (2004) reveals that the leaves of marjoram have antimicrobial activity against Bacillus anthracis, Proteus vulgaris, Salmonella stanley, S. newport, Streptococcus agalactiae, S. guneus and Aspergillus fumigatus. [31, 32]

Antibacterial activity

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., in agar diffusion assay and using S. aureus, e.coli, K.pneumoniae and pseudomonas spp.) by using dilution techniques of Kirby-Bauer method. 36. The ethanol and water extract of *O. majorana* L. have shown antimicrobial activity against Gram positive and Gram negative bacterial and its possible food applications by minimum inhibition concentration estimation. Ethanol extract had high inhibition effect against bacteria comparable to water extract. [33]

Antifungal activity

The essential oils obtained from the Marjorana leaves have shown antifungal activity against Aspergillus flavus and A. parasiticus, by observing their growth and/or mycelia inhibition through comparison wih the standard sidh(without oil) various extracts of leaves namely n-haxene, aqueous-ethanol, ethanol-ammonia extracts showed in-vitro antifungal effect against six Candida spp. Yeast strains by the disk diffusion method. The n-hexene extract has shown highest antifungal activity. [34]

Antiulcer activity

The Hydrodistilled volatile oil and methanol extract of the leaves showed Ulcer healing properties in Streptozocin-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. [35]

Antiprotozoal activity

The volatile oil and various extracts of the leaves namely n-hexane, aqueous ethanol, ethanolic ammonia extracts have shown in-vitro antiprotozoal effect against single protozoan species pentatrichomonas hominis by the disk diffusion method. [36]

Insecticidal activity

The essential oils of leaves showed insecticidal activity against fourth instars of Spodoptera littoralis and adults of Aphis fabae L. and Aspergillus spp.by total application assay and residual film assay. [37, 38]

Antiovicidal activity

The essential oils showed ovicidal and aduiticidal activities against insecticidal-susceptible and pyrethroid/malathion-resistant pediculus humanus capitis obtained from human head lice. The essential oils and its constituents particularly linolool, (-)-terpinene-4-ol and r-terpineol were found useful as fumigants with contact action in the control of *P.h.capitis* adults and eggs. [39]

Anti-gout activity

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 does dependent and found significant in decreasing uric acid, creatine, ESR, MDA and increasing reduced glutathione level. [40]

Antidiabetic activity

Methanol extract of the leaves showed antidiabetic activity in streptozotocin induced mice through various in vitro and in vivo assay. *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. [41]

Antimutagenic 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 liver and testes of mice as compared with control. [42]

Antitumor activity

The non-cytotoxic concentrations of *O. majorana* significantly inhibited the migration and invasion of the MDA-MB-231 cells by wound-healing and matrigel invasion assays. This plant also decreases the adhesion of MDA-MB-231 to HUVECs and inhibits trans endothelial migration of MDA-MB-231 through TNF-α-activated HUVECs. It suppresses the activities of matrix metalloproteinase-2 and -9 (MMP-2 and MMP-9) and phosphorylation of IκB, downregulates the nuclear level of NFκB. It reduces Nitric Oxide (NO) production in MDA-MB-231 cells. *O. majorana* promotes inhibition of tumor grow th and metastasis *in vivo*. [43]

Hepatoprotective activity

The hepatoprotective activity of methanolic extract of *Origanum majorana* in CCL4 induced liver injury of rats showed that the animals treated with the methanolic extract of *Origanum majorana* 200mg/kg and 400mg/kg b.w significantly reduced the toxic effect of CCL4. [44, 45]

Analgesic, Antiinflammatory and Antispasmodic Activity

The effects of methanol extracts of O. majorana on human platelet antiaggregant activity, which is related to the well known mechanism of action of NSAID (non-steroid anti-inflammatory drugs) through inhibition of the prostaglandins' metabolic pathway, have been studied by Okazaki et al. (1998). They found that O. majorana extracts dose-dependently inhibited platelet aggregation induced by collagen (2.0 µg/ml) or ADP (2.0 µg/ml). Successive fractionation of methanol extracts leads to isolation of an active hydroquinon -D-glucopyranoside, identified as arbutin. This strongly inhibited platelet aggregation was induced by all tested stimulating agents (collagen, ADP, arachidonic acid, thrombin). [46, 47, 48]

Immunostimulant, Antimutagenic And Anticancer Activity

According to Krukowski et al. (1998), an increase in immunoglobulin (IgG) levels was observed in reared calves, fed with a conventional concentrate supplemented by a mineral-herbal mixture containing *O. majorana* and its aqueous extracts were also able to suppress the mutagenicity of liver-specific carcinogen Trp-P-2 (Natake et al., 1989). [49]

Antitumour-promoting activity or in vitro cytotoxic effects towards different tumour cell lines were attributed also to *O. majorana* extracts or their constituents (Assaf et al., 1987; Okuyama et al., 1995; Hirobe et al., 1998). When studying cytotoxic activity of *O. majorana* water–alcoholic extracts and of isolated compounds (arbutin, methylarbutin and their aglycons – hydroquinone and hydroquinone monomethyl ether) towards cultured rat hepatoma cells (HTC line), a high dose-dependent HTC cytotoxicity of hydroquinone was observed, whilst arbutin was not active (Assaf et al., 1987). At 300 µM hydroquinone caused 40 per cent cellular mortality after 24 h of incubation, but no cells remained viable after 72 h. [50, 51]

Insect-Pollinating And Antiparasitic Activity

The use of essential oil of O. majorana in treatment of V. jacobsoni has attracted much practical attention from several authors. A combination of formic acid and of essential oil of marjoram has been shown to be very effective in treatment of Varroa mites both in laboratory trials and in field experiments (Long et al., 1997). In field experiments, that were carried out under tropical (Vietnam) and temperate (Germany) climatic conditions, formic acid was applied to a tray covered by gauze and placed on the bottom board of the hive while O. majorana essential oil was applied to two wood pieces (1.5 ml per piece), that were placed on the top bars of the combs. The combination of essential oil and formic acid, applied at 15 per cent concentration, resulted in 96.24–99.68 per cent mite mortality in tropical climate and in 97.56–99.92 per cent in temperate climatic conditions. Due to the relatively low concentrations of formic acid this combination did not affect bee mortality and was proposed as a promising practical method in the control of V. jacobsoni. The highly significant repellent activity and antiparasitic effects of essential oil of marjoram were observed towards Varroa mites, which were exposed to test wax tubes with incorporated essential oil at 0.1 per cent and 1 per cent (Kraus et al., 1994). These concentrations of O. majorana essential oil were not noxious to honeybees. Effective antiparasitic activity was observed also when essential oil of O. majorana was sprayed onto bees in colonies infested with V. jacobsoni at concentration (100 ppm), that was found non toxic to bees (Fathy and Fouly, 1997). *Origanum majorana* essential oil has been shown as a potent acaricidal agent against Acarapis woodi (Renie), the acarine disease-causing parasite that invades the tracheal system of the honeybees during winter and early spring. Infestation percentage in the bee colonies, treated with O. majorana essential oil (10 drops of oil per piece of cotton wool in a Petri dish, that was put under the combs of infested colonies) was significantly reduced already after 15 days of treatment, and after 30 days of treatment no infestation was found among the tested bees (Abou Zaid et al., 1987; Mazeed, 1987). [52]

Insecticidal, Nematicidal And Molluscicidal Activity

Essential oil of O. majorana, with terpinen-4-ol (41.6 per cent) as the major compound, affected the soil stages of phytonematodes (Rotylenchulus reniformis, Criconemella spp., Hoplolaimus spp.) and inhibited more than 80 per cent of Meloidogyne incognita juvenile hatching compared to about 3.5 per cent at the control (AbdElgawad and Omer, 1995). [53, 54]

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Conflict of Interest: None

Source of Funding: Nil