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Essential Oils Of Green Betel Leaf (*Piper Betle* L.) and Red Betel Leaf (*Piper Crocatum* Rulz And Pav): Comprehensive Overview of Components, Component Structure, Hybridization, Addition, Biological Activities and Their Benefits

Jacky Anggara Nenohai[a*], Ima Rosyida[a], Nur Indah Agustina[a], Isma Yanti Vitarisma[a], and Siti Marfuah[a]

[a] Department of Chemistry, Faculty of Mathematics and Natural Science, University of Malang, Malang, Indonesia.
* Corresponding Author: jackynenohai82@gmail.com

ABSTRACT

Essential oil is an aroma-giving liquid that comes from plant parts such as roots, stem bark, fruit, leaves, seeds, flowers, or other parts taken through distillation methods and extraction methods using organic solvents or pressed and enzymatically. Essential oils in each plant have different components and characteristics. One of the plants that can be utilized and has essential oil content is green betel leaves (*Piper betle* L.) and red betel leaves (*Piper crocatum* Ruiz and Pav). Several studies have been conducted to identify the content of betel leaves. The largest content present in green betel leaves is limonene, while the largest content of red betel leaves is sabinena which has a special structure. These red and green betel leaves have many characteristics, and benefits. The method used in this writing uses a descriptive literature review, with this study aiming to compile a comprehensive literature analysis of the components, structure, hybridization, isomerization, addition reactions, and biological activity of betel leaves covering some information based on the results of literature studies.

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1. Introduction

Essential oils are often known as essential oils and aromatic oils. Essential oils are aroma-giving liquids derived from plant parts such as roots, bark, fruits, leaves, seeds, flowers or other parts taken through distillation methods and extraction methods using organic solvents or pressed and enzymatically [1]. Extraction is a technique for separating compounds based on the difference in solute distribution between two solvents [2].

The source of essential oils is obtained from the results of plant metabolic processes formed due to reactions between chemical compounds and water. Essential oils in each plant have different components and characteristics. Most essential oils are used in the manufacture of perfumes, cosmetics, medicinal herbs, and food additives i.e. spice plants are believed to have fewer side effects than chemicals.

One plant that can be used and contains essential oils is green betel leaf (*Piper betle* L.) and red betel leaf (*Piper crocatum* Ruiz and Pav). Betel leaf is one of the plants of the family *Piperaceae* [1]. Betel leaf is usually used as an herbal medicine to cure canker sores, and vaginal discharge, as mouthwash for oral hygiene, and burn healers, and is used to inhibit bacterial growth in the media [2]. According to Gunawan & Kurniaty [3], Betel leaf (*Piper betle* L) can be used to overcome body odor, bad breath, canker sores, nosebleeds, and itching, treat vaginal

discharge, natural insecticides and become one of the active substances that can be used as mosquito repellent.

Plants that can be utilized that contain essential oils are green betel leaves (*Piper betle* L.) and red betel leaves (*Piper crocatum* Ruiz and Pav). Betel leaf belongs to the family Piperaceae [1]. Betel leaf is commonly used as an herbal medicine for stomatitis, vaginal discharge, mouthwash for oral hygiene, burn healing, and bacterial growth inhibitors in culture media [2]. According to Gunawan & Kurniaty [3], betel leaf is used to treat body odor, bad breath, stomatitis, nosebleeds, itching, and vaginal discharge, natural pesticides and one of the active ingredients that can be used as an anti-inflammatory agent.

Several studies have been conducted to identify the content of betel leaves. Green betel leaf contains 1 to 4.2% essential oil, hydroxycavikol, 7.2 to 16.7% cavikol, 2.7 to 6.2% cavibetol, 0 to 9.6% allylpyrokatekol; 2.2 to 5.6% carvakol; 26.8 to 42.5% eugenol; 4.2 to 15.8% eugenol methyl ether; 1.2 to 2.5% p-cymene; 2.4 to 4.8% cyneole; 3 to 9.8% caryophyllene; and 2.4 to 15.8% cadinene [3], while red betel leaves based on Widayani's research (2018) contain sabinena (33.35%), β-mirsena (20.18%), β-caryophyllene (7.07%), linalol (5.41%) and germacrene (4.96%) in its essential oil. GC-MS analysis of red betel leaf essential oil revealed that the main components of essential oil are monoterpenes and sesquiterpenes. The chemical composition of essential oils varies according to the geographical region of the betel leaf plant, the age of the plant, the local climate, the season, experimental conditions, and the genetic differences responsible for the variation in chemical composition. Harvesting and post-harvest treatment also affect the composition of essential oils.

Determination of compounds contained in green and red betel oil is by injecting samples into GC-MS. The spectrum obtained provides an abundance of information, retention time, and then compared to the Wiley Library data already available on the tool. Antibacterial activity tests were conducted to prove whether betel oil was able to inhibit bacteria [4].

Judging from the description of the components, structure, hybridization, isomerization, and biological activity of betel leaf above, many organic reactions occur naturally not only in laboratories or industries, but also in nature to produce new organic compounds. It is used in a variety of ways. Therefore, many types of organic reactions are grouped based on the structural changes that occur, one of which is the addition reaction. Addition reactions combine two or more molecules in the formation of a new molecule. This reaction occurs only in unsaturated compounds or compounds with double bonds (alkenes) and triple bonds (alkynes). Electrons in a bond that react with electrophiles are called electrophilic additions. Double bonds on carbon heteroatoms such as carbonyl (C=O) and imine (C=N) make carbon atoms partially positively charged, facilitating nucleophile attack. Therefore, the addition of a double bond to the heteroatomic carbon is nucleophilic [5].

Considering the potential benefits and content of betel leaf that have been described above, the purpose of the review in this article is to focus on the components and structure of essential oil components in betel leaf to determine hybridization, biological activity, and addition reactions of the main compounds of betel leaf then analyzed and associated with some information based on the findings of literature studies. Seeing the many compounds contained in green betel leaf essential oil and red betel leaf, researchers need to analyze the limitations of further research on the main components and structures of green and red betel leaf essential oil. Some of the problem formulations in this study are as follows: What are the components of the compound and what is the main chemical structure contained in the essential oils of green betel leaves (*Piper betle* L) and red betel leaves (*Piper crocatum* Rulz and Pav)? How is the hybridization, isomerization, addition reactions, and biological activity of the main compounds contained in essential oils in green betel leaves (*Piper betle* L) and red betel leaves (*Piper crocatum* rulz and pav)?

2. Research Methodology

This research method uses the literature review method. This method is a method used to analyze, describe and reduce certain information to all research results that are certain characteristics [6]. Inclusion criteria for article searches carried out include: (1) Publication is

limited to the last 5 years (2014 until 2023); (2) articles from reputable journals indexed by Eric and Google Scholar, and (3) full text and open access to articles conference papers and the result of research. In principle, data collection in this study uses research results in the form of essential oil research findings on green betel leaves (*Piper betle* L) and red betel leaves (*Piper crocatum* rulz and pav) which discuss the components, structure, and hybridization, isomerization, biological activity, and addition reactions of the main compounds of betel leaves.

3. Result and Discussion

3.1. Components of Green Betel Leaf (*Piper Betle* L) and Red Betel Leaf (*Piper Crocatum* Rulz and Pav)

Green betel leaves are traditional medicinal plants that are known to be effective in the treatment of various types of diseases. Green betel leaf (*Piper betle L.*) contains compounds such as phenolic essential oil and derivatives such as betel (*Kavibetol*) and Kavikol. About 0.8% to 1.8% of essential oils consist of *cavicol, beterphenol, eugenol, allylpyrocatechin, terpenes, cineol, caryophyllene, cadinene and manthone*. We can get this essential oil content from younger betel leaves [7]. The essential oil components of green betel leaf are described in Table 1

Table 1. Components of green betel leaf essential oil [7]

Chemical Profile of Oil Atsiri betel leaves	
Chemical Groups	**Component**
Monoterphene	*trans-sabinene hydrate* (tr)
Sesquiterpen	(E)-*caryophyllene* (0,4%), δ-*cadinene* (tr), *α-humulene* (tr), *γ-muurolene* (tr)
Alcohol	*α-cadinol* (tr), τ-*muurolol* (tr)
Ester	*Chavibetol acetate* (11,7%), *methyl salicylate* (tr), *allylpyrocatechol diacetate* (6,2%)
Aldehyde	n-*dekanal* (tr)
Phenol	*Chavicol* (0,4%), *eugenol* (0,4%), *chavibetol* (80,5%), *methyl eugenol* (0,4%)

In a study conducted by Cahyo [8], the findings of different main ingredients, namely the main component in green betel leaf essential oil, obtained the highest level, namely *limonene* (34.75%) at a retention time of 5.642. Other compounds such as trans-caryophylene (7.79%) at a retention time of 18,429, and naphthalene (5.77%) at a retention time of 21,330. Ali, Chong, Mah, et al. [9] reported several phenolic compounds such as eugenol, hydroxychavicol, isoeugenol, and allylpyrocatechol 3,4-diacetate from dried betel leaf extract stored under different storage temperature conditions for 6 months. The best stability with 100% retention was found in hydroxycavikol, while moderate stability was found in eugenol and isoeugenol during the entire storage period. Ali, Lim, and Wahida [10] also studied ultrasound-assisted extraction and maceration extraction from Piper beetle leaf powder using ethanol and water as solvents. Results revealed the highest and lowest phenolic content found to be 840 mg GAE/g (95% ethanol) and 460 mg GAE/g (50% ethanol) along with 200 mg GAE/g (water), respectively. Piper betle leaf extract using chloroform contains 1-ndodecanyloxy resorcinol and desmethylenesqualenyl deoxycepharadione-A [11]. Sarma et al. [12] focused on evaluating the antioxidant activity of two choices of betel leaf varieties (Meetha and Banarasi paan) extracts using aquades, hexane, acetone, and ethanol as solvents. The results revealed that among the extracts, ethanolic extract had the highest antioxidant (89.46%).

Red betel leaf is one type of *piper* spread in several parts of the world including Indonesia. The plant contains essential oils (monoterpenes, sesquiterpenes), alkaloids, flavonoids (auron groups), tannins-polyphenols, steroids and neolignan compounds, in addition pharmacological studies have shown that this plant has anti-inflammatory, antibacterial, antifungal, antihyperglycemic, antiproliferative and antioxidant properties. The terpenoid compounds detected on phytochemical screening most likely come from essential oils commonly found in the Piper genus. Research from Coal in Parfati [13], obtained results that red betel leaf essential oil can be isolated by steam distillation with a yield of 0.21% w/w. The results of Gas Chromatography-Mass Spectrometry analysis using the DB-5 MS column showed that Helium carrier gas detected monoterpene compounds, namely *α-thujene, α-pinene, sabinene, β-myrcene,*

α-terpinene, β-phellandrene, γ-terpinene, β-terpineol, terpinolene, α-terpineol, copaene; while sesquiterpene compounds are caryophyllene, *α-caryophyllene* and *germacrene D* [14].

The chemical components composed of essential oils in red betel leaves which have the largest percentage based on research conducted by Widayani, et al [15] are sabinena (33.35%), β-mirsena (20.18%), β-caryophyllene (7.07%), linalol (5.41%) and germakren (4.96%) [16]. GC-MS analysis of essential oil from red betel leaf revealed that the main components of essential oil are monoterpenes and sesquiterpenes. The chemical composition of essential oils varies according to geographic region, plant age, local climate, season, experimental conditions, and genetic variation that explains the variation in chemical composition. According to Batubara in Parfati [13], the essential oil component in red betel leaves is almost the same as in green betel leaves (*Piper betle L.),* the difference in green betel leaves is that there are camphene compounds classified in monoterpenes and chavicol and eugenol compounds included in phenylpropanoids, where these compounds are not found in red betel leaves.

3.2. Structure of Green Betel Leaf (*Piper Betle* L) and Red Betel Leaf (*Piper crocatum* Rulz and Pav)

The structure of green betel leaf (*Piper betle* L) identified by Cahyo [8] informed that the components contained in green betel leaf essential oil with the MAHD method carried out by GC-MS analysis are as follows:

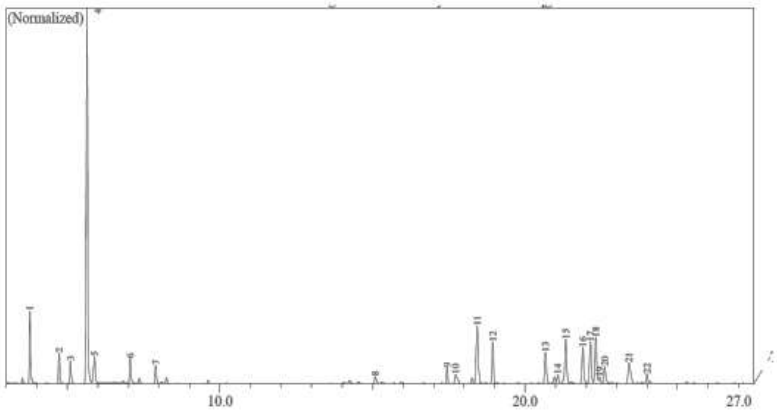

Fig 1. GC-MS Analysis of Green Betel Leaf Essential Oil Using MAHD Method [8].

Based on the results of the chromatogram, it can be seen that there are 22 types of compounds contained in green betel leaf essential oil. The most dominant compound is limonene with a percentage of 34.75%. The structure of the compound Limonene is as follows:

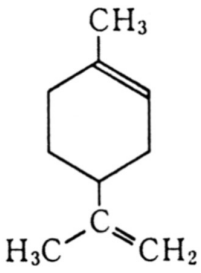

Fig 2. Relationship between temperatures and bandgap

In red betel leaves (*Piper Crocatum Rulz and Pav*), based on the results of GC-MS analysis from Setyowati [17] shows that the main components in essential oil are monoterpenes and sesquiterpenes. One example of the dominant monoterpene compound is sabinene. The results of GC-Ms can be seen in the following figure:

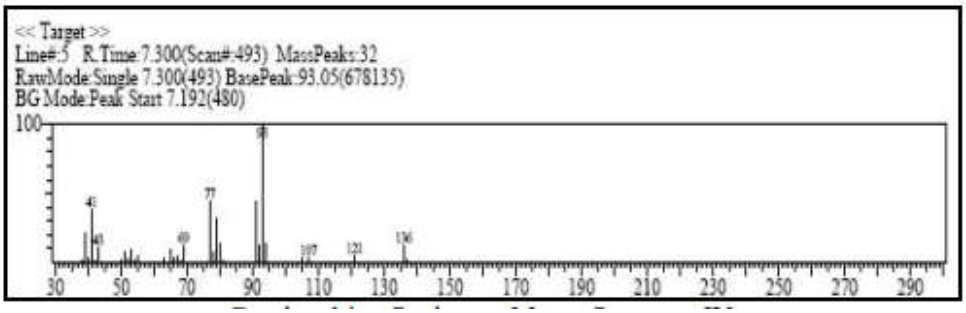

Fig 3. Mass Spectrum of Compound IV [17]

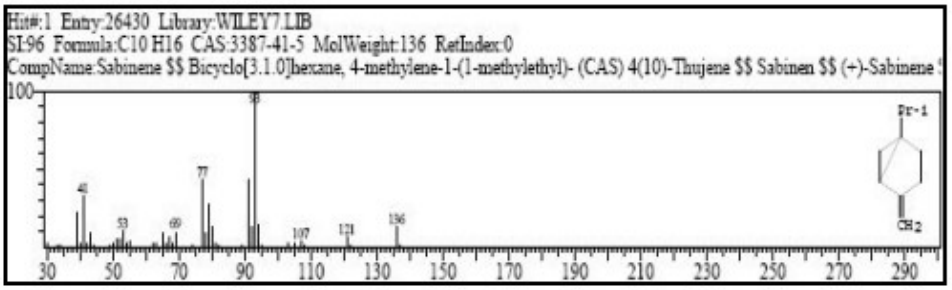

Fig 4. Mass Spectrum of Sabinene Compounds [17]

The GC-MS results in Figure 3 show that peak no. 4 has a retention time of 7,300 minutes with SI = 96 which has fragments similar to monoterpene compounds, namely sabinene in Figure 4 with molecular formulas namely $C_{10}H_{16}$ and m/e 136 [17]. The picture of the fragmentation pattern of Sabinene compounds is as follows:

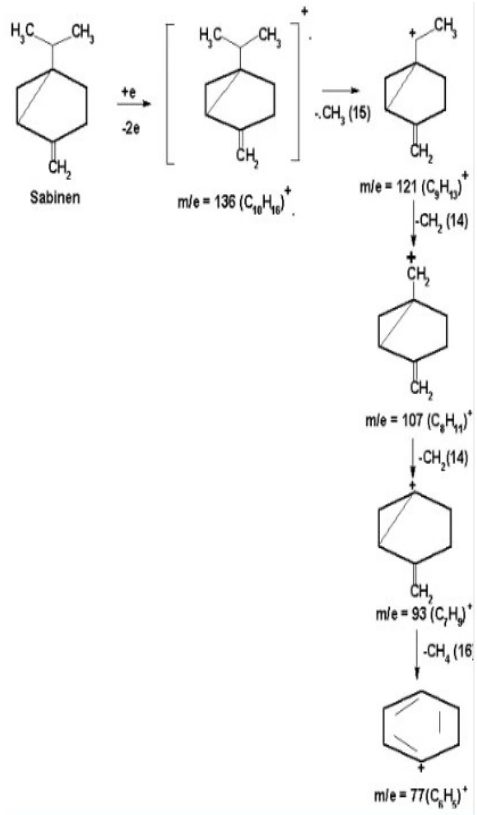

Fig 5. Sabinene Compound Fragmentation Pattern [18]

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3.3. Hybridization, Structure and Isomerization of the Largest Compound Components of Green Betel Leaf (Piper Betle L) and Red Betel Leaf (Piper Crocatum Rulz and Pav)

The dominant compound structure in green betel leaves (*Piper betle L)* is limonene and red betel leaves *(Piper crocatum* Rulz and Pav*) is* Sabinena. Both of these structures have sp^2 and sp^3 hybrid orbitals, because the C atom in both structures is bonded to 3 other atoms (sp^2) and the other C atom is bonded to 4 other atoms (sp^3). The placement of hybridization types on the structure of limonene and sabinene can be seen in the following figure:

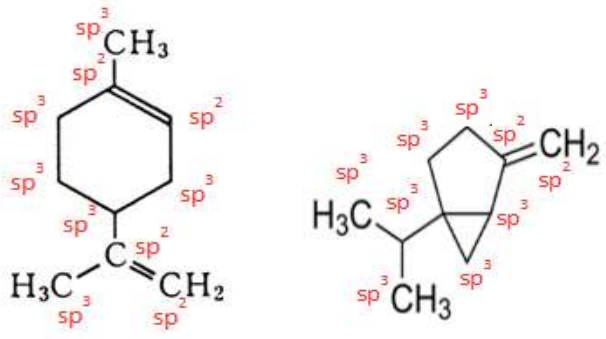

Fig 6. (a) Hybrid Orbitals on limonene compounds, (b) hybrid orbitals in sabinene compounds

In addition to hybridization, these two structures also have isomers, for example, geometric isomers with systems (R) and (S) and optical isomers. Geometric isomers with systems (R) and (S) i.e. Compounds with chiral C atoms are named according to the system convention R *(rectus*) = right and S (*sinister) =* left, or Chan-Inglod-Prelog convention, while optical isomers are configuration isomers in which the difference between enantiomer compounds lies in their interaction with other chiral compounds and their interaction with polarized light fields [5].

The geometric isomers with systems (R) and (S) in limonene compounds and sabinene compounds are as follows:

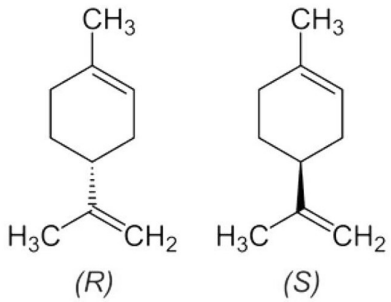

Fig 7. Geometric isomers with systems (R) and (S) in limonene compounds

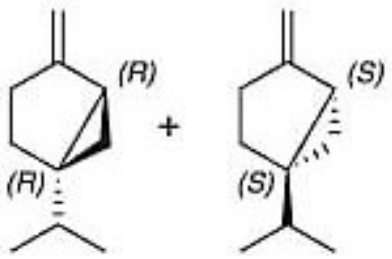

Fig 8. Geometric isomers with systems (R) and (S) in sabinene compounds

The optical isomers of limonene compounds and sabinene compounds are as follows:

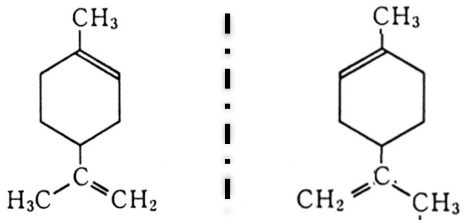

Fig 9. Optical isomers (enantiomers) of limonene compounds

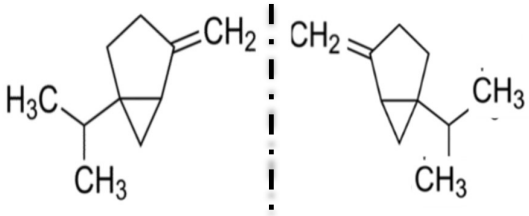

Fig 10. Optical isomers (enantiomers) of sabinene compounds

3.4. Addition Reactions of Green Betel Leaf (Piper betle L) and Red Betel Leaf (Piper crocatum Rulz and Pav) Components

The addition reaction to the components owned in green and red betel leaves wants to prove the reaction of carbon compounds that involve combining molecules so that the double bond is broken into a single bond to produce a larger molecule. This additional reaction will make the carbonyl carbon hybridize from sp2 to sp3 during the process and produce tetrahedral geometry intermediates that can undergo various types of reactions.

One example of an addition reaction that occurs in the green betel leaf component (Piper Betle L.) is the Halogen addition reaction (Br2)

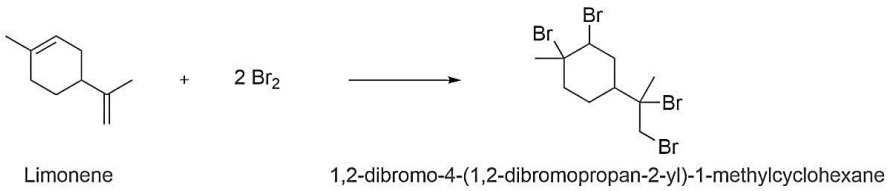

Fig 11. Limonene compound addition reaction

This reaction is also called the addition reaction of bromination, where 2 molecules of Br_2 will react with a double bond 2 in limonene compounds so that an electrophilic reaction occurs and produces compounds 1,2-dibromo-4-(1,2-dibromopropane-2-yl)-1-methylcyclohexane. The mechanism is as follows:

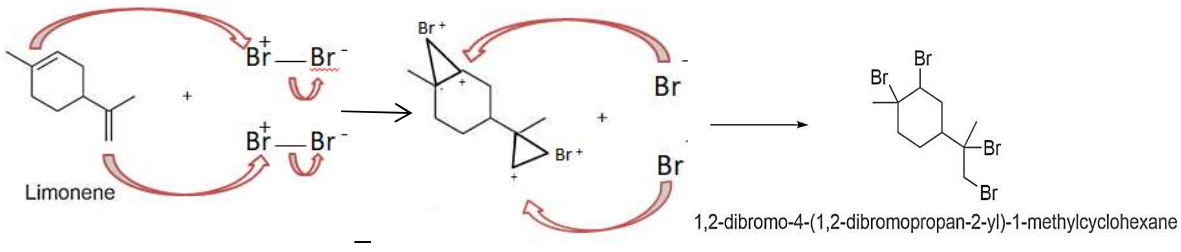

Fig 12. Limonene compound addition reaction mechanism

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An example of an addition reaction that can occur in the Red Betel Leaf component (*Piper Crocatum Rulz and Pav*) is the $KMnO_4$ addition reaction

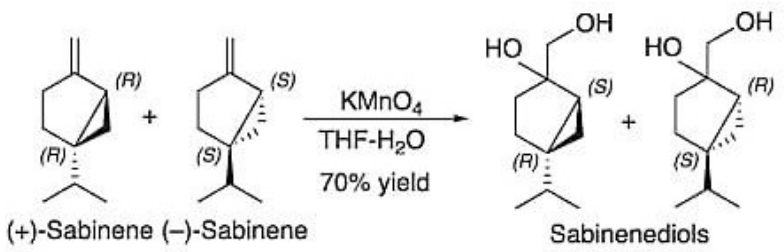

Fig 13. Addition Reaction of Sabinene compound

This $KMnO_4$ addition reaction will produce 2 OH^- groups, also called alkene dihydroxylation. The general mechanism for KMnO4 addition reaction is as follows:

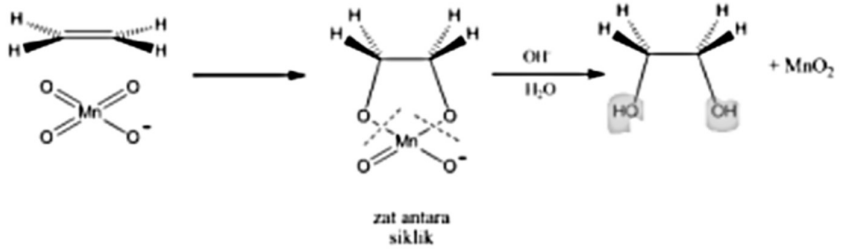

Fig 14. $KMnO_4$ addition reaction in general occurs in Sabinene compounds

3.5. Benefits and Biological Activity of Green Betel Leaf (*Piper betle* L) and Red Betel Leaf (*Piper crocatum* Rulz and Pav)

Betel leaf has a strong spicy aromatic aroma traditionally used by the people for mastication in natural raw conditions, along with other ingredients such as areca nut slices, lime, coriander, anise, cloves, cardamom, sweetener, grated coconut, diamond ash, pearls, jelly, peppermint, flavoring agent, fruit pulp, gold and silver [19]. Betel leaf is commonly used in conventional medicine as a carminative, aphrodisiac, stimulant, analgesic and cooling, antiseptic, wound healing, antiparasitic, antifungal, and antibacterial. In addition, it is also useful in the field of coronation in overcoming several diseases such as bad breath, conjunctivitis, ulcers and abscesses, headaches, hysteria, constipation, hives, mastoiditis, vaginal discharge, mastitis, inflammation of the mucous membranes of the nose and diphtheria. The sharp taste and pleasant aroma of the leaves help increase appetite, it can also act as a tonic for the brain, heart, and liver [20]. Betel leaf helps improve the health of teeth and skin. The leaves are chewed to relieve constipation in children, used as a poultice for wounds and canker sores on the nose, heated and applied to the chest to reduce cough and asthma by removing the lender. The leaves are rolled and covered with oil as a suppository and laxative in newborns. Chewing betel leaves is believed to help increase stamina and improve voice [21].

Various studies regarding its biological activity show that betel leaf provides much information about the potential of medicinal plants indicated in Table 2.

Table 2. Biological Activity of Betel Leaves from Various Extracts [22]

Extract	Biological activity
Closure	Antibacterial, Antioxidant, Anti Cancer, Anti fungal, Anti Diabetes, Neuroprotective,

Ethanol	Induces apoptosis, Antibacterial, Anticancer, Antidiabetic, Antioxidant
Methanol	Antibacterial, Anticancer, Hypopidemic
Essential Oils	Antibacteria, Antihistamine
Ethyl Acetate	Anticancer

Betel leaf has many biological activities that have many benefits, such as anticancer, antioxidant, anti-inflammatory, and anti-bacterial. Singh et al. [23] reported *hydroxychavicol* compounds present in betel leaf extract that induce bacterial cell death with DNA damage and inhibition of cell division. In addition, the antimicrobial activity of Piper betle leaf extract was studied against Vibrio alginoliticus, isolated from Asian sea bass, and late chascarrifer. Antimicrobial activity was evaluated by disc diffusion method, and 100 mg/mL of extract exerted a significant effect ($p < 0.05$) with the largest inhibitory zone (19 mm) compared to other concentrations [24]. YS Diaseptana et al. [25] discussed antibacterial activity on green and red betel leaves using the paper disk diffusion method, against gram-positive and gram-negative bacteria. The results showed that the combination of green betel and red betel showed lower antibacterial activity than green betel or red betel alone against *S.Aureus, S.Epidermidis,* and *E.Coli.*

Basak [26-28] discusses the effect of betel leaf modeling on the germination time of *Aspergillus flavus* and *Penicillium expansum* spore populations. Experimental data of spore germination rates were significantly installed (R2= 0.95%) for asymmetric models. Minimum inhibitory concentrations for germination of *A. flavus and* P. expansum *spores* were found to be 0.65 and 0.54 l/mL. Ali, Lim, and Wahida [10] evaluated and compared the added and unadded antimicrobial activity of *P.betle* extract in three types of commercially available toothpastes (*Colgate total, Paradontax, and* Darlie*) against S. aureus, E. coli, S. mutans,* and *S. salivarius*. Among 95% ethanol, 50% ethanol and aqueous extracts, TPC had the highest and growth inhibiting effect for gram-negative *E. coli*, with a MIC of 5 mg/mL found in 95% ethanol extract. Similar results were also found by Karak et al [29], where betel leaf methanol extract showed antimicrobial activity with KHM 8.196 and 0.0021 mg/mL for *E.Coli* and *S.aureus* respectively. The reason behind this difference depends on the cellular structure of bacteria having thicker cell walls in gram-positive bacteria and thinner outer membranes in gram-membrane bacteria. In another study, the antimicrobial activity (antibacterial and antifungal assay) of *Piper betle* extract was tested using ethanol, distilled water, hexane and acetone solvents against four pathogens namely *B. subtilis, E. coli, A. niger,* and *S. cerevisiae.* Among solvent extracts, ethanol extracts showed the maximum inhibitory zone against *E. coli* followed by *S. aureus.* Its gastroprotective activity helps in preventing peptic ulcers [30].

Red betel leaves can be boiled to attack diabetes. Natural antidiabetic drugs work through the enzyme glucose oxidase. Glucose oxidase enzyme is an enzyme that promotes the release of β-D-glucose electrons into gluconic acid and oxygen particles as electron acceptors [31]. In addition, the hypoglycemic properties of alkaloid and flavonoid compounds allow them to reduce blood sugar levels. Red betel leaf herb alone or with other medicinal plants to lower glucose levels in the blood by using three cups of water, boil three red betel leaves until it becomes one and a half cups of water. After the water has cooled, drink this herb three times daily before meals, each time half a glass [32].

In addition, to prevent dental caries, betel leaf has been used traditionally as a mouth freshener in India and other Southeast Asian countries. Today, diabetic disorders are becoming common in humans. It is a heterogeneous disorder of carbohydrate, lipid and protein metabolism and is characterized by high blood glucose levels due to absolute lack of insulin, since it is this deficiency that causes the body's cells not to respond well to insulin. Therefore, some antidiabetic drugs, as drugs, are used to control elevated blood glucose levels in the body. Some researchers reported that oral administration of betel leaf suspensions at 75 and 150 mg/kg body weight for 30 consecutive days to streptozotocin-induced diabetic rats led to significant reductions in blood glucose and glycosylated hemoglobin levels. Betel leaf administration in diabetic animals was also reported and in this report it was found that glucose-6-phosphatase and fructose-1,6-bisphosphatase levels decreased in the liver with

increased hexokinase levels. Betel leaf has a large role in anti-inflammatory activity which has been used as a household remedy for inflammation of the oral cavity [12].

4. Conclusion

Betel leaf is an abundant source of phenolic compounds that have many therapeutic values and are responsible for many health benefits. The components of essential oils in each carbon are different because they depend on the number of C atoms in each compound. The main or largest content of green betel leaves is limonene while the main content of red betel leaves is sabinene which can be identified using GC-MS data analysis, color reaction, TLC, and KGC. Both compounds undergo sp3 and sp2 hybridization and most have optical structural isomers and iomers that can undergo addition reactions to produce larger compounds. The biological activities of betel leaf include antimicrobial activity, antioxidant activity, antidiabetic, anticancer activity.

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