Chapter

Terpenes in Essential Oils: Bioactivity and Applications

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Abstract

Secondary metabolites from plant organisms have always been excellent options for the pharmaceutical, cosmetic, and food industries. Essential oils are a type of metabolites found in vegetables, and their chemical composition is diverse; however, monoterpenes and sesquiterpenes are inside the most abundant molecules. These terpenes have a diverse chemical composition that range from a simple molecule with carbon and hydrogen to more complex molecules with oxygenated organic groups, such as alcohols, aldehydes, ketones, and ethers. Many of these molecules with 10 and 15 carbon atoms have an especially important biological activity, being important the antimicrobial, antifungal, antioxidant, anti-inflammatory, insecticide, analgesic, anticancer, cytotoxic, among others. Some of these substances are potentially toxic, and hence, they should be handled with caution, especially when they are pure. They are easily obtained by different methods, and their industrial value grows every year, with a market of several million dollars. This chapter seeks to provide a better understanding of this type of bioactive molecules, with an emphasis in those whose information is remarkable in the scientific literature and whose value for health and human well-being makes them extremely important.

Keywords: terpenes, essential oils, bioactivity, chemical analysis

1. Introduction

Terpenes are chemical molecules synthesized from isoprene, 2-methyl-1,3 butadiene which are polymerized, thus obtaining one of nature's most diversified families of secondary metabolites.

The chemical diversity of terpenes is determined by the polymerization capacity of isoprene; because of this their classification is linked to the addition of five carbons to the basic molecular unit. The biosynthesis of the chemical precursors of isoprene, dimethylallyl pyrophosphate (DMAPP) and isopentenyl pyrophosphate (IPP) is produced by two diversified metabolic routes, the mevalonate route (MEV) and the 2C-Methyl-D-erythirol-4-phosphate (MEP) route [1].

DMAPP and IPP are hemiterpenes and are responsible of forming the various subclasses of compounds that make up the terpenes. Additionally, these isoprene polymers can be linear or can form rings and adhere to their structure oxygen and nitrogen atoms. The approximate number of known terpenes is close to 55,000 compounds [2].

Traditionally they are classified as [3]:

Hemiterpenes. These are constituted by five carbon atoms and are the basic units of the terpenes, the best-known example is 2-methyl-1,3 butadiene or isoprene.

Monoterpenes. These are constituted by 10 carbon atoms, resulting from the union of two units of isoprene, which are abundant in essential oils. Some important substances are: pinene, myrcene, limonene, thujene, etc.

Sesquiterpenes. These are formed by 15 carbon atoms, which are the result of the junction of three units of isoprene, some examples are: bisabolene, zingiberene, germacrene, caryophyllene, etc.

Diterpenes. These are formed by 20 carbon atoms or four units of isoprene; some important compounds are retinol, taxol and phytol.

Triterpenes. Squalene and several phytosterols such as sitosterol stand out among the terpenes containing 30 carbon atoms or six units of isoprene.

Tetraterpenes. These are constituted by 40 carbon atoms and eight units of isoprene, many of them are dyes like carotenes, among these the most important are carotene, lycopene and bixin.

Polyterpenes. These are composed of more than 40 carbon atoms; they are often found in gums and latex of various plant species.

2. Essential oils

Essential oils are common secondary metabolites in vegetables. From 10 to 200 compounds can be found in an essential oil, and their main characteristic is their ability to evaporate at room temperature. The chemical variability in an oil is significant; however, its components can be classified into three large groups (**Figure 1**).

Terpenes are the majority group, being monoterpenes and sesquiterpenes the most abundant. These can be present as hydrocarbons, consisting of carbon and

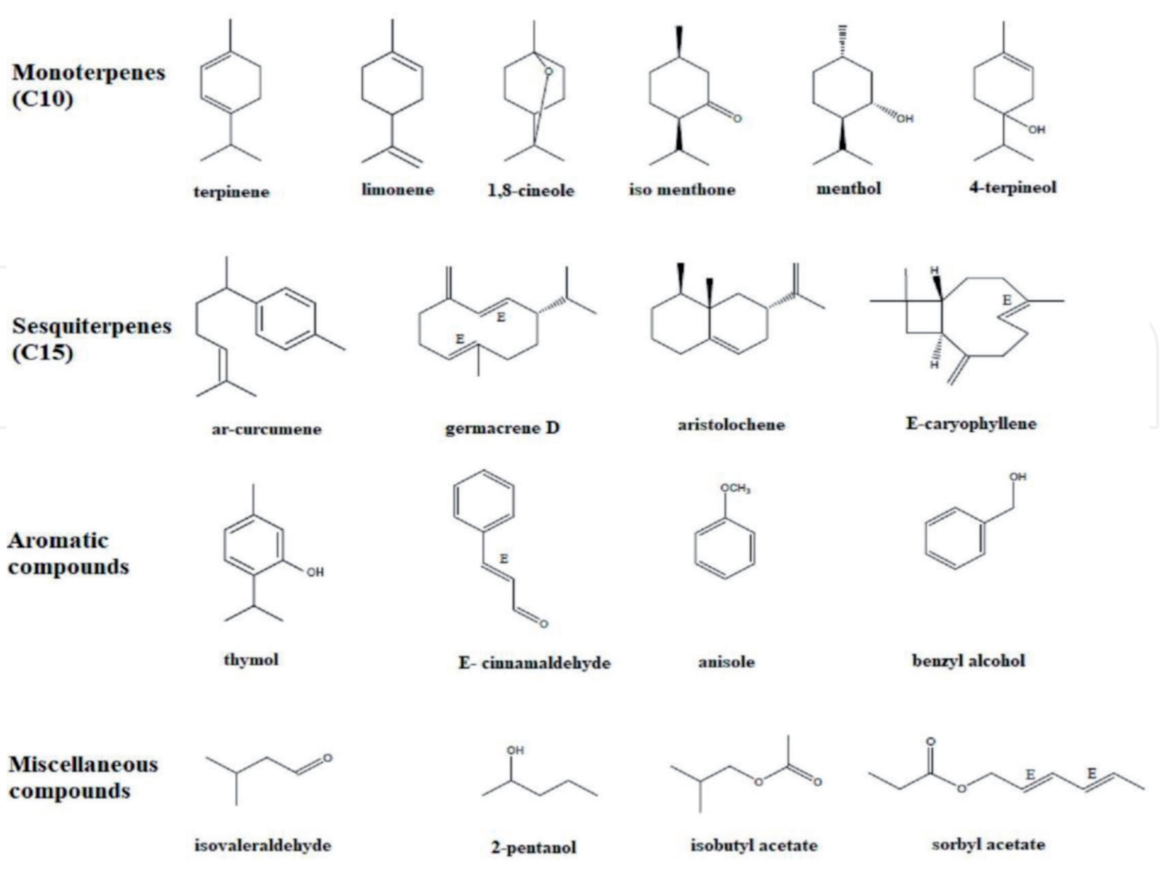

Figure 1.
Main molecules of essential oils.

hydrogen, or can have various functional groups such as alcohols, thiols, aldehydes, ketones, and ethers.

The second group of importance is aromatic compounds, many of them with an important biological activity such as derivatives of cinnamaldehyde, thymol, anethole or carvacrol.

There is a third miscellaneous group in a lower proportion that groups various molecules such as hydrocarbons, aldehydes, ketones, esters, etc. Examples of these substances are isovaleraldehyde or dodecanal.

Essential oils are usually found in low concentrations in plant organisms, ranging from 0.1 to 1%. They can exceed this value as is the case of clove oil with up to 10%, and are present in all plant organs and leaves: *Mentha piperita*, *Origanum majorana*, *Thymus vulgaris*; flowers: *Rosa damascena*, *Matricaria chamomilla*, *Lavandula officinale*; stems: *Cinnamomum verum*, *Ocotea quixos*, *Santalum álbum*; roots: *Valeriana officinale*; fruits: *Citrus bergamia*; rhizomes: *Zingiber officinale, Curcuma longa*; and seeds: *Pimpinella anisum*, *Syzygium aromaticum* and *Cuminum cyminum*.

The extraction processes are diverse, depending on the part of the plant used; the simplest and most widespread is the extraction by distillation with steam current, which does not require expensive equipment. Other methods are mechanical extraction used mainly to obtain oil from citrus pericarps, extraction using solvents which is useful when components can be affected by high temperatures and extraction using a supercritical CO_2 current, which does not need high temperatures while maintaining the chemistry of molecules, but it is very expensive to implement.

About 4000 species have been investigated by their ability to produce essential oils, but only about 30 are marketed massively globally; their main use is intended for the cosmetic industry and aromatherapy, although several of the compounds from essences could be valuable to the pharmaceutical industry. There are certainly still species whose essential oils have not been analyzed in their chemical composition or in their bioactivity, which could be interesting as a source of new secondary metabolites.

3. Chemical analysis

Since they are volatile metabolites, their low boiling points make it possible to have them as steam in a remarkably simple way; for this reason the ideal analysis is gas chromatography with GC/MS mass spectrometry.

The use of capillary columns has made it possible to have defined separations in essential oils that exceed 100 compounds, usually chromatographic separation is made in nonpolar columns with 95% dimethylpolysiloxane, due to the fact that several components of an essential oil contain polar groups such as hydroxyl (OH); the realization of these components using columns of intermediate polarity has been made. Both assays result in a complete chemical inquiry of molecules and are complementary. The correct structural elucidation is performed by combining several analyses such as comparison with spectrum databases and the theoretical and experimental determination of the retention rates of the compounds. For this purpose, there are databases, being the most used the "Identification of essential oil components by gas chomatography/mass spectrometry," with approximately 4000 compounds from essential oils [4].

The GC/MS technique is limited in the fact that it is ineffective in evaluating stereoisomers, in such cases it is necessary to use chiral columns or techniques such as nuclear magnetic resonance imaging.

A more thorough investigation of the chemical identity of the molecules of an essential oil can be done with an equipment that couples gas chromatography with spectrophotometric techniques, such as nuclear magnetic resonance imaging and infrared spectroscopy. It is also possible to analyze NMR or IR spectra in previously isolated molecules by column or thin layer chromatography [5].

4. Monoterpenes with therapeutic importance

Several monoterpenes have a diverse and useful biological activity for treating diseases and ailments; some have valuable aromatic characteristics in cosmetics and perfumery. Those molecules that have relevant information and studies are analyzed to verify their use as phytotherapeutic elements (**Figure 2**).

Pinenes. These have alpha and beta isomers; their formula is $C_{10}H_{10}$ and they are common in essential oils from conifers, although they can be found in many other species such as rosemary and lavender [6–8]; oils with high concentrations of pinenes generally have antimicrobial activity [8, 9]. Traditionally many plants containing pinene-rich essential oils are used in respiratory system disease [9].

1–8 cineol (Eucalyptol). Oxygenated monoterpene has a $C_{10}H_{18}O$ formula whose functional group is an ether that is present in many varieties of eucalyptus. Among its most noteworthy properties are analgesic, anti-inflammatory and antimicrobial [10]. Plants with eucalyptol-rich essential oils are used for expectorant and decongestant properties of the respiratory system [11].

Limonene. It is a monoterpene whose formula is $C_{10}H_{16}$; it has two optical isomers R-limonene or D- limonene and S-limonene or L-limonene, which stand out by the insecticide [12, 13] and antimicrobial properties [14].

Myrcene. It is a monoterpene whose formula is $C_{10}H_{16}$; it is the main component of *Cannabis sativa* essential oil [15]. Several studies highlight its analgesic-sedative [16, 17] and anti-inflammatory activity [18].

Linalool. It is a hydroxylated monoterpene with $C_{10}H_{18}O$ formula, its pleasant aroma makes it widely used in perfumery. Its action on the central nervous system is evidenced by its sedative, anxiolytic, analgesic and anti-inflammatory

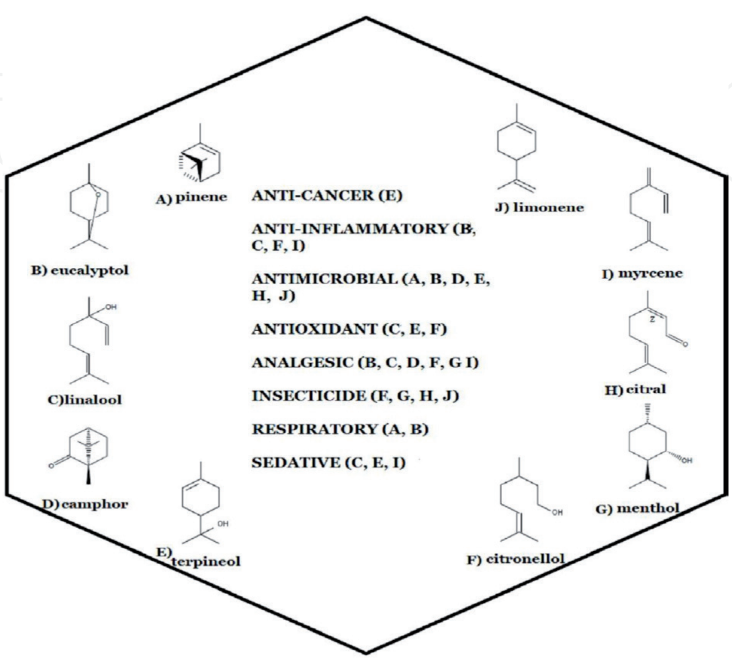

Figure 2.
Monoterpene molecules with therapeutic importance.

properties [19, 20]. Its antimicrobial and antioxidant properties have been evaluated with good results [21, 22].

Citral. It is an oxygenated monoterpene containing a group of aldehyde; its formula is $C_{10}H_{16}O$. There are two isomers known as neral (cis isomer) and geranial (trans isomer) [23], which are abundant in species such as *Backhousia citriodora* [24] and *Cymbopogon citratus* [25]. Its antimicrobial [25] and insect repellent action is noteworthy [26].

Camphor. It is an oxygenated monoterpene whose functional group is a ketone; its formula is $C_{10}H_{16}O$ and it is present in two optical isomers R and S, which are abundant in the species *Cinnamomum camphora* [27]. Traditionally camphor has been used in traditional Asian medicine, and it is known to have digestive effects, but its most important use is related to its analgesic and antiseptic effect, being very popular its inclusion in topical formulations such as liniments and creams [28, 29].

Menthol. It is a hydroxylated monoterpene, with a $C_{10}H_{20}O$ formula, which has seven isomers that are very common in mint varieties such as Peppermint. It is one of the most used compounds in the food, cosmetic, pharmaceutical industries, and pesticides, among others. Its aromatic properties are very well known [30]; however, its most noticeable and known effect is that of analgesia at the topical level [31, 32].

Terpineol. It is a hydroxylated monoterpene with a $C_{10}H_{18}O$ formula. It is known by having five isomers (α, β, γ, δ and 4-terpineol) [33], which are abundant in the essential oil of tea tree (*Malaleuca alternifolia*) [34]. The outstanding properties are antihypertensive, anticancer, antioxidant, antimicrobial, antifungal and sedative [33, 35].

Citronellol. It is a hydroxylated monoterpene with a $C_{10}H_{20}O$ formula. There are two enantiomers (+)-citronellol and (−)-citronellol [36]. The first is quite common in citronella oil, and the second is abundant in rose oil [37], which is used in perfumery. Its properties are insecticide [38], analgesic and anti-inflammatory [39], and antioxidant [40].

5. Sesquiterpenes with therapeutic importance

Several molecules with interesting properties can be found in C_{15} sesquiterpene (**Figure 3**). From a therapeutic view, there is evidence that validates its biological activity, highlighting anti-inflammatory, analgesic and anticancer trials.

Bisabolol. These are isomers, out of which stand (−)-α-Bisabolol, (−)-epi-α-Bisabolol, (+)-α-Bisabolol and (+)-epi-α-Bisabolol which are abundant in the species *Matricaria camomilla* [41], and in other species such as *Salvia runcinata* [42]. The most well-known effects in the molecule are analgesic and anti-inflammatory [43], antimicrobial and antioxidant properties; for this reason, the molecule is widely used in the cosmetic industry [44].

β-Caryophyllene. It has a $C_{15}H_{24}$ formula. It is one of the most abundant sesquiterpenes in essential oils. Various bioactivity studies have been carried out in this molecule with good results, such as analgesic [45, 46], anti-inflammatory [47] and anticancer [48].

Chamazulene. With a $C_{14}H_{16}$ formula, it is a molecule derived from the sesquiterpene matricina, which is one of the few aromatic molecules that have a blue coloration. It is found in *Matricaria camomilla*, being its most known property the anti-inflammatory [49, 50]. Several studies highlight its antioxidant effects [51, 52].

Caryophyllene oxide. It is an oxygenated sesquiterpene with a $C_{15}H_{24}O$ formula; it has properties similar to those of caryophyllene, such as analgesic and anti-inflammatory [53].

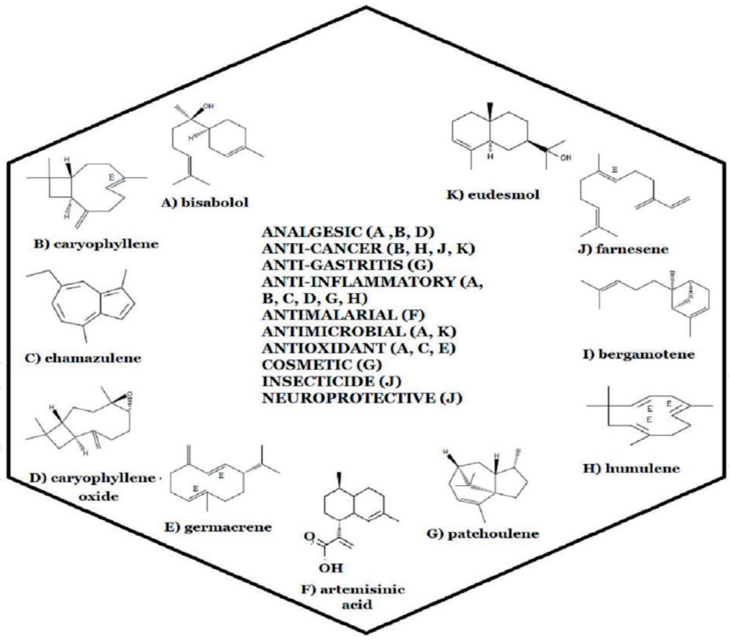

Figure 3.
Sesquiterpene molecules with therapeutic purposes.

Germacrene. It belongs to the sesquiterpenes family, and it has three double links in its structure. There are five types of germacrenes: A, B, C, D, E. Recent studies mention its antioxidant potential [5, 54].

Artemisinic acid. It has a $C_{15}H_{22}O_2$ formula, and it is one of the most interesting sesquiterpenes for health due to its antimalarial properties [55]. It is abundant in the species *Artemisia annua*, and it is generally found as a sesquiterpenic lactone [56].

Patchoulene. It is a sesquiterpene with a $C_{15}H_{24}$ formula. It is common to find its isomers α, β, α, and δ in essential oils. It is attributed to various types of bioactivity, the most relevant being those found in β-patchoulene as anti-inflammatory [57], antigastritis [58, 59], and cosmetic [60].

Humulene. Also known as α-caryophyllene, its formula is $C_{15}H_{24}$. It is named after the essential oil of the species *Humulus lupulus* [61]. It has anti-inflammatory [62, 63] and anticancer properties [64].

Bergamotene. It is a sesquiterpene with a $C_{15}H_{24}$ formula. It has four isomers α-cis, β-cis, α-trans and β-trans. It is found in several citric species such as *Citrus bergamia* [65]. One of the properties of this molecule is to act as a phero-mone [66, 67].

Farnesene. It has a $C_{15}H_{24}$ formula. It is a molecule found in several essential oils, and it is a precursor to many other sesquiterpenes since its open-chain structure and its 4-double bonds contribute to this action, as well as in the possibility of having a wide variety of isomers between geometrics and stereoisomers. Its cytotoxic and genotoxic [68], insecticide [69] and neuroprotective effects [70, 71] have been evaluated.

Eudesmol. Hydroxylated sesquiterpene with a $C_{15}H_{26}O$ formula is a very interesting molecule by the multiple positive bioactivity assays, highlighting antimicrobial and antifungal [72], anticancer [73, 74] and antiangiogenic [75].

6. Toxicity

Most of the terpenes present in essential oils have some degree of toxicity, which is not detected when consuming aromatic species directly because in most cases the oil yield is low. Many commonly used essential oil components are potentially dermal irritating with restrictions on application concentrations [76, 77]. There are also some terpenes whose toxicity is much more dangerous, such as pulegone which causes liver damage and seizures [78], and thujone that can cause dementia by being neurotoxic [79].

7. Conclusion

This brief review has shown the chemical and biological importance of low molecular weight and volatile terpenes. For this reason, components of secondary metabolites are known as essential oils. The abundance of these molecules is much higher than the one presented in this chapter, since the information presented covers those whose scientific evidence and industrial importance are references in this family of metabolites. There is still much research to be carried out on the hundreds of molecules from which there is still little or no information. There are still aromatic species whose essential oils have not yet been described and that could be a source of new monoterpenes and sesquiterpenes that are beneficial to humans.

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