Review Article

Phytochemical, Pharmacological importance of Patchouli (*Pogostemon cablin* (Blanco) Benth) an aromatic medicinal plant

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ABSTRACT

Aromatic plants have been commercially used as spices, natural flavor, raw material for essential-oil industry and other medicinal purpose. The use of essential oils continues to rise, both as a separate commodity and indirectly through a large range of beauty-care and aromatherapy products. Patchouli (*Pogostemon cablin* (Blanco) Benth; is a species from the genus Pogostemon and a bushy herb of the mint family. Patchouli leaves are the source for essential oils that constitutes more than 70 chemical compounds. The presence of these compounds imparts excellent therapeutic properties to Patchouli oils that cure various problems tormenting human beings. Production of patchouli oil in India is limited (10–15 tons/ annum). Global demand of Patchouli is 1600 tons of oil per annum with a value of 240 crores. It helps cultivators to meet the demand of the spices and pharmaceutical industry. The present communication constitutes a review on the study of phytochemistry, pharmacological activities, medicinal importance of an aromatic medicinal plant, Patchouli (*Pogostemon cablin* Blanco) Benth. A wide range of phytochemical constituents have been isolated from Patchouli (*Pogostemon cablin* (Blanco) Benth which possesses activities like antimicrobial, cytotoxic activity, antiemetic activity, analgesic, anti-mutagenic activity and anti-inflammatory activity and other important activities. Based upon the given significant information, *Pogostemon cablin* can be developed into novel natural medicine.

Keywords: aromatic plants, natural medicine, phytochemicals, Pogostemon cablin, therapeutic properties.

INTRODUCTION

Medicinal plants have provided modern medicine with numerous plant derived therapeutic agents.[1] Many parts of medicaments are based on indigenous herbals and in recent years, the interest towards the medicinal plants has increased in a great deal. Apart from this, people from different places have also taken this matter seriously by conducting various researches on plant based medicines. In the commercial market, medicinal herbs are used as raw drugs, extracts or tinctures.[2] Medicinal plants are used in aromatherapy, a form of alternative medicine that uses volatile plant materials, known as essential oils, and other aromatic compounds for the purpose of altering a person's mind, mood, cognitive function or health. Some essential oils such as tea tree[3] have demonstrated anti-microbial effects, but there is still a lack of clinical evidence demonstrating efficacy against bacterial, fungal, or viral infections.[4] However some evidence exists that essential oils may have therapeutic potential.[5]

People are settling for remedies that are not just effective but are harmless in the long run. Herbal oils are of various types depending on herbs used to extract the oil. The most important bioactive constituents of plants are alkaloids, tannins, flavonoids, and phenolic compounds.[6] Amongst popular oils, Patchouli oil extracted from *Pogostemon cablin* is known not just for its health benefits but also for its fragrance.[7] Patchouli is a perennial herb and a fragrant plant that basically grows in the tropical region throughout the world. Though patchouli oil is known for its perfumery uses and there are other medicinal properties attached with patchouli oil.[8] Patchouli oil's growing demand can be understood as it can neither be replaced inorganically nor synthesized because of its complex molecular structure.[9] Hence, the only alternative is to cultivate the plant extensively.[10] The aim of the present paper is to review the importance of patchouli extractions in the treatment of diseases that may be useful for the applications of this medicinal plant in the treatment of diseases.

Pogostemon cablin

The plant patchouli belongs to the family Lamiaceae (mint family). Traditionally it had been considered closely related to Verbenaceae.[11] The plants of this family are frequently aromatic in all parts and widely used culinary herbs such as basil, mint, rosemary, sage, savory, marjoram, oregano, thyme, lavender and perilla.[12-14] The name Patchouli was derived from Tamil (patchai: green and ellai: leaf).

Patchouli is a species from the genus Pogostemon and a bushy herb of the mint family, with erect stems, two or three feet (about 0.75 meters) in height and bearing small pale pink-white flowers. The plant is native to tropical regions of Asia and is now extensively cultivated in China, India, Thailand, Indonesia, Malaysia, Mauritius, Philippines, West Africa and Vietnam.[15] Indian demand for patchouli oil is around 220 tonnes valued at 33 crores, while global demand is to the tune of 1600 tonnes of oil per annum with a value of 240 crores.[16] The scent of patchouli is heavy, strong and used for centuries in perfumes. Even though other species of Patchouli are cultivated, *Pogostemon cablin* is considered as superior as

it grows well in warm to tropical climates.[17] The seed-bearing flowers are very fragrant and bloom in late fall.

Figure 1: *Pogostemon cablin*. Benth

In absence of modern medicinal remedies people relied on herbal remedies derived from herbs and spices. There are many medicinal herbs and spices, which find place in day-to-day uses, many of these are used as herbal remedies.[18] In patchouli fresh or dried leaves are used apart from the essential oils.[19] The flowers, leaves, and seeds of the plant give off the signature patchouli scent and even more when crushed.[20]

Scientific Classification[21]

Category	: Dicot
Kingdom	: Plantae
Subkingdom	: Tracheobionta
Super division	: Spermatophyta
Division	: Magnoliophyta
Class	: Magnoliopsida
Subclass	: Asteridae
Order	: Lamiales
Family	: Lamiaceae
Genus	: Pogostemon
Species	: Cablin
Binomial name	: *Pogostemon cablin* Benth

Synonyms **:** Patchouli, Patchouly, Pachouli.[22]

Sanskrit synonyms: Patra, Gandhaparta.[23]

Vernacular Names[24-26]

Malaysia	: Dhalum Wangi, Tilam Wangi, Nilam
English	: Patchouli
Indonesia	: Nilam Wangi (General), Nilam (Acheh), Singalon (Batak)
Thailand	: Phimsen (Bangkok)
Vietnam	: (Ho (aws) c h (uw) (ow) ng)
Philippines	: Kabling (Tagalog); Katluen (Bisaya) Kadlum (Bikol, Bisaya, Sulu)
China	: Guang Huo Xiang
Korea	: Hyangdulkkaephul
India	: Pachi (Sanskrit); Pachauli (Hindi); Pachapat, Patchouli (Bengali); Pachila, Kattam (Malayalam); Pachetene (Kannada); Pacha, Sugandhi pandi (Gujarati); Panch (Marathi)
French	: Patchouli
Spanish	: Pachuli

Commercial Cultivation of Patchouli

Commercial cultivation of the crop in India was first attempted by Tata Oil Mills in 1942. After initial stray attempts to grow the crop, its systematic cultivation started in 1962 by Central Institute of Medicinal and Aromatic Plants (CIMAP).[27] Since there is no replacement for patchouli oil; its unique market position in aroma industry has further increased.[9] Patchouli is commercially cultivated in the Indian states of Karnataka, Maharashtra, Kerala, Goa, Gujarat and Assam.[28,29] At present, the global requirement of patchouli is met mainly through the production from Indonesia. However, due to adverse conditions in Indonesia, the supply of oil is irregular. India's available infrastructure and environment can provide an opportunity to gain a major part of the world market.[30]

Essential Oils

Patchouli oil has a very earthy aroma that matures with aging. Patchouli oil is extracted from the leaves of the plant which are harvested in the wet season and then dried for several days. Dewi Haryani extracted patchouli oil using steam distillation.[31,20] Sesquiterpene cyclase patchoulol synthase was purified and characterized from *P.cablin.*[32] Molecular distillation studies were performed for purification of patchouli oil from *P.cablin.*[33] Ultrasonic extraction method used to get higher yield of patchouli oil. The ultrasound is used to penetrate into the leave cells to extract the patchouli essential oil from the leaves.[34]

The Traditional Uses of Patchouli Essential Oil

Patchouli oil can be attributed to its properties like anti-depressant, antiphlogistic, antiseptic, aphrodisiac, astringent, cicatrisant, cytophylactic, deodorant, diuretic, febrifuge, fungicide, insecticide, sedative, tonic, cicatrisant, cytophylactic, deodorant, stimulant, euphoric. It has been used in India, China and Japan for various medicinal purposes. Because of its primary antiseptic properties, it is used to treat athlete's foot, dandruff, wounds and scars. It gives relief from constipation and acts as an antidote against insect bites temporarily. Patchouli alcohol is a fragrance ingredient used in decorative cosmetics, fine fragrances, shampoos, toilet soaps, non-cosmetic products such as household cleaners and detergents.[35] 97.5 percentile use level in formulae for

use in cosmetics in general has been reported to be 0.11%,[36] which would result in a conservative calculated maximum daily exposure on the skin of 0.0028 mg/kg for high end users of these products. The volatile oil of *P. cablin* and the Chinese crude drug *Herba pogostemonis*, is widely used in the cosmetic and oral hygiene industries. Patchoulic alcohol is commonly used as an indicator for the quality assessment of dried *P. cablin*.[37] It also used as daily dosage along with other herbs for treatment of asthma.[38]

Ayurvedic Properties

The *P.cablin* is used in treatment of ayurvedic Rasa, Guna and Virya.[23]

Aromatherapy

In India this essential oil with the lyrical name of patchapat has long been used to keep moths and other insects out of linens, woolen shawls and rugs.[39] It is the characteristic scent found in Indian bedspreads and cottons. Hand-woven silk and wool rugs from Persia, India, and Turkey have dried patchouli leaves laid on them before they were rolled for shipping. To some people the scent of patchouli is exotic, sensual, and luxurious, but to others it is repellent. The leaves must be fermented and aged before being distilled, which can take as long as 24 hours. Even then, the translucent yellow oil smells harsh. As it ages, it develops patchouli's distinctive scent. It also has a reputation as an aphrodisiac, a notion that probably originated in India. All attempts to make synthetic patchouli have failed utterly.[40]

Table 1: Phytochemical constituents isolated from *Pogostemon cablin* **(**Micheal Tierra (1992); Daniel M (2006); Baby P *et al*., (2007). http://www.globinmed.com/index).

Chemical constituents				
Patchouli alcohol	3-octanone	Benzaldehyde	dimethylphenol	octanoic-acid
Pogostol	4-methyl-pentanoic-acid	b-elemene	epiguaipyridine	Ombuine
nor-patchoulinol	a-bulnesene	b-patchoulene	epoxycaryophyllene	p-vinyl-phenol
Seychellene	a-bulnesene oxide	b-pinene	Eugenol	pachypodol
nor-patchoulinol	a-bulnesone	Bulnesol	eugenol cinnamic aldehyde	patchouli-alcohol
patchoulipyridine	a-guaiene	Cadinene	g-patchoulene	Patchoulipyridine
Methylchavicol	a-guaiene oxide	Camphene	guaiacol	pentanoic-acid
Limonene	a-patchoulene	caryophyllene	guaipyridine	phenol
Pinene	a-pinene	caryophyllene-oxide	heptanoic-acid	pogostol
p-methoxycinnamaldehyde	anethole	cinnamaldehyde	humulene	pogostone
1,10-epoxy-alphabulnesene	anisaldehyde	cis-2-pentylcyclopropylcarboxylic-acid	limonene	rhamnetin
1-alpha,5-alpha-epoxy-alpha-guaiene	Apigenin	cycloseychellene	nonanoic-acid	seychellene
1-beta,5-beta-epoxy-alpha-guaiene	apigenin-7-o-beta-d-(-6"-p-coumaroyl)-glucoside	d-patchoulene	nordehydropatchoulol	tannin
2-methyl-butyric-acid	apigenin-7-o-beta-glucoside;; benzaldehyde	dehydracetic-acid	norpatchoulenol	trans-2-pentylcyclopropylcarboxylic-acid
2-methylhexanoic-acid	azulene	dhelwangin	o-cresol	

Table 2: Phytochemical constituents isolated from *Pogostemon cablin* (Guan L*et al*., 1994)

Compounds from *Pogostemon cablin*	Identification method	Reference
Patchouli alcohol	1H-NMR, IR, MS and UV	Guan L et al., 1994
Pogostone	1H-NMR, IR, MS and UV	Guan L et al., 1994
Friedelin (Isolated first time)	1H-NMR, IR, MS and UV	Guan L et al., 1994
Epifriedelinol (Isolated first time)	1H-NMR, IR, MS and UV	Guan L et al., 1994
Retusine (Isolated first time)	1H-NMR, IR, MS and UV	Guan L et al., 1994
Oleanolic acid (Isolated first time)	1H-NMR, IR, MS and UV	Guan L et al., 1994
Beta-sitosterol (Isolated first time)	1H-NMR, IR, MS and UV	Guan L et al., 1994
Daucosterol (Isolated first time)	1H-NMR, IR, MS and UV	Guan L et al., 1994

Table 3: Chemical constituents obtained from *P. cablin* (Supawan B *et al*., 2006)

Compound	Kovat's Index	% Area
Sesquiterpenes		
δ-elemene	1339	t
β-patchoulene	1380	t
β-elemene	1391	0.33
cis-thujopsene	1429	0.25
trans-caryophyllene	1418	2.24
α-guaiene	1439	7.22
γ-patchoulene	1441	3.89
α-humulene	1454	0.48
α-patchoulene	1456	2.27
Seychellene	1460	0.98
Valencene	1491	0.85
β-selinene	1485	t
α-selinene	1494	0.23
Viridiflorene	1493	1.91
Germacrene A	1503	11.73
α-bulnesene	1505	0.86
7-epi-α-selinene	1517	0.17
Oxygenated sesquiterpenes		
Longipinanol	1566	t
Globulol	1583	4.62
Patchouli alcohol	1659	60.30
Others		
1-octen-3-ol	0978	0.20

t = trace (less than 0.01)

Table 4: Phytochemical constituents

Sesquiterpene hydroperoxides 1-3	Acetone extract	Kiuchi F*et al*., 2004)
Licochalcone A	Cytotoxicity-guided fractionation	Park EJ*et al*., (1998)
Ombuin	Cytotoxicity-guided fractionation	Park EJ*et al*.,1998
5, 7-dihydroxy-3',4'- dimethoxyflavanone	Cytotoxicity-guided fractionation	Park EJ*et al*.,1998
Delta-guaiene,	GC/MS technology	Luo J*et al*., 2002
Aciphyllene	GC/MS technology	Luo J*et al*., 2002

Phytochemical Constituents of Patchouli

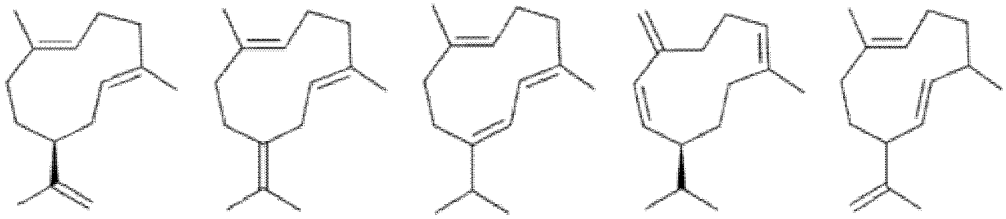
Literature survey established the fact that patchouli oil has more than 70 chemical compounds. Patchouli alcohol, pogostol, seychellene, nor-patchoulinol, patchoulipyridine, methylchavicol, limonene, pinene, p-methoxy cinnamaldehyde etc[41, 42, 43] and others have extracted phytochemical constituents from *P.cablin* through distillation process.[44-47]

Chemical constituents

Three terpenoids Germacrene, Patchoulol or patchouli alcohol, Norpatchoulenol found in patchouli oil are responsible for the typical patchouli scent.[48-50] TLC and HPLC were used to identify the possible chemical markers for evaluating the quality of the crude drug "*Pogostemoni herba*" (aerial part of *P. cablin*), a component of Kampo medicines. In addition to the reported patchouli alcohol and 2-hydroxy-6-methyl-3-(4-methylpentanoyl)-4-pyrone, three phenylethanoids (acteoside, isoacteoside, and crenatoside) were isolated from this plant material for the first time.[51]

RT-PCR strategy was developed to isolate and functionally characterize the respective patchouli oil synthase genes. Unexpectedly, only five terpene synthase cDNA genes were isolated. Four of the cDNAs encode for synthases catalyzing the biosynthesis of one major sesquiterpene,

including a gamma-curcumene synthase, two germacrene D synthases, and a germacrene A synthase. The fifth cDNA encodes for a patchoulol synthase, which catalyzes the conversion of FPP to patchoulol plus at least 13 additional sesquiterpene products.[48] The study on the chemical constituents of an essential oil of *P. cablin* was carried out by hydrodistillation of leaf explants and the oil analyzed by GC/MS and identified twenty two compounds. Among these eighteen were sesquiterpenes and three oxygenated sesquiterpenes.[52]



Germacrene A **Germacrene B** **Germacrene C** **Germacrene D** **Germacrene E**

Figure 2: Five different germacrene compounds

PHARMACOLOGICAL STUDIES

Antimicrobial Activity

Kuntal Das *et al*.,[53] evaluated the anti microbial property of patchouli oil against several microorganisms viz. *Bacillus substilis, Staphylococcus aureus, Streptococcus pyogenes, Enterobacter aerogenes, Pseudomonus aeruginosa, Escherichia coli, Klebsiella pneumoniae* and *Serratia marcescens* by agar diffusion technique and found that the dose of 300 mcg/ml patchouli oil gave maximum zone of inhibition against *Staphylococcus* (14.53±0.37) followed by 12.15 ± 0.35 against *Streptococcus*. Patchouli alcohol, a major component in patchouli oil, and the extract showed higher antibacterial activity than the mixture of *β*-sitosterol and stigmasterol and 7,3′,4-tri-O-methyleriodictyol.[54] The essential oil of *P. cablin* showed antibacterial activity against periodontopathic bacteria, including *Actinobacillus*, *Capnocytophaga*, *Fusobacterium*, *Eikenella.*[55]

Antiviral activity

The anti-influenza A (H2N2) virus activity of patchouli alcohol was studied *in vitro, in vivo* and *in silico*. The CC (50) of patchouli alcohol was above 20 µM. It could inhibit influenza virus with an IC (50) of 4.03 ± 0.23 µM. In the influenza mouse model, patchouli alcohol showed obvious protection against the viral infection at a dose of 5 $mg^{-1}kg^{-1}day$.[56] The methanol extract from the leaves of *P.cablin*, showed potent *in vitro* antiviral activity (99.8% inhibition at a concentration of 10 μgmL^{-1}) against influenza virus A/PR/8/34 (H1N1). Patchouli alcohol did not show anti-influenza virus activity against A/Guizhou/54/89 (H3N2).[57]

Anti fungal activity

P. cablin oil (100 micro g/ml) inhibited the mycelial growth of *Candida albicans*[58] as well as *Aspergillus niger* and *Aspergillus flavus* with MICs (minimal inhibitory concentrations) in the range of 0.78-12.5 mg mL^{-1}.[59]

Other Activities

Patchouli oil main constituent, patchouli alcohol was found to be toxic and repellent against *Formosan subterranean* termites.[60] The *Stomoxys calcitrans* (L.) (Diptera: Muscidae) repellency of 21 essential oils (EOs) alone or in combination with *Calophyllum inophyllum* L. (Clusiaceae), nut oil (tamanu oil) examined using an exposed human hand bioassay. Results were compared with those of commonly used repellent N, N-diethyl-3-methylbenzamide (DEET). In tests with six human male volunteers at a dose of 0.5 mg/cm^2, patchouli (protection time (PT), 3.67 h) was the most effective EO but less active than DEET (4.47h).[61] The undiluted oil of *P. cablin* showed most effective and provided 2h of complete repellency against *Culex quinquefasciatus* and *Anopheles dirus* when compare with other essential oils.[62]

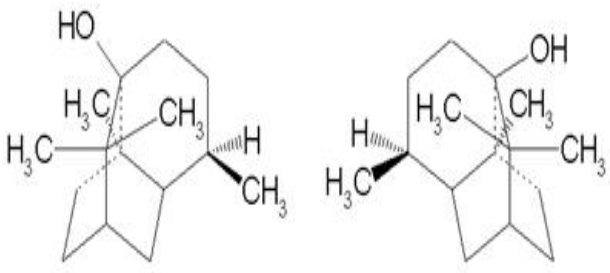


Figure 3: Patchoulol Chemical structure

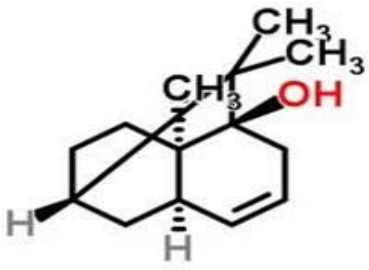


Figure 4: Norpatchoulenol Chemical structure

Evaluation of the toxicity

Patchouli oil was evaluated for toxicity against *Choristoneura rosaceana*, LC (50) and LD (50) values confirmed that patchouli oil was the most toxic to *C. rosaceana* larvae, with LC (50) = 2.8 µL mL (-1) and LD (50) = 8.0 µg insect (-1).[63]

Anti-mutagenic activity of flavonoids

Methanol extract from *P. cablin* showed a suppressive effect on *umu* gene expression of SOS response in *Salmonella typhimurium* TA1535/pSK1002 against the mutagen 2-(2-furyl)-3-(5-nitro-2-furyl) acrylamide (furylfuramide).[64]

Anti-emetic principles

n-hexane extract of patchouli alcohol, pogostol, stigmast-4-en-3-one, retusin and pachypodol exhibited anti-emetic effects.[65]

Cytotoxic activity of patchouli

Licochalcone A, ombuin, and 5, 7-dihydroxy- 3, 4 – dimethoxyflavanone were isolated from the aerial parts of *Pogostemon cablin* by cytotoxicity guided fractionation and it showed *in vitro* cytotoxicity in the P388 cell line (ED 50 9.12 µg/ml) and PI – PLCλI inhibition activity. Treatment of promyelocytic leukemia cells (HL 60) with compound Licochalcone A induced terminal differentiation with the generation of monocyte using nonspecific acid esterase assay.[45]

Location and activation of smell brain centers

Marchwicka *et al.*,[66] using MRI brain scans data determined more smell brain centers in female and male human's brains using olfactory and trigeminal nerve-mediated stimuli during stimulation by patchouli.

Studies conducted the effects of *P.cablin* essential oil inhalation on the body weight, food efficiency rate and serum leptin in SD (Sprague Dawley) rats.[67]

Recombinant Technology

Farnesyl diphosphate synthase (FPPS) of yeast has been coupled to patchoulol synthase (PTS) of plant origin (*P. cablin*). Expression of the fusion proteins in *S. cerevisiae* increased the production of patchoulol, the main sesquiterpene produced by PTS, up to 2-fold.[68] Incubations of isotopically pure (2-(2) H (1)) (E, E)-farnesyl diphosphate with recombinant patchoulol synthase (PTS) from *P. cablin* afforded a 65:35 mixture of monodeuterated and dideuterated patchoulols as well as numerous sesquiterpene hydrocarbons. Extensive NMR analyses of the labeled patchoulol mixture and comparisons of the spectra with those of unlabeled alcohol led to the conclusion that the deuterium label was located at positions (patchoulol numbering system) C5 (both isotopomers, ca. 100%) and C12 (minor isotopomer, 30-35%), that is approximately 2:1 mixture of (5-(2)H(1))- and (5,12-(2)H(2)-patchoulols.[69]

GC-MS Fingerprint Studies

The GC fingerprint performed by gas chromatography with patchouli alcohol and pogostone as chemical markers can be used for identification of patchouli oil.[70] For controlling the quality, standard fingerprint of *P.cablin* collected from different regions of China was developed by using GC-MS. Nine compounds including beta-patchoulene, caryophyllene, alpha-guaiene, seychellene, beta-guaiene, delta-guaiene, pathulenol, patchouli alcohol and pogostone were identified among 10 main peaks in *P. cablin.*[71]

Several experiments were carried out to test different habitats, collection periods, processing methods, the level of spreading manure and using agricultural chemical with the volatile oil assay of pharmacopoeia and GC-MS method.[72] A gas chromatography-tandem mass spectrometry (GC/MS/MS) method has been successfully developed for the determination of patchoulic alcohol content in the samples of dried *P. cablin* and was found to be convenient in particular to tackle the complicated matrix problems always encountered in the herbs which contain high level of essential oils.[37] The chemical constituents of the volatile oil of the stems and leaves of *P. cablin* collected from Leizhou county have been analyzed by GC-MS and found patchouli alcohol, delta-guaiene, alpha-guaiene, seychellene, alpha-patchoulene, aciphyllene, trans-caryophyllene as main constituents.[73]

Pharmacokinetics

The pharmacokinetic parameters demonstrated patchouli alcohol was consistent with the two-compartment open model and showed linear pharmacokinetics. The T1/2 beta, AUC and MRT of patchouli alcohol in patchouli oil were all higher than that of patchouli alcohol. This method is quick, precise and reliable.[74]

CONCLUSION

The literature survey revealed that Patchouli (*Pogostemon cablin* (Blanco) Benth. has been widely studied for its pharmacological activities and regarded as one of the best panacea in Ayurvedic medicine. It is a versatile plant having a wide spectrum of medicinal activities. It can be concluded that *P. cablin* is an important source of many pharmacologically and medicinally important chemicals such as sesquiterpenes and three oxygenated sesquiterpenes. There is not sufficient scientifically valid evidence to state that patchouli extract could be potentially harmful to human beings. As the global scenario is now changing towards the use of non toxic plant products,[75] development of modern drugs from *P. cablin* should be emphasized. It is also clear that much needs to be discovered, both as to the active ingredients and their biological effects. Furthermore, the information summarized here is intended to serve as a reference tool to researchers in the field of phytochemical, pharmacological studies, identification of medicinal properties of *P. cablin*. Detailed research on the chemistry and pharmacology of products

of plant origin are much essential and this may eventually lead to the discovery of medicine that can be used in the treatment of several diseases.[76] The development of these traditional systems of medicines with the perspectives of safety, efficacy and quality will help not only to preserve this traditional heritage but also to rationalize the use of natural products in the health care.

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