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Review Article

Properties and Applications of Plants of *Origanum Sp.* Genus

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Abstract

The genus *Origanum* consists of different aromatic and medicinal plants some of which are used in folk medicine and as food additives since ancient times. These plants have numerous and varied beneficial properties, among which are antibacterial, antifungal, antioxidant, anti-inflammatory, antitumor and antiviral. While a mixture of components present naturally in these plants confers myriad of benefits phenolic compounds in particular have great importance in biocidal and antioxidants properties. In this review we focus on the genus *Origanum*, discussing the beneficial and probed properties that have potential implications in health-care and dietetics.

Introduction

Phytotherapy is the science that studies the use of plant products for therapeutic purposes [1]. Medicinal plants and phytogenic products have been used for the treatment of various diseases in traditional medicine worldwide not least because of its remedial properties [2,3] and, furthermore, they have been used as human food additives due to their beneficial properties [4] such as biocidal and antioxidants. It is also important to note that currently, about 80% of the world population uses herbs as traditional remedies [2]. However, although these products are natural, they can have side effects, although less than synthetic drugs [1,2].

Among the aromatic and medicinal plants, *Origanum sp.* is an important genus belonging to the *Lamiaceae* family [5]. It consists of forty nine taxa divided into 10 sections [6,7]. Most of its species are distributed around the Mediterranean area [7], Eurasia and the North of Africa [5]. This genus is very appreciated for its volatile oil and it is characterized by a great morphological and chemical diversity [3,6]. Since antique *Origanum sp.* plants have been used in folk medicine and ethnomedicine [5,8] to treat numerous infectious diseases and pains. It is therefore important to ensure that their use is in appropriate dosages because while they confer beneficial properties in therapeutic doses over a short period of time, they however can be toxic if taken in excess [9]. In addition, it has also been demonstrated that *Origanum* species have many properties considered important from a culinary and agricultural point of view. Among them are their ovicidal, herbicidal and insecticidal activities [10,11]. They are also used as food spices to flavor food [12,13]. Furthermore, and thanks to its antimicrobial activity, plant belonging to this genus retards the growth of microorganisms in food and therefore can also be used as food preservative and flavoring agents as well as disinfectants in perfumes and soaps [3]. These plants have all the properties and beneficial activities enumerated due to the presence of different essential oils which are products of the secondary metabolism of plants [3,10]. At present, it has been demonstrated that the oils present in the whole plant give their properties [3,11,13,14]. Although essential oils can be obtained from flowers, buds, seeds, leaves, branches, barks, fruits and roots [15], they are however commonly obtained from the aerial parts of the plants.

In this review we focus on the study of the genus *Origanum*, especially in its beneficial and demonstrated properties. We have wanted to give a detailed account of many beneficial properties of *Origanum* that have potential implications in health-care and dietetics.

Properties of the *Origanum* Genus

As stated earlier, the properties of genus *Origanum* plants are many and varied, thanks to which, man has benefited from their use since ancient times. In this section we present some of the activities attributed to these plants.

Origanum species have many activities related to medical, culinary and agricultural importance. Among the properties related to medical importance are the following: gastrointestinal diseases (such as diarrhea, stomach pain, colic and gastric ulcers), respiratory diseases (e.g. asthma, cough and chest pain) [3,11,16], abnormal menstrual cycles [5], kidney and liver diseases, metabolic, hormonal and neuronal disorders and skin and urogenital system diseases [11]. They have also been used as a sedative and their biocidal properties such as antiparasitic and anthelmintic [3,5], antibacterial, antifungal and antiviral ones [3,17] have been well documented. *Origanum sp.* have also antimutagenic,

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antitumor and cytotoxic activities [17-20] as well as antioxidant, anti-inflammatory [14,16,21], antispasmodic, expectorant, carminative and antitussive properties [20]. Furthermore, *Origanum* has been used to treat nausea and rheumatism [16], arthritis, hemorrhoids, sexual diseases, animal bites and poisoning [22] and to control diabetes and obesity [11,23]. These species have been also used as carminatives, diaphoretics and tonics, and as a source of antimicrobial compounds [5].

Due to the fact that there are numerous studies about these plants, only some of them, considered as more representatives, will be discussed in more detail in this review. Furthermore, we will focus only on antibacterial, antifungal, antioxidant, anti-inflammatory, antitumor, antiparasitic, antiviral, antihyperglycemic and anticholinesterase activities.

Antibacterial activity

These plants have antibacterial activities which give them a very important role not only for treating infectious bacterial diseases, but also for using as food preservatives role, as they much delay microbial growth and better preserved food. All the studied species of the genus *Origanum* present antibacterial activity. Curiously, this activity is broad not confined to Gram negative or Gram positive bacteria thus being particularly attractive in the field of medicine. Furthermore, this plant has also activity against plants or trees pathogenic bacteria, and therefore demonstrating relevance and importance in agriculture. The antibacterial activities verified in some species of the genus *Origanum* are shown in Table 1 for Gram positive and Table 2 for Gram negative bacteria.

Infusions of both essential oils and plant extracts (either aqueous or ethanolic) can be used in antimicrobial formulations as they have activity against strains of Gram positive and negative bacteria [9,24,40]. The hydrophobicity of the essential oils allows them to be embedded in the cell and in the mitochondrial membranes and breaks them, making more permeable to throw out contents of the cell [4,15]. Different conditions such as low pH, temperature or oxygen levels enhanced the antibacterial action of essential oils. The antibacterial activity of the essential oils possibly is due to the presence of phenolic compounds such as carvacrol and thymol [10,11,20,25,30,34], and also γ-terpinene [10], linalool, p-cymene, 4-terpineol and β-caryophyllene [15,20,25]. Possibly, this activity is due to the synergism between some of the compounds present in oils [15].

Antifungal activity

As it was previously described for the antibacterial properties, the antifungal properties of these plants are very important, also regarding the possibility of treating infectious diseases and preserving food. Similarly, these plants also affect plants and trees pathogenic fungi that cause heavy losses to farmers, so they are also important for the agricultural sector. The antifungal properties studied in some species of the genus *Origanum* are shown in Table 3.

Origanum sp. essential oils and extracts (both aqueous and ethanolic) of essential oils and/or aerial parts of plants exhibit antifungal activity [45]. This antifungal activity is also due to the presence of thymol and carvacrol [34,49]. Furthermore, the quantity of carvacrol content is correlated to the antifungal activity [3].

Antioxidant activity

The oxidation reactions are very usual in the cells although they can produce Reactive Oxygen Species (ROS) and free radicals that start a series of reactions that finally damage and/or kill the cells. The antioxidants protect the cells and also their components, and thus protect the organism. The antioxidant properties of these plants have also been shown in a large number of studies and those considered as most representatives are shown in Table 4.

Table 1: Origanum species with activity against Gram positive bacteria.

Origanum species	Bacteria	References
O. syriacum	*Staphylococcus aureus*	[3]
	Enterococcus faecalis	[3,10]
	Bacillus brevis	[10]
	Bacillus megaterium	[10]
	Bacillus subtilis	[10]
	Micrococcus luteus	[10]
	Mycobacterium smegmatis	[10]
	Listeria innocua	[19]
O. vulgare	*Staphylococcus epidermidis*	[9]
	Staphylococcus aureus	[9,24-27]
	Staphylococcus saprophyticus	[24]
	Micrococcus sp	[24]
	Bacillus sp	[24]
	Bacillus cereus	[25]
	Bacillus subtilis	[25]
	Bacillus pumilis	[25]
	Enterococcus faecalis	[27]
	Listeria innocua	[28]
	Listeria monocytogenes	[28,29]
	Bochothrix thermosphacta	[30]
	Micrococcus luteus	[30]
O. dictamnus	*Staphylococcus aureus*	[13,20,31-33]
	Staphylococcus epidermidis	[13,20,31-33]
	Listeria monocytogenes	[13,33]
	Bacillus cereus	[20]
	Bacillus subtilis	[20]
	Streptococcus faecalis	[20]
	Staphylococcus hominis	[31,32]
	Streptococcus mutans	[33]
	Streptococcus viridans	[33]
O. michrophyllum	*Bacillus cereus*	[20]
	Bacillus subtilis	[20]
	Staphylococcus aureus	[20]
	Staphylococcus epidermidis	[20]
O. libanoticum	*Bacillus cereus*	[20]
	Bacillus subtilis	[20]
	Staphylococcus epidermidis	[20]
O. majorana	*Bacillus cereus*	[25]
	Bacillus subtilis	[25]
	Bacillus pumilis	[25]
	Staphylococcus aureus	[25,26]
O. acutidens	*Bacillus macerans*	[34]
	Bacillus megaterium	[34]
	Bacillus subtilis	[34]
	Clavibacter michiganense	[34]
	Enterococcus faecalis	[34]
	Staphylococcus aureus	[34]
	Staphylococcus epidermis	[34]
O. glandulosum	*Enterococcus hirae*	[35]
	Staphylococcus aureus	[35]
O. minutiflorum	*Listeria monocytogenes*	[36]
	Staphylococcus aureus	[36]

Table 2: *Origanum* species active against Gram negative bacteria.

***Origanum* species**	**Bacteria**	**Reference**
O. syriacum	*Pseudomonas aeruginosa* *Escherichia coli* *Klebsiella oxytoca* *Yersinia enterocolitica* *Klebsiella pneumoniae* *Escherichia coli O157:H7* *Proteus spp* *Yersinia enterocolitica O9* *Brucella melitensis*	[3,10] [3,10,37] [10] [10] [10,38] [38] [38] [38] [39]
O. vulgare	*Enterobacter aerogenes* *Enterobacter sakazakii* *Proteus vulgaris* *Escherichia coli* *Pseudomonas aeruginosa* *Salmonella poona* *Salmonella Enteritidis* *Salmonella Typhimurium Pseudomonas fragi* *Salmonella sp.* *Aeromonas hydrophila* *Citrobacter spp.* *Enterobacter aerogenes* *Flavobacterium spp* *Klebsiella ozaenae* *Klebsiella pneumoniae* *Proteus mirabilis* *Salmonella typhi* *Salmonella paratyphi* *Serratia marcescens* *Shigella dysenteriae* *Helicobacter pylori*	[9] [9] [9] [9,25,27,40] [9,25,40] [25] [27] [27] [30] [30] [40] [40] [40] [40] [40] [40] [40] [40] [40] [40] [40] [41]
O. dictamnus	*Salmonella enteritidis* *Salmonella typhimurium* *Escherichia coli* *Enterobacter cloacae* *Klebsiella pneumoniae* *Pseudomonas aeruginosa* *Helicobacter pylori* *Acinetobacter hemolyticusEmpedobacter brevis* *Erwinia carotovora* *Clavibacter michiganensis*	[13] [13] [13,20,33] [33] [33,42] [33,42] [41] [42] [42] [43] [44]
O. michrophyllum	*Escherichia coli*	[20]
O. majorana	*Escherichia coli* *Pseudomonas aeruginosa* *Salmonella poona* *Helicobacter pylori*	[25] [25] [25] [41]
O. acutidens	*Acinetobacter baumanii* *Acinetobacter lwoffi* *Brucella abortus* *Cedecea davisae* *Enterobacter cloacae* *Escherichia coli* *Klebsiella pneumoniae* *Morgonella morganii* *Proteus vulgaris* *Pseudomonas aeruginosa* *Pseudomonas pseudoalkaligenes* *Salmonella cholerasuis arizonae* *Salmonella enteritidis* *Serratia plymuthica* *Shigella sonnei* *Xanthomonas campestris*	[34] [34] [34] [34] [34] [34] [34] [34] [34] [34] [34] [34] [34] [34] [34] [34]
O. glandulosum	*Escherichia coli* *Klebsiella pneumoniae* *Pseudomonas aeruginosa*	[35] [35] [35]
O. minutiflorum	*Escherichia coli O157:H7* *Salmonella typhimurium*	[36] [36]

Table 3: *Origanum* species having activity against fungi.

***Origanum* species**	**Fungi**	**Reference**
O. syriacum	*Aspergillus fumigatus* *Aspergillus flavus* *Aspergillus niger* *Saccharomyces cerevisiae*	[3] [3] [3] [10]
O. dictamnus	*Candida albicans* *Candida tropicalis* *Candida glabrata* *Botrytis cinerea* *Fusarium sp.* *Aspergillus niger* *Saccharomyces cerevisiae* *Penicillium digitatum* *Yarrowia lipolytica*	[11] [11] [11] [11] [11] [13] [13] [44] [45]
O. acutidens	*Candida albicans* *Alternaria solani* *Aspergillus flavus* *Aspergillus niger* *Aspergillus varicolor* *Fusarium oxysporum* *Fusarium solani* *Microsporum canis* *Monilania fructicola* *Mortieraula alpina* *Penicillum spp.* *Rhizopus spp.* *Rhizoctonia solani* *Trichophyton rubrum*	[34] [34] [34] [34] [34] [34] [34] [34] [34] [34] [34] [34] [34] [34]
O. glandulosum	*Candida albicans* *Candida tropicalis*	[35] [35]
O. majorana	*Candida rugosa* *Debaryomyces hansenii* *Kluyveromyces marxianus* *Rhodotorula glutinis* *Rhodotorula minuta* *Saccharomyces cerevisiae* *Trichosporon cutaneum* *Yarrowia lipolytica* *Zygosaccharomyces rouxii*	[46] [46] [46] [46] [46] [46] [46] [46] [46]
O. vulgare	*Candida glabatra* *Microsporum canis* *Microsporum gypseum* *Trichophyton mentagrophytes* *Trichophyton erinacei* *Trichophyton terrestre*	[47] [48] [48] [48] [48] [48]

Essential oil and extracts (aqueous, ethanolic and cyclohexane) of aerial parts of the plants have antioxidant activity. Also, infusion and decoction processes of these extracts have this activity [8,9,11,34,53,54].

It has been shown that the antioxidant activity improves endothelial function, has anti-inflammatory properties and stimulates the DNA repair mechanism [19]. Many studies have highlighted the importance of phenolic compounds and flavonoids of essential oils in the antioxidant activity [9,25,34,51,53,54]. Viuda-Martos, et al. [19] established that the antioxidant activity is possibly due to the presence of thymol in the essential oils, while in other studies this property was mainly attributed to the presence of carvacrol [13,34], rosmarinic acid and polyphenols [34]. Liolios, et al. [11] and Lukas, et al. [22] established that this ability is also due to other polar and non-polar phenolic compounds present in the extracts which are rich in phenolic derivatives.

Table 4: *Origanum* species with antioxidant activity.

Origanum species	Method of study	Reference
O. ehrenbergii *O. syriacum* *O. vulgare* *O. majorana* *O. acutidens* *O. glandulosum*	*β*-Carotene Bleaching Inhibition [CBI]	[7] [7] [9,25] [25] [34] [50]
O. ehrenbergii *O. syriacum* *O. vulgare* *O. dictamnus* *O. syriacum* *O. minutiflorum* *O mychrophyllum* *O. libanoticum* *O. majorana* *O. acutidens* *O. compactum*	2,2'-Diphenyl-1-Picrylhydrazyl [DPPH] radical-scavenging	[7] [7,10,19] [9,25,51] [13,20] [16] [16] [20] [20] [25,52] [34] [53]
O. vulgare *O. syriacum* *O. majorana*	Reducing Power [RP]	[9] [10] [52]
O. vulgare *O. syriacum* *O. dictamnus* *O mychrophyllum* *O. libanoticum*	Ferric Reducing Antioxidant Capacity [FRAC] or Power [FRAP]	[9,51] [19] [20] [20] [20]
O. vulgare *O. majorana*	Inhibition of lipid peroxidation by TBARS assay	[9] [52]
O. syriacum *O. minutiflorum*	Ascorbate-Iron [III]-Catalyzed Phospholipid Peroxidation.	[16] [16]
O. syriacum *O. minutiflorum*	Iron [III] to Iron [II] Reducing Activity	[16] [16]
O. syriacum *O. minutiflorum*	Iron [II] Chelation Activity	[16] [16]
O. syriacum *O. minutiflorum*	Site-Specific Hydroxyl Radical-Mediated 2-Deoxy-D-ribose Degradation	[16] [16]
O. syriacum *O. minutiflorum*	Nonsite-Specific Hydroxyl Radical-Mediated 2-Deoxy-D-riboseDegradation	[16] [16]
O. syriacum	Inhibition of Lipid Peroxidation LPI of Buffered Egg Yolk by TBARS assay	[19]
O. syriacum	Determination of Oxidative Stability of Fat [RANCIMAT Assay]	[19]
O. syriacum	Ferrous Ion Chelating [FIC] Ability	[19]
O. vulgare *O. majorana*	Percent inhibition in linoleic acid system	[25] [25]
O. vulgare *O. compactum*	2,2'-Azino-Bis [3-Ethylbenzothiazoline]-6-Sulfonic acid [ABTS]; radical scavenging	[51] [53]
O. majorana	Hydroxyl radical scavenging activity	[52]
O. majorana	Hydrogen peroxide scavenging activity	[52]

Therefore, we may assume that this activity may be the result of a combination of many substances being of high importance phenolics and flavonoids compounds.

Anti-inflammatory activity

Inflammation is a non-specific physiological response to environmental stressors such as infectious microorganisms, chemical agents, physical injuries and many diseases. This process seeks to destroy the offending agent and repair the damaged tissue or organ. Activated leucocytes, endothelial cells and macrophages produce pro-inflammatory cytokines such as Interleukin (IL) IL-1b, IL-6 and TNF-α (Tumor Necrosis Factor α) among others, and anti-inflammatory cytokines such as IL-10. These cells also produce pro-inflammatory enzymes such as inducible nitric oxide synthase and cyclooxygenase, which increase the level of nitric oxide and prostaglandin E2 [55]. *Origanum* species act by inhibiting the secretion of pro-inflammatory cytokines and activating the expression of pro-inflammatory genes. Furthermore, this plant promotes the secretion of anti-inflammatory cytokines and Deactivates the expression of inflammatory genes. The anti-inflammatory activities studied for *Origanum* species are shown in Table 5.

Table 5: *Origanum* species and anti-inflammatory activity performed.

Origanum species	Anti-inflammatory activity	Reference
O. ehrenbergii	Inhibit NO synthesis in murine RAW 264.7 cell line	[7]
O.syriacum	Inhibit NO synthesis in murine RAW 264.7 cell line	[7,21]
O. vulgare spp Hirtum	Inhibit NO synthesis in murine RAW 264.7 cell line	[21]
O. vulgare	Inhibit NO synthesis in murine RAW 264.7 cell line ↓ IL-1b, IL-6 y TNF-α / ↑ IL-10 ↓ IL-1b, IL-6, GM-CSF and TNF-α in mice ↓ T helper 17 cells / ↑ T helper 2 and T regulatory cells.	[21] [55] [56] [57]

In several species of *Origanum* (e.g. *O. vulgare*, *O. vulgare spp. Hirtum* and *O. syriacum*) rosmarinic, oleanolic and ursolic acids are present, and although their concentrations vary among these species, these acids could be responsible for the anti-inflammatory activity attribute to these plants. It was observed that the three acids previously mentioned decreased the expression of inducible nitric oxide synthase and cyclooxygenase genes, showing a strong anti-inflammatory activity. It seems that rosmarinic acid inhibits lipoxygenase and cyclooxygenase, while the mechanism of action of oleanolic and ursolic acids seems to focus on the involvement of one or more signaling pathways [21].

Methanolic extracts [57] and essential oils of *O. vulgare* have showed anti-inflammatory activity. The activity of the essential oil was studied in mouse models of gastritis induced stress and contact hypersensitivity [58]. Finally, Silva, et al. [59] has suggested that carvacrol present in the essential oil probably interferes with the release and/or synthesis of inflammatory mediators such as prostanoids.

Antitumor activity

Tumors, besides being very difficult to treat because of its enormous complexity and variability, are widespread and very serious diseases. It has been demonstrated antitumor activity on some species of *Origanum*, and furthermore, they have cytotoxic activity against several tumor cell lines. *Origanum* species with cytotoxic activity against different cell lines are presented in Table 6.

Arcila-Lozano, et al. [17] reported the antimutagenic and anticarcinogenic effect of several *Origanum sp.* Generally, essential oils [13,20,55,62,65], cyclohexane [11], dichloromethane extracts [18], ethyl acetate [53,63], ethanol [53,63,64] and aqueous extracts [60] have shown antitumor activity. This antitumoral activity has been attributed to various components, including carvacrol [13], ursolic acid [18], 4-terpineol [62] and betulinic acid [63]. Moreover, several studies have shown the presence of thymoquinone in the essential oil of *Origanum sp.* Thymoquinone is a molecule with antioxidant, anti-inflammatory and analgesic properties, promising as antitumor candidate [22].

Table 6: *Origanum* species and cell lines against which have cytotoxic activity.

Origanum species	Cell line	Reference
O. dictamnus	Deletes mutagenicity of Trp-P-2 Breast cáncer, colon cancer and lung adenocarcinoma HepG2 [hepatic carcinoma] P388 y L-1210 [murine leukemia] NSCLC-N6 [bronchial epithelial tumor] LoVo [colon carcinoma]	[11] [13] [13,20] [18] [18] [20]
O. mycrophyllum	LoVo [colon carcinoma] HepG2 [hepatic carcinoma]	[20] [20]
O. libanoticum	LoVo [colon carcinoma] HepG2 [hepatic carcinoma]	[20] [20]
O. majorana	LNCaP [prostate adecocarcinoma] NIH-3T3 [mouse fibroblasts] MCF-7 [breast adenocarcinoma] HeLa [cervical cancer] Jurkat [Acute lymphocytic leukemia]	[25] [25] [25,60] [60] [60]
O. vulgare	LNCaP [prostate adecocarcinoma] MCF-7 [breast adenocarcinoma] THP-1[acute monocytic leukemia] HepG2 [hepatic carcinoma] NIH-3T3 [mouse fibroblasts] HT-29 [colon adenocarcinoma]	[25] [25,61] [55] [61] [62] [62]
O. compactum	MCF-7 [breast adenocarcinoma]	[53,63]
O. syriacum	THP-1 [acute monocytic leukemia] PMBCs [Peripheral blood mononuclear cells]	[64] [64]
O. onites	5RP7 [rat fibroblasts tumor] Rat adipose tissue endothelial cell migration	[65] [65]

Antiparasitic activity

Parasitism is a process in which an organism (parasite) depends on the host and obtains a benefit from this. In many cases, the parasites cause disease in the hosts, which can be humans, animals and plants, so that this process has a lot of medical and agricultural importance. *Origanum* species with probe anti-parasitic activity are presented in Table 7.

Antiparasitic activity has been found in the essential oils [53,66,70], and acetyl [53,68] and in methanol extracts [69]. This activity may be due to the presence of phenolic compounds in the essential oil as thymol and carvacrol that interact with the permeability of the cytoplasmic cell membrane [66]. Antiparasitic activity is also due to the presence of terpenoids and flavonoids [68]. Interestingly, in some occasions, along with the antiparasitic activity there was an improvement of the innate immune and phagocytic activity in the host [70].

Antiviral activity

Viruses are acellular microscopic infectious agents that need the cells of other organisms (hosts) to multiply. Their hosts may be humans, animals or plants. Many of these viruses cause disease, so the antiviral activity of *Origanum* species is also very important to medical and agricultural objectives. Works focus on *Origanum sp.* antiviral activity is presented in Table 8.

Table 7: *Origanum* species and parasite that they affect.

Origanum species	Parasite	Reference
O. vulgare	Affects the development of malaria Coccidium of *Eimeria tenella* Coccidium of *Eimeria sp.*	[25] [66] [67]
O. compactum	*Plasmodium falciparum* *Schistosoma haematobium*	[53] [68]
O. syriacum	Cysts and trophozoites of *Acanthamoeba castellanii*	[69]
O. laevigatum	Cysts and trophozoites of *Acanthamoeba castellanii*	[69]
O. minutiflorum	*Mixobolus sp.* [Bivalvulida/Platysporina]	[70]

Hexane, dicholoromethane, methanol [34], aqueous extracts [71] and essential oils [72] have showed antiviral activity. In the study of Sökmen, et al. [34] this activity was ascribed to the presence of rosmarinic acid. Sanchez and Aznar [72] found that the essential oil slightly reduced the infectivity of HAV while thymol present in the essential oil reduced the infectivity of norovirus, murine norovirus and feline calicivirus.

Anticholinesterase activity

Cholinesterase's are enzymes that catalyze the hydrolysis of neurotransmitters in the synaptic space, necessary to allow the cholinergic neuron to return to its resting state after activation, avoiding overstimulation and damage to the neuron or muscle. Acetyl-cholinesterase catalyzes the cleavage of acetylcholine while butyryl-cholinesterase hydrolyzes butyrylcholine. Both enzymes play an important role in the central nervous system, and their inhibitors are used in Pharmacy. Malfunctions of these enzymes results in neurodegenerative diseases where oxidative stress plays an important role. *Origanum* species with tested anticholinesterase activity are detailed in Table 9.

Mossa and Nawwar [52] attributed this activity to the presence of terpenoids as 4-terpinenol γ-terpinene, α-terpinene, p-cymene and 1,8-cineol in the essential oils of these plants, while Loizzo, et al. [73] attributed this property to the presence of thymol and carvacrol. Newly, the combination of the compounds present in the essential oils of these plants seems to be responsible for this property and provides future applications of these plants in studies focus on the prevention of neurodegenerative disorders [7,52,55].

Antidiabetes activity

Diabetes is a growing global problem characterized by insulin deficiency and the subsequent presence of blood glucose (hyperglycemia). *O. vulgare* can delay the development of diabetic complications and correct metabolic abnormalities thanks to his hypoglycemic property [5,23]. Vujicic, et al. [57] observed that methanolic extracts of *Origanum* reduced diabetes and established a normal secretion of insulin in mice with diabetes induced by antioxidant, anti-inflammatory and antiapoptotic activity in β cells. Rosmarinic acid could be involved in this activity. In the study

Table 8: *Origanum* species and virus that they affect.

Origanum species	Virus	Reference
O. acutidens	Herpes symplex virus type 1 [HSV-1]	[34]
O. vulgare	Suid herpesvirus type 1 [SuHV-1] Hepatitis A virus [HAV]	[71] [72]

Table 9: *Origanum* species and anticholinesterase activity present.

Origanum species	Affected enzyme	Reference
O. ehrenbergii	Acetyl-cholinesterasa Butyril-cholinesterasa	[7] [7]
O. syriacum	Acetyl-cholinesterasa Butyril-cholinesterasa	[7] [7]
O. majorana	Acetyl-cholinesterasa	[52]

developed by Lemhadri, et al. [74] the blood glucose levels decreased strongly in diabetic rats after treating them with *O. vulgare*. They observed that flavonoids can cause hypoglycemic effect acting separately or synergistically with other components.

Origanum Sp. as a Dietary Supplement

To the best of our knowledge, there is available few studies focus on the effects of dietary administration of *O. vulgare* on animal diets. However, the administration of these plants on diet to farm animals has yielded very good results. Dietary supplements of the essential oil from *O. vulgare* on chickens infected with *Eimeria tenella* produced weight gain of the chickens and reduced coccidiosis [66]. Similar results were observed in the study of Nosal, et al. [67], where this effect was observed against *Eimeria spp.* in rabbits (*Oryctolagus cuniculus f. domesticus*). It was also observed that the essential oil included in the diet increased weight and had positive effects against pathogenic organisms, as well as in the secretions of digestive and liver enzymes in poultry [75]. Also, there is a recent study in which the ethanolic extract of *O. vulgare* has been dietary administered to rainbow trout (*Oncorhynchus mykiss*) specimens and their innate immune response was improved [76]. In this study, one thousand and two hundreds rainbow trout were randomly allocated into two groups including placebo-treated group (control) and *O. vulgare* extract-treated group, each of three replicates. The fish were hand-fed once a day with each at a rate of 1% of feed weight in the first feeding for 8 weeks. At the end of every two weeks, blood samples were analyzed for some of hematological, biochemical and immunological parameters. Respiratory burst, phagocytosis and serum lysozyme of leucocytes was studied. The observed effects include enhancements in the innate immune response by increasing the levels of total serum proteins as albumin, globulin and lysozyme, as well as the respiratory burst and phagocytic activity of leucocytes [76].

Therefore, various studies using plants of the genus *Origanum* have yielded good results, showing that its inclusion in the diet increases the weight of the animals; helps fight infections of parasites and increase the innate immune response of the animals. These important effects on farmed animals are due to the existence in the essential oils of, among others, carvacrol, linalol, borneol, α-terpinene, γ-terpinene, α-pinene and β-pinene.

Chemical Composition

Because the primary responsibility for the properties of these plants is the essential oils, most of the chemical composition studies have focused on studying these essential oils. It has been found that although all species of the genus *Origanum* contain more or less the same components, chemical composition and concentrations of the components depends on many factors such as genotype, geographical origin, climate, type and soil composition, orientation the development of the plant, harvest time and culture conditions [3,4,15,17,77].

Essential oils of these species have alkaloids, flavonoids, phenolic and polyphenolic compounds [5,11,19,37,78]. The main components of the essential oil of these plants, in most cases, are two oxygen monoterpenes, carvacrol and thymol [3,12,78-80]. Thymol and carvacrol, which are isomeric phenols, are primarily responsible for the characteristics and properties of essential oils. The biosynthetic precursors of carvacrol and thymol are the γ-terpinene and p-cymene [11]. Although timol and carvacrol are present in most plants species and they are generally in high concentrations, other compounds are also commonly found in these plants, such as hydrocarbon monoterpenes γ-terpinene, *p*-cymene, α-terpinene, α-myrcene, α-pinene and sabinene hydrate, and oxygenated monoterpenes linalool, 4-terpineol and α-terpineol, and sesquiterpene β-caryophyllene [3,9-12,19,80].

The different *Origanum* species have chemotypes of carvacrol and thymol and thire presence and concentration varies among them and also, within different plants from the same specie [3,7]. This is very important because these chemotypes influence biosynthetic pathways and therefore, the relative proportion of parent compounds and the characteristics of essential oils [3,81]. Furthermore, some other species have carvacrol and thymol chemotypes with a high content of two hydrocarbon monoterpenes, γ-terpinene or *p*-cymene, whereas other species have high values linalool, phenols, alcohols, ethers, aldehydes and ketones [77].

While thymol has antibacterial, anti-inflammatory, anti-protozoal, antioxidant, cytotoxic and piscicide activities, and is an allelopathic agent [82], carvacrol has anti-oxidant, anti-microbial, antitumor, antimutagenic, antigenotoxic, analgesic, anti-spasmodic, anti-inflammatory, angiogenic, antiparasitic, antiplatelet, inhibiting pain, elastase, insecticide, antihepatotoxic, neuroprotective and hepatoprotective activities [83,84].

Conclusion

Plants of the genus *Origanum* have many and varied benefits that give them a great importance for being used in foods, as well as in pharmaceutical, medical and agricultural purposes. However, till present most of these beneficial effects have been seen almost exclusively in in-vitro studies, using human and mouse cell lines. It would be very interesting to perform more in vivo studies to know if the effects are comparable or not with the available in vitro effects. Until now, some in vivo studies carried out in animals have demonstrated their beneficial properties, which could make these plants good candidates for being included in animal feed, in as much that the inclusion of plants of genus *Origanum* in the diet of animals increases the weight of the animals, helps fight infections and improve the immune status.

Both, essential oils or extracts from aerial parts of the plants could be used for in vivo studies because the combination of the compounds present in them seems to be responsible of the activity of these plants, all acting synergistically.

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