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Review Article

Review on Therapeutic Activity of Pinene (C10H16): An Essential Oil

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A B S T R A C T

Pinenes are hydrocarbons, a bicyclic compound having double bond terpenoid. They are generally found in nature in different plant organs. They are the components of essential oil which are aromatic. They are found in 2 isomers i.e. alpha and beta-pinene which are extracted from plants by distillation. Pinenes are showing various therapeutics effects like anti-allergic, antioxidants, anti-schizophrenia, anti-inflammatory and hypoglycaemic etc. The common sources of pinenes are pine tree, ajwain plant (*Trachyspermum ammi*), and also in lime fruits peel. The obtained pinenes are further analyzed molecular formula and molecular weight also. IUPAC name of alpha-pinene is 2,6,6-Trimethylbicyclo [3.1.1.]hept-2-ene whereas molecular formula of alpha-pinene is $C_{10}H_{16}$ and its molecular weight is 136.23. Similarly the IUPAC name of beta-pinene is 6,6-Dimethyl-2-methylenebicyclo [3.1.1] heptane and its molecular weight and molecular formula are $C_{10}H_{16}$ and 136.23 respectively. The most common things between alpha as well as beta pinenes are that they both are bicyclic compounds, contains the same molecular formula and molecular mass. Only the positions are different from their arrangements. Thus from the given data, it can be concluded that they can be used against a wide variety of diseases.

Keywords: Pinenes, Anti- Oxidant, Terpenoids, Distillation, Essential Oils

Introduction

Essential oil is internationally defined as the product obtained by hydro-distillation, steam distillation, or dry distillation or by an appropriate mechanical process without heating (for Citrus fruit) of a plant or parts thereof.[1] These are thick gritty acidic liquids, distinguished by a strong scent, seldom coloured, and typically of reduced density than water.[2,3] Essential oils constitute just a tiny fraction of the plant composition, but they also provide the characteristics for which aromatic plants are used in the dairy, cosmetics and pharmaceutical industries.[4] The component proportions present in essential oils vary considerably.[5] The fragrance of the oil is the product of mixing the aromas of all components, and even small oil components may play a significant organoleptic function.[6] Other extraction techniques can be used to extract the volatile fraction in addition to the extraction techniques reported above, but in those cases, this cannot be called "essential oil." These techniques

include vacuum distillation, solvent extraction mixed off-line with distillation, Simultaneous Distillation-Extraction (SDE), Supercritical Fluid Extraction (SFE), and microwave-assisted extraction and hydro-distillation (MAE and MA-HD), static (S-HS), dynamic (D-HS), and high concentration headspace (HCC-HS) sampling.[1] These authors explain how all of these techniques operate synthetically.

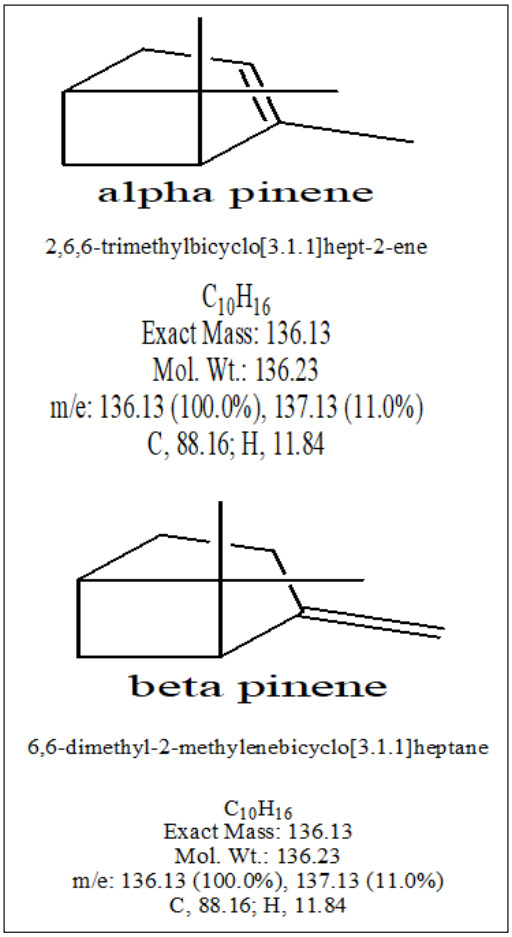

Figure 1.Chemical structures of α- and β-Pinene

Essential oils have a diverse structure, with elements from a handful to several hundred. The overwhelming majority of components found in essential oils include terpenes (oxygenated or not), with predominant monoterpenes and sesquiterpenes.[7] Pinene ($C_{10}H_{16}$) is a hydrocarbon, bicyclic, double bond, terpenoid.[8] α- and β-Pinene are two isomers (Figure 1) found in nature, for example, Essential Oils (EOs) in the pine (coniferous trees). They are among the best-known representatives of a wide monoterpene family.[9] Its boiling point is about 155°C.[9,10] β-Pinene is also a raw, colourless substance that is oil-soluble but ethanol-and water-insoluble.[10] It is also used as an important intermediate in the processing of chilled dairy goods, menthol, ionones, linalool, geraniol, citronella, lemon, citronella, and chocolate, but is primarily used in bakery items.[9] Biotransformation may create α-and β-Pinene; certain microorganisms, such as *Aspergillus spp*.[11] These two phytochemicals display different biological functions, contributing to numerous implementation and uses like fungicidal agents, colours, fragrances, and antiviral and antimicrobial agents.[12] α- as well as β-Pinene are elements of both kidney and liver drugs.[13] Despite its harmful impact on membranes, α- and β-Pinene are also used as antibacterials.[14] α- and β-Pinene has inhibitory effects on breast cancer and leukaemia.[15] The usage of pinenes goes beyond natural medicine; for example, they are extremely active in polymer synthesis.[16-19] Polymers polymerized with pine are of higher consistency over other polymers.[20] Pinenes' health risk assessment is deemed exceptional, enabling for their use in various products and is widely accepted as secure (GRAS).[21] It is thus difficult in the process of biotransformation, owing to its physicochemical features, but is often used in the processing of aroma compounds.[22]

Plants containing or producing α-Pinene, β-Pinene or both:[23–25]

Ocimum menthaefolium, *Pinus* spp.

Juniperus communis

Rosmarinus officinalis

Lavandula stoechas

Coriandrum sativum

Cuminum cyminum

Juniperus oxycedrus

Myristica fragrans

Cinnamomum verum

Melaleuca alternifolia

Achillea millefolium

Ligusticum levisticum

Pistacia lentiscus

Grindelia camporum

Piper nigrum

Pilocarpus microphyllus

Agastache rugosa

Artemisia capillaris

Eugenia aromatic

Piper guineense

Solanum erianthum

Citrus limon

Citrus bergamia

Ferula kuhistanica

Ferula clematidifolia

Extraction

A basic graphical approach was proposed for the layout of batch fractionation towers for the fractionation of multi-component formulations. With optimum reflux ratio, it can determine the volume of high purity cut one would have with the accuracy, with an optimum number of plates. This removes computer-based rigid determinations. The process is similarly successful when it comes to estimating the volume and structure of subsequent high purity breaks. The method's accuracy was developed with the realistic results from a batch fractionating column of a pilot-scale.[26]

Extraction is done by continuous fractional distillation to get pure and pinene concentration. The number of columns plays a crucial role in the purity of the extracted pinene.

Therapeutic activity of α-Pinene and β-Pinene

α-and β-Pinene are well-known members of the community of monoterpenes, which are contained in essential oils of several plants. A broad variety of biological effects have been documented involving regulation of antibiotics tolerance, anticoagulants, antitumors, antimicrobials, antimalarials, antioxidants, anti-inflammatory, anti-leishmania and analgesic impact.

Antibiotic Resistance Modulation

Bacterial pathogens have a great ability to acquire antibiotic resistance; a serious problem or threat to medical and scientific communities alike. A report revealed that in Europe about 25,000 patients die annually from multidrug-resistant infections of the bacteria.[27]

Gastroenteritis is a condition induced by a bacterium known as *Campylobacter jejuni* which is multidrug tolerant. A US study declared it a significant public health threat.[28] α-Pinene was used as a modulator for antibiotic tolerance in *C. jejuni,*[29] acting on the regulation of antibacterial tolerance and avoidance of antimicrobial efflux (detected by the mutagenesis system of insertion). This feature was tested using micro dilution of broth and aggregation of ethidium bromide assays. DNA microarrays were used to test *C. Jejuni* tolerance to α-Pinene, indicating that it may greatly alter resistance to antibiotics in *C. Jejuni* by 512 times reduction of the MIC content of ciprofloxacin, erythromycin and triclosan. In the wild-type strain, ethidium bromide was deposited at higher degrees than antimicrobial efflux mutant, suggesting that α-Pinene targets antimicrobial efflux systems. On the other hand, Griffiths et al. documented the impact of α-Pinene on the growth of some pathogens, that is to say, Nocardia sp. *Pseudomona sputida* PX1 (NCIB 10684), Sp. (P18.3) PIN18 (NCIB 10687) type, and NCIB 11671 *Pseudomonas fluorescens*. Strains were developed into α-Pinene- containing agar slants (3 g/l in media), and their development was evaluated. In (P18.3), there was no noticeable growth in the basal salt culture medium with α-Pinene, whereas fast linear growth was observed from vapour tubes in Erlenmeyer flask cultures.[30] Besides, Pseudomonas strains (NCIB 10684, 10687, and 11,671 and PL) increased rapidly with the addition of α-Pinene (0.3% v/v) to the growth medium.

Genomic Instability

Catanzaro *et al.* examined the role of α-Pinene in the Chinese hamster cell line (V79-Cl3) on genomic instability. Cells were cultivated with the fetal calf serum, penicillin, and streptomycin in Dulbecco's Modified Eagle Medium (DMEM). Different doses of α-Pinene (0, 25, 30, 35, 40, and 50 μM) were used for 1 h cell penetration (3,105 per dish). Cytotoxicity was determined by the traditional method. Morphological research shows significant development in frequencies of micro-and multi-nucleated cells. Apoptotic cells at 40 and 50 microns were seen. α-Pinene induced genetic variability, inhibiting mitotic processes, and inducing irregularity in 50% of cells. Flow cytometry has proven that the α-Pinene induced oxidative stress and the degradation of DNA.[31]

Cytogenetic and Oxidative Effects

The EO derived from coniferous plants is mainly composed of α-Pinene. Türkez and Aydin (2013) investigated α-Pinene cytogenetic and oxidative activity on human blood cells. The cultivated human blood cells were supplemented with varying doses of α-Pinene for 1–2 days (0, 10, 25, 50, 75, 100, 150 and 200 mg/l) Lactate Dehydrogenase (LDH) and MTT assays have shown a decrease in cell viability of α-Pinene at 200 mg/l. Furthermore, no significant changes were noted in the endpoints of genotoxicity rates. Total Antioxidant Capacity (TAC) and Total Oxidant Stress (TOS) levels, however, revealed changes in dose-dependence. TAC rates rose after injection by 25 and 50 mg/l of α-Pinene whereas TOS rates in human lymphocytes were decreased by 200 mg/l α-Pinene only.[32]

Anti-Leishmania Activity

The anti-Leishmania effects of Syzygium cumini leaves EO and its key components, α-Pinene, were observed in Swiss rats by Rodrigues *et al.* The anti- Leishmania results were tested using MTT techniques, and cytotoxicity of macrophages was assessed as well. Results showed that α-Pinene exerts cytotoxic effects at varying percentage levels of death (93.7%, 83.2%, and 58.4%), directly correlated with the different doses (100, 50, and 25 mg/ml, respectively) used against Leishmania *amazonensis* promastigotes. [33]

Allergic Rhinitis

α-Pinene results have been studied in BALB / c female rats with allergic rhinitis. Various doses (0.1, 1, and 10 mg/kg) of α-Pinene were administered daily to rats after the intranasal OVA challenge for 10 days, 1 h before or 1 hr. HMC-1 cells

have been cultivated into medium IMDM. HMC-1 cells with α-Pinene (0.1, 1 and 10 µg/ml) were administered for 1 h. Western blot was used to assess the distribution of the proteins. Histological analysis was carried out, too. A result showed that prior administration with α-Pinene reduces clinical symptoms, i.e. reduced number of nasal, eye and hearing fractures; spleen weight; and decreased levels of interleukin-4 and decreased levels of nasal immunoglobulin E in rats with OVA sensitivities.[34]

The Free Radical Scavenging Ability

The methods are divided into two classes for calculating free radical scavenging efficiency, according to the chemical reactions involved: reaction-based methods for the transition of hydrogen atoms and reaction-based methods for single electron transfer.[35]

Anti-inflammatory and Hypoglycemic

The goal of this research is to examine α-Pinene's anti-inflammatory and hypoglycemic behaviour and to find the amount of median lethal dose (LD50) in mice. A Probit review tool was used to examine the lethal dose levels of α-Pinene. For the calculation of anti-inflammatory behaviour seven separate classes were identified and α-Pinene was supplied at four specific doses: 0.05, 0.10, 0.25, and 0.50 ml/kg. Six separate groups composed of diabetic and safe mice were developed for the evaluation of a hypoglycemic activity. α-Pinene has been found with the highest anti-inflammatory effects with a dose of 0.50 ml/kg. α-Pinene's median effective dose (ED50) value was calculated to be 0.039 ml/kg. There were substantial rates of hypoglycemic development at the 2nd and 24th hours in diabetic mice α-Pinene. The amount of α-Pinene in LD50 was 2.076 ml/kg. We conclude, therefore, that α-Pinene is a molecule that exhibits hypoglycemic and anti-inflammatory activities.[36]

Anti- Schizophrenia

α-Pinene, a derivative of organic terpene present in coniferous plants, is used as a natural food additive and is contained in other essential oils. Several researches suggested that α-Pinene suppresses neuronal function. In this research, we investigated whether the inhalation of α-Pinene suppressing dizocilpine (MK-801-) caused schizophrenia-like behavioural disorders in mice. Mice inhaled α-Pinene 1 h before the application of the first MK-801. As behavioural trials, thirty minutes after the injection of MK-801, the open area, random locomotive operation, elevated plus labyrinth, Y-maze, tail suspension, hot plate, and grip power studies were performed. Inhalation of α-Pinene reduced mice's behaviour in the random locomotive behaviour study and while it did not inhibit the MK-801-induced enhanced locomotive activity in the open field test, the period the mice spent in the central region decreased considerably. Inhalation of α-Pinene reversed the MK-801-mediated decreased total distance traveled in the Y-maze study, while in the hot plate study it did not change the diminished antinociception threshold caused by the MK-801. The administration of MK-801 and α-Pinene inhalation throughout the tail suspension and grip power experiments did not have any impact on mouse actions. These results indicate that α-Pinene activities minimize MK-801-induced behavioural symptoms which mimic those seen in neuropsychiatric disorders. All medicinal plants and essential oils composed of α-Pinene also have the capacity for schizophrenia treatment.[37]

Conclusion

Essential oils are those which are extracted by various distillation processes and are aromatic. They are composed of various components one of them is Pinene ($C_{10}H_{16}$) which is a bicyclic, double bond, terpenoid hydrocarbon. α- and β-Pinene are two isomers found in nature. Since, both of them are isomers they both contains same molecular formula and molecular weight. Thus they can also be indicated as constitutional isomers which indicate that they hold same molecular formula but the positions or connectivity is different. Pinenes are found mostly in plant organs such as root, stem, flower, buds, etc. Pinenes are hydrocarbons which are volatile in nature so they are extracted and purified by using fractional distillation. Alpha-pinene is found in abundant amount and beta- pinene is found in fewer amounts when they are extracted. Since the beta pines are found in lesser amount pinene are distilled in fractions of batch towers in order to get the high purity. Both pinenes show essential medical benefits such as antibiotics resistance modulation, genomics instability, cytogenic and oxidative effects, anti-leishmania activity, allergic rhinitis, free radical scavenging ability, anti-inflammatory and hypoglycemic, anti-schizophrenia, etc. Along with medical uses pinenes are also used for some cleaning agents for household purposes like turpentine oils.

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Conflict of Interest: None

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