

## *Origanum compactum* Benth: A Review on Phytochemistry and Pharmacological Properties

Abdelhakim Bouyahya<sup>1,2</sup>, Abrini Jamal<sup>1</sup>, Fatima Edaoudi<sup>3</sup>, Abdeslam Et-Touys<sup>1</sup>, Youssef Bakri<sup>1</sup>, Nadia Dakka<sup>1</sup>

<sup>1</sup>Biochemistry-Immunology Laboratory, Department of Biology, Faculty of Sciences, Mohammed V University, Rabat, Morocco

<sup>2</sup>Biology and Health Laboratory, Team of Biotechnology and Applied Microbiology, Department of Biology, Faculty of Science, Abdelmalek Essaadi University, Tetouan, Morocco

<sup>3</sup>Applied Biology Laboratory, Department of Biology, Faculty of Sciences and Technologies, Tanger, Abdelmalek Essaadi University, Tetouan, Morocco

### Abstract

*Origanum compactum* Benth (*O. compactum*) is an important aromatic and medicinal plant in Morocco. It is used as a culinary condiment and largely employed in popular medicine for the treatment of ailments. Several studies recently conducted have demonstrated that *O. compactum* possesses antimicrobial, antifungal, antioxidant, antibacterial, anti-mutagenic, cytotoxic, anticancer, and anti-corrosion activities. Phytochemical investigations of this genus have resulted in the extraction of a number of important bioactive compounds. This emphasizes the need for extensive study for reporting the additional information on the mechanism of action of these effects.

**Keywords:** Essential oil; Extracts; Pharmacological properties; *Origanum compactum*

### Introduction

Oregano is the common name for the aroma and taste that comes primarily from more than 60 species of plants used worldwide as a spice. The genus *Origanum* (Lamiaceae) includes 39 species widely distributed in the Mediterranean region [1]. These plants are perennial herbs spontaneously growing in calcareous substrates. Oregano is characterized by the presence of glandular trichomes covering the aerial organs. The glandular trichomes secrete essential oils with a unique flavor, which is mainly due to its major compounds such as carvacrol, thymol and so on.

Lamiaceae family is represented in Morocco by 30 genera and 225 species (more than 90 are endemics). These species give a great ecological and economic interest. In effect, it offers many medicinal and aromatic plant species [2]. The genus *Origanum* is represented by five species (three are endemic), including *O. compactum*. Throughout Morocco, oregano, known locally as “Zaatar” and corresponding to the species *O. compactum*, is traditionally considered the biggest species for health.

Many scientific studies have been conducted to examine and justify the practices associated with Zaatar. In effect, these studies have demonstrated that essential oils and extracts from this species have many biological activities as antimicrobial, antioxidant, cytotoxic, antitumoral, anti-corrosion, etc. This review details the morphology, distribution and systemic classification of *O. compactum*, its health benefits, phytoconstituents of *O. compactum* and a detailed up-to-date literature survey of various research findings related to its ethnopharmacological property.

### Classification, Description, Distribution and Traditional Use

Botanically known as *O. compactum* Benth. and commonly as Zaatar, is the sacred plant of Morocco and is also known by various names as Zaatar, Sahtar. The plant is known in English as Oregano. *O. compactum* is perhaps the most common and the most revered of all household plants in Morocco. This aromatic shrub belongs to the family Lamiaceae and genus of *Origanum*.

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Lamiales

Family: Lamiaceae

Genus: *Origanum*

Species: *Compactum*

Binomial name: *Origanum compactum*

### Description

*O. compactum* belongs to the compactum section where successive verticillasters are reconiled fake ears contracted terminal, short and globular (spicastre). It is a perennial, chamaephyte generally pubescent, hairy stems, covered with long hair (3 mm) (Figure 1). The stem leaves are oval-ovoid, large, up to 35 mm, clearly stalked (2-8 mm). Hairy leaves, more than underside upper side margins hair long hair (3 mm). The inflorescences are in dense spikes and short, very purple, large flowers opposite (5-12 mm), sessile. The calyx is usually hairless, 3-4 mm long, 5 subequal triangular teeth (0.5-1 mm). The exserted corolla covered with very fine hairs (<0.1 mm). The floral bracts are lanceolate ovals ovoides-not membranous, stiff, leathery, sessile, truncate base, 6-8 mm long, glabrous on 2 sides, with inconspicuous glands, higher margin (top edge) ciliotée (eyelashes 0.2-0.5 mm). The floral bracts overlap each other from the base to the top of the ear and hide calyxes [3].

The principal morphological characteristic of this species is the presence of secretory organ (glandular and non glandular trichomes). This structure secretes essential oils with a unique flavor, which is

**\*Corresponding author:** Abdelhakim B, Biochemistry-Immunology Laboratory, Department of Biology, Faculty of Sciences, Mohammed V University, Rabat, Morocco, Tel: 0601350878; Fax: 0535785643; E-mail: [boyahyaa-90@hotmail.fr](mailto:boyahyaa-90@hotmail.fr)

Received April 04, 2016; Accepted May 27, 2016; Published May 30, 2016

**Citation:** Bouyahya A, Jamal A, Edaoudi F, Et-Touys A, Bakri Y, et al. (2016) *Origanum compactum* Benth: A Review on Phytochemistry and Pharmacological Properties. Med Aromat Plants 5: 252. doi:10.4172/2167-0412.1000252

**Copyright:** © 2016 Bouyahya A, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



Figure 1: *Origanum compactum* Benth.

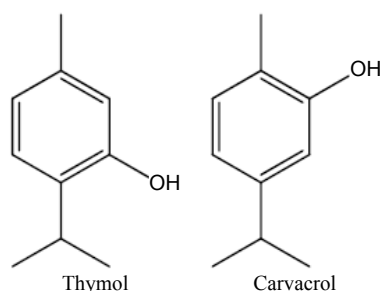


Figure 2: Structure of the main compounds (chemotypes) of *O. compactum* essential oil.

mainly due to its major compounds such as carvacrol, thymol, and so on (Figure 2) [4,5].

## Distribution

Biogeographically *O. compactum* is found in Morocco (grows in Rif, Tangier, Morocco central-northern, north western Morocco, west of southern Morocco, the Haouz, the Haut atlas and south of the Iberian Peninsula [6], South-West Spain and North Africa [7]. It is a perennial herb spontaneously growing in forests, calcareous substrates, bushes and rocky pastures of the plains and low mountains. Flowering occurs in May-July [2].

## Traditional Application

Oregano has been used a long time by Morocco population for medicinal properties and food preparation purposes. This application is no wide because of its bitterness, despite the pleasant odor. The taste is very intense, quite unpleasant and strongly bitter, so its culinary application is limited to the region of origin, such as Morocco. It is mainly used as a culinary condiment and largely employed in popular medicine for the treatment of ailments such as dysentery, colitis, bronco-pulmonary, gastric acidity, and gastro-intestinal diseases [2,8,9]. *O. compactum* is also used as preservative for the melted butter (*smen*).

## *Origanum compactum* essential oils composition

Essential oils are volatile compounds odorous found in aromatic plant [10]. The compound of essential oil are very complex and presents

very promising biological agents and accepted by consumers and exploitation for potential multi-purpose use because of their relative safety [11].

This essential oil is stored in plants in special brittle secretory organ, such as glands for *O. compactum* [12]. The yield of essential oil of plants is generally depends on plant species, geographical distribution, storage organ, collection period and method of extraction. For example, the essential oil yields flower of *O. compactum* extracted by Elbabili et al. [13] and Bouchra et al. [14] was respectively 2.10% and 5.4%. This difference in yield is attributed to geographical origin of plant collection.

Essential oils are hydrophobic and thus only slightly soluble in water. They are soluble in alcohol, non polar or weakly polar solvents, waxes and oils. Most essential oils are colorless or pale yellow, liquid and has lower density than water [15]. Essential oils are complex mixtures comprising many various compounds. Chemically they are derived from terpenes and their oxygenated compounds [15].

The chemical composition of the myrtle essential oil has been described by many authors [4,5,13,14,16-22]. Compounds that have been found in myrtle oils include  $\beta$ -Myrcene,  $\alpha$ -Phellandrene,  $\alpha$ -Terpinene, Limonene, 1,8-Cineole,  $\beta$ -Phellandrene,  $\gamma$ -Terpinene, 3-Octanone, *p*-Cymene, Terpinolene, 1-Octen-3-ol, Trans-thuyanol, Camphre, Linalol, Cis-thuyanol, Terpinene-4-ol,  $\beta$ -Caryophyllene, Pulegone,  $\alpha$ -Humulene, Neral,  $\alpha$ -Terpineol, Borneol,  $\beta$ -Bisabolene, *d*-Cadinene, *g*-Cadinene, *p*-Cymene-8-ol, Piperitenone, Caryophyllene, oxide, Thymol and Carvacrol.

All these Oregano essential oil compounds may be classified into three main categories: terpenes (monoterpene hydrocarbons and sesquiterpene hydrocarbons), terpénoides (oxygenated monoterpenes and oxygenated sesquiterpenes) and phénylpropanoïdes, but also into hydrocarbons and oxygenated compounds. The main compounds found are carvacrol, thymol, *p*-mecyne, and  $\gamma$ -terpenine (Table 1).

Environmental factors were considered to play a key role in the chemical composition of oregano oil. The fragrance and chemical composition of essential oils can vary depend on the geo-climatic location and growing conditions, including concentration of nutrients, temperature, humidity, soil type, day length, climate, altitude, amount of available water, etc. The chemical composition also depends on season or vegetative period of plant [5].

According to these factors, plant biosynthetic pathways can change the relative proportion of the primary oil components. These variations in chemical composition led to the notion of chemotypes, which are generally defined as a distinct population within the same species that

Sample	Carvacrol (%)	Thymol (%)	<i>p</i> -Cymene (%)	$\gamma$ -Terpinene (%)	References
Morocco	3.8 to 71	0 to 43.4	10.7 to 25.4	-	[16]
Rabat Morocco	58.1	9.0	11.4	7.1	[14]
Balkans	73.98	3.74	3.18	3.38	[17]
Morocco	22	19	-	23	[18]
Rabat Morocco	30.53	27.50	7.89	18.20	[4]
Morocco	36.46	29.74	24.31	1.10	[13]
Taounat Morocco	43.97	11.56	17.87	-	[19]
Morocco	58.1	9	11.4	7.1	[20]
Rabat	5.3	53	18	12	[21]
Morocco	28.5	19	-	-	[22]
Morocco	31.22	22.67	13	18.6	[5]

Table 1: The main compounds of *O. compactum* essential oil (%).

produces different chemical profiles for a particular class of secondary metabolites [10].

Therefore, all these biotope factors, genetic and epigenetic, influence the biochemical synthesis of essential oils in a particular plant. Thus, the same species of plant can produce a similar essential oil, but with different chemical composition and therapeutic activities. As shown, there is considerable variability in the composition of myrtle essential oil depending on multiple biotope factors, but the most important constituents of myrtle oil are carvacrol, thymol, p-mecyne,  $\gamma$ -terpinene.

### ***Origanum compactum* extracts composition**

A few studies aimed to investigate the chemical composition of *O. compactum* extracts; their profile constitutes polyphenolic compounds, which are grouped in three major chemical classes –phenolic acids, tannins and flavonoids. Extraction of dried and powdered aerial parts of oregano yielded thymohydroquinone, betulinic acid,  $\beta$ -amyryn, betulin, oleanolic acid, ursolic acid, aromadendrin, 21  $\alpha$ -hydroxyoleanolic acid, and 21  $\alpha$ -hydroxyursolic acid [22].

The chemical compositions of the aerial part of *O. compactum* has been evaluated by El Babili et al. [13]. The total amount of flavonoids, in oregano ethyl acetate extract, was the highest one ( $54.7 \pm 1.8$  g/kg equivalent quercetin), while the petroleum ether extract was the richest in polyphenols ( $707.8 \pm 13.4$  g/kg eq gallic acid). The anthocyanins ( $5.63 \pm 0.19$  mg eq cyaniding/kg) were present in higher amounts in the petroleum ether extract. Tannins were found in all extracts with an amount between 12.4 (ethanol extract) to 510.3 (petroleum ether extract) eq catechin (g/kg dry wt).

### **Pharmacological Activities of *Origanum compactum***

#### **Antibacterial effect**

The problems regarding application of conventional antibiotics, including antimicrobial resistance, environmental problems, cancerogenicity, side effects and high costs, have reinforced a tendency to replace synthetic antimicrobials with natural alternative agents [23]. Plant based products are among the alternative agents examined in order to replace conventional antibiotics. Accordingly, extensive research has been carried out in order to evaluate the antimicrobial effect of the essential oils and extracts which showed the ability to inhibit the growth of various pathogenic microorganisms [24].

The antibacterial properties of *O. compactum* essential oils and extracts against pathogenic bacteria were reported in many studies and obtained results are promising [19]. indicated antibacterial effect of Oregano flowers, leaves and stems essential oil against five of pathogenic bacteria of salmonella sp isolated from food borne.

Essential oil of *O. compactum* was tested against six Gram positive (*Staphylococcus aureus*, *Listeria monocytogenes* serovar 4b, *Listeria innocua* and *Enterococcus faecium*) and 4 Gram negative bacteria (*Escherichia coli* K12, *Escherichia coli* serovar O157:H7, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens* and *Bacillus subtilis*), and inhibited the growth of all tested bacteria MICs range from 0.0078 for *S. aureus* (MBLA) to over  $>1$  ml/ml for *P. aeruginosa* [4].

**Mode of antibacterial action:** Different modes of action are involved in the antimicrobial activity of essential oils and extracts. Because of the variability of quantity and chemical profiles of the essential oil and extract components, it is likely that their antimicrobial activity is not due to a single mechanism. It is considered that these

components have several sites of action at the cellular level. Generally, there are six possible mechanisms of antimicrobial action, which include:(1) disintegration of cytoplasmic membrane, (2) interaction with membrane proteins (ATPases and others), (3) disturbance of the outer membrane of gram negative bacteria with the release of lipopolysaccharides, (4) destabilization of the proton motive force with leakage of ions, (5) coagulation of the cell content, and (6) inhibition of enzymes synthesis.

The mechanism of antibacterial action seems to have a relationship with a great number of complex constituents in Eos and extracts instead of just specific bioactive metabolites, which may result in different action modes and difficult identification from molecular point of view [24,25].

Carvacrol (main compound of Origanol oil) has been demonstrated able to destabilize the cytoplasmic membrane and acts as a proton exchanger, thereby reducing the pH gradient across the cytoplasmic membrane. The resulting collapse of the proton motive force and depletion of the ATP pool eventually lead to cell death [26].

*O. compactum* essential oil showed a strong antibacterial activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. This activity may be associated with the presence of carvacrol and thymol, which is the major component of the oil. The mechanism of action is related with the capacity of *O. compactum* essential oil to induce leakage of intracellular  $K^+$  from cells, induce alterations of membrane potential and induce alterations in the bacterial membrane. These alterations led to the loss of membrane- selective permeability and thus the inhibition of respiratory activity, and also the loss of other essential enzymatic activities, all these changes led to cell death [27].

**Antibacterial action of carvacrol and thymol:** The compounds of phenolic structures, such as carvacrol and thymol presented as the main compounds (chemotypes) of OCEO, are highly active against several pathogenic bacteria. These compounds have been reported to be bacteriostatic or bactericidal agents, depending on the concentration used [28]. These compounds are highly active despite their relatively low capacity to dissolve in water [29-32]. In general, the EO having the most important antibacterial properties contain a high percentage of phenolic compounds such as carvacrol [34] and thymol [34-36].

Their mechanism of action is related to the capacity of these compounds in the disruption of the cell membrane, movement of protons, the flow of electrons, active transportation and the coagulation of the cell content [37,38].

Furthermore, carvacrol destabilizes the cytoplasmic membrane and also acts as a proton exchange, thereby reducing the pH gradient across the cytoplasmic membrane. The collapse of the force protons movement and resulting depletion of ATP pool lead to cell death [39].

The importance of the presence of the hydroxyl group in the phenolic compounds such as carvacrol and thymol was confirmed [40,41]. The relative position of the hydroxyl group on the phenol ring does not appear to strongly influence the level of antibacterial activity. Indeed, the action of thymol against *Bacillus cereus*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* appears to be comparable to that of carvacrol [36,41]. However, in a study on the effects of carvacrol and thymol, it was shown that they act differently against Gram-positive and Gram-negative species [40].

Carvacrol and thymol are able to disintegrate the outer membrane of Gram negative bacteria, releasing lipopolysaccharides (LPS) and inducing the increase in the permeability of the cytoplasmic membrane toward ATP [36].

On other hand, studies of *B. cereus* showed that carvacrol interacts with the cell membrane, which it dissolves in the phospholipid bilayer and fit between the fatty acid chains [41]. This distortion of the physical structure lead to the expansion and destabilization of the membrane, increased membrane fluidity which and consequently increase the passive permeability [41].

### Antifungal activity

The management of fungal infections possesses many problems, including a limited number of antifungal drugs, toxicity, and resistance to commonly used antifungal drugs, relapse of infections and the high costs. For that, it is very important and necessary to discover new antifungal agents to combat the strains expressing resistance to the available antifungal drugs. One of natural products used as therapeutic agent against fungi is Oregano, e.g., its essential oils and extracts. Considerable Oregano petroleum ether, hexane, chloroform and methanol extract activity were estimated by Fadel et al. against *penicillium digitatum* [42].

The petroleum ether extracts of *O. compactum* were highly active against the mycelial growth of *P. digitatum*, The effectiveness of petroleum ether extract might be due to its high levels of carvacrol, p-cymène, thymol and terpinene [14], the antifungal activity of carvacrol, the main compound of lamiaceae essential oil has been the subject of several studies [43].

The methanol 80% extracts of *O. compactum* aerial parts were also highly effective against *P. digitatum* mycelial growth. It was demonstrated that the mechanism of toxicity of total phenols against the fungi is based on the inactivation of the fungal enzymes which contain the SH group in their active sites classified the pure compounds according to their antifungal activity towards seven fungi, this activity decreases according to the type of chemical functions of compound: phenols>alcohols>aldehydes>acetones>ethers>eydrocarbures [14].

The antifungal activity of Oregano essential oil was tested against *Botrytis cinere*, and the inhibition was  $IC_{50}=35.1$  ppm). While the antifungal effect of carvacrol and thymol, the main compound of Oregano essential oil, was  $IC_{50}=18.6$  ppm and  $IC_{50}=18.9$  ppm against the same species respectively [14]. The Oregano antifungal effect may also be attributed to essential oil and phenolic compounds that are known to cause cell membranes damage, causing leakage of cellular materials and ultimately the microorganism death [44]. The antimicrobial, e.g., antifungal property of myrtle is suspected to be associated with their high contents of polyphenols and oxygenated monoterpenes.

### Antioxidant activity

Antioxidants are compounds that react with free radicals, neutralizing them and thereby preventing or reducing their damaging effects in the human body [45]. Lipid oxidation is also responsible of deterioration of fats and oils resulting in change of color, flavor and nutritive value, while oxidative stress is involved in the pathogenesis of numerous diseases [46]. In order to prevent oxidation, the addition of either synthetic or natural antioxidants to fats, fatty foods and cosmetics is a common practice. Because of its carcinogenicity, synthetic antioxidants used in products for human application are being restricted, considerably increasing interest in antioxidants of natural origin [47].

Aromatic and medicinal plants, such as myrtle, are source of natural antioxidants because of the activity of secondary metabolites, such as phenylpropanoids and essential oils. Essential oils and extracts

have been used for food preservation, pharmaceuticals, alternative medicine and natural therapies [24]. As demonstrated in several studies, the antioxidant activity of plant extracts is strongly related to phenolic content [48]. This activity is not a property of a single phenolic compound, but it is widely distributed among the phenolic phytochemical constituents. Particularly anthocyanins, flavonoids and phenolic acids seem to be responsible for the antioxidant capacity. Several methods are used to evaluate the antioxidant activity, and the obtained results depending on which method is used.

Several studies demonstrate the antioxidant activities of organic extracts and essential of *O. compactum*. In effect, Bouhdid et al. have evaluated the antioxidant activity of Oregano essential oils by three main methods: reducing power, DPPH free radical scavenging assay and b-Carotene-linoleic acid assay. The results of this study revealed evidence that the essential oil of *O. compactum* possesses a good antioxidant effect with three assays used. This antioxidant capacity was depending on the oil concentration and was attributed to the phenolic compounds present in the oil [4]. On other hand, Elbabili et al. have evaluated the antioxidant activity of Oregano essential oil, Ethyl acetate, Petroleum ether, Ethanol extract and decoction using ABTS (acid 2,2'-azino-bis(3-éthylbenz-thiazoline-6-sulfonique) radical-scavenging assay and DPPH (1,1-diphényl-2-picrylhydrazyl) free radical scavenging [13]. The results showed that the essential oil showed a higher antioxidant activity with an  $IC_{50}=2 \pm 0.1$  mg/L. Among the extracts, the aqueous extract had the highest antioxidant activity with an  $IC_{50}=4.8 \pm 0.2$  mg/L (DPPH assay). As demonstrated in several studies, the antioxidant capacity of plant extracts is strongly related to phenolic content [48].

The antioxidant activity of the phenolic compounds was attributed to its redox properties, which allow them to act as reducing agents, hydrogen donators, singlet oxygen quenchers and metal chelators [49]. Many *in vitro* studies indicate that phenolic compound like flavonoids and phenolic acid can have considerable antioxidant activity and this activity critically depends on the number and position of phenolic hydroxyls in the aromatic ring moieties [50].

Nowadays, the interest in naturally occurring antioxidants has considerably increased, because of their potential application in food, cosmetic and pharmaceutical products, in order to replace synthetic carcinogenous, and thus restricted antioxidants [46]. In addition, oligomeric proanthocyanidins, which are mainly used in vascular diseases, have an ability to trap lipid peroxides and free radicals, as well as non-competitively inhibit xanthine oxidase, which is a major generator of free radical [51].

### Cytotoxicity

Some studies have evaluated the cytotoxicity of Oregano extracts on human cell line. Elbabili et al. showed an activity against human breast cancer cells (MCF7) of the ethyl acetate extract ( $IC_{50}=30$  mg/L) and ethanol extract ( $IC_{50}=56$  mg/L). While, the petroleum ether extract and essential oil were inactive ( $IC_{50}= >100$  mg/L) [13]. Another study carried out by Chaouki et al. have shown that ethyl acetate extract of *O. compactum* had a cytotoxic effect on human breast tumor MCF-7 cells. In additionally, the same extract had a cytotoxic effect on human A549 lung cancer and SMMC-7721 hepatoma cell lines by a ( $IC_{50}=198 \pm 12$  µg/ml) and ( $IC_{50}=266 \pm 14$  µg/ml) [52].

### Anticancer activity

Some studies recently conducted have demonstrated the antitumor activity of *O. compactum* against human cancer cell lines [52,53]. The

characterization of the mechanisms involved in this effect demonstrated that this extract was an apoptosis inducer in both cell lines tested. This apoptosis induction in A549 cells was directed by activation caspase signaling triggered via modulation of Bcl-2 family proteins [53].

The main compounds of *O. compactum* essential oil were studied for their anticancer investigation. Thymol was found to be associated with cell death of many types of cell line of melanoma [54,55], osteosarcoma [56], glioblastoma [57], breast cancer [13], leukemia [58], hepatoma, lung cancer and colon cancer [59].

This action was almost related with DNA strand breaks and cell cycle block in G0/G1 phase [58]. Carvacrol is an isomer of thymol and it is widely found in *O. compactum* essential oil. It shows also a similar activity than thymol against several cancers including liver, colon, and lung [59].

### Anti-mutagenic activity

Carvacrol, the major component of oregano essential oil showed antimutagenic activity [60], which seems to be mainly linked to the induction of mitochondrial dysfunction [61].

### Insecticidal activity

More recently, the essential oil of Oregano showed strong insecticidal activity against larvae of *Spodoptera littoralis* with an LD<sub>50</sub> ≤ 0.05 ml/larva [62].

### Conclusion

*O. compactum* is used for various medicinal properties. The extract of the different parts of the plant shows various activities like antioxidant, antimicrobial, anticancer, insecticidal and anti-mutagenic activity. This review further highlights the discovered pharmacological effects and phytochemical details of *O. compactum* which provide way to further studies and research.

The authors declare that there is no conflict of interests regarding the publication of this article.

### Acknowledgements

The authors thank the: Centre National pour la Recherche Scientifique et Technique (CNRS) from Morocco for support the doctoral grant of one of the authors.

### References

- Vokou D, Kokkini S, Bessiere JM (1993) Geographic variation of Greek oregano (*Origanum vulgare* ssp. *hirtum*) essential oils. Biochem. System. Ecol. 21: 287-295.
- Benabid A (2000) Flore et écosystème du Maroc : évaluation et préservation de la biodiversité. Ibis Press, Paris, p: 357.
- Atbib M (1985) Contribution à l'étude morphologique des origans (*Origanum L.*) du Maroc et leur utilisation médicinale. Al biruniya. Rev Mar Pharm, Rabat T1 2: 107-120.
- Bouhdid S, Skali SN, Idaomar M, Zhiri A, Baudoux, et al. (2008) Antibacterial and antioxidant activities of *Origanum compactum* essential oil. Afr. J. Biotech. 7: 1563-1570.
- Belkamel A, Bammi J, Belkamel A, Douira A (2013) Study of essential oil chemical composition of an endemic Ibero-moroccan: *Origanum compactum* (Benth.). Journal of Animal Plant Science. 19: 2880-2887.
- Jahandiez E, Maire R (1934) Catalogue des plantes du Maroc - Spermaphytes et ptéridophytes. 3: 630-632.
- Tutin TG, Heywood VH, Burges NA, Moore DM, Valantine DH, et al. (1972) Flora Europaea. University Press, Cambridge. 3: 171-172.
- Bellakhdar J (1997) La pharmacopée Marocaine traditionnelle. Médecine arabe ancienne et Savoirs populaires. Ibis Press, Paris.
- Ennabili A, Ater M, Radoux M (2000) Biomasse et accumulation des NPK chez *Scirpus litoralis* et *Scirpus maritimus* aux marais Smir-Negro (NW du Maroc) Acta Bot. Barcin. 46 : 239-250.
- Djilani A, Dicko A (2012) The therapeutic benefits of essential oils. In: Bouayed J (ed). Nutrition, well-being and health. Intech, p: 178.
- Ormaney X, Sisalli S, Coutiere P (2001) Formulation of essential oils in functional perfumery. Parfums Cosmetiques Actualites 157: 30-40.
- Morone-Fortunato I, Montemurro C, Ruta C, Perrini R, Sabetta W, et al. (2010) Essential oils, genetic relationships and in vitro establishment of *Helichrysum italicum* (Roth) G. Don ssp. *italicum* from wild Mediterranean germplasm. Industrial Crops and Products. 32: 639-649.
- El Babili F, Bouajila J, Souchard JP, Bertrand C, Bellvert F, et al. (2011) Oregano: chemical analysis and evaluation of its antimalarial, antioxidant, and cytotoxic activities. J Food Sci 76: C512-518.
- Chebli B, Achouri M, Idrissi-Hassani LM, Hmamouchi M (2003). Chemical composition and antifungal activity of essential oils of seven Moroccan Labiatae against *Botrytis cinerea* Pers: Fr. J. Ethnopharmacol, 89: 165-169.
- Marin PD, Grayer RJ, Kite GC, Veljic M (2005) External flavones from *Thymus striatus* Vahl (Lamiaceae) Biochem. Syst. Ecol. 33: 1179-1182.
- Van Den Broucke CO, Lemli JA (1980) Chemical investigation of essential oil of *Origanum compactum*. Planta Med. 41: 264-266.
- Bouillot X (2007) Essential oil analysis report-Helvetica. PHARMA SA Switzerland, June.
- Oussalah M, Caillet S, Saucier L, Lacroix M (2007) Inhibitory effects of selected plant essential oils on the growth of four pathogenic bacteria: *E. coli* O157:H7, *Salmonella typhimurium*, *Staphylococcus aureus* and *Listeria monocytogenes*. Food Contr. 18: 414-420.
- Bellakhdar J, Passannanti S, Paternostro MP, Piozzi F (1988) Constituents of *Origanum compactum*. Planta Med 54: 94.
- Bellakhdar J, Idrissi A (1991) Composition chimique des huiles essentielles de 3 origans du Maroc : *Origanum compactum*, *O. grosii*, et *O. elongatum*. Actes du colloque européen d'ethnopharmacologie, Metz (France), 22-25 mars 1990. Édité par L'ORSTOM (France), pp: 440-445.
- Herouart J (1987) Utilisation de la chromatographie en phase gazeuse pour différencier quelques huiles essentielles de lamiacées, couramment prescrites en aromathérapie : Thym- Origan – Serpolet – Marjolaine. Thèse de Pharmacie, Dijon, p: 127.
- Amakran A, Hamoudane M, Ramdan B, Ben mehdi N, Ben mrid Reda, et al. (2014) Etude des propriétés antioxydants, antiglyquantes et photochimiques de l'huile essentielle d'*Origanum compactum* de Tétouan. Science Lib Editions Mersenne 6: 2111-4706.
- Gortzi O, Lala S, Chinou I, Tsaknis J (2007) Evaluation of the antimicrobial and antioxidant activities of *Origanum dictamnus* extracts before and after encapsulation in liposomes. Molecules 12: 932-945.
- Burt S (2004) Essential oils: their antibacterial properties and potential applications in foods-A review. Int J Food Microbiol 94: 223-253.
- Carson CF, Mee BJ, Riley TV (2002) Mechanism of action of *Melaleuca alternifolia* (tea tree) oil on *Staphylococcus aureus* determined by time-kill, lysis, leakage, and salt tolerance assays and electron microscopy. Antimicrob Agents Chemother 46: 1914-1920.
- Ultee A, Bennik MH, Moezelaar R (2002) The phenolic hydroxyl group of carvacrol is essential for action against the food-borne pathogen *Bacillus cereus*. Appl Environ Microbiol 68: 1561-1568.
- Bouhdid S, Abrini J, Zhiri A, Espunsky MJ, Manresa A (2009) Investigation of functional and morphological changes in *Pseudomonas aeruginosa* and *Staphylococcus aureus* cells induced by *O. compactum* essential oil. J. Appl. Microbiol. 106: 1558-1568.
- Pelczar MJ, Chan ECS, Krieg NR (1988) Control of microorganisms, the control of microorganisms by physical agents. In: Microbiology. New York: McGraw-Hill International, pp: 469-509.
- Hili P, Evans CS, Veness RG (1997) Antimicrobial action of essential oils: the effect of dimethylsulphoxide on the activity of cinnamon oil. Lett Appl Microbiol 24: 269-275.

30. Lis-Balchin M, Deans SG (1997) Bioactivity of selected plant essential oils against *Listeria monocytogenes*. J Appl Microbiol 82: 759-762.
31. Sivropoulou A, Papanikolaou E, Nikolaou C et al. (1996) Antimicrobial and cytotoxic activities of *Origanum* essential oils. Journal of Agriculture and Food Chemistry 44: 1202-5.
32. Suresh P, Ingle VK, Vijayalakshma V (1992) Antibacterial activity of eugenol in comparison with other antibiotics. Journal of Food Science and Technology 29: 254-6.
33. Periago PM, Conesa R, Delgado B et al. (2006) *Bacillus megaterium* spore germination and growth inhibition by a treatment combining heat with natural antimicrobials. Food Technology and Biotechnology 44: 17-23.
34. Cosentino S, Tuberose CI, Pisano B, Satta M, Mascia V, et al. (1999) In-vitro antimicrobial activity and chemical composition of Sardinian *Thymus* essential oils. Lett Appl Microbiol 29: 130-135.
35. Juliano C, Mattana A, Usai M (2000) Composition and *in vitro* antimicrobial activity of the essential oil of *Thymus herba-barona* Loisel growing wild in Sardinia. Journal of Essential Oil Research 12: 516-22.
36. Lambert RJ, Skandamis PN, Coote PJ, Nychas GJ (2001) A study of the minimum inhibitory concentration and mode of action of oregano essential oil, thymol and carvacrol. J Appl Microbiol 91: 453-462.
37. Davidson PM (1997) Chemical preservatives and natural antimicrobial compounds. In: Doyle MP, Beuchat LR, Montville. (Eds.), Food Microbiology: Fundamentals and Frontiers. ASM, Washington, pp: 520-556.
38. Sikkema J, de Bont JA, Poolman B (1995) Mechanisms of membrane toxicity of hydrocarbons. Microbiol Rev 59: 201-222.
39. Ultee A, Kets EP, Smid EJ (1999) Mechanisms of action of carvacrol on the food-borne pathogen *Bacillus cereus*. Appl Environ Microbiol 65: 4606-4610.
40. Dorman HJ, Deans SG (2000) Antimicrobial agents from plants: antibacterial activity of plant volatile oils. J Appl Microbiol 88: 308-316.
41. Ultee A, Bennik MH, Moezelaar R (2002) The phenolic hydroxyl group of carvacrol is essential for action against the food-borne pathogen *Bacillus cereus*. Appl Environ Microbiol 68: 1561-1568.
42. Fadel F, Ben Hmamou D, Salghi R, Chebli B, Benali O, et al. (2013) Antifungal Activity and Anti-Corrosion Inhibition of *Origanum Compactum* Extracts. Int. J. Electrochem. Sci. 8: 11019 – 11032.
43. Daferera DJ, Ziogas BN, Polissiou MG (2000) GC-MS analysis of essential oils from some Greek aromatic plants and their fungitoxicity on *Penicillium digitatum*. J Agric Food Chem 48: 2576-2581.
44. Cox SD, Mann CM, Markham JL, Bell HC, Gustafson JE, et al. (2000) The mode of antimicrobial action of the essential oil of *Melaleuca alternifolia* (tea tree oil) J Appl Microbiol 88: 170-175.
45. Pereira LR, Helena SR, Cabette and Juen L (2012) *Trichoptera* as bioindicators of habitat integrity in the Pindai'ba river basin, Mato Grosso (Central Brazil) Ann. Limnol. Int. j. lim. 48: 295-302.
46. Young IS, Woodside JV (2001) Antioxidants in health and disease. J Clin Pathol 54: 176-186.
47. Djeridane A, Yousfi M, Nadjemi B, Boutassouna D, Stocher P, et al. (2006) Antioxidant activity of some Algerian medicinal plants extracts containing phenolic compounds. Food Chemistry. 97: 654–660.
48. Zheng W, Wang SY (2003) Oxygen radical absorbing capacity of phenolics in blueberries, cranberries, chokeberries, and lingonberries. J Agric Food Chem 51: 502-509.
49. Rice-Evans CA, Miller NJ, Bolwell PG, Bramley PM, Pridham JB (1995) The relative antioxidant activities of plant-derived polyphenolic flavonoids. Free Radic Res 22: 375-383.
50. Duthie G, Crozier A (2000) Plant-derived phenolic antioxidants. Curr Opin Lipidol 11: 43-47.
51. Okuda T (2005) Systematics and health effects of chemically distinct tannins in medicinal plants. Phytochemistry 66: 2012-2031.
52. Chaouki W, Leger DY, Eljastimi J, Beneytout JL, Hmamouchi M (2010) Antiproliferative effect of extracts from *Aristolochia baetica* and *Origanum compactum* on human breast cancer cell line MCF-7. Pharm Biol 48: 269-274.
53. Chaouki W, Meddah B, Hmamouchi M (2015) Antiproliferative activity of *Origanum compactum* extract on lung cancer and hepatoma cells. Arabian Journal of Medicinal and Aromatic Plants. 1: 1.
54. He L, Mo H, Hadisusilo S, Qureshi AA, Elson CE (1997) Isoprenoids suppress the growth of murine B16 melanomas in vitro and in vivo. J Nutr 127: 668-674.
55. Satooka H, Kubo I (2012) Effects of thymol on B16-F10 melanoma cells. J Agric Food Chem 60: 2746-2752.
56. Chang HT, Hsu SS, Chou CT, Cheng JS, Wang JL, et al. (2011) Effect of thymol on Ca<sup>2+</sup> homeostasis and viability in MG63 human osteosarcoma cells. Pharmacology 88: 201-212.
57. Hsu SS, Lin KL, Chou CT, Chiang AJ, Liang WZ, et al. (2011) Effect of thymol on Ca<sup>2+</sup> homeostasis and viability in human glioblastoma cells. Eur J Pharmacol 670: 85-91.
58. Deb DD Parimala G, Saravana Devi S, Chakraborty T (2011) Effect of thymol on peripheral blood mononuclear cell PBMC and acute promyelotic cancer cell line HL-60. Chem Biol Interact 193: 97-106.
59. Slaménová D, Horváthová E, Sramková M, Marsálková L (2007) DNA-protective effects of two components of essential plant oils carvacrol and thymol on mammalian cells cultured in vitro. Neoplasma 54: 108-112.
60. Mezzoug N, Elhadri A, Dallouh A, Amkiss S, Skali NS, et al. (2007) Investigation of the mutagenic and antimutagenic effects of *Origanum compactum* essential oil and some of its constituents. Mutat Res 629: 100-110.
61. Bakkali F, Averbeck S, Averbeck D, Zhiri A, Baudoux D, et al. (2006) Antigenotoxic effects of three essential oils in diploid yeast (*Saccharomyces cerevisiae*) after treatments with UVC radiation, 8-MOP plus UVA and MMS. Mutat Res 606: 27-38.
62. Pavela R (2005) Insecticidal activity of some essential oils against larvae of *Spodoptera littoralis*. Fitoterapia 76: 691-696.