Mousavi, SS, Karami, A, Ahghighi, TM, Taban, A, Nahar, L and Sarker, S

Phytochemistry of Oliveria decumbens Vent. (Apiaceae) and its therapeutic potential: A systematic review

Phytochemistry of *Oliveria decumbens* Vent. (Apiaceae) and its therapeutic potential: A systematic review

Seyyed Sasan Mousavi[1], Akbar Karami[1]*, Tahereh Movahhed Haghighi[1], Azin Taban[1], Lutfun Nahar[2*] and Satyajit D Sarker[3]

[1]Department of Horticultural Science, Faculty of Agriculture, Shiraz University, Shiraz 71441-65186, Iran

[2]Laboratory of Growth Regulators, Palacký University and Institute of Experimental Botany, The Czech Academy of Sciences, Šlechtitelů 27, 78371 Olomouc, Czech Republic

[3]Centre for Natural Products Discovery, School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University, James Parsons Building, Byrom Street, Liverpool L3 3AF, United Kingdom

[*]*Corresponding authors:

Akbar Karami, email: akbarkarami@shirazu.ac.ir and

Lutfun Nahar, emails: nahar@ueb.cas.cz or drnahar@live.co.uk

Abstract

Oliveria decumbens Vent., an annual herb resistant to harsh environmental conditions, is an aromatic medicinal plant of the Apiaceae family. *O. decumbens* has numerous pharmacological, food and feed, and cosmetic applications. This species is endemic to Iran, Iraq, and Turkey. Published literature, available until 30 November 2022 on the morphology, phytochemistry, and bioactivity of *O. decumbens,* has been reviewed, and appraised for the potential therapeutic potential of this species, utilizing the databases, Web of Science, Google Scholar, PubMed, and Dictionary of Natural Products. The search term used was *O. decumbens*. Some manuscripts were issued on the chemical components of *O. decumbens* essential oil (EO) and various extracts. The EO of *O. decumbens* was evaluated for its chemical composition and medicinal potential against various diseases. Thymol and carvacrol constituted the primary oxygenated monoterpenes detected in substantial amounts within the EO. Additionally, diverse metabolites of *O. decumbens* were examined for their bactericidal, antioxidant, larvicidal, and immunomodulatory effects. This review article discusses morphology, phenology, and geographical distribution of *O. decumbens*

and presents a critical appraisal of its phytochemistry and therapeutic potential as documented in the published literature.

Keywords: *Oliveria decumbens*, Anti-Diabetic, Anticancer, Phytochemistry, Denak, Essential oil, phytochemicals, Pharmacology, Apiaceae

1. Introduction

Oliveria decumbens Vent. (Apiaceae), an aromatic herb thrives in untamed conditions in South-East Anatolia, Iraq, Syria, and some areas in Iran [1]. It is the only species in the *Oliveria* genus that could be found in the subtropical provinces of Khuzestan, Kermanshah, Ilam, Fars, Kohgiluyeh, and Boyer-Ahmad in southwest Iran. The herb is commonly known as "Moshkorak", "Den" or "Denak" in Iran [1,2]. A few other species, e.g., *O. aucheri* Jaub. & Spach, *O. bruguieri* Jaub. & Spach and *O. orientalis* DC. were published as new species, but have presently been recognized as synonyms of *O. decumbens*. De Candolle (1830) assigned the genus *Oliveria* to the tribe Smyrneae; Bentham & Hooker (1867) and Boissier (1878) later moved this genus to the tribe Ammineae. Afterward, the *Oliveria* was moved again to the tribe Apieae [3]. The majority of these conventional Apiaceae classification schemes were based on the morphology and anatomy of fruits. Based on DNA sequences, a thorough molecular phylogenetic investigation of the Apiaceae tribal categorization revealed that the genus *Oliveria* is related to the genus *Trachyspermum* within the Pyramidoptereae [4]. Medicinal plants can be considered as supplements to food, and they have been extensively and intensively studied for their ability to provide antioxidants and antimicrobial properties. The potential of medicinal plants to impact modern methods of food preservation is significant, as they can be used as substitutes for synthetic additives. Substituting synthetic additives with natural antioxidants from plants can help decrease the harmful effects of free radicals on the human body. Many constituents of EOs are found to exhibit antifungal properties [5,6]. Thus, it is important to characterize different types of medicinal plants for their antioxidant and antimicrobial potential. The species of the genus *Oliveria* are rich in essential oils

(EOs) that contain several bioactive substances, particularly, antibacterial agents [7], which have their usage as a food preservative in the industry to increase the shelf-life and safety of foods. Thymol, carvacrol, *p*-cymene, and γ-terpinene are only a few of the monoterpenes that are abundant in *O. decumbens* EO. The concentrations of these compounds vary depending on the geographic origin, ambient and climatic circumstances, and state of maturation [8–10]. *O. decumbens* EO has a long tradition of uses as a bactericidal, anti-*Helicobacter pylori*, insecticidal, anticholinesterase, and cytotoxic agent [9]. *O. decumbens* is a famous endemic plant of Flora Iranica used for therapeutic purposes. The Persian Traditional Medicine (PTM) recommends the plant's flower as a dry powder or infusion for dyspepsia, and diarrhea as well as an anti-inflammatory and bactericidal agent [11,12]. Various infections, cancer, inflammation, indigestion, fever, boils, abdominal pain, and diarrhea have traditionally been treated with the leaf and flower of this plant in Iran [11,13]. This plant also possesses anticholinesterase, antitumor, and insecticidal properties [9]. This plant has been reported as a remedy for skin diseases and a significant source of antioxidants, anti-inflammatory agents, anticancer, and antimicrobial compounds [14]. Its traditional use and various scientific evidences suggest that it may have a role to play in the development of new drugs or natural health products. This review article discusses the morphology, phenology, and geographical distribution of *O. decumbens* and presents a critical appraisal of its phytochemistry and therapeutic potential as documented in the published literature. To the best of our knowledge, no review article has ever been published on this plant.

2. Method of Study

The databases, Web of Science, Google Scholar, PubMed, and Dictionary of Natural Products have been explored to carry out a detailed literature search covering the materials published until 30 November 2022. *O. decumbens* was used as the search term. The obtained information was

then categorized into various classifications including morphology, geographical distribution, phytochemicals, and bioactivities.

3. Botanical, Morphological, and Phenological Description

O. decumbens is an annual herb that has rarely a decumbent growth habit that is climbing to erect [15] (Fig. 1). The stem measures 20-45 cm in height, is rigid, white, heavily branched, glabrous or infrequently hirsute, solid, terete, and has a base diameter of 2-4 mm. The petioles of the basal leaves, which quickly wither, are between 0.6 and 2.5 cm long and have a sheathing base. The lamina is 1-pinnate, 4-5 pairs of sections long, and each section is cleaved into smaller, decurrent lobes. Upper and middle cauline leaves are oblong, sub-sessile or sessile, pilose, and pinnatisect; lower cauline leaves resemble basal leaves. Umbels that range in size from 1.5 to 2.5 cm and are hairy and condensed. Bracts are found in 3–5 groups, are 3–8 mm long, obovate, dissected, and heavily pilose. Flowers are pedicellate, 15–35 hermaphrodites in number. Pedicels are hairy, 0.5-2 mm in length, somewhat thickened, and rounded. 6-8 numbers, 2.5–5 mm long, dissected, obovate, and heavily pilose bracteoles. Five distinct, persistent, ovate-triangular, acute, hairy, and 0.5-0.75 mm long sepals. Petals are five, 1-1.6 x 0.8-1.1 mm, white or pink, oblong-obovate, emarginate, and have hairs on the abaxial surface. The narrow tip is curved inward. Hairy ovary, enrolled stamens, white, approximately 1.5 mm long filaments, and subglobular, dorsally inserted anthers. Fruits 2.0-3.6 mm 1-1.6 mm, rectangular; thickly hirsute mericarps; lateral mesocarp cells. The vittae are big, almost orbicular, and oblong-elliptic. They have thin-walled epithelial cells lining them. There are two commissural vittae and one vitta per vallecula. The endocarp has a single layer and is made up of cells with thin walls. Endosperm cells have a granular interior and an uneven, polygonal shape. The fruits have dense, long, hirsute hairs with a papillose surface covering them. The stem of *Oliveria*, which is bright white and glabrous, is one of its primary characteristics [15]. Amiri et al. (2011) investigated the morphological features of the leaves and

stem of *Oliveria*. and demonstrated that non-glandular hairs cover the surface of leaves, whereas the cortical region of the cross-section of the stem reveals secretory canals. They investigated the morphology and anatomies of the fruit for their study. They discovered that *O. decumbens* fruit is rectangular, laterally compressed, and heavily hirsute. The plant ranges in height from 20 to 45 cm. Primarily gathered in the provinces of Fars, Chaharmahal & Bakhtiari, Kohgilouyeh & Boyerahmad, Boushehr, and Khuzestan at elevations of more than 2500 meters from the central Zagros mountains. This plant starts to flower in June, and there are three distinct colour phases: green, pink-purple, and white [16]. *O. decumbens* pollen grains are tricolporate, radially symmetric, monad, and polar. The pollen grains are roughly triangular with acute angles in the polar view. The colpus almost reaches the poles. The pore area can be found at the center of the colpus. The sculpting pattern is irregularly regulated in the equatorial region and striate or psilate in the polar region. However, there are times when the polar area is striate and the equatorial area is psilate-foveolate. *O. decumbens* fruit is covered in thick, long, hirsute hairs with a papillose surface [15].

Figure 1. *Oliveria decumbens* at a pink-purple flowering stage from a natural habitat (Kahnoyeh, Lar, Fars, Iran).

4. Geographical Distribution

The species of the genus *Oliveria* can be found in isolated pockets throughout Iran, Iraq, Syria, and Turkey (Fig. 2) [15]. Iran's subtropical regions, including Fars, Khuzestan, Kermanshah, Bushehr, Lorestan, Hormozgan, ChaharMahal and Bakhtiari, and Ilam provinces, are the home to only one species of the *Oliveria* genus (Fig. 3). It thrives in untamed growth in Iran's warm south and west, successfully adjusting to challenging climatic circumstances [17].

Figure 2. Geographical distribution of *O. decumbens* [15].

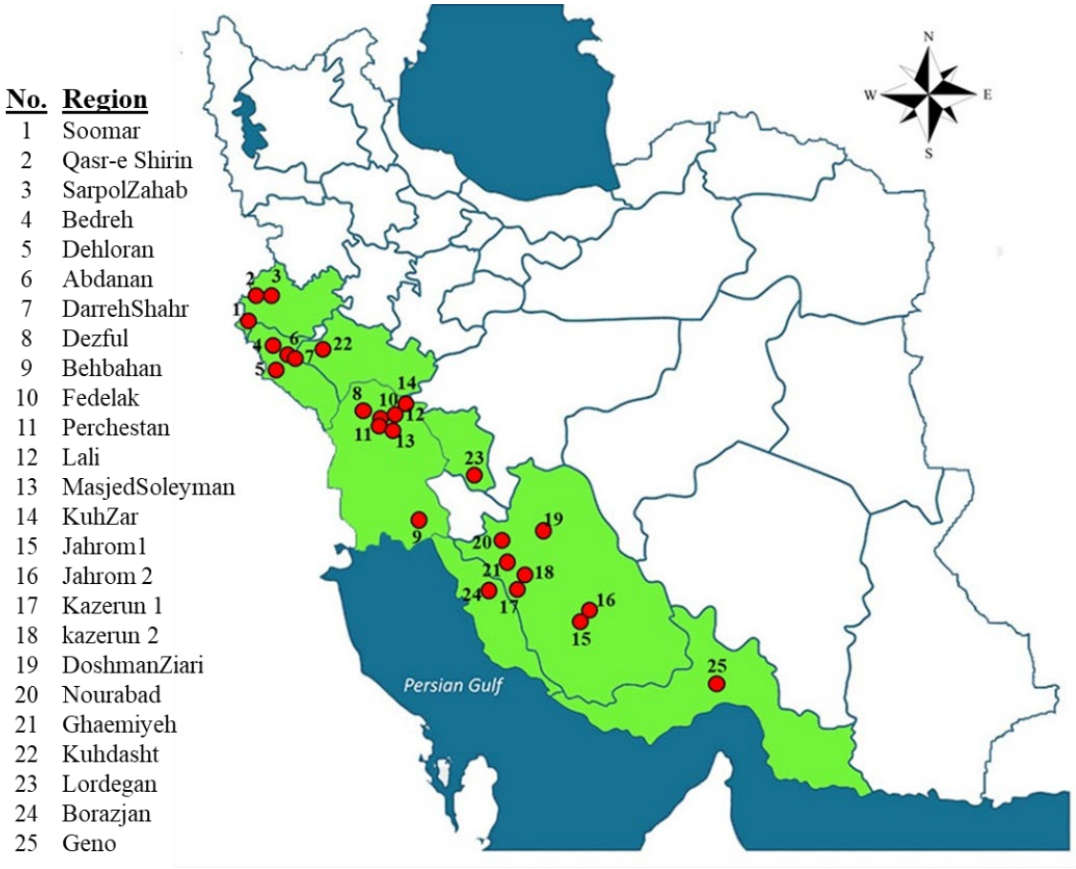

Figure 3. Map showing the distribution and locations of *O. decumbens* in Iran.

5. Phytochemicals

5.1. Essential Oil (EO)

Genetics determines the proportions of various substances in complex mixtures like EOs, yet these proportions may change depending on the environment [18]. The climatic circumstances (such as light, precipitation, and temperature), soil qualities (such as soil characteristics, and minerals), and geographical parameters (altitude, and latitude) are the most significant ecological elements that might affect the composition of EOs, both quantitatively and qualitatively (Tables 1 and 2) [19–21]. Although various studies on the *O. decumbens* EO compounds have been published [2,9,22], the connection between climatic and environmental factors and chemical compositions has never, to our knowledge, been the subject of a thorough analysis. Twelve accessions from various regions in Iran were collected for the study to recognize the impact of geographical and soil features on the compounds and quantity of *O. decumbens* EO. These accessions were then analyzed using gas chromatography coupled with a flame ionization detector (GC-FID) and gas chromatography combined with mass spectrometry (GC-MS) (Table 3) [1]. *O. decumbens* is a rich source of EO, [1,9,11,13,20]. The pink-purple phase is said to have the highest concentration of EO and its primary components [20]. However, the chemical components of *O. decumbens* EO are little known. Thymol, carvacrol, ***γ***-terpinene, and *p*-cymene were found to be the main components in earlier investigations on *O. decumbens* EO [1,13,20]. These chemicals may contribute to the medicinal effects of the EO of this plant. Sajjadi and Hoseini (2002) and Hajimehdipoor et al. (2010) reported 10 compounds in the *O. decumbens* EO, with thymol, **γ**-terpinene, *p*-cymene, myristicin, and carvacrol being the main components (Fig. 4). The variation in the chemical composition of EOs, which in turn is controlled by genetic and environmental variables, is related to the variation in those organisms' biological characteristics [23,24].

Table 1. Geographical Origins and Climate Characteristics of *O. decumbens* Habitats

Parameters	Latitude (N)	Longitude (E)	Altitude (m)	MDT (°C)	MDRH (%)	MPM (mm)	MEM (mm)	MSM (h)
O. decumbens	From 27°24'00.6"N To 34°29'02.9"N	From 45°34'27.4"E To 56°14'05.9"E	109-1699	16-28	39-53	17-41	132-259	241-279

Abbreviations: MDT, mean day temperature; MDRH, mean day relative humidity; MEM, mean evaporative per month; MPM, mean precipitation per month; MSM, mean sun hour per month.

Table 2. Soil physical characteristics of different habitats of *O. decumbens* populations.

Parameters	P (ppm)	K (ppm)	N (%)	OM (%)	TNV (%)	EC (dS/m)	pH	Sand (%)	Clay (%)	Silt (%)
O. decumbens	2-27	106-650	0.1-09	0.2-2.5	6-59	0.1-5.3	6-9	3-60	4-50	27-72

Abbreviations: EC, electrical conductivity; K, potassium; N, total nitrogen; OM, organic matter; P, phosphorus; pH, the potential of hydrogen; TNV%, total neutralizing value.

Table 3. The chemical composition of *O. decumbens* essential oil (OEO) and aromatic water (OAW) was identified by retention index and gas chromatography and gas chromatography-mass spectrometry.

No.	Compounds	Retention index	Relative percent in OEO (%)	Relative percent in OAW (%)
1	β-Pinene	976	1.8	-
2	*n*-Decane	1000	Trace	3.3
3	*p*-Cymene	1026	22.1	0.6
4	Limonene	1027	2.3	-
5	γ-Terpinene	1059	17.8	0.9
6	Linalool	1098	Trace	1.4
7	*n*-Dodecane	1200	Trace	0.7
8	Thymol	1289	25.5	37.6
9	Carvacrol	1296	23.1	52.9
10	Myristicin	1520	3.4	Trace

Retention indices (RI) were determined using a standard mixture of n-alkanes analyzed under the same chromatographic conditions on an HP-5 capillary column.

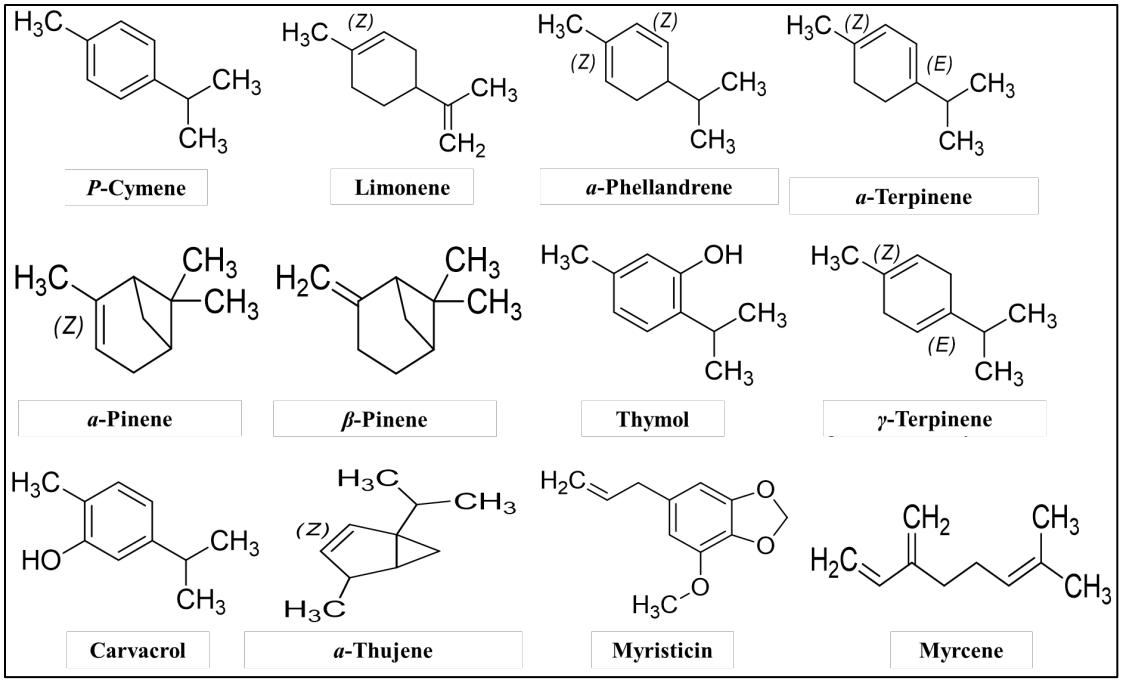

Figure 4. The chemical structure of the most important components (ACS style) of *O. decumbens* essential oil.

5.2. Extraction Methods Affecting Essential Oil Composition

Several extraction techniques, such as hydrodistillation (HD), steam distillation, and organic solvent extraction, can be used to obtain EO [25]. Due to its benefits over the traditional HD process (such as quicker extraction time and more effective heating), microwave-assisted hydrodistillation (MAHD) has recently gained popularity as a way to extract essential oils from medicinal plants [26]. In the isolation of EO from plants, an isolation method based on this technique was successfully tested [27]. This study is the identification of the volatile oil components and highlights certain drawbacks of the HD approach, including losses in the volatile chemicals and lengthy extraction times. An EO was extracted from the aerial parts of *O. decumbens* Vent. in a study using MAHD, and the outcomes were compared to the composition of the extracted EO produced using the traditional HD. The extracted oil's composition revealed some variation in these components' quantities and presence in MAHD oil as compared to HD oil. Results showed that the yield of the volatile fractions obtained using traditional HD and MAHD

was 0.79% and 0.96%, respectively. Distillation method affected E.O. constituents significantly. Differences among compounds between conventional hydrodistillation and Microwave-assisted Hydrodistillation method is shown in Figure 5 [27]. In another study, an investigation on the impact of ultrasonic pre-treatment before hydrodistillation (US-HD) on the extraction of *O. decumbens* EO was performed. According to the findings, when compared to the traditional HD procedure (where the yield is 4.4%), *O. decumbens* UA-HD provided the maximum EO yield (5.8%). The results of an analysis of EOs extracted by the UA-HD and HD procedures using GC and GC-MS revealed that thymol and carvacrol were the principal compounds that accounted for more than 60% of the EOs recovered by both techniques. Additionally, the ultrasonic pre-treatment markedly enhanced the proportion of thymol while not affecting the percentage of carvacrol. The antioxidant analysis showed that the EO obtained using the UA-HD approach (IC_{50} = 29.6 µg/mL) had better antioxidant potential than the EO obtained using the HD procedure (IC_{50} = 141.1 µg/mL). Additionally, there was no discernible variation between the cytotoxic properties of the EOs extracted utilizing the UA-HD and HD techniques. Additionally, the EO produced via the US-HD approach demonstrated a high level of insecticidal potential with an LD_{50} value of 32.7 µg/larva, compared with the HD procedure (LD_{50} = 63.2 µg/larva). Therefore, the US-HD approach is superior to the HD method in that it increases antioxidant and insecticidal properties while reducing extraction duration and energy use and improving EO production [27,28].

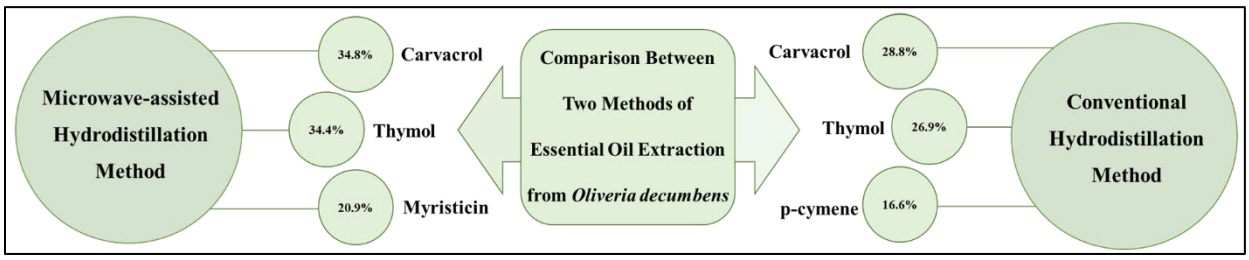

Figure 5. Comparison of E.O. compounds between two extraction methods.

5.3. Terpenes' Biosynthesis Pathways in *O. decumbens*

Isoprenoids are economically significant in both industries and agriculture. All isoprenoids have their antecedents in prenyl diphosphate. Prenyl diphosphate is produced via the MEP (2-C-methyl-D-erythritol 4- phosphate) and MVA (cytoplasmic pathway of the mevalonate) pathways. Except for plants, all living things use just one of the aforementioned channels [29]. Depending on the presence of ATP, the amount of fixed carbon, and either the plastid's MEP pathway or the cytoplasm's MVA pathway, plants regulate isoprenoid production to the greatest extent possible. Additionally, the employment of both the MEP and MVA routes shall reduce the pressure of survival in varied conditions on the many metabolites of specialized complex isoprenoid-derived biosynthesis (Figs 4) [30]. Understanding how the genes involved in both of the aforementioned pathways are expressed in various organs would give us a clear understanding of how the process works. The floral tissue has the highest levels of overexpression of MEP pathway genes, while the majority of MVA pathway genes are found in the radix. Because plastid and chloroplast make up a larger portion of flower tissue than radix, the flower's high level of MEP activity was not surprising.

6. Pharmacological Applications

Iranian traditional medicine has an illustrious history that dates back to the Babylonian-Assyrian era. The sophisticated experience of humans who have searched for valuable plants for health improvement through millennia is one of the most important ancient legacies. Many species of the Apiaceae (and some other family plants) are still utilized in folk remedies in Iran due to their high species diversity and endemism rates. In traditional Iranian medicines, *O. decumbens* is utilized for a variety of conditions, including gastrointestinal diseases and pain. In traditional medicine, *Oliveira* has been used to treat stomachaches, diarrhea, abdominal pain, fever, and skin soreness

[7,11,13]. A brief summary of the pharmacological effects of this plant species is shown in Figure 6. Numerous investigations have been carried out on this genus to demonstrate its anti-inflammatory, anti-cancer, antihemolytic, and antioxidant effects [7,9,13,22]. *O. decumbens* has been utilized as a central nervous system stimulant, and a liver and cardio tonic [31]. Moreover, it's bactericidal [9,11], antioxidant [32], and anti-*Helicobacter pylori* properties were also studied. Medicinal uses of different extracts of this plant are presented in Table 4. Also, another team worked on *O. decumbens* and investigated the bactericidal potential of the EO on the growth of *Pseudomonas aeruginosa*, *Escherichia coli*, *Streptococcus pyogenes*, and *Staphylococcus epidermidis* [11].

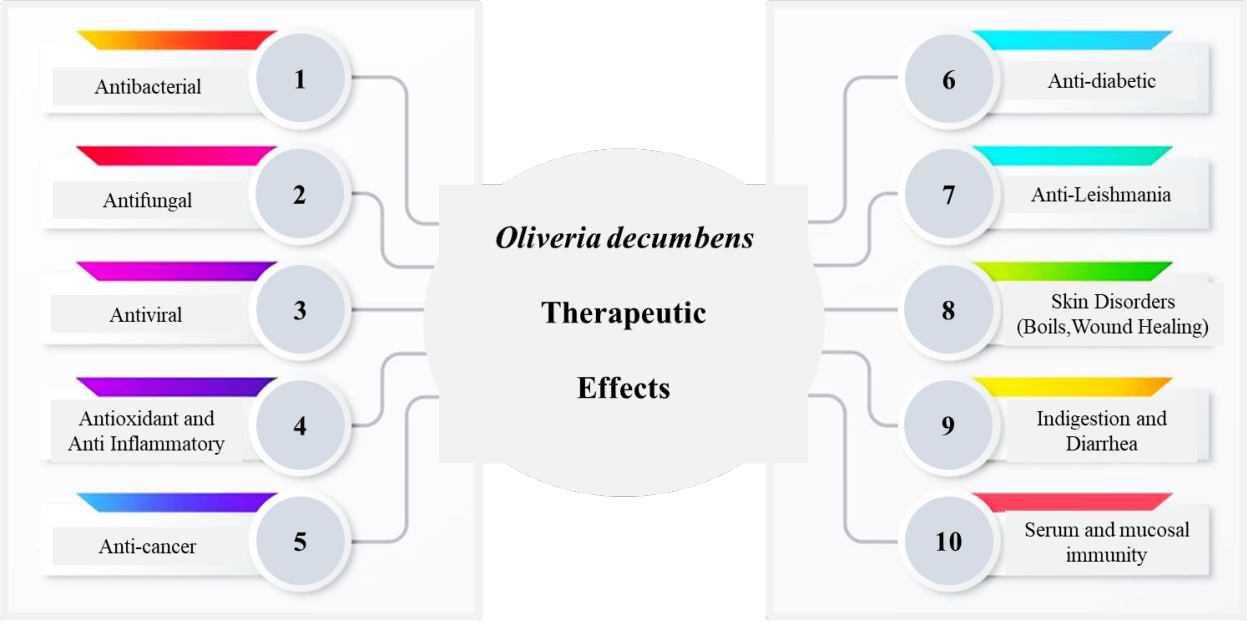

Figure 6. A Brief graphical summary of *O. decumbens* pharmacological effects.

Table 4. Various *O. decumbens* extracts and their therapeutic effects

No.	Mode of Action	Extract	References
1	Antibacterial	Hydrodistillation	(Khosravinezhad et al., 2017; Behbahani et al., 2018; Eftekhari et al., 2019; Hojjati & Ghodsi, 2019; Khoshbakht et al., 2020; Nikravan et al., 2020; Barzegar et al., 2021; Amin et al., 2022;)

2	Antifungal	Hydrodistillation	(Khajehie et al., 2017; Khosravinezhad et al., 2017; Barzegar et al., 2021)
3	Antiviral	Methanolic extract	[39]
4	Antioxidant	Hydrodistillation	(Saidi, 2014; Khajehie et al., 2017; Esmaeili et al., 2018; Vazirzadeh et al., 2019; Nikravan et al., 2020; Mollaei et al., 2021)
5	Anti-cancer	Ethanolic extract Hydro distillation	(Jamali et al., 2020; Khodavirdipour et al., 2021; Shariatzadeh et al., 2023)
6	Anti-diabetic	Hydroalcoholic Extract	[43]
7	Anti-Leishmanial	Hydroalcoholic Extract	(Khademvatan et al., 2019; Amin et al., 2022)
8	Wound Healing	Hydrodistillation	(Mahboubi et al., 2018; Amin et al., 2022)
9	Diarrhea	Hydroalcoholic Extract	[46]
10	Serum and mucosal immunity	Hydrodistillation	[40]

6.1. Antimicrobial Potential

O. decumbens essential oil demonstrated a wide range of antibacterial potential against all the investigated microbes (Table 5). The antimicrobial activity of the *O. decumbens* EO was evaluated. The EO showed strong inhibitory outcomes on Gram (+) and Gram (-) bacteria (Table 5). Additionally, it had antifungal effectiveness against *Candida albicans* and *Aspergillus niger* (Table 5). It appears that oxygenated monoterpenes, such as the well-known chemicals thymol and carvacrol, which have strong antibacterial potentials, can be linked to the antimicrobial activity of *O. decumbens* [13]. Many studies have shown that the extracted oil of *O. decumbens* exhibited strong antimicrobial and antifungal activities against filamentous fungi and yeast [11] and the antibacterial activity on bacterial strains that cause infections such as (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis,* and *Streptococcus pyogenes*) has been documented [47], while the efficiency of the herbal formulation containing *O. decumbens* EO was evaluated against methicillin-resistant *S. aureus* (MRSA) related skin wound infection in experimental mice model [7]. To evaluate anti-*Helicobacter pylori* activity, an agar dilution technique was used to measure the anti-*Helicobacter pylori* activity in an experiment. The essential

oil significantly reduced *H. pylori* (MIC= 20.4 µg/mL). Notable anti-*Helicobacter pylori* potential of *O. decumbens* EO was reported. According to a recent study, carvacrol had strong anti-*Helicobacter pylori* activity, however, its effectiveness was diminished when thymol was present [9,12]. EO extracted from *O. decumbens* aerial parts, used as an antiseptic agent and a broad-spectrum antimicrobial agent, possesses strong antibacterial activity [48]. In another study, the EO exhibited a large antimicrobial potential against the tested Gram-positive and Gram-negative bacteria and fungal strains [13]. Further research investigated the antimicrobial potential of *O. decumbens* on well-known fungi (*Candida albicans*) by using the disk diffusion agar method. The EO was reported to enclose antibacterial and antifungal effects. With increasing EO concentration, the inhibitory zone increases [33]. Haji et al (2010), reported strong antibacterial activity for *O. decumbens* EO on *Staphylococcus aureus*, *Escherichia coli*, *Aspergillus niger*, and *Candida albicans* but the low bactericidal activity on *Pseudomonas aeruginosa* [8]. Motamedi et al., (2010) stated that some microbes are resistant to the antimicrobial effects of *O. decumbens* extracts [49]. Mahboubi et al., (2008) stated that Gram-positive bacteria are more susceptible to *O. decumbens* EO's antibacterial effects than Gram-negative bacteria [50]. The antimicrobial effects of ethanolic and methanolic extracts of *O. decumbens* were also evaluated. Their results are shown in Table 5. *S. aureus* was the most susceptible strain of bacteria examined, and *O. decumbens* ethanolic extract was effective against all of them. *Salmonella typhi*, *Pseudomonas. aeruginosa*, and *Proteus. mirabilis* was more resistant to the methanolic extract than the other bacteria [49].

Table 5. Antimicrobial activity of *O. decumbens* essential oil and extracts.

	Microorganism	Plant Extract	References
Gram (+)	*Staphylococcus aureus* ATCC 6538 *Staphylococcus epidermidis* ATCC 12229 *Bacillus cereus* PTCC 1247	Essential oil	(Amin et al., 2005)
	Bacillus pumilus *Bacillus anthracis*	Ethanolic and Methanolic	[49]

	Bacillus licheniformis *Bacillus cereus* *Staphylococcus aureus* *Staphylococcus epidermidis* *Streptococcus pyogenes* *Listeria monocytogenes*		
Gram (-)	*Escherichia coli* ATCC 8739 *Pseudomonas aeruginosa* ATCC 9027 *Seratia marcenscens* PTCC 1111	Essential oil	(Amin et al., 2005)
	Escherichia coli *Salmonella typhi* *Proteus mirabilis* *Bordetella bronchiseptica* *Klebsiella pneumoniae* *Pseudomonas aeruginosa*	Ethanolic and Methanolic	[49]
Yeasts	*Aspergillus niger* ATCC 16404 *Candida albicans* ATCC 10231	Essential oil	(Amin et al., 2005)

6.2. Anti-Leishmania Activity

The primary health issue, leishmaniasis, affects millions of individuals. Leishmania infections cannot be vaccinated against, and available commercial medications are ineffective. Consequently, efforts are being made to find alternative natural therapies. *O. decumbens* hydroethanolic extract's effect on *Leishmania major* and *Leishmania infantum* was evaluated in a study. Results represented that antileishmanial activity of *O. decumbens*, on *L. major* and *L. infantum* promastigotes were affirmed with IC_{50} of 0.85 and 0.23 µg/ml after 72 h incubation. The anti-leishmania activity of the hydroethanolic extract was determined using an MTT assay. Inhibitory concentration (IC50) values were for the hydroethanolic extract of O. decumbens at 24, 48, and 72h for *L. major* promastigote 22.3, 2.7, and 0.85 µg/ml and for *L. infantum* promastigote 7.1, 1.13, and 0.23 µg/ml, respectively. Their findings demonstrated that the hydroethanolic extract of *O. decumbens* had potent anti-leishmanial activity against the forms of *L. major* and *L. infantum* promastigotes in vitro after 24, 48, and 72h of incubation ($P < 0.05$) [44].

6.3. Anticancer activity

Despite the development of conventional therapies to combat cancer, including chemotherapy, these therapies cause damage to many tissues and increase resistance leading to treatment failure. Hence, to minimize these problems, the finding of alternatives to cancer therapy is important, among which herbs have been known as a significant source of novel bioactive compounds for chemotherapeutic development [51]. Anticancer characteristics (*in vitro*) of *O. decumbens* EO were evaluated [42]. Based on the results of the MTT experiment, EO significantly reduced the vitality of 4T1 cancer cells while having no significant impact on L929 normal cells in 2D. In addition, OEO significantly reduced the proliferation of 4T1 spheroids in 3D. These findings demonstrated that OEO causes DNA damage, ROS production, mitochondrial membrane potential disturbance, and apoptosis. A cytokine assay and evaluation of EO's efficiency in 4T1 tumor-challenging mice demonstrated its anti-tumor effects and the emergence of an immune response linked to Th1 expansion. According to this study, EO can inhibit the growth of 4T1 breast cancer cell lines in 2D and 3D settings. According to the 2D data, the ROS formation, MMP decrease, and eventual induction of apoptosis are how EO exerts its inhibitory impact. This result was even seen in tumor-bearing mice treated with EO, demonstrating that EO, despite causing the death of tumor cells, exhibits anti-tumor effects because of the emergence of an antineoplastic immune response. EO may therefore be a chemical with several advantages for the treatment of breast cancer. However, additional research into the molecular processes and metabolic pathways implicated in *O. decumbens* EO's anticancer effect is required in the future [42]. Another anti-cancer study showed that by upregulating the box gene and slightly downregulating the anti-apoptosis gene bcl2, the real-time PCR demonstrated that *O. decumbens* ethanolic extract considerably triggered apoptosis in cells. Another study was aimed at investigating the pharmacological potential of *O. decumbens* essential oil (OEO) and its main compounds, focusing

on OEO's cytotoxic effects on MCF-7 breast cancer cells. Thymol, carvacrol, γ-terpinene, and p-cymene were the main OEO constituents. When MCF-7 cells were treated with OEO, the expressions of genes related to apoptosis (BIM and Bcl-2), tumor suppression (PTEN), and cell growth inhibition (AURKA), were evaluated using real-time PCR. Moreover, molecular docking was used for studying in silico the interaction of OEO principal compounds with PTEN and AURKA. The expression of AURKA was significantly reduced since the OEO treatment enhanced the expression of PTEN. Through in silico molecular docking, it was revealed that thymol, carvacrol, p-cymene, and γ-terpinene can activate PTEN and thus inhibit AURKA. Additionally, the DNA fragmentation assay, acridine orange/ethidium bromide (AO/EB) double-staining assay, and real-time PCR highlighted the fact that the OEO treatment could activate apoptosis and inhibit cell proliferation. Therefore, OEO is a viable candidate to be employed in the pharmaceutical industry, specifically as a possible agent for cancer therapy [52]. This plant EO despite inducing death in tumor cells, displays the anti-tumor effects due to the development of an anti-tumor immune response [42].

6.4. Wound healing activity

The EO of *O. decumbens* was evaluated for its wound healing property [36]. *O. decumbans'* ability to cure wounds was comparable to that of conventional skin cream. Thymol was anticipated to create the most stable complex with hydrogen bonds and hydrophobic interaction as the GSK-3 protein active site's strongest binder. *p*-Cymene, limonene, γ-terpinene, and carvacrol were the second-best binders. In addition, the healing effect of a skin dressing containing carvacrol showed that it significantly reduced the surface of a wound lesion, promoting changes in lesion depth and granulation tissue thickness. Subsequently, it was documented that carvacrol was capable of retaining the release of transforming growth factor, tumor necrosis factor-α, and interleukin 1β

during tissue repair. *O. decumbens* can also use as a wound dressing. Bacterial infections are common in wounds, which slow the healing process. Using natural antimicrobial agents can help prevent the development of bacterial resistance to conventional antibiotics. A biological polymer called chitosan has some antioxidant and antibacterial properties. In an experiment, nanofibrous scaffolds made of polyvinylpyrrolidone (PVP)/maltodextrin (MD) as the shell and chitosan (CS)/polyvinyl alcohol (PVA) as the core was created. In the center of the scaffolds that were created, *O. decumbens* EO was encapsulated. The examination of the broth microdilution revealed that the EO had substantial antibacterial action. The CS/PVA-PVP/MD and CS/PVA/EO-PVP/MD scaffolds showed appropriate mechanical characteristics. The antioxidant activity of the scaffolds was improved by the addition of the investigated EO. The antimicrobial assay of the manufactured scaffolds revealed that 10% *O. decumbens* EO loading might increase the CS/PVA-PVP/MD scaffolds' capacity for microbicidal activity and as wound dressing materials [36]. O. decumbens may have the potential as a natural wound healing agent. However, further research is needed to fully understand its mechanism of action and potential therapeutic applications [14]. Regarding anti-inflammatory docking results, the highest affinity was observed among essential oil compounds when thymol docked into the GSK-3 protein binding site. It formed hydrogen bond interactions with Asp, Tyr, and Val. Hydrophobic; Alkyl-Alkyl type interaction with Ile, Leu Ala, Val Leu, and Cys. Also, Pi-Alkyl-Pi orbital type interaction with Ile, Val, and Ala was observed. Although it is difficult to pinpoint these substances' precise molecular targets, it is possible to propose that they affect redox balance, inflammatory cytokines, and growth factors. Thymol and carvacrol play a crucial part in this process by having the ability to modify all stages of wound healing [13].

6.5. Pesticide and insecticidal activity

In the framework of a novel and eco-friendly pesticide development, plants represent a major source of effective compounds, which can be used to manage arthropod populations, formulating novel insecticides, acaricides, and repellents [53–60]. In particular, the use of botanical-based insecticides strongly reduces the chance of resistance development in targeted pests and vectors due to their multiple modes of action, including but not limited to inhibition of acetylcholinesterase, GABA, and octopamine receptors [54,61,62]. In a study, the efficacy of *O. decumbens* EO was assessed against three economically significant insects, *Culex quiquefasciatus*, *Musca domestica*, and *Spodoptera littoralis*. This EO's side effects on earthworms, *Eisenia fetida*, were evaluated. Results showed that the three target insects showed the EO to be very hazardous, on *Culex quefasciatus*, *M. domestica,* and *S. littoralis*, respectively. When evaluated at 200 mg/kg, the EO's toxicity to non-target soil insects was negligible, resulting in no or very low death of *E. fetida* [63]. Another study evaluated the insecticidal activity of *O. decumbens* E.O. It represented notable larval cabbage looper toxicity. *O. decumbens* E.O. showed an LD_{50} of 52.1 (µg larva1). Constituents of E.O. were also tested against *Trichoplusia ni* via topical application. Results showed that *ρ*-Cymene had a maximum LD_{50}, 202.8 (µg larva1), while minimum LD_{50} was achieved by Myristicin (32.7 (µg larva1)) [9].

7. Conclusion

O. decumbens is an aromatic medicinal plant that is endemic to the middle east, including some parts of Iran. *O. decumbens* EO may be utilized to treat infections and appears to be a significant source of antioxidant and antibacterial agents. It has various pharmacological activities including antiviral, anticancer, antidiabetic, and antifungal. Further research aiming at discovering phytochemicals from non-EO extracts of these plants and assessment of bioactivity of all secondary metabolites present in this plant is essential to appreciate the true potential of this plant

and to provide scientific evidence in support of its traditional medicinal uses. Since this plant has multiple and unique medicinal properties, the development of its cultivation, the separation and purification of its medicinal metabolites, and its usage in various industries, including pharmaceuticals, as a critical and vital industry, is very valuable and recommended.

Acknowledgment:

Lutfun Nahar gratefully acknowledges the financial support of the European Regional Development Fund - Project ENOCH (No. CZ.02.1.01/0.0/0.0/16_019/0000868) and the Czech Agency Grant - Project 23-05474S

References:

[1] A. Karami, T. Khoshbakht, H. Esmaeili, F. Maggi, Essential oil chemical variability in Oliveria decumbens (Apiaceae) from different regions of Iran and its relationship with environmental factors, Plants. 9 (2020) 680.

[2] H. Sereshti, Y. Izadmanesh, S. Samadi, Optimized ultrasonic assisted extraction–dispersive liquid–liquid microextraction coupled with gas chromatography for determination of essential oil of Oliveria decumbens Vent., J. Chromatogr. A. 1218 (2011) 4593–4598.

[3] I.C. Hedge, J.M. Lamond, Tribus Scandicineae, IC Hedge, JM Lamond, KH Rechinger, Al., Umbelliferae. KH Rechinger [Ed.], Flora Iran. 162 (1987) 83–110.

[4] S. Mousavi, V. Mozaffarian, K. Mummenhoff, S.R. Downie, S. Zarre, An updated lineage-based tribal classification of Apiaceae subfamily Apioideae with special focus on Iranian genera, Syst. Biodivers. 19 (2020) 89–109.

[5] K. El-Sabrout, A. Khalifah, B. Mishra, Application of botanical products as nutraceutical feed additives for improving poultry health and production, Vet. World. 16 (2023) 369.

[6] T.M. Haghighi, M.J. Saharkhiz, M. Khalesi, S.S. Mousavi, A. Ramezanian, Eco-friendly 'ochratoxin A'control in stored licorice roots–quality assurance perspective, Food Addit. Contam. Part A. 39 (2022) 1321–1336.

[7] M. Mahboubi, M.M. Feizabadi, T. Khamechian, N. Kazempour, M.R. Zadeh, F. Sasani, M. Bekhradi, The effect of Oliveria decumbens and Pelargonium graveolens on healing of

406 infected skin wounds in mice, World J. Plast. Surg. 5 (2016) 259.
407 [8] M.H. HAJI, N. Samadi, V. Mozafarian, N. Rahimifard, S.H. Shoeybi, H.M. Pirali,
408 Chemical composition and antimicrobial activity of Oliveria decumbens volatile oil from
409 West of Iran, (2010).
410 [9] M. Eftekhari, M.R.S. Ardekani, M. Amin, F. Attar, T. Akbarzadeh, M. Safavi, E.
411 Karimpour-Razkenari, M. Amini, M. Isman, M. Khanavi, Oliveria decumbens, a bioactive
412 essential oil: Chemical composition and biological activities, Iran. J. Pharm. Res. IJPR. 18
413 (2019) 412.
414 [10] S.S. Mousavi, A. Karami, T. Movahhed Haghighi, A. Tahmasebi, Lead, copper, zinc and
415 aluminum tolerance in contrasting ecotypes of Scrophularia striata, Acta Ecol. Sin. (2022).
416 https://doi.org/10.1016/j.chnaes.2022.01.005.
417 [11] B.A. Behbahani, F.T. Yazdi, A. Vasiee, S.A. Mortazavi, Oliveria decumbens essential oil:
418 Chemical compositions and antimicrobial activity against the growth of some clinical and
419 standard strains causing infection, Microb. Pathog. 114 (2018) 449–452.
420 [12] M. Eftekhari, M.R.S. Ardekani, M. Amin, M. Mansourian, M. Saeedi, T. Akbarzadeh, M.
421 Khanavi, Anti-Helicobacter pylori Compounds from Oliveria decumbens Vent. through
422 Urease Inhibitory In-vitro and In-silico Studies, Iran. J. Pharm. Res. IJPR. 20 (2021) 476.
423 [13] G. Amin, M.H.S. Sourmaghi, M. Zahedi, M. Khanavi, N. Samadi, Essential oil
424 composition and antimicrobial activity of Oliveria decumbens, Fitoterapia. 76 (2005) 704–
425 707.
426 [14] T. Jamali, G. Kavoosi, M. Safavi, S.K. Ardestani, In-vitro evaluation of apoptotic effect of
427 OEO and thymol in 2D and 3D cell cultures and the study of their interaction mode with
428 DNA, Sci. Rep. 8 (2018) 1–19.
429 [15] M. Çelik, H. Alatli, L. Gürlük, Ö.Ç. Erdoğan, Morphology, anatomy and
430 micromorphology of the genus" Oliveria"(Apiaceae), in: An. Del Jardín Botánico Madrid,
431 Real Jardín Botánico, 2021: p. 6.
432 [16] T. Khoshbakht, A. Karami, A. Tahmasebi, F. Maggi, The variability of thymol and
433 carvacrol contents reveals the level of antibacterial activity of the Essential Oils from
434 different accessions of Oliveria decumbens, Antibiotics. 9 (2020) 409.
435 [17] V. Mozaffarian, Flora of Ilam. Farhange Moaser Publication, Tehran, 936p, (2008).
436 [18] N.S. Sangwan, A.H.A. Farooqi, F. Shabih, R.S. Sangwan, Regulation of essential oil

production in plants, Plant Growth Regul. 34 (2001) 3–21.
[19] L. Llorens, J.A. Llorens-Molina, S. Agnello, H. Boira, Geographical and environment-related variations of essential oils in isolated populations of Thymus richardii Pers. in the Mediterranean basin, Biochem. Syst. Ecol. 56 (2014) 246–254.
[20] H. Esmaeili, A. Karami, F. Maggi, Essential oil composition, total phenolic and flavonoids contents, and antioxidant activity of Oliveria decumbens Vent.(Apiaceae) at different phenological stages, J. Clean. Prod. 198 (2018) 91–95.
[21] S.M.H.A.O. Nejad, H.N. Badi, A. Mehrafarin, V. Abdossi, F. Khalighi-Sigaroodi, The impact of macro environmental factors on essential oils of Oliveria decumbens Vent. from different regions of Iran, Jundishapur J. Nat. Pharm. Prod. 14 (2019).
[22] S.E. Sajjadi, S.A. Hoseini, Essential Oil Constituents of Oliveria decumbens Vent., J. Essent. Oil Res. 14 (2002) 220–221.
[23] A.R. Duarte, S.C. Santos, J.C. Seraphin, P.H. Ferri, Influence of spatial, edaphic and genetic factors on phenols and essential oils of Myrciaria cauliflora fruits, J. Braz. Chem. Soc. 23 (2012) 737–746.
[24] A. Karami, M. Khosh-Khui, H. Salehi, M.J. Saharkhiz, P. Zandi, Essential oil chemical diversity of forty-four Rosa damascena accessions from Iran, J. Essent. Oil Bear. Plants. 17 (2014) 1378–1388.
[25] M. Lo Presti, S. Ragusa, A. Trozzi, P. Dugo, F. Visinoni, A. Fazio, G. Dugo, L. Mondello, A comparison between different techniques for the isolation of rosemary essential oil, J. Sep. Sci. 28 (2005) 273–280.
[26] M. Koşar, T. Özek, M. Kürkçüoglu, K.H.C. Başer, Comparison of microwave-assisted hydrodistillation and hydrodistillation methods for the fruit essential oils of Foeniculum vulgare, J. Essent. Oil Res. 19 (2007) 426–429.
[27] F.M. Hossein, J. NasollahiIman, Comparison of different isolation methods of essential oil from Oliveria decumbens Vent.: hydrodistillation and microwave-assistHydrodistillaton, Adv. Environ. Biol. 8 (2014) 129–132.
[28] S. Mollaei, Z. Mamizadeh, S. Hazrati, H. Hashempour, The effect of ultrasonic pre-treatment on the yield, chemical composition and biological activity of essential oil in Oliveria decumbens flowers, J. Appl. Res. Med. Aromat. Plants. 24 (2021) 100313.
[29] D. Yang, X. Du, X. Liang, R. Han, Z. Liang, Y. Liu, F. Liu, J. Zhao, Different roles of the

mevalonate and methylerythritol phosphate pathways in cell growth and tanshinone production of Salvia miltiorrhiza hairy roots, PLoS One. 7 (2012) e46797.
[30] D. Ober, Gene duplications and the time thereafter–examples from plant secondary metabolism, Plant Biol. 12 (2010) 570–577.
[31] A. Ghahreman, A.R. Okhovvat, Matching the old medicinal plant names with scientific terminology. vol. 1. Farsi ed, (2004).
[32] M. Saidi, Antioxidant activities and chemical composition of essential oils from Satureja khuzestanica, Oliveria decumbens and Thymus daenensis, J. Essent. Oil Bear. Plants. 17 (2014) 513–521.
[33] M. HOJJATI, M. GHODSI, Investigation of chemical compositions and antimicrobial effects of Oliveria decumbens vent essential oil, in: B. Proc., 2019: p. 108.
[34] M. Khosravinezhad, E. Talebi, Z.N. Shivakumar, I. Nasrollahi, Essential oil composition and antimicrobial, antioxidant activities of Oliveria decumbens Vent, Int. J. Herb. Med. 5 (2017) 102–106.
[35] L. Nikravan, S. Maktabi, M. Ghaderi Ghahfarrokhi, M. Mahmoodi Sourestani, The comparison of antimicrobial and antioxidant activity of essential oil of Oliveria decumbens and its nanoemulsion preparation to apply in food industry, Iran. Vet. J. 17 (2020) 78–87.
[36] S. Barzegar, M.R. Zare, F. Shojaei, Z. Zareshahrabadi, O. Koohi-Hosseinabadi, M.J. Saharkhiz, A. Iraji, K. Zomorodian, M. Khorram, Core-shell chitosan/PVA-based nanofibrous scaffolds loaded with Satureja mutica or Oliveria decumbens essential oils as enhanced antimicrobial wound dressing, Int. J. Pharm. 597 (2021) 120288.
[37] Z.A. Amin, S.H. Sofi, H.A. Albustani, S.M. Nuraddin, Essential oil from Oliveria decumbens accelerates in vivo wound healing: a possible mechanism by the involvement of glycogen synthase kinase-3, Zanco J. Med. Sci. (Zanco J Med Sci). 26 (2022) 118–126.
[38] N. Khajehie, M.-T. Golmakani, M. Eblaghi, M.H. Eskandari, Evaluating the effects of microwave-assisted hydrodistillation on antifungal and radical scavenging activities of Oliveria decumbens and Chaerophyllum macropodum essential oils, J. Food Prot. 80 (2017) 783–791.
[39] E. Dashtimakan, F. Roodbari, M. Mohajerani, A. Mahmoudiotaghvari, Z. Zahedi, Antiviral Effects of Oliveria decumbens Vent. Extract against Herpes Simplex Virus Type

1, Sci. J. Ilam Univ. Med. Sci. 26 (2018) 113–125.
[40] A. Vazirzadeh, S. Jalali, A. Farhadi, Antibacterial activity of Oliveria decumbens against Streptococcus iniae in Nile tilapia (Oreochromis niloticus) and its effects on serum and mucosal immunity and antioxidant status, Fish Shellfish Immunol. 94 (2019) 407–416.
[41] A. Khodavirdipour, F. Haddadi, Y. Shiri, V.P. Tilak, In vitro anti-cancer activity of Oliveria decumbens vent. Extract, an endemic Persian medicinal plant, on HT-29 colorectal cancer cell line, BioRxiv. (2021).
[42] T. Jamali, G. Kavoosi, S.K. Ardestani, In-vitro and in-vivo anti-breast cancer activity of OEO (Oliveria decumbens vent essential oil) through promoting the apoptosis and immunomodulatory effects, J. Ethnopharmacol. 248 (2020) 112313.
[43] R. Siahbalaei, G. Kavoosi, Chemical composition and evaluation of anti-diabetic activity of oil extracts from Oliveria decumbens, Thymus kotschyanus, Trachyspermum ammi and Zataria multiflora, J. Food Meas. Charact. 15 (2021) 276–287.
[44] S. Khademvatan, A. Eskandari, B.S. Nejad, S. Najafi, In vitro anti-leishmanial activity of Satureja khuzestanica jamzad and Oliveria decumbens vent. Extracts on Leishmania major and Leishmania infantum promastigotes, J. Reports Pharm. Sci. 8 (2019) 149.
[45] M. Mahboubi, M. Taghizadeh, T. Khamechian, O.R. Tamtaji, R. Mokhtari, S.A. Talaei, The wound healing effects of herbal cream containing Oliveria decumbens and Pelargonium graveolens essential oils in diabetic foot ulcer model, World J. Plast. Surg. 7 (2018) 45.
[46] H.S. Gerdkohi, V. Ramezani, E. Eslahi, A. Emami, A. mohammad Ranjbar, F. Tavakoli, Effect of Hydroalcoholic Extract of Oliveria Decumbens Vent on Diarrhea and Symptoms of Morphine Withdrawal Syndrome in Mice, (2018).
[47] M. Valdivieso-Ugarte, C. Gomez-Llorente, J. Plaza-Díaz, Á. Gil, Antimicrobial, antioxidant, and immunomodulatory properties of essential oils: A systematic review, Nutrients. 11 (2019) 2786.
[48] M. Mahboubi, N. Kazempour, A. Mahboubi, The efficacy of essential oils as natural preservatives in vegetable oil, J. Diet. Suppl. 11 (2014) 334–346.
[49] H. Motamedi, E. Darabpour, M. Gholipour, S.M. Seyyednejad, Antibacterial effect of ethanolic and methanolic extracts of Plantago ovata and Oliveria decumbens endemic in Iran against some pathogenic bacteria, Int J Pharmacol. 6 (2010) 117–122.

[50] M. Mahboubi, M.M. Feizabadi, G.H. Haghi, H. Hosseini, Antimicrobial activity and chemical composition of essential oil from Oliveria decumbens Vent., Iran. J. Med. Aromat. Plants Res. 24 (2008) 56–65.
[51] A. El-Hussein, S.L. Manoto, S. Ombinda-Lemboumba, Z.A. Alrowaili, P. Mthunzi-Kufa, A review of chemotherapy and photodynamic therapy for lung cancer treatment, Anti-Cancer Agents Med. Chem. (Formerly Curr. Med. Chem. Agents). 21 (2021) 149–161.
[52] M. Shariatzadeh, A. Karami, A. Moghadam, M. Lotfi, F. Maggi, E. Ebrahimie, The Essential Oil from Oliveria decumbens Vent. (Apiaceae) as Inhibitor of Breast Cancer Cell (MCF-7) Growth, Pharmaceuticals. 16 (2023). https://doi.org/10.3390/ph16010059.
[53] M. Govindarajan, M. Rajeswary, S.L. Hoti, A. Bhattacharyya, G. Benelli, Eugenol, α-pinene and β-caryophyllene from Plectranthus barbatus essential oil as eco-friendly larvicides against malaria, dengue and Japanese encephalitis mosquito vectors, Parasitol. Res. 115 (2016) 807–815.
[54] R. Pavela, G. Benelli, Essential oils as ecofriendly biopesticides? Challenges and constraints, Trends Plant Sci. 21 (2016) 1000–1007.
[55] M.A. Tabari, M.R. Youssefi, F. Maggi, G. Benelli, Toxic and repellent activity of selected monoterpenoids (thymol, carvacrol and linalool) against the castor bean tick, Ixodes ricinus (Acari: Ixodidae), Vet. Parasitol. 245 (2017) 86–91.
[56] O.T. Adenubi, A.S. Ahmed, F.O. Fasina, L.J. McGaw, J.N. Eloff, V. Naidoo, Pesticidal plants as a possible alternative to synthetic acaricides in tick control: A systematic review and meta-analysis, Ind. Crops Prod. 123 (2018) 779–806.
[57] O.T. Adenubi, L.J. McGaw, J.N. Eloff, V. Naidoo, In vitro bioassays used in evaluating plant extracts for tick repellent and acaricidal properties: A critical review, Vet. Parasitol. 254 (2018) 160–171.
[58] G. Benelli, R. Pavela, Repellence of essential oils and selected compounds against ticks—A systematic review, Acta Trop. 179 (2018) 47–54.
[59] R. Pavela, G. Benelli, L. Pavoni, G. Bonacucina, M. Cespi, K. Cianfaglione, I. Bajalan, M.R. Morshedloo, G. Lupidi, D. Romano, Microemulsions for delivery of Apiaceae essential oils—Towards highly effective and eco-friendly mosquito larvicides?, Ind. Crops Prod. 129 (2019) 631–640.
[60] R. Pavela, F. Maggi, R. Iannarelli, G. Benelli, Plant extracts for developing mosquito

larvicides: From laboratory to the field, with insights on the modes of action, Acta Trop. 193 (2019) 236–271.

[61] M. Jankowska, J. Rogalska, J. Wyszkowska, M. Stankiewicz, Molecular targets for components of essential oils in the insect nervous system—A review, Molecules. 23 (2017) 34.

[62] M. Jankowska, B. Lapied, W. Jankowski, M. Stankiewicz, The unusual action of essential oil component, menthol, in potentiating the effect of the carbamate insecticide, bendiocarb, Pestic. Biochem. Physiol. 158 (2019) 101–111.

[63] R. Pavela, M.R. Morshedloo, H. Mumivand, G.J. Khorsand, A. Karami, F. Maggi, N. Desneux, G. Benelli, Phenolic monoterpene-rich essential oils from Apiaceae and Lamiaceae species: insecticidal activity and safety evaluation on non-target earthworms, Entomol. Gen. (2020) 421–435.