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REVIEW ARTICLE

Medicinal importance of Genus *Origanum* – A review

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Abstract

Genus *Origanum* is important medicinally as it has antimicrobial, antifungal, antioxidant, antibacterial, antithrombin ,antimutagenic, angiogenic, antiparasetic and antihyperglycaemic activities. Phytochemical investigations of the species of this genus has resulted in the extraction of a number of important bioactive compounds. This emphasizes on the need of extensive study for reporting the additional information on the medicinal importance of other unattended species of genus *Origanum*.

Introduction

Primary and secondary metabolites produced by plants, encompass a wide array of functions. Secondary metabolites have been subsequently exploited by humans for their beneficial role. At the same time essential oils and their components are also being exploited for potential multipurpose functional use (Sawamura ,2000; Ormancy *et al*.,2001; Gianni *et al*., 2005).Thus medicinal and aromatic plants are valued for their biological activities which can be justified from the fact that about 80% of the local population still depend on these plants for primary health care. The formation and accumulation of essential oil in plants has been reviewed by many workers (Guenther, 1972; Corteau, 1986; Fischer, 1991). The compounds from the plant based essential oil are useful as an alternative therapy, either directly or as models for new synthetic products (Houghton, 2000).

Origanum is an important multipurpose medicinal plant which belongs to the family Lamiaceae, tribe Mentheae and comprises of 42 species and 18 hybrids widely distributed in Eurasia and north Africa (Ietswaart,1980; Duman *et al*., 1988). It is native to the mountainous parts of Mediterranean region of Europe and Asia. Following Ietswaart's (1980) classification, the genus Origanum has been divided into 10 sections. These include:

I. Section *Amaracus* (Gleditsch) Bentham: It consists of seven species, all restricted in the east Mediterranean region. The species are mainly characterized by their usually purple bracts, 1 or 2-lipped calyces without teeth, and saccate corollas.

1. *O. boissieri* Ietswaart
2. *O. calcaratum* Jussieu
3. *O. cordifolium* (Montbret et Aucher ex Bentham) Vogel
4. *O. dictamnus* L.
5. *O. saccatum* Davis
6. *O. solymicum* Davis
7. *O. symes* Carlstrom

II. Section *Anatolicon* Bentham: It comprises of eight species, presenting a very restricted distribution in Greece, Asia Minor, Lebanon and Libya. The plants have strongly bilabiate 5-toothed calyces.

1. *O. akhdarense* Ietswaart et Boulos
2. *O. cyrenaicum* Beguinot et Vaccari
3. *O. hypericifolium* Schwarz et Davis

4. *O. libanoticum* Boissier
5. *O. scabrum* Boissier et Heldreich
6. *O. sipyleum* L.
7. *O. vetteri* Briquet et Barbey
8. *O. pampaninii* (Brullo et Furnari) Ietswaart

III. Section *Brevifilamentum* Ietswaart: This section comprises of six species which are steno-endemics mainly in the eastern part of Turkey. These species are characterized by bilabiate calyces and stamens strongly unequal in length, whose upper two are very short and included in the corolla.

1. *O.acutidens*(Handel-Mazzeti) Ietswaart
2. *O.bargyli* Mouterde
3. *O.brevidens* (Bornmuller) Dinsmore
4. *O.haussknechtii* Boissier
5. *O.leptocladum* Boissier
6. *O.rotundifolium* Boissier

IV. Section *Longitubus* Ietswaart: It consists of a single species found in a few places in the Amanus Mountains. It is mainly characterized by the slightly bilabiate calyx, the lips of the corolla are nearly at right angles to the tube and has the presence of very short staminal filaments.

1. *O. amanum* Post

V. Section *Chilocalyx* (Briquet) Ietswaart: It includes four species which are steno-endemics of South Anatolia or of the island of Crete. The plants are slightly bilabiate, conspicuously pilose in throat calyces.

1. *O. bigleri* Davis
2. *O. micranthum* Vogel
3. *O. microphyllum* (Bentham)Vogel
4. *O. minutiflorum* Schwarz et Davis

VI. Section *Majorana* (Miller) Bentham: It consists of three species. The species are characterized by 1-lipped calyces and green bracts. Among them *O. syriacum* is further subdivided into three geographically distinct varieties; these are recognised mainly from differences in their indumentum and leaf shape.

1. *O. majorana* L.
2. *O. onites* L.
3. *O. syriacum* L. Var. *syriacum*
4. Var. *bevanii* (Holmes) Ietswaart
5. Var. *sinaicum* (Boissier)) Ietswaart

VII. Section *Campanulaticalyx* Ietswaart: It consists of six local endemic species. The calyces of the plants have 5 sub equal teeth and are campanulate even when bearing fruits.

1. *O. dayi Post*
2. *O. isthmicum* Danin
3. *O. ramonense* Danin
4. *O. petraeum* Danin
5. *O. punonense* Danin
6. *O. jordanicum* Danin and Kunne

VIII. Section *Elongatispica* Ietswaart: It comprises of three steno-endemic species of North Africa, which are characterized by loose and tenuous spikes and tubular calyces with 5 equal teeth.

1. *O. elongatum* (Bunnet) Emberger et Maire
2. *O. floribundum* L.Munby
3. *O. grosii* Pau et Font Quer ex Ietswaart

IX. Section *Origanum*: It is a monospecific section consisting of the species *O. vulgare*, widely distributed in North Africa and in temperate and arid zones of Eurasia (Baser *et al*.,2010) . Introduced by humans, this species has also been encountered in North America (Ietswaart 1980). The plants of *O. vulgare* have dense spikes, and tubular 5-toothed calyces, never becoming turbinate in fruit.

1. *O.Vulgare* L.

Six subspecies have been recognised within *O. vulgare L.* based on differences in indumentum, number of sessile glands on leaves, bracts and calyces, and in size and colour of bracts and flowers.

1. Subsp. *vulgare*
2. subsp. *glandulosum* (Desfontaines) Ietswaart
3. Subsp. *gracile* (Koch) Ietswaart
4. Subsp. *hirtum* (Link) Ietswaart
5. Subsp. *viridulum* (Martrin-Donos) Nyman
6. subsp. *virens* (Hoffmannsegg and Link) Ietswaart

X. Section *Prolaticorolla* Ietswaart: It comprises of three species endemic to eastern or western parts of the Mediterranean. These species are characterized by dense spikes and tubular calyces becoming turbinate in fruiting.

1. *O. compactum* Bentham
2. *O. ehrenbergii* Boissier
3. *O. laevigatum* Boissier

Origanum species have been used for thousands of years as spice and in ethnomedicine (Fleisher and Fleisher,1988). It has antifungal, antimicrobial, insecticidal and antioxidant activities (Kokkini, 1997;Baydar *et al*., 2004; Kulisic *et al*.,2004;Bakkali *et al*., 2008). Antispasmodic, antitumoral, antifungal and analgesic activity of *Origanum* species has been reported by (Elgayar *et al*.,2001;Puertas *et al*.,2002;Sokovic *etal*.,2002;Sari *et al*.,2006). Baser, 2002; Dundar *et al*.,2008 reported that *Origanum* has been used as expectorant, antiparasitic, antihaelminthic and for gastrointestinal complaints in Turkish folk medicine. *Origanum* species are also used as a carminative, diaphoretic, stimulant and tonic (Hummer *et al*., 1999).Silva *et al*., 2012 have suggested that carvacrol present in the essential oil of *Origanum* probably interferes in the release and/or synthesis of inflammatory mediators, such as the protanoids and thus favour the healing process for gastric ulcers. Further as a folk remedy it is used against colic, cough, tooth aches and irregular menstrual cycles (Force *et al*., 2000; Kintzios 2002a). *Origanum* species are also used as powerful disinfectant, flavouring agent in perfumes and in scenting soaps (Guenther, 1949; Chiez, 1984; Kotb, 1985). As a culinary herb it is used in flavouring food products and alcoholic beverages (Aligiannis *et al*.,2001;Bendahou *et al*., 2008;Sivropoulou *et al*., 1996). Oregano has a promising potential for preventing diabetes complications in the long term and has an anti inflammatory efficacy by inhibiting soybean lipoxygenase (Koukoulitsa *et al*., 2006). The secondary metabolites of this plant have been well studied in terms of polyphenolic compounds and essential oils. Consequently, more than one hundred nonvolatile compounds have already been identified in this plant with conventional phytochemistry methods including flavonoids, depsides and origanosides (Nakatani *et al*.,1987;Lin *et al*., 2003; Koukoulitsa *et al*.,2006;Liang *et al*.,2010; Skaltsa *et al*., 2010). The species of this plant which have been subjected to chemical profiling are discussed below.

Origanum vulgare (L.) is a medicinal, perennial plant, locally known as Jungali Tulsi or Oregano or Himalayan marjoram. It is widely distributed in Mediterranean areas and Northern Africa (Ietswaaart, 1980; Kokkini, 1997). This is the only species of genus *Origanum* which is found in India. It is found in temperate Himalayas from Kashmir to Sikkim at an altitude of 1500 – 3600m . It is particularly grown in Simla Hills, the Giligit, the Nilgris and in the Kashmir valley.

Vokou *et al*.,1993 ;Kokkini *et al*., 1997; D'antuonu *et al*., 2000; Skoula, 2002 reported carvacrol and thymol as dominant components of its essential oil. Andreas *et al*., 2013 found carvacrol as dominant component in the essential oil of *O. vulgare* ssp. hirtum. Lagouri *et al*., 1993; Aeschbach *et al.*, 1994; Yanishlieva *et al*., 1999 have revealed that antioxidant effect of this plant is because of carvacrol and thymol. Mastelic *et al*., 2008 reported its antimicrobial and antioxidant properties and in addition revealed carvacrol's antiproliferative activity on tumor cells of Hela. Essential oil of this plant possesses a variety of biological activities viz. antiradical (Cervato *et al*., 2000; Ahmad *et al*., 2010a; 2010b; 2011a; 2011b), antifungal (cleff *et al*., 2010; Farag *et al*., 1989; Curtis *et al*., 1996; Sahin *et al*.,2004), antihyperglycaemic (Lemhadri *et al*., 2004), antibacterial (Dorman and Deans, 2000; Govaris *et al*., 2001; Harpaz *et al*., 2003; Burt and Reinders, 2003; Burt, 2004), antithrombin (Goun *et al*., 2002). Antioxidant (Lamaison *et al*.,1991,Lagoun and Boskou, 1996; Nakatani, 2000; Vichi *et al*., 2001; Stashenko *et al*., 2002) function of this species could become helpful agent in treatment of cancer, heart diseases and high blood pressure. Cervato *et al*., 2000 reported that antioxidant activities of *Origanum vulgare* leaves can inhibit all places of lipid peroxidative processes.

Origanum onites (L.) is distributed in Western and Southern Turkey. Baser et al., 2010 have reported that it grows naturally in Agean and Mediterranean regions of Turkey. It is a perennial species with woody stem and is commonly known as 'Turkish oregano'. An essential oil reported from this plant contains carvacrol as a major component and

has the potential to be utilized at reasonable concentrations to control tick infestations (Sevki *et al*., 2008). Diversified effects such as antispasmodic (Daferera *et al*., 2000; 2003); antibacterial (Burt, 2004); antifungal (Ultee *et al.,* 1997) have been attributed to this plant by modern pharmacological studies. It is also used in flavouring Turkish Delight candy (Facciola *et al*.,1998) and is also used in tea ,salads and meat dishes (Small *et al*., 1997).Consumption of *O. onites* distillate has beneficial effects on lipid profiles ,antioxidant status and endothelial functions in patients with mild hyperlipidaemia(Ozdemir *et al*.,2008).

Origanum syriacum commonly known as 'Syrian marjoram' is an aromatic, herbaceous and perennial plant growing wild in the Sinai desert of Egypt (Tackholm, 1974).Biblical authorities consider this plant to be referred in the Bible as hyssop particularly in the old Testament pages(Moldenke *et al.*,1952). It is a very popular culinary herb that has been used through ages in traditional medicine mainly in Lebanon and Arab world. It has antiseptic properties and has the ability to relieve stomach and intestinal pain. It is also used to treat heart problems, cough ,toothaches (Gardner *et al*.,1989), cold, anxiety and wounds(Chandler *et al*., 2004). Kamela *et al.,* 2001 and Baser *et al*., 2003 isolated thymol and carvacrol as a major constituent of its essential oil. Carvacrol is the signature chemical largely responsible for its sharp, pungent oregano flavor(Tucker *et al*.,1992).The volatile phenolic oil has been reported to be among the top 10 essential oils (Letchamo *et al*., 1995), showing antibacterial, antimycotic, antioxidative, natural food preservative and mammalian age delaying properties (Jackson and Hay, 1994; Letchamo *et al*., 1995).

Origanum majorana (L.) is an endemic medicinal plant of Cyprus and is commonly known as 'Sampsishia'. Johannes *et al*., 2002 reported sabinene linalyl acetate and Cis-sabinene hydrate from the essential oil of this plant species. It is used against common cold, as spasmolytic and as an antirheumatic. Dried leaves and flowering tips of this species are used in formulation of vermouths and bitters. The essential oil is used for flavouring sauces, condiments and other products (de Vincenzi *et al*., 1997). In India, it is used as diuretic, antiasthmatic and an antiparlytic drug (Yadava and Khare, 1995). This was a common salad herb in the 16th century(Picton *et al*.,2000). It is also used in herbal vinegars and tea can be made from its leaves(Facciola *et al*.,1998).Furthermore it has been used to treat cancer as well(Johnson *et al*.,2002; Leung *et al*., 2003).Stefanakis *et al.,*2013 have assayed the essential oil extracted from *O. marjorana L., O.onites L*. and *O.vulgare L*.ssp. hirtum as potential antibacterial agents for disinfection of rotifers(*Brachionus plicatilis*).Abdel Massih et al., 2010 suggested that Marjoram extracts exhibit antiproliferative effect and have high antioxidant activity as well.

Origanum microphyllum is a medicinal plant species of genus *Origanum*, endemic to Cretan and commonly known as 'Cretan marjoram' (Karousou ,1995) . Aligannis *et al.,* 2001and Gotsiou *et al*.,2002 isolated carvacrol, terpineol -4, linalool, sabinene, α-terpinene, ϒ-terpinene, cis-sabinene hydrate and trans -sabinene hydrate from the essential oil of this species. This small leaved oregano has a strong spicy flavor(Small *et al*.,1997).

Origanum hypericifolium is an endemic species of Turkey . It is used as a condiment, for flavouring meat and as herbal tea for treatment of common cold and stomach complaints (Baser *et al*., 1994). The essential oil of pre flowering stage extracted from this plant species is carvacrol rich.

Origanum dictamnus commonly known as 'Dittany of Crete' is native to the island of Crete ,Greece .It is used in traditional medicine in Greece and all over Europe(Christos *et al*., 2010).It possesses numerous medicinal uses like antibacterial (Aureli *et al*.,1992; Biondi *et al*., 1993;Vokou *et al*., 1993), antifungal (Arras and Picci, 1984; Collin *et al* .,1989;Paster *et al* .,1993). It is also used in cooking as well. As a culinary and medicinal herb it is used as a tonic and digestive aid(Simon *et al* .,1984;Bown *et al*.,2001) for treating kidney and liver problems , obesity and headaches(Skoula *et al*., 1997). Its flowers and bracts are used to make tea and the plant when combined with garlic, thyme, salt and pepper is used in a Saxon fish sauce(Jones *et al*., 1973).Harvala and Skaltsa, 1986, Harvala *et al*., 1987 reported that the leaves of this plant contains flavonoids and flavonoid glycosides some of which have spasmolytic activity. The essential oil has carvacrol, α- terpinene , p- cymene , caryophyllene , borneol , terpin1-en-4-ol and carvacrol methyl ether as predominant compounds. Various studies, concerning *O. dictamnus*, have shown that the oil possess strong antimicrobial activity; this activity could be attributed to the high percentage of phenolic compounds and specifically, carvacrol, thymol, p-cymene and their precursor c-terpinene (Sivropoulou *et al*.,1996). The variety of non-polar components such us fatty acids, lipids, sterols and essential oil has been identified from *O.dictamnus* (Revinthi-Moraiti *et al.,* 1985; Komaitis *et al.,* 1988).

Origanum dubium an endemic Mediterranean shrub is widely spread in Cyprus, Greece and in Southern Turkey. It is commonly called as 'Rigani'. An infusion of its leaves, flowering stems and flowers is used as a digestive aid while its essential oil when applied externally acts as an antirheumatic (Arnold *et al*., 1993). Carvacrol is the major component of its essential oil. The essential oil shows antimicrobial activity and their potential antioxidant activity was investigated and found to be significant in scavenging O_2 (Karioti *et al*., 2006). Further *O. dubium* shows inhibition of soybean lipoxygenase LOX and has high inhibitory activity(Karioti *et al*., 2006).

Origanum sipyleum **(L.)** commonly called as 'Showy Pink Oregano' is a polymorphic species of eastern Mediterranean area and is native to Western Anatolia, Turkey. It is used as a spice and against cough. It is also

beneficial for the treatment of various respiratory and gastrointestinal disorders. The essential oil of this species is rich in α- terpinene and monoterpenes (Baser *et al*.,1992) .

Origanum compactum is found in Morocco , South-West Spain and North Africa (Tutin *et al* .,1972). It is commonly called as 'Compact Oregano'. It produces one of the most powerful antimicrobial essential oil. It has antibacterial (Bouhdid, 2009), antioxidant (Bouhdid, 2008) and antifungal (Bouchra, 2003) properties. It demonstrates cytotoxic activity by oxidative stress as seen by mitochondrial damage (Bakkali ,2005). It has carvacrol , p-cymene and ϒ-terpinene as major components of its essential oil.

Origanum floribundum is recorded in Algerian site. It is used to stimulate the appetite of cattle , sheep and horses. Furthermore, it is also used against diarrhoea and other digestive disorders (Houmani *et al* ., 2002).Carvacrol , linalool , p-cymene and ϒ-terpinene were isolated by Baser *et al*.,2000 from the essential oil of this species.

Origanum acutidens is an endemic, herbaceous, and perennial plant growing mainly in calcareous and non calcareous rocks, slopes, and screes in the Central Anatolia region of Turkey (Davis 1982). The major components of *O. acutidens* oil are carvacrol , p-cymene , borneol , γ-terpinene , β-caryophyllene ,and linalool. Sokmen *et al*., 2004 has suggested that its essential oil has antagonistic activity against food-borne pathogenic bacteria and hence could be used in the food and pharmaceutical industries, and as an alternative to common synthetic antimicrobial products.

Discussion

The aim of the present review is to present comprehensive information about the medicinal importance of genus Origanum **.**Although there are 42 species of genus *Origanum*, only about less than 50% species have been subjected to chemical profiling. Other species have not been broadly subjected to chemical characterization and biological studies as evident from perusal of the literature. Current studies have shown that the essential oil, as well as their active principles possess several pharmacological properties like antimutagenic, angiogenic, antiparasitic, antiplatelet, antielastase, antihepatotoxic ones(Baser 2008). The species studied by various workers indicate that the genus *Origanum* is a potent source for isolation of a variety of bioactive molecules like terpenes, phenols, flavonoids etc. Thereby, this genus has important biological activities and acts against different types of diseases and is being used for culinary and economic uses. Furthermore it is also used as a feed additive, in honeybee breeding and in treatment of gastrointestinal ailments(Baser 2008). The recent scientific data and the rich historical evidence of its medicinal uses could support further research as well as its use as a safe herbal medicinal product. The antimicrobial activity, can promote the use of the above mentioned natural product as potent preservative and conservation agents, not only in the food industry after testing the toxic and irritating effects on humans but also in cosmetics and medical preparations. The present literature study further reveals that the biological properties of the investigated genus are not due only to their essential oils and their main compounds such as cavacrol and thymol but also to the other polar constituents acting synergistically or possessing different biological activites.

Conclusion

The synthesis of medicinally important phytochemicals by the species of genus *Origanum* has been established beyond doubt. The plant species are being used both in allopathic and traditional system of medicine as a remedial measure for number of ailments. Since, only limited species are being subjected to phytochemical investigation, there is a need to broaden this study for further phytochemical and pharmacological studies for rest of the species as well, which may prove of vital importance and could lead to new therapeutic products.. Furthermore , since the plant extracts of the genus *Origanum* and its essential oils are used as dietary supplements or for medicinal purposes ,it has become crucial to screen them for ensuring authenticity and product quality as toxic adulterants may prove to be life threatening.

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