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Review Article

A CRITICAL REVIEW ON TRADITIONAL USES, PHYTOCHEMISTRY AND PHARMACOLOGICAL USES OF *ORIGANUM VULGARE* LINN.

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ABSTRACT

The genus *Origanum* (Lamiaceae) includes 39 species widely distributed in the Mediterranean region. *Origanum vulgare* L. (*O. vulgare*) is an important aromatic and medicinal plant of the genus *Origanum*. It is used as a culinary condiment and largely employed as antimicrobial, antifungal, antioxidant, antibacterial, anti-mutagenic, cytotoxic and anticancer agent. Phytochemical investigations of this genus have resulted in the extraction of a number of important bioactive compounds such as carvacrol and thymol. Review of literature included PubMed, Science Direct searches with *'Origanum vulgare' and 'Origanum'* as initial key words. This review aims to highlight the traditional uses, phytochemistry and pharmacological uses of *O. vulgare*.

Keywords: *Origanum vulgare*, *Origanum*, Lamiaceae, Phytochemistry, Pharmacology.

INTRODUCTION

The small genus *Origanum*, (Lamiaceae), is an annual, perennial, and shrubby herb that is native to the Mediterranean, Euro-Siberian, and Irano-Siberian regions[1]. *Oregano* is the common name for the aroma and taste that comes primarily from more than 60 species of plants used worldwide as a spice. *Oregano* characterize by the presence of glandular trichomes covering the aerial organs. The glandular trichomes secrete essential oils with a unique flavor, which is mainly due to its major compounds such as carvacrol and thymol[2]. *Origanum vulgare* L. (Figure 1) is a perennial herbaceous plant belonging to the family Lamiaceae. It is widely known as a very versatile plant with many therapeutic properties such as diaphoretic, carminative, antispasmodic, antiseptic, tonic and being applied in traditional medicine systems in many countries[3]. It has been widely used in agricultural, and perfumery for its spicy fragrance[4]. However, to best of our knowledge, till date systemic studies on *O. vulgare* have not been reported. Hence, the present review aims to compile up-to-date information on the progress made in the phytochemistry and pharmacology of *O. vulgare*. Hence, we planned to collect the research articles related to *O. vulgare* from various scientific databases and write a systemic review on its traditional uses, phytochemistry and pharmacological properties.

Figure 1: Aerial parts of *Origanum vulgare*

CLASSIFICATION

Kingdom :	Plantae
Class :	Equisetopsida
Subclass :	Magnoliidae
Superorder:	Asteranae
Order :	Lamiales
Family :	Lamiaceae
Genus :	*Origanum*
Species :	*vulgare*
Scientific name:	*O. vulgare* L.

VERNACULAR NAMES

Engilsh-Oregano; Hindi-Sathra; Telgu-Mridu-maruvamu; Kannad-Maruga; Panjabi-Mirzanjosh; Unani-Marzanjosh; Gujarati-damnak; Sanskrit-damnak[5].

GENERAL DESCRIPTION AND DISTRIBUTION

Origanum species grow abundantly on stony slopes and rocky mountain areas at a wide range of altitudes (0-400 m)[6]. It is an aromatic, branched perennial herb, 30-90 cm high, found in the temperate Himalayas and from Kashmir to Sikkim, at altitudes of 1500-3600 m. Leaves broadly ovate, entire or rarely toothed; flowers purple or pink, in corymbose cymes. It is common in Shimla hills and in Kashmir valley. It is hardly and can be grown in all warm garden soils. It is propagated by seeds, cuttings, layers and root-division. It can be sown during October in plans and during March and April in the hills. The plant possesses an aromatic, thyme-like flavour. The leaves and tops cut prior to blooming are used to flavour foods[5].

PHYTOCHEMISTRY OF *ORIGANUM VULGARE*

Oregano is a widely used spice in the food industry. It is mainly used for its aromatic properties with a primary role to enhance the taste and aroma of foods. Kocic-Tanackov *et al.*[7], reported the presence of oleanolic, ursolic, caffeic, rosemarinic, lithospermic acids, flavonoids, hydroquinones, tannins, and phenolic glycosides (Figure 2).

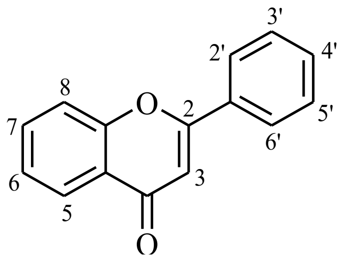
Phenolic compounds were isolated and characterized as protocatechinic acid and his phenyl glucoside, caffeic acid, rosmarinic acid; and a phenolic derivative of rosmarinic acid isolated from hexane and methanolic extracts[8] and tocopherol homologues isolated from the dichloroethane extract of *O. vulgare*[9]. In addition to the major constituents apigenin, luteolin, salvagenin, cirsimartin, diosmetin, desmethoxycentauridin, 5-hydroxy-6,7,3',4'-tetramethoxy-apigenin, apigenin 7-*O*-glucoside, luteolin 7-*O*-glucoside, luteolin 7-*O*-glucoside-6''-methylester, two new flavonoids were isolated, in minor concentration, and identified as luteolin 7-*O*-*α*-*L*-rhamnoside-4'-*O*-*β*-*D*-glucoside and quercetin 3-*O*-*β*-*D*-glucoside-4'-*O*-*α*-*L*-rhamnoside have been isolated from the methanolic extract of *O. vulgare*[10]. Major phenolic acids were identified as caffeic, *p*-coumaric, ferulic and neochlorogenic, while predominant flavonoids were characterized as quercetin, luteolin, apigenin, kaempferol and isorhamnetin[11].

A dihydrobenzodioxane derivative, origalignanol, together with nine polyphenolic compounds, salvianolic acid A, salvianolic acid C, lithospermic acid, apigenin 7-*O*-*β*-*D*-glucuronide, apigenin 7-*O*-*β*-*D*-(6 *β*-methyl) glucuronide, luteolin, luteolin 7-*O*-*β*-*D*-glucopyranoside, luteolin 7-*O*-*β*-*D*-glucuronide and luteolin 7-*O*-*β*-*D*-xylopyranoside were isolated from the aqueous ethanolic extract of the aerial parts of *O. vulgare*[12]. Flavonoid constituents were isolated from *O. vulgare* and characterized as apigenin, eriodictyol, taxifolin and dihydrokaempferol[13] and apigenin and luteolin (in insignificant quantities) were identified in acetone extracts of Greek oregano (*O. vulgare* ssp. *hirtum*)[14]. Rosmarinic acid, luteolin, luteolin glycoside, apigenin, apigeninacetyl-diglycoside and diosmetin-acetyl-glucuronide were reported[15]. Luteolin, apigenin, luteolin 7-*O*-*β*-*D*-glucuronide, apigenin 7-*O*-*β*-*D*-glucoside (cosmosiin) were isolated from the aerial parts of *O. vulgare*[16]. Bioassay-guided isolation of methanolic extract of the leaves of *O. vulgare* gave two protocatechuic acid ester derivatives, origanol A and origanol B along with ursolic acid, oleanolic acid, *β*-sitosterol, and triacontanol[17].

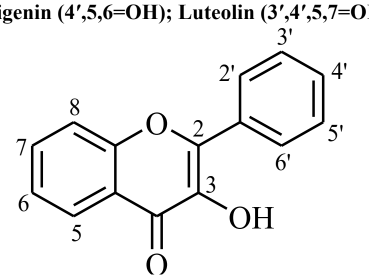
The essential oils of four wildly growing *O. vulgare* from Kumaon region (Uttarakhand, India) were reported for the presence of *p*-cymene (6.7-9.8%), *γ*-terpinene (12.4-14.0%), thymol (29.7-35.1%) and carvacrol (12.4-20.9%) as major constituents collected from Dhoulchina and Champawat (chemotype I) while the oil from Kilbury and Rushi village (chemotype II) showed linalool (6.7-9.7%), bornyl acetate (12.6-16.8%), *β*-caryophyllene (10.5-13.8%) and germacrene D (6.3-11.3%) as the major constituents[18].

Essential oils derived from six different phenophases of *O. vulgare* grown in Kumaon region of Uttarakhand, India were investigated by GC and GC-MS. Major components of oils were reported as thymol (40.9-63.4%), *p*-cymene, (5.1-25.9%), *γ*-terpinene (1.4-20.1%), bicyclogermacrene (0.2-6.1%), terpinen-4-ol (3.5-5.9%), *α*-pinene (1.6-3.1%), 1-octen-3-ol (1.4-2.7%), *α*-terpinene (1.0-2.2%), carvacrol (<0.1-2.1%), *β*-caryophyllene (0.5-2.0%) and *β*-myrcene (1.2-1.9%). Thymol, terpinen-4-ol, 3-octanol, *α*-pinene, *β*-pinene, 1,8-cineole, *α*-cubebene and (*E*)-*β*-ocimene were observed to be higher during full flowering season. The study showed that plant stage had a significant effect on the essential oil content and composition of *O. vulgare* grown in the hilly tracks of Northern India[19].

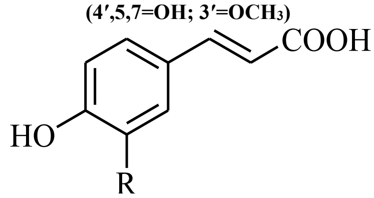
Essential oils obtained from flowers, leaves and stems of *O. vulgare* growing wild in Ardabil Province (north-west Iran), were reported to possess *β*-caryophyllene as the major constituent in all three oils (48.1%, 50.1% and 60.2%, respectively). The other major components were characterized as 1,8-cineole (11.6%), *α*-pinene (6.9%), and *γ*-cadinene (4.8%)[20]. The essential oil of *O. vulgare* growing wild in Kodjour (N. Iran) was reported for the presence of linalyl acetate, sabinene, *γ*-terpinene, *trans*-ocimene, and *cis*-ocimene and low percentages of the phenolic monoterpenoids (thymol and carvacrol) together with sesquiterpenoid (44 %) fraction *β*-caryophyllene, caryophyllene oxide, germacrene D, and *γ*-elemene[21].



Apigenin (4′,5,6=OH); Luteolin (3′,4′,5,7=OH)



Quercetin (3′,4′,5,7=OH); Kaempferol (4′,5,7=OH); Isorhamnetin (4′,5,7=OH; 3′=OCH_3)



***p*-Coumaric acid (R=H); Caffeic acid (R=OH); Ferulic acid (R= OCH_3)**

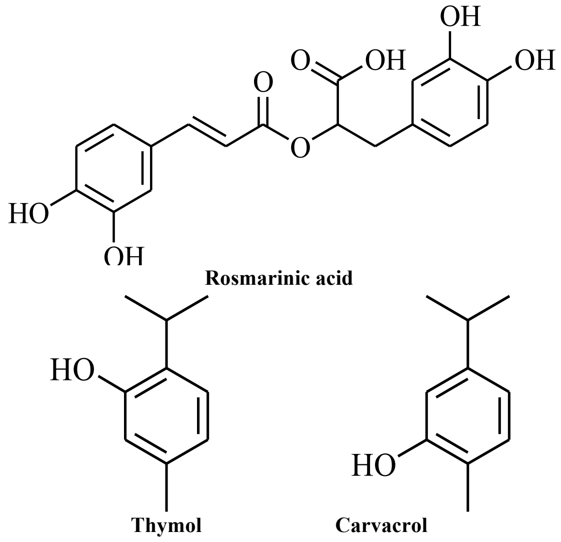


Figure 2: Chemical structures of major reported phytoconstituents of *Origanum vulgare*

PHARMACOLOGICAL BIOACTIVITIES OF *ORIGANUM VULGARE*

Oregano essential oils obtained from the genera *Origanum* is rich in carvacrol, a monoterpenic phenol isomeric with thymol. Carvacrol is responsible for the biological activities such as antimicrobial, antitumor, antimutagenic, antigenotoxic, analgesic, antispasmodic, antiinflammatory, angiogenic, antiparasitic, antiplatelet, antielastase, insecticidal, antihepatotoxic and hepatoprotective activities[22].

Antiobesity Activity
Pancreatic lipase is the most important enzyme in digestion of triglycerides. One of the strategies in prevention or treatment of obesity is altering metabolism of lipids by inhibition of dietary fat absorption. Antilipase activity was determined by turbidimetric assay. The methanolic extract of *O. vulgare* showed pancreatic lipase inhibitory activity[23].

Antihyperlipidemic Actions
Volatile oil, methanolic and aqueous extract of *O. majorana* syn. *O. vulgare* leaves showed antihyperlipidemic effects in lowering the elevated triglycerides and cholesterol levels in streptozotocin induced diabetic rats[24,25].

Anti-hyperglycaemic Potentials
The essential oil, methanolic and aqueous extract of *O. vulgare* leaves showed anti-hyperglycaemic activity by significantly decreasing blood glucose levels in STZ diabetic rats.[24] In addition, no changes were observed in basal plasma insulin concentrations after treatment in either normal or STZ diabetic rats indicating that the aqueous extract acted without changing insulin secretion[26,27]. The extracts of clonal oregano lines were reported to possess strong inhibitory activity against porcine pancreatic amylase (PPA) activity *in vitro*. PPA inhibition varied by extract and ranged from 9% to 57%. The authors also suggested that amylase inhibition by oregano extract was associated with extract total phenolic content and rosmarinic acid, protochatechuic acid, quercetin, and *p*-coumaric acid contents, as well as extract antioxidant activity and protein content[28].

Antioxidant Activity
Different extracts and essential oil of *O. vulgare* were reported to possess antioxidant activity. They showed strong DPPH scavenging activity, protective effects on lipid peroxidation in liposomes, NO and H_2O_2 neutralization activities[7,24,29,30].

Hepatoprotective Activity
Aqueous extract of *O. vulgare* leaves showed hepatoprotective activity on CCl_4-induced hepatotoxicity in normal and hepatotoxic rats by decreasing serum alanine amino transferase (ALT), alkaline phosphatase (ALP), and aspartate amino transferase (AST), lipid peroxide (LPO); and increasing GST, CAT, SOD, GPx, GR, and GSH in liver tissues[31]. The *O. vulgare* extract was reported to possess hepatoprotective activity against halothane induced hepatotoxicity by decreasing the serum levels of AST, ALT, ALP, total bilirubin (T-BIL), direct bilirubin (D-BIL) and indirect bilirubin (I-BIL) compared with group of Halothane[32].

Antifungal Effects
The essential oil of *O. vulgare* showed antifungal effects against *Aspergillus flavus*, *A. parasiticus*, *A. fumigatus*, *A. terreus* and *A. Ochraceus*[33], *Candida albicans*, *Penicillium* species, *P. aurantiogriseum*, *P. glabrum* and *P. brevicompactum*, *P. chrysogenum*; *Fusarium proliferatum*, *F. oxysporum*, *F. verticillioides*, *F. subglutinans*[7] and against the human pathogens *Malassezia furfur*, *Trichophyton rubrum*, and *Trichosporon beigelii*[34]. Antifungal activities were also reported by many other scientists[35,36].

Antibacterial Effects
Essential oil from *O. vulgare* showed antibacterial effects against *Bacillus subtilis*, *Enterobacter cloacae*, *Escherichia coli*[37], *Micrococcus flavus*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Salmonella enteritidis*, *S. epidermidis*, *S. typhimurium*, and *Staphylococcus aureus*[38] and against ulcer-associated *Helicobacter pylori*[39].

Antiurolithic Activity
The crude aqueous-methanolic extract of *O. vulgare* was reported to exhibited antiurolithic activity *by* inhibiting the slope of nucleation and aggregation; and also decreased the number of calcium oxalate monohydrate crystals produced in calcium oxalate metastable solutions and prevented as well as reversed toxic changes including loss of body weight, polyurea, crystalluria, oxaluria, raised serum urea and creatinine levels and crystal deposition in kidneys compared to their respective controls[40].

Anticancer Activity
Volatile oils and the crude ethanol and water extracts showed antiproliferative activity to the adenocarcinoma of breast cell line (MCF7)[41]. Acetone extracts inhibited *in vitro* cytotoxicity against a noncancerous African green monkey kidney (Vero) cell line and an adenocarcinoma cervical cancer (HeLa) cell line[42]. The methanolic extract showed cytotoxic effect of on HCT-116 and MDA-MB-231 cell line *in vitro* by using an MTT viability assay by inhibiting the cell growth[43].

Antinociceptive Potential
The aqueous extract of *O. vulgare* showed antinociceptive activity. The response latency of rats to thermal stimulation was recorded using Tail-Flick test. Co-administration of *O. vulgare* extract and baclofen showed significant decrease in the response latency compared to control group[44].

Antiplatelet Activity
Essential oil from *O. vulgare* showed antiplatelet activity by inhibition of clot retraction in guinea pig and rat plasma. A significant correlation between antiplatelet potency and phenyl

propanoids content was evidenced thus suggesting a key role for this moiety in the prevention of clot formation[45].

Antimelanogenic Properties

Rosmarinic acid methyl ester was isolated form *O. vulgare* showed ability to reduce tyrosinase, DOPA oxidase and melanin contents in B16 cells. The results suggested that the isolated compound possess antioxidant and depigmentation effect that may be useful in food additives and in the control of skin pigmentation[46].

CONCLUSION

Phytochemical and pharmacological studies done so far on the *O. vulgare* confirm the claims of traditional use of this plant. *O. vulgare* has immense potential for researchers and exploring it will lead to isolation and identification of new compounds which could be used as drugs for curing common and critical diseases. Pharmacological studies have demonstrated its anticancer, hepatoprotective, antimalarial, anthelmintic, antibacterial, antifungal and antioxidant activities. This review further highlights the discovered pharmacological effects and phytochemical details of *O. vulgare* which provide way to further studies and research.

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