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REVIEW ARTICLE

PHYTOCHEMICAL AND PHARMACOLOGICAL REVIEW ON *ORIGANUM VULGARE*: A POTENTIAL HERBAL CURE-ALL

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Summary

Origanum vulgare (*O. Vulgare*) is a medicinal and aromatic shrub. It is commonly used as a culinary spice and in "traditional medicine" to cure a variety of diseases. Almost all parts including roots, leaves, stems, and flowers, are employed in medical systems to treat a variety of ailments. In recent scientific literature, among other things, the plant was reported to behave clinical effectiveness against antibacterial, hyperglycemia, anthelminthic and antifungal actions. Carvacrol, limonene, thymol, ocimene, pinene, caryophyllene, terpenes-cymene, and other significant medicinal chemicals have been extracted from this genus through phytochemical studies. The phytochemical ingredients of *O. vulgare* are highlighted in this review and its traditional uses, as well as evidence-based studies on the plant's diverse pharmacological effects. This illustrates the importance of conducting a thorough investigation in order to report new information on the mechanisms of action of these impacts.

Key words: phytochemistry; Origanum vulgare; Oregano; pharmacological screening

Introduction

Oregano is the common name for the aroma and flavour of more than 60 different plant species that are used as spices all over the world. "*Origanum* (Lamiaceae)" contains 39 species that are widely dispersed in the "Mediterranean region" (1). These plants are perennial herbs that grow naturally in calcareous soils. Oregano is distinguished by glandular trichomes that cover the aerial organs. The glandular trachoma secretes "Essential Oils" with a distinct flavour, owing to key constituents including carvacrol, thymol, and others. *Origanum vulgare* was first cultivated in southern Eurasia (1). Essential oils are significantly vital in the pharmaceutical, cosmetic, and food industries. Besides this, there is proof that Oregano essential oils may have health-promoting effects (2). Plants synthesize essential oils to defend themselves from microorganisms and pests, to invite native pollinators insects, and to process signaling, but current findings have shown that essential oils may have potential health benefits. (3). It is symbolized in India by a specific organism, *Origanum vulgare* species, which is dispersed throughout the Himalayan sub-temperate

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and temperate region (4). It's a mounding herb that grows 20–80 cm tall (Figure 1), has 1–4 cm long leaves, and thrives at a 7-12 pH level (5). The blooms are coloured in white and purple, measure 3–4 mm (0.12–0.16 in) in length, and are formed into upright peaks (6). It is often referred to as the wild marjoram and belongs to the *Origanum Majorana* family (7). Oregano is the anglicized form of the word Oregano (or perhaps old Latin organ) (8).

They were both derived from the Latin word "sweet marjo," *Origanum*, and wit was taken from a Greek strain or the species that meant just "pungent herb." (9). Oros means mountain, and genos means light, hence the Greek word has a unique etymology (10). Oregano is related to majo, often titled wild marjoram and Oregano bears violet petals and spades in olive-coloured form (11). It's a lifetime, yet in colder locations, it is planted as a twelve-monthly, as it seldom lives in cold (12). In March, Oregano is planted, at a spacing of 45 cm between plants, on soil that is rich in iron and receives the most sunlight. It likes a hot, dry climate, although it can thrive in a variety of different conditions (13). Humans have created Oregano subspecies with distinct flavours and properties, and the flavours are on another level, such as spicy and sweat (14). Oregano available in stores or plants wasn't as nice as native Oregano since it lacks several characteristics, such as being bushier and having a bland, peppery flavour (15). It can pollinate more complicated strains, but the embryos aren't much better if further developed (16). The flavours of Greek *Origanum onites* and West Asian *Origanum syriacum* are identical (17). Some plants have a flavor that is similar to Oregano and sweet marjoram (18).

Much scientific research has been carried out to investigate and validate the use of Oregano. This research has shown that phytochemicals and extracts from this species exhibit a great range of biochemical characteristics, including anti-inflammatory, antioxidant, antifungal, anticancer, hepatoprotective, and so on. Morphology, distribution, and systemic classification of *O. vulgare*, as well as its health benefits, phytoconstituents, and a complete up-to-date literature evaluation of diverse study findings connected to its ethnopharmacological property, are all covered in this review.

Figure 1. *Origanum vulgare* in flowering stage (19).

Morphology

Oregano is a wood-based, aromatic perennial which grows to an altitude of 20-30 cm and is blooms between May and October (20). Leaves seem to be ovate (egg, with a broader bottom end) and 10-44 mm in length and 5-25 mm broad, on each other's stem opposite (21). The leaf edges are smooth, and the pointers vary from acute to obtuse forms (rounded) (22). Bunch is full-blown, with flowers grouped into end spikes. The corolla is 5-8 mm in length and purple white. The calyx is divided into five sepals. Four stamens are in each flower (male parts). Four nutlets are in each fruit (single-seeded units) (23).

Phytochemistry

Phytochemical testing shows that all these "chemical compounds" are observable at varying forms of extraction of Oregano, including methanol extract, water extract, and essential oil, and as such the core elements of the aerial components seem to be the primary metabolites, thymol, and carvacrol (24). The dried plant material contained four key chemical compounds: thymol, carvacrol, c-terpinene, and p-cymene, which are also found in fresh Oregano (25). *Origanum vulgare* aerial parts contain a variety of phenolic glycosides, flavonoids, terpenoids, and tannins, as well as essential oils of different combinations. The major flavonoid compounds did find in hydroalcoholic extracts, infusions, and decoctions of *O. vulgare* are luteolin 7-O-glucoside and luteolin O-glucuronide whereas rosmarinic acid has been the major phenolic acid. Caffeic acid, vanillic acid, 0-coumaric acid, and protocatechuic acid have also been found (26). Essential oils of *Oreganum vulgare* contains a high amount of acyclic monoterpenes (β-myrcene, linalyl acetate, geraniol, and linalool), monocyclic monoterpenes (carvacrol, thymol, p-cymene, and γ-terpinene), bicyclic monoterpenes (sabinene, thujene, bomeol, and α-pinene), and sesquiterpenoids (germacrene-D, β-caryophyllene, β-bisabolene, and spathulenol). Numerous researchers have found that subspecies begun to grow in the northeastern Mediterranean basin is a poor resource of volatiles with good examples of acyclic compounds, phenolic monoterpenoids, sabinyl compounds, camphane type, and a higher proportion of sesquiterpenes), but that those begun to grow in the southern area are enriched in essential oils with monoterpenoids, primarily thymol or carvacrol, which can account for at least to 70% of overall oil production (27) (Figure 2).

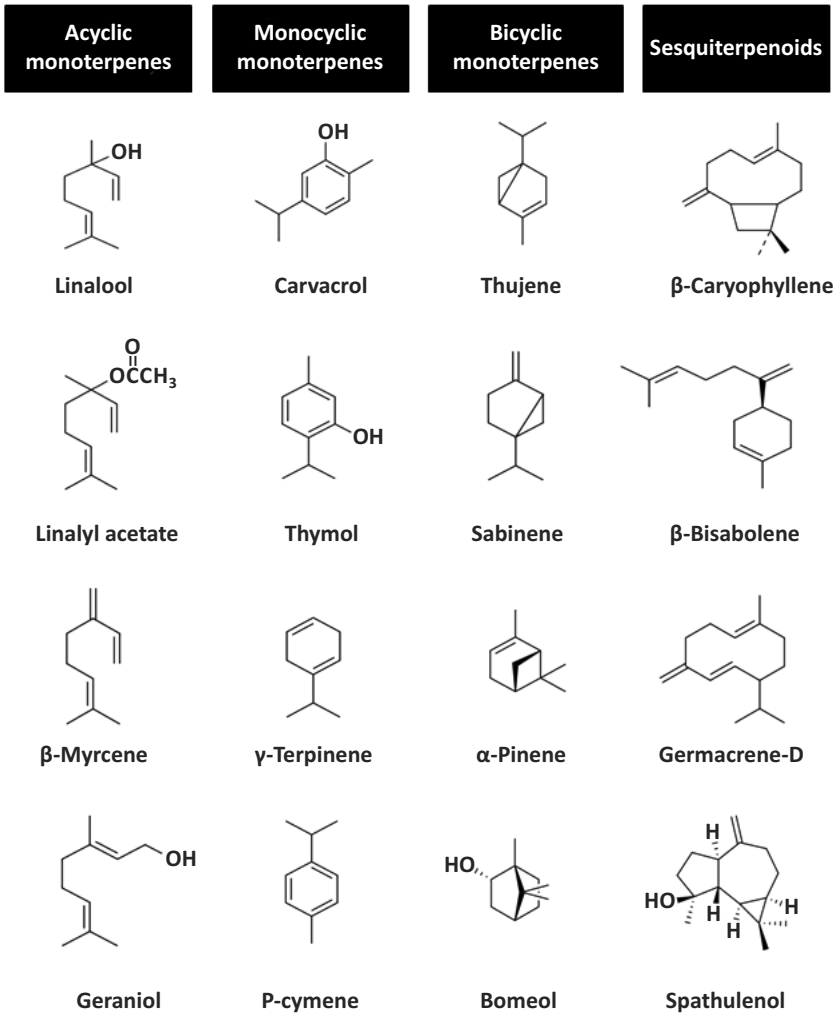

Figure 2. Phytochemical constituents.

Traditional uses

- The herb Oregano is used to treat narcotic poisoning, convulsions, and drops (28).
- Both are powerful natural bactericidal due to the high content of thymol in the essential oil of Oregano and extract of the leaf (29).
- The air-dried leaves are used to treat rheumatoid arthritis and uncomfortable swellings.
- Because of its antibacterial properties, tea of Oregano has been used to cure colds, fevers, and menstruation pain (30).
- Oregano stimulates bile flow while also helping to relieve flatulence discomfort and stomach gas discomfort (31).
- In patients with toothaches and various types of joint discomfort, diluted Oregano essential oil is recommended.
- Oregano was also utilized as an antidote to snake and insect bites that were venomous (32).

Ethnomedicinal uses

Food poisoning, bloating, indigestion, urinary issues, cough, headache, and bronchial troubles have all been treated with *Origanum vulgare* in India (33). In the past, it has been used for treating jaundice, fever, and vomiting. It includes several phytonutrients, including thymol, rosemary acid, and ursolic acid which were found to act as effective antioxidants, protecting cell structures throughout the body from oxygen-based damage (34).

Pharmacological Screening of *Origanum vulgare*

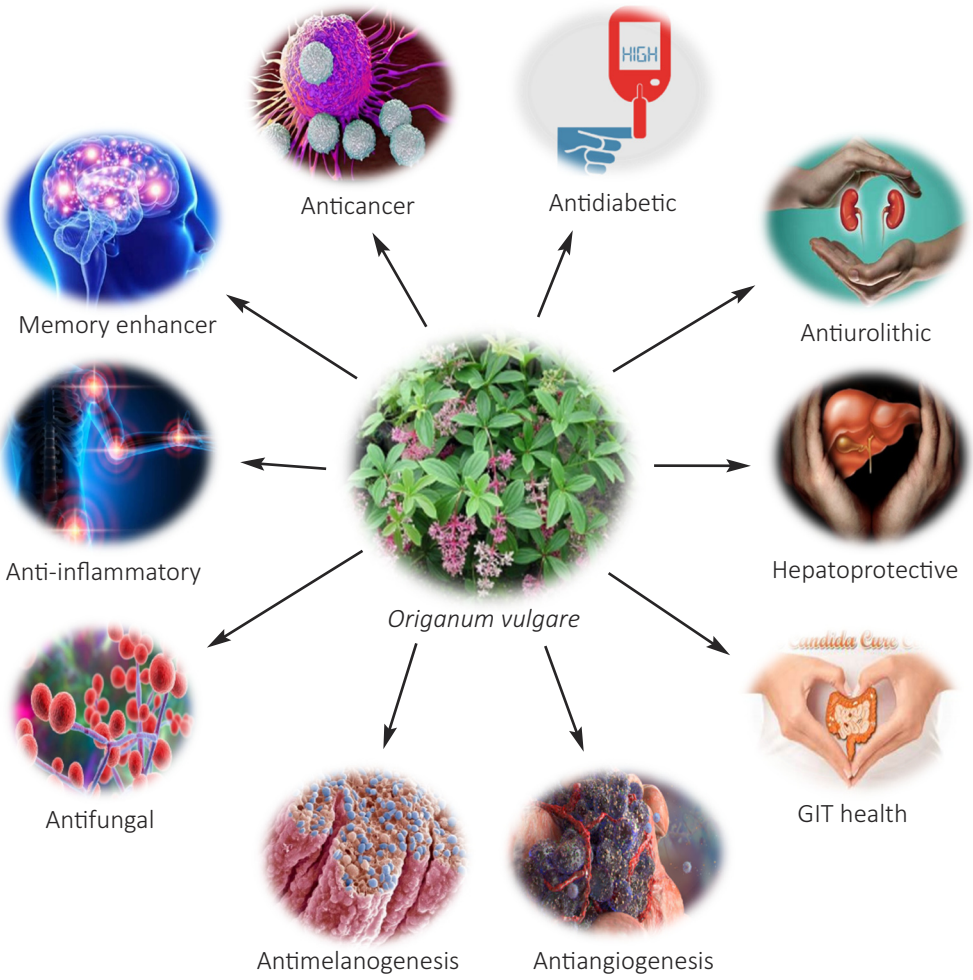

Figure 3. *Origanum vulgare* pharmacological screening.

Pharmacological properties of Oregano plant

Anti-inflammatory activity

Inflammation is the body's normal evolutionary reaction to cells serious harm, infections, and physical or chemical agents. The development of inflammatory processes is prompted during inflammation. Enzymes, prostaglandins, cytokines, prostaglandins, enzymes, reactive nitrogen species, and nitric oxide (NO) are a few instances of such mediators. Pro-inflammatory agents are overprocessed when inflammation is not treated, which can lead to pathological changes such as cancer, atherosclerosis, and arthritis.

As a result, inhibiting mediators is a critical goal in the treatment of inflammatory illnesses. (35). The anti-inflammatory efficacy of *Origanum Vulgare* was studied by Samar Javadian et al. (2015), indicating that methanolic Leaf Extract (1.5, 2.25, and 2.7 mg/ml) was used, to suppress iNOS, on microglial cells and activated mixed cells, extract of the leaf (36).

The study by Mir, R.H. et al. (2021), indicated that the extracts of *Oreganum Vulgare* suppress the pro-inflammatory cytokines (TNF-α and IL-6) and NO without influencing cell survival. (37). Oregano essential oil lowers the expression of inflammatory biomarkers (VCAM-1, MCP-1, and ICAM-1) in activated-human neonatal fibroblasts, according to a study by Han, X. et al (2017) (38). According to Conforti, F. et al. (2011) and Leyva-López, N. et al. (2016), Oregano essential oil reduces the production of NO and ROS in murine macrophage cells (39, 40).

Antioxidant activity

The impact of reactive intermediates such as superoxide anion, hydrogen peroxide (H_2O_2), hydroxyl (HO•), superoxide anion (O_2 •), alkoxyl (RO•), and peroxyl (RO_2 •) radicals on the contents of living things causes oxidative stress, which can lead to potential harm. Oxidative stress would result in significant cell proliferation, defense system hyperactivity, senescence, DNA damage, and cell death. As a result, several researchers have associated oxidative stress with the etiology of diseases including Parkinson's, Alzheimer's, chronic inflammation, some types of cancer, arthritis, some types of cancer, atherosclerosis, and diabetes (41). *Origanum vulgare* antioxidant activity (*in vitro*) was assayed using three extracts: cold water, ethanol, and hot-water extracts utilizing the DPPH and FRAP tests, by Teixeira, D. et al. (2013), the hot water had the most excellent impact on the DPPH experiment, followed by an extract of ethanol and an extract of cold water, whereas cold water had the highest potential in the FRAP assay (42).

Extracts of *Origanum vulgare* have been shown to have DPPH radical-scavenging behavior (43), radical-scavenging behavior against ABTS (44), and Ferric reduction/antioxidant ability (45), lipid oxidation retardation (46), radical-scavenging capacity in UV-induced peroxidation in the liposomal membrane (47).

Antifungal activity

The influence of the extract of *Oregano* on "Aspergillus spp." growth as well as biosynthesis of STC. Using a YES broth and an AGAR plate (sucrose yeast extract), by "Suncica Kocic-Tanackov et al" (2012). The antifungal activity of Oregano extract was demonstrated by increasing (0.2 -2.5 mL/100 mL) concentration (48).

Essential Oils of Oregano particles stuffed with nanoliposomes can be used as antifungals to T. rubrum. (49). According to Herrera-Rodrguez et al. (2019), the Emulsion of the essential oil of Mexican Oregano can be used as an antifungal to Candida albicans. (50).

Antidiabetic activity

Lemhadri, A. et al. (2004) investigated *Origanum vulgare* efficacy in diabetic rats produced by STZ (65 mg/kg i.v.). At a dosage of 20 mg/kg p.o., *Origanum vulgare* aqueous extract showed blood glucose reducing action (51), inhibition of α-glucosidase, and α-Amylase (52,53).

Anti-cancer activity

Essential oil elements may have antiproliferative properties. Their chemopreventive characteristics are due to a variety of mechanisms, including antimutagenic, antioxidant, and antiproliferative properties. The antiproliferative impact of essential oils has just been illustrated in a variety of cancer cell styles via multiple pathways (54).

The anti-tumor properties of *Oregano* were studied *in vivo* and *in vitro* by Peter Kubatka et al. (2016). N-nitroso-N-methylene causes carcinogenesis in rats. Oral administration of *Origanum* at doses of 3 and 30 g/kg. According to the findings, *Oregano* has a tumour inhibitory impact on a breast cancer model for the first time (55), Tumour sizes in illness mice should be reduced (56), Human LNCaP-prostate and MCF-7 breast (MCF-7) cancer cell designs' viability is suppressed (57)

Anti-microbial activity

Due to their anti-pathogenic features, essential oils derived from spices and herbs have received extensive research. Many *in vivo* and *in vitro* studies assays have been designed to examine essential oils' potential antibacterial, antifungal, and antiviral functions (58).

Oniga, I. et al. (2018) investigated the antimicrobial activity of *Origanum vulgare* ssp. against S. enteritidis, E. coli, L. monocytogenes, and S. aureus. The extract proved effective at inhibiting microbial growth, with varied sizes of inhibition zones compared to the standards: gentamicin for antibacterial activity. The extract was an inhibitor of all bacteria tested and had high antibacterial activity (59).

Chun, S.S. et al. (2005) investigated the antibacterial properties of *Origanum vulgare* against Helicobacter pylori. The usual agar diffusion method was used to investigate antimicrobial action against Helicobacter pylori. HPLC was used to examine phenolic profiles in Oregano extracts. The variations in phenolic acid physicochemical characteristics with C6-C3-COOH and C6-C1-COOH structures have been proposed as a factor in growth inhibition (60).

Anxiolytic activity

The anxiolytic efficacy of the aqueous extract of *Origanum vulgare* in rats was examined by Tajmah Mombeini et al. (2015). ORG was given to rats at doses of 50, 100, 200 mg/kg, along with diazepam as a controlled drug. ORG extract exhibits anxiolytic effects in the (EPM- elevated plus maze) and (OFT- open field test) (61). Bautista-Hernández, I. et al. (2021) and Amiresmaeili, et al. (2018) implied that *Origanum vulgare* extracts have anxiolytic impacts. (62, 63).

Antinociceptive activity

Origanum vulgare aqueous extract was investigated at a dose (1,3,6 g/ rat) using a test model (tail flick) as behavioral parameters to assess the antinociceptive activity of the aqueous extract of *Origanum vulgare*, by Afarineshe Khaki et al. (2013) (64).

According to Costa et al (2020) and Chabib, L. et al. (2021), Oregano has an antinociceptive activity due to the presence of monoterpene and carvacrol (65, 66).

Antiurolithic activity

Origanum vulgare was investigated in a CaOx urolithiasis animal model. The rats were given 10 and 30 mg/kg of crude methanolic aqueous extract of *Origanum vulgare*. The antiurolithic action of *Origanum* was discovered through the analysis of urine and serum samples, by Aslam Khan et al (2011) (67). ElSawy, N.A., and Mosa, O.F., (2021) proposed that *Origanum vulgare* exhibited antiurolithic impacts on calcium oxalate particle deposits via multiple mechanisms having to act at different sites via hypocalciuric, hypoxaliuric and antioxidant impact. (68).

Hepatoprotective activity

Origanum vulgare aqueous extract of the leaves was investigated at dosages (50,100,150 mg/kg p.o.) against CCl4-induced toxicity.

Researchers discovered that *Origanum vulgare*'*s* antioxidant properties can protect against CCL4-induced hepatotoxicity, Mohammad Sikander et al. (2012) (69). According to Abdel-Latif, H.M. et al. (2020) and El-sayed, M. et al. (2021), Oregano has a hepatoprotective impact related to carvacrol and thymol presence (70, 71).

Memory enhancer activity

Leaf extract of *Origanum vulgare* leaf was investigated on LTP induction and discrimination learning by V. Sheibani et al. (2010). An aqueous extract of Oregano (150, 300, and 450 mg/kg) was used. The conclusion was the aqueous extract can increase learning criteria in mice using T-maze equipment and electrophysiological recording (72). Mohajeri, M.H., and Prudence, K. (2013) proposed that Oregano improves mood as well as mental well enough in healthy people (73). Wavra, N. (2019), claimed that Oregano improves memory and brain function (74).

Antimelanogenesis

Liang et al. (2010) At 10–20 g/mL, origanoside has been shown to suppress tyrosinase activity between 16.9%–28.6% in cell culture (B16 melanoma cells). A topical gel containing origanoside was applied to the skin of mice for 10 days and showed whitening effects related to reduced pigment expression-producing genes (MITF, TRP-2, and tyrosinase) (75).

Morshedloo et al. (2018) and Nanni, V. et al. (2020) proposed that extracts of Oregano impeded tumor cell division and melanogenesis by activating cell death paths (both necroptosis and apoptosis) via DNA and mitochondria destruction (76, 77).

GIT health

Veenstra, J.P. and Johnson, J.J., (2019) investigated *Origanum vulgare* extract for food "preservation and gastrointestinal health enhancement". A single herb, such as Oregano, or a mixture of "extracts or essential oils" may have an even higher effect on "food preservation".

These herbs have also been demonstrated to boost GI health in addition to food preservation. Studies on mice have demonstrated that lowering GI inflammation and reducing the symptoms of TNBS exposure can be beneficial (78).

Feng, J. et al. (2021) proposed that essential oils of Oregano keep the improvement of epithelial barrier features, gut morphology, and mucosal immunological status by adjusting microbial communities (79).

Antiangiogenic activity

Paderes N.M. and Lagangilang A.P. (2020). Using the Chick Chorioallantoic Membrane (Cam) Assay, "researchers investigated the antiangiogenic activity of the aqueous extract of Oregano in vivo". This study found that Oregano leaf extract contains polyphenolic or phenolic compounds such as flavonoids, anthocyanins, and saponins, indicating that it can prevent angiogenesis (80).

According to Bostancolu et al. (2012), Extracts of *Origanum vulgare* inhibit in vitro tubular formation (81).

Conclusion

O. Vulgare is a valuable medicinal plant that contains a variety of bioactive compounds. Almost every part of this plant has been utilized to cure a variety of ailments in traditional medicine. In recent scientific literature, extracts of the plant have been found to have potential usefulness against inflammation, cancer, diabetes, and other

disorders. Various sections have been discovered to have biological activity that is more particularly geared toward the treatment of metabolic disorders. Focus on creating modern formulations after a thorough examination of their safety, bioactivity, pharmacodynamics, pharmacokinetics, and other factors. *O. vulgare* extracts can be used in food products, plant products, pharmaceutical products, and food preservation, depending on their application. Because Oregano is a low-cost, non-toxic herb and readily available, these factors justify the inclusion of oregano extracts or essential oils with strong phenolic compounds in the food industry. This review expands on the identified pharmacological activities and phytochemical information of *O. vulgare*, paving the way for future research studies.

Conflict of Interest

The authors declare that no conflict of interest exists for this research.

Adherence to Ethical Standards

Not applicable (review article)

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