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Anti-inflammatory, Antioxidant, anticancer and anti-microbial effect of Origanum vulgare: a systematic review

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ABSTRACT

Origanum vulgar is a perennial herb belongs to Origanum. The aim of this study was to overview its anti-inflammatory, antioxidant, anticancer and anti-microbial effects. This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases. The initial search strategy identified about 103 references. The search terms were "Origanum vulgare", "Anti-inflammatory", "Antioxidant, anticancer, antimicrobial effect", "pharmacological effects". It is commonly used for treatment of inflammatory, different kinds of cancer including Colon, lung cancers due to its most component 4-terpineol and microbial diseases. It was said to possess antioxidant effect including iron chelating, scavenging activity, and the redox state cells modification because of presence of phenolic compound including ferulic, rosmarinic, p-coumaric and caffeic, while predominant flavonoids were quercetin, apigenin kaempferol. Origanum vulgar is used for the treatment of various diseases such as different kinds of cancers and possess lots of effects as antibacterial, antioxidant, anti-inflammatory and anticancer effects. In this study, Anti-inflammatory, Antioxidant, anticancer, antimicrobial effect of this plant are presented using published articles in scientific sites. Besides, it was said to be good for cancer treatment.

Keywords: *Origanum vulgare, Phytochemicals, Anti-inflammatory, Antioxidant, anticancer, antimicrobial effect, Pharmacognosy, Alternative and complementary medicine.'*

INTRODUCTION

The use of medicinal herbs and herbal medicines is an age-old tradition and the recent progress in modern therapeutics has stimulated the use of natural product worldwide for diverse ailments and diseases [1-20]. Origanum vulgar or wild marjoram belongs to the plant family of Origanum, a genus of the mint family [Lamiaceae]. It is native to temperate western and southwestern Eurasia and the Mediterranean region [25,26].

Oregano is a perennial herb, growing from 20–80 cm tall, with opposite leaves 1–4 cm long. Oregano will grow in a pH range between 6.0 [mildly acidic] and 9.0 [strongly alkaline], with a preferred range between 6.0 and 8.0. The flowers are purple, 3–4 mm long, produced in erect spikes [27-29]. Oregano is a perennial herb possessing purple flowers and spade-shaped, olive-green leaves. It would rather to grow in a hot, relatively dry climate. Its taste is aromatic, warm, and slightly bitter varying in intensity. Factors such as climate, season, and soil composition may affect the aromatic oils. Oregano is mostly used for flavoring meat [30].

Taxonomy

Unique flavors or other characteristics of many subspecies and strains of oregano have been focused. Tastes range from spicy or astringent to more complicated and sweet [29, 30]. The related species, Origanum onites [Greece, Turkey] and *O. syriacum* [West Asia], have similar flavors. A closely related plant is marjoram from Turkey, which differs significantly in taste though, because phenolic compounds are missing from its essential oil. Some varieties show a flavour intermediate between oregano and marjoram [31].

Chemistry

Oregano contains polyphenols, including numerous flavones. Among the chemical compounds contributing to the flavour are carvacrol, thymol, limonene, pinene, ocimene, and caryophyllene[32]. The chemical compound of the essential oil of oregano are mainly monoterpenoids and monoterpenes varying widely across geographic origin and other factors. Over 60 different compounds have been identified. The most abundant compound are carvacrol and thymol but lesser abundant compounds include p-cymene, γ-terpinene, caryophyllene, spathulenol, germacrene-D, β-fenchyl alcohol and δ-terpineol [33]. Drying of the plant material affects both quantity and distribution of volatile compounds.

Beta-Caryophyllene was the major constituent in all three oils including 1, 8-cineole [11.6%], alpha-pinene [6.9%], and gamma-cadinene [4.8%]. 1-Octen-3-ol [23.8%], and 1, 8-cineole [8.5%] predominated in the leaf oil. In the stem oil, other main constituents were bicyclogermacrene [9.8%], 1, 8-cineole [6.4%], borneol [5.1%], and pinocarvone [4.4%]. γ-terpinene [pentane] as major constituents is the main component of the volatile fraction. The main components of volatile fractions were carvacrol, trans-sabinene hydrate, cis-piperitol, borneol, terpinen-4-ol, and linalool [32].

Materials and methods

This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases .The initial search strategy identified about 103 references. In this study, 53 studies was accepted for further screening and met all our inclusion criteria [in English, full text, therapeutic effects of *Origanum vulgareL* and dated mainly from the year 2002 to 2016.The search terms were “Origanum vulgare”, “anti-inflammatory” , Antioxidant, anticancer, antimicrobial effect”, “pharmacological effects”.

Antioxidant and anti-inflammatory effects

In an in vivo study, the scavenging effect of Oregano extracts at different concentrations in the survival of cancer cell lines was investigated. It was found that extract concentrations of about 100 μg.ml [-1] was more indicative in the assessment of all parameters investigated. The antioxidant defense system against the excessive production of radicals in mitochondria was sufficient. Results show that the extract possess the potential to modify the redox state of cells according to the type of disease, which is expected to be associated with oxidative stress [25].

The complete chloroplast (cp) genome of Origanum vulgare consists of 151,935 bp and includes a pair of inverted repeats (IR) of 25,527 bp separated. The variability of the cp within the genus Origanum, studied exemplarily on 16 different chloroplast DNA regions, demonstrated that in 14 regions analyzed, the variability was extremely low [max. 0.7%], while only two regions showed a moderate variability of up to 2.3%. The cp genome of Origanum vulgare contains 27 perfect mononucleotide repeats, of which 32 were di-, and 2 were trinucleotide repeats [26].

The antioxidant activities of vanillin and vanillic acid isolated from Origanum vulgare are investigated. Vanillin did not express inhibition of tyrosinase activity. The results found that vanillic acid is a significantly stronger antioxidant than vanillin in terms of free radical scavenging activity, reducing power and inhibition of lipid peroxidation and exhibited stronger antimelanogenesis performance because of the structural presence of the carboxyl group [27].

In an animal study, the anti-colon carcinogenesis effect of an aqueous extract of oregano on lipid peroxidation and anti-oxidant status was investigated. The levels of the anti-oxidants superoxide dismutase, catalase, reduced glutathione, glutathione reductase, glutathione peroxidase and glutathione-S-transferase were decreased in DMH-treated rats, but were significantly reversed on oregano supplementation. Oregano supplementation had a modulatory role on tissue lipid peroxidation and antioxidant profile in colon cancer-bearing rats, which suggested a possible anti-cancer property of oregano [28].

In an animal study, antioxidant effect of Origanum vulgare extract in preventing selenite-induced cataractogenesis was assessed. Ov extract have revealed a significant protective effect against selenite induced cataract when injected 2 times before selenite injection. It is supposed that the Ov extract is potentially possess anticataract effect due to its antioxidant mechanisms [29].The effects of a commercial extract of equal parts of oregano essential oil and sweet chestnut wood extract on oxidative status and pork quality traits were evaluated. The lipid oxidation of meat was lower in the OC group. In the cooked meat samples, OC animals had the lowest L* and H° values and the highest a* values. The OC meat received higher scores for color, taste and overall liking in both the blind and the labelled consumer tests [30].

The concentration of carnosol, rosmarinic and carnosic acids in rosemary and oregano leaves and their effect on the oxidation and colour of model pork batters was investigated. Ethanol oregano extracts containing high concentrations of phenols, mainly rosmarinic acid, efficiently prevented colour deterioration. The antioxidant effect of the studied extracts depends, not only on the concentration of phenol compounds but also on the extraction method and solvent [31].

The best conditions for the extraction of antioxidant compounds from Origanum vulgare leaves was examined. Results indicated a good correlation between TP contents and DPPH radical scavenging activity. Besides, it was indicated that phenolic compounds are powerful scavengers of free radical as demonstrated by a good correlation between TP contents and DPPH radical scavenging activity [32].

The radical scavenging activities of extract of dried leaves of oregano were compared with those of rutin, quercetin and rosmarinic acid at a concentration of 2 x 10[-5] M. The scavenging activity of 4'-O-beta-D-glucopyranosyl-3', 4’-dihydroxybenzyl protocatechuate was almost the same as that of quercetin and rosmarinic acid, but that of 4'-O-beta-D-glucopyranosyl-3', 4’-dihydroxybennzyl 4-O-methylprotocatechuate was less [33].

Antioxidant effect of oregano, lavender and lemon balm was investigated and their total phenolics and total flavonoids were determined. It was found that Origanum vulgare present the most effective antioxidant capacity in scavenging DPPH radicals [34]. In an animal study, the biotransformation and pharmacokinetics of OV-16 and oregano decoction was investigated. Results showed that when OV-16 was orally administered, free forms of OV-16, PCA, and HBA were not present in blood and the major metabolites were the glucuronides/sulfates of PCA and HBA sulfate. The serum metabolites of OV-16 exhibited free radical scavenging activity. When oregano decoction was given, the glucuronides and sulfates of PCA were the major metabolites in blood [35].

The effect of supplemental dried oregano powder [DOP] in feed on the productivity, antioxidant enzyme activity, and breast meat quality was investigated. As a result of in vivo study, DOP in the diet showed no effects on final body weight, feed intake, or feed conversion ratio. The results suggest that diets containing 0.5% and 1% DOP may beneficially affect antioxidant enzyme activity of GPx and SOD, improve meat cooking loss [36].

Antioxidant activities of five different crude extracts of Origanum vulgare L. ssp. viride [Boiss.] were determined and result showed for the first time the antiproliferative and antioxidant properties of this plant [37].

Radical-scavenging and ferric-reducing antioxidant power of Origanum vulgare was investigated in its six new phenolic compounds along with five known ones. Twelve of phenolic compounds including two new compounds exhibited significant antioxidant activity comparable to that of ascorbic acid. [38].

Anticancer effects

In vitro, the antiproliferative effect of essential oil [EO] of Origanum vulgare against human breast adenocarcinoma [MCF-7], and human colon adenocarcinoma [HT-29] was evaluated. The results show that the EO is composed mostly of 4-terpineol and induces a high cytotoxicity effect in HT-29. In the MCF-7 cell line, the EO was less effective. This study showed that O. vulgare main component is 4-terpineol and was effective in inducing cancer cell growth inhibition [38]. In a human study, anti- lung cancer effect of aqueous extract of Origanum vulgare was investigated and it showed that the biosynthesized nanoparticles were found to be impressive in inhibiting human pathogens in a dose -dependent manner [39].

Antiproliferative activity of some spices were investigated to assess their anticarcinoma activity against breast cell line. The major constituent of O vulgare was trans-sabinene hydrate [27.19%]. None of the hydro distilled essential oils of the tested plant species or their aqueous extracts demonstrated cytotoxic activity [40]. The effect of Origanum vulgare ethanolic extracts on redox balance, cell proliferation, and cell death in colon adenocarcinoma Caco2 cells was investigated. Oregano extract leads to growth arrest and cell death in a dose- and time-dependent manner. Findings suggest that oregano can exert proapoptotic effects. Besides, whole extract can be responsible for the observed cytotoxic effects [41].

Antibacterial effects

The major constituents of the ethanolic Origanum vulgare extract was examined for their cytotoxic, antioxidant, and antibacterial properties. The extract also exhibited antimicrobial properties against Gram-positive and Gram-negative bacterial strains. The oregano extract has shown cytotoxic, antioxidant, and antibacterial activities mostly attributed to carvacrol and thymol [42].

Overnight exposure of Origanum vulgare essential oil [OV] and carvacrol [CAR] did not result in direct and cross-bacterial protection. Cells subculture with increasing amounts of OV or CAR reveal few significant changes in bacterial susceptibility [43].

Antibacterial potential of infusion, decoction and essential oil of oregano against 111 Gram-positive bacterial isolates belonging to 23 different species related to 3 genera was investigated. Infusion and essential oil exhibited antibacterial activity against some bacteria. While all tested isolates were found resistant to decoction of oregano [44].

The essential oils of Origanum vulgare L. were evaluated for their antibacterial activity against 10 selected microorganisms. The result contributes to the future use of certain essential oils as natural preservatives for food products, due to their safety and positive effect on shelf life [45].

A synergistic effect between the essential oils Origanum vulgare, Pelargonium graveolens and Melaleuca alternifolia was investigated and the antifungal compound Nystatin. The essential oil O. vulgare appeared to be the most effective in inhibiting all the Candida species evaluated in this study [46]. The efficacy of Origanum vulgare L. essential oil [OVEO] and carvacrol in inhibiting the growth of Pseudomonas aeruginosa ATCC 9027 was assessed. Bacterial cells progressively subcultured in meat-based broth. The results reveal a lack of induction of tolerance in P. aeruginosa by exposure to OVEO or carvacrol in meat-based broth and in a meat model [47].

Variation in the quantity and quality of the essential oil [EO] of wild population of Origanum vulgare at different phenological stages, including vegetative, late vegetative, and flowering set, is reported. The oils of various phonological stages showed high activity against all tested bacteria, of which Bacillus subtilis was the most sensitive and resistant strain, respectively. Thus, they represent an inexpensive source of natural antibacterial substances that exhibited potential for use in pathogenic systems [48].

The ability to inhibit biofilm formation was investigated at sub-MIC levels of 200, 100, and 50 m g/ml by staining sessile cells with Safranin. Sample E showed the highest average effectiveness against all tested strains at 50 m g/ml and had inhibition percentages ranging from 30 to 52%. Oregano essential oil can inhibit the formation of biofilms of various food pathogens and food spoilage organisms [49].

The interaction effect of phenolic, nonphenolic fractions, and volatile oil of Origanum vulgare with ciprofloxacin was studied. Result shows that not only the formulation using O. vulgare and ciprofloxacin can overcome multidrug resistance but also will reduce the toxic effects of ciprofloxacin [50]. The antibacterial effect of essential oils of oregano was evaluated against 10 selected microorganisms. The data obtained contribute to the future view to use the essential oils as natural preservatives for food products due to their positive effect on their safety and shelf life [51].

The antimicrobial activity of free and microencapsulated essential oils of oregano was evaluated. EO's showed good stability after 3 months’ storage at 4°C, where antimicrobial activity of microencapsulated EO's remained the same, while free EO's decreased 41% [MXO] and 67% [EUO] from initial activity. Microencapsulation retains most antimicrobial activity and improves stability of EO's from oregano [52].

The antimicrobial activity of the essential oil from Origanum vulgare L. [OVEO] as well as its individual constituents carvacrol [CAR] and thymol [THY] were investigated. Among OVEO, CAR and, OVEO indicate that it could serve as potential sources of compounds capable of modulating drug resistance [53].

Antimicrobial activities of the essential oils of Origanum vulgare and some other herbs against microorganisms, including multiple antibiotic-resistant bacteria, were investigated. Result found that all the essential oils used in this study were very effective against Gram-positive and Gram-negative bacteria, and the antimicrobial activities of the essential oils varied depending on the species, subspecies, or variety [54].

Antimicrobial activity of the essential oil-rich fractions of oregano were investigated against six different microbial species. Result showed that All of the extraction showed antimicrobial activity against all of the microorganisms tested, although the most active fraction was the fraction with 7% ethanol at 150 bar and 40 degrees C. besides, C. albicans was the most sensitive microorganism to the oregano extracts, carvacrol being the most effective [55]. Antioxidant and antimicrobial activities of essential oils obtained from were evaluated. Essential oils obtained by CH and SFME at different microwave powers inhibited the survival of Listeria monocytogenes, Salmonella typhimurium, and Escherichia coli O157:H7, whereas survival of Staphylococcus aureus was not influenced. [56].

Antilisterial activities of Origanum vulgare essential oils was tested against 41 strains of Listeria monocytogenes. The oil of O. vulgare was consisted of three components constituted 70% of the oil including thymol [33%], gamma-terpinene [26%], and p-cymene [11%]. Use of O. vulgare essential oils can constitute a powerful tool in the control of L. monocytogenes in food and other industries [57].

DISCUSSION

Major phenolic acids identified in this herb were shown to be ferulic, rosmarinic, p-coumaric and caffeic, while predominant flavonoids were quercetin, apigenin kaempherol caused its antioxidant activity [34]. Besides, 4-[3,4-Dihydroxybenzoyloxymethyl]phenyl- O-beta-D-glucopyranoside [OV-16] is a polyphenolic glycoside isolated from oregano contribute to its antioxidative activity. In addition, the findings showed that the antioxidant effect of the studied extracts depends, not only on the concentration of phenol compounds [rosmarinic acid, carnosol and carnosic acid], but also on the extraction method and solvent. O. vulgare was effective in inducing cancer cell growth inhibition due to its most component 4-terpineol [38]. Antibacterial activities of this plant was found mostly attributed to carvacrol and thymol [42]. Thymol and carvacrol were among the main components of EO's and their free and microencapsulated inhibitory activity was tested against M. luteus, showing an additive combined effect.

CONCLUSION

Origanum vulgar is used for the treatment of various diseases such as different kinds of cancers and possess lots of effects as antibacterial, antioxidant, anti-inflammatory and anticancer effects. In this study, Anti-inflammatory, Antioxidant, anticancer, antimicrobial effect of this plant are presented using published articles in scientific sites. Besides, it was said to be good for cancer treatment. The data obtained contribute to the future view to varied new properties of this plant and identification of new chemical compounds especially in human studies.

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