Patchouli (Pogostemon cablin Benth): Chemistry, Biology, and Anti-inflammatory Activities: A Review

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Abstract: Patchouli (*Pogostemon cablin* Benth) is an essential oil and an aromatic medicinal plant, industrially valued due to widely used in flavours, fragrance and pharmaceuticals. Recently, researchers are showing deep interest towards patchouli alcohol. In Indonesia, patchouli is commonly known as 'nilam' which stand for Nederlands Indische Land ook Acheh Maatscappij. Understanding the chemistry, biology, and anti-inflammatory activities allows its utilization in medicine, toiletries, perfumery and insecticides. This review provides a comprehensive information on chemical compositions of patchouli species and its extracts by gas chromatography-mass spectroscopy (GC-MS) and gas chromatography-flame ionization detection (GC-FID). The biological activities of patchouli towards microorganisms is also being reviewed. This review also provides an additional information on anti-inflammatory activities of *Pogostemon cablin* Benth.

1 INTRODUCTION

Nowadays, the natural product from plants are widely used as herbal medicines and health therapy to treat various diseases. Some products including essential oils, dyes, cosmetics, and drugs also derived from natural products. Currently, several medicinal and aromatic plants are widely cultivated by farmers and industrial agricultural both large and small scale to obtain plants metabolites that are indispensable for industrial needs (Lubbe and Verpoorte, 2011). The aromatic plants are capable to produce some essentials oils that are useful for several therapeutics such as pharmaceutical, perfume and food industries. For example, perfumes, cosmetics, and other health products used 90% of essential oils sourced from plants.

In Indonesia, patchouli oil (*Pogostemon cablin* Benth) is commonly known as 'NILAM' which stand for Nederlands Indische Land ook Acheh Maatscappij. *P. cablin* is an herbaceous plant, spread in Southeast Asia, especially Vietnam, Malaysia, Thailand, and Indonesia. *P. cablin* mainly contains of patchouli alcohol, this compound is functioned as long-lasting aroma or as fixative in perfumes industries. This compound commonly used as indicator to determine the quality of essential oils from patchouli (Anonis, 2006). Patchouli alcohol, commonly used in the perfume manufacturing industry and some products such as soap, detergents, body lotions, and cosmetics (Swamy and Sinniah, 2015), deodorants, and insecticides (Hasegawa et al., 1992).

P. cablin is also known contain several metabolites such as sesquiterpenes, hydrocarbons, patchoulol, patchoulene, bulnesene, guaiene, caryophyllene, elemene, and copaene. *P. cablin* also contains others bioactive compounds such as flavonoids and glycosides (Hasegawa et al., 1992). In addition, patchouli oil is also widely used as aromatherapy to increase sexual arousal (aphrodisiac), to mitigate depression, and anxiety to calm nerves. Several studies reported that patchouli oil are potentials used for treatments of antimicrobial, analgesic, antioxidant, antiplatelet, aphrodisiac, antithrombotic, antidepressant, antimutagenic,

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fibronolytic, antiemetic, and cytotoxic activity (Swamy and Sinniah, 2015; Chakrapani et al., 2013; Priya et al., 2014). In this review, we described some chemicals compounds containing in *P. cablin* and the biological activities on some bacteria, fungi and others microorganisms. In this review, the anti-inflammatory activities of *P. cablin* also communicated.

2 CHEMICALS COMPOSITION OF PATCHOULI OIL (*Pogostemon cablin* benth)

Patchouli oil contains some secondary metabolites and some volatile and in-volatile compounds. Some of these compounds are described as shown below.

2.1 Phytochemicals

The phytochemicals screening results showed that *P. cablin* contains several secondary metabolites including monoterpenoids, triterpenoids, sesquiterpenoids, phytosterols, flavonoids, organic acids, lignins, glycosides, alcohols and aldehydes. The main of phytochemicals from *P. cablin* were patchouli alcohol, α-patchoulene, β-patchoulene, α-bulnesene, seychellene, norpatchoulenol, pogostone, eugenol and pogostol (Mallapa et al., 2016).

2.2 Volatile Chemical Composition of *Pogostemon cablin* Benth

P. cablin generally contains volatile and non-volatile compounds. The volatile compounds generally derived from the leaves and stems such as monoterpenes, sesquiterpenes, and alcohol. Ling mentioned that *P. cablin* consisting of patchouli alcohol (31.86%), seychellene (9.58%), α-guaiene (8.82%), δ-guaiene (8.65%), δ-patchoulene (8.8%) 8.48%), ß-patchoulene (6.91%), and pogostone (3.83%) (Ling et al., 1992). Zang also reported that 96% compounds containing in *P. cablin* were generally in the form of volatile compounds (Zhnag et al., 2003). Some volatile compounds such as geranium ketone, 7-patchoulene, α-patchoulene, α-bulnesene, 5-cedrol and eucalyptus oil ketene. Zhou also reported that the aerial part of *P. cablin* contains four compounds derived from patchoulene namely 8α, 9α-dihydroxypatchoulol; 3α, 8α-dihydroxypatchoulol; 6α-hydroxypatchoulol and 2ß, 12-dihydroxypatchoulol (Zhou et al., 2011). Zhou also successfully identified four sesquiterpenoid compounds from the aerial part of *P. cablin* such as (5R) -5-hydroxypathoulol, (9R) -9-hydroxypatchoulol, (8S) -8-hydroxypatoulol and (3R) -3-hydroxypathoulol (Zhou et al., 2011). The main structure of terpenoids contained in volatile oil from *P. cablin* can be seen in Figure 1.

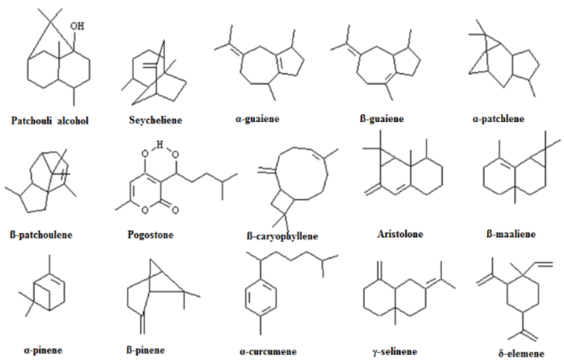

Figure 1: The main structure of terpenoids contained in volatile oil from *P. cablin.*

2.3 Non-volatile Chemical Composition of *Pogostemon cablin* Benth

Besides volatile compounds, *P. cablin* also contains several non-volatile compounds. Guan reported that two flavones compounds such as retusine (1) and pachypodol (2) also available in *P. cablin*. Guan also reported that ethanolic extracts from leaves and stems of *P. cablin* contain four non-volatile compounds (flavonoids glycosides) such as isorhamnetin-3-O-ß-D-galactoside (3), hyperoside (4), 3,5,8,3',4'-pentahydroxy-7-methoxyflavone-3-O-β-D-galactoside (5) and isisolidone-7-O-α-L-rhamnopyranoside (6). Some researchers also reported several other types of flavone compounds such as 3α-hydroxypatchoulane-3-O-β-D-glucopyranoside (7), 15-hydroxypatchoulol 15-O-β-D-glucopyranoside (8) (Ding et al. (2009) Friedelin (9), epifriedelinol (10), oleanolic acid (11), ß-sitosterol (12), eugenol (13), cinnamaldehyde (14), benzaldehyde (15), patchoulipyridine (16), epiguaipyridine (17), and daucosterin (18) [Guan et al., 1994; Itokawa et al., 1981; Treasure 2005). (Figure 2).

Ding reported that ethanolic and buthanolic extracts from leaves and stems of *P. cablin* contains several glycosides compunds such as apigenin 7- (O-methylglucuronide), apigenin-7-galacturonide, luteolin 7-O- (6-O-methyl-β-D-glucuronopyranoside), quercetin-7-β-D-glucoside, syringaresinol-β-D-glucoside, verbascoside, orobanchoside and campneoside I (Ding et al., 2009).

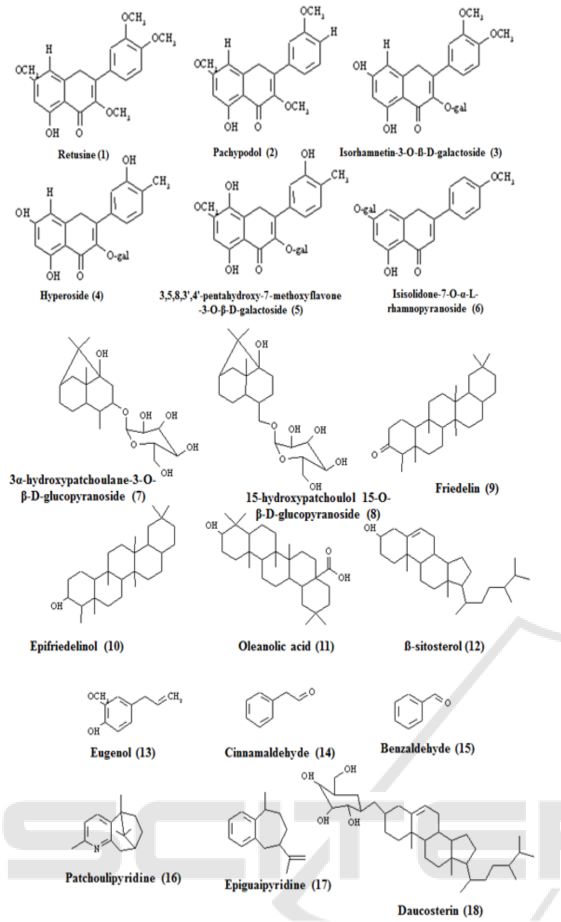

Figure 2: Structure of some non-volatile compounds apart from flavonoids in *P. cablin.*

However, the quality of essential oils from *P. cablin* is highly depend on chemotypes and others factor such as environmental conditions, ways of adaptation, climate, gene quality, dryness of leaves, geographical location (geographical index), and time of harvest. The research conducted by Blank. mentioned that *P. cablin* planted in different harvest seasons would have different chemotypes both qualitatively and quantitatively. Interestingly, the main compound of patchouli alcohol (patchoulol) was founded in all plants that planted in different seasons (Blank et al., 2011). (Table 1).

Besides the harvesting seasons, the chemical content of the patchouli alcohol was also strongly influenced by the geographical indication. Yunhui reported that patchouli alcohol and pogostone from *P. cablin* were differences in percentage of yield of 36 samples in three provinces in China (Guangdong, Guangxi and Hunan Provinces) (Yinhui et al.,2006)., Figure 3.

Table 1: The percentage of main volatile compounds from *P. cablin* Benth in different seasons of harvesting time using *gas chromatograph equipped with a flame ionization detector (GC-FID)* (Blank et al., 2011).

Main volatile compounds	Percentage of abundance compounds (%) each harvest time			
	1^{st}	2^{nd}	3^{th}	4^{th}
α-Pinene	0.00	0.00	0.00	0.00
ß-Pinene	0.00	0.00	0.00	0.00
Limonene	0.00	0.00	0.00	0.00
Acetophenone	0.00	0.00	0.00	0.00
ß-Patcoulene	2.30	2.81	2.62	2.02
ß-Elemene	0.72	0.39	1.06	0.45
ß-Caryophyllene	2.41	1.18	2.24	1.53
α-Guaiene	7.43	3.73	5.99	4.44
Seychellene	5.01	3.01	4.58	3.25
α-Humulene	0.63	0.30	0.33	0.32
α-Patcoulene	3.14	1.71	2.81	1.95
α-Bulnesene	10.32	5.82	8.37	6.48
(E)nerolidol	0.00	0.00	0.00	0.00
Caryophyllene oxide	0.00	0.00	0.00	0.00
ß-Atlantol	0.00	0.54	1.01	1.17
Pogostol	4.18	5.04	4.30	5.06
Pathoulol	55.25	68.41	61.17	62.15

Note: 1^{st}: harvest (May 2008); 2^{nd}: harvest (August 2008); 3^{th}: harvest (November 2008); and 4^{th}: harvest (February 2009)

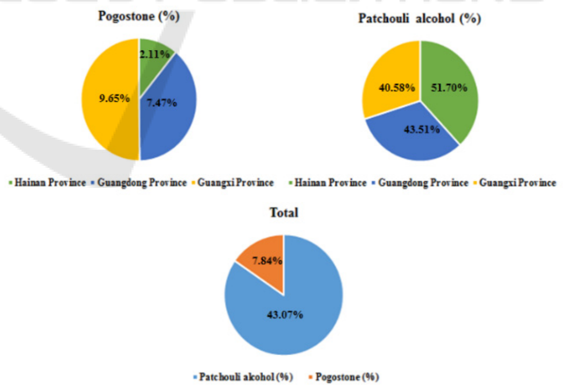

Figure 3: The percentages of patchouli alcohol and pogostone from 36 samples of *P. cablin* in three provinces in China (Yinhui et al.,2006).

Yunhui also mentioned that Guangdong Province (S1-S23) had percentage of patchouli alcohol and pogostone were 43.51 and 7.47%, respectively. While, Guangxi Province (S24-S33) had percentage of patchouli alcohol and pogostone were 40.81 and 9.65%, respectively. Interestingly, the samples from Hunan Province (S34-S36) had the highest patchouli alcohol content (51.70%) and the lowest pogostone content (2.11%). These results indicate that plant sources (cultivation sources), growth temperature (climate) and time of growth (harvesting time) greatly affect the chemical composition of essential oils of *P. cablin* (Yinhui et al.,2006).

3 BIOLOGY ACTIVITIES

3.1 Antibacterial Activities

Luo reported that aqueous *P. cablin* extract possess antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Enteritis coccus* and *Aerobacter aerogenes*. Interestingly, this extract has antibacterial activity against *Staphylococcus aureus* significantly, but does not show activity against *Escherichia coli* (Luo, 2005). Pattnaik mentioned that patchouli oil was effective in inhibiting on 20 bacterial strains and 12 fungal strains. He also mentioned that the patchouli oil derived from several countries with geographical differences such as China, India, and Indonesia showed antifungal activity against 17 of pathogenic fungi, and effective against 16 commensal bacteria from the skin, mucous membranes, nails, feet and armpits (Pattnaik et al., 1996). Hammer also mentioned that *P. cablin* extract were effective in inhibiting *Acenitobacter baumanii*, *Aeromonas veronii*, *Candida albicans*, *Enterococcus faecalis*, *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Salmonella enteric* and *Staphyllococcus aureus*. The organics leave extracts of *P. cablin* were reported have significant activity against *Escherichia coli, Escherichia aerogenes, Bacillus substilis,* and *Staphylococcus aureus.* Among all the compounds contained in patchouli oil, pogostone and (-) - patchoulol have the greatest therapeutic effect on bacteria (Hammer et al., 1999).

3.2 Antifungal Activities

The research conducted by Kocevski showed that patchouli oil has antifungal activity against 11 fungal types. However, it has no activity against *Aspergillus flavus*, *Aspergillus niger* and *Escherichia coli*, but showed antifungal activity against several *Aspergillus species* at concentration of 44.52% (Kocevski et al., 2013). Yang reported that patchouli alcohol, α-bulnesene and patchoulene isolated from P. cablin from China have activity on 12 types of dermatophytes (dermatophytes) with MIC_{50} values were around 50-400 µg / L (Yang et al., 2000). In addition, the combination of patchouli oil and sodium artesunate has a synergistic effect on *Plasmodium berghei* (Liu et al., 2000). Yu also reported that pogostone from *P. cablin* had antifungal activity against clinical isolate of *Candida albicans* at concentrations of 50-400 µg / ml both in vitro and in vivo (Yu et al., 2012). Lie showed that pogostone from *P. cablin* is also effective as candidiasis especially against *Vulvovaginal candidiasis* (Lie et al., 1994).

3.3 Antiviral Activities

P. cablin extracts were reported have anti-influenza activity against the FMI virus in vivo to the mouse model by evaluating the pulmonary index, while the methanolic extract of *P. cablin* leaves was known have antiviral activity against influenza viruses (Kiyohara et al., 2012). Gao reported that patchouli alcohol in volatile oils obtained from isolation using HPLC showed antiviral activity against H1N1 with an IC_{50} value of 2,635 µM. In addition, Gao also reported that the methanol and ethyl acetate extracts of *P. cablin* had an excellent antiviral effect against the coxsackie B virus, with IC50 values of 26.92 and 13.84 µg / ml, respectively (Gao et al., 2009). *P. cablin* was also known to have effects on Herpes simplex types I and II in people with HIV-AIDS (Buckle, 2002). However, until now it has not been known exactly how the mechanism of action of *P. cablin* as an antivirus.

3.4 Insecticidal Activities

P. cablin leaf extract at a concentration of 1% (w / w) was known to be effective as a repellent against *Stegobium paniceum* (Kardian, 1997). Chun reported that patchouli oil was effective against *Lasioderma serricorne*, *Sitophilus zeamais*, *Tribolium confusum*, *Falsogastrallus sauteri*, and *Coptotermes formosanus* Shiraki (Chun et al., 2000). Patchouli oil is also effective as a repellent for mosquitoes *Ades aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus* (Trongtokit et al., 2005; Albuquerque et al., 2013; Gokulakrishnan et al., 2013). Petroleum ether extract of *P. cablin* leaves was also reported to be effective against *Dermatophagoides farina* (Wu et al., 2010). Progostone compounds from P. cablin were also reported effective as larvicidal, antifeedant, pupicidal activities against *Spodoptera litura* and *Spodoptera exigua* (Huang et al., 2014).

3.5 Nematicidal Activities

Wiratno reported that patchouli oil from *P. cablin* has nematicidal activity against root-knot nematode of *Meloidogyne incognita* with a mortality rate of around 4 ± 5.6% with IC_{20}, IC_{50}, and IC_{90} values was more than 19.2 mg / ml (Wiratno et al., 2009). Patidar also reported that *P. cablin* extract at a concentration of 500 ppm had nematicidal effect on second stage juveniles (J2) *Meloidogyne incognita* with a percent mortality of 28.25% after 48 hours of incubation of time (Patidar et al., 2016).

4 ANTIOXIDANT EFFECTS

Hussin reported that patchouli oil had antioxidant activity and radical scavenging by DPPH assay. The results of the antioxidant effect test also showed that patchouli oil from *P. cablin* had a higher activity than mannitol. Polysaccharide compounds from P. cablin are reported to be able to remove hydroxyl radicals (•OH) and superoxide radicals (O_2•) (Hussin et al., 2012). Other results also show that *P. cablin* is very effective in protecting A172 cells (human neuroglioma cell line) from necrosis and apoptosis induced by hydrogen peroxide (H_2O_2), which is indicated by the ability of P. cablin act as reactive oxygen (ROS)-scavenger (Kim et al., 2010). In addition, patchouli alcohol reported able to reduce the level of ROS and Ca^{2+} ions to cells induced by Aß25-35. P. cablin is also reported to be able to protect the intestinal barrier function by protecting membrane's fluidity of epithelial cells through regulation of NO and TNF-α in serum. The volatile oil from *P. cablin* has also been reported to have an antitussive and expectorant effect on ammonia-induced mice (Xie and Tang, 2009).

5 ANTI-INFLAMMANTORY ACTIVITIES

It has been reported that methanolic extract of *P. cablin* possess anti-inflammatory activity by reduced the level of malondialdehyde in paw endema on mice by increasing the antioxidant activity of enzymes in the liver (Lu et al., 2011). Lu also mentioned that this extract was able to reduce the level of superoxide dismutase activity, glutathione peroxidase, gluthathione reductase, COX-2 and TNF-α in paw endema of mice. The extract of *P. cablin* also reported have strongest anti-inflammatory response by regulation of interleukin-1β (IL-1β) and prostaglandin E (2). Yu also reported that patchouli alcohol from Pogostemonis plant mice was able to inhibit ear edema and paw edema in xylene and carrageenan-induced mice at concentration of 10-40 mg / kg body weight of mice. The patchouli alcohol was also able to reduce the production of TNF-α, IL-1ß, iNOS, and COX-2 in hind paw to carrageenan-induced mice (Yu et al., 2011). In addition, Jin also reported that patchouli alcohol has anti-inflammatory activity against RAW264.7 and HT-29 cell lines through suppressing ERK mediated by the NF-κB pathway (Jin et al., 2013). Li mentioned that pogostone has an anti-inflammatory effect and could be potential developed as septic shock therapy (Li et al., 2014). Besides that, Park reported that aqueous *P. cablin* extract was be able to suppressed colon inflammation by suppressing the expression of pro-inflammatory cytokines (Park et al., 2014).

6 CONCLUSIONS AND RECOMMENDATIONS

This review tries to summarize the latest research related to the phytochemical content, biological activity and anti-inflammatory effect of *P. cablin.* The chemical constituents of *P. cablin* were strongly influence by several factors including environmental conditions, adaptation methods, climate, gene quality, dryness of leaves, harvest time, and its geographical location. However, further research needed to develop patchouli oil as drug candidate particularly for anti-inflammatory drugs.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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