Review

Kazakh Ziziphora Species as Sources of Bioactive Substances

Karel Šmejkal 1,*, Milan Malaník 1, Karlygash Zhaparkulova 2, Zuriyadda Sakipova 2, Liliya Ibragimova 2, Galya Ibadullaeva 2 and Milan Žemlička 3

1 Department of Natural Drugs, Faculty of Pharmacy, University of Veterinary and Pharmaceutical Sciences Brno, Brno 61242, Czech Republic; milan.malanik@seznam.cz
2 Department of Pharmaceutical Technology, Faculty of Pharmacy, Kazakh National Medical University, Almaty 050000, Kazakhstan; zhaparkulovakarlygash@mail.ru (K.Z.); sakipova.zb@gmail.com (Z.S.); ibadullaeva.g@kaznmu.kz (L.I.);
3 Department of Pharmacognosy and Botany, The University of Veterinary Medicine and Pharmacy in Košice, Košice 04181, Slovakia; zemlicka1@gmail.com
* Correspondence: karel.smekal@post.cz; Tel.: +420-72-424-3643

Academic Editor: Derek J. McPhee
Received: 19 May 2016; Accepted: 18 June 2016; Published: 25 June 2016

Abstract: Ziziphora species represent the prototypical example of the Lamiaceae family. The phytochemicals present in Ziziphora include monoterpenic essential oils, triterpenes and phenolic substances belonging to the flavonoids. In Kazakh traditional medicine, Ziziphora species possess several medicinal uses. In particular, Z. bungeana Lam. and Z. clinopodioides Lam. are used for the treatment of illnesses related to the cardiovascular system or to combat different infections. Unfortunately, the majority of the information about the complex Ziziphora species is only available in Russian and Chinese language, therefore, we decided gather all available information on Kazakhstan Ziziphora, namely its content compounds, medicinal uses and published patents, to draw the attention of scientists to this very interesting plant with high medicinal potential.

Keywords: Ziziphora; essential oil; flavonoid; triterpene; cardiovascular; antibacterial

1. Introduction

1.1. Taxonomy of Ziziphora spp. and Their Typical Habitat

Taxonomy of Ziziphora spp. is complicated, as its world population is represented by more than 30 different species. This genus belongs to a very large Lamiaceae family with very similar taxonomic signs. In the flora of Kazakhstan, this genus can be subdivided into six species: Z. bungeana Lam., Z. clinopodioides Lam., Z. interrupta Juz., Z. pamiroalaica Juz., Z. tenuior L., and Z. vichodceviana Tkatsch. ex Tuylaganova. It is not completely clear if Z. bungeana is not simply a subspecies derived from Z. clinopodioides [1].

Ziziphora plants are annual or perennial and herbaceous or sub-shrubby. Their leaves are short petiolate or sub-sessile; the leaf blade is abaxially glandular. Verticillasters are scattered on the leaf axils or crowded in a terminal capitulum; floral leaves occur as large as stem leaves or can be reduced. Ziziphora species blossom from June to September according to the surrounding conditions. The calyx of Ziziphora plants appears to be narrowly cylindrical, straight to slightly curved, 13-veined, villous, annulated at throat, obscurely 2-lipped, with the upper lip 3-toothed and lower lip 2-toothed; the teeth are subequal, close together, rarely divergent after anthesis. The corolla limb of the flower is 2-lipped: upper lip straight, margin entire, apex emarginate; lower lip spreading, 3-lobed, and middle lobe narrower than suborbicular lateral lobes. The anterior stamens are fertile, reaching the upper corolla lip, and posterior stamens are rudimentary, short, or absent; anther cells are linear, with only
1 or 2 of them developed, and the others tend to be reduced to an appendage or absent. The style apex is unequally 2-cleft, and the posterior lobe is short. The fruits are ovoid and smooth nutlets. As mentioned, around the world, there are about 25–30 species in Africa, Asia and Europe, and four different species in China. Kazakhstan flora is represented by six different species. The morphology of *Z. bungeana* and *Z. clinopodioides* is described in detail, and information about the phytochemically less explored species *Z. tenuior*, *Z. pamiroalaica*, *Z. vichodceviana* and *Z. interrupta* can be found here [2,3].

*Z. bungeana* Lam. are aromatic subshrubs with woody roots. The stems are numerous, obliquely ascending to sub-erect, 12–30 cm long, woody at the base, branched, densely retrorse, pubescent, especially at apex. The petioles are pubescent; the leaves are narrowly lanceolate to ovate-lanceolate, rarely ovate, 5–15 mm × 1.5–6 mm, sub-glabrous or pubescent, conspicuously glandular, base cuneate to attenuate, margin entire, apex acute to slightly obtuse. The verticillasters are crowded in globose or semiglobose terminal capitula; the floral leaves are reduced, mostly ascending or horizontal. The pedicel is 1–3 mm long. The calyx is tubular, 5(–7) mm, obscurely glandular; the teeth are subequal and acute. The corolla rose, ca. 8 mm, tube pubescent, and lateral lobes are circular. Usually, 2 stamens are fertile, and the posterior stamens are short or absent. The flowering period is typically in Aug-Sep. *Z. bungeana* grows in gravelly hillsides, semi-desert areas, or sandy beaches, at altitudes of 700–1100 m above sea level in the areas of Xinjiang (China), Kazakhstan, Kyrgyzstan, Mongolia, Russia, Tajikistan, Turkmenistan, and Uzbekistan [2].

*Z. clinopodioides* Lam. has a thick and woody rhizome. The stems are numerous, simple, erect, 8–40 cm long, rarely branched, but branching on the top, somewhat ascending, covered with short hairs bent down. The leaves are petiolate, ovate or oblong-ovate, 10–25 mm long, 3–10 mm wide, with entire or unclearly rarely toothed margin. The leaves are point-ferruginous, smooth or sparsely short-haired. The flowers are gathered in dense apical capitately inflorescences surrounded by small bracts. The calyx is covered with short hairs, corolla is 10–12 mm long, pink or light purple outside, short and fluffy, tubular, twice as long as the limb, with the upper lip oblong to oval and notched, the middle part of the lower lip almost formy and villous, and lateral lobes spit ovate. *Z. clinopodioides* Lam. grows typically on the open rocky and gravelly slopes of hills and mountains, on rocky riverbanks, and also on the steppe meadows [2].

1.2. The Traditional Utilization of Ziziphora spp.

*Z. clinopodioides* is well known in Chinese traditional medicine as lip vanilla, leaflet mint or mountain mint. According to Chinese Materia Medica, it is used as a tranquilizing agent. It is also used to treat palpitations, insomnia, cold and fever, and oedema. It is usually administered orally as a decoction prepared by placing 15–18 g of the plant in boiling water to brew a tea. *Z. clinopodioides* is found to have been used in folk medicine to treat fevers and headaches in Xinjiang, China [4]. It is also a medicinal plant used in traditional Uighur medicine for many purposes, e.g., treatment of heart disease, high blood pressure, asthma, hyperhidrosis, palpitation, insomnia, edema, cough, bronchitis, lung abscess and other diseases [5,6]. *Z. clinopodioides* leaves, flowers and stems are frequently used as wild vegetables or additives in food to obtain a strong aroma and flavour [7].

*Z. clinopodioides* (known as blue mint bush in Turkish and Iranian traditional medicine) is well known for its antibacterial action [8]. *Ziziphora* species are used frequently also in Turkish and Iranian folk medicine, mainly as infusions for sedative, stomachic, carminative and other effects. Their antiseptic and wound healing effect is also well known [6,9]. In Anatolia, *Z. clinopodioides* is used as a wild vegetable or aroma and flavour adding spice. The plant is locally known as Kirnanesi and is prepared as an aromatic tea for treating gastrointestinal disorders and for its carminative, antiseptic and wound-healing properties [6]. Furthermore, it used as a culinary agent for manufacturing a special type of cheese [10,11].

*Z. tenuior* L. (known as raushangul in Kazakh language and kakuti in Persian language; kakuti-e kuhi is the Persian name of *Z. clinopodioides* according to Beikmohammadi [8]), is used in traditional medicine for treatment of fever, dysentery, uterus infection and as an analgesic. It is used also to combat
different gastrointestinal disorders, especially as a carminative, or as a remedial agent for diarrhoea or nausea. The essential oils and main components pulegone (53), thymol (62), menthone/isomenthone (44) and piperitone (45) could be the compounds responsible for the above-mentioned medicinal properties [12]. *Z. tenuior* has high content of essential oil, meaning it is a good raw source of pulegone (53) which is widely used in the food and drug industry [13,14]. Sezik et al. found this plant (local name Chulhuulva) to have hypotensive properties in their ethnopharmacological research on the medicinal plants of Uzbekistan [13].

*Z. bungeana* herb is used in Uygur medicine to prepare oral decoction which relieves respiratory distress, dizziness and other symptoms connected to cardiovascular diseases like coronary heart disease or hypertension [14].

### 2. *Ziziphora* Phytochemistry and Pharmacology

The previous investigations which were carried out on the *Ziziphora* genus with aim to elucidate the phytochemical profiles were mainly focused on its essential oil composition, and this will be discussed in the following text. In addition to essential oils, the *Ziziphora* species can be sources of flavonoids, caffeic acid derivatives, fatty acids, triterpenes and sterols. Ding et al. attempted to determine the effect of growth stage of *Z. clinopodioides* on the content and composition of essential oils, terpenoids, phenolics and flavonoids, showing that essential oil content was higher during the flowering period from non-volatile compounds and only the total flavonoid content was strongly affected by the growth stage [15]. Similar results were shown by Razmjoue and Zarei, where the essential oil content was correlated to temperature, relative moisture and height above sea level [16]. The habitat was also a factor affecting the content of the compounds present in the essential oils of *Z. clinopodioides* [17]. Moreover, different chemovars were identified during the chemical analysis of *Z. clinopodioides* and Iranian *Z. clinopodioides* ssp. *rigida*. The content of main essential oils components varied and allowed authors to classify analyzed species into pulegone/neomenthol, pulegone, pulegone/1,8-cineol, neomenthol and 1,8-cineol/terpinen-4-ol chemotypes [18,19].

Water and ethanol extracts of *Z. clinopodioides* showed no activity against several bacterial species, but some activity against COX-1 was recorded [20]. When different extracts from *Z. clinopodioides* subsp. *rigida* were tested for antibacterial activity against several Gram-positive and Gram-negative bacterial strains, only low activity was noted (with the exception of deodorized hot water and water-soluble methanol extracts against *Bacillus subtilis* and methanol and water-insoluble methanol extract against *E. coli*) [21]. However, methanol-water extracts of *Z. clinopodioides* and *Z. tenuior* showed low activity against several Gram-positive and Gram-negative microbial species in other assays [22].

The efficacy of methanolic extract obtained from *Z. clinopodioides* for treating inflammatory bowel disease was tested using the dextran sulphate-induced colitis model in mice. The parameters of inflammatory process were observed and it was found that TNF-α and NO levels were decreased, and the level of antioxidative defence was restored to almost the normal level [23]. Promising results in mice model of acetic acid-induced colitis showed also the water soluble portion of methanolic extract of *Z. clinopodioides*, however, compounds responsible for effect were probably not the components of essential oil [24]. The effect observed in this assay could be connected with antioxidant activity, as myeloperoxidase and TBARS levels were decreased by pretreatment of mice with different *Z. clinopodioides* extract concentrations. All doses of *Z. clinopodioides* showed significantly lowered score values of macroscopic and microscopic evaluations of colons, the effect of *Z. clinopodioides* at concentration of 300 mg/kg was comparable to that of prednisolone. The anti-inflammatory potential of *Ziziphora* was confirmed also by further study which showed, that ethanolic extract of *Z. tenuior* is active in induction of CD40 expression on dendritic cells and it can modulate the immunity response by affection of cytokine secretion, what at least partially explains the traditional usage of this plant in treatment of immunity related diseases [25]. *Z. tenuior* hydroalcoholic extract showed the antinociceptive activity (against visceral pain) in acetic acid-induced writhing assay in mice [26].
The methanolic extract of Z. clinopodioides subsp. rigida showed higher DPPH scavenging effect than the essential oil and other types of extracts [21].

Ziziphora extracts were tested for their potential cytotoxic effect in gastric cancer AGS cell line and showed promising cytotoxic activity [27].

Z. tenuior methanol and ethanol extracts showed the ability to decrease the bitterness of caffeine and showed some antioxidant activity, making Z. tenuior a promising food additive [28]. Some experiments also showed the reducing power of the water extract of Z. tenuior in the process of the formulation of silver nanoparticles [29].

The following chapters present an overview of the compounds identified from Kazakhstan Ziziphora species and their biological effects. Tables 1–4 outline the Ziziphora compounds and their activities. The information pertaining to each single compound which was isolated or identified in Kazakhstan Ziziphora species is presented here to attract attention to these interesting plants with several possible uses. The data in this research were collected using the Scifinder portal, Web of Knowledge and Science Direct. The search included articles published till April 2016, which are written in English (with limited number of papers in Russian language). The search was conducted using each single compound detected in Ziziphora as keyword. The articles that presented results of compounds added to mixtures as well as those that appeared in congress abstracts were not considered in this review.

2.1. Patents

There are several patents registered for the Ziziphora species and their application (or application of their isolated compounds) in the area of medicine. Capsules containing the mixture of dried aerial part extract Z. bungeana with Artemisia rupestris and Arctium lappa extracts are used to treat different viral infections of the upper respiratory tract. The patent applications also include the assays on the antipyretic activity of the extract in rabbits, anti-inflammatory activity in rats and antitussic activity in mice. The antiviral activity of the preparation was also evaluated in vitro [30].

The method for obtaining the flavonoid fraction of the Z. bungeana extract was also patented, combining the extraction of the Z. bungeana aerial part with organic solvent, with the dispersion of the extract into aqueous phase and filtration through macroporous resin, further washed with ethanol to get a flavonoid-rich extract [31]. This flavonoid fraction is believed to be useful in the treatment of cardiovascular diseases. Other patents cover the usage of Z. bungeana polyphenol and flavonoid fraction [32]. A flavonoid preparation from Z. bungeana to treat cardiovascular disorders is also patented [33].

Z. clinopodioides is also a component of Chinese traditional medicinal preparation for the treatment of paroxysmal supraventricular tachycardia [34]. Z. clinopodioides essential oil can be used as an oral spray to improve hygiene of oral cavity, suppress inflammation and suppress the growth of oral pathogenic bacteria [35]. Z. clinopodioides essential oil can be used in agriculture. The method for obtaining this oil and its application as an anti-fungal preparation against plant pathogenic fungus Sclerotinia sclerotiorum was patented [36]. The HPLC fingerprint for Z. clinopodioides compounds has also been developed using reversed-phase chromatography of diosmin (7), linarin (8) and pulegone (53) [37].

2.2. Phenolics

Z. clinopodioides was extracted with aim to obtain extracts with different polarity compounds to determine the total polyphenol and flavonoid content. As shown, phenolic substances are concentrated in the ethyl acetate extract, similar to flavonoids, phenolic acids and some other phenolics [5]. However, the analysis of the literature on the isolation of flavonoids or further phenolics from Ziziphora showed the presence of mainly lipophilic compounds of aglycone type (Table 1). From flavonoids, only a limited number of glycosides (diosmin (7) and linarin (8)) was isolated.
Table 1. Phenolic substances isolated from Kazakhstan *Ziziphora* species. (N.f.—not found).

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of *Ziziphora* | Biological Activity |
|------------------------|-----------------------------------------------|----------------------|
| **Flavonoids**         |                                               |                      |
| Apigenin (1)           | *Z. tenuior* [38], *Z. clinopodioides* [4,39,40] | Vasoactive activity (IC$_{50}$ 189.4 ± 12.4 µM) [39]; Some inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4]; Review on apigenin (1) on breast cancer [41]; Anticancer activity review [42-44]; Review on apigenin (1) impact on gastric cancer [45]; General review on the impact of apigenin (1) on health and disease [46] |
| Chrysin (2)            | *Z. clinopodioides* [39]                      | Vasoactive activity (IC$_{50}$ 347.8 ± 23.9 µM) [39]; Some inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4]; Anticancer activity reviewed [47]; Recent general review on bioactivities of chrysin (2) and its derivatives [50] |
| Luteolin (3)           | *Z. clinopodioides* [4]                       | Some inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4]; Anticancer [51,52]; Review on anti-inflammatory and neuroprotective effect [53,54]; Neurotrophic effects [55]; Anti-allergic [56]; Anti-atherogenic [57]; Cardioprotective [58]; General reviews on luteolin (3) [59,60] |
| Thymonin (4)           | *Z. clinopodioides* [39,61]                   | Low vasoactive activity (IC$_{50}$ not calc.) [39]; Toxicity against *Artemia* saline larvae [62]; Antiradical [63]; Weak antibacterial effect [61] |
| Acacetin (5)           | *Z. clinopodioides* [39]                      | Low vasoactive activity (IC$_{50}$ not calc.) [39]; Inhibition of angiogenesis [64,65]; Induction of apoptosis in different cancer cell lines [66-70]; Inhibition of TNF-related apoptosis [71]; Anticancer [72,73]; Induction of melanogenesis in B16F10 cells [74]; Cytotoxic against HL-60 cells cells [75]; Interaction with telomeres [76]; Antimetastatic effect [77,78] |

**Chemical Structure**

![Chemical Structure](image-url)
Some inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4].

Table 1. Phenolic substances isolated from Kazakhstan Ziziphora species. (N.f.—not found).

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphora | Biological Activity |
|-------------------------|-----------------------------------------------------|---------------------|
| Diosmetin (6)           | *Z. clinopodioides* [4]                              | Some inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4]. Cytotoxic against HL-60 cells [75]. Induction of melanogenesis in B16F10 cells [73,74]. Review on bioactivity [79]. |
| Dioxin (7)              | *Z. clinopodioides* [80]                             | Antidiabetic activity (reviewed by Abdurrazak et al. [81]). Review on clinical use [82]. |
| Linarin (8)             | *Z. clinopodioides* [44,80]                          | Inhibition of mucin production and secretion in airways epithelial cells [83]. Hepatoprotective [64]. Potential inhibitor of CDK4 in retinoblastoma [85]. Neuroprotective [86]. Inhibition of acetylcholinesterase [87]. Anti-inflammatory [88]; Anti-inflammatory in vivo [89]. Depressant effect on CNS [90,91]. |
| Ziziphorin A (9)        | *Z. tenuior* [39]                                    | Glucosidase inhibitor (review by Benalla et al. [97]). |
| Ziziphorin B (10)       | *Z. tenuior* [39]                                    | Low vasorelaxant activity (IC50 not calc.) [39]. Review on its potential in treatment of cardiovascular diseases [92]. Review on its potential in treatment of neurodegenerative diseases [93]. |
| 5,7,2′-trihydroxyflavone-2′-O-β-D-glucopyranoside (11) | *Z. clinopodioides* [44]                             | Low vasorelaxant activity (IC50 not calc.) [39]. |

Other Phenolics

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphora | Biological Activity |
|-------------------------|-----------------------------------------------------|---------------------|
| Acetovanillone (syn. apocynin) (12) | *Z. clinopodioides* [39]                              | Low vasorelaxant activity (IC50 not calc.) [39]. Review on its potential in treatment of cardiovascular diseases [92]. Review on its potential in treatment of neurodegenerative diseases [93]. |
| 4-Hydroxyacetophenone (syn. piceol) (13) | *Z. clinopodioides* [39]                              | Low vasorelaxant activity (IC50 not calc.) [39]. |

Other Phenolics
| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of *Ziziphus* | Biological Activity |
|------------------------|---------------------------------------------------|---------------------|
| Acetophenone (14)      | Z. tenuior [94]                                   | Tyrosinase inhibition [95] |
|                        |                                                   | Acaricidal effect [96] |
|                        |                                                   | H                   |
|                        |                                                   | H                   |
| Picein (15)            | Z. clinopodioides [14,44]                         | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] |
|                        |                                                   | Glucosidase inhibitor (review by Benalla et al. [97]) |
|                        |                                                   | O-Glc               |
|                        |                                                   | H                   |
| 2-Methoxy-4-vinylphenol (16) | Z. clinopodioides [15] | n.f. |
| Caffeic acid (17)      | Z. clinopodioides [80]                           | Anticancer potential reviewed [98] |
|                        |                                                   | Protection of endothelial cells (review by Fuentes and Palomo [99]) |
|                        |                                                   | General review on applications [100] |
| Ethyl ester of caffeic acid (18) | Z. clinopodioides [4] | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] |
|                        |                                                   | Antihypertensive [101,102] |
|                        |                                                   | Anti-inflammatory [103–105] |
|                        |                                                   | Antidiabetic [106] |
|                        |                                                   | Inhibitory activity against amyloidogenesis [107] |
|                        |                                                   | Antioxidative [108–111] |
|                        |                                                   | Anticancer [112] |
| Rosmarinic acid (19)   | Z. clinopodioides [80]                           | Review on pharmaceutical and clinical usage [113] |
|                        |                                                   | General review on applications [115] |
|                        |                                                   | Review on anticancer potential [116] |
| Salicylic acid (20)    | Z. clinopodioides [80]                           | Effect on cardiovascular system reviewed [117] |
|                        |                                                   | Pharmacological importance reviewed [118] |
| Benzoic acid (21)      | Z. clinopodioides [4]                            | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] |
|                        |                                                   | Properties reviewed here [119] |
### Table 1. Cont.

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of *Ziziphus* | Biological Activity                                                                                     | Chemical Structure |
|-------------------------|-----------------------------------------------------|--------------------------------------------------------------------------------------------------------|--------------------|
| (Z)-3-Hexen-1-ol benzoate (22) | *Z. tenuior* [94] | n.f.                                                                                                   |                    |
| Benzylalcohol glucoside (23) | *Z. clinopodioides* [4] | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4]          | ![Chemical Structure](image) |
| Phenethylalcohol glucoside (24) | *Z. clinopodioides* [4] | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4]          | ![Chemical Structure](image) |
| Eugenol (25)             | *Z. tenuior* [94] | Insecticidal (against *L. serricorn*) [126]                                                            | ![Chemical Structure](image) |
|                         |                       | Acaricidal activity [127]                                                                               |                    |
|                         |                       | Antibacterial [128]                                                                                     |                    |
|                         |                       | Inhibition of tyrosine kinase [129]                                                                     |                    |
|                         |                       | Review on antibacterial effect against cariogenic bacteria [131]                                       |                    |
|                         |                       | Review on possible synergy of eugenol containing essential oils and eugenol (25) with antibiotics [132]|                    |
|                         |                       | Review on antioxidative effect [133]                                                                    |                    |
|                         |                       | General properties reviewed here [134]                                                                   |                    |
Several aglycons, which can be called as dietary aglycons (like apigenin (1) and luteolin (3)) were also obtained. Typically, from Lamiaceae plants, lipophilic methoxylated aglycons were extracted, e.g., thymonin (4) or acacetin (5). Some relatively uncommon fatty acid-substituted flavones ziziphorin A and B (9 and 10) were isolated from Z. tenuior [38]. Furthermore, several phenolic acids and their esters, like caffic acid (17) and its ethyl ester (18) and rosmarinic acid (19), salicylic acid (20) and benzoic acid (21), and derivatives of benzyl alcohol were detected in Ziziphora species (Table 1). The bioactivity of Ziziphora flavonoids was studied for several single compounds; therefore, we will mention the activities in connection to possible Ziziphora use. Generally, flavonoids from Ziziphora species showed antioxidant, anti-inflammatory, venoprotective and anticancer activity. Several lipophilic flavonoids showed also antibacterial properties.

The antioxidant activity of flavonoid substances depends on the arrangement of the functionalities on the skeleton. Especially, the substitution and number of hydroxyl groups affects the antioxidant activity mediated by radical scavenging and metal ion chelation. As the substitution of Ziziphora-isolated flavonoids is not entirely favourable for scavenging and chelation, the antioxidant effect may be more related with suppression of ROS formation either by inhibition of enzymes or by upregulation or protection of antioxidant defences. Flavonoids contribute to ROS generation inhibition by the affection of the enzymes involved in their production, like microsomal monooxygenase, glutathione S-transferase, mitochondrial succinoxidase, NADH oxidase, and others. The antioxidant activity of Z. clinopodioides was tested by several methods (DPPH, superoxide, and hydroxyl radical scavenging activity). Given the high polyphenol and flavonoid content, the greatest activity was observed in ethyl acetate extract [5]. Monoterpenic glucoside shizonepetoside A (83) and simple flavonoids apigenin (1), luteolin (3) and diosmetin (6) showed potent inhibitory effects on NO production. The stereochemistry of monoterpenic glucosides is important for this effect according to these results [4]. Vasorelaxant activity was shown by those Z. clinopodioides extracts that had high concentration of polyphenolic substances [135]. The mechanism of its vasorelaxant action was also elucidated. The bioactivity guided separation of CH₂Cl₂ part of a hydroalcoholic extract of the whole plant, using an in vitro model of rat-isolated thoracic aortic rings led to isolation of several compounds, from which apigenin (1) and chrysin (2) showed the greatest activity [39]. Therefore, some structure-activity relationships can be assumed: the presence of 4′-hydroxy group of flavonoid, no methyl substitution at C-4′ and absence of continual substitution at positions 5, 6 and 7 of the flavonoid skeleton [39]. These results should be interpreted carefully, as these tests were carried out ex vivo on normal rat aortas, and differences can be observed after application of compounds or extracts to hypertonic animals or human.

In general, lipophilic flavonoids (flavonoids aglycons or methoxylated and prenylated flavonoids) are synthesized by plants as a part of defence against microbial infection; therefore, they can be used for antimicrobial therapy in humans. Lipophilic flavonoids isolated from Ziziphora species like chrysin (2), acacetin (5) or thymonin (4) have antimicrobial effects and are components of, for example, propolis, a well-known antimicrobial active material [50,61]. Antibacterial flavonoids probably possess multiple cellular targets rather than one specific site of action. One of their actions at the molecular level is to form a complex with proteins through nonspecific forces such as hydrogen bonding and hydrophobic effects as well as covalent bond formation. Thus, their mode of antimicrobial action may be related to their ability to inactivate microbial adhesins, enzymes, cell envelope transport proteins, and others [136]. Lipophilic flavonoids can also kill microbes by causing disruption of the microbial membranes [136]. Therefore, the presence of a number of lipophilic flavonoids can contribute to overall antibacterial effect of the traditional medicinal usage of Ziziphora extracts.

As it is well known, inflammation is a normal biological process in response to tissue injury, microbial pathogen infection, and chemical irritation. Inflammation is initiated by migration of immune cells from the blood vessels and release of mediators at the site of damage. This process is followed by further recruitment of inflammatory cells and release of reactive oxygen and nitrogen species and pro-inflammatory cytokines to combat the cause of inflammation, and later to repair
caused damage. Acute inflammatory process is rapid and self-limiting, but prolonged inflammation triggers chronic disorders. Natural products are often used to combat diseases connected with chronic inflammation [137,138]. The effectiveness of methanolic extract obtained from *Z. clinopodioides* for treating inflammatory bowel disease was tested in dextran sulphate-induced colitis model in mice. The parameters of inflammatory process were observed and it was found that the TNF-α level and NO level were decreased and level of antioxidative defence was restored to almost normal level [23]. *Ziziphora* is relatively rich in flavonoids, which can be considered responsible for the anti-inflammatory potential of this plant. Flavonoids like apigenin (1) [46], luteolin (3) [53,54], diosmin (7) [82], its aglycone diosmetin (6) [79] and linarin (8) [88,89] are reported to possess anti-inflammatory effects.

Caffeic acid (17) and its derivatives are often connected with different therapeutical applications: their potential anticancer activity was well reviewed [98], their effects on the cardiovascular system were reviewed by Fuentes and Palomo [99] and a large review on general applications of caffeic acid (17) was published recently [100]. Similar activities were observed for caffeic acid ethylester (18). This compound showed antihypertensive, antioxidant and anti-inflammatory activities that can be connected with usage of *Ziziphora* against diseases of cardiovascular system [101–112]. Similarly, rosmarinic acid (19) possesses various activities, also connected with civilization diseases like cardiovascular system illnesses, chronic inflammations and cancer [113–116].

### 2.3. Triterpenes and Steroids

There is not much information about triterpenes obtained from *Ziziphora* species, however, their presence is confirmed and some unpublished results showed their relatively high concentrations. The main triterpenic compounds identified till date in *Ziziphora* spp. are oleanolic acid (26), ursolic acid (27) and maslinic acid (28), together with daucosterol (29) as a representative of plant steroids. The bioactivity of all these compounds was well reviewed (with the exception of 29) [139,140].

Oleanolic acid (26) and maslinic acid (28) are representatives of β-amyrin type of pentacyclic triterpenes with the carboxyl group at position C-17 of the triterpenic skeleton. Both these compounds are relatively abundant in nature and are active components of many plants with medicinal properties. Oleanolic (26) and maslinic (28) acids and their derivatives are often used as components in medical drugs with effect on the cardiovascular system. These compounds help combat different so-called “civilization” diseases, for example cardiovascular diseases including atherosclerosis and diabetes, and even cancer. This could be because they have anti-inflammatory and antioxidative properties, and both cytoprotective and cytotoxic activity depending on the conditions and type of cells. Albeit, their activity is relatively indistinctive, and the multiple potentials of these triterpenes makes them good candidates for semi-synthesis and synthesis of potent drugs [141]. Ursolic acid (27) is an α-amyrin type of triterpene, again with carboxylic function at C-17. Similarly to oleanolic (26) and maslinic (28) acid, it can be isolated from several plant species with potent medicinal properties [142]. Similar to previously mentioned triterpenic acids, it shows activities beneficial in the treatment of civilization diseases like for example cancer, cardiovascular diseases or chronic inflammations [142].

Concerning the folk usage and effects of *Ziziphora*, oleanolic acid (26) and maslinic (28) acid have been found to affect the cardiovascular system. Both these compounds work against LDL oxidation, thus showing antiatherogenic properties. Oleanolic acid (27) also causes vascular smooth muscle relaxation. 28 acts as a strong antioxidant and possesses hypoglycemic properties; it was found to reduce the insulin resistance in the mouse model of genetic type 2 diabetes. 26 is also a potent antioxidant interfering with the glutathione redox cycle, affecting the Fenton reaction, NADPH oxidase, Nrf2 and others [142]. Its anti-inflammatory effects are connected mainly with interaction with NF-κB, STAT3 dimerization and overall inhibition of gene expression of pro-inflammatory factors (COX, iNOS) [142].
Table 2. Triterpenic substances isolated from Kazakhstan *Ziziphora* species. (N.f.—not found).

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of *Ziziphora* | Biological Activity | Chemical Structure |
|-------------------------|-----------------------------------------------------|---------------------|--------------------|
| Oleanolic acid (26)     | *Z. clinopodioides* [4,80,143]                      | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] | ![Chemical Structure](https://example.com/oleanolic_acid.png) |
|                         |                                                     | General review on bioactivity and mechanisms of effect [143,144] | |
| Ursolic acid (27)       | *Z. clinopodioides* [4,80,145]                      | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] | ![Chemical Structure](https://example.com/ursolic_acid.png) |
|                         |                                                     | Cytotoxicity against HL-60 and LLC cell line [145] | |
|                         |                                                     | Recent general review on bioactivity [142] | |
|                         |                                                     | Review on anticancer potential [147,148] | |
| Maslinic acid (28)      | *Z. clinopodioides* [4]                            | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] | ![Chemical Structure](https://example.com/maslinic_acid.png) |
|                         |                                                     | Cytotoxicity against HL-60 and LLC cell line [145] | |
|                         |                                                     | Recent review on bioactivity [139,144] | |
|                         |                                                     | Review on anti-inflammatory potential [149] | |
| Daucosterol (29)        | *Z. clinopodioides* [44]                           | Immunosuppressive effect [159] | ![Chemical Structure](https://example.com/daucosterol.png) |
|                         |                                                     | Anti-inflammatory activity [151], anti-inflammatory in ear edema assay [152], topical anti-inflammatory activity in the mouse ear edema model [153], weak 5-LOX inhibitory activity [154] | |
|                         |                                                     | DPPH and ABTS scavenging effect [155], antioxidant [156], inhibitory effect on nitric oxide production in LPS-activated RAW264.7 cells [157] | |
|                         |                                                     | Antinociceptive [158] | |
|                         |                                                     | Some anticomplementary activity [159] | |
|                         |                                                     | Neuropeptrotic [160,161], promotion of proliferation of neural stem cells [162], Inhibition of acetylcholinesterase [163] | |
|                         |                                                     | Inhibition of cancer cell proliferation [164], induction of apoptosis [165], antiproliferative [166], cytotoxic [167], antiproliferative activity against HL-66, K562, HepG2 and CNE-1 cell lines [168] | |
|                         |                                                     | Inhibition of MDA-MB-231 cancer cell migration [169], Ability to activate PPAR and PPARγ [170] | |
|                         |                                                     | Inhibition of α-glucosidase [171] | |
|                         |                                                     | Antibacterial effect against *E. coli* [172], against *H. pylori* and *S. aureus* [173], against *E. coli* and *S. aureus* [174], against *Bacillus subtilis* and *S. aureus* [175] | |
|                         |                                                     | Inhibitory effect on reverse transcriptase [176] | |
|                         |                                                     | Suppression of HCl/ethanol-induced gastric lesions [177] | |
|                         |                                                     | Inhibitory activity against osteoclast differentiation by suppressing TRAP activity in RANKL-induced RAW 264.7 macrophage cells [178] |
Ziziphora species extracts are also connected with antibacterial effect, and the activity of ursolic acid (27) was proven against numerous Gram-positive and Gram-negative bacteria, including vancomycin-resistant Enterococcus and different Mycobacterium tuberculosis strains. Some antiviral, anti-parasitic and antifungal activity was also observed [142]. However, the authors of the majority of the cited papers are right in that more studies should be carried out to prove these effects in vivo in humans [144].

Daucosterol (29) is a natural phytosterol—a glucoside derived from β-sitosterol. As we did not find relevant information about its bioactivity, we tried to summarise its effects in Table 2. Several activities of daucosterol (29) are again in accordance with therapeutic potential of Ziziphora species observed both in folk medicine and scientific studies. The anti-inflammatory effect of daucosterol (29) was observed both in vitro and in vivo [152,153] and a 5-LOX inhibitory effect was observed [154]. Daucosterol (29) also acts as scavenger of free radicals in vitro [155] and as an antioxidant [156] and it inhibits nitric oxide production in LPS-activated RAW264.7 cells [157]. Furthermore, 29 showed antiproliferative [164,166] and cytotoxic [167] activity against different cancer cell lines; it induces apoptosis [165] and inhibits MDA-MB-231 cancer cell migration [169]. Some antimicrobial activities of 29 were observed, mainly against E. coli, S. aureus and H. pylori. The inhibition of H. pylori growth can be beneficial in the treatment of gastric ulcer lesions, because daucosterol (29)-mediated suppression of HCl/ethanol-induced gastric lesions was observed by Jeong et al. [177].

2.4. Essential Oil

The essential oils are probably the most studied part of Ziziphora phytochemical components (Table 3). As could be expected for Lamiaceae, these essential oils are predominantly composed of monoterpenic compounds; however, several sesquiterpenic substances and some other compounds were also identified by GC-MS analysis (see Table 3). The hydrodistillation is the commonly used method for obtaining Ziziphora essential oils, but the method used for obtaining Z. tenuior essential oil by supercritical fluid extraction (SFE) with higher yield was also published [179]. It is clear that the relative ratios of components vary according to the frequently occurring chemotypes in the family Lamiaceae, environmental factors and also extraction method [180–182]. For example, although we can see biochemical convergence among the Z. clinopodioides from different locations, owing to the frequent occurrence of chemotypes, different patterns in the composition of the oils are common. As mentioned above, the variability of essential oils components in Ziziphora species is really high and chemovars of one species can be found in very related habitats, as showed for example by Khodaverdi-Samani et al., who identified several chemovars of Z. clinopodioides ssp. rigida in limited area of southwestern Iran (Alpine type mountains). The essential oils obtained by hydro-distillation (content ranged from 0.12 to 0.98 mL/100 g of dry weight) were analyzed by GC and GC/MS to prove that the main chemical compositions were pulegone (53) (5.19% to 57.85%), limonene (38) (0.26% to 12.79%), 1,8-cineole (72) (0.00% to 27.4%), bornyl acetate (69) (0.47% to 9.37%), piperitenone (46) (0.70% to 9.05%) and menthol derivatives (for example 58) [19]. Other study revealed Z. clinopodioides as plant rich in carvacrol (73) 52.7%, linalool (66) 15.9% and menthol (56) 14% [183]. Further literature survey indicated that the oils of Ziziphora species have been found to be rich in pulegone (53) and thymol (62), but there are also analysis showing low or no concentration of these substances in Z. clinopodioides essential oil [184]. The composition of Z. clinopodioides essential oil is strongly influenced by flowering stage [182]. Also, the composition of Z. tenuior and Z. pamiroalaica essential oil may vary strongly [185]. Z. bungeana and Z. clinopodioides were analysed by the same group [185], same as Z. vychodceviana [186].
Table 3. Mono and sesquiterpenic substances isolated from Kazakhstan *Ziziphora* species (N.f.—not found).

| Name of Compound and ID | Isolation/Detection in *Ziziphora* spp. (Percentage Content when Given) | Biological Activity | Chemical Structure |
|-------------------------|-------------------------------------------------|--------------------|--------------------|
| **Monoterpenes**        |                                                 |                    |                    |
| **Myrcene** (syn. β-myrcene) (30) | *Z. clinopodioides* (0.6%–1.9%) [9,15,185] | Antibacterial, antitermitic, antifungal [187] | ![Monoterpenes Myrcene](image) |
|                        | *Z. clinopodioides subsp. rigida* (0.2%) [21] | Low fungicidal activity against various species of insects [190,191] | ![Monoterpenes Myrcene](image) |
|                        | *Z. clinopodioides subsp. bungeana* (0.3%) [201] | Anti-inflammatory activity in the mouse model of pleurisy induced by LPS [193] | ![Monoterpenes Myrcene](image) |
|                        | *Z. tenuior* (0.1%) [179,202] | Protective effect against t-BOOH induced mutagenesis [194] | ![Monoterpenes Myrcene](image) |
|                        | *Z. tenuior* n.f. [94] | Insecticidal activity against *A. albopictus* | ![Monoterpenes Myrcene](image) |
| **(Z)-β- Ocimene** (31) | *Z. clinopodioides* (1.1%) [184] | Antibacterial [187] | ![Monoterpenes Ocimene](image) |
|                        | *Z. clinopodioides subsp. bungeana* [201] | Antituberculosis (against *M. tuberculosis* and *M. gypseum*), Antifungal (against *C. albicans*, *A. niger*, *A. flavus*, *E. coli*, *P. aeruginosa*, and *S. aureus*) [203,204] | ![Monoterpenes Ocimene](image) |
| **(E)-β- Ocimene** (32) | *Z. clinopodioides* (1.2%) [184] | Antifungal (against *C. albicans*, *C. tropicalis*, *C. krusei*, *C. glabrata*, *A. niger*, *A. flavus*, *E. coli*, *P. aeruginosa*, and *S. aureus*) [203,204] | ![Monoterpenes Ocimene](image) |
| 3,7-Dimethyl-1,3,7-octatriene (33) | *Z. tenuior* [94] | n.f. | ![Monoterpenes Ocimene](image) |
| **α-Thujene** (34) | *Z. clinopodioides* (0.1%–1.2%) [35,184] | Antibacterial, antitermitic, antifungal [187] | ![Monoterpenes Thujene](image) |
|                        | *Z. clinopodioides subsp. rigida* (0.1%) [21] | Some cytotoxic activity [189] | ![Monoterpenes Thujene](image) |
|                        | *Z. tenuior* (0.4%) [94,179] | Sedative and motor relaxant effects in mice [192] | ![Monoterpenes Thujene](image) |
| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of *Ziziphora* (Percentage Content when Given) | Biological Activity | Chemical Structure |
|-------------------------|----------------------------------------------------------------------------------|---------------------|-------------------|
| α-Phellandrene (35)     | Z. clinopodioides (0.3%) [184]                                                   | Insecticidal activity against various species of insects [192,193]; larvicidal activity against various mosquito species [205,206]; Antinociceptive activity assessed in various chemical-induced nociception models in rodents [207,208]; Antidepressant activity in rats [208]; Induction of autophagy in human liver tumour cells [209]; induction of necrosis [210]; induction of apoptosis in mice leukaemia WEHI-3 cells in vitro [211]; promotion of the immune response by increasing the level of T-cells, monocytes and macrophages in BALB/c mice in vivo [212] |
|                         | **Z. clinopodioides** (2.0%) [184]                                                | Inhibition of P-glycoprotein-mediated transport of different substances [213]; Suppression of CNS in mice [214,215]; Some topical anti-inflammatory activity in carrageenan-induced paw edema in rats [216]; Antioxidant activity in various free radical scavenging tests [217,219]; Antifungal activity tested against some food spoilage yeasts [219]; Larvicidal activity against mosquitoes *Aedes aegypti* and *A. albopictus* [219]; Antiviral activity against herpes simplex virus type 1 in vitro [220]; Review on some effects on cardiovascular system [221]; Trypanocidal activity against *Trypanosoma cruzi* [222] |
| α-Terpinene (36)        | Z. clinopodioides subsp. rigida [21]                                              | Anti-inflammatory (inhibition of NO production in LPS-stimulated RAW-264.7 macrophages) [223]; Inhibition of acetylcholinesterase and butyrylcholinesterase [224] |
|                         | **Z. clinopodioides subsp. bungeana** (0.1%) [201]                               | Inhibition of P-glycoprotein-mediated transport of different substances [213]; Anti-inflammatory (inhibition of NO production in LPS-stimulated RAW-264.7 macrophages) [223]; Inhibition of acetylcholinesterase and butyrylcholinesterase [224]; Suppression of CNS in mice [214,215,225]; Inhibition of P-glycoprotein-mediated transport of different substances [213]; Inhibition of P-glycoprotein-mediated transport of different substances [213]; Antioxidant activity in various free radical scavenging tests [217,219]; Antiviral activity against herpes simplex virus type 1 in vitro [220]; Review on some effects on cardiovascular system [221]; Antiproliferative (tested on primary rat neurons and N2a neuroblastoma cells) [226]; some cytotoxic activity [190]; Trypanocidal activity against *Trypanosoma cruzi* [222] |
| Terpinolene (37)        | Z. clinopodioides (0.1%–0.2 %) [184]                                             | Antioxidant activity in various free radical scavenging tests [217,219]; protective effect against LDL-oxidation [230]; Review on some effects on cardiovascular system [221]; Antiviral activity against influenza A/PR/8 virus subtype H1N1 [231] |
|                         | **Z. clinopodioides subsp. rigida** (0.5%) [21]                                  | Inhibition of P-glycoprotein-mediated transport of different substances [213]; Anti-inflammatory (inhibition of NO production in LPS-stimulated RAW-264.7 macrophages) [223]; Inhibition of acetylcholinesterase and butyrylcholinesterase [224]; Suppression of CNS in mice [214,215,225]; Inhibition of P-glycoprotein-mediated transport of different substances [213]; Antioxidant activity in various free radical scavenging tests [217,219]; Antiviral activity against herpes simplex virus type 1 in vitro [220]; Review on some effects on cardiovascular system [221]; Antiproliferative (tested on primary rat neurons and N2a neuroblastoma cells) [226]; some cytotoxic activity [190]; Trypanocidal activity against *Trypanosoma cruzi* [222] |
|                         | **Z. clinopodioides subsp. bungeana** (0.1%) [201]                               | Inhibition of P-glycoprotein-mediated transport of different substances [213]; Anti-inflammatory (inhibition of NO production in LPS-stimulated RAW-264.7 macrophages) [223]; Inhibition of acetylcholinesterase and butyrylcholinesterase [224]; Suppression of CNS in mice [214,215,225]; Inhibition of P-glycoprotein-mediated transport of different substances [213]; Antioxidant activity in various free radical scavenging tests [217,219]; Antiviral activity against herpes simplex virus type 1 in vitro [220]; Review on some effects on cardiovascular system [221]; Antiproliferative (tested on primary rat neurons and N2a neuroblastoma cells) [226]; some cytotoxic activity [190]; Trypanocidal activity against *Trypanosoma cruzi* [222] |
|                         | **Z. tenuior** (0.51%–7.82%) [232]                                               | Inhibition of P-glycoprotein-mediated transport of different substances [213]; Anti-inflammatory (inhibition of NO production in LPS-stimulated RAW-264.7 macrophages) [223]; Inhibition of acetylcholinesterase and butyrylcholinesterase [224]; Suppression of CNS in mice [214,215,225]; Inhibition of P-glycoprotein-mediated transport of different substances [213]; Antioxidant activity in various free radical scavenging tests [217,219]; Antiviral activity against herpes simplex virus type 1 in vitro [220]; Review on some effects on cardiovascular system [221]; Antiproliferative (tested on primary rat neurons and N2a neuroblastoma cells) [226]; some cytotoxic activity [190]; Trypanocidal activity against *Trypanosoma cruzi* [222] |
### Table 3. Cont.

| Monoterpenes | Isolation/Detection in Kazakhstan spp. of Ziziphus (Percentage Content when Given) | Biological Activity | Chemical Structure |
|--------------|---------------------------------------------------------------------------------|---------------------|--------------------|
| Z. clinopodioides [11,15] | Insecticidal (against red imported fire ant) [233] | Fumigation activity against stored-product pest insects [234] | ![Chemical Structure](image) |
| 3-Methyl-6-(1-methyl-ethylidene)-cyclohexene (syn. pseudolimonene) | Z. tenuior (0.51%–7.82%) [232] | Insecticidal (against red imported fire ant) [233] | ![Chemical Structure](image) |
| 3-Isopropenyl-5,5-di-methyl-cyclopentene | Z. tenuior (0.04%) [179] | n.f. | ![Chemical Structure](image) |
| 4-Methyl-1-(1-methyl-ethenyl)-cyclohexene (syn. 3,8-p-menthadiene) | Z. tenuior [94] | n.f. | ![Chemical Structure](image) |
| 3-Methyl-6-(1-methyl-ethylidenec)-cyclohexene (syn. Isoterpinolene, 2,4-p-mentadiene) | Z. tenuior [94] | n.f. | ![Chemical Structure](image) |
| 3-Isoeugenyl-5,5-di-methyl-cyclopentene | Z. tenuior [94] | n.f. | ![Chemical Structure](image) |
### Table 3. Cont.

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphus (Percentage Content when Given) | Biological Activity | Chemical Structure |
|-------------------------|---------------------------------------------------------------------------------|---------------------|--------------------|
| Menthone (44)           | *Z. clinopodioides* (6.2%–13.3%) [238]                                        | Antifungal effect against *C. albicans*, synergy with fluconazole [239], antimicrobial activity against tested strains of bacteria, yeast and pathogenic fungi [240,241]
|                         |                                                                                 | Insecticidal activity tested against various stored grain pests and vectors [242], moderate insecticidal activity against *Sitophilus zeamais* [243]
|                         |                                                                                 | Antidepressant-like effects in an unpredictable chronic mild stress mouse model of depression [244] |
| Piperitone (45)          | *Z. clinopodioides* (4.18%) [11]                                               | Repellent activity against ants of the genus *Crematogaster* [245], insecticidal activity against larvae of *Spodoptera littoralis* [246] and against *Callosobruchus maculatus* [247]
|                         | *Z. clinopodioides subsp. rigidida* (1.4%) [21]                                | Increase in antimicrobial activity of furazolidone and nitrofurantoin against bacteria of the family Enterobacteriaceae [248,249]
|                         | *Z. clinopodioides subsp. bungana* (0.6%) [201]                               | Fungicidal activity against *Aspergillus flavus* [250] |
| Piperitenone (46)        | *Z. clinopodioides* (5.3%) [11]                                                | Antibacterial activity against 52 Gram-positive and Gram-negative bacterial species, disc diffusion method [11]
|                         | *Z. clinopodioides subsp. rigidida* (17.4%) [21]                              | Insecticidal activity against *Sitophilus zeamais* [243] |
| p-Menth-4-en-3-one (47)  | *Z. tenuior* (0.5%) [202]                                                      | n.f. |
| Piperritone oxide (48)   | *Z. persica* (0.32%) [251]                                                    | Antibacterial activity against 19 Gram-positive and Gram-negative bacterial species [252] |
| Piperritone oxide (49)   | *Z. clinopodioides* (0.16%) [11]                                               | Antimicrobial activity against strains of bacteria, yeast and pathogenic fungi [241,252]
|                         |                                                                                 | Insecticidal activity against the West Nile virus mosquito *Culex pipiens* larvae [253]
|                         |                                                                                 | and against various stages of *Aedes aegypti* [254]
|                         |                                                                                 | Antinociceptive activity in acetic acid-induced writhing test and in the second phase of formalin test [255]
|                         |                                                                                 | Antiviral activity against herpes simplex virus type 1 [256] |
Table 3. Cont.

| Name of Compound and ID | Isolation/Detection in Kazakhstan app. of Ziziphora (Percentage Content when Given) | Biological Activity | Chemical Structure |
|------------------------|---------------------------------------------------------------------------------|---------------------|-------------------|
| Verbenone (50)         | Z. clinopodioides subsp. rigida (0.2%) [21]                                     | Antifungal activity against Botrytis cinerea [237] | ![Chemical Structure](image) |
|                        |                                                                                 | Fumigation activity against stored-product pest insects [234] |                     |
|                        |                                                                                 | Insecticidal activity against Acanthoscelides obtectus [256] |                     |
| 2-Acetyl-4,4-dimethyl-  | Z. tenuior (2.49%) [94]                                                          | n.f.                | ![Chemical Structure](image) |
| cyclopet-2-enone (51)  |                                                                                 |                     |                     |
| 2-Isopropyl-5-methyl-3-| Z. tenuior [94], Z. tenuior (1.6%) [179]                                        | n.f.                | ![Chemical Structure](image) |
| cyclohexen-1-one (52)  |                                                                                 |                     |                     |
| Pulegone (53)          | Z. tenuior (86.29%–87.06%) [259]                                                | Insecticidal [260]  | ![Chemical Structure](image) |
|                        |                                                                                 | Fumigation activity against stored-product pest insects [234] |                     |
|                        |                                                                                 | Anti-inflammatory activity reviewed [261] |                     |
|                        |                                                                                 | Analgesic activity reviewed [199] |                     |
|                        |                                                                                 | Review on metabolism and toxicity [200] |                     |
| 3-Methyl-6-(1-methyl-ethenyl)-  | Z. tenuior (0.3%–1%) [94,259]                                                  | n.f.                | ![Chemical Structure](image) |
| 2-cyclohexen-1-one (syn. |                                                                                 |                     |                     |
| Isopiperitenone) (54)  |                                                                                 |                     |                     |
| Carvotanacetone (55)   | Z. tenuior [94]                                                                 | Cytotoxic activity against MCF-7 and Hep-G2 cells [262] | ![Chemical Structure](image) |
|                        |                                                                                 | Antifungal activity against tested phytopathogenic fungi [263] |                     |
| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphus (Percentage Content when Given) | Biological Activity | Chemical Structure |
|-------------------------|---------------------------------------|--------------------|-------------------|
| Menthol (56)            | Z. clinopodioides (0.13%) [11]        | Antifungal against Candida albicans, synergy with fluconazole [239] | ![Menthol](https://example.com/menthol.png) |
|                         | Z. clinopodioides subsp. rigida (0.1%) [21] | Fumigant activity [264] |       |
|                         | Z. clinopodioides subsp. bungeana (0.3%) [201] | Antifungal activity against Candida albicans, synergy with fluconazole [239] | ![Ziziphus](https://example.com/ziziphus.png) |
|                         | Z. tenuior (0.1%) [184] | Antifungal activity against Candida albicans, synergy with fluconazole [239] | ![Methyle acetate](https://example.com/methyle acetate.png) |
| Neo-menthol (58)        | Z. clinopodioides subsp. rigida (2.1%) [21] | Antibacterial activity against Escherichia coli [270] | ![Neo-menthol](https://example.com/neo-menthol.png) |
|                         | Z. clinopodioides subsp. bungeana (0.3%) [201] | Acaricidal activity against Tyrophagus putrescentiae [271] |       |
| Neo-isomenthol (59)     | Z. clinopodioides subsp. bungeana (0.3%) [201] | Sedative in the pentobarbital-induced sleep test in mice [272] | ![Neo-isomenthol](https://example.com/neo-isomenthol.png) |
| Menthol acetate (60)    | Z. clinopodioides (0.1%) [184] | n.f. | ![Menthol acetate](https://example.com/menthol acetate.png) |
| Isomenthol acetate (61) | Z. clinopodioides subsp. rigida (0.5%) [21] | n.f. | ![Isomenthol acetate](https://example.com/isomenthol acetate.png) |
### Table 3. Cont.

| Monoterpenes | Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of *Ziziphus* (Percentage Content when Given) | Biological Activity | Chemical Structure |
|--------------|-------------------------|---------------------------------------------------------------------------------|-------------------|-------------------|
|              |                         | Z. clinopodioides (0.17%–5.56%)                                               | Antibacterial (Bacillus cereus, Micrococcus flavus, S. aureus, Listeria monoceptogenes, E. coli, P. aeruginosa, Proteus mirabilis, Salmonella typhimurium) | ![Chemical Structure](attachment:image1) |
|              |                         | [15,184]                                                                        |                   |                   |
| Thymol (62)  |                         | Z. clinopodioides subsp. rigida (8%)                                           | Antifungal (Penicillium funiculosum and P. ochrochloron, Aspergillus fumigatus, A. niger, A. flavus, A. ochraceus, C. albicans, Trichoderma viride) | ![Chemical Structure](attachment:image2) |
|              |                         |                                                                                 |                   |                   |
|              |                         | Z. tenuior [94]                                                                 | Low antimycotic activity | ![Chemical Structure](attachment:image3) |
|              |                         |                                                                                 | Antiviral (HSV-1)   |                   |
|              |                         |                                                                                 | Antigenotoxic (bleomycin-induced DNA damage) |                   |
|              |                         |                                                                                 | Anti-inflammatory activity in carrageenan-induced paw edema, MPO activity and poritionitis in rats |                   |
|              |                         |                                                                                 | Anti-inflammatory activity in LPS-stimulated mouse mammary epithelial cells via inhibition of the NF-κB and MAPKs signalling pathways |                   |
|              |                         |                                                                                 | Protective effect on radiation-induced apoptosis in Chinese hamster lung fibroblast V79 cells |                   |
|              |                         |                                                                                 | DNA-protective effects against H_{2}O_{2}-induced DNA lesions in human hepatoma HepG2 cells |                   |
|              |                         |                                                                                 | Hepatoprotective effect against t-BHP-induced oxidative damage in Chang liver cells |                   |
|              |                         |                                                                                 | Protective effect against cisplatin-induced nephrotoxicity in rats |                   |
|              |                         |                                                                                 | Protective effect against UVA- and UVB-induced lipid peroxidation in NCTC 2544 cell line |                   |
|              |                         |                                                                                 | Protective effects on cardiovascular system |                   |
|              |                         |                                                                                 | Gastroprotective effects in the acute and chronic ulcer models in rats |                   |
|              |                         |                                                                                 | Positive allosteric modulator of the GABA_{A} receptors in primary cultures of mouse cortical neurons |                   |
|              |                         |                                                                                 | Anti-hyperglycemic and anti-hyperlipidemic activity in high fat-induced type 2 diabetic C57BL/6j mice |                   |
|              |                         |                                                                                 | Protective effect in nephropathy |                   |
|              |                         |                                                                                 | Analgesic activity reviewed |                   |
|              |                         |                                                                                 | Review on metabolism and toxicity |                   |
|              |                         | Z. clinopodioides (0.3%–2.2%)                                                   | Antiviral (HSV-1)   | ![Chemical Structure](attachment:image4) |
|              |                         | [184]                                                                           |                   |                   |
|              | cis-Sabinene hydrate (63)|                                                                                 |                   |                   |
|              | Z. clinopodioides subsp. bungeana [201]                                       |                                                                                 |                   |                   |
Table 3. Cont.

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphus (Percentage Content when Given) | Biological Activity | Chemical Structure |
|-------------------------|----------------------------------------------------------------------------------|---------------------|--------------------|
| **trans-Sabinene hydrate (64)** | Z. clinopodiformis subsp. rigida (0.1%) [21] | Antiviral (HSV-1) [282]; Moderate repellent (against tick Amblyomma americanum) [303] | ![Chemical Structure](image1) |
| | Z. tenuior [94] | | |
| **Z. clinopodiformis (2.7%) [185]** | Z. clinopodiformis subsp. rigida (12.5%) [21] | n.f. | ![Chemical Structure](image2) |
| | Z. tenuior (53.9%) [179] | | |
| **p-Menth-3-en-8-ol (65)** | Anti-inflammatory (in carrageenan-induced edema and inhibition of hyperalgesia induced by L-glutamate and prostaglandin E2 in rats) [311]; anti-inflammatory (through inhibition of the expression of TNF-α and IL-6 in LPS-stimulated RAW 264.7 cells) [312]; anti-inflammatory (in cigarette smoke-induced ALI in mice through inhibiting NF-κB and MAPKs signalling pathways) [325]; suppression of expression of IL-1β and IL-6 in TNBS-induced colitis in mice [326]; Penetration enhancer [327], increasing of the brain bioavailability of different drugs [326]; Antimycotic (against C. albicans) [307], against M. ramamnianus [308] |
| **Linalool (66)** | Antimicrobial (against Enterobacter cloaceae) [287], against E. coli [233]; Moderate repellent (against tick Amblyomma americanum) [303]; Repellent against mosquitoes [309]; Anti-inflammatory (in cigarette smoke-induced ALI in mice through inhibiting NF-κB activation) [313] | ![Chemical Structure](image3) |
| | Z. clinopodiformis (1.8%-7.9%) [184] | Mechanicidal (against snail Oncomelania hupsensis) and cercaricidal (against Schistosoma japonicum) [310]; Anti-inflammatory (in carrageenan-induced edema and inhibition of hyperalgesia induced by L-glutamate and prostaglandin E2 in rats) [311]; anti-inflammatory (through inhibition of the expression of TNF-α and IL-6 in LPS-stimulated RAW 264.7 cells) [312]; anti-inflammatory (in cigarette smoke-induced ALI in mice through inhibiting NF-κB and MAPKs signalling pathways) [325]; suppression of expression of IL-1β and IL-6 in TNBS-induced colitis in mice [326]; Penetration enhancer [327], increasing of the brain bioavailability of different drugs [326]; Antimycotic (against C. albicans) [307], against M. ramamnianus [308] |
| | Z. clinopodiformis subsp. rigida [21] | Protective effect against 1-BOOH induced mutagenesis [194] | |
| | | Review on some effects on cardiovascular system [221]; Sedative and anxiolytic [320]; antidepressant [321]; GABA<sub>A</sub> receptor modulation [322] | |
| | | Analgesic activity reviewed [199] | |
| | | Review on metabolism and toxicity [200] | |
| **Borneol (67)** | Z. clinopodiformis (0.9%-1.2%) [184] | Inhibition of nicotinic acetylcholine receptor [323] | ![Chemical Structure](image4) |
| | | DNA-protective effects against H<sub>2</sub>O<sub>2</sub> in primary rat hepatocytes and testicular cells [324]; Anti-inflammatory in an ALI model in mice through inhibition of the NF-κB and MAPKs signalling pathways [325]; suppression of expression of IL-1β and IL-6 in TNBS-induced colitis in mice [326]; Penetration enhancer [327], increasing of the brain bioavailability of different drugs [326]; Antimycotic (against C. albicans) [307], against M. ramamnianus [308] |
| | | Antiviral (HSV-1) [282] | |
### Table 3. Cont.

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphus (Percentage Content when Given) | Biological Activity | Chemical Structure |
|------------------------|-------------------------------------------------------------------------------------|---------------------|--------------------|
| α-Terpineol (66)       | Z. tenax (0.14%) [202]                                                             | Vasorelaxant effect on rat thoracic aorta artery rings [330] | [Chemical Structure Image] |
|                        | Z. tenax (0.14%) [202]                                                             | Positive modulation of the activation of GABA_A receptors [331] |                     |
|                        | Z. tenax (0.14%) [202]                                                             | Potentiation of Sc-C-induced apoptosis in human hepatocellular carcinoma cells [332] |                     |
|                        | Z. tenax (0.14%) [202]                                                             | Prolonging anaesthesia time of propofol by inhibiting its glucuronidation [333] |                     |
| Bornyl acetate (69)    | Z. clinopoides (3.3%) [184]                                                       | Antifungal (against Pyrenophora arenaria) [334] | [Chemical Structure Image] |
|                        | Z. clinopoides (3.3%) [184]                                                       | Insecticidal against Callosobruchus chinensis and Sitophilus oryzae [228] |                     |
|                        | Z. clinopoides (3.3%) [184]                                                       | Anti-inflammatory in an ALI model in mice [335] and in human chondrocytes [336] |                     |
|                        | Z. clinopoides (3.3%) [184]                                                       | Antiabortion in pregnant mice [337] |                     |
|                        | Z. clinopoides (3.3%) [184]                                                       | Cytotoxic (Eca-109, HepG2, HT29, MDA-MB-231, PC-3, SGC7901, SW1990 and U2-OS) and a normal cell line (HL-7702) [338] |                     |
| Terpinen-4-ol (70)     | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Sedative and anæsthetic (on silver catfish juveniles) [339], depressant effect on the CNS and significant anticonvulsant activity probably due to interaction with GABA receptors [340,341] | [Chemical Structure Image] |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Low inhibition of acetylcholinesterase and butyrylcholinesterase [224] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Relase effect on vascular smooth muscle [342] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Review on some effects on cardiovascular system [221] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Anticancer (melanoma) [343], antiproliferative activity in two murine cancer cell lines through induction of necrosis and cell cycle arrest [344], induction of apoptosis in non-small cell lung cancer [345], anti-tumoral activity in human melanoma cells by induction of caspase-dependent form of apoptosis [346] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Antiviral activity against influenza APR8 virus subtype H1N1 [235] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Anti-inflammatory (inhibition of NO production in LPS-stimulated RAW-264.7 macrophages) [223] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Anti-inflammatory [216], anti-inflammatory activity in a murine model of oral candidiasis [347], suppression of the production of TNFα, IL-1β, IL-6, IL-10 and PGE2 by LPS-activated monocytes [348] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Antibacterial against MRSA and CoNS [349] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Low antinemotocidal activity [381] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Antimycotic (C. albicans) [307,350] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Trypanocidal activity against Trypanosoma brucei [222] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Insecticidal (against L. serricorne) [351] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Antifungal [187,390,392], antimicrobial activity [306] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Antiviral activity against influenza APR8 virus subtype H1N1 [235] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Enhancement of GABA modulation [355] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Anticancer (melanoma cells) [343] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Insecticidal (against L. serricorne) [351] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Inhibition of the acetic acid-induced writhing and formalin-induced nociception in mice [354] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Analgesic activity reviewed [199] |                     |
|                        | Z. clinopoides (0.36%-18.2%) [15,184]                                              | Review on metabolism and toxicity [200] |                     |
| 1,8-Cineole (72)       | Z. clinopoides (5.4%–21.6%) [185]                                                 | Antimicrobial activity (MDR resistant bacteria) [355] | [Chemical Structure Image] |
|                        | Z. clinopoides (5.4%–21.6%) [185]                                                 | Hypocholesteremic (through inhibition of HMG-CoA reductase and conversion of squalene to lanosterol [319] |                     |
|                        | Z. clinopoides (5.4%–21.6%) [185]                                                 | Analgesic activity reviewed [199] |                     |
|                        | Z. clinopoides (5.4%–21.6%) [185]                                                 | Review on some effects on cardiovascular system [221] |                     |
|                        | Z. clinopoides (5.4%–21.6%) [185]                                                 | Review on metabolism and toxicity [200] |                     |
### Table 3. Cont.

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphus (Percentage Content when Given) | Biological Activity | Chemical Structure |
|-------------------------|-----------------------------------------------------------------------------------|---------------------|--------------------|
| Carvacrol (73) Z. clinopodioides (8.7%) [184], Z. clinopodioides (52.7%) [183] | Antifungal (Penicillium funiculosum and P. ochrochloron, Aspergillus fumigatus, A. niger, A. flavus, A. ochraceus, C. albicans, T. verrucosus) [187,273,277] | Low antinematocidal activity [281] | ![Carvacrol](image) |
| Ziziphoroside A (4) | Antileishmanial (against L. chagasi) [279] | Review on synergic effect with antibiotics [132] | ![Ziziphoroside A](image) |
| | Cytotoxic (HeLa, B16, MCF-7, 3T3, MRC-5 cells) [284], against P815 and PBMC [284], antiproliferative effects on a human metastatic breast cancer cell line, MDA-MB 231 [360]; induction of apoptosis in HL-60 and Jurkat cells by mitochondria-mediated pathway through the involvement of caspase-3 [361] | DNA-protective effects against H$_2$O$_2$-induced DNA lesions in human hepatoma HepG2 cells [295], antioxidant [273,297,299], anti-inflammatory (inhibition of NO production in LPS-stimulated RAW-264.7 macrophages) [223], anti-inflammatory effect by reducing the production of IL-1β and prostanoids, possibly through the induction of IL-10 release [384], Anti-generotic [287] | ![Ziziphoroside](image) |
| | Anti-inflammatory effect through inhibition of edema induced by carrageenan, histamine, serotonin or PGE$_2$; against Anopheles gambiae Anxiolytic, GABA$_A$ receptor modulation [322,365] | Bronchodilatory effect in guinea pigs [386] | ![Bronchodilatory](image) |
| | Antinociceptive activity in mice in the acetic acid-induced abdominal constriction, formalin and hot-plate tests [367] | Acetyl- and butyrylcholinesterase inhibitory activity [269,368] | ![Acetyl- and butyrylcholinesterase](image) |
| | DNA-protective effects against human metastatic breast cancer cell line, MDA-MB 231 [360]; induction of apoptosis in HL-60 and Jurkat cells by mitochondria-mediated pathway through the involvement of caspase-3 [361]| Analgesic activity reviewed [199] | ![Analgesic](image) |
| | Review on anti-inflammatory, antioxidant, and immunological effects [292] | Review on some effects on cardiovascular system [221] | ![Review on cardiovascular](image) |
| | Review on some effects on cardiovascular system [221] | General reviews on 73 [369,370] | ![General reviews on cardiovascular](image) |
| 2-Methyl-5-[(1-methyl-ethyl)phenol acetate (syn. carvacryl acetate) (74) Z. tenius [94] | Anthelmintic Haemonculus contortus [371] | Anthelmintic Haemonculus contortus [371] | ![Anthelmintic Haemonculus contortus](image) |
| | Anti-inflammatory effect through inhibition of edema induced by carrageenan, histamine, serotonin or PGE$_2$ [372] | Anti-inflammatory effect through inhibition of edema induced by carrageenan, histamine, serotonin or PGE$_2$ [372] | ![Anti-inflammatory](image) |
| | Anxiolytic-like effect probably through acting on the GABAergic system [373,374] | Anxiolytic-like effect probably through acting on the GABAergic system [373,374] | ![Anxiolytic-like effect](image) |
| trans- p-Mentha-2,6-dienol (syn. trans-leopiperitenol) (75) Z. tenius [94] | n.f. | n.f. | ![n.f.](image) |
Ziziphoroside C (81) Z. clinopodioides [4] Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4]

**Table 3. Cont.**

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphus (Percentage Content when Given) | Biological Activity | Chemical Structure |
|-------------------------|-----------------------------------------------------------------------------------|---------------------|--------------------|
| cis-Verbenol (76)       | Z. clinopodioides subsp. rigida (0.1%) [21]                                      | Antibacterial (multi-drug resistant E. coli) [329] | ![Chemical Structure of cis-Verbenol](attachment) |
|                         |                                                                                   | Insecticidal activity (against Latasaemus serricornus) [351] |                     |
|                         |                                                                                   | GABA<sub>A</sub> receptor modulation [322] |                     |
|                         |                                                                                   | Repellent activity against *Anopheles gambiَ* [375] |                     |
|                         |                                                                                   | Anti-ischemic and anti-inflammatory activity [376] |                     |
| trans-Verbenol (77)     | Z. clinopodioides subsp. rigida (0.1%) [21]                                      | Antibacterial (multi-drug resistant E. coli) [329] | ![Chemical Structure of trans-Verbenol](attachment) |
|                         |                                                                                   | GABA<sub>A</sub> receptor modulation [322] |                     |
| Cuminyl aldehyde (syn. cumaldehyde) (78) | Z. clinopodioides subsp. rigida (0.8%) [21]                                      | Tyrosinase inhibitory activity [377] | ![Chemical Structure of Cuminyl aldehyde](attachment) |
|                         |                                                                                   | Suppression of melanin formation in cultured murine B16-F10 melanoma cells [378] |                     |
|                         | Z. clinopodioides (0.12%–0.24%) [15]                                             |                     |                     |
| Ziziphoroside A (79)    | Z. clinopodioides [4]                                                             | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] | ![Chemical Structure of Ziziphoroside A](attachment) |
| Ziziphoroside B (80)    | Z. clinopodioides [4]                                                             | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] | ![Chemical Structure of Ziziphoroside B](attachment) |
| Ziziphoroside C (81)    | Z. clinopodioides [4]                                                             | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] | ![Chemical Structure of Ziziphoroside C](attachment) |
| Schizonepetoside C (82) | Z. clinopodioides [4]                                                             | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] | ![Chemical Structure of Schizonepetoside C](attachment) |
| Schizonepetoside A (83) | Z. clinopodioides [4]                                                             | Some inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] | ![Chemical Structure of Schizonepetoside A](attachment) |
| 9-O-Glucopyranosyl-p-menthan-3-one (84) | Z. clinopodioides [4]                                                             | Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4] | ![Chemical Structure of 9-O-Glucopyranosyl-p-menthan-3-one](attachment) |
### Monoterpenes

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphus (Percentage Content when Given) | Biological Activity | Chemical Structure |
|------------------------|------------------------------------------------------------------------------------|---------------------|--------------------|
| 4α,7α,7αα-Nepeta-lactone (85) | *Z. tenuior* (0.5%) [94,179] | Some activity against *Helicobacter pylori* [379] and repellent activity against mosquitoes [380] | ![](image) |

### Sesquiterpenes

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphus (Percentage Content When Given) | Biological Activity | Chemical Structure |
|------------------------|------------------------------------------------------------------------------------|---------------------|--------------------|
| Germacrene B (86)      | *Z. clinopodioides* (1.1%) [11] | n.f. | ![](image) |

**Table 3. Cont.**
| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphora (Percentage Content When Given) | Biological Activity | Chemical Structure |
|-------------------------|-----------------------------------------------------------------|---------------------|-------------------|
| Caryophyllene oxide (β-caryophyllene oxide) (90) | Z. clinopodioides (0.5%) [184] | Antithermic [187], antifungal [308,384], antimicrobial [385] | ![Chemical Structure](image1.png) |
|                         | Z. tenuior (0.11%–0.32%) [94,179,202] | Modest cytotoxic activity against tested human tumor cell lines [387] | ![Chemical Structure](image2.png) |
|                         | Z. tenuior (0.2%) [184] | Anti-cancer effects through the modulation of the PI3K/AKT/mTOR/S6K1 and MAPK signalling [388] | ![Chemical Structure](image3.png) |
| Caryophyllene (syn. β-caryophyllene, trans-caryophyllene, (E)-caryophyllene) (91) | Z. tenuior (0.22%) [94,179] | Antifungal, antibacterial [187] | ![Chemical Structure](image4.png) |
|                         | Z. tenuior (0.2%) [184] | Antiprotozoal (T. cruzi, L. infantum) [390] | ![Chemical Structure](image5.png) |
|                         | Z. tenuior (0.2%) [184] | Antihyperglycemic effect by decreasing blood glucose and increasing plasma insulin in diabetic rats [391] | ![Chemical Structure](image6.png) |
|                         | Z. tenuior (0.2%) [184] | Antioxidant effect and inhibition of 5-lipoxygenase in CCL4-induced fibrosis in rats [392] | ![Chemical Structure](image7.png) |
|                         | Z. tenuior (0.2%) [184] | Anti-inflammatory effect through the inhibition of TNFα and PGE2 and it is also effective in reducing PAF-, bradykinin-, ovoalbumin-induced mouse paw edema [393,394] | ![Chemical Structure](image8.png) |
| α-Humulene (syn. α-Caryophyllene) (92) | Z. clinopodioides (2.7%–4.5%) [184] | Antimicrobial activity against Propionibacterium acnes (MIC of 3.13 µg/mL) [395] | ![Chemical Structure](image9.png) |
|                         | Z. clinopodioides (2.7%–4.5%) [184] | Antiproliferative activity against several cancer cell lines (MCF-7, PC-3, M4BEU, CT-26, human amelanotic melanoma cell line C32, renal cell adenocarcinoma ACHN, hormone-dependent prostate carcinoma LNCaP; A-549 and human colon adenoarcinoma cell line DLD-1) [396–401] | ![Chemical Structure](image10.png) |
| δ-Cadinene (93) | Z. tenuior [94] | Antimicrobial activity against Streptococcus pneumoniae strains resistant to β-lactamic antimicrobials (MIC of 31.25 µg/mL) [402] | ![Chemical Structure](image11.png) |
|                         | Z. tenuior [94] | Antibacterial activity against Propionibacterium acnes (MIC of 3.13 µg/mL) [395] | ![Chemical Structure](image12.png) |
| δ-Cadinene (93) | Z. tenuior [94] | Antileishmanial effect against L. donovani [403] | ![Chemical Structure](image13.png) |
| τ-Cadinol (94) | Z. tenuior [94] | Weak antmite activity against Dermatophagoides pteronyssinus [404] | ![Chemical Structure](image14.png) |
|                         | Z. tenuior [94] | Good antifungal activity against brown rot fungi Lasioderma serricorne and weak antifungal activity against white rot fungi Coriolus versicolor [405] | ![Chemical Structure](image15.png) |
|                         | Z. tenuior [94] | Anti-wood-decay fungal activity [274,406] | ![Chemical Structure](image16.png) |
| Patchouli alcohol (95) | Z. clinopodioides (0.1%–1.04 %) [15] | Anti-inflammatory activity through inhibition of over-expression of iNOS and IL-6 in LPS-stimulated RAW264.7 and TNF-a HT-29 cells [407,408], anti-inflammatory effect in vivo in rats [409] | ![Chemical Structure](image17.png) |
|                         | Z. clinopodioides (0.1%–1.04 %) [15] | Gastroprotective [410] | ![Chemical Structure](image18.png) |
|                         | Z. clinopodioides (0.1%–1.04 %) [15] | Review on metabolism and toxicity [200] | ![Chemical Structure](image19.png) |
Molecules 2016, 21, 826 26 of 53

Table 3. Cont.

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of Ziziphus (Percentage Content When Given) | Biological Activity | Chemical Structure |
|-------------------------|------------------------------------------------------------------------------------|---------------------|--------------------|
| (Z)-6,10-dimethyl-5,9-undecadien-2-one (syn. Z-geranylacetone, nerylacetone) | Z. tenuior [94] | n.f. | ![Chemical Structure](image1) |
| Cyclohexane, 1-ethenyl-1-methyl-2-(1-methylthienyl)-4-(1-methylthylidene) (97) | Z. tenuior [94] | n.f. | ![Chemical Structure](image2) |
| Spathulenol (98) | Z. tenuior [94] | Antimicrobial activity against S. aureus and P. mirabilis [385] | ![Chemical Structure](image3) |
| Bicyclo[5.2.0]no-nane, 2-methylene-4,8,8-tri-methyl-4-vinyl (99) | Z. tenuior [94] | Antimicrobial, anti-inflammatory, antihyperlipidemic, antioxidant activities [411] Repellent activity against Tribolium castaneum and Myzus persicae [412] | ![Chemical Structure](image4) |
| 2-Methylene-6,8,8-trimethyl-tricyclo-[5.2.2.0(1,6)]undecan-3-ol (100) | Z. tenuior [94] | n.f. | ![Chemical Structure](image5) |
| Ar-turmerone (101) | Z. tenuior [94] | Significant repellent action against S. zearali; and toxic effect against Spodoptera frugiperda [413], insecticidal activities against Nilaparvata lugens and Plutella xylostella [414] Inhibition of platelet aggregation induced by collagen (IC50, 14.4. µM) and arachidonic acid (IC50, 43.6. µM) and no effect on PAF and thrombin-induced platelet aggregation on washed rabbit platelets [415]; anti-inflammatory effects through blocking of NF-κB, JNK and p38 MAPK signalling pathways in amyloid β-stimulated microglia [416] Review on activity [417] | ![Chemical Structure](image6) |
Essential oils are almost always complex mixtures of numerous substances, and therefore their biological effects are often described as the result of a synergism of all molecules or they mirror major activities of molecules present at the highest concentrations [418]. Moreover, the synergistic action is beneficial because the bacteria can undergo adaptation to maintain their membrane functionality in the presence of sub-inhibitory concentrations of antibacterial compounds and the resistance can occur, but the complex action of essential oil can help suppress this resistance [419].

Therefore, only the biological activities of essential oils in their entirety or of their main compounds have usually been evaluated. There are some reports about bioactivities of Ziziphora essential oils, mainly connected with evaluation of antibacterial activity. Moreover, antioxidant properties and anti-inflammatory effect was evaluated using different methods. 5-LOX was inhibited by Z. clinopodioides essential oil (could be due to the presence of compounds structurally related to fatty acids serving as substrate of LOX) [420].

Generally, the major compounds reflect the biophysical and biological characteristics of the parent essential oils quite well (as visible for example for Origanum oil and carvacrol [73] [421]), and the exhibition of their effects depends on their concentration [422,423]. The very complex mixture of compounds present in essential oil also strongly affects the smell, thickness, texture, colour and cell penetration [424], lipophilic or hydrophilic attraction and fixation on cell walls and membranes, and cellular distribution [418]. Therefore, it is sometimes better to analyse the activity of the entire essential oil and compare it with the activity of pure main components. However, some reports highlight the antagonism of single components of essential oil [281,425], so the information about the activity of pure compounds could be useful. As visible from Table 3, we tried to summarize all information about biological effects of compounds present in Ziziphora essential oils available in recent literature, but for some compounds the information is missing or it is scarce.

Reports on the essential oils of different Ziziphora species often discuss their antibacterial activity. The essential oils obtained from different Kazakh Ziziphora species are generally rich in oxygenated monoterpene (see Table 3); their antibacterial effect can be attributed to the presence of these compounds; however, this effect is not the consequence of the presence of oxygenated monoterpenes only. Z. clinopodioides essential oils were found to be effective against both Gram-negative and Gram-positive bacterial species [184,426]. The presence of thymol (62) could be responsible for the antibacterial activity. The activity of Z. tenuior essential oil was lower [426]. Similar results have been presented by Salehi et al. [21], showing good activity of Z. clinopodioides subsp. rigida essential oil against several bacterial strains (with the exception of insensitive P. aeruginosa). Thymol (62) and pulegone (53) showed at least partial responsibility for the antibacterial effects of these materials. Also, the assays carried out on Z. clinopodioides subsp. bungeana essential oils showed activity against both Gram-positive and negative bacterial species, and pulegone (53) and 1,8-cineole (72) were assigned as compounds responsible for the effect [201]. The high concentration of pulegone (53) is mentioned when the antimicrobial activity of essential oils is analysed: it showed activity especially against C. albicans and S. typhimurium. C. albicans was found to be susceptible to pulegone (53), which was found to be twice as effective as nystatin [427,428].

In other test, the antibacterial activity of essential oil and methanolic extract from Z. clinopodioides was compared using 52 Gram-positive and Gram-negative bacterial species, with disc diffusion method [11]. Both tested materials varied in level of activity, with much higher activity of essential oil. Pulegone (53), limonene (38), and piperitone (45) appeared to be the most active substances; however, further information about antibacterial activity of these compounds is not abundant.

We attempted to summarise compounds found in the literature with the antibacterial effect of Ziziphora essential oils and, if possible, their underlying mechanisms (Table 3). Carvacrol (73) and thymol (62) are placed in the first place, as their antibacterial and antiseptic effect is well known [429]. Their synergic action has been described previously and is well reviewed [369]. Carvacrol (73) acts on B. cereus via depletion of intracellular ATP pool, changes the membrane potential and increase the permeability of membrane for protons and potassium. Carvacrol (73) integrates into the lipidic
monolayer of the cell membrane, changes its fluidity and damaging its functions [430]. There are evidences of other mechanisms of antibacterial effect, such as interaction with DNA. Moreover, application of carvacrol (73) has been found to inhibit the formation of bacterial biofilm, which is one of the mechanisms of bacterial resistance [369].

Thymol (62), an aromatic p-menthane type monoterpen phenol, isomeric to carvacrol (73), is established as a good antimicrobial agent, interacting both with outer and inner cytoplasmic cell membranes via incorporation of the polar head group region into the lipid bilayer. This interaction changes the properties of the cell membrane and leads to its increased permeability/disintegration [431–433]. Moreover, thymol (62) can also up- or down-regulate the genes encoding the outer membrane protein synthesis. Beside this, it is able to inhibit the enzymes involved in protection against thermal stress, to affect the synthesis of ATP or to alter citric acid metabolic pathways [434,435].

As mentioned above, carvacrol (73) and thymol (62) exert a synergic effect, similar to many other combinations of components of essential oils against different common human pathogens (carvacrol/thymol (73/62), terpinene-4-ol/myrcene (70/31), carvacrol/p-cymene (73), eugenol/thymol (25/62), eugenol/carvacrol (25/73), cinnamaldehyde/eugenol (106/25), citronellol/geraniol and others) [436–438]. The synergic action of p-cymene and carvacrol (73) combination is based on the high affinity of p-cymene to the cytoplasmic membrane and its bonding to the membrane causes its expansion, altering its potential and resulting in its higher sensitivity to the action of carvacrol (73) [358]. Some of these combinations of compounds with synergic activities are also present in Ziziphora essential oils. The mechanism of thymol (62) and carvacrol (73) synergism was also elucidated and reviewed [132,439]; however, the mechanistic studies describing the mechanisms of synergy are relatively scarce. Owing to their hydrophobic nature, 73 and 62 interact with the lipid bilayer of cytoplasmic membranes, causing loss of integrity and leakage of cellular material. This effect can, in general, increase the permeability of the membrane to other antimicrobial compounds by general disintegration of the membrane or by formation of a large number of pores.

The synergic activity of some terpenoids can be also observed for other organisms than bacteria, e.g., Meloidogyne incognita [440]. Synergic activity was observed also during development of insecticides (pulegone (53)/perillaldehyde) [260].

Of note, essential oil components of the thymol (61) and carvacrol (72) type can act as antagonists, as several essential oils showed lower activity than their single monoterpenic components [281]. The review of Bassolé and Juliani [439] showed some examples of synergic, additive or even antagonistic activity of well-known components of essential oils in different bacterial species.

Carvacrol (72) and thymol (61) are often mentioned as inhibitors of growth of food-borne pathogens. These pathogens are represented for example by different strains of Salmonella, Shigella, E. coli or Clostridium. The activity of the essential oils of Z. tenuior and Z. clinopodioides against food-borne bacteria has been proven by Aliakbarlu and Shameli [426]. Together with the results of experiments on the antiradical activity of Z. clinopodioides essential oil, which showed better activity than Z. tenuior [426], Z. clinopodioides essential oils can be seen as promising food preservatives. This observation is supported by some other reports that examined the single components identified in Ziziphora essential oils (Table 3).

The hypolipidemic activity of aromatic water obtained by mixing the Z. tenuior essential oil in water was proven in tests on cholesterol-fed rabbits. However, the levels of measured parameters of hypercholesterolemia were not restored to basal levels [202]. Several patent applications cover the usage of Ziziphora in the treatment of some cardiovascular diseases. It is clear that the components of essential oils obtained from Ziziphora species can affect the cardiovascular system, as visible from data reviewed in Table 3. The cardiovascular activities of thymol (61), carvacrol (72), limonene (38), α-terpineol (71), terpinen-4-ol (70), linalool (66) and menthol (56) were reviewed by Santos et al. [221]; however, this review examined a limited number of literature sources. The effects of linalool (66) were tested in a human study, and the activity of several compounds (72, 38, 56, 61, 70 and 71) was examined in animal studies.
Table 4. Miscellaneous substances isolated from Kazakhstan *Ziziphora* species (N.f.—not found).

| Name of Compound and ID | Isolation/Detection in Kazakhstan spp. of *Ziziphora* (Percentage Content When Given) | Biological Activity | Chemical Structure |
|-------------------------|--------------------------------------------------------------------------------------|---------------------|--------------------|
| Styrene (102)           | *Z. tenuior* [94]                                                                   | n.f.                | ![Styrene](image)   |
| Benzaaldehyde (103)     | *Z. tenuior* [94]                                                                   | Weak antifungal activity against wood decay fungi [441]         | ![Benzaaldehyde](image) |
| 2-Methyl-3-methylbutyl-butanoic acid ester (104) | *Z. tenuior* [94]                                                                   | Antimicrobial activity against *Listeria monocytogenes* and *Salmonella typhimurium* [442] | ![2-Methyl-3-methylbutyl-butanoic acid ester](image) |
| *n*-Amyl isovalerate (105) | *Z. tenuior* [94]                                                                   | n.f.                | ![n-Amyl isovalerate](image) |
| 3-Phenyl-2-propanal (syn. cinnamaldehyd) (106) | *Z. tenuior* [94]                                                                   | Antibacterial, antifungal, antidiabetic, anti-inflammatory, antiproliferative activities ([132,443] Inhibition of tyrosin kinase [129] | ![3-Phenyl-2-propanal](image) |
| 2,4,4,6-Tetramethyl-6-phenyl-1-heptene (107) | *Z. tenuior* [94]                                                                   | n.f.                | ![2,4,4,6-Tetramethyl-6-phenyl-1-heptene](image) |
| Benzophenone (108)      | *Z. tenuior* [94]                                                                   | Photosensitization of lipid peroxidation due to H-abstraction by its long lived triplet state [444] | ![Benzophenone](image) |
Photosensitization of lipid peroxidation due to H-abstraction by its long lived triplet state [444] Could be effective repellent against Anopheles species [445] Increasing of total cholesterol level [448] Reduction of LDL cholesterol [448] Weak inhibitory activity on NO production stimulated by LPS and IFN-γ in RAW 264.7 cells [4]
Further, linalool (66) and 1,8-cineol (72) showed hypcholesterolemic activity via inhibition of HMG-CoA reductase and inhibition of cholesterol synthesis [318,319]. Endo-borneol (68) exerts a vasorelaxant effect on rat thoracic aorta artery rings [330] and terpin-4-ol (70) has a relaxant effect on vascular smooth muscle [332].

Several components of Ziziphora essential oils were tested and found to possess antioxidant activity, proven in both in vitro and in vivo assays. For example, monoterpenic α-terpinene (36), terpinolene (37) [217,218], thymol (62) [293], borneol (67) [324], carvacrol (73) [273,294,297,299], and sesquiterpenic caryophylene (91) [392] were found to possess antioxidant activity. The antioxidant activity of Lamiaceae essential oils is known, so they can be used in their entirety or their single compounds can be used as food preservatives; moreover, their antibacterial activity and relative non-toxicity makes them more beneficial than some synthetic antioxidants.

Potential Toxicity

Monoterpenic pulegone (53) is present in many Lamiaceae plants. It is commonly connected with potential toxic effect of so called pennyroyal oil. In high doses, it can cause hepatic failure, central nervous system toxicity, gastritis, renal and pulmonary toxicity, and, in very serious cases, death [451,452]. Assays carried out on mice showed its hepatotoxicity and pulmonary toxicity [451,453]. The toxic potential of pulegone (53) is connected to its extensive metabolism in liver, which includes its oxidation to menthofuran, p-cresol and other compounds. These compounds can be further metabolized and cause depletion of glutathione; then, they can covalently bind to proteins and modify their function, causing cell injury [454].

3. Conclusions

The traditional medicine of Kazakhstan uses Ziziphora species (Lamiaceae) to combat several diseases. Especially, Z. bungeana Lam. and Z. clinopodioides Lam. are used for the treatment of illnesses connected with cardiovascular system or to combat different infections. We gathered information about four Kazakh Ziziphora species, their traditional utilization and the compounds identified in extracts obtained from these plants. This review presented information about each compound and their bioactivities. We can conclude that as a typical example of the Lamiaceae family, phytochemicals present in Ziziphora are represented especially by monoterpenic essential oil, phenolic substances belonging to the flavonoids and phenolic acids, and triterpenes. The presence of these particular compounds with confirmed activity can be seen as proof of the traditional use and validation of numerous patent applications. We hope that the review on the compounds isolated from Ziziphora, their medicinal uses and published patents will draw the attention of scientists to this very interesting plant with high medicinal potential.

Acknowledgments: Thanks to kontroluje.me for English language corrections.

Author Contributions: K.Š. and M.M. performed the literature search, wrote the manuscript and provided the final corrections. K.Z., Z.S., G.I., L.I. performed the literature search and analyzed sources in Russian language. M.Ž. performed search and provided the final corrections.

Conflicts of Interest: The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

References

1. Bimursaev, A.A. Fitochemitscheskoe Izutchenie Zizifory bungovskoj (Phytochemical Study of Ziziphora bungeana). Dissertation Thesis, Khakh National Medical University, Alma-Ata, Russia, 1985.
2. Xi-wen, L.; Hedge, I.C. Lamiaceae. In Flora of China; Xiwen, Z.W., Raven, P.H., Eds.; Science Press: Beijing, China; Missouri Botanical Garden Press: St. Louis, MO, USA, 1994; Volume 17.
3. Pavlov, N.V. Flora Kazakhstan; Academia nauk KazSSR: Almaty, Russia, 1964.
4. Furukawa, M.; Oikawa, N.; Imohata, T.; Makino, M.; Ogawa, S.; Iida, T.; Fujimoto, Y.; Kitanaka, S. Monoterpane Glucosides from Ziziphora clinopodioides (Labiatae). Chem. Pharm. Bull. 2012, 60, 397–401. [CrossRef] [PubMed]
5. Tian, S.; Shi, Y.; Zhou, X.; Ge, L.; Upur, H. Total polyphenolic (flavonoids) content and antioxidant capacity of different Ziziphora clinopodioides Lam. Extracts. Pharmacog. Mag. 2011, 7, 65–68.
6. Baytop, T.; Turkiyede, B.; Tedavi, I.U. Yayinlari. Eczacilik Fak 1996, 40, 444.
7. Masournia, M.; Shams, A. Elemental Determination and Essential Oil Composition of Ziziphora clinopodioides and Consideration of its Antibacterial Effects. Asian J. Chem. 2013, 25, 6553–6556.
8. Beikmohammadi, M. The Evaluation of Medicinal Properties of Ziziphora clinopodioides. World Appl. Sci. J. 2011, 12, 1635–1638.
9. Ozturk, Y.; Aydin, S.; Tecik, B.; Baser, K.H.C. Effects of essential oils from certain Ziziphora species on swimming performance in mice. Phytother. Res. 1995, 9, 225–227. [CrossRef]
10. Tarakci, Z.; Coskun, H.; Tuncturk, Y. Some properties of fresh and ripened herby cheese, a traditional variety produced in Turkey. Food Technol. Biotech. 2004, 42, 47–50.
11. Ozturk, S.; Ercisli, S. Antibacterial activity and chemical constitutions of Ziziphora clinopodioides. Food Control 2007, 18, 535–540. [CrossRef]
12. Ghassemi, N.; Ghadianian, M.; Ghaemmaghami, L.; Kiani, H. Development of a Validated HPLC/Photodiode Array Method for the Determination of Isomenthone in the Aerial Parts of Ziziphora tenuior L. Gundishapur J. Nat. Pharm. Prod. 2013, 8, 180–186. [CrossRef] [PubMed]
13. Sezik, E.; Yesilada, E.; Shadidoyatov, H.; Kulivey, Z.; Nigmatullaaev, A.M.; Aripov, H.N.; Takaishi, Y.; Takeda, Y.; Honda, G. Folk medicine in Uzbekistan I. Toshkent, Djizzax, and Samarqand provinces. J. Ethnopharmacol. 2004, 92, 197–207. [CrossRef] [PubMed]
14. Ajiaikebaier, A.; Shi, H.; Abduwuufuer, R. Preparation and Use of Ziziphora General Flavone. Chinese Patent CN 10513448 8 B, 1 August 2012.
15. Ding, W.; Yang, T.; Liu, E.; Tian, S. Effect of different growth stages of Ziziphora clinopodioides Lam. on its chemical composition. Pharmacog. Mag. 2014, 10. [CrossRef]
16. Razmjoue, D.; Zarei, Z. Study on the ecological specifications effects (climate and height) on chemical compounds of Ziziphora medicinal plant essential oil (Ziziphora clinopodioides Lam.) in Fars province, Iran. J. Chem. Biol. Phys. Sci. 2015, 5, 3049–3066.
17. Jamzad, M.; Jamzad, Z.; Mokhber, F.; Ziareh, S.; Yari, M. Variation in essential oil composition of Mentha longifolia var. chlorodichtya Rech.f. and Ziziphora clinopodioides Lam. growing in different habitats. J. Med. Plant Res. 2013, 7, 1618–1623.
18. Sonboli, A.; Atri, M.; Shafiei, S. Intraspecific variability of the essential oil of Ziziphora clinopodioides ssp. rigida from Iran. Chem. Biodivers. 2010, 7, 1784–1789. [CrossRef] [PubMed]
19. Khodaverdi-Samani, H.; Pirbalouti, A.G.; Shirmardi, H.-A.; Malekpoor, F. Chemical composition of essential oils of Ziziphora clinopodioides Lam. (endemic Iranian herb) collected from different natural habitats. Iranian J. Trad. Know. 2011, 15, 57–62.
20. Jeppesen, A.S.; Soelberg, J.; Jäger, A.K. Antibacterial and COX-1 Inhibitory Effect of Medicinal Plants from the Pamir Mountains, Afghanistan. Plants 2012, 1, 74–81. [CrossRef] [PubMed]
21. Salehi, P.; Sonboli, A.; Eftekhari, F.; Nejad-Ebrahimi, S.; Yousefzadi, M. Essential Oil Composition, Antibacterial and Antioxidant Activity of the Oil and Various Extracts of Ziziphora clinopodioides subsp. rigida (BOISS.) RECH.f. from Iran. Biol. Pharm. Bull. 2005, 10, 1892–1896. [CrossRef]
22. Mahboubi, A.; Kamalonejad, M.; Ayatollahi, A.M.; Babaean, M. Total phenolic content and antibacterial activity of five plants of Labiatae against four foodborne and some other bacteria. Iranian J. Pharm. Res. 2014, 13, 559–566.
23. Amini-Shirazi, N.; Hoseini, A.; Rajnbar, A.; Mohammadirad, A.; Khoshakhlagh, P.; Yasa, N.; Abdollahi, M. Inhibition of Tumor Necrosis Factor and Nitrosative/Oxidative Stresses by Ziziphora Clinopodioides (Kahlioni); A Molecular Mechanism of Protection Against Dextran Sodium Sulfate-Induced Colitis in Mice. Toxicol. Mech. Methods 2009, 19, 183–189. [CrossRef] [PubMed]
24. Ghafari, H.; Yasa, N.; Mohammadirad, A.; Dehghan, G.; Zaman, M.J.; Nikfar, S.; Khorasani, R.; Minaie, B.; Abdollahi, M. Protection by Ziziphora clinopodioides of acetic acid-induced toxic bowel inflammation through reduction of cellular lipid peroxidation and myeloperoxidase activity. Hum. Exp. Toxicol. 2006, 25, 325–332. [CrossRef] [PubMed]
25. Azadmehr, A.; Latifi, R.; Mosalla, S.; Hajighaee, R.; Shahnazi, M. Immunomodulatory effects of *Ziziphora tenuior* L. extract on the dendritic cells. *Daru* 2014, 22, 63. [CrossRef] [PubMed]

26. Ghahhari, J.; Vaezi, G.; Shariatifar, N.; Zendehdel, K.M. The study of hydroalcoholic extract of *Ziziphora tenuior* on visceral pain with writhing test in mice. *Horm. Med. Sci.* 2009, 15, 24–29.

27. Ghazanfari, T.; Yaraee, R.; Shams, J.; Rahmati, B.; Radjadian, T.; Hakimzadeh, H. Cytotoxic effect of four herbal medicines on gastric cancer (AGS) cell line. *Food Agric. Immunol.* 2013, 24. [CrossRef]

28. Entezary, A.; Neamatshahi, M.M.; Khodaparast, M.H.H.; Farjam, M.K.N.; Nematshahi, N.; Mohammadi, M. The effects of adding extracts of *Ziziphora* (*Ziziphora tenuior*) as flavoring to chewing gums and the study of the release of caffeine from these extracts. *Eur. J. Exp. Biol.* 2013, 3, 307–312.

29. Sadeghi, B.; Gholamhoseinpoor, F. A study on the stability and green synthesis of silver nanoparticles using *Ziziphora tenuior* (Zt) extract at room temperature. *Spectrosc. Acta Pt. A Mol. Biomol. Spectr.* 2015, 134, 310–315. [CrossRef] [PubMed]

30. Weijun, Y.; Bo, C.; Yan, M.; Tuerxunjiang, D.; Wencai, X.; Chong, L.; Jiang, H.; Hairula, M.; Tuhehongda, Z. Compound *Ziziphora bungeana* Capsule, and Preparation Method and Application Thereof. Chinese Patent CN102895304 (A), 30 January 2013.

31. Ajiaikebaier, A.; Shi, H.; Abuduwufuer, R. Preparation and Use of *Ziziphora* General Flavone. CN 101513448 A, 26 August 2009.

32. Jiang, H.; Yang, W.; Feng, S.; Abudushalamu, M. *Ziziphora clinopodioides* Lam. Extract and Production Method Thereof and Application Thereof in Cardiovascular Drugs. Chinese Patent CN101623324 (B), 1 February 2012.

33. Yang, W.; Hairula, M.; Chong, L.; Jiang, H. *Ziziphora bungeana* Dripping Pills, Production Method Thereof and Application of Dripping Pills as Cardiovascular Medicament. Chinese Patent CN102048813 (A), 11 May 2011.

34. Zheng, S.; Meng, X.; Zhu, H.; Xu, M. Traditional Chinese Medicine Compound for Treating Paroxysmal Supraventricular Tachycardia. Chinese Patent CN102861169 (A), 9 January 2013.

35. Bahaerguli, A.; Zhu, X.; Xu, X.; Bao, E. Kazak Medicine *Ziziphora clinopodioides* Lam. Oral Cavity Spray. Chinese Patent CN101485621 (A), 22 July 2009.

36. Wang, Y.; Ban, X.; He, J.; Huang, B.; Zeng, H.; Jun, T.; Chen, Y. Preparation Method of *Ziziphora clinopodioides* Volatile Oil and Function Thereof of Preventing and Treating Sclerotinia Rot of Rape. Chinese Patent CN102093932 (B), 14 November 2012.

37. Tian, S.; Zhou, X.; Hammulati, W.; Yu, Q.; Liu, H.; Ge, L. *Ziziphora clinopodioides* Lam Fingerprint and Establishment Method Thereof. Chinese Patent CN102662019 (A), 12 September 2012.

38. Mehmood, R.; Imran, M.; Malik, A.; Tareen, R.B. Ziziphorins A and B. New flavonoids from *Ziziphora tenuior*. *Z. Naturforsch. Sect. B J. Chem. Sci.* 2010, 65, 1397–1400. [CrossRef]

39. Senejoux, F.; Demougeot, C.; Kerram, P.; Aisa, H.A.; Berthelot, A.; Bévalot, F.; Girard-Thernier, C. Bioassay-guided isolation of vasorelaxant compounds from *Ziziphora clinopodioides* Lam. (Lamiaceae). *Fitoterapia* 2012, 83, 377–382. [CrossRef] [PubMed]

40. Ye, Y.; Liu, B.Y.; Zou, G.; Aisa, H.A. Chemical constituents of *Ziziphora clinopodioides*. *Chem. Nat. Compd.* 2012, 48, 681–682. [CrossRef]

41. Nabavi, S.M.; Habtemariam, S.; Daglia, M.; Nabavi, S.F. Apigenin and Breast Cancers: From Chemistry to Medicine. *Anti-Cancer Agents Med. Chem.* 2015, 15, 728–735. [CrossRef]

42. Bao, Y.Y.; Zhou, S.H.; Fan, J.; Wang, Q.Y. Anticancer mechanism of apigenin and the implications of GLUT-1 expression in head and neck cancers. *Future Oncol.* 2013, 9, 1353–1364. [CrossRef] [PubMed]

43. Babcook, M.A.; Gupta, S. Apigenin: a promising anticancer agent for the modulation of the insulin-like growth factor (IGF) axis in prostate cancer. *Biomed. Res.* 2012, 23, 55–68.

44. Shukla, S.; Gupta, S. Apigenin: A Promising Molecule for Cancer Prevention. *Pharm. Res.* 2010, 27, 962–978. [CrossRef] [PubMed]

45. Lefort, E.C.; Blay, J. Apigenin and its impact on gastrointestinal cancers. *Mol. Nutr. Food Res.* 2013, 57, 126–144. [CrossRef] [PubMed]

46. Shukla, S.; Gupta, S. Role of apigenin in human health and disease. In *Beer in Health and Disease Prevention*; Preedy, V.R., Ed.; Academic Press: Burlington, MA, USA, 2009; pp. e202–e216.

47. Nabavi, S.F.; Braidy, N.; Habtemariam, S.; Orhan, I.E.; Daglia, M.; Manayi, A.; Gortzi, O.; Nabavi, S.M. Neuroprotective effects of chrysin: From chemistry to medicine. *Neurochem. Int.* 2015, 90, 224–231. [CrossRef] [PubMed]
48. Kasala, E.R.; Bodduluru, L.N.; Madana, R.M.; V, A.K.; Gogoi, R.; Barua, C.C. Chemopreventive and therapeutic potential of chrysin in cancer: Mechanistic perspectives. *Toxicol. Lett.* 2015, 233, 214–225. [CrossRef] [PubMed]
49. Kasala, E.R.; Bodduluru, L.N.; Barua, C.C.; Gogoi, R. Chrysin and its emerging role in cancer drug resistance. *Chem.-Biol. Interact.* 2015, 236, 7–8. [CrossRef] [PubMed]
50. Liu, Y.; Song, X.; He, J.; Zheng, X.; Wu, H. Synthetic derivatives of chrysin and their biological activities. *Med. Chem. Res.* 2014, 23, 555–563. [CrossRef]
51. Tuorkey, M.J. Molecular targets of luteolin in cancer. *Eur. J. Cancer Prev.* 2016, 25, 65–76. [CrossRef] [PubMed]
52. Kapoor, S. Luteolin and its inhibitory effect on tumor growth in systemic malignancies. *Exp. Cell Res.* 2013, 319, 777–778. [CrossRef] [PubMed]
53. Nabavi, S.F.; Braidy, N.; Gortzi, O.; Sobarzo-Sanchez, E.; Daglia, M.; Skalicka-Woźniak, K.; Nabavi, S.M. Luteolin as an anti-inflammatory and neuroprotective agent: A brief review. *Brain Res. Bull.* 2015, 119. [CrossRef] [PubMed]
54. Theoharides, T.C. Luteolin as a therapeutic option for multiple sclerosis. *J. Neuroinflammation* 2009, 6, 29. [CrossRef] [PubMed]
55. Maruoka, H.; Shimoke, K. Mechanisms of neurotrophic activities via low-molecular-weight compounds: Post-transcriptional regulation in PC12 cells and neurons. *Clin. Pharmacol. Biopharm.* 2013, 51, 003. [CrossRef]
56. Kritas, S.K.; Saggini, A.; Varvara, G.; Murmura, G.; Caraffa, A.; Antinolfi, P.; Toniato, E.; Pantalone, A.; Neri, G.; Frydas, S.; et al. Luteolin inhibits mast cell-mediated allergic inflammation. *J. Biol. Reg. Homeos. Ag.* 2013, 27, 955–959.
57. Jiang, D.; Li, D.; Wu, W. Inhibitory effects and mechanisms of luteolin on proliferation and migration of vascular smooth muscle cells. *Nutrients* 2013, 5, 1648–1659. [CrossRef] [PubMed]
58. Xu, T.; Li, D.; Jiang, D. Targeting cell signaling and apoptotic pathways by luteolin: Cardioprotective role in rat cardiomyocytes following ischemia/reperfusion. *Nutrients* 2012, 4, 2008–2019. [CrossRef] [PubMed]
59. Lopez-Lazaro, M. Distribution and biological activities of the flavonoid luteolin. *Mini-Rev. Med. Chem.* 2009, 9, 31–59. [CrossRef] [PubMed]
60. Seelinger, G.; Merfort, I.; Schempp, C.M. Anti-oxidant, anti-inflammatory and anti-allergic activities of luteolin. *Planta Med.* 2008, 74, 1667–1677. [CrossRef] [PubMed]
61. Oganesyan, G.B.; Galstyan, A.M.; Mnatsakanyan, V.A.; Paronikyan, R.V.; Ter-Zakharyan, Y.Z. Phenols and flavonoids of *Ziziphus clinopodioides* and *Satureja atropatana* from the Mediterranean flora. *Khimiya Prirodnykh Soedinenii* 1991, 2, 286–287.
62. Gohari, A.R.; Saeidnia, S.; Gohari, M.R.; Moradi-Afrapoli, F.; Malmir, M.; Hadjiakhoondi, A. Bioactive flavonoids from *Satureja atropatana* and *Ziziphora clinopodioides* flavonoids of *luteolin*. *Planta Med.* 2008, 74, 327–331. [CrossRef] [PubMed]
63. Dugas, A.J.; Castaneda-Acosta, J.; Bonin, G.C.; Price, K.L.; Fischer, N.H.; Winston, G.W. Evaluation of the Total Peroxyl Radical-Scavenging Capacity of Flavonoids: Structure-Activity Relationships. *J. Nat. Prod.* 2000, 63, 327–331. [CrossRef] [PubMed]
64. Bhat, T.A.; Nambiar, D.; Tailor, D.; Pal, A.; Agarwal, R.; Singh, R.P. Acacetin Inhibits In Vitro and In Vivo Angiogenesis and Downregulates Stat Signaling and VEGF Expression. *Cancer Prev. Res.* 2013, 6, 1128–1139. [CrossRef] [PubMed]
65. Liu, L.-Z.; Jing, Y.; Jiang, L.L.; Jiang, X.E.; Jiang, Y.; Rojanasakul, Y.; Jiang, B.H. Acacetin inhibits VEGF expression, tumor angiogenesis and growth through AKT/HIF-1α pathway. *Biochem. Biophys. Res. Commun.* 2011, 413, 299–305. [CrossRef] [PubMed]
66. Kim, C.D.; Cha, J.D.; Li, S.; Cha, I.H. The mechanism of acacetin-induced apoptosis on oral squamous cell carcinoma. *Arch. Oral Biol.* 2015, 60, 1283–1298. [CrossRef] [PubMed]
67. Shim, H.Y.; Park, J.H.; Paik, H.D.; Nah, S.Y.; Kim, D.S.; Han, Y.S. Acacetin-induced apoptosis of human breast cancer MCF-7 cells involves caspase cascade, mitochondria-mediated death signaling and SAPK/JNK1/2-c-Jun activation. *Mol. Cells* 2007, 24, 95–104. [PubMed]
68. Singh, R.P.; Agrawal, P.; Yin, D.; Agarwal, C.; Agarwal, R. Acacetin inhibits cell growth and cell cycle progression, and induces apoptosis in human prostate cancer cells: Structure-activity relationship with linarin and linarin acetate. *Carcinogenesis* 2005, 26, 845–854. [CrossRef] [PubMed]
69. Pan, M.H.; Lai, C.S.; Hsu, P.C.; Wang, Y.J. Acacetin Induces Apoptosis in Human Gastric Carcinoma Cells Accompanied by Activation of Caspase Cascades and Production of Reactive Oxygen Species. *J. Agric. Food Chem.* 2005, 53, 620–630. [CrossRef] [PubMed]
70. Hsu, Y.L.; Kuo, P.L.; Liu, C.F.; Lin, C.C. Acacetin-induced cell cycle arrest and apoptosis in human non-small cell lung cancer A549 cells. *Cancer Lett.* 2004, 212, 53–60. [CrossRef] [PubMed]

71. Warat, M.; Szlisszka, E.; Korzonek-Szlacheta, I.; Kröl, W.; Czuba, Z.P. Chrysins, apigenin and acacetin inhibit Tumor Necrosis Factor-related apoptosis-inducing ligand receptor-1 (TRAIL-R1) on activated RAW264.7 macrophages. *Int. J. Mol. Sci.* 2014, 15, 11510–11522. [CrossRef] [PubMed]

72. Kim, H.R.; Park, C.G.; Jung, J.Y. Acacetin (5,7-dihydroxy-4'-methoxylavone) exhibits in vitro and in vivo anticancer activity through the suppression of NF-κB/Akt signaling in prostate cancer cells. *Int. J. Mol. Med.* 2014, 33, 317–324. [PubMed]

73. Jung, S.K.; Kim, J.E.; Lee, S.Y.; Lee, M.H.; Byun, S.; Kim, Y.A.; Lim, T.G.; Reddy, K.; Huang, Z.; Bode, A.M.; et al. The PI10 subunit of PI3-K is a therapeutic target of acacetin in skin cancer. *Carcinogenesis* 2014, 35, 123–130. [CrossRef] [PubMed]

74. Horibe, I.; Satoh, Y.; Shiota, Y.; Kumagai, A.; Horike, N.; Uesato, S.; Sugie, S.; Obata, K.; Kawahara, H.; et al. Induction of melanogenesis by 4'-O-methylated flavonoids in B16F10 melanoma cells. *J. Nat. Med.* 2013, 67, 705–710. [CrossRef] [PubMed]

75. Ninomiya, M.; Nishida, K.; Tanaka, K.; Watanabe, K.; Koketsu, M. Structure-activity relationship studies of 5,7-dihydroxyflavones as naturally occurring inhibitors of cell proliferation in human leukemia HL-60 cells. *J. Nat. Med.* 2013, 67, 460–467. [CrossRef] [PubMed]

76. Boussouar, A.; Barette, C.; Nadon, R.; Saint-Léger, A.; Broucsault, N.; Ottaviani, A.; Firozhoussen, A.; Lu, Y.; Lafanèchère, L.; Gilson, E.; et al. Acacetin and chrysin, two polyphenolic compounds, alleviate telomeric position effect in human cells. *Mol. Ther. Nucleic Acids* 2013, 2, e116. [CrossRef] [PubMed]

77. Fong, Y.; Shen, K.H.; Chiang, T.A.; Shih, Y.W. Acacetin inhibits TPA-induced MMP-2 and u-PA expressions of human lung cancer cells through inactivating JNK signaling pathway and reducing binding activities of NF-κB and AP-1. *J. Food Sci.* 2010, 75, 30–38. [CrossRef] [PubMed]

78. Shen, K.H.; Hung, S.H.; Yin, L.T.; Huang, C.S.; Chao, C.H.; Liu, C.L.; Shih, Y.W. Acacetin, a flavonoid, inhibits the invasion and migration of human prostate cancer DU145 cells via inactivation of the p38 MAPK signaling pathway. *Mol. Cell. Biochem.* 2010, 333, 279–291. [CrossRef] [PubMed]

79. Patel, K.; Gadewar, M.; Tahilyani, V.; Patel, D.K. A review on pharmacological and analytical aspects of diosmetin: A concise report. *Chin. J. Integr. Med.* 2013, 19, 792–800. [CrossRef] [PubMed]

80. Tian, S.; Yu, Q.; Wang, D.; Upur, H. Development of a rapid resolution liquid chromatography-diode array detector method for the determination of three compounds in *Ziziphora clinopodioides* Lam from different origins of Xinjiang. *Pharmacog. Mag.* 2012, 8, 280–284.

81. Abdurrazak, M.; Rao, M.U.S.; Ado, A.B.; Mohd, K.S.; Thant, Z. Some natural products and their secondary metabolites attributed towards diabetic cure: a review. *Int. J. Pharm. Pharm. Sci.* 2013, 5, 89–95. [CrossRef]

82. Lafanechère, L.; Gilson, E.; et al. Acacetin and chrysin, two polyphenolic compounds, alleviate telomeric position effect in human cells. *Mol. Ther. Nucleic Acids* 2013, 2, e116. [CrossRef] [PubMed]

83. Yoon, Y.P.; Lee, H.J.; Kim, Y.H.; Luyen, B.T.T.; Hong, J.H.; Lee, C.J. Effects of cynaroside, cynarin and linarin on secretion, production and gene expression of airway MUC5AC mucin in NCI-H292 cells. *Nat. Prod. Sci.* 2013, 19, 792–800. [CrossRef] [PubMed]

84. Kim, S.J.; Cho, H.I.; Kim, S.J.; Park, J.H.; Kim, J.S.; Kim, Y.H.; Lee, S.K.; Kwak, J.H.; Lee, S.M. Protective effect of linarin against d-galactosamine and lipopolysaccharide-induced fulminant hepatic failure. *Eur. J. Pharmacol.* 2014, 738, 66–73. [CrossRef] [PubMed]

85. Sivashanmugam, M.; Raghunath, C.; Vetrivel, U. Virtual screening studies reveal linarin as a potential natural inhibitor targeting CDK4 in retinoblastoma. *J. Pharmacol. Pharmacother.* 2013, 4, 256–264. [PubMed]

86. Lou, H.; Fan, P.; Perez, R.G.; Lou, H. Neuroprotective effects of linarin through activation of the PI3K/Akt pathway in amyloid-β-induced neuronal cell death. *Bioorg. Med. Chem.* 2011, 19, 4021–4027. [CrossRef] [PubMed]

87. Fan, P.; Hay, A.E.; Marston, A.; Hostettmann, K. Acetycholinesterase-Inhibitory Activity of Linarin from *Buddleja davidii*, Structure-Activity Relationships of Related Flavonoids, and Chemical Investigation of *Buddleja nitida*. *Pharm. Biol.* 2008, 46, 596–601. [CrossRef]
Molecules 2016, 21, 826

89. Wu, J.; Feng, J.Q.; Zhao, W.M. A new lignan and anti-inflammatory flavonoids from Kerria japonica. J. Asian Nat. Prod. Res. 2008, 10, 435–438. [CrossRef] [PubMed]

90. Fernandez, S.P.; Wasowski, C.; Loscalzo, L.M.; Granger, R.E.; Johnston, G.A.; Paladini, A.C.; Marder, M. Central nervous system depressant action of flavonoid glycosides. Eur. J. Pharmacol. 2006, 539, 168–176. [CrossRef] [PubMed]

91. Fernandez, S.; Wasowski, C.; Paladini, A.; Marder, M. Sedative and sleep-enhancing properties of linarin, a flavonoid-isolated from Valeriana officinalis. Pharmacol. Biochem. Behav. 2004, 77, 399–404. [CrossRef] [PubMed]

92. Yu, J.; Weiwer, M.; Linhardt, R.J.; Dordick, J.S. The role of the methoxyphenol apocynin, a vascular NADPH oxidase inhibitor, as a chemopreventative agent in the potential treatment of cardiovascular diseases. Curr. Vasc. Pharmacol. 2008, 6, 204–217. [CrossRef] [PubMed]

93. ’t Hart, B.A.; Copray, S.; Philippens, I. Apocynin, a low molecular oral treatment for neurodegenerative disease. BioMed. Res. Int. 2014, 298020. [CrossRef]

94. Pakniyat, E.; Mousavi, M. Improvement of GC-MS Analysis of Shahrbabak Cynanchum paniculatum and Acaricidal Changes by Introducing Functional Radicals. Food Sci. Technol. Res. 2013, 19, 609–615. [CrossRef]

95. Kim, M.G.; Yang, J.Y.; Lee, H.S. Acaricidal Potentials of Active Properties Isolated from Kerria japonica. BioMed. Res. Int. 2014, 21

96. Su, P.; Shi, Y.; Wang, J.; Shen, X.; Zhang, J. Anticancer Agents Derived from Natural Cinnamic Acids. Anti-Cancer Agents Med. Chem. 2015, 15, 980–987. [CrossRef]

97. Benalla, W.; Bellahcen, S.; Bnouham, M. Anti diabetic medicinal plants as a source of alpha glucosidase inhibitors. Curr. Diabetes Rev. 2010, 6, 247–254. [CrossRef] [PubMed]

98. Zhu, T.H.; Yu, Y.Y.; Cao, S.W. Tyrosinase inhibitory effects and antioxidant properties of paeonol and its analogues. Food Sci. Technol. Res. 2013, 19, 609–615. [CrossRef]

99. Fuentes, E.; Palomo, I. Mechanisms of endothelial cell protection by hydroxycinnamic acids. Anal. Meth. 2014, 6, 3203–3210. [CrossRef]

100. Bhullar, K.S.; Lassalle-Claux, G.; Touaibia, M.; Rupasinghe, H.P. Antihypertensive effect of caffeic acid and its analogs through dual renin-angiotensin-aldosterone system inhibition. Eur. J. Pharmacol. 2014, 730, 125–132. [CrossRef] [PubMed]

101. Li, Q.L.; Li, B.G.; Zhang, Y.; Gao, X.P.; Li, C.Q.; Zhang, G.L. Three angiotensin-converting enzyme inhibitors from Rabdosia coetsa. Phytomedicine 2008, 15, 386–388. [CrossRef] [PubMed]

102. Silva, T.; Borges, F.; Edraki, N.; Alizadeh, M.; Rupasinghe, H.P. Antihypertensive effect of caffeic acid and its analogs through dual renin-angiotensin-aldosterone system inhibition. Eur. J. Pharmacol. 2014, 730, 125–132. [CrossRef] [PubMed]

103. Chiang, Y.M.; Lo, C.P.; Chen, Y.P.; Wang, S.Y.; Yang, N.S.; Kuo, Y.H.; Shyur, L.F. Ethyl caffeate suppresses NF-κB activation and its downstream inflammatory mediators, iNOS, COX-2, and PGE2 in vitro or in mouse skin. Br. J. Pharmacol. 2005, 146, 352–363. [CrossRef] [PubMed]

104. Yokoyama, T.; Kosaka, Y.; Mizuguchi, M. Inhibitory Activities of Propolis and Its Promising Component, Caffeic Acid Phenethyl Ester, against Amyloidogenesis of Human Transthyretin. J. Med. Chem. 2014, 57, 8928–8935. [CrossRef] [PubMed]

105. Wang, J.; Gu, S.S.; Pang, N.; Wang, F.Q.; Pang, E.; Cui, H.S.; Wu, X.Y.; Wu, F.A. Alkyl caffeates improve the antioxidant activity, antitumor property and oxidation stability of edible oil. PLoS ONE 2014, 9, e95909. [CrossRef] [PubMed]

106. Williams, L.K.; Li, C.; Withers, S.G.; Brayer, G.D. Order and Disorder: Differential Structural Impacts of Myricetin and Ethyl Caffeate on Human Amylase, an Antidiabetic Target. J. Med. Chem. 2012, 55, 10177–10186. [CrossRef] [PubMed]

107. Yokoyama, T.; Kosaka, Y.; Mizuguchi, M. Inhibitory Activities of Propolis and Its Promising Component, Caffeic Acid Phenethyl Ester, against Amyloidogenesis of Human Transthyretin. J. Med. Chem. 2014, 57, 8928–8935. [CrossRef] [PubMed]

108. Wang, J.; Gu, S.S.; Pang, N.; Wang, F.Q.; Pang, E.; Cui, H.S.; Wu, X.Y.; Wu, F.A. Alkyl caffeates improve the antioxidant activity, antitumor property and oxidation stability of edible oil. PLoS ONE 2014, 9, e95909. [CrossRef] [PubMed]

109. Hradkova, I.; Merkl, R.; Smidrlak, J.; Kyselka, J.; Filip, V. Antioxidant effect of mono- and dihydroxyphenols in sunflower oil with different levels of naturally present tocopherols. Eur. J. Lipid Sci. Technol. 2013, 115, 747–755. [CrossRef] [PubMed]
110. Garrido, J.; Gaspar, A.; Garrido, E.; Miri, R.; Tavakkoli, M.; Pourali, S.; Saso, L.; Borges, F.; Firuzi, O. Alkyl esters of hydroxycinnamic acids with improved antioxidant activity and lipophilicity protect PC12 cells against oxidative stress. Biochimie 2012, 94, 961–967. [CrossRef] [PubMed]

111. Frega, N.G.; Boselli, E.; Bendia, E.; Minardi, M.; Benedetti, A. Ethyl caffeate: Liquid chromatography-tandem mass spectrometric analysis in Verdicchio wine and effects on hepatic stellate cells and intracellular peroxidation. Anal. Chim. Acta 2006, 563, 375–381. [CrossRef]

112. Lee, H.N.; Kim, J.K.; Kim, J.H.; Lee, S.J.; Ahn, E.K.; Oh, J.S.; Seo, D.W. A mechanistic study on the anti-cancer activity of ethyl caffeate in human ovarian cancer SKOV-3 cells. Chem.-Biol. Interact. 2014, 219, 151–158. [CrossRef] [PubMed]

113. Amoah, S.K.; Sandjo, L.P.; Kratz, J.M.; Biavatti, M.W. Rosmarinic Acid—Pharmaceutical and Clinical Aspects. Planta Med. 2016, 82, 388–406. [CrossRef] [PubMed]

114. Nabavi, S.F.; Tenore, G.C.; Bagheri, A.; Khaledi, H.K.; Kianpour, M.; Bouali, M.; Pournaghib, A.; Nabavi, S.M. The Cellular Protective Effects of Rosmarinic Acid: From Bench to Bedside. Curr. Neurovasc. Res. 2015, 12, 98–105. [CrossRef] [PubMed]

115. Kim, G.D.; Park, Y.S.; Jin, Y.H.; Park, C.S. Production and applications of rosmarinic acid and structurally related compounds. Appl. Microbiol. Biotechnol. 2015, 99, 2083–2092. [CrossRef] [PubMed]

116. Hossan, M.S.; Rahman, S.; Bashar, A.B.M.A.; Rahmatullah, M. Rosmarinic acid: A review of its anticancer activity and the cardiovascular system. Nutr. J. 2014, 13, 63. [CrossRef] [PubMed]

117. Mahdi, J.; Al-Musayib, N.; Mahdi, E.; Pepper, C. Pharmacological Importance of Simple Phenolic Compounds on Inflammation, Cell Proliferation and Apoptosis with a Special Reference to β-d-Salicin and Hydroxybenzoic Acid. Eur. J. Inflamm. 2013, 11, 327–336.

118. Opgrande, J.L.; Brown, E.E.; Hesser, M.; Andrews, J. Benzoic acid. In Kirk-Othmer Encyclopedia of Chemical Technology, 5th ed.; Seidel, A., Ed.; John Wiley & Sons: Hoboken, New Jersey, NJ, USA, 2004; Volume 3, pp. 625–637.

119. Ina, H.; Yamada, K.; Matsumoto, K.; Miyazaki, T. Effects of benzyl glucoside and chlorogenic acid from Nepenthes mirabilis plant against oxidative stress. Biochimie 2014, 96, 21–28. [CrossRef] [PubMed]

120. Du, S.S.; Yang, K.; Wang, C.F.; You, C.X.; Geng, Z.F.; Guo, S.S.; Deng, Z.W.; Liu, Z.L. Chemical Constituents and Activities of the Essential Oil from Nepenthes mirabilis. Arch. Pharmacal. Res. 2015, 38, 1774–1782.

121. Du, S.S.; Yang, K.; Wang, C.F.; You, C.X.; Geng, Z.F.; Guo, S.S.; Deng, Z.W.; Liu, Z.L. Chemical Constituents and Activities of the Essential Oil from Myristica fragrans against Cigarette Beetle Lasioderma serricorne. Chem. Biodivers. 2014, 11, 1449–1456. [CrossRef] [PubMed]

122. Do Nascimento, A.F.; da Camara, C.A.; da Moraes, M.M.; Ramos, C. Essential oil composition and acaricidal activity of Schinus terebinthifolius from Atlantic forest of Pernambuco, Brazil against Tetramychus urticae. Nat. Prod. Commun. 2012, 7, 129–132. [PubMed]

123. Duman, A.D.; Telci, I.; Dayisoylu, K.S.; Digrak, M.; Demirtas, I.; Alma, M.H. Evaluation of bioactivity of linalool-rich essential oils from Ocimum basilicum and Coriandrum sativum varieties. Nat. Prod. Commun. 2010, 5, 969–974. [PubMed]

124. Wang, W.; Chen, W.; Yang, Y.; Liu, T.; Yang, H.; Xin, Z. New Phenolic Compounds from Tetranychus urticae and Activities of the Essential Oil from Myristica fragrans and the cardiovasular system. J. Agric. Food Chem. 2003, 51, 178–180.

125. Luyen, B.T.T.; Tai, B.H.; Thao, N.P.; Cha, J.Y.; Lee, H.Y.; Lee, Y.M.; Kim, Y.H. Anti-inflammatory components of Chrysanthemum indicum flowers. Bioorg. Med. Chem. Lett. 2015, 25, 266–269. [CrossRef] [PubMed]

126. Mook-Jung, I.; Kim, H.F.; Wenzhe, T.; Tezuka, Y.; Kadota, S.; Nishijo, H.; Jung, M.W. Neuroprotective effects of compounds on the oriental crude drugs, Rhodiola sacra, S. sachalinensis and Tokaku-joki-to, against β-amyloid toxicity, oxidative stress and apoptosis. Biol. Pharm. Bull. 2003, 26, 1101–1104. [CrossRef] [PubMed]

127. Frega, N.G.; Boselli, E.; Bendia, E.; Minardi, M.; Benedetti, A. Ethyl caffeate: Liquid chromatography-tandem mass spectrometric analysis in Verdicchio wine and effects on hepatic stellate cells and intracellular peroxidation. Anal. Chim. Acta 2006, 563, 375–381. [CrossRef]

128. Lee, H.N.; Kim, J.K.; Kim, J.H.; Lee, S.J.; Ahn, E.K.; Oh, J.S.; Seo, D.W. A mechanistic study on the anti-cancer activity of ethyl caffeate in human ovarian cancer SKOV-3 cells. Chem.-Biol. Interact. 2014, 219, 151–158. [CrossRef] [PubMed]

129. Amoah, S.K.; Sandjo, L.P.; Kratz, J.M.; Biavatti, M.W. Rosmarinic Acid—Pharmaceutical and Clinical Aspects. Planta Med. 2016, 82, 388–406. [CrossRef] [PubMed]

130. Nabavi, S.F.; Tenore, G.C.; Bagheri, A.; Khaledi, H.K.; Kianpour, M.; Bouali, M.; Pournaghib, A.; Nabavi, S.M. The Cellular Protective Effects of Rosmarinic Acid: From Bench to Bedside. Curr. Neurovasc. Res. 2015, 12, 98–105. [CrossRef] [PubMed]

131. Kim, G.D.; Park, Y.S.; Jin, Y.H.; Park, C.S. Production and applications of rosmarinic acid and structurally related compounds. Appl. Microbiol. Biotechnol. 2015, 99, 2083–2092. [CrossRef] [PubMed]

132. Hossan, M.S.; Rahman, S.; Bashar, A.B.M.A.; Rahmatullah, M. Rosmarinic acid: A review of its anticancer action. World J. Pharm. Pharm. Sci. 2014, 3, 57–70.

133. Juurlink, B.H.J.; Azouz, H.J.; Aldalati, A.M.Z.; Altinawi, B.M.; Ganguly, P. Hydroxybenzoic acid isomers and the cardiovascular system. Nutr. J. 2014, 13, 63. [CrossRef] [PubMed]

134. Mahdi, J.; Al-Musayib, N.; Mahdi, E.; Pepper, C. Pharmacological Importance of Simple Phenolic Compounds on Inflammation, Cell Proliferation and Apoptosis with a Special Reference to β-d-Salicin and Hydroxybenzoic Acid. Eur. J. Inflamm. 2013, 11, 327–336.

135. Opgrande, J.L.; Brown, E.E.; Hesser, M.; Andrews, J. Benzoic acid. In Kirk-Othmer Encyclopedia of Chemical Technology, 5th ed.; Seidel, A., Ed.; John Wiley & Sons: Hoboken, New Jersey, NJ, USA, 2004; Volume 3, pp. 625–637.

136. Ina, H.; Yamada, K.; Matsumoto, K.; Miyazaki, T. Effects of benzyl glucoside and chlorogenic acid from Prunus munce on angiotensin converting enzyme, aldosterone and corticosterone levels in rat plasma. Nat. Med. 2003, 57, 178–180.
130. Bahramsoltani, R.; Farzaei, M.H.; Farahani, M.S.; Rahimi, R. Phytochemical constituents as future antidepressants: A comprehensive review. Rev. Neurosci. 2015, 26, 699–719. [CrossRef] [PubMed]

131. Freires, I.A.; Denny, C.; Benso, B.; de Alencar, S.M.; Rosalen, P.L. Antibacterial activity of essential oils and their isolated constituents against cariogenic bacteria: A systematic review. Molecules 2015, 20, 7329–7358. [CrossRef] [PubMed]

132. Langeveld, W.T.; Veldhuizen, E.J.A.; Burt, S.A. Synergy between essential oil components and antibiotics: A review. Cr. Rev. Microbiol. 2014, 40, 76–94. [CrossRef] [PubMed]

133. Sánchez-Quesada, C.; López-Biedma, A.; Warleta, F.; Campos, M.; Beltrán, G.; Gaforio, J.J. Bioactive derivatives as anticancer agents. J. Pharmacogn. Phytochem. 2013, 2, 214–222. [CrossRef]

134. Kashyap, D.; Tuli, H.S.; Sharma, A.K. Ursolic acid (UA): A metabolite with promising therapeutic potential. J. Agric. Food Chem. 2013, 61, 12173–12182. [CrossRef] [PubMed]

135. Paszel-Jaworska, A.; Romaniuk, A.; Rybczynska, M. Molecular Mechanisms of Biological Activity of Oleanolic Acid—A Source of Inspiration for A New Drugs Design. Mini-Rev. Org. Chem. 2014, 11, 330–342. [CrossRef]

136. Cushnie, T.P.; Lamb, A.J. Antimicrobial activity of flavonoids. Int. J. Antimicrob. Agents 2005, 26, 343–356. [CrossRef] [PubMed]

137. Hosek, J.; Smejkal, K. Flavonoids as anti-inflammatory agents. In Encyclopedia of Inflammatory Diseases; Parnham, M.J., Ed.; Birkhauser Verlag AG: Basel, Switzerland, 2016; In press.

138. Pan, M.H.; Lai, C.S.; Ho, C.T. Anti-inflammatory activity of dietary flavonoids. Food Funct. 2010, 1, 15–31. [CrossRef] [PubMed]

139. Lozano-Mena, G.; Sanchez-Gonzalez, M.; Juan, M.E.; Planas, J.M. Maslinic acid, a natural phytoalexin-type triterpenoid from olives—an exciting nutraceutical? Molecules 2014, 19, 11538–11559. [CrossRef] [PubMed]

140. Rodríguez-Rodriguez, R. Oleanolic Acid and Related Triterpenoids from Olives on Vascular Function: Molecular Mechanisms and Therapeutic Perspectives. Curr. Med. Chem. 2015, 22, 1414–1425. [CrossRef] [PubMed]

141. Paszel-Jaworska, A.; Romaniuk, A.; Rybczynska, M. Molecular Mechanisms of Biological Activity of Oleanolic Acid—A Source of Inspiration for A New Drugs Design. Mini-Rev. Org. Chem. 2014, 11, 330–342. [CrossRef]

142. Kashyap, D.; Tuli, H.S.; Sharma, A.K. Ursolic acid (UA): A metabolite with promising therapeutic potential. Life Sci. 2016, 146, 201–213. [CrossRef] [PubMed]

143. Tian, S.; Shi, Y.; Yu, Q.; Upur, H. Determination of oleanolic acid and ursolic acid contents in Ziziphora clinopodioides Lam. by HPLC method. Pharmacog. Mag. 2010, 6, 116–119. [CrossRef] [PubMed]

144. Sánchez-Quesada, C.; López-Biedma, A.; Warleta, F.; Campos, M.; Beltrán, G.; Gaforio, J.J. Bioactive properties of the main triterpenes found in olives, virgin olive oil, and leaves of Olea europaea L. f. afford the treatment of asthma through activation of β2AR and inhibition of NF-κB. Lat. Am. J. Pharm. 2015, 34, 291–295.
152. Huang, L.J.; Gao, W.Y.; Li, X.; Zhao, W.S.; Huang, L.Q.; Liu, C.X. Evaluation of the In Vivo Anti-inflammatory Effects of Extracts from Pyrus bretschneideri Rehd. J. Agric. Food Chem. 2010, 58, 8983–8987. [CrossRef] [PubMed]

153. Mavar-Manga, H.; Haddad, M.; Pieters, L.; Baccelli, C.; Penge, A.; Quetin-Leclercq, J. Anti-inflammatory compounds from leaves and root bark of Alchornea cordifolia (Schumach. & Thonn.) Muell. Arg. J. Ethnopharmacol. 2008, 115, 25–29. [PubMed]

154. Kim, J.S.; Kim, J.C.; Shim, S.H.; Lee, E.J.; Jin, W.; Bae, K.; Son, K.H.; Kim, H.P.; Kang, S.S.; Chang, H.W. Chemical constituents of the root of Dystaenia takeshimana and their anti-inflammatory activity. Arch. Pharmacal. Res. 2006, 29, 617–623. [CrossRef]

155. Luo, W.; Zhao, M.; Yang, B.; Shen, G.; Rao, G. Identification of bioactive compounds in Phyllanthus emblica L. fruit and their free radical scavenging activities. Food Chem. 2009, 114, 499–504. [CrossRef]

156. Guo, X.D.; Wang, M.; Gao, J.M.; Shi, X.W. Bioguided fraction of antioxidant activity of ethanol extract from tartary buckwheat bran. Cereal Chem. 2012, 89, 311–315. [CrossRef]

157. Qing, Z.J.; Wang, Y.; Hui, L.Y.; Yong, L.W.; Long, L.H.; Ao, D.J.; Xia, P.L. Two new natural products from the fruits of Alpinia oxyphylla with inhibitory effects on nitric oxide production in lipopolysaccharide-activated RAW264.7 macrophage cells. Arch. Pharmacal. Res. 2012, 35, 2143–2146. [CrossRef] [PubMed]

158. Kim, J.S.; Kim, J.C.; Shim, S.H.; Lee, E.J.; Jin, W.; Bae, K.; Son, K.H.; Kim, H.P.; Kang, S.S.; Chang, H.W. Chemical constituents of the root of Dystaenia takeshimana and their anti-inflammatory activity. Arch. Pharmacal. Res. 2006, 29, 617–623. [CrossRef]

159. Luo, W.; Zhao, M.; Yang, B.; Shen, G.; Rao, G. Identification of bioactive compounds in Phyllanthus emblica L. fruit and their free radical scavenging activities. Food Chem. 2009, 114, 499–504. [CrossRef]

160. Chung, M.J.; Lee, S.; Park, Y.I.; Lee, J.; Kwon, K.H. Neuroprotective effects of phytosterols and flavonoids promotes the proliferation of neural stem cells. J. Steroid Biochem. Mol. Biol. 2014, 140, 90–99. [CrossRef] [PubMed]

161. Jiang, L.H.; Yuan, X.L.; Yang, N.Y.; Zou, Y.J.; Zhao, F.M.; Chen, J.P.; Wang, M.Y.; Lu, D.X. Daucosterol protects neurons against oxygen-glucose deprivation/reperfusion-mediated injury by activating IGF1 signaling pathway. J. Steroid Biochem. Mol. Biol. 2015, 152, 45–52. [CrossRef] [PubMed]

162. Jiang, L.H.; Yang, N.Y.; Yuan, X.L.; Zhou, Y.J.; Zhao, F.M.; Chen, J.P.; Wang, M.Y.; Lu, D.X. Daucosterol promotes the proliferation of neural stem cells. J. Steroid Biochem. Mol. Biol. 2014, 140, 90–99. [CrossRef] [PubMed]

163. Bahadori, M.B.; Dinparast, L.; Valizadeh, H.; Farimani, M.M.; Ebrahimi, S.N. Bioactive constituents from roots of Salvia syriaca L.: Acetylcholinesterase inhibitory activity and molecular docking studies. S. Afr. J. Bot. 2016, 106, 1–4. [CrossRef] [PubMed]

164. Zhao, C.; She, T.; Wang, L.; Su, Y.; Qu, L.; Gao, Y.; Xu, S.; Cai, S.; Shou, C. Daucosterol inhibits cancer cell proliferation by inducing autophagy through reactive oxygen species-dependent manner. Life Sci. 2015, 137, 37–43. [CrossRef] [PubMed]

165. Esmaeili, M.A.; Farimani, M.M. Inactivation of PI3K/Akt pathway and upregulation of PTEN gene are involved in daucosterol, isolated from Salvia sahendica, induced apoptosis in human breast adenocarcinoma cells. S. Afr. J. Bot. 2014, 93, 37–47. [CrossRef] [PubMed]

166. Manayi, A.; Saeidnia, S.; Ostad, S.N.; Hadijakhooindi, A.; Ardekani, M.R.; Vazirian, M.; Akhtar, Y.; Khanavi, M. Chemical constituents and cytotoxic effect of the main compounds of Lythrum salicaria L. Z. Naturforsch. C J. Biosci. 2013, 68, 367–375. [CrossRef]

167. Salimi, M.; Ardestaniyan, M.H.; Mostafapour, K.H.; Saieidnia, S.; Gohari, A.R.; Amanzadeh, A.; Sanati, H.; Sepahdar, Z.; Ghorbani, S.; Salimi, M. Anti-proliferative and apoptotic activities of constituents of chloroform extract of Juglans regia leaves. Cell. Prolif. 2014, 47, 172–179. [CrossRef] [PubMed]

168. Zeng, X.; Li, C.Y.; Wang, H.; Qiu, Q.; Qiu, G.; He, X. Unusual lipids and acylglucosylsterols from the roots of Livistona chinensis. Phytochem. Lett. 2013, 6, 36–40. [CrossRef] [PubMed]

169. Lee, D.Y.; Lee, S.J.; Kwak, H.Y.; Jung, L.; Heo, J.; Hong, S.; Kim, G.W.; Baek, N.I. Sterols isolated from Nuruk (Rhizopus oryzae KSD-815) inhibit the migration of cancer cells. J. Microbiol. Biotechnol. 2009, 19, 1328–1332. [CrossRef] [PubMed]
170. Gao, D.; Zhang, Y.L.; Xu, P.; Lin, Y.X.; Yang, F.Q.; Liu, J.H.; Zhu, H.W.; Xia, Z.N. In vitro evaluation of dual agonists for PPARγ/β from the flower of *Edgeworthia gardneri* (wall.) Meisn. *J. Ethnopharmacol.* **2015**, *162*, 14–19. [CrossRef] [PubMed]

171. Sheng, Z.; Dai, H.; Pan, S.; Wang, H.; Hu, Y.; Ma, W. Isolation and characterization of an α-glucosidase inhibitor from *Musa* spp. (Baxijiao) flowers. *Molecules* **2014**, *19*, 10563–10573. [CrossRef] [PubMed]

172. Chen, W.H.; Liu, W.J.; Wang, Y.; Song, X.P.; Chen, G.Y. A new naphthoquinone and other antibacterial constituents from the roots of *Xanthium sibircum*. *Nat. Prod. Res.** **2015**, *29*, 739–744. [PubMed]

173. Lee, D.G.; Lee, A.Y.; Kim, S.J.; Lee, S. Antibacterial phytosterols and alkaloids from *Lycoris radiata*. *Nat. Prod. Sci.* **2014**, *20*, 107–112.

174. Cho, E.J.; Choi, J.Y.; Lee, K.H.; Lee, S. Isolation of antibacterial compounds from *Prunus mume* and their inhibitory effects on osteoclast differentiation by suppressing tartrate-resistant acid phosphatase activity. *Arch. Pharm. Res.* **2015**, *38*, 186–192. [CrossRef] [PubMed]

175. Darbandi, T.; Honarvar, B.; Sinaei Nobandegani, M.; Rezaei, A. Extraction of *Ziziphus tenuior* essential oil using supercritical CO₂. *Eur. J. Exp. Biol.* **2013**, *3*, 687–695.

176. Kimura, T.; Jyo, M.; Nakamura, N.; Komatsu, K.; Shimotohno, K.; Shimotohno, K.; Kakiuchi, N. Inhibitory effect of Tibetan medicinal plants on viral polymerases. *J. Trad. Med.* **2003**, *20*, 243–250.

177. Jeong, J.S.; Lee, J.-H.; Lee, S.H.; Jeong, C.S. Suppressive actions of *Astragali Radix* (AR) ethanol extract and isolated astragaloside I on HCl/ethanol-induced gastric lesions. *Biomol. Ther.* **2009**, *17*, 62–69. [CrossRef]

178. Yan, X.T.; Lee, S.-H.; Li, W.; Jang, H.D.; Kim, Y.H. Terpenes and sterols from the fruits of *Prunus mume* and their inhibitory effects on osteoclast differentiation by suppressing tartrate-resistant acid phosphatase activity. *J. Chem. Ecol.* **2009**, *35*, 518–525. [CrossRef] [PubMed]

179. Amiri, H. Influence of growth phase on the essential oil composition of *Ziziphus clinopodioides* Lam. *Nat. Prod. Res.* **2009**, *23*, 601–606. [CrossRef] [PubMed]

180. Barra, A. Factors affecting chemical variability of essential oils: A review of recent developments. *Chem. Nat. Compd.* **2008**, *44*, 4, 387–389. [CrossRef]

181. Aghajani, Z.; Assadian, F.; Masoudi, S.; Chalabian, F.; Esmaili, A.; Tabatabaei-Anaraki, M.; Rustaiyan, A. Chemical composition and In Vitro Antibacterial Activities of The Oil *Ziziphus clinopodioides* and *Z. capitata* subsp. *capitata* from Iran. *Chem. Nat. Compd.* **2008**, *44*, 4, 387–389. [CrossRef]

182. Kasumov, F.Y.; Kyazimov, I.M.; Dembtskii, A.D.; Ismailov, N.M. Component composition of the essential oils of *Ziziphus* species. *Chem. Nat. Compd.* **1988**, *23*, 636–637. [CrossRef]

183. Aghajani, Z.; Assadian, F.; Masoudi, S.; Chalabian, F.; Esmaili, A.; Tabatabaei-Anaraki, M.; Rustaiyan, A. Chemical composition and In Vitro Antibacterial Activities of The Oil *Ziziphus clinopodioides* and *Z. capitata* subsp. *capitata* from Iran. *Chem. Nat. Compd.* **2008**, *44*, 4, 387–389. [CrossRef]

184. Kasumov, F.Y.; Kyazimov, I.M.; Dembtskii, A.D.; Ismailov, N.M. Component composition of the essential oils of *Ziziphus* species. *Chem. Nat. Compd.* **1988**, *23*, 636–637. [CrossRef]

185. Ladis, Z.; El-arami, S.A. Fumigant and Contact Toxicities of Monoterpenes to *Sitophilus oryzae* (L.) and *Tribolium castaneum* (Herbst) and their Inhibitory Effects on Acetylcholinesterase Activity. *J. Chem. Ecol.* **2009**, *35*, 518–525. [CrossRef] [PubMed]

186. Abdelgaleil, S.A.M.; Mohamed, M.I.E.; Badawy, M.E.I.; El-arami, S.A. Fumigant and Contact Toxicities of Monoterpenes to *Sitophilus oryzae* (L.) and *Tribolium castaneum* (Herbst) and their Inhibitory Effects on Acetylcholinesterase Activity. *J. Chem. Ecol.* **2009**, *35*, 518–525. [CrossRef] [PubMed]

187. Liu, Z.L.; Du, S.S. Fumigant components from the essential oil of *Evodia rutaecarpa* Hort unripe fruits. *Eur. J. Chem.* **2011**, *8*, 1937–1943.
192. Ciftci, O.; Tanyildizi, S.; Godekmerdan, A. Curcumin, myrcene and cineol modulate the percentage of
193. do Vale, T.G.; Furtado, E.C.; Santos, J.G., Jr.; Viana, G.S.B. Central effects of citral, myrcene and limonene,
194. Mitic-Culafic, D.; Zegura, B.; Nikolic, B.; Vukovic-Gacic, B.; Knezevic-Vukevic, J.; Filipic, M. Protective
effect of linalool, myrcene and eucalyptol against t-butyl hydroperoxide induced genotoxicity in bacteria
195. Hsieh, L.C.; Hsieh, S.L.; Chen, C.T.; Chung, J.G.; Wang, J.J.; Wu, C.C. Induction of
196. Ciftci, O.; Ozdemir, I.; Tanyildizi, S.; Yildiz, S.; Oguzturk, H. Antioxidative effects of curcumin,
197. Ciftci, O.; Oztanir, M.N.; Cetin, A. Neuroprotective Effects of
198. Bonamin, F.; Moraes, T.M.; dos Santos, R.C.; Kushima, H.; Faria, F.M.; Silva, M.A.; Junior, I.V.; Nogueira, L.;
199. Guimarães, A.G.; Quintans, J.S.; Quintans-Júnior, L.J. Monoterpenes with analgesic activity—A systematic
200. Sonboli, A.; Mirjalili, M.H.; Hadian, J.; Ebrahimi, S.N.; Yousefzadi, M. Antibacterial Activity and Composition
201. Jaeger, W. Metabolism of terpenoids in animal models and humans. In Handbook of Essential Oils
202. Piccinelli, A.C.; Santos, J.A.; Konkiewitz, E.C.; Oesterreich, S.A.; Formagio, A.S.; Croda, J.; Ziff, E.B.;
203. Valente, J.; Zuzarte, M.; Goncalves, M.J.; Lopes, M.C.; Cavaleiro, C.; Salgueiro, L.; Cruz, M.T. Antifungal,
204. Cheng, S.S.; Huang, C.G.; Chen, Y.J.; Yu, J.J.; Chen, W.J.; Chang, S.T. Chemical compositions and larvicidal
205. Perumalsamy, H.; Kim, N.J.; Ahn, Y.J. Larvicidal activity of compounds isolated from
206. Lima, D.F.; Brandao, M.S.; Moura, J.B.; Leitão, J.M.; Carvalho, F.A.; Miúra, L.M.; Leite, J.R.; Sousa, D.P.;
207. Hsieh, L.C.; Hsieh, S.L.; Chen, C.T.; Chung, J.G.; Wang, J.J.; Wu, C.C. Induction of α-Phellandrene on
208. Piccinelli, A.C.; Santos, J.A.; Konkiewitz, E.C.; Oesterreich, S.A.; Formagio, A.S.; Croda, J.; Ziff, E.B.;
209. Hsieh, L.C.; Hsieh, S.L.; Chen, C.T.; Chung, J.G.; Wang, J.J.; Wu, C.C. Induction of α-Phellandrene on

[CrossRef] [PubMed]
210. Hsieh, S.L.; Li, Y.C.; Chang, W.C.; Chung, J.G.; Hsieh, L.C.; Wu, C.C. Induction of Necrosis in Human Liver Tumor Cells by α-Phellandrene. *Nutr. Cancer* 2014, 66, 970–979. [CrossRef] [PubMed]

211. Santos, M.R.V.; Moreira, F.V.; Fraga, B.P.; de Souza, D.P.; Bonjardim, L.R.; Quintans-Júnior, L.J. Cardiovascular effects of monoterpene terpinolene from the oil of *Citrus junos* and (+)-limonene on emotional behavior in mice. *Flavour Fragr. J.* 2012, 27, 416–424. [PubMed]

212. Astani, A.; Reichling, J.; Schnitzler, P. Comparative study on the antiviral activity of selected monoterpenes derived from essential oils. *Phytother. Res.* 2010, 24, 673–679. [CrossRef] [PubMed]

213. Okumura, N.; Yoshida, H.; Nishimura, Y.; Kitagishi, Y.; Matsuda, S. Terpinolene, a component of herbal sage, downregulates AKT1 expression in K562 cells. *Oncol. Lett.* 2012, 3, 321–324. [PubMed]

214. Bonesi, M.; Menichini, F.; Tundis, R.; Loizzo, M.R.; Conforti, F.; Passalacqua, N.G.; Statti, G.A.; Menichini, N.G. α-Phellandrene-induced apoptosis in mice leukemia WEHI-3 cells in vitro. *Environ. Toxicol.* 2015. [CrossRef] [PubMed]

215. Ito, K.; Ito, M. The sedative effect of inhaled terpinolene in mice and its structure-activity relationships. *J. Nat. Med.* 2013, 67, 833–837. [CrossRef] [PubMed]

216. Aydin, E.; Turkez, H.; Tasdemir, S. Anticancer and antioxidant properties of terpinolene in rat brain cells. *Phytother. Res.* 2015, 29, 1674–1681. [CrossRef] [PubMed]

217. Yoshida, N.; Koizumi, M.; Adachi, I.; Kawakami, J. Inhibition of P-glycoprotein-mediated transport by terpenoids contained in herbal medicines and natural products. *Food Chem. Toxicol.* 2006, 44, 2033–2039. [CrossRef] [PubMed]

218. Astani, A.; Reichling, J.; Schnitzler, P. Comparative study on the antiviral activity of selected monoterpenes derived from essential oils. *Phytother. Res.* 2010, 24, 673–679. [CrossRef] [PubMed]

219. Adegoke, G.O.; Iwahashi, H.; Komatsu, Y.; Obuchi, K.; Iwahashi, Y. Inhibition of food spoilage yeasts and aflatoxigenic moulds by monoterpene of the spice *Aframomum danielli*. *Flavour Fragr. J.* 2000, 15, 147–150. [CrossRef]

220. Bourgou, S.; Pichette, A.; Marzouk, B.; Legault, J. Bioactivities of black cumin essential oil and its main terpenes from Tunisia. *S. Afr. J. Bot.* 2010, 76, 210–216. [CrossRef]

221. Santos, M.R.V.; Moreira, F.V.; Fraga, B.P.; de Souza, D.P.; Bonjardim, L.R.; Quintans-Júnior, L.J. Cardiovascular effects of monoterpenes: A review. *Rev. Bras. Farmacogn.* 2011, 21, 764–771. [CrossRef]

222. Baldissera, M.D.; Grando, T.H.; Souza, C.F.; Gressler, L.T.; Stefani, L.M.; da Silva, A.S.; Monteiro, S.G. In vivo action of terpinolene against *Trichosanthes foetida* (L.) and *Aedes aegypti* adults. *Microtoena patchoulii* and *α*-tocopherol and *β*-carotene effectively prevents oxidation of LDL. *Phytomedicine* 2005, 12, 416–423. [CrossRef] [PubMed]

223. Bousso, S.; De Broucker, T.; Colson, L.; Janbon, J.; Ratte, J.; Verwee, K. Antioxidant activities of selected monoterpenes from *Melaleuca alternifolia* Oil and Its Components. *J. Agric. Food Chem.* 2004, 52, 3025–3034. [CrossRef] [PubMed]

224. Bonechi, G.O.; Iwahashi, H.; Komatsu, Y.; Obuchi, K.; Iwahashi, Y. Inhibition of food spoilage yeasts and aflatoxigenic moulds by monoterpene of the spice *Aframomum danielli*. *Flavour Fragr. J.* 2000, 15, 147–150. [CrossRef]

225. Chang, S.S.; Chang, H.T.; Lin, C.Y.; Chen, P.S.; Huang, C.G.; Chen, W.J.; Chang, S.T. Insecticidal activities of leaf and twig essential oils from *Clausena excavata* against *Aedes aegypti* and *Aedes albopictus* larvae. *Pest Manag. Sci.* 2009, 65, 339–343. [CrossRef] [PubMed]
231. Garozzo, A.; Timpanaro, R.; Bisignano, B.; Furneri, P.M.; Bisignano, G.; Castro, A. In vitro antiviral activity of Melaleuca alternifolia essential oil. Lett. Appl. Microbiol. 2009, 49, 806–808. [CrossRef] [PubMed]

232. Pirbalouti, A.G.; Amirkhosravi, A.; Bordbar, F. Diversity in the chemical composition of essential oils of Ziziphus tenuis as a potential source of pulegone. Chemija 2013, 24, 234–239.

233. Vogt, J.T.; Shelton, T.G.; Merchant, M.E.; Russel, S.A.; Tanley, M.J.; Appel, A.G. Efficacy of the three citrus oil formulations against Solenopsis invicta Buren (Hymenoptera: Formicidae), the red imported fire ant. J. Agric. Urban Entomol. 2002, 19, 159–171.

234. Lee, S.; Peterson, C.J.; Coats, J.R. Fumigation toxicity of monoterpenoids to several stored product insects. J. Stored Prod. Res. 2003, 39, 77–85. [CrossRef]

235. Rozza, A.L.; Moraes, T.M.; Kushima, H.; Tanimoto, A.; Marques, M.O.; Bauab, T.M.; Hiruma-Lima, C.A.; Pellizzon, C.H. Gastroprotective mechanisms of Citrus lemon (Rutaceae) essential oil and its majority compounds limonene and β-pinene: Involvement of heat-shock protein-70, vasoactive intestinal peptide, glutathione, sulphydryl compounds, nitric oxide and prostaglandin E2. Chem.-Biol. Interact. 2011, 189, 82–89. [CrossRef] [PubMed]

236. Erasto, P.; Viljoen, A.M. Limonene—A review: Biosynthetic, ecological and pharmacological relevance. Nat. Prod. Commun. 2008, 3, 1193–1202.

237. Maróstica, M.R., Jr.; Pastore, G.M. Limonene and Its Oxyfunctionalized Compounds—Biotransformation by Microorganisms and Their Role as Functional Bioactive Compounds. Food Sci. Biotechnol. 2009, 18, 833–841.

238. Sharopov, F.S.; Setzer, W.N. Chemical diversity of Ziziphus clinopodioides: Composition of the essential oil of Z. clinopodioides from Tajikistan. Nat. Prod. Commun. 2011, 6, 695–698. [PubMed]

239. Samber, N.; Khan, A.; Varma, A.; Manzoor, N. Synergistic anti-candidal activity and mode of action of Mentha piperita essential oil and its major components. Pharm. Biol. 2015, 53, 1496–1504. [CrossRef] [PubMed]

240. Jirovetz, L.; Buchbauer, G.; Bail, S.; Denkova, Z.; Slavchev, A.; Stoyanova, A.; Schmidt, E.; Geissler, M. Antimicrobial activities of essential oils of mint and peppermint as well as some of their main compounds. J. Essent. Oil Res. 2009, 21, 363–366. [CrossRef]

241. Hussain, A.I.; Anwar, F.; Nigam, P.S.; Ashraf, M.; Gilani, A.H. Seasonal variation in content, chemical composition and antimicrobial and cytotoxic activities of essential oils from four Mentha species. J. Sci. Food Agric. 2010, 90, 1827–1836. [CrossRef] [PubMed]

242. Kumar, P.; Mishra, S.; Malik, A.; Satya, S. Insecticidal properties of Mentha species: A review. Ind. Crops Prod. 2011, 34, 802–817. [CrossRef]

243. Herrera, J.M.; Zunino, M.P.; Dambolena, J.S.; Pizzolitto, R.P.; Ganan, N.A.; Lucini, E.I.; Zygadlo, J.A. β-ketones as natural insecticides against Sitophilus zeamais. Ind. Crop. Prod. 2015, 70, 435–442. [CrossRef]

244. Xue, J.; Li, H.; Deng, X.; Ma, Z.; Fu, Q.; Ma, S. 1-Menthone confers antidepressant-like effects in an unpredictable chronic mild stress mouse model via NLRP3 inflammasome-mediated inflammatory cytokines and central neurotransmitters. Pharmacol. Biochem. Behav. 2015, 134, 42–48. [CrossRef] [PubMed]

245. Bowers, W.S.; Ortego, F.; You, X.; Evans, P.H. Insect repellents from the Chinese prickly ash Zanthoxylum bungeum. J. Nat. Prod. 1993, 56, 935–938. [CrossRef]

246. Abdelgaleil, S.A.M.; Abbassy, M.A.; Belal, A.S.H.; Rasoul, M.A.A. Bioactivity of two major constituents isolated from the essential oil of Artemisia judaica L. Biosciences. Technol. 2008, 99, 5497–5490. [CrossRef] [PubMed]

247. Ketoh, G.K.; Koumaglo, H.K.; Glitho, I.A.; Huignard, J. Comparative effects of Cymbopogon schoenanthus essential oil and piperitone on Callosobruchus maculatus development. Fitoterapia 2006, 77, 506–510. [CrossRef] [PubMed]

248. Shahverdi, A.R.; Rafii, F.; Tavassoli, F.; Bagheri, M.; Attar, F.; Ghahraman, A. Piperitone from Mentha longifolia var. chordeictya Rech F. reduces the nitrofurantoin resistance of strains of Enterobacteriaceae. Phytother. Res. 2004, 18, 911–914. [CrossRef] [PubMed]

249. Shahverdi, A.R.; Mirzaie, S.; Rafii, F.; Kakavand, M.; Foroumadi, M. A. Monoterpenes as nitrofurantoin resistance modulating agents: Minimal structural requirements, molecular dynamics simulations, and the effect of piperitone on the emergence of nitrofurantoin resistance in Enterobacteriaceae. J. Mol. Model. 2015, 21, 198. [CrossRef] [PubMed]

250. Cárdenas-Ortega, N.C.; Zavala-Sanchez, M.A.; Aguirre-Rivera, J.R.; Pérez-González, C.; Pérez-Gutiérrez, S. Chemical Composition and Antifungal Activity of Essential Oil of Chrysactinia mexicana Gray. J. Agric. Food Chem. 2005, 53, 4347–4349. [CrossRef] [PubMed]
251. Ozturk, S.; Ercisli, S. The chemical composition of essential oil and in vitro antibacterial activities of essential oil and methanol extract of Zizipora persica Bunge. *J. Ethnopharmacol.* 2006, 106, 372–376. [CrossRef] [PubMed]

252. Oumzi1, H.; Ghoulami, S.; Rhajouiti, M.; Illidrissi, A.; Fkhir-Tetouani, S.; Faid, M.; Benjuoud, A. Antibacterial and antifungal activity of essential oils of Mentha suaveolens. *Phytother. Res.* 2002, 16, 727–731. [CrossRef] [PubMed]

253. Koliopoulou, G.; Pitarokili, D.; Kioulos, E.; Michaelakis, A.; Tzakou, O. Chemical composition and larvicidal evaluation of Mentha, Salvia, and Melissa essential oils against the West Nile virus mosquito Culex pipiens. *Parasitol. Res.* 2010, 107, 327–335. [CrossRef] [PubMed]

254. Han, J.; Kim, S.I.; Choi, B.R.; Lee, S.G.; Ahn, Y.J. Fumigant toxicity of lemon eucalyptus oil constituents of *Melaleuca alternifolia*. *Phytochemistry* 2013, 80, 56–62. [CrossRef] [PubMed]

255. Meepagala, K.M.; Kuhajek, J.M.; Sturtz, G.D.; Wedge, D.E. Vulgarone B, the Antifungal Constituent in the Essential Oil of *Cymbopogon vulgaris* (Poaceae). *J. Nat. Prod.* 2002, 65, 1333–1336. [CrossRef] [PubMed]

256. Thodgdon-A, J.; Inprakhon, P. Composition and biological activities of essential oils from *Lippia alba* L. *Phytother. Res.* 2009, 23, 101–104. [CrossRef] [PubMed]

257. Kamatou, G.P.; Vermaak, I.; Viljoen, A.M.; Lawrence, B.M. Menthol: A simple monoterpene with remarkable biological properties. *Phytochemistry* 2013, 96, 15–25. [CrossRef] [PubMed]

258. Papachristos, D.P.; Karamanoli, K.I.; Stamopoulos, D.C.; Menkissoglu-Spiroudi, U. The relationship between the chemical composition of three essential oils and their insecticidal activity against *Acanthoscelides obtectus* (Say). *Pest Manag. Sci.* 2004, 60, 514–520. [CrossRef] [PubMed]

259. Meepagala, K.M.; Kuhajek, J.M.; Sturtz, G.D.; Wedge, D.E. Vulgarone B, the Antifungal Constituent in the Essential Oil of *Cymbopogon vulgaris* (Poaceae). *J. Nat. Prod.* 2002, 65, 1333–1336. [CrossRef] [PubMed]

260. Kamatou, G.P.; Vermaak, I.; Viljoen, A.M.; Laurence, B.M. Menthol: A simple monoterpene with remarkable biological properties. *Phytochemistry* 2013, 96, 15–25. [CrossRef] [PubMed]

261. Rozza, A.L.; Meira de Faria, F.; Souza Brito, A.R.; Pellizzon, C.H. The gastroprotective effect of menthol: involvement of anti-apoptotic, antioxidant and anti-inflammatory activities. *PLoS ONE* 2014, 9, e86686. [CrossRef] [PubMed]

262. Tripathi, A.K.; Prajapati, V.; Ahmad, A.; Aggarwal, K.K.; Khanuja, S.P. Piperitenone oxide as toxic, repellent, and reproduction retardant toward malarial vector *Anopheles stephensi* (Diptera: Anophelinae). *J. Med. Entomol.* 2004, 41, 691–698. [CrossRef] [PubMed]

263. Orhan, I.; Kartal, M.; Kan, V.; Sener, B. Activity of essential oils and individual components against acetyl- and butyrylcholinesterase. *Z. Naturforsch. C J. Biosci.* 2008, 63, 547–553.

264. Sezik, E.; Tümen, G.; Başer, K.H.C. Zizipora tenuior L. a new source of pulegone. *Flav. Fragr. J.* 1991, 6, 101–104. [CrossRef] [PubMed]

265. Ozturk, S.; Ercisli, S. The chemical composition of essential oil and in vitro antibacterial activities of essential oil and methanol extract of *Zizipora persica* Bunge. *J. Ethnopharmacol.* 2006, 106, 372–376. [CrossRef] [PubMed]

266. Kamatou, G.P.; Vermaak, I.; Viljoen, A.M.; Laurence, B.M. Menthol: A simple monoterpene with remarkable biological properties. *Phytochemistry* 2013, 96, 15–25. [CrossRef] [PubMed]

267. Orhan, I.; Kartal, M.; Kan, V.; Sener, B. Activity of essential oils and individual components against acetyl- and butyrylcholinesterase. *Z. Naturforsch. C J. Biosci.* 2008, 63, 547–553.

268. Han, J.; Kim, S.I.; Choi, B.R.; Lee, S.G.; Ahn, Y.J. Fumigant toxicity of lemon eucalyptus oil constituents of *Melaleuca alternifolia*. *Phytochemistry* 2013, 80, 56–62. [CrossRef] [PubMed]

269. Orhan, I.; Kartal, M.; Kan, V.; Sener, B. Activity of essential oils and individual components against acetyl- and butyrylcholinesterase. *Z. Naturforsch. C J. Biosci.* 2008, 63, 547–553.

270. Osawa, K.; Saeki, T.; Yasuda, H.; Hamashima, H.; Sasatsu, M.; Arai, T. The antibacterial activities of peppermint oil and green tea polyphenols, alone and in combination, against enterohemorrhagic *Escherichia coli*. *Biocontrol. Sci.* 1999, 4. [CrossRef]
271. Park, J.H.; Yang, J.Y.; Lee, H.S. Acaricidal activity of constituents derived from peppermint oil against Tyrophagus putrescentiae. *J. Food Protect.* 2014, 77, 1819–1823. [CrossRef] [PubMed]

272. De Sousa, D.P.; Raphael, E.; Brocksom, U.; Brocksom, T.J. Sedative effect of monoterpene alcohols in mice: A preliminary screening. *Z. Naturforsch. C J. Biosci.* 2007, 62, 563–566. [CrossRef]

273. Giweli, A.A.; Dzamic, A.M.; Sokovic, M.D.; Ristic, M.S.; Marin, P.D. Chemical composition, antioxidant and antimicrobial activities of essential oil of *Thymus algeriensis* wild-growing in Libya. *Cent. Eur. J. Biol.* 2013, 8, 504–511. [CrossRef]

274. Ho, C.L.; Su, Y.C. Composition, antioxidant and antimicrobial activities of the leaf essential oil of *Lippia gracilis* from Taiwan. *Nat. Prod. Commun.* 2012, 7, 109–112. [PubMed]

275. Bouchra, C.; Achouri, M.; Hassani, L.M.I.; Hmamouchi, M. Chemical composition and antifungal activity of essential oils of seven Moroccan Labiatae against *Botrytis cinerea* Pers: Fr. *J. Ethnopharmacol.* 2003, 89, 165–169. [CrossRef]

276. Kurdelas, R.R.; Lopez, S.; Lima, B.; Feresin, G.E.; Zygadło, J.; Zacchino, S.; Lópe, M.L.; Tapia, A.; Freile, M.L. Chemical composition, anti-insect and antimicrobial activity of *Baccharis darwinii* essential oil from Argentina, Patagonia. *Ind. Crop Prod.* 2012, 40, 261–267. [CrossRef]

277. Zuzarte, M.; Goncalves, M.J.; Cavaleiro, C.; Cruz, M.T.; Benzarti, A.; Marongiu, B.; Maxia, A.; Piras, A.; Salgueiro, L. Antifungal and anti-inflammatory potential of *Lavandula stoechas* and *Thymus herba-barona* essential oils. *Ind. Crop Prod.* 2013, 44, 97–103. [CrossRef]

278. Ahmad, A.; Khan, A.; Manzoor, N. Reversal of efflux-mediated antifungal resistance underlies synergistic activity of two monoterpeneones with fluconazole. *Eur. J. Pharm. Sci.* 2013, 48, 80–86. [CrossRef] [PubMed]

279. Farias-Junior, P.A.; Rios, M.C.; Moura, T.A.; Almeida, R.P.; Alves, P.B.; Blank, A.F.; Fernandes, R.P.M.; Scher, R. Leishmaniacidal activity of carvacrol-rich essential oil from *Lippia sidoides* Cham. *Biol. Res.* 2012, 45, 399–402. [CrossRef] [PubMed]

280. Mota, M.L.; Lobo, L.T.; Costa, J.M.; Costa, L.S.; Rocha, H.A.; Rocha e Silva, L.F.; Pohl, A.M.; Neto, V.F. In vitro and in vivo antimalarial activity of essential oils and chemical components from three medicinal plants found in northeastern Brazil. *Planta Med.* 2012, 78, 658–664. [CrossRef] [PubMed]

281. Ntalii, N.G.; Ferrari, F.; Giannakou, I.; Menkissoglou-Spirouidi, U. Phytochemistry and Nematicidal Activity of the Essential Oils from 8 Greek Lamiaceae Aromatic Plants and 13 Terpene Components. *J. Agric. Food Chem.* 2010, 58, 7856–7863. [CrossRef] [PubMed]

282. Santoyo, S.; Jaime, L.; Garcia-Risco, M.R.; Ruiz-Rodriguez, A.; Reglero, G. Antiviral Properties of Supercritical CO2 Extracts from Oregano and Sage. *Int. J. Food Prop.* 2014, 17, 1150–1161. [CrossRef]

283. Melo, J.O.; Fachin, A.L.; Rizo, W.F.; Jesus, H.C.R.; Arrigoni-Blank, M.F.; Alves, P.B.; Marins, M.A.; França, S.C.; Blank, A.F. Cytotoxic effects of essential oils from three *Lippia gracilis* Schauer genotypes on HeLa, B16, and MCF-7 cells and normal human fibroblasts. *Genet. Mol. Res.* 2014, 13, 2691–2697. [CrossRef] [PubMed]

284. Jaafari, A.; Mouse, H.A.; Rakib, E.M.; Tilaoui, M.; Benbakhta, C.; Boulli, A.; Abbad, A.; Ziad, A. Chemical composition and antitumor activity of different wild varieties of Moroccan thyme. *Rev. Bras. Farmacogn.* 2011, 21, 45–54. [CrossRef] [PubMed]

285. Pathania, A.S.; Guru, S.K.; Verma, M.K.; Sharma, C.; Abdullah, S.T.; Malik, F.; Chandra, S.; Katech, M.; Bhushan, S. Disruption of the PI3K/AKT/mTOR signaling cascade and induction of apoptosis in HL-60 cells by an essential oil from *Monarda citriodora*. *Food Chem. Toxicol.* 2013, 62, 246–254. [CrossRef] [PubMed]

286. Deb, D.D.; Parmala, G.; Saravana Devi, S.; Chakraborty, T. Effect of thymol on mononuclear cell PBMC and acute promyelotic cancer cell line HL-60. *Chem.-Biol. Interact.* 2011, 193, 97–106. [CrossRef] [PubMed]

287. Vicuna, G.C.; Stashenko, E.E.; Fuentes, J.L. Chemical composition of the *Lippia origanoides* essential oils and their antigenotoxicity against bleomycin-induced DNA damage. *Fitoterapia* 2010, 81, 343–349. [CrossRef] [PubMed]

288. Riella, K.R.; Marinho, R.R.; Santos, J.S.; Pereira-Filho, R.N.; Cardoso, J.C.; Albuquerque-Junior, R.L.; Thomazzi, S.M. Anti-inflammatory and cicatrizing activities of thymol, a monoterpene of the essential oil from *Lippia gracilis*, in rodents. *J. Ethnopharmacol.* 2012, 143, 656–663. [CrossRef] [PubMed]

289. Liang, D.; Li, F.; Fu, Y.; Cao, Y.; Song, X.; Wang, T.; Wang, W.; Guo, M.; Zhou, E.; Li, D.; et al. Thymol Inhibits LPS-Stimulated Inflammatory Response via Down-Regulation of NF-κB and MAPK Signaling Pathways in Mouse Mammary Epithelial Cells. *Inflammation* 2014, 37, 214–222. [CrossRef] [PubMed]
290. Zhou, E.; Fu, Y.; Wei, Z.; Yu, Y.; Zhang, X.; Yang, Z. Thymol attenuates allergic airway inflammation in ovalbumin (OVA)-induced mouse asthma. *Fitoerapia* **2014**, *96*, 131–137. [CrossRef] [PubMed]
291. Wei, Z.; Zhou, E.; Guo, C.; Fu, Y.; Yu, Y.; Li, Y.; Yao, M.; Zhang, N.; Yang, Z. Thymol inhibits *Staphylococcus aureus* internalization into bovine mammary epithelial cells by inhibiting NF-κB activation. *Microb. Pathog.* **2014**, *71*, 15–19.
292. Alavinezhad, A.; Boskabady, M.H. Antiinflammatory, Antioxidant, and Immunological Effects of *Carum copticum* L. and Some of Its Constituents. *Phytother. Res.* **2014**, *28*, 1739–1748. [CrossRef] [PubMed]
293. Archana, P.R.; Rao, B.N.; Ballal, M.; Rao, B.S. Thymol, a naturally occurring monocyclic dietary phenolic. *Archives of Phytochemistry* **2016**, *7*, 14–22. [CrossRef]
294. Zhou, E.; Fu, Y.; Wei, Z.; Yu, Y.; Li, Y.; Yao, M.; Zhang, N.; Yang, Z. Thymol attenuates allergic airway inflammation in ovalbumin (OVA)-induced mouse asthma. *Fitoerapia* **2014**, *96*, 131–137. [CrossRef] [PubMed]
295. El-Sayed, E.S.M.; Mansour, A.M.; Abdul-Hameed, M.S. Thymol and Carvacrol Prevent Doxorubicin-Induced Cardiotoxicity by Abrogation of Oxidative Stress, Inflammation, and Apoptosis in Rats. *J. Biochem. Mol. Toxic.* **2016**, *30*, 37–44. [CrossRef] [PubMed]
296. Calo, R.; Visone, C.M.; Marabini, L. Thymol and *Thymus vulgaris* L. activity against UVA- and UVB-induced damage in NCTC 2544 cell line. *Mutat. Res. Gen. Tox. Environ.* **2015**, *791*, 30–37. [CrossRef] [PubMed]
297. Kazemi, M.; Rostami, H. Chemical composition and biological activities of Iranian *Achillea wilhelmsii* L. essential oil: A high effectiveness against *Candida* spp. and *Escherichia* strains. *Nat. Prod. Res.* **2015**, *29*, 286–288. [CrossRef] [PubMed]
298. Alitonou, G.; Tchobo, F.; Avlessi, F.; Sohounhloue, D.K.; Menut, C. Inhibitory effects of *Aeollanthus pubescens* Benth. from Benin: A Potential Source of Essential Oil with High Antiradical Efficiency. *J. Essent. Oil Bear. Plants* **2012**, *15*, 308–314. [CrossRef]
299. Kavoosi, G.; Teixeira da Silva, J.A.; Saharkhiz, M.J. Inhibitory effects of *Zataria multiflora* essential oil and its main components on nitric oxide and hydrogen peroxide production in glucose-stimulated human monocyte. *Food Chem. Toxicol.* **2012**, *50*, 3079–3085. [CrossRef] [PubMed]
300. Ribeiro, A.R.S.; Diniz, P.B.F.; Pinheiro, M.S.; Albuquerque-Júnior, R.C.L.; Thomazzi, S.M. Gastroprotective effects of thymol on acute and chronic ulcers in rats: The role of prostaglandins, ATP-sensitive K⁺ channels, and gastric mucus secretion. *Chem.-Biol. Interact.* **2016**, *244*, 121–128. [CrossRef] [PubMed]
301. García, D.A.; Bujons, J.; Vale, C.; Suñol, C. Allosteric positive interaction of thymol with the GABA receptor in primary cultures of mouse cortical neurons. *Neuropharmacology* **2016**, *100*, 29–38. [CrossRef] [PubMed]
302. Saravanan, S.; Pari, L. Role of thymol on hyperglycemia and hyperlipidemia in high fat diet-induced type 2 diabetic C57BL/6J mice. *Eur. J. Pharmacol.* **2015**, *761*, 279–287. [CrossRef] [PubMed]
303. Saravanan, S.; Pari, L. Protective effect of thymol on high fat diet induced diabetic nephropathy in C57BL/6J mice. *Chem.-Biol. Interact.* **2016**, *245*, 1–11. [CrossRef] [PubMed]
304. Basch, E.; Ulbricht, C.; Hammerness, P.; Bevins, A.; Sollars, D. Thyme (*Thymus vulgaris* L.), thymol. *J. Herb. Pharmacother.* **2004**, *4*, 49–67. [CrossRef] [PubMed]
305. Oh, J.; Bowling, J.J.; Carroll, J.F.; Demirici, B.; Başer, K.H.C.; Leininger, T.D.; Bernier, U.R.; Hamann, M.T. Natural product studies of U.S. endangered plants: Volatile components of *Lindera melissifolia* (Lauraceae) repel mosquitoes and ticks. *Phytochemistry* **2012**, *80*, 28–36. [CrossRef] [PubMed]
306. Park, S.N.; Lim, Y.K.; Freire, M.O.; Cho, E.; Jin, D.; Kook, J.K. Antimicrobial effect of linalool and α-terpineol against periodontopathic and cariogenic bacteria. *Anaerobe* **2012**, *18*, 369–372. [CrossRef] [PubMed]
307. Bader, A.; Panizzi, L.; Cioni, P.L.; Flamini, G. *Achillea ligustica*: Composition and antimicrobial activity of essential oils from the leaves, flowers and some pure constituents. *Cent. Eur. J. Biol.* **2007**, *2*, 206–212. [CrossRef]
308. Ellouze, I.; Abderrabba, M.; Saboua, N.; Mathieu, F.; Lebrihi, A.; Bouajila, J. Seasonal variation impact on *Citrus aurantium* leaves essential oil: Chemical composition and biological activities. *J. Food Sci.* **2012**, *77*, 173–180. [CrossRef] [PubMed]
309. Müller, G.C.; Junnula, A.; Butler, J.; Kravchenko, V.D.; Revay, E.E.; Weiss, R.W.; Schlein, Y. Efficacy of the botanical repellents geraniol, linalool, and citronella against mosquitoes. *J. Vector Ecol.* **2009**, *34*, 2–8. [CrossRef] [PubMed]
310. Yang, F.; Long, E.; Wen, J.; Cao, L.; Zhu, C.; Hu, H.; Ruan, Y.; Okanurak, K.; Hu, H.; Wei, X.; et al. Linalool, derived from Cinnamomum camphora (L.) Presl leaf extracts, possesses molluscidal activity against Oncomelania hupensis and inhibits infection of Schistosoma japonicum. Parasite Vector 2014, 7, 407. [CrossRef] [PubMed]

311. Peana, A.T.; De Montis, M.G.; Sechi, S.; Sircana, G.; D’Aquila, P.S.; Pippia, P. Effects of (−)-linalool in the acute hyperalgesia induced by carrageenan, L-glutamate and prostaglandin E2. Eur. J. Pharmacol. 2004, 497, 279–284. [CrossRef] [PubMed]

312. Luo, M.; Cui, X.; Xue, J.; Chi, G.; Gao, R.; Deng, X.; Guan, S.; Wei, J.; Soromou, L.W.; Feng, H.; et al. Anti-inflammatory effects of linalool in RAW 264.7 macrophages and lipopolysaccharide-induced lung injury model. J. Surg. Res. 2013, 180, e47–e54. [CrossRef] [PubMed]

313. Maeda, H.; Yamazaki, M.; Katagata, Y. Kuromoji (Litsea glaucescens) essential oil: Identification of β-pinene and linalool as active principles. J. Ethnopharmacol. 2012, 151, 268–274. [CrossRef] [PubMed]

314. Cho, S.Y.; Jun, H.J.; Lee, J.H.; Jia, Y.; Kim, K.H.; Lee, S.J. Linalool reduces the expression of 3-hydroxy-3-methylglutaryl CoA reductase via sterol regulatory element binding protein-2- and ubiquitin-dependent mechanisms. FEBS Lett. 2011, 585, 3289–3296. [CrossRef] [PubMed]

315. Gu, Y.; Ting, Z.; Qiu, X.; Zhang, X.; Gan, X.; Fang, Y.; Xu, X.; Xu, R. Linalool preferentially induces robust apoptosis of a variety of leukemia cells via upregulating p53 and cyclin-dependent kinase inhibitors. Toxicology 2010, 268, 19–24. [CrossRef] [PubMed]

316. Guzman-Gutierrez, S.L.; Gomez-Cansino, R.; Garcia-Zebadua, J.C.; Jimenez-Perez, N.C.; Reyes-Chilpa, R. Effects of inhaled linalool, 1,8-cineole, and simvastatin on human cell lines. Chem.-Biol. Interact. 2014, 214, 57–68. [CrossRef] [PubMed]

317. Linck, V.M.; Da Silva, A.L.; Figueiró, M.; Caramão, E.B.; Moreno, P.R.H.; Elisabetsky, E. Effects of inhaled linalool in anxiety, social interaction and aggressive behavior in mice. Phytomedicine 2010, 17, 679–683. [CrossRef] [PubMed]

318. Guzman-Gutierrez, S.L.; Gomez-Cansino, R.; Garcia-Zebadua, J.C.; Jimenez-Perez, N.C.; Reyes-Chilpa, R. Antidepressant activity of Litsea glaucescens essential oil: Identification of β-pinene and linalool as active principles. J. Ethnopharmacol. 2012, 143, 673–679. [CrossRef] [PubMed]

319. Kessler, A.; Sahin-Nadeem, H.; Lummis, S.C.R.; Weigel, I.; Pischetsrieder, M.; Buettner, A.; Villmann, C. Antidepressant activity of Litsea glaucescens essential oil: Identification of β-pinene and linalool as active principles. J. Ethnopharmacol. 2012, 143, 673–679. [CrossRef] [PubMed]

320. Linck, V.M.; Da Silva, A.L.; Figueiró, M.; Caramão, E.B.; Moreno, P.R.H.; Elisabetsky, E. Effects of inhaled linalool in anxiety, social interaction and aggressive behavior in mice. Phytomedicine 2010, 17, 679–683. [CrossRef] [PubMed]

321. Horvathova, E.; Slamenova, D.; Marsalkova, L.; Sramkova, M.; Wsolova, L. Effects of borneol on the level of DNA damage induced in primary rat hepatocytes and testicular cells by hydrogen peroxide. Food Chem. Toxicol. 2009, 47, 1318–1323. [CrossRef] [PubMed]

322. Zhong, W.; Cui, Y.; Yu, Q.; Xie, X.; Liu, Y.; Wei, M.; Ci, X.; Peng, L. Modulation of LPS-Stimulated Pulmonary Inflammation by Borneol in Murine Acute Lung Injury Model. Inflammation 2014, 37, 1148–1157. [CrossRef] [PubMed]

323. Juhás, S.; Cikos, S.; Czikkova, S.; Vesela, J.; Il’kova, G.; Hájek, T.; Domaracka, K.; Domaracky, M.; Bujnakova, D.; Rehák, P.; et al. Effects of Borneol and Thymoquinone on TNBS-Induced Colitis in Mice. Folia Biol. 2008, 54, 1–7. [PubMed]
328. Zhang, Q.; Wu, D.; Wu, J.; Ou, Y.; Yu, C.; Han, B.; Zhang, Q. Improved blood-brain barrier distribution: Effect of borneol on the brain pharmacokinetics of kaempferol in rats by in vivo microdialysis sampling. *J. Ethnopharmacol.* 2015, 162, 270–277. [CrossRef] [PubMed]

329. Asili, J.; Emami, S.A.; Fynolghozat, R.; Noghbab, Z.S.; Bazzaz, B.S.F.; Sahebkar, A. Chemical Composition and in Vitro Efficacy of Essential Oil of Seven *Artemisia* Species Against ESBL Producing Multidrug-Resistant *Escherichia coli*. *J. Essent. Oil Bear. Plants* 2015, 18, 124–145. [CrossRef]

330. Silva-Filho, J.C.; Oliveira, N.N.; Arcanjo, D.D.; Quintans-Júnior, L.J.; Cavalcanti, S.C.; Santos, M.R.; Oliveira Rde, C.; Oliveira, A.P. Investigation of Mechanisms Involved in (−)-Borneol-Induced Vasorelaxant Response on Rat Thoracic Aorta. *Basic Clin. Pharmacol. Toxicol.* 2012, 110, 171–177. [CrossRef] [PubMed]

331. Granger, R.E.; Campbell, E.L.; Johnston, G.A.R. (+)- And (−)-borneol: efficacious positive modulators of GABA action at human recombinant α1β2γ2L GABA<sub>A</sub> receptors. *Biochem. Pharmacol.* 2005, 69, 1101–1111. [CrossRef] [PubMed]

332. Su, J.; Lai, H.; Chen, J.; Li, L.; Wong, Y.S.; Chen, T.; Li, X. Natural Borneol, a Monoterpenoid Compound, Potentiates Selenocystine-Induced Apoptosis in Human Hepatocellular Carcinoma Cells by Enhancement of Cellular Uptake and Activation of ROS-Mediated DNA Damage. *PLoS ONE* 2013, 8, e63502. [CrossRef] [PubMed]

333. Lin, A.L.; Shangari, N.; Chan, T.S.; Remirez, D.; O’Brien, P.J. Herbal monoterpenic alcohols inhibit propofol metabolism and prolong anesthesia time. *Life Sci.* 2006, 79, 21–29. [CrossRef] [PubMed]

334. Letessier, M.P.; Svoboda, K.P.; Walters, D.R. Antifungal Activity of the Essential Oil of *Hyssopus officinalis*. *J. Phytopathol.* 2001, 149, 673–678. [CrossRef]

335. Chen, N.; Sun, G.; Yuan, X.; Hou, J.; Wu, Q.; Soromou, L.W.; Feng, H. Inhibition of lung inflammatory responses by bornyl acetate is correlated with regulation of myeloperoxidase activity. *J. Surg. Res.* 2014, 186, 436–455. [CrossRef] [PubMed]

336. Yang, H.; Zhao, R.; Chen, H.; Jia, P.; Bao, L.; Tang, H. Bornyl Acetate Has an Anti-inflammatory Effect in Human Chondrocytes Via Induction of IL-11. *IUBMB Life* 2014, 66, 854–859. [CrossRef] [PubMed]

337. Wang, X.; Ma, A.; Shi, W.; Geng, M.; Zhong, X.; Zhao, Y. Quercetin and Bornyl Acetate Regulate T-Lymphocyte Subsets and INF-γ/IL-4 Ratio In Utero in Pregnant Mice. *Evid.-Based Complement. Altern. Med.* 2011, 745262. [CrossRef]

338. Yan, R.; Yang, Y.; Zou, G. Cytotoxic and apoptotic effects of *Lindera strychnifolia* leaf essential oil. *J. Essent. Oil Res.* 2014, 26, 308–314. [CrossRef]

339. Nobrega, F.F.F.; Salvadori, M.G.S.S.; Masson, C.J.; Mello, C.F.; Nascimento, T.S.; Leal-Cardoso, J.H.; de Sousa, D.P.; Almeida, R.N. Monoterpenoid terpinen-4-ol: efficacious positive modulators of GABA<sub>A</sub> receptors. *Basic Clin. Pharmacol. Toxicol.* 2013, 110, 52–58. [CrossRef] [PubMed]

340. Silva, L.L.; Garlet, Q.I.; Benovit, S.C.; Dolci, G.; Mallmann, C.A.; Bürger, M.E.; Baldisserotto, B.; Longhi, S.J.; Masson, C.J.; Mello, C.F.; and their isolated components in silver catfish (*Rhamdia quelen*). *J. Phytopathol.* 2001, 149, 771–779. [CrossRef] [PubMed]

341. Aoshima, H.; Oda, K.; Orihara, Y.; Hara, A.; Shigemori, Y.; Tan, N.; Koda, H.; Kiso, Y. Effects of essential oils on the response of GABA<sub>A</sub> receptors, sleeping time in mice induced by sleeping drug and plasma adrenocorticotropic hormone levels of rats. *Aroma Res.* 2009, 10, 58–64.

342. Bozzuto, G.; Colone, M.; Toccaicili, L.; Stringaro, A.; Molinari, A. Tea tree oil might combat melanoma. *Planta Med.* 2011, 77, 54–56. [CrossRef] [PubMed]

343. Greay, S.J.; Ireland, D.J.; Kissick, H.T.; Levy, A.; Beilharz, M.W.; Riley, T.V.; Carson, C.F. Induction of necrosis and cell cycle arrest in murine cancer cell lines by *Melaleuca alternifolia* (tea tree) oil and terpinen-4-ol. *Cancer Chemoth. Pharm.* 2010, 65, 877–888. [CrossRef] [PubMed]

344. Wu, C.S.; Chen, Y.J.; Chen, J.J.W.; Shieh, J.J.; Huang, C.H.; Lin, P.S.; Chang, G.C.; Chang, J.T.; Lin, C.C. Terpinen-4-ol Induces Apoptosis in Human Nonsmall Cell Lung Cancer in Vitro and in Vivo. *Evid. Based Complement. Altern. Med.* 2012, 12, 818261. [CrossRef] [PubMed]
346. Calcabrini, A.; Stringaro, A.; Toccacieli, L.; Meschini, S.; Marra, M.; Colone, M.; Salvatore, G.; Mondello, F.; Arancia, G.; Molinari, A. Terpinen-4-ol, the main component of \textit{Melaleuca alternifolia} (tea tree) oil inhibits the in vitro growth of human melanoma cells. \textit{J. Investig. Dermatol.} 2004, 122, 349–360. [CrossRef] [PubMed]

347. Ninomiya, K.; Hayama, K.; Ishijima, S.A.; Maruyama, N.; Irie, H.; Kurihara, J.; Abe, S. Suppression of inflammatory reactions by terpinen-4-ol, a main constituent of tea tree oil, in a murine model of oral candidiasis and its suppressive activity to cytokine production of macrophages in vitro. \textit{Biol. Pharm. Bull.} 2013, 36, 838–844. [CrossRef] [PubMed]

348. Hart, P.H.; Brand, C.; Carson, C.F.; Riley, T.V.; Prager, R.H.; Finlay-Jones, J.J. Terpinen-4-ol, the main component of the essential oil of \textit{Melaleuca alternifolia} (tea tree oil), suppresses inflammatory mediator production by activated human monocytes. \textit{Inflamm. Res.} 2000, 49, 619–626. [CrossRef] [PubMed]

349. Loughlin, R.; Gilmore, B.F.; McCarron, P.A.; Tunney, M.M. Comparison of the cidal activity of tea tree oil and terpinen-4-ol against clinical bacterial skin isolates and human fibroblast cells. \textit{Lett. Appl. Microbiol.} 2008, 46, 428–433. [CrossRef] [PubMed]

350. Hammer, K.A.; Carson, C.F.; Riley, T.V. Antifungal activity of the components of \textit{Melaleuca alternifolia} (tea tree) oil. \textit{J. Appl. Microbiol.} 2003, 95, 853–860. [CrossRef] [PubMed]

351. You, C.; Guo, S.; Zhang, W.; Yang, K.; Geng, Z.; Du, S.; Wang, C.; Deng, Z. Identification of repellent and insecticidal constituents from \textit{Artemisia mongolica} essential oil against \textit{Lasioderma serricorne}. \textit{J. Chem.} 2015, 2015. [CrossRef]

352. Cosentino, S.; Tuberoso, C.I.G.; Pisano, B.; Satta, M.L.; Mascia, V.; Arzedi, E.; Palmas, F. \textit{In-vitro} antimicrobial activity and chemical composition of Sardinian \textit{Thymus} essential oils. \textit{Lett. Appl. Microbiol.} 1999, 29, 130–135. [CrossRef] [PubMed]

353. Has, A.T.C.; Islam, M.R.; Baburin, I.; Hering, S.; Osman, H.; Mohamad, H.; Abdullah, J.M. The inhibitory activity of nutmeg essential oil on GABA\textsubscript{A} \textalpha{}1\textbeta{}2\textgamma{}2s receptors. \textit{Biomed. Res.} 2014, 25, 543–550.

354. Quintans-Júnior, L.J.; Oliveira, M.G.; Santana, M.F.; Santana, M.T.; Guimarães, A.G.; Siqueira, J.S.; de Sousa, D.P.; Almeida, R.N. \textalpha{}-Terpineol reduces nociceptive behavior in mice. \textit{Pharm. Biol.} 2011, 49, 583–586. [CrossRef] [PubMed]

355. Mulyaningsih, S.; Sporer, F.; Reichling, J.; Wink, M. Antibacterial activity of essential oils from \textit{Eucalyptus} and of selected components against multidrug-resistant bacterial pathogens. \textit{Pharm. Biol.} 2011, 49, 893–899. [PubMed]

356. Klein, G.; Ruben, C.; Upmann, M. Antimicrobial Activity of Essential Oil Components Against Potential Food Spoilage Microorganisms. \textit{Curr. Microbiol.} 2013, 67, 200–208. [CrossRef] [PubMed]

357. Bagamboula, C.F.; Uyttendaele, M.; Debereve, J. Inhibitory effect of thyme and basil essential oils, carvacrol, thymol, estragol, linalool and \textalpha{}-cymene towards \textit{Shigella sonnei} and \textit{S. flexneri}. \textit{Food Microbiol.} 2004, 21, 33–42. [CrossRef]

358. Ultee, A.; Slump, R.A.; Steging, G.; Smid, E.J. Antimicrobial activity of carvacrol toward \textit{Bacillus cereus} on rice. \textit{J. Food Prot.} 2000, 63, 620–624. [PubMed]

359. Sanchez, C.; Aznar, R.; Sanchez, G. The effect of carvacrol on enteric viruses. \textit{Int. J. Food Microbiol.} 2015, 192, 72–76. [CrossRef] [PubMed]

360. Arunasree, K.M. Anti-proliferative effects of carvacrol on a human metastatic breast cancer cell line, MDA-MB 231. \textit{Phytomedicine} 2010, 17, 581–588. [CrossRef] [PubMed]

361. Bhakkialakshmi, E.; Suganya, N.; Sireesh, D.; Krishnamurthi, K.; Devi, S.S.; Rajaguru, P.; Ramkumar, K.M. Carvacrol induces mitochondria-mediated apoptosis in HL-60 promyelocytic and Jurkat T lymphoma cells. \textit{Eur. J. Pharmacol.} 2016, 772, 92–98. [CrossRef] [PubMed]

362. Llana-Ruiz-Cabello, M.; Gutierrez-Praena, D.; Pichardo, S.; Moreno, F.J.; Bermúdez, J.M.; Aucejo, S.; Cameán, A.M. Cytotoxicity and morphological effects induced by carvacrol and thymol on the human cell line Caco-2. \textit{Food Chem. Toxicol.} 2014, 64, 281–290. [CrossRef] [PubMed]

363. Zeytinoglu, H.; Incsel, Z.; Baser, K.H.C. Inhibition of DNA synthesis by carvacrol in mouse myeloblast cells bearing a human N-RAS oncogene. \textit{Phytomedicine} 2003, 10, 292–299. [CrossRef] [PubMed]

364. Lima, M.S.; Quintans-Júnior, L.J.; de Santana, W.A.; Kaneto, C.M.; Soares, M.B.P.; Villarreal, C.F. Anti-inflammatory effects of carvacrol: Evidence for a key role of interleukin-10. \textit{Eur. J. Pharmacol.} 2013, 699, 112–117. [CrossRef] [PubMed]
365. Melo, F.H.C.; Venâncio, E.T.; de Sousa, D.P.; de França Fonteles, M.M.; de Vasconcelos, S.M.M.; Viana, G.S.B.; de Sousa, F.C. Anxiolytic-like effect of Carvacrol (5-isopropyl-2-methylphenol) in mice: Involvement with GABAergic transmission. *Fund. Clin. Pharmacol*. 2010, 24, 437–443. [CrossRef] [PubMed]

366. Boskabady, M.H.; Mah Taj, L.G. Lung inflammation changes and oxidative stress induced by cigarette smoke exposure in guinea pigs affected by *Zataria multiflora* and its constituent, carvacrol. *RMC Complement. Altern. Med.* 2015, 15. [CrossRef] [PubMed]

367. Melo, F.H.C.; Rios, E.R.V.; Rocha, N.F.M.; Citó, M.C.O.; Fernandes, M.L.; de Sousa, D.P.; de Vasconcelos, S.M.M.; de Sousa, F.C. Antinociceptive activity of carvacrol (5-isopropyl-2-methylphenol) in mice. *J. Pharm. Pharmacol*. 2012, 64, 1722–1729. [CrossRef] [PubMed]

368. Jukic, M.; Politeo, O.; Maksimovic, M.; Milos, M.; Milos, M. In vitro acetylcholinesterase inhibitory properties of thymol, carvacrol and their derivatives thymoquinone and thymohydroquinone. *Phytother. Res.* 2007, 21, 259–261. [CrossRef] [PubMed]

369. Friedman, M. Chemistry and multifunctional bioactivities of carvacrol (4-isopropyl-2-methylphenol), a component of essential oils produced by aromatic plants and spices. *J. Agric. Food Chem.* 2014, 62, 7652–7670. [CrossRef] [PubMed]

370. Baser, K.H.C. Biological and pharmacological activities of carvacrol and carvacrol bearing essential oils. *Curr. Pharm. Des.* 2008, 14, 3106–3119. [CrossRef] [PubMed]

371. Andre, W.P.P.; Ribeiro, W.L.C.; Cavalcante, G.S.; dos Santos, J.M.L.; Macedo, I.T.F.; de Paula, H.C.B.; de Morais, S.M.; de Melo, J.V.; Beviluca, C.M.L. Comparative efficacious and toxic effects of carvacryl acetate and carvacrol on sheep gastrointestinal nematodes and mice. *Vet. Parasitol*. 2016, 218, 52–58. [CrossRef] [PubMed]

372. Damasceno, S.R.B.; Oliveira, F.R.A.; Carvalho, N.S.; Brito, C.F.; Silva, I.S.; Sousa, F.B.M.; Silva, R.O.; Sousa, D.P.; Barbosa, A.L.R.; Freitas, R.M.; et al. Carvacryl acetate, a derivative of carvacrol, reduces nociceptive and inflammatory response in mice. *Life Sci.* 2014, 94, 58–66. [CrossRef] [PubMed]

373. Pires, L.F.; Costa, L.M.; Cardoso de Almeida, A.A.; Silva, O.A.; Santos Cerqueira, G.; de Sousa, D.P.; Pires, R.M.; Satyal, P.; de Freitas, R.M. Neuropharmacological effects of carvacryl acetate on δ-aminolevulinic dehydratase, Na+, K+-ATPase activities and amino acids levels in mice hippocampus after seizures. *Chem. Biol. Interact.* 2015, 226, 49–57. [CrossRef] [PubMed]

374. Pires, L.F.; Costa, L.M.; Silva, O.A.; Cerqueira, G.S.; de Sousa, D.P.; de Freitas, R.M. Anxiolytic-like effects of carvacryl acetate, a derivative of carvacrol, in mice. *Pharmacol. Biochem. Behav.* 2013, 112, 42–48. [CrossRef] [PubMed]

375. Omolo, M.O.; Okinyo, D.; Ndiege, I.O.; Lwande, W.; Hassanali, A. Repellency of essential oils of some Kenyan plants against *Anopheles gambiae*. *Phytochemistry* 2004, 65, 2797–2802. [CrossRef] [PubMed]

376. Choi, I.Y.; Lim, J.H.; Hwang, S.; Lee, J.C.; Cho, G.S.; Kim, W.K. Anti-ischemic and anti-inflammatory activity of (S)-cis-verbenol. *Free Radical Res.* 2010, 44, 541–551. [CrossRef] [PubMed]

377. Kubo, I.; Kinst-Hori, I. Tyrosinase Inhibitors from Cumin. *J. Agric. Food Chem.* 1998, 46, 5338–5341. [CrossRef]

378. Nitoda, T.; Fan, M.D.; Kubo, I. Effects of Cuminaldehyde on Melanoma Cells. *Phytother. Res.* 2008, 22, 809–813. [CrossRef] [PubMed]

379. Kalpoutzakis, E.; Aliagiannis, N.; Mentis, A.; Mitaku, S.; Charvala, C. Composition of the essential oil of two *Nepeta* species and in vitro evaluation of their activity against *Helicobacter pylori*. *Planta Med.* 2001, 67, 880–883. [CrossRef] [PubMed]

380. Birkett, M.A.; Hassanali, A.; Hoglund, S.; Pettersson, J.; Pickett, J.A. Repellent activity of catmint, *Nepeta cataria*, and iridoid nepetalactone isomers against Afro-tropical mosquitoes, ixodid ticks and red poultry mites. *Phytochemistry* 2011, 72, 109–114. [CrossRef] [PubMed]

381. Bruce, T.J.A.; Birkett, M.A.; Blande, J.; Hooper, A.M.; Martin, J.L.; Khambay, B.; Prosser, I.; Smart, L.E.; Wadham, L.J. Response of economically important aphids to components of *Hemizygia petiolata* essential oil. *Pest Manag. Sci.* 2005, 61, 1115–1121. [CrossRef] [PubMed]

382. Santos, T.G.; Dognini, J.; Begnini, I.M.; Rebelo, R.A.; Verdi, M.; de Gasper, A.L.; Dalmarco, E.M. Chemical characterization of essential oils from *Zataria multiflora* and antibacterial activity of their major compounds. *J. Braz. Chem. Soc.* 2013, 24, 164–170. [CrossRef]

383. Nascimento, A.M.A.; Brandao, M.G.L.; Oliveira, G.B.; Fortes, I.C.; Chartone-Souza, E. Synergistic bactericidal activity of *Eremanthus erythropappus* oil or β-bisabolene with ampicillin against *Staphylococcus aureus*. *Antonie Leeuwenhoek* 2007, 92, 95–100. [CrossRef] [PubMed]
384. Cakir, A.; Kordali, S.; Zengin, H.; Izumi, S.; Hirata, T. Composition and antifungal activity of essential oils isolated from *Hypericum hyssopifolium* and *Hypericum heterophyllum*. *Flavour Fragr. J.* 2004, 19, 62–68. [CrossRef]

385. Ulubelen, A.; Topcu, G.; Eriş, C.; Sönmez, U.; Kartal, M.; Kurucu, S.; Bozk-Johansson, C. Terpenoids from *Salvia sclarea*. *Phytochemistry* 1994, 36, 971–974. [CrossRef]

386. Chavan, M.J.; Wake, P.S.; Shinde, D.B. Analgesic and anti-inflammatory activity of caryophyllene oxide from *Annona squamosa* L. bark. *Phytomedicine* 2010, 17, 149–151. [CrossRef] [PubMed]

387. Sibanda, S.; Chigwada, G.P.; Melvin, G.; Gwebu, E.T.; Noletto, J.A.; Schmidt, J.M.; Rea, A.I.; Setzer, W.N. Composition and bioactivity of the essential oil of *Heteropyxis divulsa* from Zimbabwe. *J. Ethnopharmacol.* 2004, 92, 107–111. [CrossRef] [PubMed]

388. Park, K.R.; Nam, D.; Yun, H.M.; Lee, S.G.; Jang, H.J.; Sethi, G.; Cho, S.K.; Ahn, K.S. β-Caryophyllene oxide inhibits growth and induces apoptosis through the suppression of PI3K/AKT/mTOR/S6K1 pathways and ROS-mediated MAPKs activation. *Cancer Lett.* 2011, 312, 178–188. [CrossRef] [PubMed]

389. Leal, S.M.; Pino, N.; Stashenko, E.E.; Martínez, J.R.; Escobar, P. AntipROTOzoal activity of essential oils derived from *Piper* spp. grown in Colombia. *J. Essent. Oil Res.* 2013, 25, 512–519. [CrossRef]

390. Zhang, W.J.; You, C.X.; Yang, K.; Chen, R.; Wang, Y.; Wu, Y.; Geng, Z.F.; Chen, H.P.; Jiang, H.Y.; Su, Y.; et al. Bioactivity of essential oil of *Artemisia argyi* Lev. et Van. and its main compounds against *Lasioderma serricorne*. *J. Oleo Sci.* 2014, 63, 829–837. [CrossRef] [PubMed]

391. Basha, R.H.; Sankaranarayanan, C. β-Caryophyllene, a natural sesquiterpene lactone attenuates hyperglycemia mediated oxidative and inflammatory stress in experimental diabetic rats. *Chem.-Biol. Interact.* 2016, 245, 50–58. [CrossRef] [PubMed]

392. Calleja, M.A.; Vieites, J.M.; Montero-Melendez, T.; Torres, M.I.; Faus, M.J.; Gil, A.; Suárez, A. The antioxidant effect of β-caryophyllene protects rat liver from carbon tetrachloride-induced fibrosis by inhibiting hepatic stellate cell activation. *Brit. J. Nutr.* 2013, 109, 394–401. [CrossRef] [PubMed]

393. Fernandes, E.S.; Passos, G.F.; Medeiros, R.; da Cunha, F.M.; Ferreira, J.; Campos, M.M.; Pianowski, L.F.; Calixto, J.B. Anti-inflammatory effects of compounds α-humulene and (→-)trans-caryophyllene isolated from the essential oil of *Cordia verbenacea*. *Eur. J. Pharmacol.* 2007, 569, 228–236. [CrossRef] [PubMed]

394. Passos, G.F.; Fernandes, E.S.; da Cunha, F.M.; Ferreira, J.; Pianowski, L.F.; Campos, M.M.; Calixto, J.B. Anti-inflammatory and anti-allergic properties of the essential oil and active compounds from *Cordia verbenacea*. *J. Ethnopharmacol.* 2007, 110, 323–333. [CrossRef] [PubMed]

395. Kubo, I.; Muroi, H.; Kubo, A. Naturally occurring antiacne agents. *J. Nat. Prod.* 1994, 57, 9–17. [CrossRef] [PubMed]

396. Loizzo, M.R.; Tundis, R.; Menichini, F.; Saab, A.M.; Statti, G.A.; Menichini, F. Cytotoxic activity of essential oils from Labiatae and Lauraceae families against in vitro human tumor models. *Anticancer Res.* 2007, 27, 3293–3300. [PubMed]

397. Sylvestre, M.; Longtin, A.P.A.; Legault, J. Volatile leaf constituents and anticancer activity of *Bursera simaruba* (L.) Sarg. essential oil. *Nat. Prod. Commun.* 2007, 2, 1273–1276. [CrossRef] [PubMed]

398. Sylvestre, M.; Pichette, A.; Longtin, A.; Nagau, F.; Legault, J. Essential oil analysis and anticancer activity of leaf essential oil of *Croton flavens* L. from Guadeloupe. *J. Ethnopharmacol.* 2010, 103, 99–102. [CrossRef] [PubMed]

399. Sylvestre, M.; Pichette, A.; Lavoie, S.; Longtin, A.; Legault, J. Composition and cytotoxic activity of the leaf essential oil of *Comptonia peregrina* (L.) Coulter. *Phytother. Res.* 2007, 21, 536–540. [CrossRef] [PubMed]

400. Venditti, A.; Bianco, A.; Nicoletti, M.; Quassinti, L.; Bramucci, M.; Lupidi, G.; Vitali, L.A.; Petrelli, D.; Papa, F.; Vittori, S.; et al. Phytochemical analysis, biological evaluation and micromorphological study of *Stachys alopecuros* (L.) Benth. subsp. *divulsa* (Ten.) Grande endemic to central Apennines, Italy. *Fitoterapia* 2013, 90, 94–103. [PubMed]

401. Tundis, R.; Peruzzi, L.; Menichini, F. Phytochemical and biological studies of *Stachys* species in relation to chemotaxonomy: A review. *Phytochemistry* 2014, 102, 7–39. [CrossRef] [PubMed]

402. Pérez-López, A.; Cirio, A.T.; Rivas-Galindo, V.M.; Waksman de Torres, N. Activity against *Streptococcus pneumoniae* of the essential oil and δ-cadinene isolated from *Schinus molle* fruit. *J. Essent. Oil Res.* 2011, 23, 25–28. [CrossRef]
403. Zheljazkov, V.D.; Cantrell, C.L.; Tekwani, B.; Khan, S.I. Content, Composition, and Bioactivity of the Essential Oils of Three Basil Genotypes as a Function of Harvesting. *J. Agric. Food Chem.* 2008, 56, 380–385. [CrossRef] [PubMed]

404. Chang, S.T.; Chen, P.F.; Wang, S.Y.; Wu, H.H. Antimite activity of essential oils and their constituents from *Taiwania cryptomerioides*. *J. Med. Entomol.* 2001, 38, 455–457. [CrossRef] [PubMed]

405. Chang, S.T.; Wang, S.Y.; Wu, C.L.; Chen, P.F.; Kuo, Y.H. Comparison of the antifungal activity of cadinane skeletal sesquiterpenoids from *Taiwania (Taiwania cryptomerioides) Hayata* heartwood. *Holzforschung* 2000, 54, 241–245. [CrossRef]

406. Ho, C.L.; Liao, P.C.; Su, Y.C. Composition and antimicrobial activities of the leaf essential oil of *Machilus zuihoensis* from Taiwan. *Rev. Bras. Farmacogn.* 2012, 22, 277–283. [CrossRef]

407. Jeong, J.B.; Choi, J.; Lou, Z.; Jiang, X.; Lee, S.H. Patchouli alcohol, an essential oil of *Pogostemon cablin*, exhibits anti-tumorogenic activity in human colorectal cancer cells. *Int. Immunopharmacol.* 2013, 16, 184–190. [CrossRef] [PubMed]

408. Xian, Y.F.; Li, Y.C.; Ip, S.P.; Lin, Z.X.; Lai, X.P.; Su, Z.R. Anti-inflammatory effect of patchouli alcohol isolated from *Pogostemon Herba* in LPS-stimulated RAW264.7 macrophages. *Exp. Ther. Med.* 2011, 2, 545–550. [PubMed]

409. Li, Y.C.; Xian, Y.F.; Ip, S.P.; Su, Z.R.; Su, J.Y.; He, J.J.; Xie, Q.F.; Lai, X.P.; Lin, Z.X. Anti-inflammatory activity of patchouli alcohol isolated from *Pogostemon Herba* in animal models. *Fitoterapia* 2011, 82, 1295–1301. [CrossRef] [PubMed]

410. Zheng, Y.F.; Xie, J.H.; Xu, Y.F.; Liang, Y.Z.; Mo, Z.Z.; Jiang, W.W.; Chen, X.Y.; Liu, Y.H.; Yu, X.D.; Huang, P.; et al. Gastroprotective effect and mechanism of patchouli alcohol against ethanol, indomethacin and stress-induced ulcer in rats. *Chem.-Biol. Interact.* 2014, 222, 27–36. [CrossRef] [PubMed]

411. Prakasia, P.P.; Nair, A.S. Chemical fingerprint of essential oil components from fresh leaves of *Glycosmis pentaphylla* (Retz.) Correa. *Pharma Innov.* 2015, 3, 50–56.

412. García, M.; Gonzales-Coloma, A.; Donadel, O.J.; Ardanaz, C.E.; Tonn, C.E.; Sosa, M.E. Insecticidal effects of *Flourensia oolepis* (Asteraceae) essential oil. *Biochem. Syst. Ecol.* 2007, 35, 181–187. [CrossRef]

413. Tavares, W.S.; Freitas, S.S.; Grazziotti, G.H.; Parente, L.M.L.; Lião, L.M.; Zanuncio, J.C. Insecticidal and Anti-Inflammatory Activities of Essential Oils of Selected Aromatic Plants from Tajikistan. *Foods* 2012, 14, 13–20. [CrossRef] [PubMed]

414. Lee, H.K.; Park, C.; Ahn, Y.J. Insecticidal activities of asarones identified in *Taiwania cryptomerioides* rhizomes and effects on *Sitophilus zeamais* (Coleoptera: Curculionidae) and *Plutella xylostella* (Lepidoptera: Yponomeutidae). *Appl. Entomol. Zool.* 2002, 37, 459–464. [CrossRef]

415. Lee, H.S. Antiplatelet property of *Curcuma longa* L. rhizome-derived ar-turmerone. *Bioresour. Technol.* 2006, 97, 1372–1376. [CrossRef] [PubMed]

416. García, M.; Gonzales-Coloma, A.; Donadel, O.J.; Ardanaz, C.E.; Tonn, C.E.; Sosa, M.E. Insecticidal effects of *Flourensia oolepis* Blake (Asteraceae) essential oil. *Biochem. Syst. Ecol.* 2007, 35, 181–187. [CrossRef]

417. Kumar, V. Turmeric (*Curcuma longa*): A valuable traditional medicine. *Pharma Rev.* 2006, 4, 77–80.

418. Bakkali, F.; Averbuck, S.; Averbuck, D.; Idaomar, M. Biological effects of essential oils—A review. *Food Chem. Toxicol.* 2008, 46, 446–475. [CrossRef] [PubMed]

419. Di Pasqua, R.; Bettis, G.; Hoskins, N.; Edwards, M.; Ercolini, D.; Mauriello, G. Membrane toxicity of antimicrobial compounds from essential oils. *J. Agric. Food Chem.* 2007, 55, 4863–4870. [CrossRef] [PubMed]

420. Sharopov, F.; Braun, M.S.; Gulmurodov, I.; Khalifaev, D.; Isupov, S.; Wink, M. Antimicrobial, Antioxidant, and Anti-Inflammatory Activities of Essential Oils of Selected Aromatic Plants from Tajikistan. *Foods* 2015, 4, 645–653. [CrossRef]

421. Ipek, E.; Zeytinoğlu, H.; Okay, S.; Tuylu, B.A.; Kucuoglu, M.; Baser, K.H.C. Genotoxicity and antigenotoxicity of *Origanum* oil and carvacrol evaluated by Ames *Salmonella*/microsomal test. *Food Chem.* 2005, 93, 551–556. [CrossRef]

422. Franzios, G.; Mirotsou, M.; Hatziapostolou, E.; Kral, J.; Scouras, Z.G.; Mavragani-Tsipidou, P. Insecticidal and genotoxic activities of mint essential oils. *J. Agric. Food Chem.* 1997, 45, 2690–2694. [CrossRef]

423. Santana-Rios, G.; Orner, G.A.; Amantana, A.; Provost, C.; Wu, S.Y.; Dashwood, R.H. Potent antimutagenic activity of white tea in comparison with green tea in the *Salmonella* assay. *Mutat. Res.* 2001, 495, 61–74. [CrossRef]
424. Cal, K. Skin penetration of terpenes from essential oils and topical vehicles. *Planta Med.* **2006**, *72*, 311–316. [CrossRef] [PubMed]
425. Savelev, S.; Okello, E.; Perry, N.S.L.; Wilkins, R.M.; Perry, E.K. Synergistic and antagonistic interactions of anticholinesterase terpenoids in *Salvia lavandulaefolia* essential oil. *Pharmacol. Biochem. Behav.* **2003**, *75*, 661–668. [CrossRef]
426. Aliakbarlu, J.; Shameli, F. In vitro antioxidant and antibacterial properties and total phenolic contents of essential oil from *Thymbra vulgaris*, *T. kotschyanus*, *Z. tenuior* and *Z. clinoiodides*. *Turk. J. Biochem.* **2013**, *38*, 425–431. [CrossRef]
427. Duru, M.E.; Oztürk, M.; Ugur, A.; Ceylan, Ö. The constituents of essential oil and in vitro antimicrobial activity of *Micromeria ciliata* from Turkey. *J. Ethnopharmacol.* **2004**, *94*, 43–48. [CrossRef] [PubMed]
428. Sivropoulou, A.; Kokkini, S.; Lanaras, T.; Arsenakis, M. Antimicrobial activity of mint essential oils. *J. Agric. Food Chem.* **1995**, *43*, 2384–2388. [CrossRef]
429. Radulovic, N.S.; Blagojevic, P.D.; Stojanovic-Radic, Z.Z.; Stojanovic, N.M. Antimicrobial Plant Metabolites: Structural Diversity and Mechanism of Action. *Curr. Med. Chem.* **2013**, *20*, 932–952. [CrossRef] [PubMed]
430. Nowotarska, S.; Nowotarski, K.; Friedman, M. Effect of structure on the interactions between five natural antimicrobial compounds and phospholipids of bacterial cell membrane on model monolayers. *Molecules* **2014**, *19*, 7497–7515. [CrossRef]
431. Helander, I.M.; Alakomi, H.; Latva-Kala, K.; Mattila-Sandholm, T.; Pol, I.; Smid, E.J.; Gorris, L.G.M.; von Wright, A. Characterization of the action of selected essential oil components on Gram-negative bacteria. *J. Agric. Food Chem.* **1998**, *46*, 3590–3595. [CrossRef]
432. Lambert, R.J.W.; Skandamis, P.N.; Coote, P.J.; Nychas, G.J. A study of the minimum inhibitory concentration and mode of action of oregano essential oil, thymol and carvacrol. *J. Appl. Microbiol.* **2001**, *91*, 453–462. [CrossRef] [PubMed]
433. Walsh, S.E.; Maillard, J.Y.; Russell, A.D.; Catrenich, C.E.; Charbonneau, D.L.; Bartolo, R.G. Activity and mechanisms of action of selected biocidal agents on Gram-positive and negative bacteria. *J. Appl. Microbiol.* **2003**, *94*, 240–247. [CrossRef] [PubMed]
434. Horváth, G.; Kovács, K.; Kocsis, B.; Kustos, I. Effect of thyme (*Thymus vulgaris* L.) essential oil and its main constituents on the outer membrane protein composition of *Erwinia* strains studied with microfluid chip technology. *Chromatographia* **2009**, *70*, 1645–1650. [CrossRef]
435. Di Pasqua, R.; Mamone, G.; Ferranti, P.; Ercolini, D.; Mauriello, G. Changes in the proteome of *Salmonella enterica* serovar Thompson as stress adaptation to sublethal concentrations of thymol. *Proteomics* **2010**, *10*, 1040–1049. [CrossRef] [PubMed]
436. Lachowicz, K.J.; Jones, G.P.; Briggs, D.R.; Bienvenu, F.E.; Wan, J.; Wilcock, A.; Coventry, M.J. The synergistic preservative effects of the essential oils of sweet basil (*Ocimum basilicum* L.) against acid-tolerant food microflora. *Lett. Appl. Microbiol.* **1998**, *26*, 209–214. [CrossRef] [PubMed]
437. Moleyar, V.; Narasimham, P. Antibacterial activity of essential oil components. *Int. J. Food Microbiol.* **1992**, *16*, 337–342. [CrossRef]
438. Mulyaningsih, S.; Sporer, F.; Zimmermann, S.; Reichling, J.; Wink, M. Synergistic properties of the terpenoids aromadendrene and 1,8-cineole from the essential oil of *Eucalyptus globulus* against antibiotic-susceptible and antibiotic-resistant pathogens. *Phytomedicine* **2010**, *17*, 1061–1066. [CrossRef] [PubMed]
439. Bassolé, I.H.N.; Juliani, H.R. Essential oils in combination and their antimicrobial properties. *Molecules* **2012**, *17*, 3989–4006. [CrossRef] [PubMed]
440. Ntalí, N.G.; Ferrari, F.; Giannakou, I.; Menkissoglu-Spiroudi, U. Synergistic and antagonistic interactions of terpenes against *Meliodogyns incognita* and the nematicidal activity of essential oils from seven plants indigenous to Greece. *Pest Manag. Sci.* **2011**, *67*, 341–351. [CrossRef] [PubMed]
441. Wanghen, P.F.; Chang, S.T. Antifungal activities of essential oils and their constituents from indigenous cinnamon (*Cinnamomum osmophloem*) leaves against wood decay fungi. *Bioresource Technol.* **2005**, *96*, 813–818.
442. Larsen, A.G.; Knoechel, S. Antimicrobial activity of food-related *Penicillium* sp. against pathogenic bacteria in laboratory media and a cheese model system. *J. Appl. Microbiol.* **1997**, *83*, 111–119. [CrossRef] [PubMed]
443. Jayaprakasha, G.K.; Rao, L.J.M. Chemistry, Biogenesis, and Biological Activities of *Cinnamomum zealamicum*. *Cr. Rev. Food Sci.* **2011**, *51*, 547–562. [CrossRef] [PubMed]
444. Bosca, F.; Miranda, M.A. Photosensitizing drugs containing the benzophenone chromophore. *J. Photochem. Photobiol. B Biol.* 1998, 43. [CrossRef]

445. Ogunlesi, M.; Okiei, W.; Ofor, E.; Osibote, A.E. Analysis of the essential oil from the dried leaves of *Euphorbia hirta* Linn (Euphorbiaceae), a potential medication for asthma. *Afr. J. Biotechnol.* 2009, 8, 7042–7050.

446. Zavala-Sanchez, M.A.; Perez-Gutierrez, S.; Perez-Gonzalez, C.; Sanchez-Saldivar, D.; Arias-Garcia, L. Antidiarrhoeal activity of nonanal, an aldehyde isolated from *Artemisia ludoviciana*. *Pharm. Biol.* 2002, 40, 263–268. [CrossRef]

447. Kobaisy, M.; Tellez, M.R.; Webber, C.L.; Dayan, F.E.; Schrader, K.K.; Wedge, D.E. Phytotoxic and fungitoxic activities of the essential oil of kenaf (*Hibiscus cannabinus*) leaves and its composition. *J. Agric. Food Chem.* 2001, 49, 3768–3771. [CrossRef] [PubMed]

448. Grundy, S.M.; Denke, M.A. Dietary influences on serum lipids and lipoproteins. *J. Lipid Res.* 1990, 31, 1149–1172. [PubMed]

449. Dilika, F.; Bremner, P.D.; Meyer, J.J.M. Antibacterial activity of linoleic and oleic acids isolated from Helichrysum pedunculatum: A plant used during circumcision rites. *Fitoterapia* 2000, 71, 450–452. [CrossRef]

450. Seidel, V.; Taylor, P.W. In vitro activity of extracts and constituents of *Pelargonium* against rapidly growing mycobacteria. *Int. J. Antimicrob. Ag.* 2004, 23, 613–619. [CrossRef] [PubMed]

451. Anderson, I.B.; Mullen, W.H.; Meeker, J.E.; Khojasteh-Bakht, S.C.; Oishi, S.; Nelson, S.D.; Blanc, P.D. Pennyroyal toxicity: measurement of toxic metabolite levels in two cases and review of the literature. *Ann. Intern. Med.* 1996, 124, 726–734. [CrossRef] [PubMed]

452. Woolf, A. Essential oil poisoning. *J. Toxicol. Clin. Toxicol.* 1999, 37, 721–727. [CrossRef] [PubMed]

453. Gordon, W.P.; Forte, A.J.; McMurtry, R.J.; Gal, J.; Nelson, S.D. Hepatotoxicity and pulmonary toxicity of pennyroyal oil and its constituent terpenes in the mouse. *Toxicol. Appl. Pharm.* 1982, 65, 413–424. [CrossRef]

454. Zhou, S.; Koh, H.L.; Gao, Y.; Gong, Z.Y.; Lee, E.J.D. Herbal bioactivation: The good, the bad and the ugly. *Life Sci.* 2004, 74, 935–968. [CrossRef] [PubMed]

© 2016 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC-BY) license (http://creativecommons.org/licenses/by/4.0/).