

1 *Review*

## 2 **Plants of the Genus *Zingiber* as Source of** 3 **Antimicrobial Agents: from Tradition to Pharmacy**

4 **Mehdi Sharifi-Rad<sup>1</sup>, Elena Maria Varoni<sup>2</sup>, Bahare Salehi<sup>3,\*</sup>, Javad Sharifi-Rad<sup>4,\*</sup>, Karl R.**  
5 **Matthews<sup>5</sup>, Seyed Abdulmajid Ayatollahi<sup>4,6</sup>, Farzad Kobarfard<sup>4,7</sup>, Salam A. Ibrahim<sup>8</sup>, Dima**  
6 **Mnayer<sup>9</sup>, Zainul Amiruddin Zakaria<sup>10,11</sup>, Majid Sharifi-Rad<sup>12</sup>, Zubaida Yousaf<sup>13</sup>, Marcello Iriti<sup>14,\*</sup>,**  
7 **Adriana Basile<sup>15</sup>, Daniela Rigano<sup>16,\*</sup>**

8 <sup>1</sup>Department of Medical Parasitology, Zabol University of Medical Sciences, Zabol 61663-335, Iran;

9 [mehdi\\_sharifirad@yahoo.com](mailto:mehdi_sharifirad@yahoo.com)

10 <sup>2</sup>Dipartimento di Scienze Biomediche, Chirurgiche ed Odontoiatriche, Università degli Studi di Milano, Italy;

11 [elena.varoni@unimi.it](mailto:elena.varoni@unimi.it)

12 <sup>3</sup>Zabol Medicinal Plants Research Center, Zabol University of Medical Sciences, Zabol, Iran;

13 [bahar.salehi007@gmail.com](mailto:bahar.salehi007@gmail.com)

14 <sup>4</sup>Phytochemistry Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran;

15 [javad.sharifirad@gmail.com](mailto:javad.sharifirad@gmail.com)

16 <sup>5</sup>Department of Food Science, Rutgers University, New Brunswick, NJ 08901, New Jersey, USA;

17 [bijan@sebs.rutgers.edu](mailto:bijan@sebs.rutgers.edu)

18 <sup>6</sup>Department of Pharmacognosy, School of Pharmacy, Shahid Beheshti University of Medical Sciences Tehran,

19 Iran; [majid\\_ayatollahi@yahoo.com](mailto:majid_ayatollahi@yahoo.com)

20 <sup>7</sup>Department of Medicinal Chemistry, School of Pharmacy, Shahid Beheshti University of Medical Sciences,

21 Iran; [farzadkf@yahoo.com](mailto:farzadkf@yahoo.com)

22 <sup>8</sup>Food Microbiology and Biotechnology Laboratory, 171 Carver Hall, College of Agriculture and

23 Environmental Sciences North Carolina A & T State University Greensboro, NC 27411-1064;

24 [ibrah001@ncat.edu](mailto:ibrah001@ncat.edu)

25 <sup>9</sup>Faculty of Agricultural Engineering and Veterinary Medicine, Lebanese University, Dekwaneh, Beirut 6573,

26 Lebanon; [d\\_mnayer@yahoo.fr](mailto:d_mnayer@yahoo.fr)

27 <sup>10</sup>Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia,

28 Selangor, 43400 Serdang, Malaysia; [dr\\_zaz@yahoo.com](mailto:dr_zaz@yahoo.com)

29 <sup>11</sup>Integrative Pharmacogenomics Institute (iPROMISE), Level 7, FF3 Building, Universiti Teknologi MARA,

30 42300 Puncak Alam, Selangor, Malaysia; [dr\\_zaz@yahoo.com](mailto:dr_zaz@yahoo.com)

31 <sup>12</sup>Department of Range and Watershed Management, Faculty of Natural Resources, University of Zabol,

32 Zabol 98615-538, Iran; [majid.sharifirad@gmail.com](mailto:majid.sharifirad@gmail.com)

33 <sup>13</sup>Department of Botany, Lahore College for Women University, Jail Road Lahore, Pakistan;

34 [mussabuswaeshal@hotmail.com](mailto:mussabuswaeshal@hotmail.com)

35 <sup>14</sup>Department of Agricultural and Environmental Sciences, Milan State University, Milan, Italy;

36 [marcello.iriti@unimi.it](mailto:marcello.iriti@unimi.it)

37 <sup>15</sup>Department of Biological Sciences—Plant Biology Section, University of Naples “Federico II”, Naples 80126,

38 Italy; [adbabile@unina.it](mailto:adbabile@unina.it)

39 <sup>16</sup>Department of Pharmacy, University Federico II of Naples, via D. Montesano 49, CAP 80131, Naples, Italy;

40 [drigano@unina.it](mailto:drigano@unina.it)

41  
42 \* Correspondences:

43 [bahar.salehi007@gmail.com](mailto:bahar.salehi007@gmail.com) (B.S.); [javad.sharifirad@gmail.com](mailto:javad.sharifirad@gmail.com) (J.S.-R.); [marcello.iriti@unimi.it](mailto:marcello.iriti@unimi.it) (M.I.);

44 [drigano@unina.it](mailto:drigano@unina.it) (D.R.); Tel.: +98-22-51-790 (B.S.); Tel.: +98-88-200-104 (J.S.-R.); Tel.: +39-02-5031-6766 (M.I.);

45 Tel.: +39 081 679897 (D.R.)

51 **Abstract:** Plants of the genus *Zingiber* (Family Zingiberaceae) are widely used throughout the world  
52 as food and medicinal plants. They represent very popular herbal remedies in various traditional  
53 healing systems; in particular, rhizome of *Zingiber* spp. plants has a long history of ethnobotanical  
54 uses because of a plethora of curative properties. Antimicrobial activity of rhizome essential oil has  
55 been extensively confirmed *in vitro* and attributed to its chemical components, mainly consisting in  
56 monoterpene and sesquiterpene hydrocarbons such as  $\alpha$ -zingiberene, ar-curcumene,  $\beta$ -bisabolene  
57 and  $\beta$ -sesquiphellandrene. In addition, gingerols have been identified as the major active  
58 components in the fresh rhizome, whereas shogaols, dehydrated gingerol derivatives, are the  
59 predominant pungent constituents in dried rhizome. *Zingiber* spp. may thus represent a promising  
60 and innovative source of natural alternatives to chemical food preservatives. This approach would  
61 meet the increasing concern of consumers aware of the potential health risks associated with the  
62 conventional antimicrobial agents in food. This narrative review aims providing a literature  
63 overview on *Zingiber* spp. plants, their cultivation, traditional uses, phytochemical constituents and  
64 biological activities.

65 **Keywords:** *Zingiber*; ginger; essential oil; rhizome; herbal remedies; traditional healing systems;  
66 food preservatives  
67

---

## 68 1. Introduction

69 Today's consumers are becoming more aware of the link between diet and health. For instance,  
70 Mediterranean diet, possesses a plethora of bioactive phytochemicals, e.g. polyphenols and  
71 melatonin [1,2], which can contribute to its beneficial effects against chronic-degenerative disorders,  
72 including cancer, cardiovascular diseases and diabetes [3-5]. This trend is leading to increasing  
73 demand for the use of natural ingredients as food supplements and preservatives. In addition,  
74 increasing number of microorganisms that are not only antibiotic resistant, but are more tolerant to  
75 existing preservative techniques is of worldwide concern [6]. Plant derived extracts that have  
76 biological activities, such as antimicrobial, antidiabetic or antihypertensive effects have the potential  
77 to fulfill the need for safe natural preservatives [7-12]. Therefore, much emphasis has been focused  
78 on the investigation of plant derived natural sources of antimicrobials, compounds that could  
79 potentially replace chemical preservatives and synthetic antimicrobial ingredients [13-17].

80 Herbs and spices, which are important part of the human diet, have been used for thousands of  
81 years to enhance the flavor, color and aroma of food. In addition to boosting flavor, herbs and spices  
82 are also known for their preservative, antioxidant, antimicrobial and other medicinal properties  
83 [8,16,18]. The genus *Zingiber*, belonging to the family Zingiberaceae, comprises about 85 species of  
84 herbs mostly grown in Asia, Central, South America and Africa [19]. Although different members of  
85 this genus are somewhat similar in morphology, they differ widely in their pharmacological and  
86 therapeutic properties [20].

87 The most popular spice, ginger, comes from the underground stems or rhizomes of the plant  
88 *Zingiber officinale* Roscoe. It has been widely reported in literature that ginger is consumed worldwide  
89 as a spice and flavoring agent and is attributed to have many medicinal properties [19,21-23].

90 The essential oil (EO) from *Zingiber* rhizome is pale yellow to light-amber, contains both  
91 aromatic and pungent compounds and can be extracted with yields ranging from 1.5-3.0%,  
92 depending on the quality of the crop [24].

93 Phytochemical investigation of the rhizomes of several *Zingiber* spp. has revealed the presence  
94 of bioactive compounds such as gingerols, shogaols, diarylheptanoids, phenylbutenoids, flavanoids,  
95 diterpenoids and sesquiterpenoids [22]. The gingerols are identified as the major active components  
96 in the fresh rhizome of the plant. In addition, shogaols, dehydrated gingerol derivatives, are the  
97 predominant pungent constituents in dried ginger [25].

98 *Zingiber* plants possess various pharmacological and physiological effects and are common  
99 ingredients in traditional medicines. The rhizomes have been shown to be effective in the treatment  
100 of several medical conditions including stomach problems, nausea, vomiting, epilepsy, sore throat,

101 cough, common cold, bruises, wounds, liver complaints, rheumatism, muscular pains,  
102 atherosclerosis, migraine headaches, high cholesterol, ulcers, and stomach discomfort [26]. In  
103 addition, phenolic compounds, especially the gingerols, in ginger root, have been shown to have  
104 chemopreventive effects that have been associated with their antioxidant and anti-inflammatory  
105 activities [26].

106 The EOs of *Zingiber* rhizomes are used for preserving various foods against autoxidation and  
107 microbial spoilage because of their antioxidant and antimicrobial properties [24,27,28]. Many *in vitro*  
108 studies demonstrated the antimicrobial potential of *Zingiber* plant extracts against both gram positive  
109 (*Bacillus cereus*, *Staphylococcus aureus*) and gram negative (*Escherichia coli*, *Salmonella typhi*,  
110 *Pseudomonas aeruginosa*, *Klebsiella pneumonia*) bacteria [29]. The EOs also exhibited significant  
111 antifungal activity against *Candida glabrata*, *C. albicans* and *Aspergillus niger* [19]. These results suggest  
112 that EO of *Zingiber* plant could be used in the treatment of many bacterial and fungal diseases as well  
113 as in food preservation as natural preservative [20,24]. The main aim of this paper is to provide an  
114 overview of the biological activity of the *Zingiber* spp. EOs and their components, focusing on the  
115 potential application of *Zingiber* plants as natural preservatives for foods.  
116

## 117 2. Genus *Zingiber* Plant Cultivation

118 Most *Zingiber* spp. plants are aromatic, perennial herbs with the characteristic of growing  
119 horizontal or fibrous rhizomes. They are cultivated in many countries, though these plants prefer  
120 moist, tropical conditions. Ginger thrives in well drained soils like sandy loam, clay loam, red loam  
121 or lateritic loam. A friable loam with a pH of 6.0 to 6.5 rich in humus is optimal for production of  
122 *Zingiber*. The crop prefers a temperature range of 19-28°C and a humidity of 70-90% [30]. Before  
123 cultivation, the land needs to be ploughed 4 to 5 times. Ginger is propagated by portions of rhizomes  
124 known as seed rhizomes. Preserved seed rhizomes are carefully cut into small pieces of 2.5-5.0 cm  
125 length weighing 20-25 g; each of the piece should have one or two buds. China, Indonesia, Nigeria,  
126 Philippines, Thailand and India are the main ginger producers. Ginger reaches full maturity in 210-  
127 240 days after planting. Harvesting of ginger for vegetable purpose starts after 180 days based on the  
128 demand. As ginger is used in many different forms and high amounts are consumed in the countries  
129 where it is grown or is used to provide seeds for the next crop, it is difficult to get accurate figures of  
130 trade of *Zingiber* [31,32]. To enhance the productivity of crop, in some countries, at the time of  
131 planting, people use decomposed cattle manure or compost at 25-30 tons/ha, either by broadcasting  
132 over the beds prior to planting or applied in the pits at the time of planting. Rhizome seed generation  
133 is difficult and expensive. Therefore, people are looking for other techniques to cultivate *Zingiber* cost  
134 effectively. A transplanting technique in ginger by using single bud sprouts (about 5 g) is  
135 recommended to produce high quality planting material with reduced cost. The technique involves  
136 raising transplants from single sprout seed rhizomes in the pro-tray and planting in the field after 30-  
137 40 days. This technique is greatly useful to reduce the quantity of rhizome seed [30]. To improve the  
138 quality, in some countries, crop rotation and intercropping techniques are also used. Ginger is usually  
139 intercropped in coconut, areca nut, coffee and orange plantations in Kerala and Karnataka [30].  
140 Changes in soil fertility for improved growth of ginger under different quantity of pigeon pea  
141 hedgerow alley management gave significant increase in ginger yield [33]. Another important  
142 technique is propagation by using internodal cuttings [34]. Aeroponic cultivation of ginger has also  
143 been introduced [35], as well as micropropagation and cytogenetic assessment [36].  
144

## 145 3. Chemical Composition of Essential Oils Obtained from Genus *Zingiber* Plants

146 The genus *Zingiber* is widely used in the world for its medicinal and biological properties [37].  
147 Among this genus, *Z. officinale* (ginger) is well known and mostly studied for its health benefits  
148 [38,39].

149 As previously introduced, the color of *Z. officinale* EO varies from pale yellow to light amber and  
150 the extraction yield ranges from 1.5 to 3% [40]. Different studies have documented their biological  
151 properties such as antimicrobial, antioxidant, cytotoxic, insecticidal [41,42], anti-inflammatory effects  
152 [39] as well as food preservative characteristics [43].

153 These properties have been attributed to the chemical components of *Z. officinale* EO, mainly  
154 consisting in monoterpene and sesquiterpene hydrocarbons (Fig. 1) [42]. The most abundant  
155 compounds are  $\alpha$ -zingiberene, responsible for the distinctive flavor and aroma, geranial, ar-  
156 curcumene,  $\beta$ -bisabolene,  $\beta$ -sesquiphellandrene and neral [27,44-46]. Other pungent constituents  
157 found in lower amount are gingerol and shogaol [47].

158 However, the amount and the composition of the bioactive substances may vary among  
159 different *Zingiber* species, and according to different factors such as the extraction methods, the  
160 geographic and the growing conditions, the harvest time etc. [46-49]. Table 1 shows the major  
161 constituents of EOs from different *Zingiber* species, the extraction methods used and their biological  
162 activities.

163 *Z. officinale* EO was obtained using different extraction methods including conventional  
164 hydrodistillation, microwave-assisted hydrodistillation, solvent free microwave hydrodistillation  
165 and improved solvent-free microwave extraction with three types of microwave-absorption medium.  
166 Results showed that  $\alpha$ -zingiberene was the most abundant compound found in all EOs studied  
167 ranging from 17.4 to 25.4%, followed by ar-curcumene (14.1-16.4%),  $\beta$ -bisabolene (9.9-12.5%) and  $\beta$ -  
168 sesquiphellandrene (9.7-13.4%) [46]. These results are in accordance with those obtained from dried  
169 ginger rhizome EO, showing that the major components were  $\alpha$ -zingiberene (29.5%) and  
170 sesquiphellandrene (18.4%) [50]. Again,  $\alpha$ -zingiberene was reported as a major constituent (28.62%)  
171 found in the fresh rhizome EO of *Z. officinale*, followed by camphene (9.32%), ar-curcumene (9.09%)  
172 and  $\beta$ -phellandrene (7.97%) [45].

173 A comparative chemical composition was conducted on fresh and dry rhizome EOs belonging  
174 to *Z. officinale* cv. Nedumangadu.  $\alpha$ -Zingiberene was the major compound found both in fresh and  
175 dry ginger EOs (28.6 and 30.9%, respectively). Fresh ginger EO also contained geranial (8.5%), ar-  
176 curcumene (5.6%) and  $\beta$ -bisabolene (5.8%), whereas ar-curcumene (11%),  $\beta$ -bisabolene (7.2%),  $\beta$ -  
177 sesquiphellandrene (6.6%) and germacrene-D (4.2%) were present in the dry ginger EO. Fresh ginger  
178 EO exhibited higher antibacterial activity due to the oxygenated compounds (29.2%) which are higher  
179 than in dry ginger EO (14.4%) [51].

180 Many *Z. officinale* cultivars were studied and compared for their EO composition. Seventeen  
181 cultivars from north India were studied for their chemical composition and the major components  
182 were camphene ( $8.49 \pm 0.41\%$ ), neral ( $4.95 \pm 0.34\%$ ), geranial ( $12.36 \pm 0.46\%$ ),  $\alpha$ -zingiberene ( $20.98 \pm$   
183  $2.34\%$ ) and  $\beta$ -sesquiphellandrene ( $7.96 \pm 0.66\%$ ) [52].

184 Three sub Himalayan ginger cultivars, namely Gorubathane, Shingboi and Thingria were  
185 studied for their EO composition. Results showed that  $\alpha$ -zingiberene (32.2%) and  $\beta$ -  
186 sesquiphellandrene (10.9%) were the major compounds in Gorubathane EO, whereas  $\alpha$ -zingiberene  
187 (12.58%) and ar-curcumene (9.89%) were mostly present in Thingria EO. However, geranial (20.07%)  
188 and neral (9.44%) were the main constituents found in Shingboi EO [44].

189 The composition of EO may vary not only within different ginger cultivars, but also according  
190 to the parts of the plant studied, as demonstrated by Sivasothy et al., [22] who showed that the  
191 composition of EO obtained by hydrodistillation of the leaves and rhizomes of *Z. officinale* var.  
192 Rubrum Theilade were different. In fact,  $\beta$ -caryophyllene (31.7%) was the major compound found in  
193 the leaf oil, while rhizome oil was predominantly rich in monoterpenoids, such as camphene (14.5%),  
194 geranial (14.3%) and geranylacetate (13.7%).

195 Regarding the extraction methods used, water and steam distillation were used to obtain EO  
196 from Vietnamese *Z. officinale*. The main EO components obtained by water distillation were  $\alpha$ -  
197 curcumene (11.7%) and  $\beta$ -bisabolene (4.1%), while those obtained by steam distillation were ar-  
198 curcumene (12.6%),  $\alpha$ -zingiberene (10.3%),  $\beta$ -bisabolene (8.1%) and  $\beta$ -sesquiphellandrene (7.4%). The  
199 difference in the composition can be because, during water distillation, the raw material was in  
200 contact with water, which is not the case during steam distillation. As a result, the extraction method  
201 used may affect the composition of the EO released [48]. The chemical composition of the *Z. officinale*  
202 EOs previously cited is in accordance with a number of studies which reported the presence of these  
203 major compounds, though found in different amounts [28,39,53].

204 Ginger EO rich in constituents such as  $\beta$ -sesquiphellandrene (27.16%), caryophyllene (15.29%),  
205  $\alpha$ -zingiberene (13.97%),  $\alpha$ -farnesene (10.52%) and ar-curcumene (6.62%) showed high antimicrobial  
206 and antioxidant activities [28]. *Z. officinale* EO rich in ar-curcumene (59%),  $\beta$ -myrcene (14%), 1,8-cineol  
207 (8%), citral (7.5%) and  $\alpha$ -zingiberene (7.5%) exhibited high anti-inflammatory effects [54]. Ginger EO  
208 containing geranial (25.9%),  $\alpha$ -zingiberene (9.5%), (E,E)- $\alpha$ -farnesene (7.6%), neral (7.4%) and ar-  
209 curcumene (6.6%) as major components was an effective antibacterial and antifungal agent, as well  
210 as a more powerful antioxidant than butylated hydroxyanisole (BHA) [27].  $\alpha$ -Zingiberene, a key  
211 component of ginger EO, was found in low amount (1.64%) in the study conducted by Mesomo et al.  
212 [37]. The main components were ar-curcumene (11.32%), geranial (10.66%) followed by camphene  
213 (4.88%),  $\beta$ -bisabolene (4.45%) eucalyptol (3.14%), isobornyl formate (1.95%).

214 Apart from the common ginger (*Z. officinalis*), many wild and cultivated species of this genus  
215 have been studied across the world and characterized for the beneficial phytochemicals present in  
216 rhizome EO[54].

217 The chemical composition of a species native to Thailand, *Zingiber cassumunar* Roxb., showed  
218 that major compounds were sabinene (36.71-53.50%),  $\gamma$ -terpinene (5.27-7.25%), terpinen-4-ol (21.85-  
219 29.96%) and (E)-1-(3-,4-dimethoxyphenyl) butadiene (0.95-16.16%). The EO yield ranged from 1.26%  
220 to 1.37% [49]. These results are in agreement with recent results on *Z. cassumunar* rhizome EO where  
221 the major constituents were terpinen-4-ol ( $40.5 \pm 6.6\%$ ) and sabinene ( $17.4 \pm 1.4\%$ ) [55]. These  
222 phytochemicals have shown various pharmacological properties, including anti-inflammatory,  
223 antifungal and antibacterial effects [56]. The chemical composition of *Z. cassumunar* EO from Malaysia  
224 showed that 6,9,9-tetramethyl-2,6,10-cycloundecatrien-1-one (60.77%) and  $\alpha$ -caryophyllene (23.92%)  
225 were the most abundant components [57].

226 The effects of the growing conditions, different cultivation areas and harvest time were studied  
227 to compare the composition of EOs from *Zingiber montanum* Koenig. Results showed differences in  
228 their constituents according to these exogenous factors. The major components measured were  
229 sabinene (52.64-56.34 %), terpinen-4-ol (7.16-10.17%) and (E)-1-(3-,4-dimethoxyphenyl) butadiene  
230 (10.88– 14.7%) [58].

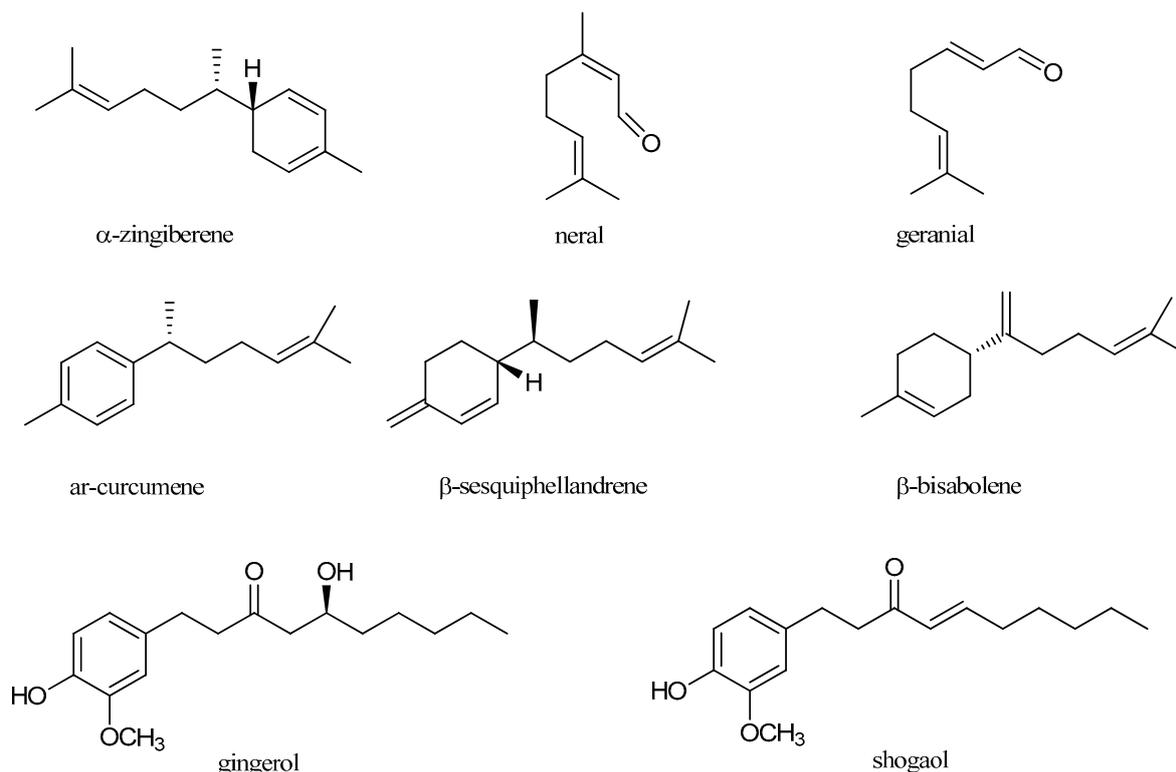
231 Coral ginger (*Zingiber corallinum* Hance), an herbal remedy in traditional Chinese medicine, was  
 232 studied for its rhizome EO. Sabinene (53.38%),  $\alpha$ -terpinene (3.23%),  $\gamma$ -terpinene (2.16%), terpinen-4-  
 233 ol (22.66%),  $\beta$ -sesquiphellandrene (1.41%) and 1,4-bis(methoxy)-triquinacene (9.64%) were the major  
 234 compounds [59].

235 The chemical composition of *Zingiber zerumbet* (L.) Sm. var. *Darcyi* EO obtained by  
 236 hydrodistillation from the rhizome showed that zerumbone (69.9%),  $\alpha$  humulene (12.9%), humulene  
 237 epoxide II (2.5%), caryophyllene oxide (1.1%) and camphene (1.9%) were the major constituents [60].

238 *Zingiber nimmonii* (J. Graham) Dalzell is an endemic species from the Western Ghats, in South  
 239 India. The major components of the rhizome EO were different from the rhizome EO obtained from  
 240 other species. The major constituents were myrcene (5.1%),  $\beta$ -caryophyllene (26.9%),  $\alpha$ -humulene  
 241 (19.6%) and  $\alpha$ -cadinol (5.2%) [61]. These results are also in accordance with Sabulal et al. [19] who  
 242 showed that *Z. nimmonii* EO is a unique caryophyllene-rich natural source.

243 *Zingiber moran* is a local ginger variety endemic to north-east Indian region, rich in camphene,  
 244 citral, and linalool [54]. *Zingiber wrayi* var. *Halabala* C.K.Lim, a local herb from the Bala Forest in  
 245 Narathiwat (Thailand), was investigated for its EO composition. Four compounds including *trans*-  
 246 anethole (96.5%), estragol, camphor and *m*-phenylphenol [62].

247  
 248



249  
 250  
 251  
 252  
 253

**Figure 1.** Chemical structures of major components of *Z. officinale*.

254 **Table 1:** Extraction methods, major constituents and biological activities of *Zingiber* spp. essential oils.

Plant	Extraction methods	Major compounds	Biological activities	References
<i>Z. officinale</i>	Hydrodistillation	ar-curcumene (11.32%), geranial (10.66%), camphene (4.88%), eucalyptol (3.14%), isobornyl formate (1.95%), $\alpha$ -zingiberene (1.64 %)	Antibacterial	[37]
<i>Z. officinale</i>	Hydrodistillation, microwave assisted hydrodistillation, solvent-free microwave hydrodistillation, improved solvent-free microwave extraction	$\alpha$ -zingiberene (17.4- 25.4%), ar-curcumene (14.1-16.4%), $\beta$ -bisabolene (9.9-12.5%), $\beta$ -sesquiphellandrene (9.7-13.4%)	NR*	[46]
<i>Z. officinale</i>	Hydrodistillation	Geranial (25.9%), $\alpha$ -zingiberene (9.5%), (E,E)- $\alpha$ -farnesene (7.6%), neral (7.4%), ar-curcumene (6.6%)	Antibacterial, antifungal, antioxidant	[28]
Three sub-Himalayan <i>Z. officinalis</i> cultivars (Gorubathane, Shingboi Thingria)	Hydrodistillation	Gorubathane: $\alpha$ -zingiberene (32.2%), $\beta$ -sesquiphellandrene (10.9%); Thingria: $\alpha$ -zingiberene (12.58%), ar-curcumene (9.89%); Shingboi: geranial (20.07%), neral (9.44%)	NR	[44]
Fresh and dry <i>Z. officinale</i> var. Nedumangadu	Hydrodistillation	Fresh ginger: $\alpha$ -zingiberene (28.6%), geranial (8.5%) ar-curcumene (5.6%), $\beta$ -bisabolene (5.8%); Dry ginger: $\alpha$ -zingiberene (30.9%), ar-urcumene (11%), $\beta$ -bisabolene (7.2%), $\beta$ -sesquiphellandrene (6.6%), germacrene-D (4.2%)	Antibacterial, antifungal	[51]
<i>Z. officinale</i>	Hydrodistillation	$\alpha$ -zingiberene (28.62%), camphene (9.32%), ar-curcumene (9.09%), $\beta$ -phellandrene (7.97%)	Antifungal, antioxidant	[45]

<i>Z. officinale</i>	Hydrodistillation	$\beta$ -sesquiphellandrene (27.16%), caryophyllene (15.29%), zingiberene (13.97%), $\alpha$ -farnesene (10.52%), ar-curcumin (6.62%)	Antibacterial, antioxidant	[28]
<i>Z. montanum</i>	Hydrodistillation	Sabinene (52.64-56.34%), terpinen-4-ol (7.16-10.17%), (E)-1-(3-4-dimethoxyphenyl) butadiene (10.88-14.7%)	NR	[58]
<i>Z. cassumunar</i> (three native cultivars)	Hydrodistillation	Sabinene (36.71-53.50%), $\gamma$ -terpinene (5.27-7.25%), terpinen-4-ol (21.85-29.96%), (E)-1-(3-4-dimethoxyphenyl) butadiene (0.95-16.16%)	NR	[49]
<i>Z. cassumunar</i>	Steam distillation	6,9,9-tetramethyl-2,6,10-cycloundecatrien-1-one (60.77%), $\alpha$ -caryophyllene (23.92%)	Slight antimicrobial	[57]
<i>Z. officinale</i>	Steam distillation	ar-curcumene (59%), b-myrcene (14%), 1,8-cineol (8%), citral (7.5%), and $\alpha$ -zingiberene (7.5%)	Inflammatory effects	[39]
<i>Z. zerumbet</i> var. <i>Darcyi</i>	Hydrodistillation	zerumbone (69.9%), $\alpha$ -humulene (12.9%), humulene epoxide II (2.5%), caryophyllene oxide (1.1%), camphene (1.9%)	NR	[60]
<i>Z. corallinum</i>	Steam distillation	Sabinene (53.38%), $\alpha$ -terpinene (3.23%), $\gamma$ -terpinene (2.16%), terpinen-4-ol (22.66%), $\beta$ -sesquiphellandrene (1.41%), 1,4-bis(methoxy) triquinacene (9.64%)	NR	[59]
<i>Z. nimmonii</i>	Hydrodistillation	Myrcene (5.1%), $\beta$ -caryophyllene (26.9%), $\alpha$ -humulene (19.6%), $\alpha$ -cadinol (5.2%)	Larvicidal and repellent	[31]
<i>Z. nimmonii</i>	Hydrodistillation	$\beta$ -caryophyllene (42.2%), $\alpha$ -humulene, $\alpha$ -caryophyllene (27.7%)	Antimicrobial	[19]
<i>Z. moran</i>	Hydrodistillation	Camphene, citral, linalool	Cytotoxic	[54]
<i>Z. wrayi</i> var. <i>Halabala</i> ,	Steam distillation	<i>Trans</i> -anethole (96.5%)	Antibacterial	[62]

\*NR, not reported

257

## 258 4. The genus *Zingiber* in Traditional Healing Systems

259

### 260 4.1. Medicinal Uses of Ginger

261 Ginger (*Z. officinale*) is an important plant with several medicinal, ethnomedicinal and  
262 nutritional values. Among different biological activities, ginger has demonstrated anti-inflammatory,  
263 antioxidant, anti-emetic, analgesic, and antimicrobial activities. Overall, they can be mainly ascribed  
264 to 6-gingerol and 6-shogaol, which represent the major compounds in ginger rhizomes, among  
265 hundreds of molecules isolated [63,64].

266 According to recent literature, ginger anti-inflammatory properties are mediated by the  
267 inhibition of 5-lipoxygenase or prostaglandin synthetase, which reduces biosynthesis of  
268 prostaglandins, leukotrienes and pro-inflammatory cytokines such as IL-1, IL-8; TNF- $\alpha$ , and NF $\kappa$ B  
269 [63]. One clinical trial, indeed, reported its beneficial effects in reducing pro-inflammatory cytokines  
270 of patients suffering from osteoarthritis [65]. In addition, the antioxidant activity of the *Z. officinale*  
271 extract [66] has been *in vitro* demonstrated to inhibit the hydroxyl radicals and the lipid peroxidation  
272 products. This was consistent with further studies in animal models, which revealed as it acted by  
273 enhancing antioxidant enzyme defenses and serum glutathione [67]. Similar effects were attributed  
274 to ginger single constituents, namely 6-gingerol, 8-gingerol, 10-gingerol, and 6-shogaol [68] as well  
275 as geranial and neral,  $\alpha$ -zingiberene, camphene,  $\alpha$ -farnesene,  $\beta$ -sesquiphellandrene [69] and  
276 zingerone [67]. 6-Shogaol, in particular, showed the most potent antioxidant and anti-inflammatory  
277 properties, due to the presence of  $\alpha$ ,  $\beta$ -unsaturated ketone moiety [67], while zingerone exhibited, in  
278 mice, protection against radiation-induced toxicity, increasing antiapoptotic molecules (Bcl-2) while  
279 reducing the proapoptotic ones (Bax) [70].

280 Together, the above reported antioxidant and anti-inflammatory properties of ginger support  
281 its preventive role against a plethora of chronic-degenerative diseases [71], including cancer,  
282 cardiovascular disorders, and diabetes.

283 Although still under debate, anticancer activity of ginger is, as mentioned above, mainly related  
284 to the high content of 6-gingerol and 6-shogaol. Ginger and related bioactive molecules, indeed, are  
285 effective in controlling, *in vitro*, viability and invasiveness of colorectal, gastric, ovarian, liver, skin,  
286 breast, and prostate cancer cells [67]. Recent evidence supports, in particular, the role of zingerone  
287 supplementation as chemopreventive agent, reducing cancer incidence in dimethyl hydrazine treated  
288 rats; the mechanism included the inhibition of cell proliferation, the induction of cell apoptosis, and  
289 the suppression of NF- $\kappa$ B and heme oxygenase (HO)-1 expression [70]. The proapoptotic effect and  
290 the promotion of cell cycle arrest in hepatoma and prostate cancer cells were ascribed to the activation  
291 of caspase cascade and the impairment of the nuclear translocation of NF- $\kappa$ B, particularly by 6-  
292 gingerol [70], which was also able to inhibit angiogenesis and invasiveness in the murine cancer  
293 models [70]. Anti-angiogenetic activity of 6-gingerol occurs by the inhibition of the vascular  
294 endothelial growth factor (VEGF), while its anti-metastatic activity could be ascribed to regulation of  
295 matrix metalloproteinases 2/9 transcription [64]. Another active compound contained in ginger is  
296 zerumbone, which induced apoptosis in pancreatic carcinoma cells, through p53 signal pathway and  
297 increasing the activity of caspase-3 [70]. In humans, the chemopreventive effect of ginger has been  
298 mainly investigated against colorectal cancer, in virtue of its anti-inflammatory effects, similarly to

299 those of aspirin. Ginger significantly lowered COX-1 protein expression in patients at increased risk  
300 for colorectal cancer [72], but with no effect on eicosanoid levels [73].

301 The role of ginger in reducing cardiovascular diseases and diabetes is highly related to its ability  
302 in controlling body weight, and reducing serum levels of glucose and lipids. Indeed, a study showed  
303 that ginger significantly decreased glucose, total cholesterol, triglycerides, free fatty acids, LDL and  
304 VLDL, whilst raised HDL in serum of rats with diabetic or fed with a high fat diet [67]. These effects  
305 are mainly related to zingerone [70], and less to shogaols [64]. Recently, in high fat diet fed animals,  
306 zingerone and 6-gingerol both possessed high lipolytic activity: the former by increasing the activity  
307 of norepinephrine-sensitive lipases, enhancing basal lipolysis and isoprenaline-induced lipolysis in  
308 adipocytes [64], while the latter by reducing the levels of fatty acid synthase and adipocyte-specific  
309 fatty acid binding protein [64]. In addition, 6-gingerol could prevent diabetes via the improvement  
310 of adipocyte dysfunction, since it caused the inhibition of the TNF- $\alpha$  mediated down-regulation of  
311 adiponectin expression, as well as arachidonic acid pathway in turn inhibiting anti-platelet  
312 aggregation [64]. A clinical trial showed that ginger consumption enhanced thermogenesis and  
313 reduced feeling of hunger, suggesting a potential role in weight control [74]. In patients with type 2  
314 diabetes, ginger improved glycemic index, total antioxidant capacity [75], insulin sensitivity and lipid  
315 profile, reducing c-reactive protein and prostaglandin E<sub>2</sub> [76,77]. In peritoneal dialysis patients, for  
316 whom one of the major risk factors for cardiovascular disease is serum triglyceride concentration, the  
317 latter resulted reduced by daily administration of 1,000 mg ginger [78].

318 As antimicrobial agent, ginger extract exhibited higher antifungal than antibacterial effects *in*  
319 *vitro*, showing anti-*Candida* activity against strains isolated from patients. This finding was related to  
320 the high anti-biofilm activity against *C. albicans*, at concentrations ranging from 0.625 mg/mL to 5  
321 mg/mL [79]. Ginger was also effective against other fungal strains, such as *Fusarium* spp, and it  
322 inhibited the growth of fungi that were resistant to amphotericin B and ketoconazole [80-82]. Among  
323 bacteria, it showed efficacy against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Acinetobacter*  
324 *Baumannii* [79], *Escherichia Coli*, *Bacillus subtilis* and *Salmonella Typhi* [83]. Furthermore, 6-gingerol and  
325 12-gingerol showed antibacterial activity against periodontal bacteria [83], so that a clinical trial was  
326 performed to test a polyherbal mouthwash containing, among the others, the hydroalcoholic extract  
327 of *Z. officinale*; noteworthy, it was effective in reducing gingival and plaque indices similarly to  
328 chlorhexidine mouthwash [84]. On the other hand, the antidiarrheal activity of 6-gingerol has been  
329 accredited to its ability to bind to the toxin produced by *Vibrio cholera*, rather than due to direct  
330 antibacterial activity [64].

331 Nausea and emesis are among the most common adverse effects of chemotherapeutics as well  
332 as frequent events during pregnancy and post-surgery anesthesia. At preclinical level, 6-gingerol  
333 showed efficacy in rats against cisplatin-induced nausea and vomiting [64]. Along these lines, a  
334 number of clinical trials and related systematic reviews and meta-analysis now support the efficacy  
335 of ginger in reducing hyperemesis during pregnancy [85,86] as well as in alleviating nausea and  
336 vomiting during chemotherapy, especially for breast cancer [87]. Similarly, ginger appeared to reduce  
337 post-anesthesia emesis in gynecological surgery [88] and after antituberculosis drug administration  
338 [89].

339 Analgesic and antipyretic activities of ginger can be ascribed to 6-gingerol, as shown in rats [64].  
340 Injection of 10  $\mu$ g of 6-gingerol into the rat spinal cord was found to be effective in ameliorating  
341 neuropathic pain, via vanilloid receptor-mediated pathway [64]. In humans, ginger intake produced

342 pain relief in primary dysmenorrhea similarly to conventional analgesic drugs [90,91], while  
343 remaining controversial in case of osteoarthritis [92,93]. In addition, it showed abortive effect against  
344 migraine [94] particularly when administered early and in presence of mild migraine [95].

345 Further activities include gastroprotective, immunomodulatory, anti-allergy and  
346 hepatoprotective properties, in all cases mainly related to 6-gingerol [64]. In particular, ginger  
347 reduced the gastropathy induced by some drugs, such as anti-tuberculosis agents [96] and nonsteroid  
348 anti-inflammatory drugs [97]

349 Due to these overwhelming activities supported by preclinical evidences, people of different  
350 cultures have traditionally applied ginger as medicinal agent since a long time ago. A vast body of  
351 anecdotal evidence, which can be used to support ginger uses and efficacy, can be found in various  
352 traditional systems of medicine belonging to Indian, Unani, Chinese, Japanese and other cultures  
353 [98].

354

#### 355 4.1.2. *Ginger in the Indian System of Medicine*

356 Ginger plays an important role in traditional Indian medicine. It is also used as an ingredient in  
357 traditional Indian drinks. Fresh ginger is one of the main spices used for making dishes, both  
358 vegetarian and non-vegetarian foods. In the Ayurveda system of medicine, ginger, either fresh or  
359 dry, has been widely used as a common household remedy for various illnesses [99,100]. Commonly,  
360 both types of ginger, which have similar properties, act as an appetizer, carminative, and stomachic  
361 [101]. Other than that, ginger is acrid, analgesic, antirheumatic, antiphlegmatic, diuretic and  
362 aphrodisiac. Ginger is also used to treat asthma, bronchitis, piles, eructation, and ascites, to help  
363 cleanse the throat, is useful for the voice (corrective of larynx affections), subsides vomiting, relieves  
364 flatulence and constipation, acts as a remedy for cough and relieves neck pain. In addition, the  
365 Ayurveda system also cited that ginger has anti-inflammatory and anti-edematous activities. Due to  
366 its hot property, ginger can cause dryness and, thus, is anti-diarrheal [30]. Moreover, ginger is applied  
367 externally to boils and enlarged glands, and internally as a tonic in Cambodia [102]. According to  
368 Nadkarni [103], ginger also strengthens memory and removes obstruction in the vessels, incontinence  
369 of urine, and nervous diseases.

370 Specifically, the fresh ginger is used together with honey and ghee as a remedy for cough or  
371 alone as a remedy for acute ascites with dropsy arising from liver cirrhosis. Additionally, the juice is  
372 applied as a strong diuretic [102]. The outer skin of ginger is used as a carminative and is said to be  
373 a remedy for opacity of cornea. On the other hand, the dry ginger has been reported to possess  
374 antiarthritic and antifilarial activities [102] while the paste of dry ginger with water is effective in  
375 recovering from fainting and is also applied externally to the eyelids. In addition, the ginger powder  
376 can also be used as a snuff. The dry ginger, in combination with dry rock salt, long pepper and black  
377 pepper is powdered and then mixed with fresh ginger juice and used as a gargle, and for the  
378 treatment of phlegmatic affections of the heart, head, neck, and chest. Moreover, the combination can  
379 also exert remarkable effects against all types of severe fevers and their associated symptoms.

380 Other than its uses to treat human affections, ginger is used of in veterinary as a stimulant and  
381 carminative, in indigestion in horses and cattle, in spasmodic colic of horses, and to prevent gripping  
382 by purgatives [104].

383

#### 384 4.1.3. *Ginger in the Chinese and Japanese Systems of Medicine*

385 Ginger rhizome is an important drug in the Chinese and Japanese medicinal systems [98]. In  
386 Chinese medicine, the fresh ginger (*Rhizoma Zingiberis Recens*) is used as an antiemetic, antitussive,  
387 or expectorant, and is used to induce perspiration and dispel cold, whereas the dried ginger is used  
388 for stomachache, vomiting, and diarrhea accompanied by cold extremities and faint pulse [105]. In  
389 Chinese Materia Medica, Benskey and Gamble [105] cited that ginger has the ability to: *i*) release the  
390 exterior and disperses cold - used for exterior cold patterns; *ii*) warm the middle burner and alleviates  
391 vomiting - used for cold in the stomach, especially when there is vomiting; *iii*) disperse cold and  
392 alleviates coughing, used for coughing from acute wind, cold cough patterns, and chronic lung  
393 disorders with phlegm; *iv*) reduce the poisonous effects of other herbs - used to detoxify or treat  
394 overdoses of other herbs such as *Radix Aconiti Carmichaeli Praeparata* (*Fuzi*) or *Rhizoma Pinelliae*  
395 *Ternata* (*Ban Xia*).

396

#### 397 4.1.4. *Ginger in the Unani System of Medicine*

398 In the Unani system, ginger is used for its anthelmintic, aphrodisiac, carminative, digestive, and  
399 sedative properties; in headache, lumbago, nervous diseases, pains, and rheumatism; and for  
400 strengthening of memory [103]. Ginger is also used in veterinary medicine in horses and cattle for  
401 rheumatic complaints, as an antispasmodic and a carminative in atonic indigestion [106,107].

402

#### 403 4.2. *Examples of Ginger Species and their Uses in Traditional Medicine*

404 Ginger has been used as traditional medicine since ancient times. It is considered as a medicinal  
405 plant as with several curative properties in treating different diseases. In the following sections are  
406 reported some ginger species known for their medicinal properties.

407

#### 408 4.2.1. *Zingiber officinale* Roscoe

409 *Z. officinale* is the best known *Zingiber* plant in the ginger family and is also referred to as garden  
410 ginger or common ginger. This ginger is used in Ayurveda and Chinese medicine, as previously  
411 mentioned, in both fresh and dried preparations, for curing heart problems, treat stomach upset,  
412 diarrhea, headaches, and nausea. Other than that, *Z. officinale* has also been used to promote the  
413 release of bile from the gall bladder, reduce joint pain from arthritis, treat heart and lung diseases;  
414 relief cough and cold, throat infection and even the removal of warts and corns. In both the Chinese  
415 and Japanese systems of medicine, fresh ginger is used for its warming properties and as a remedy  
416 for coughs and nausea, whereas dried ginger is indicated for ailments of the digestive system. In  
417 aromatherapy, the essential oil of ginger is used for muscle and joint pain, sprains, colds, nausea,  
418 diarrhoea, alcoholism and helping the healing of broken bones [108-110]. The rhizome of *Z. officinale*  
419 can also be prepared as a tea for indigestion and increasing the blood circulation and sense of well-  
420 being [111]. In addition, the rhizome extracts have been used in Malay traditional culture to treat  
421 various types of ailments such as inflammatory- and pain-mediated diseases, worm infestation, and  
422 diarrhea.

423

#### 424 4.2.2. *Zingiber montanum* (J.Koenig) Link ex A.Dietr.

425 The rhizomes of *Z. montanum*, also known as “cassumunar ginger”, are used throughout tropical  
426 Asia primarily as a carminative and stimulant for the stomach, and against diarrhea and colic

427 [112,113]. The pounded rhizome is traditionally used in Indonesia as a poultice against headache  
428 while the Malaysians used the rhizome internally as a vermifuge and for postpartum medication.  
429 Moreover, in Laos the rhizome is applied against abscesses, fever, colic, diarrhea and other intestinal  
430 disorders, as a depurative, as well as a poison antidote, whereas, in Thailand, the rhizomes are taken  
431 against asthma and used as the main ingredient in massage oil to relieve muscle pain [112,114]. Other  
432 than that, the rhizome paste is consumed orally by the people leaving in Northeast India to treat  
433 dyspepsia and stomach bloating [113,114].

434

#### 435 4.2.3. *Zingiber mioga* (Thunb.) Roscoe

436 Also known as Japanese ginger or myoga ginger, this perennial herb is native to Japan, China  
437 and the southern part of Korea. The subterranean stem and young flower buds of this species can be  
438 used to cure menstrual irregularity, leucorrhea, heart disease, and eye inflammation. It can also be  
439 used as an expectorant. In addition, *Z. mioga* is used to treat cough and rheumatism in China and  
440 consumed throughout Japan to relieve insect bites, eye inflammation, cough and rheumatism  
441 [115,116].

442

#### 443 4.2.4. *Zingiber spectabile* Griff.

444 Native to maritime Southeast Asia such as peninsular Malaysia and peninsular Thailand, it is a  
445 species of ginger commonly known in the west as "beehive ginger". Different parts of *Z. spectabile* are  
446 widely used in the Malay traditional medicine to treat various ailments. For examples, the pounded  
447 leaves are used as poultice to treat swelling or applied topically to the required part of the body to  
448 treat burns, backaches, headaches and back pain [116]. The juice from leaves has been used by the  
449 Temuan tribe, which is one of the indigenous populations found in Ayer Hitam Forest, Perak,  
450 Malaysia, to treat eye infections and to soothe swollen eyes [117]. In Thailand, the fresh pounded leaf  
451 infusion can be used to wash the infected eyelids or treat inflammation of the eye [118]. Moreover,  
452 the paste of *Z. spectabile* fresh leaves is patched onto open wounds to heal them, while the water  
453 obtained from boiling the leaves is said to be effective against sinus ailments, and is used as a facial  
454 and nasal wash. The rhizomes are used in the treatments of cancer, cough and asthma, as a stimulant,  
455 tonic and germicide. *Z. spectabile* is also used in recipes for medicinal bath by mothers after giving  
456 birth and during the maternity period, especially for post-natal bath by boiling the whole plant [119].

457

#### 458 4.2.5. *Zingiber zerumbet* (L.) Sm.

459 *Z. zerumbet*, also known as shampoo ginger and native to India, is found in many tropical  
460 countries. The rhizome extracts of this species have been used to treat a diverse range of ailments.  
461 For examples, the Hawaiians applied the fresh pounded rhizome as medicine for indigestion and  
462 other ailments. Traditionally, the ground rhizomes, mixed with a ripe noni (*Morinda citrifolia* L.) fruit,  
463 can be used to treat severe sprains while the pulp, placed in a cloth, can be loosely bound around the  
464 injured area. The cooked and softened rhizome can also be used to treat toothache or caries by  
465 pressing it into the hollow and left for as long as was needed, while the ground and strained rhizome  
466 material is mixed with water and drunk to treat a stomachache [120].

467

468 Other than that, the rhizome of *Z. zerumbet* has been generally cited to be used in the treatment  
469 of inflammation, diarrhea, stomach cramps, bacterial infections, fever, flatulence, allergies and  
poisoning. The powdered rhizomes are used in the treatment of ear infections and toothache, while

470 the tea of *Z. zerumbet* rhizome is used to treat stomach disease. In addition, the juice of cooked  
471 rhizome can be used in the treatment of worm infection in children. The leaves are also used in  
472 therapies for joint pain [121].

473

#### 474 4.2.6. *Zingiber ottensii* Valetton

475 In Indonesia, the stem is traditionally used as part of a sedative lotion by the Javanese people,  
476 while, in Sumatra, the stem is used as potherb for postpartum care. On the other hand, the traditional  
477 midwives in Perak, Malaysia, used the rhizomes and leaves as a poultice applied on the body of the  
478 women in confinement. In addition, the leaves are used as a poultice for lumbago [122]. The pungent  
479 rhizomes are pounded into a poultice and used by women after childbirth, or are added to a mixture  
480 to make a sedative lotion or a tonic [123].

481

482

### 483 5. Essential Oil Obtained from Genus *Zingiber* Plants as a Food Preservative

484

485 Consumers are increasingly concerned with the use of chemical agents in foods. The desire to  
486 seek novel food antimicrobials is not out of fear that microbes in food have developed resistance to  
487 traditional food antimicrobials. Traditional food antimicrobials are proven and remain extremely  
488 effective in achieving shelf life and food safety goals. When traditional antimicrobials are evaluated  
489 under real food processing/handling conditions, antimicrobial resistance does not appear to be a  
490 major phenomenon [124]. The concern of many consumers centers on the potential health risks that  
491 may be associated with the antimicrobial itself and its by-products. The consumer today values  
492 products that have “natural” preservatives and a “clean label” or products with no artificial  
493 ingredients and chemicals.

494 A wealth of new technologies including high hydrostatic pressure, ionization radiation, and  
495 bioactive packaging can reduce or eliminate the need for utilization of traditional food preservatives.  
496 The major drawback of these technologies is associated with cost and feasibility of use in a range of  
497 food products. In the past decade, increased attention has been focused on the utilization of plant  
498 essential oils as natural antimicrobials in foods. Essential oils have been found to exhibit a broad  
499 range of activity against spoilage and pathogenic bacteria associated with food. Essential oils derived  
500 from *Thymus vulgaris* (thyme), *Origanum majorana* (marjoram), *Origanum vulgare* (oregano), *Ocimum*  
501 *basilicum* (basil), *Cymbopogon citratus* (lemon grass), and *Caryophyllus aromaticus* (clove) have been  
502 evaluated for the ability to control or inactivate various foodborne pathogens *in vitro* or in select foods  
503 [125]. A key advantage to the use of essential oils from those plants is they are considered generally  
504 recognized as safe (GRAS) for use in food.

505 As previously introduced, ginger is an important spice used throughout Asia and has gained  
506 considerable global popularity as an ingredient in food due to its unique flavor. The flavor is derived  
507 from both volatile and non-volatile compounds; these include gingerol, shogaol, and zingiberene.  
508 Compounds important to antimicrobial activity include camphene, linalool,  $\alpha$ -pinene, and borneol.  
509 Antimicrobial activity of ginger essential oils has been evaluated against *Aeromonas hydrophila*,  
510 *Bacillus subtilis*, *Bacillus cereus*, *Listeria monocytogenes*, *Salinococcus roseus*, *Halococcus turkmenicus*,  
511 *Halococcus morrhuae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Salmonella* spp., *Escherichia coli*,

512 *Vibrio cholera*, *Vibrio parahaemolyticus*, *Aspergillus niger*, *Mucor* spp., *Candida albicans*, and *Penicillium*  
513 spp. [8,125-128].

514 The part of the plant (leaf or rhizome) utilized and method of extraction of essential oils can have  
515 a profound impact on antimicrobial activity [37,129]. Much of the research on antimicrobial activity  
516 of essential oils of ginger has been conducted *in vitro* which is similar for essential oils from other  
517 plants. Although this is a good starting point, the level of antimicrobial activity observed may not be  
518 comparable in a complex food matrix. Ginger essential oils extracted from leaf and rhizome exhibited  
519 antibacterial activity against *B. licheniformis*, *B. spizizenii*, *S. aureus*, *E. coli*, *K. pneumoniae*, and *P. stutzeri*  
520 (MIC = 0.16-0.63 mg/mL) [22]. In general, activity was higher against the Gram-positive bacteria  
521 evaluated. These findings are in agreement with others studies where ginger essential oils were  
522 evaluated against Gram-positive and Gram-negative bacteria using disc-diffusion or broth assays  
523 [24,130,131].

524 The antimicrobial activity of ginger essential oil is comparable or higher than essential oils from  
525 other plants. A comparison of ginger, eucalyptus, and sweet orange essential oils found that ginger  
526 essential oil exhibited the highest antibacterial activity [85]. However, *V. parahaemolyticus* was  
527 resistant to all the essential oils evaluated. Ginger, thyme, coriander, marjoram, mustard, chamomile,  
528 licorice and nigella essential oils were evaluated for their activity against Gram-negative and Gram-  
529 positive foodborne pathogens [132]. Ginger, thyme, and coriander showed the highest antibacterial  
530 inhibition against the strains of bacteria tested.

531 Yeasts and molds can present relevant problems in food. Yeasts are associated with food  
532 spoilage and present no human health concern, whereas molds are associated with spoilage and can  
533 produce mycotoxins which, in the worst case scenario, can result in chronic toxicity and death.  
534 Essential oils of ginger exhibited poor activity against *Penicillium* spp. (MIC = 869.2 mg/mL) and no  
535 activity against *A. niger* [24]. These results are in agreement with other reports [86]. In contrast, ginger  
536 essential oil was reported to inhibit the growth of *Fusarium verticillioides* (MIC = 2500 µg/mL) and the  
537 production of fumonisin B1 and fumonisin B2 at concentrations of 4000 and 2000 µg/mL, respectively  
538 [88]. The growth of yeasts, *Candida tropicalis* and *Candida utilis*, was not inhibited by exposure to  
539 ginger essential oil [131].

540 The antimicrobial effect of ginger essential oil against microorganisms associated with food is  
541 clearly demonstrated through *in vitro* studies. However, the dearth of literature on evaluation of  
542 ginger essential oil in food is surprising, compared with reports on antimicrobial efficacy in foods of  
543 essential oils from other plants [8,125] A potential application of ginger essential oil is the control of  
544 microorganisms on fresh and fresh-cut fruits and vegetables that are intended to be consumed  
545 without a cooking step. Shredded green or unripe papaya is used in several types of Asian cuisine,  
546 including Thai papaya salad. The ability of three amounts of ginger essential oil (5, 10 or 15 µL) to  
547 control bacterial, mold, and yeast growth in shredded green papaya stored at 13 °C for 4 days was  
548 evaluated. The populations of bacteria and yeasts were approximately 3-log lower on shredded green  
549 papaya treated with the highest concentration of ginger essential oil compared to the untreated  
550 control. Control of mold growth could not be evaluated since none of the packages exhibited mold  
551 growth [128]. Raw poultry can be contaminated with *Salmonella*, *Campylobacter*, or both. Often,  
552 poultry carcasses are rinsed or immersed in a water bath containing an antimicrobial chemical (e.g.,  
553 chlorine). The practice is used in part to reduce the microbial load, including foodborne pathogens,  
554 on the carcass prior to packaging and shipment to the consumer. Utilization of essential oils to control

555 microorganisms on poultry carcasses would likely be met with a positive response by consumers.  
556 Chicken breast and whole leg samples were immersed for 2 min in various concentrations of ginger  
557 essential oil (1:150, 1:250 and 1:550) and then total aerobic bacteria, *E. coli*, *S. aureus* and *Salmonella*  
558 populations determined [89]. A highly significant reduction in population of total aerobic bacteria, *E.*  
559 *coli*, *S. aureus* and *Salmonella* occurred following treatment. Indeed, higher than a 3-log reduction in  
560 the populations of *E. coli* and *Salmonella* on the surface of chicken was achieved. These results suggest  
561 ginger essential could be used as an alternative to traditional antimicrobial chemicals for the  
562 treatment of poultry carcasses.

563 On what concerns safety issue, ginger is included among spices provided from natural sources  
564 generally recognized as safe (GRAS) by the American Food and Drug Administration (FDA) [133].  
565 From clinical trials, we can remark which concentrations can be considered of reasonably safe for  
566 human consumption. The daily dose of oral administration of ginger ranged from 500 mg/day to 1000  
567 mg/day; at these concentrations, adverse effects were rare and mainly in form of gastrointestinal  
568 discomfort [85,92]. Considering ginger metabolites (6-, 8- and 10-gingerols and 6-shogaols), a clinical  
569 trial on healthy volunteers showed no toxicity up to 2000 mg [134]. At preclinical level, using rat  
570 animal model, the acute oral lethal dose of ginger essential oil was found over 5 g/kg of weight, and  
571 certain teratogenicity, embryonic loss and mutagenicity could not be definitely ruled out [135,136].

572 The research reported on the efficacy of ginger essential oil to inactivate and control microbial  
573 populations *in vitro* and in association with food is encouraging. Many more studies should be  
574 completed using essential oil of ginger in or on complex foods before solid conclusions can be  
575 advanced with respect to its utility. These studies should also evaluate organoleptic changes  
576 including impact on taste, odor, and color. A key factor in use of ginger essential oil as an  
577 antimicrobial in food or food processing will be cost. Seismic shifts in consumer food preferences  
578 have occurred in recent years. Consumer acceptance of the essential oil of ginger as an alternative to  
579 traditional food preservatives will likely be met with enthusiasm even if the cost of the product  
580 increases slightly.

581

## 582 6. Conclusions

583 Indian, Chinese, Japanese, Unani systems of medicine use ginger extracts to deal with pain and  
584 inflammatory disease since decades. At the end of this survey,, members of the genus *Zingiber*  
585 represent a promising and innovative source of natural bioactive agents, mainly gingerols, shogaols  
586 and zingerone.

587 Clinical evidence suggests their efficacy, in particular, in managing hyperemesis related to  
588 pregnancy or chemotherapy. As antimicrobial agents, ginger essential oils appear especially effective  
589 in the management of food contaminations, increasing shelf life of food. Given their reasonable safety  
590 data, members of the genus *Zingiber* may constitute a valid alternative towards common drugs to  
591 manage nausea and vomiting, and towards chemical food preservatives. The latter issue meets the  
592 increasing concern of consumers aware of the potential health risks associated with the conventional  
593 antimicrobials in food.

594

595 **Author Contributions:** All authors contributed equally in the preparation of the manuscript.

596 **Conflicts of Interest:** The authors declare no conflict of interest.

597

598 **References**

- 599 1. Iriti, M.; Varoni, E.M.; Vitalini, S. Melatonin in traditional Mediterranean diets. *J Pineal Res.* **2010**, *49*,101-5.
- 600 2. Iriti, M.; Varoni, E.M. Melatonin in Mediterranean diet, a new perspective. *J Sci Food Agric.* **2015**, *95*, 2355-
- 601 9.
- 602 3. Iriti M.; Varoni, E.M. Chemopreventive potential of flavonoids in oral squamous cell carcinoma in human
- 603 studies. *Nutrients.* **2013**, *5*, 2564-76.
- 604 4. Varoni, E.M.; Lo Faro, A.F.; Sharifi-Rad, J.; Iriti, M. Anticancer Molecular Mechanisms of Resveratrol. *Front*
- 605 *Nutr.* **2016**, *12*, 3:8.
- 606 5. Varoni, E.M.; Vitalini, S.; Contino, D.; Lodi, G.; Simonetti, P.; Gardana, C. Sardella, A.; Carrassi, A.; Iriti, M.
- 607 Effects of red wine intake on human salivary antiradical capacity and total polyphenol content. *Food Chem*
- 608 *Toxicol.* **2013**, *58*, 289-94.
- 609 6. Gyawali, R.; Ibrahim, S.A. Natural products as antimicrobial agents. *Food Control* **2014**, *46*, 412-429.
- 610 7. Burt, S. Essential oils: their antibacterial properties and potential applications in foods -a review. *Int. J. Food*
- 611 *Microbiol.* **2004**, *94*, 223-253.
- 612 8. Tajkarimi, M.M.; Ibrahim, S.A.; Cliver, D.O. Antimicrobial herb and spice compounds in food. *Food control*
- 613 **2010**, *21*, 1199-1218.
- 614 9. Sharifi-Rad, J.; Salehi, B.; Varoni, E.M.; Sharopov, F.; Yousaf, Z.; Ayatollahi, S.A.; Kobarfard, F.; Sharifi-Rad,
- 615 M.; Afdjei, M.H.; Sharifi-Rad, M.; Iriti, M. Plants of the *Melaleuca* Genus as Antimicrobial Agents: From
- 616 Farm to Pharmacy. *Phytother Res.* **2017**, *7*. doi: 10.1002/ptr.5880.
- 617 10. Sharifi-Rad, J.; Soufi, L.; Ayatollahi, S.A.; Iriti, M.; Sharifi-Rad, M.; Varoni, E.M.; Shahri, F.; Esposito, S.;
- 618 Kuhestani, K.; Sharifi-Rad, M. Anti-bacterial effect of essential oil from *Xanthium strumarium* against shiga
- 619 toxin-producing *Escherichia coli*. *Cell Mol Biol (Noisy-le-grand)*. **2016**, *62*, 69-74.
- 620 11. Azzimonti, B.; Cochis, A.; Beyrouthy, M.E.; Iriti, M.; Uberti, F.; Sorrentino, R.; Landini, M.M.; Rimondini,
- 621 L.; Varoni, E.M. Essential Oil from Berries of Lebanese Juniperus excelsa M. Bieb Displays Similar
- 622 Antibacterial Activity to Chlorhexidine but Higher Cytocompatibility with Human Oral Primary
- 623 Cells. *Molecules* **2015**, *20*, 9344-57.
- 624 12. Sharifi-Rad, M.; Tayeboon, G.S.; Sharifi-Rad, J.; Iriti, M.; Varoni, E.M.; Razazi, S. Inhibitory activity on type
- 625 2 diabetes and hypertension key-enzymes, and antioxidant capacity of *Veronica persica* phenolic-rich
- 626 extracts. *Cell Mol Biol (Noisy-le-grand)*. **2016**, *62*, 80-5.
- 627 13. Bor, T.; Aljaloud, S.O.; Gyawali, R.; Ibrahim, S.A. *Antimicrobials from herbs, spices, and plants*. In
- 628 Encapsulations: Nanotechnology in the Agri-Food Industry, vol. 2 (ed Alexandru M Grumezescu),
- 629 Academic press, pp 269-288, 2016.
- 630 14. El-Ghorab, A.H.; Nauman, M.; Anjum, F.M.; Hussain, S.; Nadeem, M.A. Comparative study on chemical
- 631 composition and antioxidant activity of ginger (*Zingiber officinale*) and cumin (*Cuminum cyminum*). *J. Agr.*
- 632 *Food Chem.* **2010**, *58*, 8231-8237.
- 633 15. Gyawali, R.; Hayek, S.A.; Ibrahim, S.A. Plant extracts as antimicrobials in food products: mechanisms of
- 634 action, extraction methods, and applications. In T.M. Taylor (Ed.), *Handbook of natural antimicrobials for food*
- 635 *safety and quality*. Woodhead Publishing, 2014.
- 636 16. Hayek, S.A.; Gyawali, R.; Ibrahim, S.A. Antimicrobial natural products. In A. Mendez-Vilas (Ed.) *Microbial*
- 637 *pathogens and strategies for combating them: Science, technology and education (Vol. 2)*; (pp. 910-921).
- 638 Formatex Research Center, 2013.
- 639 17. Sharifi-Rad, J.; Salehi, B.; Stojanović-Radić, Z.Z.; Fokou, P.V.T.; Sharifi-Rad, M.; Mahady, G.B.; Sharifi-Rad,
- 640 M.; Masjedi, M.R.; Lawal, T.O.; Ayatollahi, S.A.; Masjedi, J.; Sharifi-Rad, R.; Setzer, W.N.; Sharifi-Rad,
- 641 M.; Kobarfard, F.; Rahman, A.U.; Choudhary, M.I.; Ata, A.; Iriti, M. Medicinal plants used in the treatment
- 642 of tuberculosis - Ethnobotanical and ethnopharmacological approaches. *Biotechnol Adv.* **2017** pii: S0734-
- 643 9750(17)30077-0.
- 644 18. Sharifi-Rad, J.; Sureda, A.; Tenore, G.C.; Daglia, M.; Sharifi-Rad, M.; Valussi, M.; Tundis, R.; Sharifi-Rad,
- 645 M.; Loizzo, M.R.; Ademiluyi, A.O.; Sharifi-Rad, R.; Ayatollahi, S.A.; Iriti, M. Biological Activities of
- 646 Essential Oils: From Plant Chemoecology to Traditional Healing Systems. *Molecules* **2017**, *22*, pii: E70.
- 647 19. Sabulal, B.; Dan, M.; Kurup, R.; Pradeep, N.S.; Valsamma, R.K., George, V. Caryophyllene-rich rhizome oil
- 648 of *Zingiber nimmonii* from South India: chemical characterization and antimicrobial activity. *Phytochemistry*
- 649 **2006**, *67*, 2469-2473.
- 650 20. Ghosh, S.; Majumder, P.B.; Mandi, S.S. Species-specific AFLP markers for identification of *Zingiber officinale*,
- 651 *Z. montanum* and *Z. zerumbet* (Zingiberaceae). *Genet. Mol. Res.* **2011**, *10*, 218-229.

- 652 21. Stoilova, I.; Krastanov, A.; Stoyanova, A.; Denev, P.; Gargova, S. Antioxidant activity of a ginger extract  
653 (*Zingiber officinale*). *Food Chem.* **2007**, *102*, 764-770.
- 654 22. Sivasothy, Y.; Chong, W.K.; Hamid, A.; Eldeen, I.M.; Sulaiman, S.F.; Awang, K. Essential oils of *Zingiber*  
655 *officinale* var. *rubrum* Theilade and their antibacterial activities. *Food Chem.* **2011**, *124*, 514-517.
- 656 23. Sharma, P.K.; Singh, V.; Ali, M. Chemical composition and antimicrobial activity of fresh rhizome essential  
657 oil of *Zingiber officinale* Roscoe. *Pharmacogn. J.* **2016**, *8*, 185-190.
- 658 24. Bellik, Y. Total antioxidant activity and antimicrobial potency of the essential oil and oleoresin of *Zingiber*  
659 *officinale* Roscoe. *Asian Pac. J. Trop. Dis.* **2014**, *4*, 40-44.
- 660 25. Jiang, H.; Xie, Z.; Koo, H.J.; McLaughlin, S.P.; Timmermann, B.N.; Gang, D.R. Metabolic profiling and  
661 phylogenetic analysis of medicinal *Zingiber* species: Tools for authentication of ginger (*Zingiber officinale*  
662 Rosc.). *Phytochemistry* **2006**, *67*, 1673-1685.
- 663 26. Shukla, Y.; Singh, M. Cancer preventive properties of ginger: a brief review. *Food Chem. Toxicol.* **2007**, *45*,  
664 683-690.
- 665 27. Singh, G.; Kapoor, I.P.S.; Singh, P.; de Heluani, C.S.; de Lampasona, M.P.; Catalan, C.A.N. Chemistry,  
666 antioxidant and antimicrobial investigations on essential oil and oleoresins of *Zingiber officinale*. *Food Chem.*  
667 *Toxicol.* **2008**, *46*, 3295-3302.
- 668 28. El-Baroty, G.S.; El-Baky, H.A.; Farag, R.S.; Saleh, M.A. Characterization of antioxidant and antimicrobial  
669 compounds of cinnamon and ginger essential oils. *Afr. J. Biochem. Res.* **2010**, *4*, 167-174.
- 670 29. Kumar, G.; Karthik, L.; Rao, K.B. A review on pharmacological and phytochemical properties of *Zingiber*  
671 *officinale* Roscoe (Zingiberaceae). *J. Pharm. Res.* **2011**, *4*, 2963-2966.
- 672 30. Jayashree, E.; Kandiannan, K.; Prasath, D.; Rashid Pervez, Sasikumar B.; Senthil Kumar C.M.; Srinivasan,  
673 V.; Suseela Bhai, R.; Thankamani, C.K. Ginger. ICAR-Indian Institute of Spices Research Kozhikode - 673  
674 012, Kerala, 2015
- 675 31. Govindarajan, V.S. Ginger - chemistry, technology, and quality evaluation: Part 1. *Crit. Rev. in Food Sci.*  
676 *Nutr.* **1982**, *17*, 1-96.
- 677 32. Sutarno, H.; Hadad, E.A.; Brink, M. *Zingiber officinale* Roscoe. In : de Guzman, C.C. and Siemonsma, J.S.  
678 (Editors) : Plant Resources of South-East Asia No 13. Spices. Backhuys Publishers, Leiden, The Netherlands.  
679 pp. 239-244, **1999**.
- 680 33. Nwaogu, E.N. Soil fertility changes and their effects on ginger (*Zingiber officinale* Rosc.) yield response in  
681 an ultisol under different pigeon pea hedgerow alley management in South Eastern Nigeria. *Afr. J. Agr.*  
682 *Res.* **2014**, *9*, 2158-2166.
- 683 34. Davidson, A. The Oxford Companion to Food, Second Edition. Oxford University Press, Oxford, 2006.
- 684 35. Anita, L.H.; Lindy, A.B.; Gene, A.G.. Aeroponic cultivation of ginger (*Zingiber officinale*) rhizomes. Proc. VII  
685 IS on Prot. Cult. Mild Winter Climates Eds. D.J. Cantliffe, P.J. Stoffella & N. Shaw Acta Hort. 659, ISHS,  
686 2003.
- 687 36. Archana, D.; Vigya, K.; Latha, R. Micropropagation and cytogenetic assessment of *Zingiber* species of  
688 Northeast India. *Biotechnol.* **2013**, *3*, 471-479.
- 689 37. Mesomo, M.C.; Corazza, M.L.; Ndiaye, P.M.; Dalla Santa, O.R.; Cardozo, L.; Scheer, A. de P. Supercritical  
690 CO<sub>2</sub> extracts and essential oil of ginger (*Zingiber officinale* R.): Chemical composition and antibacterial  
691 activity. *J. Supercrit. Fluid.* **2013**, *80*, 44-49.
- 692 38. An, K.; Zhao, D.; Wang, Z.; Wu, J.; Xu, Y.; Xiao, G. Comparison of different drying methods on Chinese  
693 ginger (*Zingiber officinale* Roscoe): Changes in volatiles, chemical profile, antioxidant properties, and  
694 microstructure. *Food Chem.* **2016**, *197*, 1292-1300.
- 695 39. Nogueira de Melo, G.A.; Grespan, R.; Fonseca, J.P.; Farinha, T.O.; da Silva, E.L.; Romero, A.L.; Cuman,  
696 R.K.N. Inhibitory effects of ginger (*Zingiber officinale* Roscoe) essential oil on leukocyte migration in vivo  
697 and in vitro. *J. Nat. Med.* **2011**, *65*, 241-246.
- 698 40. Fernandes, R.V. de B.; Borges, S.V.; Silva, E.K.; da Silva, Y.F.; de Souza, H.J.B.; do Carmo, E.L.; Botrel, D.A.  
699 Study of ultrasound-assisted emulsions on microencapsulation of ginger essential oil by spray drying. *Ind.*  
700 *Crop Prod.* **2016**, *94*, 413-423.
- 701 41. Babarinde, S.A.; Sunnie-Ododo, M.O.; Akanbi, W.B.; Oyegoke, O.O.; Tijani, R.; Olaobaju, S.F. Comparative  
702 susceptibility of two developmental stages of hide beetle (*Dermestes maculatus* Degeer, 1774) to ginger  
703 (*Zingiber officinale* Roscoe) essential oil. *J. of the Saudi Society of Agric. Sci.* 2016, in press

- 704 42. Pushpanathan, T.; Jebanesan, A.; Govindarajan, M. The essential oil of *Zingiber officinalis* Linn  
705 (Zingiberaceae) as a mosquito larvicidal and repellent agent against the filarial vector *Culex quinquefasciatus*  
706 Say (Diptera: Culicidae). *Parasitol. Res.* **2008**, *102*, 1289–1291.
- 707 43. Azizi, S.; Mohamad, R.; Rahim, R.A.; Moghaddam, A.B.; Moniri, M.; Ariff, A.; Namvab, F. ZnO-Ag core  
708 shell nanocomposite formed by green method using essential oil of wild ginger and their bactericidal and  
709 cytotoxic effects. *Appl. Surf. Sci.* **2016**, *384*, 517–524.
- 710 44. Nampoothiri, S.V.; Venugopalan, V.V.; Joy, B.; Sreekumar, M.M.; Menon, A.N. Comparison of essential oil  
711 composition of three ginger cultivars from sub Himalayan region. *Asian Pac. J. Trop. Biomed.* **2012**, *2*, S1347–  
712 S1350.
- 713 45. Singh, G.; Maurya, S.; Catalan, C.; de Lampasona, M.P. Studies on essential oils, Part 42: chemical,  
714 antifungal, antioxidant and sprout suppressant studies on ginger essential oil and its oleoresin. *Flavour*  
715 *Frag. J.* **2005**, *20*, 1–6.
- 716 46. Wang, Z.; Wang, L.; Li, T.; Zhou, X.; Ding, L.; Yu, Y.; Zhang, H. Rapid analysis of the essential oils from  
717 dried *Illicium verum* Hook. f. and *Zingiber officinale* Rosc. by improved solvent-free microwave extraction  
718 with three types of microwave-absorption medium. *Anal. Bioanal. Chem.* **2006**, *386*, 1863–1868.
- 719 47. Lin, R.-J.; Chen, C.-Y.; Lu, C.-M.; Ma, Y.-H.; Chung, L.-Y.; Wang, J.-J.; Yen, C.-M. Anthelmintic constituents  
720 from ginger (*Zingiber officinale*) against *Hymenolepis nana*. *Acta Trop.* **2014**, *140*, 50–60.
- 721 48. Stoyanova, A.; Konakchiev, A.; Damyanova, S.; Stoilova, I.; Suu, P.T. Composition and antimicrobial  
722 activity of ginger essential oil from Vietnam. *J. Essent. Oil Bear. Pl.* **2006**, *9*, 93–98.
- 723 49. Sukatta, U.; Rugthaworn, P.; Punjee, P.; Chidchenchey, S.; Keeratinijakal, V. Chemical composition and  
724 physical properties of oil from Plai (*Zingiber cassumunar* Roxb.) obtained by hydrodistillation and hexane  
725 extraction. *Kasetsart J. (Nat. Sci.)* **2009**, *43*, 212–217.
- 726 50. Onyenekwe, P.C.; Hashimoto, S. The composition of the essential oil of dried Nigerian ginger (*Zingiber*  
727 *officinale* Roscoe). *Eur. Food Res. Technol.* **1999**, *209*, 407–410
- 728 51. Sasidharan, I.; Nirmala, M. Comparative chemical composition and antimicrobial activity fresh & dry  
729 ginger oils (*Zingiber officinale* Roscoe). *Int. J. Curr. Pharm. Res.* **2010**, *2*, 40–43.
- 730 52. Ravi Kiran, C.; Chakka, A.K.; Padmakumari Amma, K.P.; Nirmala Menon, A.; Sree Kumar, M.M.;  
731 Venugopalan, V.V. Essential oil composition of fresh ginger cultivars from North-East India. *J. Essent. Oil*  
732 *Res.* **2013**, *25*, 380–387.
- 733 53. Nerilo, S.B.; Rocha, G.H.O.; Tomoike, C.; Mossini, S.A.G.; Grespan, R.; Mikcha, J.M.G.; Machinski, M.  
734 Antifungal properties and inhibitory effects upon aflatoxin production by *Zingiber officinale* essential oil in  
735 *Aspergillus flavus*. *Int. J. Food Sci. Technol.* **2016**, *51*, 286–292.
- 736 54. Das, A.; Kasoju, N.; Bora, U.; Rangan, L. Chemico-biological investigation of rhizome essential oil of  
737 *Zingiber moran*—native to Northeast India. *Med. Chem. Res.* **2013**, *22*, 4308–4315.
- 738 55. Chaiyana, W.; Anuchapreeda, S.; Leelapornpisid, P.; Phongpradist, R.; Viernstein, H.; Mueller, M.  
739 Development of microemulsion delivery system of essential oil from *Zingiber cassumunar* Roxb. rhizome  
740 for improvement of stability and anti-inflammatory activity. *AAPS Pharm. Sci. Tech.* **2017**, *18*, 1332–1342.
- 741 56. Boonyanugomol, W.; Krairiwattana, K.; Rukseree, K.; Boonsam, K.; Narachai, P. In vitro synergistic  
742 antibacterial activity of the essential oil from *Zingiber cassumunar* Roxb against extensively drug-resistant  
743 *Acinetobacter baumannii* strains. *J. Infect. Public Health* **2017**, *10*, 586–592.
- 744 57. Kamazeri, T.S.A.T.; Samah, O.A.; Taher, M.; Susanti, D.; Qaralleh, H. Antimicrobial activity and essential  
745 oils of *Curcuma aeruginosa*, *Curcuma mangga*, and *Zingiber cassumunar* from Malaysia. *Asian Pac. J. Trop. Med.*  
746 **2012**, *5*, 202–209.
- 747 58. Manochai, B.; Paisooksantivatana, Y.; Choi, H.; Hong, J.H. Variation in DPPH scavenging activity and  
748 major volatile oil components of cassumunar ginger, *Zingiber montanum* (Koenig), in response to water  
749 deficit and light intensity. *Sci. Hortic.* **2010**, *126*, 462–466.
- 750 59. Zhannan, Y.; Shiqiong, L.; Quancai, P.; Chao, Z.; Zhengwen, Y. GC-MS analysis of the essential oil of Coral  
751 Ginger (*Zingiber corallinum* Hance) rhizome obtained by supercritical fluid extraction and steam distillation  
752 extraction. *Chromatographia* **2009**, *69*, 785–790.
- 753 60. Rana, V.; Verdeguer, M.; Blasquez, M. Chemical composition of the essential oil of *Zingiber zerumbet* var.  
754 *darcyi*. *Nat Prod Commun.* **2012**, *7*, 1369–70.
- 755 61. Govindarajan, M.; Rajeswary, M.; Arivoli, S.; Tennyson, S.; Benelli, G. Larvicidal and repellent potential of  
756 *Zingiber nimmonii* (J. Graham) Dalzell (Zingiberaceae) essential oil: an eco-friendly tool against malaria,  
757 dengue, and lymphatic filariasis mosquito vectors *Parasitol. Res.* **2016**, *115*, 1807–1816.

- 758 62. Chairgulprasert, V.; Prasertsongsun, S.; Wichaporn, W. Chemical constituents of the essential oil and  
759 antibacterial activity of *Zingiber wrayi* var. *halabala*. *Songklanakarin J. Sci. Technol.* **2005**, *27*, 813–8.
- 760 63. Kubra, I.R.; Rao, L.J. An impression on current developments in the technology, chemistry, and biological  
761 activities of ginger (*Zingiber officinale* Roscoe). *Crit. Rev. Food Sci. Nutr.* **2012**, *52*, 651–88.
- 762 64. Semwal, R.B.; Semwal, D.K.; Combrinck, S.; Viljoen, A.M. Gingerols and shogaols: Important nutraceutical  
763 principles from ginger. *Phytochemistry* **2015**, *117*, 554–68.
- 764 65. Mozaffari-Khosravi, H.; Naderi, Z.; Dehghan, A.; Nadjarzadeh, A.; Fallah Huseini, H.  
765 Effect of Ginger Supplementation on Proinflammatory Cytokines in Older Patients with Osteoarthritis: O  
766 utcomes of a Randomized Controlled Clinical Trial. *J. Nutr. Gerontol. Geriatr.* **2016**, *35*, 209–18.
- 767 66. Stoilova, I.; Krastanov, A.; Stoyanova, A.; Denev, P.; Gargova, S. Antioxidant activity of a ginger extract  
768 (*Zingiber officinale*). *Food Chem.* **2007**, *102*, 764–770.
- 769 67. Mashhadi, N.S.; Ghiasvand, R.; Askari, G.; Hariri, M.; Darvishi, L.; Mofid, M. R.; Anti-Oxidative and  
770 Anti-Inflammatory Effects of Ginger in Health and Physical Activity: Review of Current Evidence. *Int. J.*  
771 *Prev. Med.* **2013**, *4*, S36–S42.
- 772 68. Si, W.; Chen, Y.P.; Zhang, J.; Chen, Z.Y.; Chung, H.Y. Antioxidant activities of ginger extract and its  
773 constituents toward lipids. *Food Chem.* **2018**, *239*, 1117–1125.
- 774 69. Höferl, M.; Stoilova, I.; Wanner, J.; Schmidt, E.; Jirovetz, L.; Trifonova, D.; Stanchev, V.; Krastanov, A.  
775 Composition and Comprehensive Antioxidant Activity of Ginger (*Zingiber officinale*) Essential Oil from  
776 Ecuador. *Nat. Prod. Commun.* **2015**, *10*, 1085–90.
- 777 70. Ahmad, B.; Rehman M.U.; Amin, I.; Arif, A.; Rasool, S.; Bhat, S.A.; Afzal, I.; Hussain, I.; Bilal, S.; Mir M.U.R.  
778 A Review on Pharmacological Properties of Zingerone (4-(4-Hydroxy-3-methoxyphenyl)-2-butanone). *Sci.*  
779 *World J.* **2015**, *816364*, 6.
- 780 71. Mohd Yusof Y.A. Gingerol and Its Role in Chronic Diseases. *Adv. Exp. Med. Biol.* **2016**, *929*, 177–207.
- 781 72. Jiang, Y.; Turgeon, D.K.; Wright, B.D.; Sidahmed E.; Ruffin, M.T.; Brenner, D.E.; Sen, A.; Zick, S.M. Effect  
782 of ginger root on cyclooxygenase-1 and 15-hydroxyprostaglandin dehydrogenase expression in colonic  
783 mucosa of humans at normal and increased risk for colorectal cancer. *Eur. J. Cancer Prev.* **2013**, *22*, 455–60.
- 784 73. Zick, S.M.; Turgeon, D.K.; Ren, J.; Ruffin, M.T.; Wright, B.D.; Sen, A.; Djuric, Z.; Brenner D.E. Pilot Clinical  
785 Study of the Effects of Ginger Root Extract on Eicosanoids in Colonic Mucosa of Subjects at Increased Risk  
786 for Colorectal Cancer. *Mol. Carcinog.* **2015**, *54*, 908–915.
- 787 74. Mansour M.S.; Ni, Y.M.; Roberts, A.L.; Kelleman, M.; Roychoudhury, A.; St-Onge, M.P. Ginger  
788 consumption enhances the thermic effect of food and promotes feelings of satiety without affecting  
789 metabolic and hormonal parameters in overweight men: a pilot study. *Metabolism.* **2012**, *61*, 1347–52.
- 790 75. Shidfar, F.; Rajab, A.; Rahideh, T.; Khandouzim, N.; Hosseini, S.; Shidfar, S. The effect of ginger (*Zingiber*  
791 *officinale*) on glycemic markers in patients with type 2 diabetes. *J. Complement. Integr. Med.* **2015**, *12*, 165–70.
- 792 76. Arablou, T.; Aryaeian, N.; Valizadeh, M.; Sharifi, F.; Hosseini, A.; Djalali, M. The effect of ginger  
793 consumption on glycemic status, lipid profile and some inflammatory markers in patients with type 2  
794 diabetes mellitus. *Int. J. Food Sci. Nutr.* **2014**, *65*, 515–20.
- 795 77. Mozaffari-Khosravi, H.; Talaei, B.; Jalali, B.A.; Najarzadeh, A.; Mozayan, M.R. The effect of ginger powder  
796 supplementation on insulin resistance and glycemic indices in patients with type 2 diabetes: a randomized,  
797 double-blind, placebo-controlled trial. *Complement. Ther. Med.* **2014**, *22*, 9–16.
- 798 78. Tabibi, H.; Imani, H.; Atabak, S.; Najafi, I.; Hedayati, M.; Rahmani, L. Effects of Ginger on Serum Lipids  
799 and Lipoproteins in Peritoneal Dialysis Patients: A Randomized Controlled Trial. *Perit. Dial. Int.* **2016**, *36*,  
800 140–5.
- 801 79. Aghazadeh, M.; Bialvaei, A.Z.; Aghazadeh, M.; Kabiri, F.; Saliyani, N.; Yousef, M.; Eslami, H.; Kafli H.S.  
802 Survey of the Antibiofilm and Antimicrobial Effects of *Zingiber officinale* (in Vitro Study). *Jundishapur J.*  
803 *Microbiol.* **2016**, *9*, e30167.
- 804 80. Wang, H.; Ng, T.B. An antifungal protein from ginger rhizomes. *Biochem. Biophys. Res. Commun.* **2005**, *336*,  
805 100–4.
- 806 81. Nguefack, J.; Leth, V.; Amvam, Zollo, P.H.; Mathur, S.B. Evaluation of five essential oils from aromatic  
807 plants of Cameroon for controlling food spoilage and mycotoxin producing fungi. *Int. J. Food Microbiol.*  
808 **2004**, *94*, 329–34.
- 809 82. Ficker, C.E.; Arnason, J.T.; Vindas, P.S.; Alvarez, L.P.; Akpagana, K.; Gbeassor, M.; De Souza, C.; Smith,  
810 M.L. Inhibition of human pathogenic fungi by ethnobotanically selected plant extracts. *Mycoses.* **2003**, *46*,  
811 29–37.

- 812 83. Rahmani, A.H.; Al shabrmi, F.M.; Aly, S.M. Active ingredients of ginger as potential candidates in the  
813 prevention and treatment of diseases via modulation of biological activities. *Int. J. Physiol. Pathophysiol.*  
814 *Pharmacol.* **2014**, *6*, 125–136.
- 815 84. Mahyari, S.; Mahyari, B.; Emami, S.A.; Malaekheh-Nikouei, B.; Jahanbakhsh, S.P.; Sahebkar, A.;  
816 Mohammadpour, A.H. Evaluation of the efficacy of a polyherbal mouthwash containing *Zingiber*  
817 *officinale*, *Rosmarinus officinalis* and *Calendula officinalis* extracts in patients with gingivitis: A  
818 randomized double-blind placebo-controlled trial. *Complement Ther. Clin. Pract.* **2016**, *22*, 93-8.
- 819 85. Viljoen, E.; Visser, J.; Koen, N.; Musekiwa, A. A systematic review and meta-analysis of the effect and safety  
820 of ginger in the treatment of pregnancy-associated nausea and vomiting. *Nutr J.* **2014**, *13*, 20.
- 821 86. McParlin, C.; O'Donnell, A.; Robson, S.C.; Beyer, F.; Moloney, E.; Bryant, A.I. Bradley, J.; Muirhead, C.R.;  
822 Nelson-Piercy, C.; Newbury-Birch, D.; Norman, J.; Shaw, C.; Simpson, E.; Swallow, B.; Yates, L.; Vale, L.  
823 Treatments for Hyperemesis Gravidarum and Nausea and Vomiting in Pregnancy: A Systematic Review.  
824 *JAMA* **2016**, *316*, 1392-1401.
- 825 87. Marx, W.; Ried, K.; McCarthy, A.L.; Vitetta, L.; Sali, A.; McKavanagh, D.; Isenring, L. Ginger-Mechanism  
826 of action in chemotherapy-induced nausea and vomiting: A review. *Crit. Rev. Food Sci Nutr.* **2017**, *57*, 141-  
827 146.
- 828 88. Bone, M.E.; Wilkinson, D.J.; Young, J.R.; McNeil, J.; Charlton, S. Ginger root--a new antiemetic. The effect  
829 of ginger root on postoperative nausea and vomiting after major gynaecological surgery. *Anaesthesia* **1990**  
830 *45*, 669-71.
- 831 89. Emrani, Z.; Shojaei, E.; Khalili, H. Ginger for Prevention of Antituberculosis-induced Gastrointestinal  
832 Adverse Reactions Including Hepatotoxicity: A Randomized Pilot Clinical Trial. *Phytother. Res.* **2016** *30*,  
833 1003-9.
- 834 90. Shirvani, M.A.; Motahari-Tabari, N.; Alipour, A. The effect of mefenamic acid and ginger on pain relief in  
835 primary dysmenorrhea: a randomized clinical trial. *Arch. Gynecol. Obstet.* **2015**, *291*, 1277-81.
- 836 91. Ozgoli, G.; Goli, M.; Moattar, F. Comparison of effects of ginger, mefenamic acid, and ibuprofen on pain in  
837 women with primary dysmenorrhea. *J. Altern. Complement. Med.* **2009**, *15*, 129-32.
- 838 92. Bartels, E.M.; Folmer, V.N.; Bliddal, H.; Altman, R.D.; Juhl, C.; Tarp, S.; Zhang, W.; Christensen, R. Efficacy  
839 and safety of ginger in osteoarthritis patients: a meta-analysis of randomized placebo-controlled trials.  
840 *Osteoarthritis Cartilage* **2015**, *23*, 13-21.
- 841 93. Bliddal, H.; Rosetzky, A.; Schlichting, P.; Weidner, M.S.; Andersen, L.A.; Ibfelt, H.H.; Christensen, K.;  
842 Jensen, O.N.; Barslev, J. A randomized, placebo-controlled, cross-over study of ginger extracts and  
843 ibuprofen in osteoarthritis. *Osteoarthritis Cartilage* **2000**, *8*, 9-12.
- 844 94. Maghbooli, M.; Golipour, F.; Moghimi Esfandabadi, A.; Yousefi, M. Comparison between the efficacy of  
845 ginger and sumatriptan in the ablative treatment of the common migraine. *Phytother. Res.* **2014**, *28*, 412-5.
- 846 95. Cady, R.K.; Schreiber, C.P.; Beach, M.E.; Hart, C.C. Gelstat Migraine (sublingually administered feverfew  
847 and ginger compound) for acute treatment of migraine when administered during the mild pain phase.  
848 *Med. Sci. Monit.* **2005**, *11*, PI65-9.
- 849 96. Emrani, Z.; Shojaei, E.; Khalili, H. Ginger for Prevention of Antituberculosis-induced Gastrointestinal  
850 Adverse Reactions Including Hepatotoxicity: A Randomized Pilot Clinical Trial. *Phytother Res.* **2016**, *30*,  
851 1003-9.
- 852 97. Drozdov, V.N.; Kim, V.A.; Tkachenko, E.V.; Varvanina, G.G. Influence of a specific ginger combination on  
853 gastropathy conditions in patients with osteoarthritis of the knee or hip. *J. Altern Complement. Med.* **2012**,  
854 *18*, 583-8.
- 855 98. Remadevi, R.; Surendran, E.; Ravindran, P.N. Properties and medicinal uses of ginger. In: *Ginger: The*  
856 *Genus Zingiber* (Eds. K. Nirmal Babu, P. N. Ravindran). CRC Press, Boca Raton, FL, **2004**.
- 857 99. Nirmal Babu, K.; Ravindran, P.N. *Ginger: The Genus Zingiber*. CRC Press, Boca Raton, FL, **2004**.
- 858 100. Kumar, K.M.P.; Asish, G.R.; Sabu, M.; Balachandran, I. Significance of gingers (*Zingiberaceae*) in Indian  
859 System of Medicine - Ayurveda: An overview. *Anc Sci. Life.* **2013**, *32*, 253-261.
- 860 101. Aiyer, K.N.; Kolammal, M. *Pharmacognosy of Ayurvedic Drugs of Kerala*. Vol. 9. Department of  
861 Pharmacognosy, University of Kerala, Trivandrum, India, **1996**.
- 862 102. Kirtikar, K.R.; Basu, B.D. *Indian medicinal plants* (Vol. 1-4) 2<sup>nd</sup> ed. Bishen Singh Mahendrapal Singh, Delhi,  
863 India. Pp. 2971, **1991**.
- 864

- 865 103. Nadkarni, K.M. Indian Medicinal plants and drugs – their medicinal properties and uses. Asiatic  
866 Publishing House, New Delhi, India, p. 450, **1998**.
- 867 104. Pruthy, J.S. *Spices and Condiments*. National Book Trust of India, New Delhi, India, **1979**.
- 868 105. Benskey, D.; Gamble, A. (eds.) *Chinese Herbal Medicine: Materia Medica*, Eastland Press, Seattle, **1986**.
- 869 106. Blumenthal, M. (ed.) The complete German Commission E Monographs. *Therapeutic Guide to Herbal*  
870 *Medicine*. American Botany Council, Austin, TX.
- 871 107. Pakrashi, S.C.; Pakrashi, A. *Ginger*. Vedams, New Delhi, **2003**.
- 872 108. O'Hara, M.; Keifer, D.; Farrel K.; Kemper, K. A review of 12 commonly used medicinal herbs. *Arch. Fam.*  
873 *Med.* **1998**, *7*, 523-536.
- 874 109. Awang, D.V.C. *Ginger*. *Can. Pharm. J.* **1992**, *125*, 309–311
- 875 110. Gupta, S.K.; Sharma A. Medicinal properties of *Zingiber officinale* Roscoe - A Review. *IOSR J. Pharm. Biol.*  
876 *Sci.* **2014**, *9*, 124-129.
- 877 111. Honolulu Advertiser (2005). Canoe Plants of Ancient Hawai'i.  
878 <https://www.canoepplants.com/awapuhi.html>. Accessed on 18th February 2017.
- 879 112. Wolff, X.Y.; Astuti, I.P.; Brink, M. *Zingiber* G.R. Boehmer. Plant Resources of South-East Asia (PROSEA)  
880 No. 13: Spices: 233-238, 1999.
- 881 113. Datiles, M.J.; Acevedo-Rodríguez, P. (2014). *Zingiber montanum* (cassumunar ginger). Centre for  
882 Agriculture and Biosciences International (CABI) website. <http://www.cabi.org/isc/datasheet/57536>.  
883 Accessed on 2nd March 2017.
- 884 114. Anasamy, T.; Abdul, A.B.; Sukari, M.A.; Abdelwahab, S.I.; Mohan, S.; Kamalidehghan, B.; Azid, M.Z. A  
885 Phenylbutenoid Dimer, cis-3-(3',4'-Dimethoxyphenyl)-4-[(E)-3''',4'''-Dimethoxystyryl] Cyclohex-1-ene,  
886 Exhibits Apoptogenic Properties in T-Acute Lymphoblastic Leukemia Cells via Induction of p53-  
887 Independent Mitochondrial Signalling Pathway. *Evid. Based Complement. Alternat. Med.* **2013**. Article  
888 ID 939810, 14.
- 889 115. Mihashi, H.; Okada, M. Illustrated medicinal plants of the world in colour. Hokuryūkan Co., Ltd.; Tokyo:  
890 1988. p. 666. (In Japanese)
- 891 116. Wiart, C.; Medicinal Plants of China, Korea, and Japan: Bioresources for Tomorrow's Drugs and Cosmetics.  
892 1st. CRC Press; Boca Raton, FL: 2012. p. 67.
- 893 117. Farifah Hanum, I.; Hamzah, N. The Use of Medicinal Plant Species by the Temuan Tribe of Ayer Hitam  
894 Forest, Selangor, Peninsular Malaysia. *Pertanika J. Trap. Agric. Sci.* **1999**, *22*, 85 – 94.
- 895 118. Weiss, E.A. *Spice Crops*. CABI. p. 338, 2002.
- 896 119. Chee, B.J. "The Spectacular Ginger: *Zingiber spectabile*". September 2010. Malaysian Naturalist: 12–13.
- 897 120. Koga, A.Y.; Beltrame, F.L.; Pereira, A.V. Several aspects of *Zingiber zerumbet*: a review. *Rev. Bras. de*  
898 *Farmacognosia.* **2016**, *26*, 385–391.
- 899 121. Mahmood, N.D.; Nasir, N.L.; Rofiee, M.S.; Tohid, S.F.; Ching, S.M.; The, L.K.; Salleh, M.Z.; Zakaria, Z.A.  
900 *Muntingia calabura* L.: A Review on Its Traditional Uses, Chemical Properties and Pharmacological  
901 Observations. *Pharm. Biol.* **2014**, *52*, 1598 – 1623.
- 902 122. Burkill, I.H. Dictionary of Economic Products of the Malay Peninsula (Volume 2), Ministry of Agriculture  
903 and Cooperatives Malaysia, Kuala Lumpur, pg. 2344-2345, 1966.
- 904 123. Jansen P.C.M. *Zingiber ottensii* (PROSEA). In: Plant Resources of Southeast Asia. [http://uses.plantnet-](http://uses.plantnet-project.org/en/Zingiber_ottensii_(PROSEA))  
905 [project.org/en/Zingiber\\_ottensii\\_\(PROSEA\)](http://uses.plantnet-project.org/en/Zingiber_ottensii_(PROSEA)). Accessed on 29<sup>th</sup> March 2017 *Medicinal properties of Zingiber*  
906 *officinale* Roscoe – A Review [www.iosrjournals.org](http://www.iosrjournals.org) 126 | Page, 2017
- 907 124. Riazi, S.; Matthews, K.R. Failure of foodborne pathogens to develop resistance to sanitizers following  
908 repeated exposure to common sanitizers. *Int. Biodeterior. Biodegr.* **2011**, *65*, 374–378.
- 909 125. Pandey, A.K.; Kumar, P.; Singh, P.; Tripathi, N.N.; Baipai, V.K. Essential oils: Sources of antimicrobials and  
910 food preservatives. *Front. Microbiol.* **2017**, *7*, 2161.
- 911 126. Islam, K.; Rowsni, A.A.; Khan, Md. M.; Kabir, Md. S. Antimicrobial activity of ginger (*Zingiber officinale*)  
912 extracts against food-borne pathogenic bacteria. *Int. J. Sci. Technol.* **2014**, *3*, 867 – 871.
- 913 127. Prasad, M.M.; Seenayya, G. Effect of spices on the growth of red halophilic cocci isolated from salt cured  
914 fish and solar salt. *Food Res. Int.* **2000**, *33*, 793-798.
- 915 128. Sa-nguanpuag, Kanlayanarat, K.S.; Srilaong, V.; Tanprasert, K.; Techavuthipornng, C. Ginger (*Zingiber*  
916 *officinale*) Oil as an antimicrobial agent for minimally processed produce: A case study in shredded green  
917 papaya. *Int. J. Agric. Biol.* **2011**, *13*, 895-901.

- 918 129. Ortiz, M. Antimicrobial activity of onion and ginger against two foodborne pathogens *Escherichia coli* and  
919 *Staphylococcus aureus*. *MOJ Food Proc. Tech.* 1: 00021. **2015** DOI: 10.15406/mojfpt.2015.01.00021.
- 920 130. Debbarma, J.; Kishore, P.; Nayak, B.B.; Kannuchamy, N.; Gudipati, V. Antibacterial activity of ginger,  
921 eucalyptus and sweet orange peel essential oils on fish-borne bacteria. *J. Food Proc. Pres.* **2013**, *37*, 1022–1030
- 922 131. Jeevani Osadee Wijekoon, M.M.; Bhat, R.; Karim, A.A.; Fazilah, A. Chemical composition and  
923 antimicrobial activity of essential oil and solvent extracts of torch ginger inflorescence (*Etilingera elatior*  
924 Jack.). *Int. J. Food Prop.* **2013**, *16*, 1200-1210.
- 925 132. Mohamed, H.G.; Gaafar A.M.; Soliman. A. Antimicrobial activities of essential oil of eight plant species  
926 from different families against some pathogenic microorganisms. *Res. J. Microbiol.* **2016**, *11*, 28-34.
- 927 133. Gottardi, D.; Bukvicki, D.; Prasad, S.; Tyagi, A.K. Beneficial Effects of Spices in Food Preservation and  
928 Safety. *Front Microbiol.* **2016**, *7*, 1394. doi: 10.3389/fmicb.2016.01394
- 929 134. Zick, S.M.; Djuric, Z.; Ruffin MT, Litzinger AJ, Normolle DP, Alrawi S, Feng MR, Brenner DE.  
930 Pharmacokinetics of 6-gingerol, 8-gingerol, 10-gingerol, and 6-shogaol and conjugate metabolites in  
931 healthy human subjects. *Cancer Epidemiol. Biomarkers Prev.* **2008** *17*, 1930-6.
- 932 135. Chrubasik, S.; Pittler, M.H.; Roufogalis, B.D. *Zingiberis rhizoma*: a comprehensive review on the ginger effect  
933 and efficacy profiles. *Phytomedicine* **2005**, *12*, 684-701.
- 934 136. Marcus, D.M.; Snodgrass W.R. Do no harm: avoidance of herbal medicines during pregnancy. *Obstet*  
935 *Gynecol.* **2005**, *105*, 1119-1122.

936

937

938