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Diversity, Utility, Analytical Methods and Use Implications of Aroma-active Compounds from Select Angiosperm Families

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Authors' contributions

This review was carried out in collaboration between all authors. Author SJA designed the study and wrote the first draft; authors NNI, AAA and TA reviewed the draft and managed the references; and authors BKT, BUE, JA and MG approved the study. Authors SJA, NNI and JA prepared the final draft. All authors read and approved the final manuscript.

Review Article

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ABSTRACT

Introduction: An "aroma-active compound" (AAC) has a "flavor"- ie: a "distinct taste and odor". An example is menthol. All aromatic plants (APs), including some medicinal plants, such as *Mentha×piperita* (Family Lamiaceae), produce a group of fat-soluble secondary metabolites called "essential oils" (EOs) for various ecophysiological reasons. An EO has

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a "flavor" because it contains one or more AACs. A typical EO is a complex mixture of several AACs, with wide ranging, dose-dependent pharmacological/ toxic effects. Owing to their complexity and variability, many EOs need to be standardized to ISO's criteria. Professional use of EOs/ AAPs in food and drugs is controlled by good manufacturing practice (GMP).

Aim: Given the immense diversities in sources, chemical structures, and bioactivities of EOs/ AACs, which are greatly patronized in foods and drugs, this review focused on their: i) sources in plants, beneficial attributes and liabilities; and ii) chemistry and analytical methods, in order to gain a better insight into their regulation in foods and drugs.

Methodology: Using the 2009 Angiosperm Phylogenic Grouping (APG) of plants as a guide, pertinent literature was perused to ascertain: i) the taxa of APs; ii) their EOs/ AAPs; and iii) the methods for analyzing EOs/ AACs in raw materials (RMs) and finished products (FPs).

Results: The literature revealed scores of AACs with varying health implications. But their levels in samples are usually unknown, or extremely hard to ascertain, owing to costs and complexities of the methods used.

Conclusions: Given the wide ranging effects of EOs/ AAPs vis-à-vis the dearth of data on their levels in samples, it is recommended that their regulation in FPs should focus on: i) controlling the wholesomeness of RMs; and ii) on enforcing strict GMP in using such RMs. Meanwhile relevant agencies should sponsor research into more cost-effective methods.

Keywords: Aroma-active compound (AAC); drug, essential oil (EO); flavor; food; good manufacturing practice (GMP); international organization for standardization (ISO) analytical method; regulation.

1. INTRODUCTION

1.1 Aromatic Plants, Spices, Essential Oils and Aroma-active Compounds

An "aromatic plant" (AP) refers to a plant used in food and/ or medicine because of its "flavor" (taste and smell) and other biological attributes of a named part, such as the fruit, seed, leaf, bark, stem, or root. For example, nutmeg tree (*Myristica fragrans)* is the source of two spices: mace, from the seed covering; and nutmeg, from the seed cotyledon. A "spice" usually refers to a fresh or dry whole plant or its part that is used because of its flavor. The flavor of an AP or spice is due a "mixture of oily substances" extractable from the AP or spice. That mixture is called "essential oil" (EO). EOs may be defined as pure or partly purified mixtures of hydrophobic/ lipophilic substances, usually extractable as a liquid from a named AP or spice. An EO has taste and smell because it contains volatile aroma-active compounds (AACs) - ie: chemical entities that evoke a distinct taste and smell in humans. An EO may be called the "oil of" the plant from which it was extracted, usually by distillation, expression, or solvent extraction. An EO is termed "essential" in the sense that it has a distinct aroma reminiscent of the plant from which it was extracted. Most EOs contain terpenes, terpenoids and other hydrophobic/ lipophilic substances with molecular weights below, or slightly above, 300 daltons. EOs or the plants or spices containing AACs were well known since antiquity for their use in cosmetics, foods and drugs [1,2].

1.2 Issues and Terminologies Associated with the Term "Essential Oil"

A typically EO is a highly complex mixture of several scores of individual AACs that are volatile and mostly liquid, or sometimes solid, at room temperature. EOs are not "oils" in the classical sense of being "liquid fats" like many triglycerides of plants that are liquid at room temperature, but they share with such oils a poor solubility in water. Unlike most triglycerides (fixed oils) and many mineral, paraffin, or petroleum oils that may be practically tasteless and odorless, a typical EO has taste and smell hence it is used as a "flavor". However, if an EO is tasteless or is distinguished only by its smell, it is termed a "fragrance". While flavors are used in foods, medicines and cosmetics, fragrances are more commonly associated with cosmetics, perfumes and toiletries. This review is concerned with EOs/ AACs or flavors associated with a select range of medicinal and aromatic plants (MAPs). Such MAPs or their spices have been known since antiquity, and have not only been the cause of many wars and voyages in the past, but are even today a major item of world politics and commerce [2].

2. SELECT AROMATIC ANGIOSPERMS

2.1 Scope of the Study/ Families of Plants Selected

2.1.1 Scope of the study

Using the most current angiosperm phylogenetic grouping (APG III) of flowering plants [3-5] as a guide, pertinent literature on the chosen plants and their EOs/ AACs was diligently perused to ascertain the following:

- The taxa of the chosen plant.
- The diversity, utilization, and liabilities of the EOs/ AACs.
- The chemical composition, structures, and biological effects of the EOs/AACs.
- The methods of analyses of the EOs/ AAPs in raw materials and finished products.

2.1.2 Families of the plants selected

A preliminary survey of aromatic flowering plants and of flavors commonly used in products worldwide revealed the following Angiospermae families as the most commonly patronized:

- Apiaceae
- Ericaceae
- Erythroxylaceae
- Lamiaceae
- Myrtaceae
- Piperaceae
- Solanaceae
- Rutaceae
- Zingiberaceae

The survey revealed that many medicinal and aromatic plants (MAPs) thrive in most regions of the globe that supports vegetation, but their greatest abundance is in the tropics, where "about 400 species, from 67 Angiospermae families" produce EOs of commercial importance [4]. Chemically, the AACs in these plants fall into the following classes:

- Phenolics
- Esters
- Terpenes
- Terpenoids
- Others

Terpenes and terpenoids are the dominant classes of AACs, followed closely by phenolics and esters. The "others" category includes aldehydes, ethers, ketones, and various lipid-soluble entities. Further details on the foregoing plants and AAPs are revealed below.

2.2 Apiaceae Members

2.2.1 Introduction

Apiaceae is also called the "carrot" or "parsley" family. It has many aromatic plants that have hollow stems. It is the 16th largest family in APG classification, with 434 genera/ 3,700 species [5]. Popular members include anise, caraway, carrot, celery, coriander, cumin, dill, fennel, hemlock, parsley, and parsnip, among others.

2.2.2 Botany

Botanically the Apiaceae family members have the follow key features:

2.2.2.1 Habit

- Most are annual, biennial or perennial herbs, but a few are shrubs or trees.

2.2.2.2 Leaves

- In the herbs the leaves tend to aggregate toward the base.
- The leaves are variable in size and alternately arranged, or alternate with the upper leaves becoming nearly opposite.
- In some taxa, the texture of the leaves is leathery, fleshy, or even rigid, but they always have stomata.
- Crushing the leaves commonly emits a distinct smell – aromatic, or fetid.

2.2.2.3 Inflorescence

- The flowers are nearly always aggregated in terminal umbels, simple or compound, often umbelliform cymes, which is why the family used to be called: Umbelliferae.
- The flowers are usually hermaphroditic and actinomorphic (ie: symmetrical).
- The flowers are nearly perfectly pentamerous, with 5 each of petals, sepals, and stamens.

2.2.2.4 Fruit

- The fruits are usually a schizocarp, ie: dry fruit with separable carpels.
- The seeds usually have oily endosperms, with much triglycerides.
- The fatty acid - petroselinic acid occurs universally in Apiaceae, but rarely outside it.

2.2.3 Chemistry

Apiaceae members contain aldehydes, esters, ethers, ketones, and phenolics, including estrogenic entities. The chemistry, biological effects, and uses of the EOs/ AACs, and some of the members containing such EOs/ AACs are indicated in Table 1.

2.3 Ericaceae

2.3.1Introduction

Ericaceae, or the heath family, thrives in acidic and infertile habitats. It is the 14th largest family among the Angiosperms, with 126 genera/4000 species [24]. There are many well-known and economically important members, including the cranberry, blueberry, huckleberry, azalea, and rhododendron. Common heath genera are: *Erica*, *Daboecia*, and *Calluna* [24,25]. Heather (or *Calluna*) is listed among 38 plants used to prepare Bach flower remedies – a form of Alternative Medicine [26]. The family is widely distributed except at the poles and specific places like deserts and tropical lowlands. Like other stress-tolerant plants, many members have mycorrhizal fungi that assist in extracting nutrients from infertile land. Many members also have evergreen foliage to conserve nutrients, and are used as herbal medicines in various health conditions [26,27].

2.3.2 Botany

2.3.2.1 General habit

The Ericaceae contains a morphologically diverse range of taxa, including herbs, dwarf shrubs, shrubs and trees [27].

2.3.2.2 Leaves

The leaves are usually alternate or whorled, simple and without stipules [27].

2.3.2.3 Flowers

Members of Ericaceae bear hermaphrodite flowers that exhibit show considerable variability. The petals are often fused (ie: sympetalous) with shapes ranging from narrowly tubular to funnel-like or widely bowl-shaped. The corollas are usually radially symmetrical (ie: actinomorphic) but many flowers of the genus *Rhododendron* are zygomorphic, ie: bilaterally symmetrical [27].

2.3.3 Chemistry

2.3.3.1 Some methyl salicylate (MS) producing plants

Many plant families, including many Ericaceae members produce methyl salicylate (MS) in very small quantities, but the families/ genus/ species most famous for MS production are:

- Gaultheria [28], including Gaultheria procumbens-the wintergreen or eastern teaberry [29-33].
- Betula in the family Betulaceae, such as *B. lenta*, the black birch.

- All species of the genus *Spiraea* in the family Rosaceae, the meadowsweets.
- Coca - *Erythroxylum coca* (Erythroxylaceae) also produce significant amounts of methyl salicylate.
- *Gaultheria procumbens* (eastern teaberry, checkerberry, boxberry, or American wintergreen) is a species of *Gaultheria* native to northeast of the US [28].

A brief review of *Gaultheria procumbens* is presented in the next subsection.

2.3.4 *Gaultheria procumbens*

2.3.4.1 Habit and habitat

Gaultheria procumbens is a small low-growing shrub, typically reaching 10–15 cm tall. The leaves are evergreen, elliptic to ovate, 2–5cm long and 1–2cm wide, and when crushed, emit a distinct aroma, characteristic of the oil of wintergreen. The plant is calcifuge (ie: failing inlimestone or alkaline soils, but thriving in acidic soils). It tends to grow best as part of the heath complexin a forest setting, but generally produces fruit only in sunnier areas [29].Although *G. procumbens* can reproduce by seeds, it normally spreads vegetatively by means of its long rhizomes [29]. However, since the rhizomes are only within the top 20–30 mm of soil (ie: shallow-rooted), the plant may not survive most forest fires. Unlike most other plants, which require warmth to grow, the seeds of *G. procumbens* must be kept cold (even by refrigeration) for 2 months to stimulate them to grow.

2.3.4.2 Flowers

The flowers are bell-shaped, 5 mm long, white, borne solitary or in short racemes, ie: an inflorescence in which the flowers are borne on short stalks along a long main stem, as in the lily of the valley. The fruit looks like a berry, but is actually a dry capsule surrounded by fleshy calyx, 6–9mm diameter [30-32].

2.3.4.3 Use in food and medicine

The fruit and leaf of *G. procumbens* are edible - minty and pleasantly sour. The aerial parts make a well flavored tea that is quite popular, being known by over 28 common names [31]. But for the leaves to yield their essential oil sufficiently, they must be fermented for 3 days, or more [32]. By virtue of its content of MS, which largely accounts for the plant's pleasant flavor, *G. procumbens* has been in use in food and medicine since antiquity, not only in Europe but in the America [33]. As shown in Table 2, MS is related to aspirin – an analgesic, antipyretic and antiinflammatory.

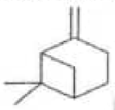
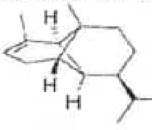
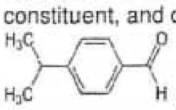
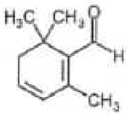
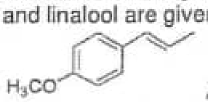
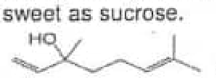
2.4 Erythroxylaceae

2.4.1 Introduction

Erythroxylaceae (or coca family) is an Angiosperm family of trees and shrubs consisting of 4 genera and approximately 240 species [3,23,34,35]. The four genera are:

- *Aneulophus*
- *Erythroxylum*
- *Nectaropetalum*
- *Pinacopodium*

Table 1. Apiaceae EOs/ AACs and their sources, attributes, effects and uses

EOs/ AACs/ Structures/ Examples	Attributes/ Effects/ Uses/ other comments
Angelica root oil (ARO) has > 60 AACs including pinenes that occur in large amounts in ARO [6]; and copaene that occurs in small amounts in [7].  β-Pinene Pinenesare the key AAC of Gymnosperms, but occur in Angiosperms.  Copaene Example: *Angelica archangelica* contains all the AACs shown in the right column[8].	ARO's key AACs are: Pinenes, camphene, sabinene, phellandrenes, myrcene, limonene, cryptone, bisabolene, ocimenes, p-cymene, terpinolene, bornyl acetate, humulene oxide, tridecanolide, pentadecanolide, and copaene [7].Uses of ARO obtained from *Angelica archangelica*: • Alleviates digestive/ hormonal problems • Immune booster / detoxifier • Promote restful sleep and peak circulation • Calms emotional distress/ nervousness Pinenes and copaene are used by many insects as semiochemicals. Copaene (found first in *Copaifera* spp.) is proposed for controlling *Ceratitis capitata* – an agro-pest in Mediterranean zones [7].
Cumin oil (CO): Structures of cuminaldehyde – a defining constituent, and of safranal are given.  Cuminaldehyde Cuminaldehyde contributes to the aroma of many EOs use in food and cosmetics. It inhibits the fibrillation and may be of help in Parkinsonism and dementia [9].  Safranal Chemical analysis of *Cuminum cyminum* oil from *China reveals scores of AACs. The oil is used in food and medicine [10].*	The key AACs of CO are: cuminaldehyde, cuminic acid, cymene, dipentene, limonene, phellandrene, and pinene, λ-terpinene, and safranal [10,11]. Its attributes/ health benefits include: • Bactericidal/ antiseptic/ detoxifier • Carminative/ digestive • Diuretic/ stimulant/ anti-spasmodic/ tonic • Emenagogue/ induce r of menstruation. Black cumin oil (BCO) refers to *Nigella sativaoil.* Safranal is an effective anticonvulsant – a GABA receptor agonist [12,13]. It is strongly antioxidant/ free radical scavenger [14,15] and cytotoxicity to cancer cells in vitro [16]. It has also been shown to have antidepressant properties [17,18].
Anise oil (AO): Structures of 2 key constituents - anethole and linalool are given[19-22]:  Anethole Anethole is a phytoestrogen. It is 13xas sweet as sucrose.  Linalool Linalool is also called β-linalool. Example: *Pimpinella anisum* (aniseed) has all the AACs in the right column [19]	Key constituents of AO are: anethole, pinenes, camphene, safrole, anisaldehyde, acetoanisole and linalool. AO's attributes/ effects/ uses are [20]: • Antispasmodic/ anti-menstrual cramps [10] • Carminative/ stomachic/ expectorant • Antiseptic/ insecticide to head-lice. • Diuretic/ stimulant • Others: galactagogue and laxative Linalool occurs in spice plants/ flowers with many commercial uses based on its aroma -floral, with a touch of spiciness. It has a soothing effect, and occurs in > 200 tropical and boreal plants [21,22].

Linalool is said to be "one of the most widely used substances to soothe away emotional stress" [22]. Conium maculatum (Hemlock) is an Apiaceae member, but has a fetid smell. Unlike other Apiaceae in the Table, hemlock is not used in food due to the presence of coniine-a deadly poison. Hemlock is a perennial herb native to Europe, Mediterranean region, and South Africa [23]

The tree or shrubs are tropical, occurring in South America, Java and Zimbabwe. All the 4 genera occur in South America. *Erythroxylum* occur in both Java (as *E. coca*) and Zimbabwe (as *E. emarginatum*). The most popular species of the family is *Erythroxylum coca*, or coca plant-the source of the cocaine.

2.4.2 Botany

2.4.2.1 Habit

Erythroxylaceae members are trees or shrubs [34,35], and are hairless all-round (glabrous). *Stipules* may be present or absent, and when present, are *intrapetiolar (ie: within the leafstalk).*

2.4.2.2 Leaves

The leaves occur alternately, are simple, and entire. They contain, in addition to coca alkaloids, a small quantity of EO (0.06-0.13%w/w) whose main constituent is methylsalicyclic acid (MS). Other constituents are methyl alcohol and acetone [28]

2.4.2.3 Flowers

The flowers have the following characteristics:

- Occur between leaf and branch (ie: axillary)
- Are solitary or in bunches (ie: fascicles)
- Actinomorphic
- Bisexual
- There are 5 non-overlapping (ie: valvate) sepals
- There are 5 petals 5, each having an adaxial ligule-like appendage with nectar
- There are 10 stamens, usually forming a tube
- The ovary is superior, 2- or 3-locular, with 1 ovule per loculus

2.4.2.4 Fruit

The fruit is a 1-seeded fleshy drupe [34,35]

2.5 Lamiaceae

2.5.1 Introduction

Lamiaceae, or the mint family, enlarged in the 1990s, has a worldwide distribution. It has about 236 genera/ 7000 species [36]. The largest genera are *Salvia*-900, *Scutellaria*-360, *Stachys*-300, *Plectranthus*-300, *Hyptis*-280, *Teucrium*-250, *Vitex*–250, *Thymus*-220, and *Nepeta* 200 [37].

2.5.2 Chemistry

Lamiaceae members are mostly aromatic in all parts and include many widely used culinary herbs like basil, hyssop, lavender, marjoram, mint, oregano, rosemary, sage, savory, and thyme [36,37]. However, some are shrubs or tree. They are easy to cultivate by stem cuttings, and many are widely cultivated for their aromatic qualities. While many Lamiaceae members are desired for their edible leaves, others are grown for their seeds. Mint (*Mentha arvensis*) oil, commonly used in toothpastes, pharmaceuticals and aromatherapy, is a popular product of the family [37]. Others include Vietnamese miniature "beef-steak-plant" (*Mosla dianthera*), whose oil contains 62 AACs, including: carvone and limonene as most abundant, followed by limonene oxide (lemon/floral), β-caryophyllene, and α-humulene; and a further 20 AACs, including linalool 1-octen-3-one (mushroom/earthy) hexenol (grassy/leafy/metallic), myrcene (plastic/sweet), α-thujene (soy sauce/grassy), and dihydrocarvone (spearminty/pepperminty). On the basis of the aroma characteristics and intensity, it was concluded that (-)-carvone was responsible for the characteristic aroma of miniature beef-steak-plant [38]. More lately, GC–MS analysis of Korean *Mosla dianthera* oil revealed the presence of 29 AACs accounting for 97.74% of terpenoids and AACs. The major compounds were: Elemicin (16.51%), thymol (14.77%), β-caryophyllene (14.49%), iso-elemicin (9.22%), α-asarone (6.09%) and α-caryophyllene (5.26%). The oil had significantly reduced lung viral titers, inhibited pneumonia, and enhanced antioxidant activity in the lungs of virus infected mice [39]. AACs that can be extracted from wild mint (*Mentha Arvensis Piperascens*) include menthol, menthone, iso-menthone, neo-menthol, limonene, methyl acetate, piperitone, β-caryophyllene, α-pinene, and β-pinene [40-43]. Some outstanding AACs of Lamiaceaeare shown in Table 2.

2.6 Myrtaceae

2.6.1 Introduction

The Myrtaceae (Myrtle family) has thousands of species that include several popular plants:

- Allspice
- Clove
- Eucalyptus
- Guava
- Myrtle

All Myrtaceae members are woody trees or shrubs. All have EOs in one or parts, especially the leaves. Since APG III, the numbers of genera and species have been rising almost yearly. The most recent estimates are: >5650 species in 130-150 genera. The family has wide distribution in the tropics and warm-temperate. Members are common in the world's biodiversity hotspots, eg: the Amazon. The member *Eucalyptus regnans* is the tallest Angiosperm tree [3,23,50].

2.6.2 Botany

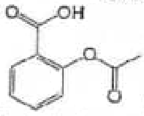
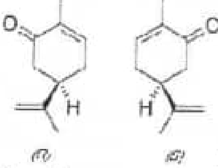
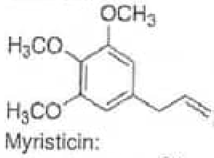
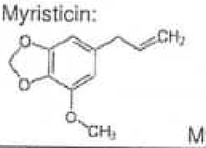
2.6.2.1 Vascular bundle

A key distinguishing feature of Myrtaceaeis that the phloem is located on both sides of the xylem, not just outside the xylem as in most other plants.

2.6.2.2 Leaves

The leaves are ever green, alternate, or mostly opposite, simple, and usually with an entire margin.

Table 2. Ericaceae and lamiaceae EOs/ AACs and their sources, attributes and uses

EOs/ AACs/ structures/ examples	Attributes/ effects/ uses/ other comments
Methyl salicylate (wintergreen oil): Is an AAC produced by many plants (mostly *Gaultheria*) but especially wintergreens, hence the common name. It is used both as a flavor and a fragrance. It is a key constituent of in liniments and balms.  Methyl salicylate (MS) Key producers other than *Gaultheria* are: • *Betula* spp. (family: *Betulaceae*) especially *B. lenta* - black birch • *Speiraea* (family: Rosaceae)- also called the meadowsweets. • Erythroxylaceae, eg: Coca plant It is noteworthy that MS is a fragrant liquid, but two related compounds – salicyclic acid (SA) and acetylsalicylic acid (ASA) are odorless solids	MS is produced as an anti-herbivore defense. Infection with herbivorous insects releases MS that attracts beneficial killer insects. MS is also used as a pheromone to warn other plants of pathogens. In humans MS has the following effects: • High doses for treating joint/ muscular pain • Low doses as a flavoring - highest level of MS in candy is 0.04% w/w. Notably: • MS is an antiseptic in Listerine mouthwash • MS is the ingredient sought after in de-cocainized coca leaf used in Coke. MS is produced by the methylation of the acetyl OH of salicyclic acid shown below:  Salicyclic acid (SA). Major plant producers of SA however, are: • Salicaceae, eg: *Sax alba* (white willow) • Thermogenic plants, eg: voodoo lilies • Tobacco, especially virus-infected.  Acetylsalicylic acid (ASA: Aspirin) Acetylation of the phenyl OH of salicyclic to aspirin – the famous analgesic, antipyretic and antiinflammatory
The following AACs occur not only in the oils of Apiaceae (eg: *Carum* and *Anethum*) but also in the EOs of Lamiaceae (eg: *Mosla* and *Mentha*): Carvone:  Carvone Elemicin:  Elemicin Myristicin:  Myristicin	*S*-(+)-Carvone is the key constituent (50-70%) of *Carum* seeds EO [41]. It also occurs 40-60% in *Anethum* seed EO and in mandarin orange peel EO. *R*-(–)-Carvone is abundant (50-80%) in *Mentha spicata* (spearmint) oil [42]. But most of *R*-(–)-carvone used in commerce is synthesized from *R*-(+)-limonene [43]. Many EOs, like gingergrass oil, contain a mixture of both enantiomers. Many EOs, eg: peppermint oil, contain trace quantities of carvones. Carvones are especially responsible for the flavor of caraway, dill and spearmint, which have been in use for millennia in food [43,44]. *R*-(-)-Carvone is used in air fresheners. *S*-(+)-Carvone is used to prevent premature sprouting of potatoes. (*R*)-(–)-Carvone has been proposed for use as a mosquito repellent [45,46]. Elemicin and Myristicin are phenylpropenoids and are a constituent of many EOs. Example: nutmeg oil contains 2.4%w/w of elemicin, while mace oil contains 10.5%w/w [47]. Elemicin also comprises 2.4%w/w of *Canarium luzonicum* (Manila elemi) oil [47]. Both elemicin and myristicin are psychoactive [48,49]. For example, the anticholinergic-like effects of raw nutmeg have been attributed to elemicin and myristicin [44]. Similarly, elemicin is also known to be partially responsible for the psychoactive effects of nutmeg [49].

It is to be noted that many of the AACs such as limonene, myrecene, pinenes, phenylpropenoids, among others, are present in many EOs irrespective of Family. For example many Apiaceae and Lamiaceae EOs have pinenes. Similarly many Lamiaceae and Myristicaceaecontain phenylpropenoids

2.6.2.3 Flowers

The flowers have a base number of 4 or 5 petals, but mostly 5. In some genera, the petals are exceedingly minute, or absent. The stamens are usually very conspicuous, brightly colored, and numerous.

2.6.3 Chemistry

Some members, eg: guava, bear fruits rich in ascorbic acid. As stated earlier all Myrtaceae members bear EOs in one or more parts. For example clove and eucalyptus oils are respectively from the flower buds of clove (*Syzygium* or *Eugenia*) and leaves of *Eucalyptus*. Some of the AACs of these EOs are shown in Table 3.

2.6.3 "Guava"- *Psidium guajava*

"Guava" fruits are popular and edible. The guava tree or shrub is *Psidium guajava* (Myrtaceae). It has oil in all parts. The guava fruit is the most frequently eaten fruit within the family. Guavas have tough dark leaves that are opposite, simple, elliptic to ovate and 5–15 cm long. When crushed, the leaves emit an aroma. The flowers are white, with five petals and numerous stamens. Like clove oil, guava oil can be derived from the leaves or other parts. It is reputed to be nourishing and soothing to the skin and to have antitumor properties owing to its high lycopene content and high β-carotene [72].

2.7 Piperaceae

2.7.1 Introduction

With from 2012, Piperaceae (the Pepper family) was considered to consist of about 2000 species in 5 genera [73]. Older documents had the same number of species in 10-13 genera [3,23]. Two genera, *Piper* and *Peperomia*, stand out as containing most of peppers [73].

2.7.2 Botany

Peppers are pantropical in distribution and may be small trees, shrubs, vines or herbs. *Piper nigrum*, the source of black and white peppers, is the most outstanding Piperaceae, and is a vine. Peppers tend to have slightly swollen or jointed nodes, ie: the points at which leaves attach to the stem or branch.

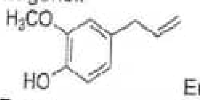
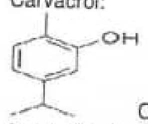
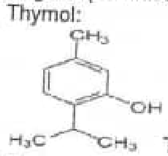
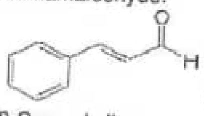
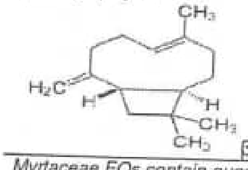
2.7.2.1 Leaves

The leaves of Piperaceae, which have a pungent flavor, grow singly. They are alternate or rarely opposite or whorled, stipules are adnate to petiole or absent.

2.7.2.2 Flowers

The bisexual or less commonly unisexual flowers, are minute, lack perianth, and are usually densely packed into rat-tail like spikes. Each flower is associated with a peltate, umbrella-like bract. The and roecium consists of 1-10 stamens. The compound pistil has a superior ovary and consists of 1-5carpels with a single locule and a solitary basal ovule.

Table 3. Myrtaceae EOs/ AACs and their attributes, uses and pertinent comments

EOs/ AACs/ structures/ examples	Attributes/ effects/ uses/ other comments
All Myrtaceae species, eg: allspice and clove have EOs in their parts. Clove has the following Eos [50-52]: • Bud oil, consisting of 60–90% eugenol/ eugenyl acetate, caryophyllene and others • Leaf oil, consisting of 82–88% eugenol, little or no acetate and minor others • Stem oil, consisting of 90–95% eugenol and minor others On the whole the key phytochemicals of clove oils are: phenylpropanoids, especially eugenol, but elemicin and myristicin [51] also occur. Others are carvacrol and thymol, cinnamaldehyde and β-caryophyllene. Eugenol:  Eugenol Eugenolisslightly soluble in H_2O, with spicy, clove-like aroma. It also occurs in nutmeg[59], cinnamon, basil and bay leaf, among others [51,59-61]. Carvacrol:  Carvacrol Some plants containing carvacrol: *Mornarda* (Lamiaceae), *Nigella* (Ranunculaceae), *Thymus vulgaris* (Lamiaceae) and others Thymol:  Thymol Plants containing carvacrol: *Momarda* (Lamiaceae), *Nigella* (Ranunculaceae), *Thymus vulgaris* (Lamiaceae), *Trachyspermum* (Apiaceae) and others. Cinnamaldehyde:  Cinnamaldehyde β-Caryophyllene  β-Caryophyllene	Allspice is *Pimenta dioca. The key AAC of its EO is eugenol.* Clove is *Syzygium aromaticum, Eugenia caryophyllata,* or *Eugenia aromaticum*). Clove oils are the most used of Myrtaceae oils: • In dentistry as an analgesic and antiseptic • In home remedy for dental pain relief • In aromatherapy • In flavoring foods and some medicines • In combination with garlic oil and sodium lauryl sulfate in cat deterrent sprays • Its high refractive index of 1.53 is useful in microscopy • Control of molds and their spores Despite US-FDA's down-grading, the efficacy of clove oil/ eugenol has been upheld [53,54]. Carvacrol: Is a monoterpenoid phenol, with a pungent, warm odor of oregano [55]. It is an effective antioxidant [56] and antiseptic, with a wide antimicrobial spectrum [57]. Thymol: Is isomeric with carvacrol, and occurs in thyme (*Thymus vulgaris*: Lamiaceae) and APs. It is a white crystalline solid, with a pleasant aroma, is antiseptic, and contributes for thymes flavor. Cinnamaldehyde: Is pale yellow, viscous liquid that occurs in the bark of cinnamon trees and other APs. It is responsible for cinnamon's pleasant flavor and contributes to that of clove oil [51,58]. Cinnamon's or cinnamaldehyde's health benefits are attributable to its antibacterial, antifungal, antimicrobial, astringent and anticlotting properties. β-Caryophyllene: Is a bicyclic sesquiterpene that occurs in EOs of many plants: clove, black pepper, Indian hemp rosemary, hops [62-68]. It occurs as a mixture with isocaryophyllene and α-humulene (or α-caryophyllene). In mice β-caryophyllene is a selective agonist of cannabinoid receptor type-2 (CB2) in some organs, and to exert significant cannabimimetic effects in such organs. It does not bind to the centrally expressed cannabinoid receptor type-1 (CB1) and hence does not exert psychomimetic effects. The ability of trained dogs to detect β-caryophyllene oxide is the basis for using such dogs for cannabis identification [67]

Myrtaceae EOs contain eugenol. Most contain detectable amounts of other AACs. The richest source of β-caryophyllene (51.75 %w/w) is Piper guineense [69]. β-Caryophylleneis thought to partly account for Niprisan's use in managing sickle cell crisis [63,64]. Other rich sources of β-caryophyllene are: Cannabis sativa (3.8–37.5 %w/w [69]; Cinnamomum tamala (3.4–18.4 %w/w) [70]; and clove: 1.7-19.5 %w/w [71]

2.7.2.3 Fruit

The fruit is a berry or drupe. The seeds have a minute embryo and a mealy perisperm [73].

2.7.2.4 Stems and roots

Piperaceae members are often rhizomatous, and can be terrestrial or epiphytic. The stems can be simple or branched.

2.7.3 Some examples of *Piper*

Piper species are mostly shrubs, woody vines (lianas), and small trees. Many are used in medicines and in food and beverages as spices and seasonings.

2.7.3.1 Piper nigrum

Piper nigrum is a 9-metre woody climber native to the Indian subcontinent. It can be cultivated in most tropical regions where soil moisture is constantly high and temperatures are warm. The pungency of *Piper* peppers is attributed to chavicine, piperine and piperidine.

2.7.3.2 Pipercubeba

This species of cubeb pepper, and is of particular importance in Southeast Asia, especially Vietnam, where it is a major cash crop. It is used in various medicines and for flavoring cigarettes and bitters.

2.7.3.3 Piperbetle

In China and Japan, and other Far East countries, the leaves of the betel pepper (*P. betle)* are commonly chewed with betel nut (*Areca catechu*) and lime, for recreation.

2.7.3.4 Piper guineense

Piper guineense is also called "Climbing black pepper" [63], West African black pepper, Ashanti pepper, Guinea cubeb, Benin pepper, or "uziza" pepper. It is native to the tropical rain forest of Africa, where it thrives mainly in the wild. It is, however, partly cultivated in Southern Nigeria, where the leaves and seeds are used to flavor soup [63].

2.7.3.5 Piper methysticum

A recreational drink of Fiji and other Pacific Islands, variously known as "kava", is made from the root of *P. methysticum*. Kava has narcotic and sedative effects.

2.7.4 Chemistry

Among the AACs that occur in Piperaceae, particularly in the leaves, fruits, and roots of *Piper* species, or in EOs derived from such parts, are: capsaicinoids like piperine and chavicine; terpenes likeα-phellandrene and α-pinene; terpenoids like linalool, α-thujone, and terpinen-4-ol; and Phenylpropanoids like elemicin and myristicin. A few of the foregoing AACs are illustrated in Table 4, with pertinent comments.

2.8 Solanaceae

2.8.1 Introduction

Solanaceae, or the nightshade, or potato family, consists of about 98 genera/ 2,700 species [74], or 102 genera/ 2,500 species [75]. The family contains members that have immense economic importance, as food and drug sources. These include:

- *Atropa belladonna*-deadly nightshade, also called belladonna
- *Capsicum annuum*-chilies (high in capsaicin) or sweet pepper (low in capsaicin)
- *Solanum tuberosum*–Irish potato, white potato, or simply, potato
- *Solanum melongena*–garden egg, or eggplant
- *Solanum lycopersicum*,or*Lycopersicon esculentum*–tomato
- *Nicotiana tabacum*-tobacco
- *Datura stramonium*–Jimsonweed, contains toxic cyanogens

The family has been included in this review solely because of the intensely spicy phytochemical, capsaicin, which occurs in some varieties *Capsicum annuum*. However, the following points deserve to be mentioned [69-71]:

- Members of the Solanaceae are distributed globally, but are most abundant in the neotropics, where about 40 genera are endemic.
- Temperate regions such the North America contain only about 50 species.
- The genus *Solanum* has almost half of all the species Solanaceae.

2.8.2 Botany

Solanaceae members may be herbs, vines, lianas, shrubs, or trees, but are rather most frequently creeping or lianous. The distinguishing family characteristics are:

2.8.2.1 Leaves

The leaves are alternate, usually simple, and lack stipules [69].

2.8.2.2 Flowers

- The flowers are bisexual and actinomorphic or only slightly zygomorphic.
- The perianth and androecium whorls are isomerous and usually are 5- or 4- or 6-merous.
- The calyx is synsepalous, ranging from tubular to deeply split.
- The corolla is sympetalous and ranges from forms with a short tube and rather long, reflexed lobes to forms with a long tube and short lobes.
- The stamens are distinct, alternating with the lobes of the corolla, and adnate to the corolla tube or perigynous zone.
- The gynoecium consists of a single compound pistil of 2 carpels, a single style, and a superior ovary with 2 or rarely more locules by false partitioning, each with usually numerous ovules.
- A nectary disk is often present at the base of the ovary [69].

2.8.2.3 Fruit

The fruit is a berry or septicidal capsule [70].

2.8.3 Chemistry

As stated earlier, Solanaceae is included in this review solely because of capsaicin-containing genus–*Capsicum* (family: Solanaceae). Yet capsaicin is not an oil, nor is it fragrant, unlike the EOs/ AACs encountered so far. All the spices or APs mentioned so far are used in food and medicines because of their fragrant and tasty EOs/ AACs. By contrast *Capsicum* peppers are used mainly on account of the intense spiciness of capsaicin, which is an odorless crystalline substance. Whereas Solanaceae is most noted for a range of cyclic-nitrogen alkaloids, like atropines; *Capsicum* is best known for-nitrogen alkaloids called "capsaicinoids". Capsaicinoids-typified by capsaicin. Capsaicinoids have been figured into this review because: Whereas the *Piper* species are best noted for their EOs/ AACs, much of their spiciness is due to capsaicinoids not EOs/ AACs. For example, the spiciest constituent of *Piper* is piperine and its isomers, which are capsaicinoids. The structures and attributes of EOs/ ACCs and capsaicinoids in *Piper;* and of capsaicinoids in *Capsicum*, are presented in Table 4.

2.9 Rutaceae

2.9.1 Introduction

Rutaceae, rue, or citrus family includes shrubs and trees and a few herbaceous perennials [85]. The family consists of 160 genera and 1,700 species distributed throughout the world, especially in the tropics and warm temperate [86]. The largest numbers are found in Africa and Australia, often in semiarid woodlands. The most economically important and most internationalized species are of the *Citrus* [85-88]:

- Grapefruit–*Citrusparadisi*
- Sweet orange-*Citrus sinensis*
- Sour orange-*Citrus aurantium*
- Mandarin orange or Tangerine–Citrus *reticulata*
- Citron-*Citrus medica*
- Lemon-*Citrus×limon*
- Lime-*Citrus aurantifolia*, the key lime

2.9.2 Botany

2.9.2.1 Habit

- Most species are shrubs, a few are herbs, eg: *Dictamnus*–burning bush [82]
- Most are aromatic with oil-containing cavities on the leaves
- Many species have oil in their flowers, eg: neroli oil is got from *C. aurantium* flowers
- Many have thorns.

2.9.2.2 Leaves

- The leaves are usually opposed and compound, and without stipules.
- The leaves have pellucid glands. Hence crushing the leaves releases aromatic oils typical of citrus-the basis for the synapomorphic identification test for Rutaceae.

2.9.2.3 Flower

The flowers are, or have [81,82]:

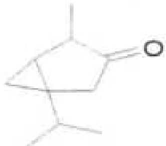
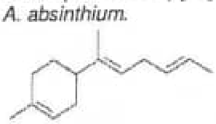
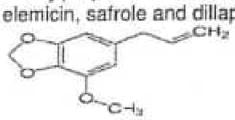
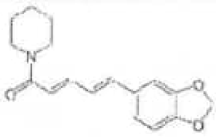
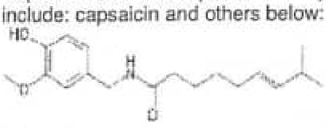
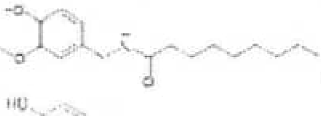
- Mostly perfect, ie: contain male and female organs in same flower - hermaphroditic, or sometimes unisexual, ie: having separate male and female flowers on same plant-monoecious.
- Bractless, solitary or in cyme, rarely in raceme, and mainly pollinated by insects.
- Mostly radially symmetrical
- Petals–5 in number, and mostly separate
- Sepals–5, or 3 in number, and mostly separate
- Stamen-5-10, eg: 5 in *Skimmia;* and up to 10 or more in *Citrus*, usually separate or in groups.
- Stigma-usually single, with 2-5 united carpels
- Ovaries-sometimes separate, but styles are fused

2.9.2.4 Fruit

The fruit of Rutaceae are very variable:

- Berry–a fleshy seed-containing fruit, eg: tomatoes and bananas. *Triphasia* species bear berries.
- Drupe-a fruit with thin outer skin, soft pulpy middle, and hard stony central part (pit) that encloses a seed, eg: apricots, plums, and almonds. *Amyris* species bear drupes.
- Hesperidium - a fruit consisting of thick leathery rind and soft segmented pulp, eg: all citrus fruits. Hesperidiums are actually specialized berries.
- Samara ("key")-a dry indehiscent, one-seeded, winged fruit, eg: ash, sycamore, or elm tree fruit. Keys or samaras usually grow in bunches. The hop tree (*Ptelea trifoliata*) bears samaras.
- Schizocarp - a dry compound fruit that splits at maturity into several indehiscent one-seeded carpels. *Helietta* species bear schizocarps.
- Capsule-a fruit containing seeds that it releases by splitting open when it is dry and mature. *Ruta* species bear capsules.

Table 4. EOs/ AACs in Piperaceae and capsaicinoids in Piperaceae and Solanaceae

EOs/ AACs/ structures/ examples	Attributes/ comments on select constituents
Piperaceae EOs/ AACs, eg: of *Piper nigrum*'sor*guineense*'sinclude: thujones, pinenes, camphenes, sabinenes, phellandrenes, myrcenes, caryophyllene, farnesene, linalool, bisabolene, terpineol and others.  β-Thujone Thujones [72,73]: Are monoterpenoids that occur in many conifers: especially *Thuja* (Cupressaceae) and *Juniperus* (Cupressaceae); and Angiosperms, eg:*Origanum, Mentha* and *Salvia* (Lamiaceae) [76] and *Artemisia*(Asteraceae) –notably *A. absinthium*.  α-Bisabolene Bisabolenes: Are sesquiterpenes in EOs of cubeb (Piperaceae), lemon (Rutaceae) and oregano (Lamiaceae). Phenylpropanoids: Those present in Piperaceae are: myristicin, elemicin, safrole and dillapiol.  Myristicin  Elemicin Among the capsaicinoids present are: piperine and its enantiomers such as chavicine.  Piperine Capsaicinoids: Those present in *Capsicum* (Solanaceae) include: capsaicin and others below:  Capsaicin  Dihydrocapsaicin  Nordihydocapsaicin	Thujone: Is a diastereomeric monoterpene, with 2 forms: (–)-α-thujone and (+)-β-thujone [71]. [2] It has a menthol-type aroma. It is regulated in food since it modulates brain GABA and $5\text{-}HT_3$ receptors [77]. Bisabolenes: Act as semiochemicals/ insecticidal. β-bisabolene has a balsamic odor [4] and is approved in EU as a food additive. It is an intermediate in the biosynthesisofhernandulcin, a natural sweetener. Myristicin and Dillapiol: Also occur in parsley/ dill (Apiaceae). Note-1: Eugenolis a phenylpropanoid Note-2: Eugenol is a key AAC of clove (Myrtaceae), *Cinnamomum* (Lauraceae), nutmeg (Myristicaceae). Elemicin: Accounts for 2.4 -10.5%w/w of nutmeg and mace oils; and 2.4% w/w of elemi (Burseraceae) tree oil [78]. Nutmeg's anticholinergic effects are attributable to elemicin [79] and myristicin [80]; and for the use of elemi oil or resin in bronchitis,catarrh and severe cough. Piperine and capsaicin: Both are insecticidal. Their spiciness arises from activation of heat/ acidity sensing ion channels on pain sensing neurons [81,82]. Capsaicin: Is used as analgesic in topical creams, nasal sprays and dermal patches at levels of 0.025-0.25%w/w. It is applied with other rubefacients to relieve muscle/ joint aches/ pains [83]. Spiciness [83]: Measured in Scoville Heat Unit: (SHU) for some capsaicinoids are: • Capsaicin: 16×10^6 • Dihydrocapsaicin: 15×10^6 • Nordihydrocapsaicin: 9.1×10^5 • Shogaol: 1.6×10^5 • Piperine: 1.0×10^5 • Gingerol: 6.0×10^4 Values show for example that piperine is only 0.1% as spicy or "hot" as capsaicin.

P. guineense, for example,has 5-8%w/w piperine–a capsaicinoid, accounting for most of its "heat". Pipers also have much terpenes/ terpenoids, eg: β-caryophyllene that are less spicy but aromatic. The phenylpropanoids have various medicinal used. Rotundone [84]- a key contributor to P. guineense' flavor, also occurs in oregano and thyme (Lamiaceae) and "coco-grass" or "nut-grass"- Cyperus rotundus(Cyperaceae)

Follicle - a dry dehiscent one-celled many-seeded fruit, eg: milkweed, which has a single carpel and opens along one suture. *Zanthoxylum* species bear follicles.

It is evident from the foregoing that seed numbers vary widely within Rutaceae [86,87].

2.9.3 Chemistry

Any given Rutaceae EO (eg: orange oil) contains over 100 phytochemicals, which may include: terpenes, terpenoids, coumarins, phenylpropanoids, limonoids, among others [87,88].Table 5 lists some of the outstanding AACs of 4 *Citrus* species, while Table 6 lists those of *Dictamnus albus* and 5 *Zanthoxylum* species. Table 7 shows some more EOs/AACs of Rutaceae. Wherever possible in Tables 5-7 chemical structures are used as illustrations.

2.9.3.1 Limonoids

Limonoids are phytochemicals (secondary metabolites) that abound in citrus and other Rutaceae members and in some Meliaceae (mahoganyfamily) members. Some limonoids are being investigated for a variety of effects and uses, such as: antibacterial, antidiabetic, antifungal, antineoplastic, antimalarial and antiviral [87-89]. Some, such as azadirachtin from the neem tree, are used as insecticides [89]. Structurally, limonoids consist of variations of a central furanolactone core. The prototype consists of four 6-membered rings and a furan ring (Table 6). Chemically, limonoids are classed as "tetranortriterpenes", or "tetranortriterpenoids". Citrus fruits contain the limonoids: limonin, nomilin and nomilinic acid, while both neem seeds and leaves contain the limonoid: azadirachtin [89].

2.9.3.2 Tetranortriterpenoids

The tetranortriterpenoid class of phytochemicals is most exemplified by azadirachtin, which is extracted from neem tree [89]: *Azadirachta indica* (Meliaceae). Azadirachtin has insecticidal properties, and mimics insect hormone called ecdysone that regulates insect pupation–a stage in metamorphosis. Application of azadirachtin on insects therefore interferes with their development, which eventually kills them. Azadirachtin is a limonoid [89].

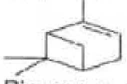
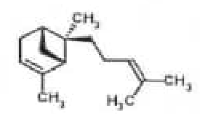
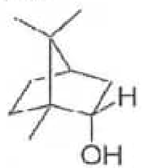
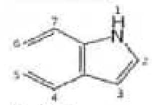
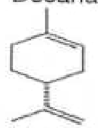
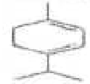
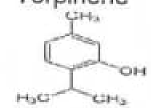
2.9.3.3 Hydroxy-alpha sanshool (HAS)

Hydroxy-alpha sanshool (HAS) is a bioactive phytochemical from the *Zanthoxylum*species, especially "Sichuan pepper" (*Z. simulans*, or *Z. bungeanum*). HAS is responsible for the numbing, tingling sensation (paresthesia) caused by eating food cooked with Sichuan pepper. The mechanism by which HAS induces paresthesia is still being debated. But HAS is an agonist of pain-integrating cation channels: transient receptor potential vanilloid - member 1 (TRPV1) and transient receptor potential cation channel, subfamily A, member 1 (TRPA1). In addition, newer evidence suggests that the two-pore domain potassium channels are primarily responsible for HAS's effects [90]. The word *"Sanshool"* in HAS is derived from the Japanese termfor "Sichuan pepper".

2.9.3.4 TRPV1

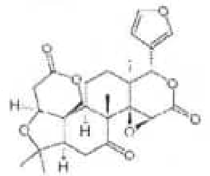
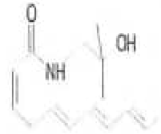
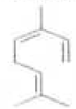
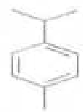
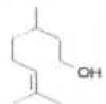
The function of *TRPV1* is to detect and regulate changes in body temperature. *TRPV1* also provides sensation of scalding heat and pain (nociception). It is activated by capsaicinoids such as piperine in black pepper and capsaicin in chili pepper [81-83].

Table 5. AACs of Select *Citrus* oils listed in descending order abundance

Top AACs of Select *Citrus* peel oils/ *Citrus aurantium* (neroli) flower oil					
Grapefruit	**Lemon**	**Lime**	**Neroli flower**	**Orange**	**Tangerine**
Pinene	Pinene	Pinene	Pinene	Limonene> 90%	Limonene
Sabinene	Camphene	Myrcene	Camphene	Pinene	Pinene
Myrcene	Sabinene	Limonene	Terpinene	Sabinene	Myrcene
Limonene	Myrcene	Terpinolene	Nerol	Myrcene	Terpinene
Geraniol	Terpinene	Cineole	NAC	Octanal	Citronellal
Linalool	Linalool	Linalool	Farnesol	Linalool	Linalool
Citronellal	Bisabolene	Borneol	Geraniol	Carene	Neral
DAC	Limonene	Citral	Linalool	Decanal< 0.3%	NAC
NRA	Bergamotene	NAC	Nerolidol		GAC
Terpinenol	Nerol	GAC	LAC		Geraniol
	Neral		MAT		Thymol
			Indole		Carvone
 Pinene: α- and β-isomers exist. The α-isomer is the main form	 α-Bergamotene:detected in lemon only	 Borneol: 2 pleasantly flavored isomers	 Farnesol  Indole	 Limonene: The D-isomer occurs at > 90% in rinds	 Terpinene  Thymol

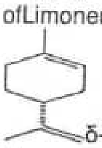
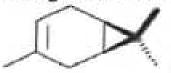
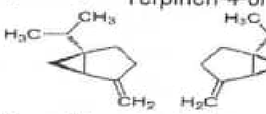
Careful inspection of the lists might explain, for example, the richer flavor of neroli oil as compared to all the others. Similarly, the richer flavor of tangerine oil as compared to those of grapefruit and orange oils can be explained. The richer flavor of lemon and lime oils as compare to that of orange oil can also be explained by studying the list. The difference between lemon and lime flavors deduced from the lists. The presence of anthranilate and indole in neroli oil, and the non-detection of limonene in the same may be noteworthy. Generally, the following esters tend to have an even richer flavor than terpenes or terpenoids: DAC - Decylacetate; NAC-Nerylacetate; GAC-Geranylacetate; MAT-Methylanthranilate; LAC–Linalylacetate

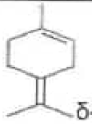
Table 6. AACs/ other phytochemicals in oils of *Dictamnus* and *Zanthoxylum* species

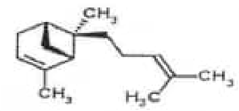
AACs/ other items in OEs from fruits/ leaves of *Dictamnus albus* and *Zanthoxylum* species					
***D. albus* [87]**	***Z. fagara***	***Z. simulans***	***Z. armatum***	***Z. rhesta***	***Z. piperitum***
Alkaloids Limonoids Triterpenoids Flavonoids Sesquiterpenoids Coumarins Phenylpropanoids Others	Alkaloids Coumarins HAS Others	Myrcene Limonene Cineole Ocimene HAS Others	Linalool Limonene MCN Cineole Others	Sabinene Limonene Pinene Cymene Terpinene Terpineol HAS Others	Citronellal Citronellol Hexenal HAS Others
			 		
Limonin – a limonoid. Occurs in neem also [89]	Hydroxy-α-sanshool (HAS). HAS affects functions of some ion channels*[90]*.	Ocimene has 2 forms: cis (above) and trans form. Both have pleasant flavors	Cineole is also called Eucalyptol. It has pleasant flavor and is insecticidal	Cymene: A semiochemical with pleasant flavor	Citronellol: 2 forms exist in lemon grass oil (50%) and in rose (18-55%) and others

Z. fagara occurs in tropical Africa and America. It is mentioned as useful in herbal management of sickle cell crisis [91]. Z. simulans occurs in Asia, especially Taiwan. It is also called "Sichuan pepper". Z. armatum occurs in Asia, especially Nepal. Z. rhesta is popular in India cuisine, while Z. piperitum is highly prized Japanese cuisine. Z. acanthopodium especially contains citronellal and limonene, among others, and is popular in Indonesia [92,93]. MCN: Methylcinnamate

Table 7. Rutaceae EOs/ AACs structures and attributes with pertinent comments

EOs/ AACs/ structures/ examples	Attributes/ effects/ uses/ other comments
Orange oil: Over 100 AACs (mostly terpenes/terpenoids) occur in orange peels. Examples: The topmost AACs of Italian orange peel EO by % content are: δ-limonene-93.67, α-pinene- 0.65, myrcene-2.09, β-pinene/ sabinene-1.00, octanal-0.41, linalool-0.31, carene- 0.31 and decanal -0.27 [96]. Structures ofLimonene/Carene are:  δ-Limonene Limonene: Is a colorless cyclic terpene, with strong lemon smell.  δ-3-Carene Carene: Is a bicyclic terpene in many EOs, eg: citrus oils. It has a sweet/ pungent odor. Grapefruit oil: Is got from peels by cold compression. Yield: 0.5 - 1 %, and consists of a-pinene, sabinene, myrcene, limonene, geraniol, linalool, citronellal, decyl acetate, neryl acetate and terpinen-4-ol.  Terpinen-4-ol  Sabinene Lime oil is extracted from *Citrus aurantifolia* (also known as Citrus medica var. acida and C. latifolia) of the Rutaceae family and is also known as Mexican and West Indian lime, as well as sour lime. Chemical composition The main constituents in the distilled lime oil, like the one normally sold is a-pinene, b-pinene, myrcene, limonene, terpinolene, 1,8-ceneole, linalool, borneol, citral and traces of neral acetate and geranyl acetate.  Myrcene	Limonene: It is used in synthesis of carvone and as a renewable cleanser. As a chiral molecule, δ-limonene is the natural enantiomer. It is got from citrus by centrifugation or distillation. Racemic limonene is dipentene [92]. Carene: Is water-insoluble; oil-miscible, and can be a skin irritant or CNS depressant. Other sources are: rosemary, pine, and cedar. Grapefruit oil: is extracted from Citrus paradisi (also known as *Citrus racemosa* and *C. maxima*) from the Rutaceae and is also called shaddock. This refreshing oil helps to boost digestion, benefits the immune system by helping to clear the lymphatic system, helps with skin problems, and can be used for muscle stiffness, water retention and for bolstering the nervous system. Terpinen-4-ol: is a terpene with a molecular weight of 154. It is deemed the primary active ingredient of tea tree oil [93,94]. It is also the compound of highest concentration in the EOs of nutmeg (Myristicaceae). Sabinene: is a natural bicyclic monoterpene with the molecular formula $C_{10}H_{16}$. It is isolated from the EOs of a variety of plants including holm oak - *Quercus ilex*(Fagaceae) and Norway spruce- *Picea abies*(Pinaceae). It has a strained ring system with cyclopentane fused to cyclopropane. Sabinene is one of the chemicals contributing to the spiciness of black pepper (Piperaceae). It is also a major constituent of carrot seed oil (Apiaceae). It occurs in tea tree - oil - *Melaleuca alternifolia* (Myrtaceae) and in the EO of nutmeg. Lemon: The main chemical components of lemon oil are α-pinene, camphene, β-pinene, sabinene, myrcene, a-terpinene, linalool, β-bisabolene, limonene, nerol, neral, and the rarest: α-bergamotene.


δ-Terpinene (or Terpinolene)


α-Bergamotene

α-Bergamotene is also known as: (-)-exo-alpha-bergamotene, (-)-trans-alpha-bergamotene, bergamotene (Z,.alpha.,cis), cis-.alpha.-Bergamotene. Formula: $C_{15}H_{24}$ Molecular Weight: 204. It is a key components flavors and fragrances containing lemon oil.

Most parts, especially the fruits and leaves of Rutaceae contain large numbers of various terpenes/ terpenoids and other secondary plant metabolites with distinct aroma-active attributes [95-97]. More than 100 compounds have, for example, been isolated from Dictamnusalbus that include: alkaloids, limonoid triterpenoids, flavonoids, terpenoids, coumarins, and phenylpropanoids [87]

2.9.3.5 TRPA1

TRPA1 is a protein that in humans is encoded by the *TRPA1* gene [93-95]. TRPA1 is an ion channel located on the plasma membrane of many human and animal cells. This ion channel is best known as a sensor for environmental irritants, pain, cold and stretch [94,95].

2.10 Zingiberaceae

2.10.1 Introduction

Zingiberaceae, or the gingerfamily, consist of several familiar and unfamiliar aromatic perennial herbs that have creeping horizontal or tuberous rhizomes. The family about 52 genera and over 1300 species, distributed throughout tropical Africa, Asia, and the Americas. Many species are important spices, or medicinal plants [98-108], including:

- Ginger (Root ginger)-*Zingiber*
- Galangal-*Alpinia galanga*
- Turmeric–*Curcuma*
- Myoga-*Zingiber mioga* [99]
- *Amomum* species, eg: true cardamom [100,101]
- *Elettaria* species [102,103]
- *Aframomum* species, eg: Alligator pepper, Korarima , and grains of paradise [104-108]

2.10.2 Botany

2.10.2.1 Habit

Zingiberaceae members are perennials that frequently have sympodial (forked) fleshy rhizomes (underground stems). They may grow to 6m height. A few species are epiphytic, ie: supported by other plants and with aerial roots exposed. The rolled-up sheathing bases of leaves often form an apparent short aerial stem. The commonly green sepals differ in texture and color from the petals, which may be brightly colored is some members [98].

2.10.2.2 Leaves

The leaves are alternate and distichous (ie: growing in vertical rows on opposite sides of a stem), the base sheathing and the blade mostly linear to elliptic with penni-parallel, strongly ascending veins.

2.10.2.3 Flowers

The flowers are bisexual, strongly zygomorphic, and often are associated with conspicuous floral bracts in a spike or raceme. The perianth is in two whorls:

- An herbaceous or membranous 3-lobed or spathaceous tubular calyx.
- A petaloid tubular corolla with 3 lobes.

The androecium typically consists of:

- One fertile stamen
- One large opposing petaloid labellum representing 2 connate staminodia
- Two smaller flanking petaloid staminodia

The gynoecium consists of:

- One compound pistil of 3 carpels
- One style nestled in a channel of the filament and anther of the fertile stamen
- One inferior ovary with typically 3 locules, each containing numerous axile ovules.

Only rarely is the ovary is unilocular with parietal placentation.

2.10.2.4 Fruit

The fruit is a loculicidal capsule or is berrylike.

2.10.3 Chemistry

Zingiberaceae plant parts used as spices may one of the following that contain EOs/ AACs and other phytochemicals [98,99]:

- Rhizome, eg: ginger, galangal, and tumeric
- Shoot/ Flower bud, eg:myogaginger-*Zingiber mioga* [99]
- Seed, eg:black cardamom-*Amomum subulatum* [100]; false cardamom-*Amomum corrorima* [101]; green or true cardamom-*Elettaria cardamomum* [102]; Ceylon cardamom-*Elettaria repens* [103]

Illustrations of the foregoing are given in the following subsections and Table 8.

2.10.3.1 Chemistry of Zingiberaceae rhizomes used as spices

The rhizome of ginger (*Zingiber officinale*) contains the following AACs:

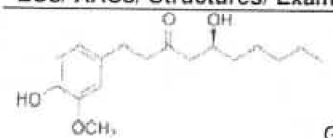
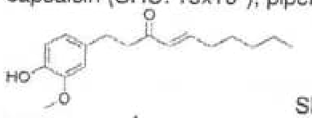
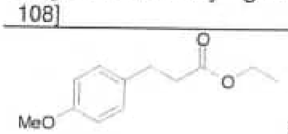
- Terpenes: zingiberene, and others such as: camphene and pinene

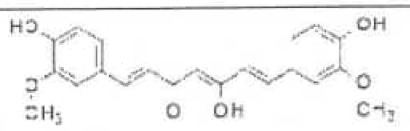
- Terpenoids: bisabolene, borneol, cineole, geranial, geraniol, neral, nerol and terpineol
- Esters: geranyl acetate
- Capsaicin-like phenolics with alkyl ketone group: gingerol, zingerone, and shogaol

The structures of zingiberene, gingerol, zingerone, and shogaol are shown in Table 8. The rhizome of galangal (*Alpinia galanga*) contains the following as key AACs:

- Zingiberene
- Ethyl cinnamate (25%)
- Ethyl p-methoxycinnamate (30%)
- p-Methoxycinnamic acid

Table 8. Zingiberaceae EOs/ AACs structures, attributes and pertinent comments

EOs/ AACs/ Structures/ Examples	Attributes/ effects/ uses/ other comments
 Gingerol (SHU: $6x10^4$) Gingerol, zingerone and shogaol in ginger are like capsaicin (SHU: $15x10^6$), piperine (SHU: $10x10^4$)  Shogaol (SHU:$16X10^4$)  Zingiberene Zingiberene is a key ingredient of ginger oil [106-108]	Gingerol is pungent, oily and yellow liquid at room temperature, has the following attributes: • Can form crystals at low temperatures • Is the key active of fresh ginger. • Converts to zingerone on cooking or to shogaol on drying or storage [107]. Gingerol or ginger oil is reputed to be: • Antipyretic [109] • Effective against rheumatoid arthritis in rats [110]. • A potential drug against: Colon Cancer [111]; Breast cancer cells [112]; Ovarian cancer [113]; and Pancreatic Cancer [114]
 Ethyl-p-methoxycinnamate In addition to some of ginger's AACs, galangal oil has: • Ethyl cinnamate (EC) - 25% w/w • Ethyl p-methoxycinnamate (EPMC) - 30%w/w • p-Methoxycinnamic acid EC occurs in/ imparts aroma to cinnamon oil [115].	Galangal oil is used as/ reputed for: • A spice to flavor food • An aid to relieve respiratory distress • An aid to relieve rheumatism • An adjuvant to drugs used against infections of mucous membranes, eg: catarrhal infections. • The *p*-methoxy derivatives are monoamine oxidase inhibitors [116].
Turmeric is popular for non-volatile, slightly bitter and spicy crystalline "curcuminoids", typified by "curcumin".	Curcuminoids are phenolics responsible for turmeric's yellowness. Curcumin exhibits keto-enol tautomerism - the enol is more stable [118]. It is appreciated in food for: • Its appealing yellow color imparted to

 Curcumin Curcumin is a diarylheptanoid. It is the key curcuminoid of turmeric – *Curcuma longa*. Other curcuminoids are desmethoxycurcumin and bis-desmethoxycurcumin [117].	foods, eg: curries. Its EU's number is E100 • Its slightly bitter and spicy taste Curcumin is turmeric's key bioactive for most health uses [5 curcumin], eg: skin, liver, stomach and respiratory disorders [119].
The flower buds and shootsof myogaginger (*Zingiber mioga*) and the seeds of *Amomum*, *Elettaria* and *Aframomum* species are used as spices because they contain similar AACs as ginger, eg: zingiberene, paradol (analogous to gingerol) and some of the commoner AACs like pinene and cineole [99-104].  Paradol	Paradol is deemed a key bioactive of spices from *Zingiber*, *Amomum*, *Elettaria* and *Aframomum* species responsible for their antioxidant and antitumor effects [119].Reports of these include: • Myoga is cytotoxic to cancer cells [99]. • Korarima seeds are used as a tonic, carminative and laxative in Ethiopia[120] • In Nigeria Grains of Paradise may be added to antisickling mixtures. They are also valued for warming and digestive effects [121,122].

AACs of Zingiberaceae occur in rhizomes, shoots/ flower buds, and seeds. They include: i) zingiberene; ii) gingerol - rhizomes; iii) paradol - seeds/ others; and iv) the commoner terpenes/ terpenoids. Gingerol and paradol are analogous to capsaicinoids, but turmeric contains curcuminoids

The structure of ethyl p-methoxycinnamate is given in Table 8. The rhizome of tumeric (*Curcuma longa*) contains some of the AACs of ginger, especially zingiberene, but turmeric is best known for its content of a group of non-volatile, slightly bitter and spicy crystalline phytochemicals called "curcuminoids", typified by "curcumin"(diferuloylmethane)–a brightly yellow substance that gives turmeric and some curries (those containing turmeric and other spices) their characteristic yellow color. Other curcuminoids found in turmeric are:

- Demethoxycurcumin
- Bisdemethoxycurcumin

The structure of curcumin is given in Table 8.

2.10.3.2 Chemistry of Zingiberaceae flower buds/ shoots used as spices

The flower buds and shoots of myoga ginger (*Zingiber mioga*) are flavorful and have EO presumably with some similarities to ginger oil in terms of AACs. For use, myoga ginger flower buds and shoots are mostly shredded into fine bits before incorporating the spices in cooking, mainly in Japan and South Korean. There is a dearth of literature on myoga ginger oil, but the spice is reputed to have cytotoxic constituents that have potentially anti-carcinogenic properties [99].

2.10.3.3 Chemistry of Zingiberaceae seeds used as spices

Amomum species includeblack cardamom, eg: *Amomum subulatum* [100]; and Korarima or false cardamom-*Amomum corrorima* [101], whose seeds are used as spices and have a strong camphorous flavor, and presumably some AACs such as zingiberene and paradol that are the same or similar to those of *Zingiber officinale*. Paradol Table 8 is analogous to ginger's gingerol.

Elettaria genus includes two species native to southeastern Asia: *Elettaria cardamomum* (green or true cardamom) and *Elettaria repens* (Ceylon cardamom). The seeds of both have chemical characteristics similar to those of the *Amomum* species [100,101].

The seeds of *Aframomum* species have similar chemical characteristics as *Amomum* and *Elettaria* species, and include three African species: Korarima or Ethiopian cardamom (*Aframomum corrorima*-alternative name of *Amomum corrorima* [101], "Grains of Paradise" – *Aframomum melegueta* [104], and "Alligator pepper" or Mbongospice (*Aframomum danielli* or *Aframomum citratum* [105].

3. RELEVANCE OF GMP/ ISO STANDARDS TO UTILIZATION OF EOs/AACs

APs or spices are "generally regarded as safe" (GRAS) flavorings, or additives, in foods, drinks, medicines and cosmetic. But extracted EOs usedin industrial production of foods (eg: ice cream and confectionaries), beverages (eg: sodas, beers and spirits) and pharmaceuticals (eg: syrups and elixirs) need to be handled professionally in accordance with strict "good manufacturing practice" (GMP). This is because the EOs or AAPs are secondary plant metabolites produced to ensure the plant's survival, and as such, can produce dramatic physiological effects, including unwanted effects, if misused. It therefore, became necessary for safety and good trade practice for standards to be developed for EOs. The International Organization for Standardization (ISO) has established over 130 standards on EOs. Examples include:

- ISO 3217:1974, for "Oil of lemongrass"
- ISO/TR210:1999, for "General rules for packaging, conditioning and storage" of EOs
- ISO 7359:1985, for "Analysis of EOs by gas chromatography on packed columns"
- ISO 16928 for "Essential oil of ginger [*Zingiber officinale* Roscoe]"
- ISO 22972:2004 Essential oils -- Analysis by GC on chiral capillary columns
- ISO 3061:2008 for "Oil of black pepper (*Piper nigrum* L.)"
- ISO 4720:2009, for "Nomenclature"
- ISO 25157:2013, for "Essential oil of rose, Chinese Kushui type"
- ISO 3528:2012 for "Essential oil of mandarin, Italian type (Citrus reticulata Blanco)"
- ISO 9235:2013 for "Aromatic natural raw materials – Vocabulary"

These standards and others are listed in ISO catalog [123] and are widely used to guide production, quality control, marketing, storage, and use of EOs worldwide. Without GMP and ISO or similar standards it would be impossible to properly regulate the use of flavors in products like Coke, Pepsi, Fanta, Sprite, 7-Up, Mountain Dew, Miranda, and other sodas.

4. ANALYSIS OF AACs IN SPICES, OILS AND FINISHED PRODUCTS

4.1 Equipment and Techniques Used in Flavor Analysis with Pertinent Comments

Equipment and techniques used in beverage flavor research include, among others:

- Liquid-liquid continuous extraction/solvent-assisted flavor evaporation (LLCE/SAFE) is a technique used in extracting AAPs from products [124].
- Gas chromatography-olfactometry (GCO) is a technique used for detecting AAPs. It works in conjunction with another technique called aroma extract dilution analysis (AEDA). This technique is well described and used by Hausch [125].
- Solid phase microextraction (SPME) combined with stable isotope dilution assays (SIDA) is used in quantifying AACs [126].
- Gas chromatograph-mass spectroscope (GC-MS) equipped with a comprehensive library is a requirement for flavor chemistry.
- High performance liquid chromatography (HPLC). It is, for example, often essential and convenient in flavor analysis to quantify benzoic acid in beverages using HPLC.

4.2 Retention Time Locked Methods

Two Retention Time Locked Methods (RTLMs) for analyzing EOs/ AACs have been described by David and coworkers [127].

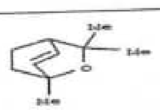
- The first was a gas chromatography-flame ionization detector (GC-FID) analyses performed on an Agilent 6980 GC equipped with a split/splitless inlet. Separation was done on a 50mx0.32 mm idx1.05µm HP-5 column (β=72): Agilent part number 19091J-215.
- The second was a gas chromatography-mass spectrometry (GC-MS) analyses performed on an Agilent 6980 GC equipped with a split/splitless inlet in combination with an Agilent 5973N MSD.

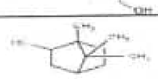
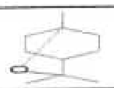
Retention times (RTs) for each of 400 AACs were determined using both methods. These led to the creation of two RT databases. Thus AACs in food, spices and EOs can be searched for automatically based on RTs and/or mass spectra.

4.3 Typical Concentrations of AACs in Finished Products

Table 9 shows levels of AACs in three lemon-lime sodas: Sprite, Serra Mist and 7Up.

Table 9. Levels of aroma-active compounds (AACs) in three regulated products

Molecule	Structure	Concentration of component in ng/g of de-carbonated soda as Mean or (Range at 95% Confidence Interval)		
		Sprite	Sierra Mist	7Up
Dehydrocineole		1550 (1360-1740)	2630 (2380-2890)	2750 (2490-3010)
Linalool		220 (202-239)	296 (277-314)	378 (353-403)
Borneol		201 (189-213)	53.8 (52.6-55.1)	58.6 (52.1-65.1)
Octanal		168 (155-181)	449 (411-487)	347 (332-362)
Decanal		61.3 (54.8-67.8)	191 (183-199)	133 (121-145)
Geraniol		47.5 (39.9-55.0)	67.5 (59.3-75.7)	119 (105-132)
Nonanal		33.5 (31.8-35.2)	54.3 (53.7-55.0)	42.1 (35.5-48.6)

Nerol		32.9 (29.5-36.4)	35.0 (29.8-40.2)	49.5 (43.2-55.9)
Isoborneol		32.5 (29.8-35.3)	16.0 (14.4-17.7)	12.2 (10.8-13.6)
Cineole (Eucalyptol)		29.7 (28.3-31.1)	17.4 (16.9-17.9)	15.5 (15.2-15.7)
Geranial (e-Citral)		5.64 (3.36-7.91)	6.58 (4.65-8.52)	10.0 (6.11-13.9)
Neral (z-Citral)		3.58 (2.46-4.70)	3.83 (2.65-5.01)	4.59 (3.56-5.63)

The data are after Hausch [125], using liquid-liquid continuous extraction/solvent-assisted flavor evaporation (LLCE/SAFE), gas chromatography-olfactometry (GCO) and solid phase microextraction (SPME) combined with stable isotope dilution assays (SIDA). The masses of de-carbonated beverages were: Sprite-97.4±1.55; Sierra Mist - 97.8±1.50; and 7Up-99.0±0.18% w/w of their carbonated masses [125]. Note: µg/g is equivalent to mg/kg or parts per million (ppm); and ng/g is equivalent to µg/kg or parts per billion (ppb)

5. USE IMPLICATIONS OF EOs/ AACs OF SELECT SPICES

5.1 Pharmacology and Toxicology of Eos/ Aacs

5.1.1 Permeabilization of membranes as a general effect of Eos

Both the therapeutic and toxicological effects of EOs/ AACs are concentration-depend, and have much to do with their ability to "permeabilize" barriers, ie: make cell walls and all membranes permeable. Their small size (mostly <300 Daltons) and lipophilic character are both critical to this ability. But the specific effects of an EO depend upon its composition of AACs and their functional groups. A typical EO, composed of many lipophilic AACs, may have no specific cellular target [128], rather as a composite lipophile, it can transverse cell walls, cell membranes, cytoplasmic membranes, as well as nuclear membranes. It can disrupt the molecular structure of cellulose, mucoproteins, lipoproteins, and phospholipids complexes, and in so doing, permeabilize these structures, and compromise their functions. Irrespective of cell type, permeabilization of membranes may lead to one or more of the following:

- Loss of ions
- Reduction of membrane potential
- Collapse of the proton pump
- Depletion of the ATP pool

EOs can even coagulate the cytosol with irreversible damage to enzymes and other proteins [128]. Thus, while concentrated EOs are indiscriminately injurious to both economic (eg: normal human cells) and non-economic (eg: bacterial, or cancer cells) species, appropriately diluted EOs may have selective effects, and hence be therapeutic.

5.1.2 Selective use of EOs/ AACs as poisons, medicines, flavorings, and additive to cosmetics

Undiluted EOs are oily liquids that can be dangerous even in small quantities if taken internally or applied on the skin. Even a diluted EO, may contain enough AACs to cause harmful effects, such as:

- Abortion
- Cancer
- Gynecomastia
- Irritation, photo-toxicity
- Sensitization
- Liver damage
- Jaundice and other systemic derangements
- In extreme cases coma or death [129].

Despite the foregoing liabilities, EOs can be beneficial as medicines, flavorings, and as additive to cosmetics, if used in accordance with professional directions. The health benefits and liabilities of a selection of spices or EOs/ AACs are briefly presented below.

5.2 Specific Benefits and Liabilities of Some Spices or EOs/ AACs

5.2.1 Ginger (*Zingiber officinale*) oil

Ginger (family: Zingiberaceae) is used worldwide for preparing various foods and beverages for centuries because of the flavor of its oil, which is associated with many health benefits [130]. These benefit and occasional liabilities, in cases of misuse, are enumerated below:

5.2.1.1 Benefits of ginger oil

- Analgesic/ anti-pyretic/ rubefacient
- Anti-emetic/ carminative/ laxative
- Antispasmodic/ expectorant
- Bacteriostatic/ bactericidal
- Psychostimulant/ stomachic/ tonic
- Relief of colds and flu symptoms
- Sudorific/ diaphoretic)

5.2.1.2 Liabilities of ginger oil

- Mild irritation of sensitive skin and mucous membranes
- Mild photosensitivity, ie: a chemically induced change in the skin that makes people more sensitive to light.

5.2.2 Hops (*Humulus lupulus*) oil

5.2.2.1 Introduction

The common hops plant (family: Moraceae) produces small dioecious flowers, but only the female plant produces the flowers, or fruit, called "hops". Hops are used in malts and beers for their bitter flavor.

5.2.2.2 Components of hops oil

Hops oil contains humulene, humulone, and isohumulone that give beers their bitterness and aroma. The oil also contains: many common terpenes and terpenoids; xanthohumol-a prenylated chalconoid reputed to be anti-cancer and anti-oxidant [131]; isoxanthohumol-a prenylflavonoid with limited estrogenic activity [132]; and 8 prenylnaringenin–a prenylflavonoid with high estrogenic activity [133]. Parkes [134] ascribed the hoppy aroma and sedative effect of hops to humulene and amyl-alcohol respectively.

5.2.2.3 Benefits of hops oil

- Hops are used in brewing because their antibacterial properties favor the activity of yeast over less desirable microbes; and for flavor, especially balancing malt's sweetness with bitterness.
- In herbal medicine, hops are used similarly to valerian, as a remedy for anxiety, restlessness, and insomnia [135].
- Hops are also used in preparations for relief of menstruation-related problems, ie: in hormone replacement therapy [135,136].

5.2.2.4 Liabilities of hops oil

- Dermatitis often results from harvesting hops. Some 3% of the persons engaged in harvesting hops suffer from skin lesions in the face, hands, and legs [137].

5.2.3Black pepper oil

The oil black pepper - *Piper nigrum* (Piperaceae) contains well over 30 AACs including α-phellandrene, α-pinene, β-caryophyllene, β-bisabolene, β-farnesene, β-pinene, camphene, limonene, myrcene, sabinene, linalool, α-thujone, and terpinen-4-ol, among others, including capsaicinoids and phenylpropanoids Table 4. Some of its benefits and occasional liabilities are stated below.

5.2.3.1 Benefits of black pepper oil

- Analgesic-relieves sore muscles and joints; and useful as an anodyne/ antiseptic in dental care
- Anti-inflammatory
- Antiseptic/ antipyretic–indicated for enteric fever; and chills, flu, and colds
- Antispasmodic
- Anti-toxic/ laxative
- Aphrodisiac–boost serum levels of androgens [138,139].
- Diaphoretic–it also helps to disperse bruising by increasing circulation to the skin.
- Digestive-boosts the digestive system
- Diuretic-stimulates the kidneys
- Nerve tonic–increase warmth of the body and mind
- Rubefacient-useful in rheumatism; increases circulation
- Relieves exhaustion, muscular aches, physical and emotional coldness
- Stimulates saliva flow, appetite, peristalsis, and tones colon muscles
- Tonic - especially of the spleen, hence boosting the immune system

5.2.3.2 Liabilities black pepper oil

The only liability of therapeutic/ nutritional use of black pepper oil is:

- Mild irritation to skin and mucous membrane, which are rare.

5.2.4 Clove oil

Clove oil contains eugenol, eugenyl acetate, caryophyllene, isocaryophyllene [140]. Some of its benefits and occasional liabilities are stated below.

5.2.4.1 Benefits of clove oil

- Analgesic–especially for pain due to arthritis, rheumatism, sprains, strains, and toothache
- Asthma
- Bronchitis

5.2.4.2 Liabilities of clove oil

- Irritant to the skin and mucous membrane and dermal
- According to Tisserand [141], clove oil should be avoided, or used with extreme caution in:
    - Alcoholism
    - Anticoagulant medications
    - Disease of the kidney and liver
    - Hemophilia
    - Prostatic cancer

5.3 Specific Benefits and Liabilities of Capsaicin

5.3.1 Capsaicin

Capsaicin, an irritant to all mammals, is not an oil, but a crystalline substance. It is included here because it is the ingredient that gives chili peppers (*Capsicum*) much of their characteristics, including flavor.

5.3.1.1 Benefits of capsaicin

- Many worldwide "enjoy the heat" imparted by capsaicin [142], hence the age long demand for chili-spiced products.
- The claim that some experience euphoria from ingesting capsaicin, can be ascribed to pain-stimulated release of endorphins, evidenced by the blockade of that effect by naloxone or opiates which compete for sites on a common receptor [143].
- Capsaicin (0.025-0.25%w/w), with or without rubefacients, is used in topical ointments, or in dermal patches or plasters to relieve muscle or arthritic pain, or pain due to post-herpetic neuralgia [144,145].
- Capsaicin cream is used to reduce itching/ inflammation caused by psoriasis [142].
- Capsaicin selectively binds TRPV1-a heat-activated calcium channel that opens in the range: 37-45ºC. In pain and heat-sensing neurons, capsaicin bound TRPV1 causes the ion channel to open below 37ºC, which is why capsaicin is linked to the sensation of heat [146].
- Capsaicin induces apoptosis in prostate and lung cancer cells [147]. Capsaicin also directly inhibits the growth of leukemic cells [148].

5.3.1.2 Liabilities

Liabilities of capsaicin-based therapies may include:

- Burning sensation in the face, eyes, and finger; hence the need to wear face masks, goggles, and hand gloves when applying capsaicin-based therapies.
- The use capsaicin-based products (eg: pepper spray) in riot control owes to the burning effects of capsaicin on the face and mucous membranes.
- Even the minutest quantities of capsaicin inhaled, provoke sneezing and breathing difficulties.

6. CONCLUSION

Aromatic plants (APs), spices, and essential oils/ aroma-active compounds (EOs/ AACs) played and continue toplay a major role in human civilization by virtue of their uses in foods, medicines, and cosmetics. They are used by scientists, technologists and physicians for various purposes, because of their fragrances (smells only) or flavor (tastes and smells) or other biochemical attributes. They are generally used in very low concentrations (parts per billion, eg: µg/kg). In higher concentrations (parts per million, eg: mg/kg), they act as powerful drugs or poisons, yet their levels both in raw materials (RMs) and finished products (FPs) are often unknown becauseof the immense difficulties and costs of the methods used for their analyses. On the basis of the foregoing therefore, it is recommended that: i) industrial/ professional uses of EOs/ ACCs in foods, medicines, and aromatherapy should always be with standardized EOs/ AACs (as per ISO) and follow strict codes of practice (as in GMP); ii) the uses of APs and spices to flavor foods and medicines, or as nutritional supplements, should focus on the sources and wholesomeness of such RMs; iii) home uses of EOs/ AACs are not recommended unless guided by manufacturer's instructions; and iv) in order to enhance the regulation of EOs/ AACs in foods, medicines, and cosmetics, it is needful for chemists to devise more cost-effective analytical methods for EOs/ AACs.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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