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SCHEMATIC LITERATURE REVIEW: CONTENT OF A-FARNESENE COMPOUNDS AS AN ANTI-VIRUS

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ABSTRACT

Indonesia is a country with a tropical climate, where the air temperature tends to be humid and causes various viruses and bacteria to multiply quickly and easily. Compound α-farnesene is one of the compounds that are often found in living things. This compound has many functions that are very useful in life. The last few months we have come out of the Coronavirus pandemic, but we must remain vigilant about the virus. The erratic weather in Indonesia also makes us maintain our health and anticipate viruses as well as the weather that can be anytime and the weather is pleasant. Therefore, the author is interested in making an article regarding the review of the content of the compound α-farnesene as an antiviral. The method used by the author in this study is a description using the literature review method. Beginning with various literatures discussing the structure, name, uses, properties, reactions, and activities of the compound α-farnesene, continued by reviewing the literature and ending with making conclusions about the function of the compound α-farnesene as an antiviral.

Review Paper

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Keywords: Antiviral, Compound α-Farnesene, Literature Review Method.

INTRODUCTION

Indonesia is one of the countries with a tropical climate, where the air temperature tends to be humid and causes various viruses and bacteria to multiply easily (Chen et al., 2021; Saputra, 2022). It is very important to maintain the body's immune resistance, and apart from that, it is always necessary to be aware of viruses or bacteria that might be able to attack the body. One way is to always consume foods that can be used as antibiotics, antibacterials, and antivirals (Kumar et al., 2022). These functions are not only found in supplements. Therefore, we must know what compounds are contained in supplements or food so that they can be used as antibiotics, antibacterials, or antivirals.

The α-farnesene compound is a compound that is often found in living things such as apples, pears, and several other fruits (Zhu et al., 2020). In addition, this compound is also found in several flowers, such as the fried plate flower and the frangipani flower. In several studies, this compound was also found in beetles and some marine animals (Wang et al., 2020). Although it is still rare to know about this compound, it turns out that it has many functions that are very useful in life. This α-farnesene compound is usually separated from plants by steam distillation or extraction, and the result is essential oil.

This essential oil, which contains α-farnesene compound with a pleasant smell, can be used as an antiviral, a fragrance, and so on (Lu & Qiao, 2020; Wang et al., 2020). So, it is very unfortunate if only a few people are familiar with this compound. Therefore, in this article, we will write a review of one of the functions of the α-farnesene compound as an antiviral. This antivirus is always needed in life to protect the body from various viruses that may approach our bodies anytime and anywhere. With this

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article, it is hoped that it can optimize understanding of the function of α-farnesene as an antivirus. So that we can find out about various foods that contain these compounds to fight viruses.

MATERIALS AND METHODS

The research method used in this study is a description using the literature review method with searches related to α-farnesene compounds, viruses, and antivirals. Journal reference searches were carried out through national and international journals obtained from Google Scholar, PubMed, NCBI, and others with the keywords "alpha farnesene", "virus", and "antivirus". The article used is official and conforms to keywords related to the title of the literature review. Several journals with certain criteria were obtained, including trusted national or international journals.

Based on the selection criteria in the literature review, this was carried out using inclusion criteria. These inclusion criteria include the contents of the article in accordance with what will be discussed with the research problem under study; The year of publication of the article discussed is at least the last 10 years; Literature search on predetermined sites providing international journals; Research articles that can be accessed in full (full text). After that, the contents of the various journals found were narrowed down according to the purpose for which this article was written. Using a careful study, where material has been pursed, discussed, and explained, conclusions can be drawn regarding the review of α-farnesene compounds as antivirals.

RESULT AND DISCUSSION

Compound Structure and Name

The common name α-farnesene, accompanied by the IUPAC name (3E.6E)-3.7.11-trimethyl-1.3.6.10-dodecatriene (**Figure 1**). Alpha forms in α-farnesene compounds as four stereoisomers that differ about the geometry of two of the three internal double bonds. α-farnesene compounds also belong to a class of organic compounds known as sesquiterpenoids, which are terpenes with three successive isoprene units.

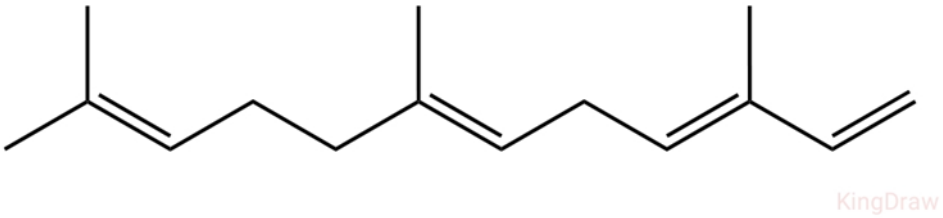

Figure 1 Structure of (3E.6E)-3.7.11-trimethyl-1.3.6.10-dodecatriene

Utility

1. Food additives (*flavoring*)

The compound α-farnesene is a constituent of the natural coating of apples, pears, and several other fruits. This makes α-farnesene a potential biomarker for consumption of these foods (Du et al., 2022; Ehlers et al., 2021). As we know, fruits that contain α-farnesene compounds have a good taste. So it can be concluded that besides being able to produce a fragrant smell, this compound can also be used as a food *flavoring* because it can create a delicious taste.

2. Fragrance

α-farnesene compound is a terpene compound that has 3 isoprene. Terpene is a hydrocarbon compound that is produced by plants. Isoprene is a compound consisting of 10 and 15 C atoms (Du et al., 2022). This isoprene compound has the characteristic of being able to give off a fragrant smell. For that reason, this α-farnesene compound is widely used as an ingredient in giving fragrance to fragrances, essential oils, and several other fragrance products, such as perfume. Farnesene compounds, which are long chain hydrocarbon compounds ($C_{15}H_{24}$) have many applications in lubricants, cosmetics, fragrances, and biogels (Schotte et al., 2021).

3. Biofuel

Farnesene compounds, which are long-chain hydrocarbon compounds ($C_{15}H_{24}$), have many applications in lubricants, cosmetics, fragrances, and biogels (Grenz et al., 2019). In optimizing its production, this farnesene compound will be chemically synthesized, then expressed in cyanobacteria so that farnesene is synthesized via the MEP pathway. Farnesene was excreted from the engineered cyanobacterium, evaporated into the flask head chamber, and recovered by adsorption in the resin column.

4. Pest Control

In several journals, it is explained that, based on the results of research, it was found that pesticides were derived from natural ingredients and were more environmentally friendly. The pesticides come from lime, kecombrang, noni, Pontianak oranges, kaffir limes, grapefruits, and several other fruits. As for its use, it utilizes the content of flavonoids, phenolic compounds, saponins, alkaloids, and terpenoids (Ningsih, et al. 2021). As already explained, the content of essential oils used as pesticides contains terpenoid compounds, one of which is an α-farnesene compound. The same thing is explained in the explanation of the functions of basil and lime as insecticides. In these plants, there are active compounds such as linalol, augenol, methyl cinnamate, α-farnesene, *β*-ocimene, and several other compounds (Islamy & Asngad. 2018).

5. Antimicrobial

In several recent reports, it was reported that α-farnesene which is an acyclic sesquiterpene compound, has an antimicrobial function. Antimicrobials have the function of killing bacteria that can harm the body. For example, in the explanation of the essential oil of a plate of fried flowers. The essential oil of sunflower oil has the highest constituent components, namely linalool and (E,E) α-farnesene. This essential oil has antimicrobial activity against several bacteria, such as *Escherichia coli*, *Candida albicans*, *Campylobacter jejuni*, *Listeria monocytogenes*, and *Staphylococcus aureus*, and can inhibit several other pathogens.

6. Antivirus

The use of ginger as a family medicinal plant shows that ginger has biological activities, one of which is antiviral. Where many chemical compounds were found in ginger, one of which is a terpene compound. Some of the terpene components in ginger that are considered the main constituents of essential oils are *β*-seskuipellandrene, α-farnesene, *β*-bisabolene, and α-curcumene compounds. This shows that the α-farnesene compound has antiviral activity.

7. Composition of essential oils (reducing symptoms of Covid-19)

In a research journal by Joyce Kelly R. da Silva, et al in 2020. Starting from the function of essential oils as antivirals, Kelly and several of her friends hypothesized that essential oils could be used to fight the Covid-19 virus. So, they conducted a study in which they explained that the main protease of SARS-CoV-2Mpro, is a cysteine protease, which is important for processing polyproteins translated from the Covid-19 virus RNA (Grenz et al., 2019). Examined in terms of essential oil content, the compound with the best docking normalization value was the farnesene hydrocarbon compound. Where in the first place is (E) *β*-farnesene, and followed by (E,E) α-farnesene.

Characteristic

The physical properties of alpha-farnesene compounds are as follows in **Table 1.**

Table 1 Physical Properties of Alpha-Farnesene

Physical Form/Smell	**Colorless to Pale Yellow-Green Liquid with a Fruity Odor**
Boiling point	260°C until 262°C
Solubility	0.01053 mg/L
Polarity	Non polar
Density	0.834-0.845
Molecular mass	204.35
Refractive index	1940-1500

α-farnesene belongs to a class of organic compounds commonly known as sesquiterpenoids. It is a terpene with three successive isoprene units. It has the physical properties of a colorless to pale green-yellow liquid with a fruity flavor because α-farnesene is a constituent of the natural coating of apples, pears, and other fruits, as well as ginger (Zhang & Tiefenbacher, 2019). The boiling point of α-farnesene is 260°C to 262°C, the molecular mass is 204.35, and it has a solubility of 0.01053 mg/L, so that α-farnesene is insoluble in water, slightly soluble in ethanol, and soluble in benzene (Chuang et al., 2021). The α-farnesene compound is a nonpolar compound because the structure of the α-farnesene compound consists of three bonds: carbon single bonds, carbon double bonds, and carbon bonds with hydrogen. The single bond between carbon and carbon is a nonpolar bond that cancels each other's dipole moments. The double bond between carbon and

carbon is also a nonpolar bond that cancels each other's dipole moment, the bond between carbon and hydrogen is a nonpolar covalent bond. Therefore, the polarity of the α-farnesene compound as a whole is a nonpolar compound because it consists of polar bonds that cancel each other's dipole moments.

Reaction

The reaction that occurs in this compound is a biochemical reaction. If the α-farnesene compound is reacted with diphosphate it will produce fernyl diphosphate. The reaction between (3E.6E)-α-farnesene and diphosphate can be seen in **Figure 2**.

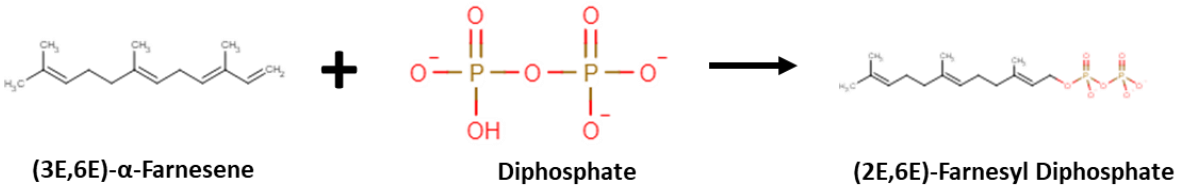

Figure 2 Reaction between (3E.6E)-α- Farnesene and Diphosphate

Fernesene is reacted with pyrophosphate to produce farnesyl pyrophosphate through a biosynthetic process. The reaction between (3E.6E)-α-farnesene and pyrophosphate can be seen in **Figure 3**.

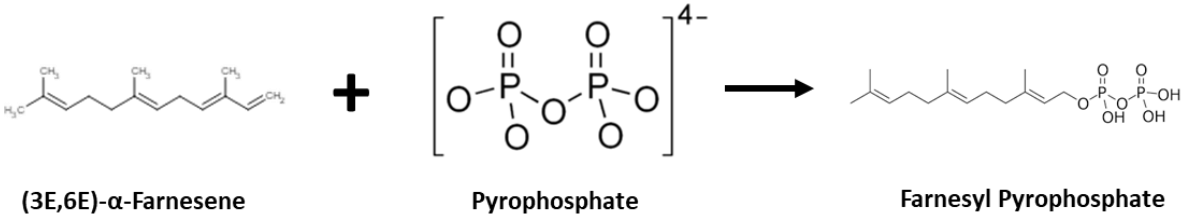

Figure 3 Reaction between (3E.6E)-α- Farnesene and Pyrophosphate

This sesquiterpene synthesis can catalyze the production of (E,E)-α-farnesene which can be used for the storage of fruits. The catalytic process produced four isomers: (E,E)-α-farnesene, (Z,E)-α-farnesene, (E,Z)-α-farnesene, and (Z,Z)-α-farnesene (Chuang et al., 2021). The mixture of isomeric forms of farnesyl diphosphate can convert geranyl diphosphate to monoterpenes (E)-β-ocimene, linalol, and β-miricen.

Activity of α-Farnesene as an Antiviral in Reducing the Symptoms of Covid-19

The compounds contained in essential oils have been screened for 171 components against the SARS-CoV-2 protein using a molecular docking technique. Among the 171 compounds that were filtered, one of them contained α-farnesene compounds. It is said that α-farnesene shows better binding with SARS-CoV-2 Mpro, which indicates that this essential oil component, when administered alone or in a mixture, can inhibit viral replication (Tan et al., 2020). Non-structural protein 15 (Nsp15), the endoribonuclease of SARS-CoV, is required for successful viral infection (Bhardwaj et al. 2006).

α-farnesene showed the best binding with Nsp15. RNA replication is catalyzed by RNA-dependent RNA polymerase (RdRp) in viral RNA and is an important step in viral replication. Thus, it becomes a viable target for antiviral chemotherapy. The SARS-CoV-2 Spike (S) protein helps viral cells attach to human cells by interacting with the angiotensin-converting enzyme 2 (ACE2) protein present on the host cell, making this interface a promising target for preventing the binding of SARS-CoV-2 to the host cell (Suenaga-Hiromori et al., 2022; Yu et al., 2023). The best binding to human angiotensin-converting enzyme 2 (ACE2) was observed with α-farnesene.

In the case of the SARS-CoV-2 spike protein, relatively better binding was observed with α-farnesene. Overall, Alpha-Farnesene exhibits better binding potential to target proteins. These phytochemicals are found in varying amounts in the essential oils of various plants that may be used to treat Covid-19, but better data from preclinical and clinical trials is needed.

CONCLUSION

The α-farnesene compound, which has the IUPAC name (3E.6E)-3.7.11-trimethyl-1.3.6.10-dodecatriene, is a terpene compound with 3 isoprene. This compound has uses as a food additive

(*flavoring*), fragrance, pest control, biofuel, antimicrobial, antiviral, and a constituent of essential oils that can reduce the symptoms of Covid-19. The α-farnesene compound is a non-polar compound, so it has very low solubility in water. However, this compound is soluble in organic solvents, such as benzene and diphosphate. One of the functions of α-farnesene as an antiviral can be seen from its activity, which can reduce the symptoms of Covid-19 through essential oils. In the case of the SARS-CoV-2 spike protein, relatively better binding was observed with α-farnesene. Overall, α-farnesene shows better binding potential to target proteins. These phytochemicals are found in varying amounts in the essential oils of various plants that can be used to treat Covid-19.

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