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# Areas of Utilization of *Origanum acutidens* (Hand.-Mazz.) Ietswaart and Carvacrol

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## Abstract

*Origanum acutidens* (Hand.-Mazz.) Ietswaart is an endemic plant growing in the eastern part of Turkey. *Origanum acutidens*, rich in rosmarinic acid, has a high antioxidant effect. The essential oil of this plant is rich in carvacrol. The plant has chemotypes containing up to 90% carvacrol. Carvacrol also has a comprehensive range of uses from health to food. According to results obtained from previous studies, carvacrol has a lethal effect against some cancer cells. Furthermore, carvacrol has antifungal and antibacterial effects and it is lethal for some agriculturally harmful insect species. In this study, we have compiled the details of various research findings related to the morphology, natural distribution and synonymous of *Origanum acutidens*, its karyological and histological features, its content and yield of essential oil and its pharmacological property and the effects of carvacrol based on an exhaustive literature review. Such knowledge could contribute to the design of new and more effective technologies for the increased use and in the number of plant-based drugs for plant and human health. Using alternative and integrative strategies such as phytochemicals against harmful insect families, bacteria and fungi in agricultural areas and storage conditions are among current necessities. In addition, this review may contribute to provide a new and additional perspective on cancer treatment by combining the finding that the carvacrol in the essential oil of *Origanum acutidens*is effective against cancer cells**.**

## Article Info

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## Keywords

Essential oil, endemic plant, anti-cancer, antibacterial, antifungal.

## Introduction

The word *Origanum* comes from the words that mean mountain ornament in Greek (oros= mountain, ganos = ornament). The genus *Origanum* belongs to the Lamiaceae family and is commonly known as oregano and marjoram. Origanum genus includes about 900 species in the world (Davis 1982; Baser 2002).Turkey is considered the gene centre of this genus because 22 species and four subspecies are represented. They are grouped into eight sections and 14 species are endemic to Turkey. One such endemic species is *Origanum acutidens* (Hand.-Mazz.) Ietswaart. *Origanum acutidens* (Hand.-Mazz.) Ietswaart is an endemic plant growing in the eastern part of Turkey (Bakis *et al.*, 2011) and it is rich in carvacrol (Baser *et al.*, 1997; Figueredo *et al.*, 2006; Kordali *et al.*, 2008).

*Origanum* species have a great economic importance (Kokkini, 1996; Kizil *et al.*, 2009). Turkey played a key role in oregano trade with about 15,000 tonnes of product worth $60 million exported in 2014 (Sari and Altunkaya 2015). *Origanum* species have been used for tens of thousands of years (Tepe *et al.*, 2016). Some endemic *Origanum* species including *O. acutidens* are used as herbal teas in the regions where they grow

(Tumen *et al.,* 1995). In addition, Origanum species are widely used as culinary herbs, in alcoholic beverages and to flavor food products (Aligiannis *et al.,* 2001; Bendahou *et al.,* 2009; Cetin *et al.,* 2011).

This genus is rich in bitter substances and essential oils (Baytop, 1999, Esen *et al.,* 2007; Kordali *et al.,* 2008). It was stated that *p*-cymene (7.5–14.0%) and carvacrol (66.0–72.0%) were the primary components of the essential oils of *O. acutidens* (Baser *et al.,* 1997, Sokmen *et al.,* 2004, Figueredo *et al.,* 2006). Kordali *et al.,* (2008) reported that *O. acutidens* essential oil and its aromatic monoterpene components showed potent antifungal activity against plant pathogens, fungi and phytotoxic effects against *A. retroflexus*, *R. crispus*. and *C. albüm.*

Natural plants are used in the pharmaceutical industry for developing new drugs (Tohma *et al.,* 2017). Actually, the main sources of natural antioxidants are fruits, vegetables and green plants. Consumption of natural antioxidants can reduce the risk of cancer, cataracts, cardiovascular diseases, brain dysfunction (Aras, 2016). *Origanum* species are also traditionally used as diuretics, sedatives, antiflatulants, antiseptics and diaphoretics and also in the treatment of gastrointestinal diseases and constipation (Baytop, 1999).

In parallel with the developments in the chemical sector, the manufacturing of chemical drugs has become easier, therefore interest in plant-derived components has decreased. However, the adverse effects caused by chemical drugs have recently attracted interest in plant components again (Avcı and Bayram, 2013). Nowadays, scientists are interested in plant-based drug materials because the adverse effects seen in chemical drugs are less common in plant-based drugs and disease strains are more resistant to chemical-based antibiotics (Dülger *et al.,* 1999). This review is based on a detailed exhaustive literature survey of various research findings related to the morphology, natural distribution and synonymous with *Origanum acutidens*, its karyological and histological features, content and yield of essential oil of *Origanum acutidens* and its pharmacological property and the effects of carvacrol.

## Herbal properties and description

*O. acutidens* (Hand.-Mazz.) Ietswaart grows as endemic in Turkey's East Anatolia Region and it has very beautiful flowers with white to pale yellow or pink corollas that flower between June and August (Ietswaart and Ietswaart, 1980; Davis, 1982). It is a perennial herbaceous plant. *O. acutidens* grows on limestone and on non-calcareous soils, between 1000 - 3000 m, sometimes in shady places. *O. acutidens* needs very little moisture during the growing season. The pleasant fragrance of the leaves has long been a source of fascination. The intensely fragrant leaves of *O. acutidens* can be used in the landscaping of cities and in rock gardens as an alternative ornamental plant (Tubives, 2013).The plant height of *O. acutidens* may be up to 50 cm, it is lintless with a half-bushy form; the leaves are almost stalkless, ovata is obtuse and dull blue green in dimensions 5-30 x 4-24 mm. The small flower status resembling a crown is 10-35 x 10-30 mm. Bracts are almost orbicular, obovate or elliptical and 7-22 x 6-20 mm in dimensions, the hill is acute or obtustur, it is yellowish green and rarely slightly purplish red. Vertisillastrum has 2-12 flowers. Calix 5-7.5 mm in size and corolla is 10-16 mm long light white or pink in color (Figure 1). The upper filaments are 2 mm thick and the bottom filaments are 10 mm thick. *O. acutidens* is also akin to *O. rotundifolium*, from which it differs in its ovate leaves and its slightly scabrous stems (Ietswaart and Ietswaart, 1980). The average of fresh herb yields (220.4 gr), drug herbal yield (63.12 gr), drug leaf yield (41.31 gr), leaf/leaf + scape ratio (%54.47), number of side branches (8), plant crown width (43.11 cm), plant height (37.06 cm) and chlorophyll content (49.54 SPAD) were determined in the study investigating the vegetative and yield properties of *O. acutidens* collected from 5 different provinces and 70 different locations in Turkey (Karagoz, 2018).

## Natural distribution and synonymous

*Amaracus haussknechtii* (Boiss.) Briq. var. acutidensHand.-Mazz is synonymous with *Origanum acutidens* (Davis, 1982). This plant is grown in Gümüşhane (Torul), Erzurum (Ispir, Aşkale and Çat), Artvin (Yusufeli), Sivas (Zara), Tunceli, Malatya, Bitlis Erzincan (Tercan, İliç, Kemah and Otlukbeli), Hakkari and Bingol provinces in Turkey (Sezen, 2006; Karagöz, 2018). The region with the highest plant density and diversity in Turkey is the Ispir district of Erzurum province and Coruh basin (Çakmakçı *et al.,* 2008; Karagoz, 2018; Figure 2).

## Karyological and histological features

The basic chromosome number of *Origanum acutidens* species is x= 15, and diploid chromosome numbers were found as 2n=30. Chromosomes have median region (m)

and submedian (sm) centromers (Gedik *et al.,* 2014; Figure 3). The total chromosome length of *Origanum acutidens* ranges from 1.13-1.91 µm and arm rates vary from 1.26-2.37 µm. The karyotype formula of *Origanum acutidens* is 5m+10sm. While the centromeric index varies between 29.65-44.07 µm, the relative lengths of chromosomes vary between 5.06-8.50 µm. The total haploid chromosome length of the species is 22.48 µm. The intrachromosomal asymmetry index is 0.45 and the interchromosomal asymmetry index is 0.13 (Gedik *et al.,* 2014).

## Content and yield of essential oil

Essential oils are mixtures that are obtained from plants or plant drugs, which are strongly odorous and are liquid at room temperature and can be dragged by water vapor. They are called "etheric oils" since they vaporize like ether (Şarer *et al.,* 1985). The percentages of essential oils obtained from the *Origanum acutidens* range from 0.73 to 1.7% (Cosge *et al.,* 2009; Çakmakçı *et al.,* 2009a). Essential oil of *O. acutidens* contains 35 different components (Figueredo *et al.,* 2012; Çakmakçı *et al.,* 2009b). Essential oil of *Origanum acutidens* contains high amounts of carvacrol. Carvacrol rates in some studies with *Origanum acutidens* are as follows: Kordali *et al.,* (2008) determined 87.00% carvacrol; Tozlu *et al.,* (2011) 86.99% carvacrol; Figueredo *et al.,* (2012) 76.20% carvacrol; Cosge *et al.,* (2009) 67.51% carvacrol; Baser *et al.,* (1997) 66.25% carvacrol and Goze *et al.,* (2010) determined 65.00% carvacrol. The main component of this oil is carvacrol followed by p-cymene. Other important oil components are borneol, thymol, beta-caryophyllene, gamma-terpinene, linalool, eugenal, camphor, linalyl acetate, beta-myrcene, alpha-pinene, camphene, 3-octanone and alpha-terpinene (Çakmakçı *et al.,* 2008). In addition, there is more than 20% thymol in the *Origanum acutidens* chemotypesin the eastern Anatolia region (Karagoz, 2018). These chemotypes have a more pleasant odour due to the blending of thymol and carvacrol. In addition, these chemotypes are thought to be more effective in the fight against bacteria and fungi (Kordali *et al.,* 2008).

## Antimicrobial and insecticidal effect

Bacteria and fungi have adverse effects on the safety, quality and protection of food. Adults and larvae of some insect species are one of the main causes of crop losses (Isman, 2000). These types of insects can be controlled with biological, chemical, physical methods or a combination of these methods (Thomas, 2001). Synthetic chemicals are broadly used in fighting plant diseases. These chemicals can cause toxic residues in treated products (Barnard *et al.,* 1997; Isman, 2000). Synthetic pesticides which have slow biodegradation can cause environmental pollution (Barnard *et al.,* 1997; Misra and Pavlostathis, 1997) Excessive use of synthetic herbicides can cause soil and groundwater contamination (Duke *et al.,* 2000). Using natural herbal drugs is very important due to these damages of chemical drugs in agriculture. Studies on *O. acutidens* essential oil showed that this plant can be used against harmful insect families, bacteria and fungi through their phytochemicals in agricultural areas and storage conditions (Caglar *et al.,* 2007; Kordali *et al.,* 2008; Kürşat *et al.,* 2009; Dadas oglu *et al.,* 2011; Tozlu *et al.,* 2011; Kordali *et al.,* 2013; Gulec *et al.,* 2014; Kesdek *et al.,* 2015).

## Antioxidant activity

Artificial antioxidants have negative effects on health, especially when they are over-consumed (Lennerz *et al.,* 2015). Rosmarinic acid, which is an important antioxidant, is found in the essential oil of *O. acutidens*. Antioxidants obtained from natural species are preferred by consumers since they are healthier, safer and more convenient food (Shim *et al.,* 2011). Rosmarinic acid the main components of which are rosemary extracts is responsible for a number of functions and associated health benefits. DPPH, CUPRAC and FRAP methods were used in a study carried out to determine the antioxidant level of *Origanum acutidens* leaves. As a result, high concentrations of quinic acid (3200.84 ppb), rosmarinic acid (11158.99 ppb) and naringenin (1238.45 ppb) were determined quantitatively (Aras *et al.,* 2017).

## Utilization of the *Origanum acutidens Origanum acutidens* (HAND.-MAZZ.) Ietswaartas an ornamental plant

Most Origanum species grow exclusively on calcareous soils, stony slopes and in rocky places, some are even strictly limited to cliffs. Most Origanum species are best grown in well drained, limy soil, in a sunny location preferably in a rock garden or under alpine housing conditions (Ietswaart and Ietswaart, 1980). *Origanum acutidens* is a promising ornamental plant that can be widely used in urban landscape management (Bağdat 2006; Yildirim, 2013). It is suitable for use as a border plant in rock gardens (Yildirim, 2013). *Origanum acutidens* has arching, showy, bright pink flowers and stems with large chartreuse bracts. Due to its aromatic fragrance and capacity for attracting butterflies and bees,

it can be preferred in theme gardens. Its intense and aromatic odour makes it suitable for areas designed for disabled people and in improvement gardens. Aesthetic effects can be created when it is used with colorful plants such as red, yellow, orange etc. The plant can also be used as additional material in cut flower bouquets or as cutting greens. The aerial parts of plants prepared as cut flowers can be dried and used for decorative purposes indoors.

## Effects of carvacrol and carvacrol

Carvacrol, a phenolic compound, is a thymol isomer. Carvacrol is essential and alkaline. While carvacrol is slowly soluble in water, it is more soluble in alcohol and ether. As a powerful antiseptic, carvacrol is used in medicine and included in the composition of oral preparations. Artificial carvacrol is produced from d-limonene synthesized carvone or p-simendene (Boydağ, 1996). The chemical formula of carvacrol is $C_{10}H_{14}O$. The molecular weight of carvacrol is 150.221 g $mol^{-1}$. Carvacrol is especially abundant in the Labiatae family. *Origanum*oil (80%) is a rich source of carvacrol (PubChem 2019; Figure 4a, b).

Recent studies have shown that carvacrol is very effective against cancer cells and carvacrol is a completely organic matter (Arunasree, 2010; Babili *et al.,* 2011; Potočnjak*et al.,* 2018). The carvacrol component was found to be effective against prostate cancer cells (Khan *et al.,* 2018). Antitumor effects have been observed for carvacrol (Andersen 2006). Studies indicate that lung cancer cells, oral cancer cells and brain tumors were blocked with the use of carvacrol (Junk *et al.,* 2018; Liang *et al.,* 2012; Liang and Lu, 2012; Ozkan and Erdogan, 2012). In a study on grape tomatoes, the antimicrobial effects of carvacrol and chlorine against salmonella were compared. As a result, the use of carvacrol reduced the level of salmonella on the tomato. According to the researchers, carvacrol did not affect the nutritional value, antioxidant content, look and taste of the tomatoes either (Lu and Wu, 2010). Studies have shown that carvacrol is effective against *Salmonella* and *Escherichia coli*, *Campylobacter jejuni* and *Listeria monocytogenes* (Obaidat and Frank, 2009; Van *et al.,* 2012; Upadhyay *et al.,* 2012). Salmonella colonies on celery were destroyed by carvacrol (Ravishankar *et al.,* 2010). *Candida albicans* taken from patients using dentures were tested against carvacrol. The test proved that carvacrol was very effective against *Candida albicans*. As a result of this study, it was concluded that carvacrol in oregano oil may be a natural treatment for *Candida albicans* (Marcos-Arias *et al.,* 2011). The oxidation of LDL cholesterol is dangerous for health because of its accumulation along the artery walls. One of several plant oils is the essential oil of oregano which has protective effects for LDL against copper-induced oxidation. This effect is associated with carvacrol (Kulišić *et al.,* 2007).

The Ministry of Health of Soviet Russia approves a plant-based drug system that includes carvacrol and other plant components as therapeutic support for blood sugar abnormalities. Although carvacrol used in this application does not come from oregano, it has been reported that the drug trials reduced blood sugar without adverse effects (Kemertelidzeetal., 2012). Redness and swelling are present in almost all forms of injury or irritation. In tests, carvacrol suppresses COX-2 expression generated by redness. Therefore, clinical evidence suggests that carvacrol can reduce redness and swelling. While many plant-based essential oils have this potential, the study has shown that carvacrol offered the highest efficacy (Hotta, 2010). Except for personal hygiene, carvacrol can also be used as a cleaning agent. In one of the studies, its activity was examined as a surface cleaning agent. Desai (2012) reported that concentrates of Oregano oil removed Listeria biofilms from plastic and stainless steel surfaces. This result shows that carvacrol can be used as a cleaning agent even in nonorganic environments (Desai, 2012).

The number of cancer cases has increased considerably due to changes in nutritional habits, use of alcohol and tobacco, chronic infections, exposure to harmful chemicals and radiation, changes in lifestyle and environmental pollution (Gautam *et al.,* 2014) Unfortunately, there is no drug that is absolutely effective in treating cancer. New highly effective drugs with low toxicity and minor environmental impact are needed. There are opportunities for innovation in drug discovery with natural products (Cai *et al.,* 2004). Carvacrol can provide a new perspective on cancer treatment. *Origanum acutidens* was shown to have antitumor activity against breast cancer cell lines in a study that investigated the antiprolipherative properties of *Origanum acutidens* on breast cancer (Tuncer *et al.,* 2013). In a study carried out to investigate the effects of the cytotoxic and radical scavenging of the *Origanum acutidens* essential oil it was manifested that the essential oil had an inhibitory effect on two human cancer cell lines, namely HT-29 and HeLa. According to these results and other reported studies, this observed high effect may be attributed to the presence of the carvacrol

component in the essential oil(Altuntaşand Demirtas, 2017). As a result, studies show that carvacrol obtained from *Origanum acutidens* and other origanum species has a lethal effect on cancer cells. New researches on carvacrol and *Origanum acutidens* can provide new hopes for cancer patients.

**Figure.1** Leaves and calyces (a and b); flower with bracts in a cross section of the *O. Acutidens* (Ietswaart and Ietswaart, 1980)

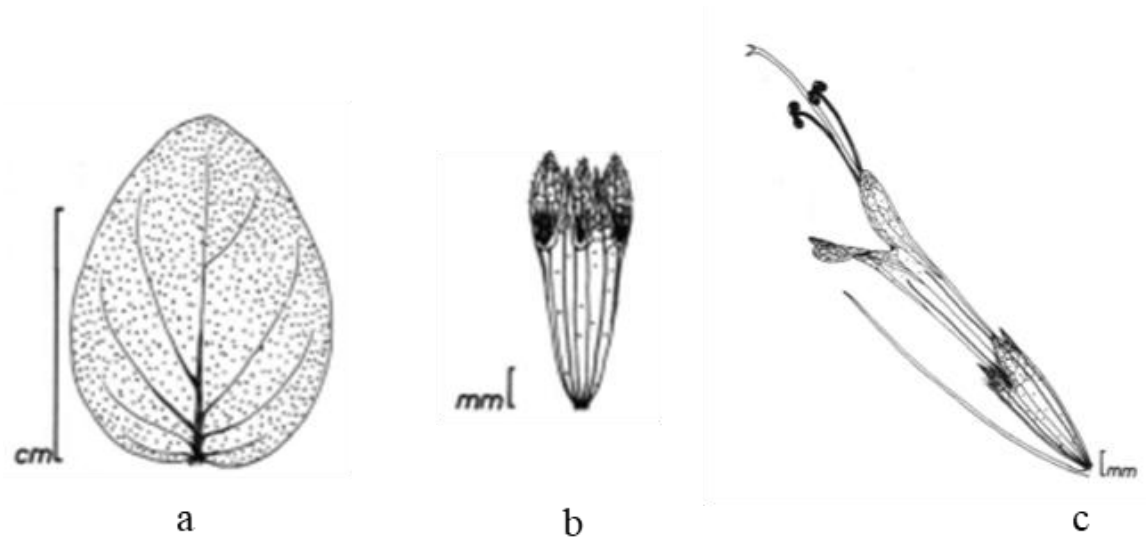



**Figure.2** Intensity of *Origanumacutidens* in Ispir (a) and general view of *Origanumacutidens* (b) (Karagoz, 2018)

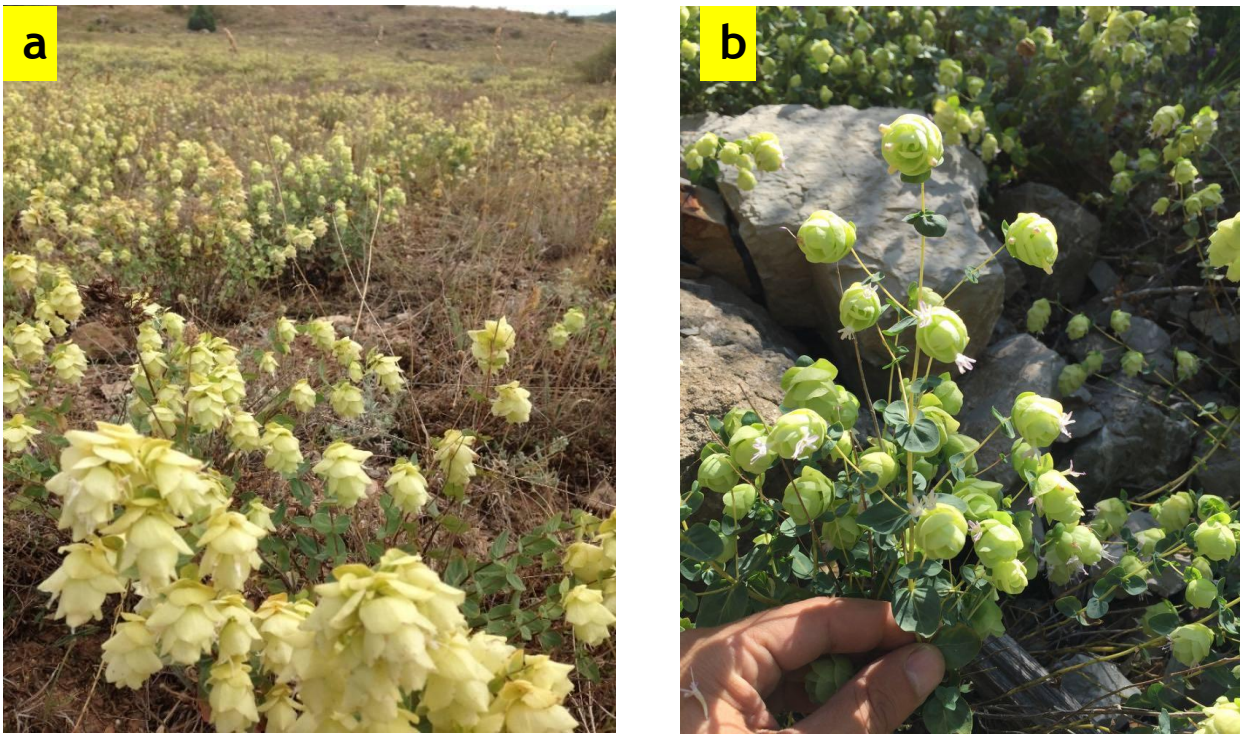


**Figure.3** Metaphase chromosomes Scala bar 10 µm (Gedik *et al.*, 2014)

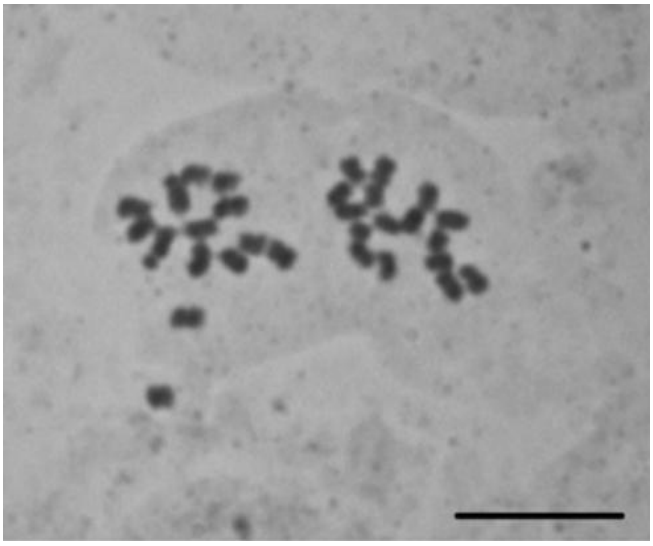
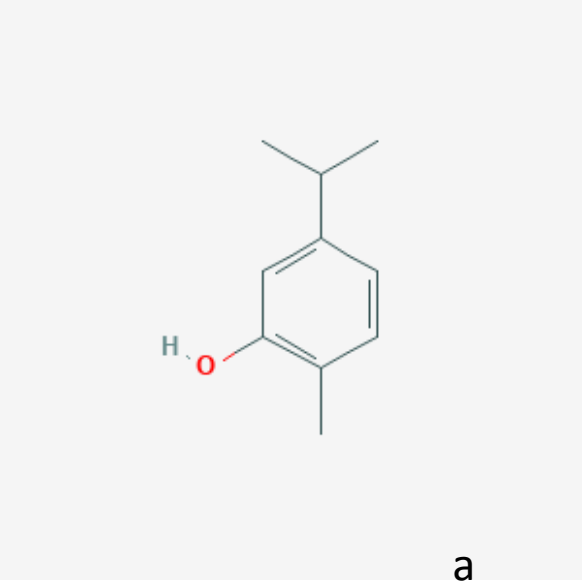
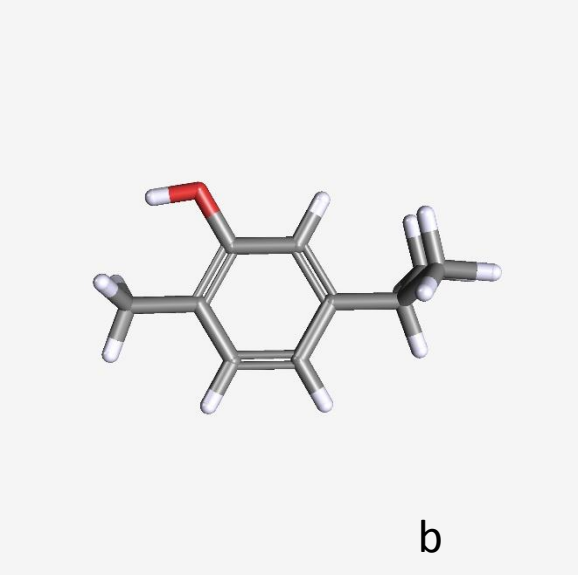


**Figure.4** 2D structure of carvacrol (a); 3D conformer of carvacrol (b) (PubChem CID: 10364)




## Conclusion

In this study, based on exhaustive literature review, we have compiled the various detailed research findings related to the morphology, natural distribution and synonymous with *Origanum acutidens*, its karyological and histological features, content and yield of essential oil and the pharmacological property and effects of carvacrol. Unfortunately, the habitat of *Origanum acutidens* grown as endemic in Turkey has been gradually decreasing due to human pressure such as new road and dam construction. The future of *Origanum acutidens* which is quite rich in terms of carvacrol needs to be secured. Further research will be conducted to evaluate the experimental effect of essential oil of *Origanum acutidens* identified from this review on the antimicrobial and insecticidal effects, antioxidant activity and effectiveness against cancer cells, redness and swelling.

**Competing Interests:** Authors have declared that no competing interests exist.

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