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Review

Antimicrobial Activity and Other Biological Properties of Oregano Essential Oil and Carvacrol

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Abstract

Oregano species, especially members of *Origanum* genus, have drawn attention owing to their various biological activities for the last decades besides their traditional uses as flavoring herb in many cuisines throughout ages in human history. These activities are mainly dependent on type and content of the extract as well as oregano species. Essential oils extracted from oreganos are well-known bioactive agents characterized by a broad spectrum of activities ranged from antimicrobial to insecticidal. Phytochemical studies have revealed that oregano essential oil (OEO) is composed of mainly these bioactive compounds: terpenoids, phenolic acids, triterpene acids, hydroquinones, flavonoids, hydrocarbons, sterols, pigments, fatty acids, tocopherols, and inorganic compounds, which are responsible for its diverse bioactivities. The monoterpene carvacrol constitutes around 50% of the oregano essential oil. In this context, the present review was conducted to review oregano essential oil and its major active component carvacrol.

Keywords: Antimicrobial activity; Bioactivity; Carvacrol; Essential oil; Oregano.

1. Introduction

The history of oregano usage extends to early ages of mankind as old as 50.000-70.000 BC. It has been mainly used as a flavoring herb in many cuisines around the world, especially Mediterranean region where it naturally distributes. However, each culture used it for various purposes throughout its history, such as wedding ornament, cure for various ailments, perfume and additive to snuff.

According to PubMed database, the first scientific report about oregano bioactivity has been published in 1945 [1]. Since then the interest in bioactivity of oregano has drastically increased in parallel with the improvements in the phytochemical studies which resulted in the isolation and determination of various bioactive substances from *Origanum* species. The main groups of these compounds are terpenoids, phenolic acids, triterpene acids, hydroquinones, flavonoids, hydrocarbons, sterols, pigments, fatty acids, tocopherols and inorganic compounds. These groups are mainly found in oregano essential oils (OEOs), which include the carvacrol and thymol as major bioactive components and various extracts. Thanks to these bioactive molecules *Origanum* species are being used and tested for acaricidal, anticancer, antidiabetic, antiviral, antimicrobial, antioxidant, insecticidal, larvicidal, hepatoprotective, genotoxic/antigenotoxic, cardiorespiratory, anti-inflammatory, fumigant toxicity, cholinesterase inhibitory, and analgesic activities as well as effects on endothelial function, colitis (colonal injury), and gastrointestinal tract.

The present article is aimed to review the recent scientific reports about bioactivities of the oregano oil and carvacrol by discussing their act of mechanism.

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2. Bioactivities of Oregano Essential Oil and Carvacrol

2.1. Antibacterial Properties

Antibacterial properties of oregano species vary widely; a great number of pathogenic or nonpathogenic bacterial species are affected by the essential oils, several extracts and some of bioactive compounds naturally found in several parts of these plants. Pathogens and saprophytic bacteria, which directly or indirectly cause sickness, spoilage and eventually economical loss, are more remarkable groups among the oregano sensitive bacterial species due to their

importance in human, animal, plant or environmental safety.

Human pathogens directly affect the health of the individual and the community. Therefore, they come first among the studies focus on antibacterial properties of oregano species and there are many related studies in the literature. Some of the species investigated in these studies are *Acinetobacter baumannii*, *Chryseomonas luteola*, *Corynebacterium xerosis*, *Enterobacter aerogenes*, *Enterococcus faecalis*, *Klebsiella pneumonia*, *Listeria monocytogenes*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Staphylococcus aureus*, *S. haemolyticus*, *S. lugdunensis*, *S. sciuri*, *Stenotrophomonas maltophilia*, *Streptococcus mutans*, *Vibrio alginolyticus* and *Yersinia enterocolitica*. Antibacterial potential of oregano species against animal pathogens, plant pathogens and saprophytic bacteria also has come to the forefront in research because of close interactions between mankind and other organisms and even the environment. Antagonistic effects of oregano preparations and several bioactive compounds such as carvacrol and thymol isolated from these preparations have been extensively investigated (a) on animal pathogens such as *Aeromonas hydrophila*, *A. salmonicida* and *Listonella anguillarum*; (b) on plant pathogens such as *Clavibacter michiganensis*, *Erwinia amylovora*, *E. carotovora*, *E. chrysanthemi*, *Pseudomonas cichorii, P. helianthi*, *P. syringae* and *Xanthomonas malvacearum*; (c) and on the other bacterial species closely related with safety of various organisms and the environment such as *Bacillus amyloliquefaciens*, *B. cereus*, *B. megaterium*, *B. subtilis*, *Brevibacillus brevis*, *E. cloacae*, *Escherichia coli*, *Micrococcus luteus* and *Mycobacterium smegmatis*. Table 1 summarizes some of important antibacterial studies related with oregano species in the literature.

Recent studies focused on the mode of action mechanisms showed that antibacterial properties of oregano species are mainly dependent on the presence of aromatic monoterpenes such as carvacrol and thymol. Essential oils and other extracts of oregano species are rich in such bioactive molecules and especially carvacrol has been intensively studied as a model compound to understand fundamentals of the antibacterial activity. In a related study performed with *Bacillus cereus*, carvacrol treatment caused loss of the ion gradient in the target cell via depleting the intracellular ATP pool, changing the membrane potential, and increasing the permeability of the cytoplasmic membrane for protons and potassium ions. These vital changes eventually resulted in the death of the target cell. Although this mechanism has been observed in many species of oregano sensitive bacteria, the intermediate steps of the antibacterial process are still unknown [2]. In a recent study, the emerging opportunistic nosocomial multidrug resistant pathogen *A. baumannii* (Ab-MDR) were challenged by oreganum essential oil [3]. Results indicated that OEO has antimicrobial effects on Ab-MDR via cell membrane destabilization and disruption. Additionally, researchers combined the OEO with polymyxin B and the combination results in up to 16-fold reduction of polymyxin B MIC.

In addition to antimicrobial effects, oregano oil and carvacrol are proven to be inhibitors of certain genes especially virulence genes in enterohaemorrhagic *E. coli* [4] and previously it was also shown that while flagellin expression was inhibited, chaperonins were upregulated.

To exemplify the use of oregano oil as an additive to inhibit bacteria caused food spoilage, low-fat cheese was treated with oregano essential oil by Artiga-artigas et al. [5]. The shelf life low-fat cheese is limited due to the microbial development on its surface reducing their quality, especially if they are cut. To increase the shelf life by inhibiting microbial growth on the surface of the cheese, a nanoemulsion containing oregano oil in combination with mandarin fibers were used to form antimicrobial coatings on the cheese surface. According to the study, immersion of the cut cheese pieces in the nanoemulsion including at least 2% oregano oil inhibits the contamination of the cheese by external pathogens such as *Staphylococcus aureus* thus the shelf life of the low-fat cheese has increased.

2.2. Antigenotoxic Activity

There has been always an intensive interest in mutations because of their detrimental effects on human, other organisms and the environment. Recent knowledge on the relationship between mutagenesis and its critical role in various diseases, especially in formation of genetic disorders, has raised the scientific attention to the mutation-based genotoxicity and antigenotoxicity studies. Among these studies, researches especially related to natural preservative components or bioactive compounds, which show protective activities against mutagens in various ways, are noteworthy.

In one of the earlier studies, two desmutagen compounds, 3,5,7-trihydroxy-2-phenyl-4*H*-1-benzopyran-4-one (galangin) and 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4*H*-1-benzopyran-4-one (quercetin), were isolated from *O. vulgare* and it was shown that both molecules have significant antimutagenic activity against 3-amino-1-methyl-5*H*-pyrido[4,3-*b*]indole (Trp-P-2, a dietary carcinogen) [6]. In similar studies, it was first shown that methanol extract from *O. vulgare* had a significant antigenotoxic activity against various mutagens [7], and then luteolin 7-*O*-xyloside and luteolin 7-*O*-glucuronide were determined as two of bioactive flavonoid compounds responsible for the observed antimutagenic activity [8,9]. In a recent study, antigenotoxic property of essential oil from *O. vulgare* was shown in human lymphocytes [10].

Antigenotoxic potential of essential oil *from O. onites* was evaluated by using *Salmonella typhimurium* mutant tester strains TA98 and TA100. Results of this

study showed that the oil and its major constituent carvacrol strongly inhibited mutagenicity induced by 4-nitro-*o*-phenylenediamine and 2-aminofluorene in both strains with or without metabolic activation [11]. Antigenotoxic effects of essential oil from *O. compactum* were also shown in diploid *Saccharomyces cerevisiae* and *Drosophila melanogaster* as model organisms for eukaryotic systems [12,13]. These studies revealed that the oil strongly inhibits the mutagenic activities of 254-nm UVC radiation, 8-methoxypsoralen (8-MOP) plus UVA radiation, urethane (URE) and methylmethane sulfonate (MMS), and carvacrol is mainly responsible for this ultimate activity. A recent study also revealed that essential oils of *O. onites* and *O. minutiflorum* have antigenotoxic activities against potassium dichromate ($K_2Cr_2O_7$) and cobalt chloride ($CoCl_2$) induced mutagenesis in *D. melanogaster* [14]. In addition, *O. majorana* is known as one of the important oregano species with antigenotoxic properties and its aqueous extracts and essential oil show significant inhibitory activity on various mutagens [15,16].

2.3. Antitumor Activity

Several recent studies revealed anti-cancer potential of oregano essential oil. Cell cultures of rat embryonic fibroblasts and rat adipose tissue endothelial cells were treated with *O. onites* essential oil for 24, 48 and 96 hours. After the treatment cell cultures were tested in terms of apoptosis, cell migration, proliferation and angiogenesis. Results showed that while the oregano essential oil inhibits angiogenesis, cell proliferation and migration, it also induces apoptosis [17].

As a component of oregano oil, carvacrol has been tested as a novel antitumor agent on several types of cancer cells. Although action mechanism of carvacrol on cancerous cells varies between different cancer cell lines, generally it inhibits the proliferative pathways and/or upregulates the inhibitors of these pathways. Carvacrol was tested on Tca-8113 oral squamous cancer cells and was found to be inducing G1/S cell cycle arrest through downregulation of CDK regulator CCND1 and CDK4. It was also found to be upregulating CDK inhibitor P21. In addition, treatment of Tca-8113 cells with carvacrol resulted in downregulation of anti-apoptotic proteins Bcl-2, Cox-2, and upregulation of Bax [18].

Carvacrol has been shown to reduce prostate cancer cell proliferation, migration and invasion in two of the prostate cancer cell lines (PC-3 and DU145) [19]. It was known that in PC-3 and DU145 cancer cell lines, proliferation, migration and invasion is regulated by a TRPM7 membrane channel and its subsequent pathways. Carvacrol has been shown to block TRPM7 and the subsequent pathways thus reducing the proliferation, migration and invasion of the cancer cells TRPM7 blockage by carvacrol also showed similar effects on glioblastoma cells [20] and breast cancer cell lines by [21]. At higher concentrations, carvacrol were identified as an apoptosis inducer in hepatocellular carcinoma (HepG2) cell line [22].

Beside the anti-tumor properties of the carvacrol, it also helps to prevent the carcinogenic effects of chemicals. When rats injected with a carcinogenic agent (1,2-dimethylhydrazine) that causes colon carcinoma and supplemented with carvacrol in their diet, it was observed that the carvacrol diet significantly decreased the number of tumor incidents [23].

2.4. Antifungal Activity

As in the antibacterial activity mechanism, carvacrol also damages the cell membrane of fungi and leads to cytoplasmic leakage. Carvacrol and thymol inhibits the ergosterol synthesis, which constitutes the backbone of the fungal cell membrane [24,25]. It was also shown that carvacrol induces a Ca^{2+} ion burst from the cell and acidification of the cytosol, thus leading the loss of cell viability [26]. When the RNA's or the carvacrol-induced cells were analyzed, it was revealed that the response of these cells resembles to the cells under Ca^{2+} stress. Another antifungal activity of the carvacrol is to disrupt the endoplasmic reticulum integrity of the fungi and inducing unfolded protein response (UPR) [27]. In another study, oregano essential oil was used to inhibit the growth of *Aspergillus* species and it was found to be one of the best three aspergillus growth inhibiting essential oils [28].

In addition to that, since carvacrol and thymol are cell membrane disturbing agents, they were also combined with antifungal and antibacterial compounds to enhance the effect of these compounds. This combination was used to treat a mammalian fungal pathogen *Pythium insidiosum in vitro*. The study revealed a synergistic effect in combination of essential oils with the chemicals that increased the effectiveness of the treatment by 11 to 46% [29,30].

The opportunistic pathogen *Candida albicans* were exposed to twelve different essential oils on agar plates by employing the disc diffusion method. Six of the essential oils including oregano oil inhibited the growth of the fungus more efficiently than the antifungal drug Clotrimazole [31].

Oregano oil found to be inhibiting the fungal growth even in the volatile form. For instance, a tomato pest, *Sclerotinia sclerotiorum* were treated with volatile oregano oil and its mycelial growth was found to be inhibited at the concentrations of 0.3 µg/ml [32].

In an interesting study, cats were infected with zoophilic and zoonotic dermatophyte *Microsporum canis* was washed with a shampoo including oregano essential oil as a supplementary treatment to oral antifungal administration [33]. Oregano essential oil included shampoo treatment appeared to be effective to cure the infection.

Another example for antifungal activity of carvacrol were demonstrated on *Botrytis cinerea*, a stem and fruit rot causing pathogen [34]. It was shown that thymol and carvacrol exhibited strong anti-fungal activity against the pathogen by disrupting the

membrane permeability of *B. cinerea*. These results indicate thymol and carvacrol are good alternatives to conventional fungicides against *B. cinerea* in controlling grey molds in horticultural products.

2.5. Acaricidal/Insecticidal/Larvacidal Activity

Oregano oil and carvacrol are not only effective on microorganisms but also on some of the insect species. Because of this property, it has potential uses in animal husbandry.

The veterinary skin disease, animal acariasis which is caused by the parasitic acars reduces the yield and quality of the animal products. Conventionally this disease is treated with chemical drugs. As an example, the rabbit parasitic mite *Psoroptes cuniculi* were treated with oregano oil *in vitro* and *in vivo*. Results showed that the 0.05% and 0.02% of the oregano oil has killed all the parasites within 1h and 6h, respectively [35].

Oregano oil was also used to repel and kill the insect in the stored grains. When the oregano oil is applied at 1 ml/L, maize weevil and larger grain borer is killed within 48 hours in the maize storages. In addition to that oregano oil act as a repellent, therefore the storage stayed insect free [36].

There are also some reports indicating that the oregano oil can be used as a larvacidal. It was shown that after 24 hours of treatment, oregano oil has LC_{50} value of 258 mg/L against the mosquito larvae (*Culex pipiens*) [37]. In more comprehensive study larvae of the mosquito species of *Anopheles stephensi*, *A. subpictus*, *Culex quinquefasciatus* and *C. tritaeniorhynchus* were treated with oregano essential oil in concentrations of 30, 60, 90 and 120, 150 µg/ml for 24 h. Mortality rate of larvae was found to be increased in a dose-dependent manner and for 150 µg/ml dose mortality rates were between 95.2% (for *C. quinquefasciatus*) to 100% (for *A. stephensi*) [38].

2.6. Antispasmodic Activity

Antispasmodics are the compounds that relieve cramps or spasms of the stomach, intestines and bladder. They are commonly used for the treatment of different gastrointestinal disorders. Antispasmodic activity of the oregano has been known for decades [39]. Van Den Broucke and Lemli [39] isolated guinea pig ileum and rat vas deferens and contracted them by using carbachol. After 5 minutes oreganum oil pre-treatment of ileum and vas deferens, effect of contraction agent carbachol was mitigated. These results indicated the antagonistic effect of oreganum oil against carbachol. Khan et al. [15] showed that because of its antispasmodic activity, carvacrol is a potential choice for treating the kidney stones.

The effect of the essential oils extracted from Mexican oreganos (*Poliomintha longiflora* and *Lippia graveolens*) on carbachol- and histamine-induced guinea-pig ileum contractions was assessed. The results revealed that both of the essential oils provoked a concentration-dependent inhibition of the tone and amplitude of the guinea pig ileum induced contractions [40].

2.7. Antiurolithic Activity

One of the problems of the urinary tract is the formation of calcium oxalate crystals (CaOx) in kidneys. Effects of oregano oil on kidney stones were investigated *in vitro* and *in vivo* [15]. According to the study, oregano extract inhibited CaOx nucleation and aggregation. *In vivo* studies resulted in increased urine output in a similar manner as the diuretic drug hydrochlorothiazide which also helps expulse CaOx crystals. *In vitro* studies indicated that, oregano oil blocks calcium channels and causes a relaxation in the bladder stripes that contracted via carbachol and high K^+ concentrations, thus helps expulsion of the kidney stones from the urinary tract.

2.8. Antinociceptive and Anti-inflammatory Activity

There are cases where the oregano was used as a potential pain reliever. In one of the studies, researchers used aqueous extract of *O. vulgare* leaves and they administered the extract to cerebro spinal fluid of rats thus targeting the central nervous system [41]. According to the study, injection of oreganum extract caused an analgesic effect on the rats in dose-dependent manner. Researchers also concluded that the oreganum is possibly effecting opioid pathway.

Cyclooxygenase-2 (COX-2) plays a key role in inflammation and circulatory homeostasis. Expression of the COX-2 is controlled by a system that involves the peroxisome proliferator-activated receptors (PPAR). Human macrophage-like cells were treated with oregano essential oil and carvacrol and it was observed that the carvacrol suppressed lipopolysaccharide-induced COX-2 mRNA and protein expression [42]. This finding suggested that carvacrol regulates COX-2 expression via its agonistic effect on PPAR, thus suppressing the inflammatory response.

When the mice were treated with acetic acid to induce abdominal writhing carvacrol reduced the number of writhing compared to the control group. Additionally, carvacrol also significantly inhibited both the early (neurogenic pain) and the late (inflammatory pain) phases of formalin-induced licking in mice [43]. The researcher also found out that carvacrol significantly inhibits the pain caused by capsaicin, glutamate and heat [44].

2.9. Antidiabetic Activity

Diabetes is one of the main health problems of modern world. In a pilot study, a combination of essential oils containing oregano essential oil lowered the circulating glucose levels in rats suggesting an enhancement in insulin sensitivity [45]. However, there was no direct link to the oregano effect on diabetes. Methanol extract of oregano oil was tested for its protective effect against Streptozotocin-induced type 1 diabetes in mice and it was found that oregano oil protected the mice from type 1 diabetes development [46]. The protective effect of

the oil was attributed to its antioxidant, anti-inflammatory and anti-apoptotic properties. A similar result also observed when the Streptozotocin-induced mice were treated with ethyl acetate extract of oregano [47].

2.10. Antioxidant Activity

Most of the metabolic activities results in production of reactive oxygen species (ROS) and ROS are maintained at low levels by various enzymatic systems participating in the *in vivo* redox homeostasis under normal conditions. In case of excessive ROS production and/or a deficiency of antioxidants result in endogenous oxidative stress. Hydrogen peroxide is one of the main oxidative stress agents and it was studied in several projects. On the other hand, oregano has been proved to alleviate oxidative stress in some studies. For instance, oregano oil was tested on hydrogen peroxide produced oxidative stress on porcine small intestinal epithelial cells (IPEC-J2) [11]. In another work, ROS scavenging activity of the *O. dictamnus* essential oil and its components were tested against the chemical 2,2-diphenyl-1-picrylhydrazyl (DPPH) [48]. For both of the works, the results revealed significant antioxidant activity of essential oil and the carvacrol. However, no antioxidant activity was observed for the other oil components *γ*-terpinene, *p*-cymene and linalool.

Oregano essential oil was also used as a food additive for enriching the antioxidant capacity of the food substances, thus preserving longer the aroma, taste and color via strengthen the stability of the substance against oxidative degradation. Some of the tested oregano species as an antioxidant food additives are *O. onites* (oregano), *O. dictamnus* (dittany) [49], *O. vulgare* [50].

Because of its antioxidant capacity oregano active film was proved to increase the shelf life of fresh beef steaks [51,52]. When the oregano essential oil is combined with the other compounds, such as chitosan, its antioxidant and antimicrobial effects can be boosted to even higher levels [53].

Vascular smooth muscle cell (VSMC) migration and proliferation are key processes occurs during atherosclerosis. Carvacrol inhibits migration and proliferation of many normal and cancerous cells [54,55] Because of its antioxidant activity carvacrol was shown to diminish the elevation of ROS generation in response to platelet-derived growth factor (PDGF) in rat aorta smooth muscle cells thus inhibiting aortic sprout outgrowth [56].

2.11. Vasorelaxant and Cardiovascular Activity

Monoterpenes has been known for their cardiovascular effects [57]. Carvacrol was tested on anaesthetized mice to determine cardiovascular effects of *p*-cymene is one of the components of oregano oil and it is the precursor of carvacrol. Rat aorta was treated with monoterpenic phenol isomers, carvacrol, thymol and *p*-cymene and it was reported that the monoterpenes have a relaxing effect on the vascular smooth muscle [58], [59]. In a similar work, administration of carvacrol to anaesthetized rats at 100 µg/kg concentration resulted in decreased heart rate, lower arterial pressure and decreased systolic and diastolic pressure [60].

2.12. Antiobesity Activity

Obesity is one of the health concerns of the modern life. The activity of oregano oil and carvacrol has been investigated in some studies. In these studies, carvacrol inhibited intracellular fat deposition by blocking various pathways thus the adipogenesis.

Rosiglitazone-mediated DRIP205/TRAP220 (transcription factor complex) activation of PPAR*γ* is classified among the "adipogenic factors", those promotes adipogenesis and adipocyte differentiation in cell culture and thus weight gain in humans [61]. Extracts of oregano and almost all the associated substances moderately antagonized PPAR*γ* activation. In an initial study oregano extracts were found to have antagonistic effects against PPAR*γ* [62]. Oregano oil containing PPAR antagonists contributes to weight loss, thus making the oregano extracts as a potential food supplements for weight reduction.

Animal models for obesity is generally achieved by feeding a mouse with a high fat diet (HFD). Antiobesity effects of carvacrol on such a model was reported by Cho et al. [63]. The mice fed with HFD together with 0.1% carvacrol showed lowered fat-pad weights in comparison to HFD fed mice. The researchers also tested the carvacrol on mice embryonic 3T3-L1 cell line, which differentiates to adipocytes under certain conditions. Carvacrol treatment on 3T3-L1 cells significantly reduced the intracellular fat accumulation and blocked the differentiation of cells to adipocytes. Researchers suggested that carvacrol inhibits visceral adipogenesis by suppressing BMP-, FGF-1- and galanin-mediated signaling cascades. Additionally, carvacrol attenuates the production of pro-inflammatory cytokines in the visceral adipose tissues by inhibiting TLR2- and TLR4-mediated signaling pathways. Supportingly, Spalletta et al. showed that carvacrol reduces the adipose differentiation 40% in 3T3-L1 murine cell line and 30% in human mesenchymal stem cell line (WJ-MSC) by blocking the transcription of ChREBP transcription factor [64].

2.13. Other Biological Activities

2.13.1. Therapeutic Hypothermia Effect

Therapeutic hypothermia is a technique in which a patient's core temperature is mildly lowered intentionally by some chemicals to trick the body's sensory system to sense the body is warmer than it should be, thus signaling to body to lower the core temperature. The technique has some benefits for patients after cardiac arrest, for the treatment of stroke and traumatic brain injury. In a study, carvacrol was injected by the intraperitoneally and intravenously to mice and rats [65]. Carvacrol is an antagonist and activator of transient receptor potential vanilloid-3

(TRPV3) which is a component of the temperature sensory system. At safe doses of carvacrol, temperature dropped modestly and higher doses caused toxic effects. Study suggested that carvacrol has a limited potential for being used as a hypothermical agent.

2.13.2. Antidepressant Activity

Carvacrol showed potential antidepressant effects on mice. When it is given to the mice orally before the forced swimming test and tail suspension tests, immobility time of mice decreased significantly. These findings indicated that carvacrol has an antidepressant like effect on mice [66]. Researchers also indicated that the underlying mechanism of antidepressant like effect of the carvacrol is based on increase in dopamine levels in the synaptic cleft meaning carvacrol acts on the dopaminergic system.

2.13.3. Anxiolytic Activity

Anxiolytics are the drugs to inhibit anxiety. In a couple of study, it has been shown that the oregano oil has anxiolytic effects on mice. Melo et al. [67] tested mice in maze test after fed them with carvacrol containing food and they observed that carvacrol has some anxiolytic activities on mice without showing any sedative or myorelaxant effects.

2.13.4. Antiplatelet Activity

Antiplatelet drugs are used to decrease platelet aggregation. They are generally used in prevention of thrombotic cardiovascular diseases. Venous blood was treated with platelet activating factor (PAF), adenosine diphosphate and arachidonate to induce platelet aggregation. Platelet aggregation results in thromboxane A2 (TXA_2) production normally. However, when carvacrol is added to the media together with these platelet aggregation factors a significant decrease observed in the TXA_2 production which confirms the antiplatelet activity of carvacrol [68].

3. Conclusion

In this review, it was aimed to overview the diversity of bioactivities of oregano essential oil and its major active component carvacrol. Since oregano essential oil and carvacrol have been subjected in a great number of studies, the present review cannot cover all the studies in the literature. However, it was designed to represent main concepts and recent updates.

In modern world, there has been a growing demand for natural drug alternatives to conventional synthetic chemicals since they have shortcomings and side effects. For instance, present antibiotics are incapable of inhibiting several resistant bacteria [69-72] and some of current insecticides cause undesirable genetic changes on both treated plant and insect species [73]. In this perspective, oregano essential oil and its constituents are promising bioactive agents to replace and/or improve the inappropriate conventional treatments. Our present knowledge on bioactive properties of oregano species indicates that they will potentially play a crucial role in the development of novel natural formulations in near future.

Table 1. Antibacterial properties of oregano species

Bacteria	Importance	Antagonistic Oregano Component	References
A. baumannii	An opportunistic human pathogen that causes nosocomial infections	Essential oils from *O. vulgare*, *O. majorana*, *O. onites* and *O. acutidens*	[71,72,74-77]
A. lwoffii	An opportunistic pathogenic bacterium that cause diseases in immunocompromised humans	Essential oil, hexane extract, dichloromethane extract, methanol/$CHCl_3$ extract and deodorised methanol/$CHCl_3$ extract from *O. syriacum* var. *bevanii*	[78]
A. hydrophila	A pathogenic bacterium that generally infects fish and amphibian species	Essential oils from *O. minutiflorum*, *O.* onites, *O. vulgare*, *O. acutidens* and *O. heracleoticum*	[78,79,80-84]
		Carvacrol and thymol	[13]
A. salmonicida	A fish pathogen that severely impacts trout populations and other species	Essential oils from *O. vulgare* and *O. onites*	[83,85]
B. amyloliquefaciens	A non-pathogenic and root-colonizing bacterium with potential use as a biocontrol agent	Essential oils from *O. minutiflorum* and *O. onites*	[76,79]

Table 1. *Cont.*

B. cereus	A bacterium that causes several types of foodborne diseases	Essential oils from *O. vulgare*, *O. onites*, *O. minutiflorum*, *O. compactum*, *O. heracleoticum* and *O. acutidens*	[79,86-89]
		Methanol extract of *O. onites*	-
		Carvacrol and thymol	[86,90,91]
B. megaterium	A non-pathogenic bacterium with environmental significance.	Methanol extract of *O. majorana*, essential oil and aqueous infusion of *O. vulgare*, extracts of *O. onites*	[76,92-94]
B. subtilis	A non-pathogenic bacterium with environmental and industrial significance	Essential oils from *O. onites*, *O. minutiflorum*, *O. vulgare*, *O. majorana*, *O. compactum* and *O. saccatum*	[79,95-97]
		Methanol extract of *O. majorana*	[92]
		Carvacrol	[96]
B. brevis	A non-pathogenic bacterium with environmental significance	Essential oil from *O. onites*	[76]
C. luteola	An opportunistic pathogen that causes bacteremia, meningitis, prosthetic valve endocarditis, peritonitis in humans and animals	Essential oil from *O. onites*	[76]
C. michiganensis	A plant pathogen that severely impacts tomatoes and potatoes and cause substantial economic losses worldwide	Essential oils from *O. rotundifolium* and *O. onites*	[76,98]
C. michiganensis ssp. *michiganensis*	A plant pathogen that is responsible for bacterial wilt and canker of tomato	Essential oil from *O. onites*	[76]
C. xerosis	A bacterium that is important as a pathogen in immunosuppressed patients	Essential oils from *O. onites*, *O. minutiflorum* and *O. vulgare*	[79,99]
E. aerogenes	An opportunistic human pathogen that causes nosocomial infections with various symptoms	Essential oil from *O. onites*, essential oil and aqueous infusion of *O. vulgare*	[76,80]
E. cloacae	A non-hazardous bacterium	Essential oils from *O. onites*, *O. acutidens* and *O. vulgare*	[76,89,100]
E. faecalis	A human pathogen that cause endocarditis and septicemia, urinary tract infections, meningitis and other types of infections	Essential oils from *O. vulgare*, *O. bilgeri, O. minutiflorum*, *O. onites* and *O. heracleoticum*	[79,88,101,102]
		Carvacrol and thymol	[30]
E. amylovora	A plant pathogen that is the causative agent of fire blight disease, severely affects apples, pears, and some other members of the family Rosaceae	Essential oils from *O. compactum*, *O. vulgare* and *O. onites*	[76,103]

Table 1. *Cont.*

E. carotovora	Another plant pathogen that cause fire blight like disease	Essential oils from *O. vulgare*, *O. onites* and *O. dictamnus*	[104]
E. chrysanthemi	A plant pathogen that infects several members of various plant families with economic importance such as Amaryllidaceae, Apiaceae, Asparagaceae, Asteraceae, Begoniaceae, Brassicaceae, Bromeliaceae, Convolvulaceae, Poaceae and Solanaceae	Essential oil from *O. onites*	[76]
E. coli	Some strains are non-pathogenic. Some are opportunistic pathogens that can cause gastroenteritis, urinary tract infections, neonatal meningitis and various types of infections. Moreover, several strains of *E. coli* are a major cause of foodborne illness	Essential oils from *O. heracleoticum*, *O.* dictamnus, O. *vulgare*, *O. acutidens* and *O. onites*	[4,18,35,76,105]
		Carvacrol	[4]
K. pneumonia	An opportunistic pathogen that damages animal and human lungs	Essential oil from *O. acutidens*	[18]
		Ethyl acetate, acetone and methanol extract of *O. onites*	[94]
L. monocytogenes	A bacterium that is one of the most virulent foodborne pathogens and causes listeriosis	Essential oils from *O. minutiflorum*, *O. onites*, *O. compactum*, *O. heracleoticum*, *O. vulgare* and *O. acutidens*	[4,8,77,105-107]
		Carvacrol	[4]
L. anguillarum	An animal pathogen that infects various marine and fresh water fishes, bivalves and crustaceans	Essential oil from *O. onites*	[76]
		Ethanolic extract from *O. vulgare*	[108]
M. luteus	An opportunistic pathogen which is responsible for nosocomial infections	Essential oils from *O. minutiflorum*, *O. onites*, *O. vulgare* and *O. hypericifolium*	[8,109,110]
M. smegmatis	An opportunistic pathogen that may cause diseases in humans in some very rare cases	Essential oils from *O. minutiflorum* and *O. onites*	[8]
		Essential oil and extracts from *O. vulgare* subsp. *virens* and extracts from *O. vulgare* subsp *hirtum*	[111,112]
P. mirabilis	A human pathogen that is responsible for the formation of kidney stones	Essential oil and aqueous infusion of *O. vulgare*	[80,100]
		Essential oils from *O. heracleoticum* and *O. onites*	[17,76]

Table 1. *Cont.*

P. vulgaris	A human pathogen that cause nosocomial infections including wound infections, septicemia and pneumonia	Essential oils from *O. vulgare*, *O. minutiflorum*, *O. onites*, *O. hypericifolium* and *O. acutidens*	[8,18,99,110]
		Methanol extract of *O. majorana*	[92]
		Carvacrol	[89,101,113]
		Thymol	[69,101,113]
		Eugenol	[113]
P. aeruginosa	A bacterium with a broad-spectrum pathogenicity that infects and causes diseases in plants, animals and humans	Essential oils from *O. acutidens*, *O. onites*, *O. vulgare* and *O. heracleoticum*	[17,18,114]
		Methanolic extracts from *O. syriacum* and *O. majorana*	[92,115]
		Carvacrol, thymol and eugenol	[113]
P. cichorii	A plant pathogen with high economic impact on lettuce, celery and chrysanthemum crops	Extracts and essential oil from *O. onites*	[76]
P. fluorescens	A pathogenic bacterium that cause illness in humans	Extracts and essential oil from *O. onites*	[76]
P. helianthi	A plant pathogenic bacterium that infects a variety of plants	Extracts and essential oil from *O. onites*	[76]
P. stutzeri	An opportunist pathogenic bacterium that cause illness in humans	Extracts and essential oil from *O. onites*	[76]
P. syringae	A plant pathogen that infects a great variety of plant species	Essential oils from *O. vulgare* and *O. compactum*	[103,116]
		Extracts and essential oil from *O. onites*	[76]
P. syringae pv. *syringae*	A plant pathogen that infects plant species belong to genera Syringa, Prunus and Phaseolus	Extracts and essential oil from *O. onites*	[76]
		Essential oils from *O. vulgare* and *O. compactum*	[103]
P. syringae pv. *tomato*	A plant pathogen that infects tomatoes	Extracts and essential oil from *O. onites*	[76]
S. typhimurium	A pathogenic bacterium that infects animals and humans	Essential oils from *O. vulgare*, *O. majorana*, *O. hypericifolium*, *O. heracleoticum*, *O. onites*, *O. minutiflorum* and *O. acutidens*	[4,18,117-120]
		Carvacrol	[4,118]
S. aureus	Some strains are non-pathogenic. Some are pathogens that can cause skin infections such as a skin abscess and respiratory infections such as sinusitis. Moreover, several strains of *S. aureus* cause foodborne diseases	Essential oils from *O. onites*, *O. vulgare*, *O. glandulosum*, *O. dictamnus*, *O. minutiflorum*, *O. majorana*, *O. bilgeri* and *O. heracleoticum*	[8,17,35,76,86, 102,107,121,122]
		Essential oil and various extracts obtained from *O. acutidens* and methanol extract of *O. majorana*	[77,92]
S. epidermidis	An opportunistic pathogen that especially infects patients with compromised immune systems	Essential oils from *O. vulgare*, *O. onites*, *O. calcaratum* and *O. scabrum*	[99,123,124]

Table 1. *Cont.*

S. haemolyticus	A well-known opportunistic pathogen in humans	Essential oil from *O. onites*	[76,121]
S. lugdunensis	A human pathogen closely related with a broad variety of infections	Essential oil from *O. onites*	[76,121]
S. sciuri	A human pathogen that cause endocarditis, peritonitis, septic shock, urinary tract infection, pelvic inflammatory disease and wound infections	Essential oils from *O. onites*, *O. vulgare* and *O. majorana*	[76,121,125]
		Mixtures of carvacrol/thymol/*p*-cymene and carvacrol/thymol	[125]
S. maltophilia	A human pathogen that cause diseases	Essential oils from *O. vulgare* and *O. onites*	[70,76,114]
S. mutans	A bacterium that is one of the major causative agents of tooth decay in humans	Essential oils from *O. onites* and *O. vulgare*	[76,126]
V. alginolyticus	A pathogenic marine bacterium that causes otitis and wound infection	Essential oil from *O. onites*	[76]
V. splendidus	A pathogenic bacterium that cause toxic effects on bivalves and vibriosis in marine life	Essential oil from *O. onites*	[76]
X. malvacearum	A plant pathogen that infects cotton plant and cause seedling blight, leaf spot, blackarm and boll rot	Essential oil from *O. onites*	[76,127]
X. axonopodis pv. *malvacearum*	A plant pathogen that infects cotton plant and cause leaf spots	Essential oil from *O. onites*	[76]
X. axonopodis pv. *vesicatoria*	A plant pathogen that infects peppers and tomatoes and cause leaf spots	Essential oil from *O. onites*	[76,98]
X. axonopodis pv. *campestris*	A plant pathogen that infects crucifers	Essential oil from *O. onites*	[76]
X. axonopodis pv. *vitians*	A plant pathogen that is the causal agent of bacterial leaf spot of lettuce	Essential oil from *O. onites*	[76]
X. axonopodis pv. *pelargonii*	A plant pathogen that infects several plants such as *Pelargonium peltatum* and *Pelargonium hortorum*	Essential oil from *O. onites*	[76]
X. campestris pv. *raphani*	A plant pathogen that infects radishes	Essential oil from *O. onites*	[76]
X. campestris pv. *zinnia*	A plant pathogen that infects *Zinnia* species	Essential oil from *O. onites*	[76]
Y. enterocolitica	A human pathogen that cause diarrhea	Essential oils from *O. minutiflorum*, *O. onites*, *O. vulgare* and *O. majorana*	[8,128]
		Extracts of *O. sipyleum*	[129]

Conflict of Interest

The authors declare no conflict of interest.

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