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Biomedical Significance of Terpenes: An Insight

Sabitha Kandi[1], Vikram Godishala[2], Pragna Rao[3], K.V. Ramana[4,*]

[1]Department of Biochemistry, Chalmeda AnandRao Institute of Medical Sciences, Karimnagar, Telangana, India
[2]Department of Biotechnology, Vaagdevi Degree and PG College, Warangal, Telangana, India
[3]Department of Biochemistry, Manipal University, Manipal, Karnataka, India
[4]Department of Microbiology, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India
*Corresponding author: ramana_20021@rediffmail.com

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Abstract Terpenes are polymers of isoprenoid units. These isoprenoid units are five carbon compounds and are favorite nature's building blocks. In terpenes these isoprenoids are arranged in a regular head to tail fashion. The side chains of Vitamin A, E, K, squalene (unsaturated hydrocarbon found in shark, humans) are all constituents of terpenes. Terpenes emit fragrances which allow them to be used as insect repellants, aids in pollination, perfume preparation, cosmetics and also has many medicinal values if used in required quantities. Adverse usage of terpenes has toxic effects like seizures, CNS depression, nausea vomiting etc.

Keywords: *terpenes, isoprenoid unit, squalene*

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1. Introduction and Historical Background

History of terpenes dates back to various civilizations. The essential oils were used in the ancient Egypt for various ceremonies. Camphor was introduced by Arabs around 11th century. The process of distillation of oils from rosemary and sage was described by Arnaud de Villanosa (1th century). Analyses of oils obtained from plants started by JJ Houston in 1818. Dumas proposed the name 'Terpene" derived from turpentine. In 1887, Wallah O proposed that isoprenoid unit (5C) is present always in terpenes. The structure of beta carotene from carrot was isolated by Wackenrodder and its correct molecular formula was determined by Will Statter [1,2,3,4].

2. Molecular Structure of Terpenes

Terpenes are polymers of five carbon hydrocarbon isoprene and are miscellaneous lipids found in all living organisms and natural products [5,6,7]. The isoprene (5C) unit is the nature's favorite building block. Terpenes have many isoprene units attached in a regular head to tail fashion [8]. The side chains in vitamin A, E, K, beta carotene, squalene are examples of terpenes (Figure 1).

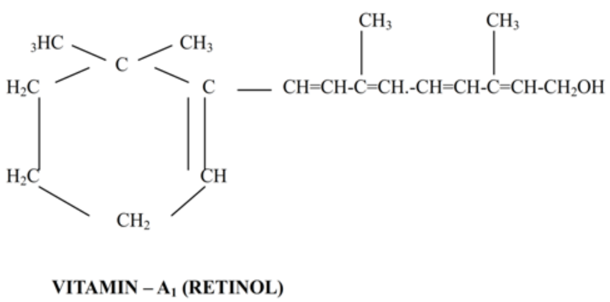

Figure 1. Molecular structure of terpenes as observed as a side chain in Vitamin A

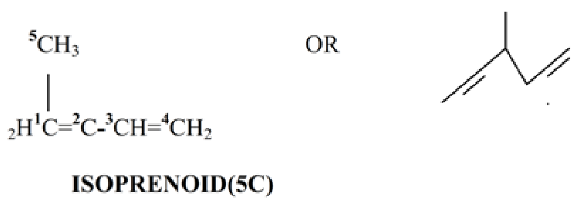

Figure 2. The molecular Structure of terpenes as observed in polymers of isoprenoid units (5C)

Natural rubber is polyterpene containing hundreds of isoprenes arranged in a regular linear order. The terpenes of natural product emits characteristic fragranance [9,10]. The products derived from terpenes in living organism makes it special as it leads to formation of squalene, cholesterol, sidechains of fat soluble vitamins like A,E,K and ubiquinone (a component of Electron Transport Chain). By definition terpenes are volatile, unsaturated aromatic hydrocarbons found in all living organisms and essential oils of plants [11]. Termites swallow tail butterflies, conifers, citrus plants, eucalyptus tree etc. The molecular Structure of terpenes includes polymers of isoprenoid units (5C) (Figure 2).

The number of carbons present in terpenes is multiples of 5. The isoprenoid units are arranged in head to tail fashion to form terpenes. Terpenoids are also terpenes but contain an oxygen atom [11]. Terpenes are released by trees more actively in warmer weather and acts as a natural form of cloud seeding. The clouds reflect sunlight, allowing the forest to regulate its temperature [12].

3. Classification of Terpenes

Terpenes are classified based on the attached isoprenoid unit as Monoterpens (2 isoprenoid units and 10 carbon atoms), Sesquiterpenes (3 isoprenoid units and 15 carbon atoms), Diterpenes (4 isoprenoid units and 20 carbon atoms), Sesterterpenes (5 isoprenoid units and 25 carbon atoms), Triterpenes (6 isoprenoid units and 30 carbon atoms), Tetraterpenes (8 isoprenoid units and 40 carbon atoms) and Polyterpenes (many isoprenoid units). There are two metabolic pathways for biosynthesis synthesis of terpenes [13], including the Mevalonic acid pathway and Methyl erythritol Phosphate / Deoxy Xylulose Phosphate pathway. The Mevalonic acid pathway is similar to cholesterol synthesis via the enzyme HMG-CoASH reductase. These reactions take place in the cytosol (Figure 3).

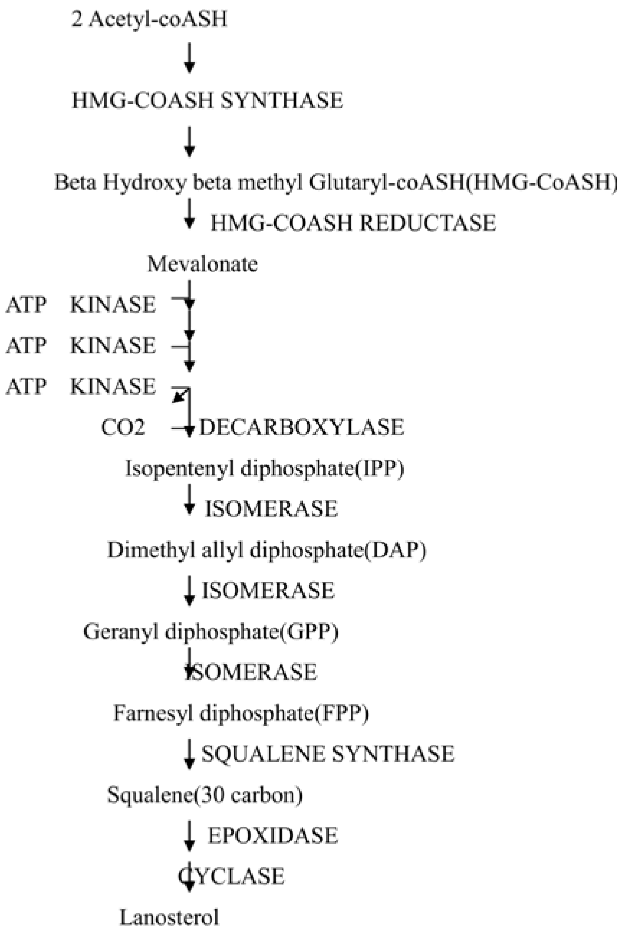

Figure 3. The Mevalonic acid pathway that occurs in cytosol of living cells

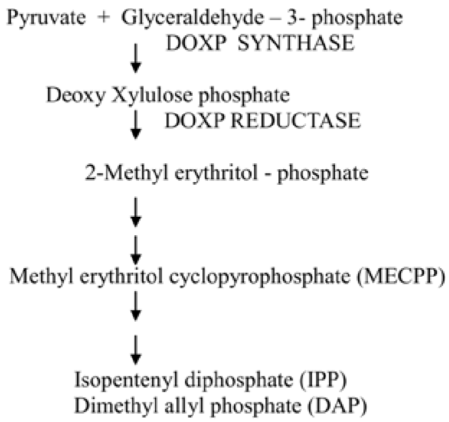

Figure 4. The Methyl erythritol phosphate or non-mevalonic acid pathway which occurs in plastids of plants, apicomplexa group of protozoa and many bacteria

In this pathway, the formation of isopentenyl didphosphate, a 5 carbon compound is the initial stage of terpene formation. The squalene that is formed in this pathway, a 30 carbon cyclic compound is an unsaturated hydrocarbon present in shark and mammalian liver and human sebum. The squalene leads to synthesis of cholesterol, carotenoids, ubiquinone. The Methyl erythritol phosphate or Deoxy xylulose phosphate pathway (DOXP) is also called non-mevalonic acid pathway which occurs in plastids of plants, apicomplexa group of protozoa and many bacteria (Figure 4).

After the formation of IPP and DAP the pathway is similar in both. Synthesis of all higher terpenes/terpenoids occurs via formation of GPP and FPP. Terpene synthesis pathways occurring in various living organisms include bacteria (MAP and MEP), Algae (MAP), Plants (MAP and MEP), Animals (MAP) and Fungi (MAP) [14,15].

4. Biomedical Importance of Terpenes

The biomedical importance of terpenes includes their use in the preparation of perfumes. The natural products such as menthol, citrus, spices are terpenes mostly used in the perfume preparation. Terpenes are also used as insect repellants. The main constituent of many insect repellants is citronella, Limonene from citrus plants, eucalyptus, lavender, mint. They appear in the leaves, bark, roots, and flowers of these plants. Terpenes present in these plants naturally wards off insects acting as insect repellant. Turpentine oil, Chamomile and Arnica, Shark derived oils are terpenes used in the preparation of cosmetics. The characteristic fragrances of terpenes make them to use in aromatherapy. Terpenes like Limonene, Pinene are used as air fresheners. They elevate the mood of an individual. Because of their pungent smell, terpenes naturally wards off insects and herbivores and aid in the pollination.

5. Madicinal Value of Terpenes

The medicinal uses of terpenes and their derivatives include the use of eucalyptus oil and clover leaf oils in dentistry. Eucalyptus oil helps in the stimulating the secretion of mucus hence acts as expectorant. Terpenes also act as diuretics and helps in relieving gastrointestinal spasms (Eucalyptus oil). Terpenes are added to creams and ointments to relieve pain and itching. Terpenes also possess antimicrobial properties thus, helps to fight microorganisms resistant to antibiotics such as yeast and other fungi [16,17]. Terpenes like menthol when consumed as a tea aids to reduce flatulence and indigestion. Other uses of terpenes include the preparations of rubber and resins, as natural agricultural pesticides. Terpenes are also used by termites (Nasutitermitinae family) to attack enemy insects by a mechanism called a fontanellar gun.

Adverse/ Toxic effects of terpenes and their derivatives include depressive effects on Central Nervous System (CNS) and respiratory disorders in case of aspiration of increased quantities. Clinical symptoms of terpene overdose/poisoning are nausea; vomiting and seizures. Children are the most common victims of terpene poisoning by accidental ingestion. Certain Terpenes present in plant oils have hallucinogenic effects and might lead to drug abuse.

6. Conclusion and Future Perspectives

Terpenes are naturally occurring chemical substances produced both from plants and animals. In the era of emerging multi-drug resistance, where microorganisms resistant to most of the antimicrobial agents available are fast spreading, research is on to find alternatives to antibiotics. Non-infectious conditions including cancers have been known to contribute to extensive morbidity and mortality in humans. Research must be encouraged in future to evaluate the anti-microbial (bactericidal, fungicidal, anti-parasitic and virucidal) and anti-cancer properties of terpenes and their derivatives. Medicinal properties of terpenes and terpenoids need to be extensively evaluated for their anti-tumor activity, anti-microbial properties, anti-inflammatory effects, anti-hyperglycemic properties, treatment for neuropsychological disorders and other potential uses that may include and not limited to treatment of autoimmune allergic skin disorders, cleansing environment of toxic chemicals, treatment of water and in preparation of plant pesticides

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