

Epigenetics of Betel Leaf Essential Oil: A Determinant of Industrial Niche of the Cultivar

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Piper betle (betel) plants are profusely grown in different states of India. The conventional greenhouse structure known as barejas (baroj) produces best quality betel leaves with huge export potential. The creeper is grown vegetatively from stem cutting and the green foliage produces high quality essential oil that is being utilized in the medicinal, pharmaceutical and aroma industry. The vegetative mode of propagation of this plant species under semi-*in vitro* condition inside baroj structure generated a number of cultivars due to diverse epigenetic regulation. The cultivars respond separately in non-identical habitat generating epi-variants. The aroma compound expresses differential seasonal, morpho-anatomical, chemotypic profile. This distinction may aid the farmers and oil manufacturer-cum exporters to utilize the creeper for diverse applications. The chemotypic variation of leaves and non-leafy segments made this plant a potential bio-prospecting agent. This plant has potential to substitute a number of indigenous and exotic medicinal plants in extraction of important volatile and non-volatile compounds. The unsold, additional leaves along with non-leafy organ from betel-vines could be utilized for cultivar specific essential oil extraction. The oil extraction and purification may enrich the aroma-therapy sector and medicinal industry along with contribution towards agricultural waste management and additional income generation for betel farmers.

Key words: *Piper betle*, epigenetic, betel leaf essential oil, multi-purpose use, cultivar, agri-waste-management, industrial niche

Indian *Piper betle* (*P. betle*) creepers produce high quality betel leaves in conventional greenhouse structure called pan-baroj (pan-barejas). Most of the cultivars of Indian subcontinent shows high level of Betel Leaf Essential Oil (BLEO) recovery from fresh as well as partially degraded leaves. The highly perishable betel leaves causes huge post-harvest loss of farmers reaching up-to 70 % in selected cases. The waste leaves causes environmental pollution and ecological imbalance^[1]. In glut season and erratic weather condition, farmers sell betel leaves in throw away prices, additionally, the temporary baroj structure requires annual maintenance. This high value crop has good export potential. If Betel Leaf Export Consignment (BLEC) shows a slight deviation from the standard betel advisory published by Agricultural Processing and Export Development Authority (APEDA) or Indian phytosanitary authority that leads to rejection of the whole consignment. This problem is faced by the exporters and they lose interest in betel leaf export after multiple non-compliance related rejection. Betel

leaves are highly perishable and domestic left-over and rejected export consignment remains unutilized, experiences *in situ* decays and harbors huge microbial load^[2]. Both the on-farm wastage as well as export loss could be mitigated by utilization of the excess leaves in extraction and purification of BLEO. An in depth study of cultivar specific component profiling of oil will not only increase the efficient BLEO extraction rather reveal the ultimate market value of the plants in suitable pharmaceutical industry. The precise component profiling of *Piper* cultivars could assist in extraction of novel bioactive compounds without application of metabolic engineering or biotechnological interventions. The information on epigenetic variation of betel leaves could be a boon for the BLEO industry. The available Omics data on

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betel could be successfully exploited for estimating the prospect of different cultivars for domain specific industrial utilization^[3]. The recent shift of the aroma industry towards natural plant based ingredient could play key role in utilization of this BLEO^[4]. This plant could replace some indigenous and exotic aromatic plants showing similar chemo-profiles in herbal drug industry. Information on the aroma profile of betel creeper could be useful as alternative for high value endangered aroma germplasm of the world. In this paper an attempt is taken to unwrap the epigenetics of this miraculous creeper as a potential alternative of popular aromatic germplasms in phyto-pharmaceutical sector.

FACTORS AFFECTING BLEO PRODUCTION AND RECOVERY

The high perishability of the leaves along with oscillating demand in domestic and international market causes great hindrance for the betel farmers and sellers. The rotten leaves causes severe bacterial and fungal infection^[5]. The detection of any pathogen in betel consignment causes non-compliance and a total ban on betel leaf export of the whole country. Betel leaves could be stored for only 4 d-6 d in ambient environmental condition but BLEO could remain intact for more than 3 y^[6]. The high storage life and lucrative cost of the BLEO is the reason behind its extraction. The vegetative mode of propagation inside a closed conventional greenhouse structure causes noticeable variation in the production of betel leaves and nature of Essential Oil (EO). The differential intercultural operation leads to variation in the performance of the cultivars. The variation in essential oil production is dependent on seasonal variation of compound accumulation^[7], histological diversity^[8], sexual dimorphism^[9], ecological^[2] as well as climatic influence^[10] on numerous betel leaf cultivars. This epigenetic regulation has potential for betel waste management, signature compound identification, extraction and securing the industrial niche of the plant.

Leaf bio marking:

The EO recovery in betel germplasm depends on different varieties and the application of different processes. The fresh or partially decomposed leaves could be taken for oil extraction. The leaf colour of betel shows significant difference from light green, dark green, yellow, red to even black in some cultivars. The leaf colour may act as a morphological marker in cultivar identification^[11] and during examination of chemotypic diversity of BLEO. The variable colour

may have developed due to the presence of particular signature compound and could act as an excellent morphological identifier in taxonomic management of the germplasms. The leaf morphological studies are regarded as the cheapest and rapid method for plant diversity studies^[12]. The organoleptic and microscopic evaluation of the leaves reveals, marker important for cultivar identification. The presence of abundant pearl like secretory cell in Bangla cultivar of betel leaves distinguishes it from other cultivars. In kapoori cultivar, multi-layered epidermis, cuticular hypodermis and presence of silicified cell in the upper leaf surface proclaims its drought tolerant nature^[13]. In South Indian cultivar Siguramani the presence of cylindrical finger like glandular trichomes and 3-4 layered secretory cell distinguishes it from others. Sessile secretory glandular trichomes and single mucus canal is characteristic of Pachaikodi cultivar^[14]. The ash value, total soluble solid content of the leaves could additionally provide information on epigenetic variation of the cultivar performance under different inter-cultural operation^[15].

Variation in oil content in betel leaves:

The Indian betel leaf export industry mainly emphasizes the export of raw leaves for mastication purpose. In India about 10 % of the total production of betel leaves remain surplus and subjected to wastage every year particularly during the rainy season. To mitigate the problem the extraction of essential oil from well-demanded varieties of betel leaves could be taken up during monsoon when the export and domestic market demand experiences drastic reduction^[16]. The average oil content in the Bangla cultivar was 1.7 % and in the Mitha cultivar it was 2.0 % whereas in the Sanchi it was only 0.8 % on dry weight basis^[17]. In Sada Bangla cultivar 1.8 % oil recovery was noticed with the application of modified hydro-distillation method^[10]. The information on BLEO recovery is not available for Kali Bangla/Jhalpata, Kharibangla cultivars. Bagerhati, which is a prominent cultivar of West Bengal, India was also neglected and data is not available regarding the oil content. This oil, which is the major ingredient imparting particular aroma and medicinal properties to the betel leaves, can be preserved for more than 3 y.

The oil has a multidimensional potential for utilization in cottage industry for manufacturing of numerous commercial products like medicine, gutkha (chewable mouth freshener), incense sticks, fragrant and flavoring agent etc. The establishment of a rural industry for extraction of essential oil from betel leaves could be initiated at a very reasonable initial investment of Rs.

30 000-40 000/-(400-500 USD) in bareja adjacent region^[16]. This mission may minimize the wastage of surplus betel leaves besides increasing the agro-industrial employment opportunities in the betel leaf growing regions of India and other betel leaf producing countries.

Morpho-anatomical variation and sexual dimorphism of BLEO:

The leaf biomass determines the economic yield in betel trade and increased biomass increases the prospect of more oil recovery. Leaf biomass production and composition depends on gender, location, season, agronomic technologies, and propagation method of a cultivar^[3]. Additionally the leaf oil content of petiole^[18], inflorescence^[19], rhizomes^[20] and root^[21] of betel leaf cultivars were regarded as promising inclusion for biomedicine manufacturers and food additive sector. It is important to analyze the potential of all the parts of *P. betle* creeper to maximize the need based utilization of different plant organ and reduction in the waste generation during climatic adversities. The saline belt of Indian subcontinent produces good quality betel leaves but the vines are devastated by super-cyclones in every year. The Sagar Meetha and Sagar Bangla produces highest quantity of essential oil in comparison to other cultivars of India. In such condition the different parts of the uprooted creeper could be separated, sorted and utilized for need based oil utilization from separate organs.

Additionally, the sexual dimorphism influences biomass production and the ultimate constituent diversity of the said biomass. The sexual dimorphism affects the leaf length, width, weight regulating economic yield of commercial cultivars. Leaf yield regulates the economic turnover of the prominent cultivars. The male plants have narrowly ovate leaves and female possess cordate leaves^[2]. In clonally propagated plants, in absence of flowering, the leaf morphology is usually utilized for discrimination of male and female plants. In a study of wild betel cultivar it is noticed that female plant produces more than 62.9 % monoterpenes while male produces 60.93 % sesquiterpenes hydrocarbons. The female plants under stress condition produces some excess metabolite than the male partners including monoterpenes and oxygenated monoterpenes^[22]. Higher amount of phenol and other antioxidants were produced in females. A quantitative difference in acetylation of phenols was observed between genders. Gender associated qualitative and quantitative difference

ultimately influence the metabolite production and drug efficacy, recovery and yield in specific taxons^[23]. The clonal propagation also leads to change in ploidy level in sexes and may produce larger leaf in some varieties^[24]. In West Bengal, India majority of the betel-vines display sexual dimorphism and indirectly influences bio-prospect of the cultivated germplasm.

Seasonal fluctuation of BLEO:

Seasonal oscillation regulates production of different bioactive compounds. Difference in temperature, rainfall, humidity regulates the production of different compounds in *P. betle*. The volatile and non-volatile compounds accumulate within the oil glands in differential amounts. Gas Chromatography-Mass Spectroscopy (GC-MS) based analysis of the leaf extract on the accumulation of various metabolites in *Piper*^[22], detected maximum storage of chemical constituents in winter and lowest in monsoon. Cluster analysis of the 8 cultivated varieties on the basis of 45 non-polar components revealed seasonal variation of components, though some major components remain unaffected irrespective of season. The growers and medicine industry may focus on seasonal extraction of different phyto-compounds^[23]. Additionally epigenetic variation led to the production of multiple volatile and non-volatile aroma constituents in different developmental stages of the plant^[24]. The clonal propagation mechanism leads to perpetuation of mitotically transmissible epigenetic traits by allowing promiscuous movement of diffusible epigenetic factors through plasmodesmata^[25].

Histological and seasonal variation in monoterpenes and sesquiterpenes were also noticed in this aromatic species. Unbiased analysis of the *Piper* metabolome could specify the distinct role of genotype, developmental stages and environmental effects on Secondary metabolite (SC) production^[26]. The increase in biomass could regulate the percentage of essential oil recovery and competitive production and distribution of bioactive compounds regulating ultimate aroma-architecture of the genotype. GC-MS study of volatile and non-volatile components along with Principle Component Analysis (PCA) shows eugenol and sesquiterpenoids were responsible for seasonal variation of BLEO^[27]. The quantitative and qualitative chemotypic profile of cultivars showed noticeable variation and the variation of BLEO signifies the operation of epigenetic factors as an operative force in BLEO diversification^[28]. In different orchards of a single locality the plant types perform differently leading to differential orchard

performance. The *in vivo* diffusion of selective epigenetic compounds through plasmodesmata may be the influence behind this orchard to orchard variation of same genotype^[29]. In Indian subcontinent betel leaf based business exhibits seasonal influence and extraction and exploitation of a broad spectrum of EO could possible and prospective with respect to season and demand of the pharmaceutical sector.

Geographical variation of BLEO:

The epigenetic control mechanism affects the omic-architecture of clonally propagated plants affecting the chemo-diversity. In *Piper* significant variation of secondary metabolites are noticed pertaining to geographical variation. The varietal performance deviates in different geographical region mainly due to the accumulation of different secondary metabolites. The *P. betle* might have originated in the South-Eastern region of Asia in Indonesia or Thailand but in India all the cultivars of *P. betle* shows the presence of eugenol and chavibetol as major constituent of BLEO^[30-34]. In Philippine and Malaysia the major compound was identified as chavibetol and its acetate^[35,36]. The betel leaves of Democratic Kampuchea shows the presence of Alpha (α)-pinene and sabinene as major component^[20]. The Taiwan type shows presence of chavibetol, safrole and myrcene^[37]. Presence of saponin and glycoside is noticed in black betel of Africa^[38]. Safrole followed by

chavibetol are the major BLEO constituents of Srilanka. Malabulath cultivar of Srilanka shows unique presence of allylpyrocatecholdiacetate^[39]. The major compound in Malabulath oil is allylpyrocatecholdiacetate which is regarded as the third major compound in common betel oil of Lanka. This chemical composition of the BLEO of Lanka shows proximity with Indian cultivar Deshawari^[40]. The presence of different varieties could be recognized and marked by their chemo-diversity. In India the Northern, Eastern and Southern varieties shows distinct difference in overall chemical composition^[41].

The popular cultivars of our state of West Bengal such as Bangla, Mitha and Sanchi, Sadabangla, kalibangla has number of valuable components but the signatory compound remain present in trace quantity and unique to a cultivar^[3]. The discriminatory component could play significant role in cultivar biomarking. The presence of estragole and anethole provides the sweet fragrance to the Meetha cultivar and is unique to the Meetha cultivar of West Bengal^[42]. In Bangla cultivar of Bangladesh, the signatory compound were oxophorone and 9-epi- β -caryophyllene but in Sanchi the presence of H-indole was prominent^[43]. The study on trace element is rare and requires replicated confirmatory study establishing the validity of the signature compound for authentic biomarking of promising cultivars. The cultivar could be classified on the basis of the presence of signature compounds in the betel plant types (Table 1).

TABLE 1: SIGNATURE COMPOUNDS OF DIFFERENT CHEMOTYPES OF BETEL LEAVES OF ASIA

Country	Signature compound	Reference
Philippine	Hydroxychavicol	Ilao ^[35]
Malaysia	Chavibetol, eugenol acetate	Jantan <i>et al.</i> ^[36]
Taiwan	Safrole, myrcene	Chang <i>et al.</i> ^[37]
Africa	Saponin, glycoside	Junairiah <i>et al.</i> ^[38]
Sri Lanka	Safrole, allylpyrocatechol, eugenol	Mohottalage <i>et al.</i> ^[39]
Indonesia	4-allyl phenylacetate	Alighiri <i>et al.</i> ^[7]
Vietnam	Isoeugenol, isoeugenol acetate	Thanh <i>et al.</i> ^[20]
Bangladesh	Eugenol, α -celinene, oxophorone, 9-epi- β -caryophyllene	Islam <i>et al.</i> ^[43]
Thailand	Chavicol, chavibetol	Nagabhushan <i>et al.</i> ^[44]
Nepal	Chavibetol, chavibetol acetate	Satyral <i>et al.</i> ^[45]

Performance of non-leafy organs for oil recovery:

P. betle plant is a store house of essential chemicals, though the performance of the leafy part is being evaluated by several researchers, the BLEO recovery from non-foliage tissues are scanty. The petiole, inflorescence, rhizome contains different valuable components and could be utilized for oil extraction. In betel leaf storage, the removal of petiole increases the longevity of the leaf. This segments could be evaluated for commercial oil extraction as it is removed for long term storage of betel leaves the excised petiole could be utilized for essential oil extraction. The petiole shows presence of methyl undecanoate, dodecanoic acid, 3-methyl-butyl-dodecanoate and lauryl alcohol, that has great potential in flavor and cosmetics industry^[18]. A novel hydroxychavicol dimer, 2-(g'-hydroxychavicol)-hydroxychavicol was isolated from the roots of *P. betle* along with five known compounds, hydroxychavicol, aristolactam AII, aristolactam BII, piperolactam A and cepharadione A^[44-46]. The structures of these isolated compounds were elucidated by spectroscopic methods. Compounds 1 and 2 exhibited inhibitory effects on the generation of superoxide anion and the release of elastase by human neutrophils.

The extract of Indian *P. betle* roots furnished novel aristolactam AII and a phenyl propene, characterized as 4-allyl resorcinol, with the petroleum-ether extract yielded a diketosteroid, viz., stigmast-4-en-3,6-dione^[47]. Diverse alkaloids and lignans present in stems of *P. betle* were elucidated by spectral analysis as piperine, pellitorine, N-isobutyl-2E, 4E-dodecadienamide, dehydropiperonaline, piperdardine, piperolein-B, guineensine, (2E, 4E)-N-isobutyl-7-(3', 4'-methylenedioxyphenyl)-2, 4-heptadienamide, syringaresinol-O-beta-D-glucopyranoside, pinoresinol. The compounds were isolated as novel types for stem^[48]. The rhizome oil of *P. betle* contains 40 compounds with δ -cadinene, α -cadinol, T-cadinol and T-muurolol as major constituents^[19]. The extraction and identification of several novel compounds from betel non-leafy parts bear prospect of enhancement of natural drug extraction. The plant organs may act as bio-factory for drug, therapeutic and organoleptic studies.

PROMINENT BETEL LEAF CHEMOTYPES OF WEST BENGAL WITH AGRO-INDUSTRIAL POTENTIAL

In *P. betle* the chemical polymorphism is well established leading to formation of eight distinct chemotypes predominantly on the basis of essential oil

present in leaves. The prominent cultivars of the state of West Bengal, India are Bangla, Meetha, Kalibangla and Bagerhati. Those cultivars could be utilized for extraction of chavicol, eugenol, eugenol acetate and anethole respectively. Sanchi, Haldia, Ghanegate and Manikdanga also shows promise as expensive medicinal cultivar^[16,3]. The signature compounds of all the eight cultivar holds enormous potential to be used in a spectrum of pharmaceutical and aroma-industry and assist in boosting local business and enhancing indigenous economy. Additionally the rhizome oil may form another significant biomarker. The available metabolomics data could be used to identify the transcriptomics and genetic ontogeny of volatile compounds^[49,50]. The molecular genetic study and information on genomics is less in *Piper* but the metabolomic data could be utilized for exploring the unexplored territory of epigenomic details of betel plants. The aroma-omic of betel-leaf has potential medicinal uses. The details of pre-clinical trials with betel leaf extract and essential oil in human diseases could throw light on the epigenomic performance and intricacies of this prominent creeper (Table 2 and fig. 1)^[51-64].

EPIGENETIC CONTROL OF VARIABILITY IN BLEO PRODUCTION

The spectrum of secondary metabolites and aroma-compound produced by *P. betle* under diverse environmental stimuli suggests the occurrence of a strong epigenetic control mechanism. The selective production of a compound in one season and then trace occurrence or total disappearance of the same compound in BLEO in next season suggests strong transcriptional as well as translational regulation. In plants methylation, acetylation/deacetylation controls gene repression and expression^[65]. The cis and trans acting elements in cell controls the gene action and metabolite production. The covalent modification of conserved proteins in packaged Deoxyribonucleic Acid (DNA) controls epigenomics of different plants. Down regulation of genomic DNA in plants assist in conservation of energy to control biotic and abiotic stresses^[66]. The less production of some compounds in selected season in *P. betle* may be a defense mechanism by resource storage. An array of non-coding Ribonucleic Acids (RNAs) might have played predominant role in performance of distinct landraces^[67]. In several plants it has been noticed nitrogen assimilation, vernalization, pigmentation, photo-morphogenesis, male sterility, flowering, spore production, biotic and abiotic stresses

were mediated by essential non-coding RNAs^[68-73]. Histone acetylation and cytosine methylation regulates the promoter, regulator and enhancer action in post-transcriptional operations. The natural environmental factor or exogenous application of chemical compounds could assist in the recovery of commercially suitable epigenetic variants.

PROSPECT OF BETEL CREEPER AS SUBSTITUTE OF AROMA-PLANTS

Plant normally produces diverse bioactive compounds with different health benefits and nutritional productivity. These compounds are mainly related to defense mechanism of the plant or indirectly assist in successful propagation. *Piper* plant reserves a spectrum of monoterpenes and sesquiterpenes with more than 10 % additional products^[74]. In *Freesia hybrida* the synergistic expression and hierarchical regulatory activity of transcription factors regulate the linalool production in different varieties of flowers.

A regulatory gene showed two-fold activity in transcriptional modulation. It controls both the nature of secretory trichome formation in flower petals along with sequential expression of terpene biosynthesis gene^[75]. In a similar manner in different betel cultivars the cascading activity of different transcription factor and associated cis acting elements activates/deactivates diverse candidate of terpenoid family. This event leads to histological, quantitative and qualitative variation in the composition of secondary metabolites in *P. betle* cultivars. Apart from *P. betle* several other species such as *P. betle* var. *nigra*^[76], *Piper crocatum*^[77], *Piper sarmentosum*^[78] has potential to replace several aromatic plants as biophore for herbal drugs. Thus betel creeper could substantially replace a number of aromatic medicinal plant as biophore for extraction of multiple bioactive compounds. In this way the plant has potential to assist pharmaceutical industry as replacement of endangered indigenous or exotic plants in Indian subcontinent or in other countries as well (Table 3)^[79-92].

TABLE 2: PRE-CLINICAL STUDIES OF BLEO AS A POTENT PHARMACEUTICAL AGENT

Clinical area	Type of action	Reference
Anti-breast cancer	Significant suppression and migration of cell lines MCF-7 at a dose of 25 µg/ml of leaf extract	Boontha <i>et al.</i> ^[51]
Human colorectal adeno carcinoma	200 µg/ml leaf extract triggers micro-tubule polymerization and cell cycle arrest	Looi <i>et al.</i> ^[52]
Anti-cancer property	100 µg/ml of leaf extract inhibited treated KB cells with 43.42 % viability	Veettil <i>et al.</i> ^[53]
Anti-diabetic property	Anti-diabetic assay by α-amylase and α-glucosidase enzyme inhibition (IC ₅₀) at 26.2 µg/ml and 96.8 µg/ml by methanolic extract of Kapoori Meetha cultivar	Satapathy <i>et al.</i> ^[54]
Antithrombin activity	Thrombin substrate III and thrombin inhibition (IC ₅₀) at 165.5 µg/ml by methanolic leaf extract	Shekhar <i>et al.</i> ^[55]
Antioxidant activity	The ethyl acetate leaf extract shows highest anti-proliferative activity against MCF-7 cell lines in RPMI 1640 medium with IC ₅₀ value of 65 µg/ml	Alfiana <i>et al.</i> ^[56]
Anti-candida activity	The disc-diffusion assay using <i>Candida albicans</i> showed a MIC value of 0.1-2 mg/ml with a liquid formulation of 5 % BLEO	Biswal <i>et al.</i> ^[57]
Episiotomy effect	A topical combination of 2 ml cinnamon oil and 20 % red betel leaf extract accelerate wound healing and reduce perineal pain in episiotomy incision model in Swiss mice	Meinisasti <i>et al.</i> ^[58]
Anti-estrogenic activity	1 g/kg/day aqueous and methanolic leaf extract showed significant decrease in the duration of proestrus and estrus and reduction in the number of estrous cycle in female albino rats	Bhattacharya <i>et al.</i> ^[59]
Anti-acne property	15 % ethanolic extract of betel leaves shows strongest inhibitory zone of 15.35 mm in pure <i>Propionibacterium</i> culture equivalent to clindamycin gel	

Healing of stomach ulcer	120 mg/kg of leaf extract shows 78.28±2.8 % protection in indomethacin induced stomach ulcerated rats	Abraham <i>et al.</i> ^[60]
Antinociceptive activity	100-200 mg/kg methanolic extract of leaf shows analgesic activity in hot-plate technique in Swiss-albino mice and Wister rats. Dose dependent variation in latency time was noticed with supra-spinal response of the test subjects	Alam <i>et al.</i> ^[61]
Anti-inflammatory activity	10-250 µg/ml of methanolic leaf extract shows anti-inflammatory activity with a maximum viability of 87.74 % in RAW 264.7 cells treated with 1 µg/ml of <i>Escherichia coli</i> LPS	Rintu <i>et al.</i> ^[62]
Immuno-protective property	Oral administration of aqueous leaf extract of 225 mg/kg 1 h before radiation exposure shows radio-protective activity in Swiss female mice with a reduction of 34.78 % of micro-nucleated cells in post-irradiation (24 h) bone-marrow samples	Verma <i>et al.</i> ^[63]
Rheumatoid arthritis treatment	200-400 mg/kg of methanolic leaf extract shows recovery from joint damage in male albino Wister rats in dose dependent manner	Murugesan <i>et al.</i> ^[64]

Note: MCF-7: Michigan Cancer Foundation-7; IC₅₀: half-maximal Inhibitory Concentration; RPMI: Roswell Park Memorial Institute and LPS: Lipopolysaccharide

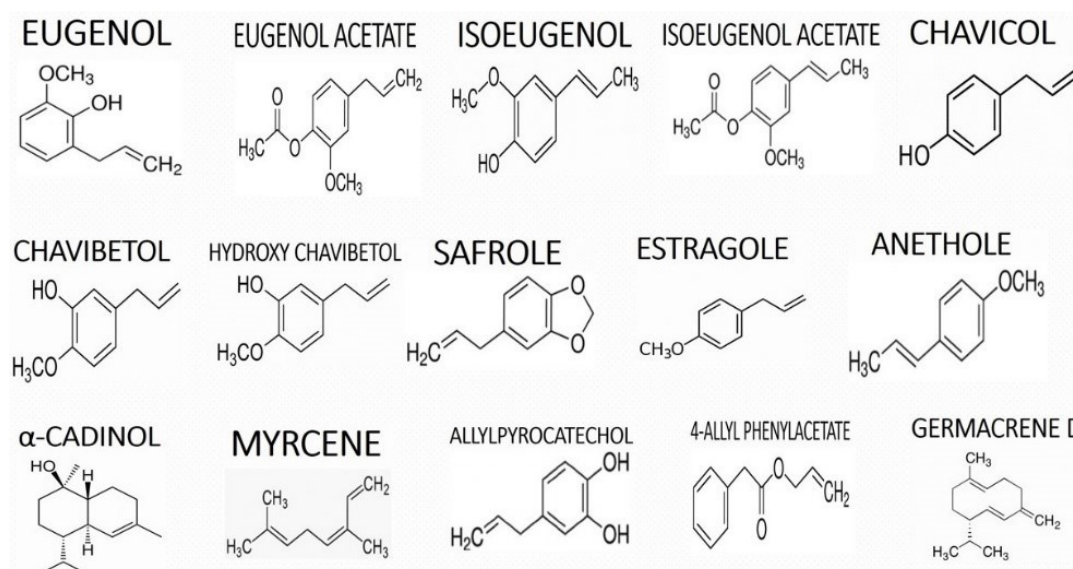


Fig. 1: Major chemical compounds present in *P. betle* chemotypes of West Bengal, India

TABLE 3: *P. betle* CREEPER AS POTENTIAL ALTERNATIVE OF AN ARRAY OF MEDICINAL PLANTS

Scientific name	Name of the plant	Signature compound	Piper cultivar	Reference
<i>Cymbopogon nardus</i>	Citronella	Methyl eugenol	Bangla	Tan <i>et al.</i> ^[79]
<i>Syzygium aromaticum</i>	Clove	Eugenol	Meetha	Khalil <i>et al.</i> ^[80]
<i>Petunia hybrid</i>	Petunia	Isoeugenol	Vietnameze	Koeduka <i>et al.</i> ^[81]
<i>Cinnamomum verum</i>	Cinnamon	Acetyl eugenol	Maghai	Khalil <i>et al.</i> ^[80]
<i>Acacia nilotica</i>	Gum arabic	Eugenol acetate	Kalibangla	Abdulhamid <i>et al.</i> ^[82]
<i>Ocotea pretiosa</i>	Canelafuncho	Safrole	Sanchi	Lima <i>et al.</i> ^[83]
<i>Bursera copallifera</i>	Copal ancho	Germacrene-D	Siguramani	Noge <i>et al.</i> ^[84]
<i>Pimpinella anisum</i>	Anise	Anethole	Meetha	Duta <i>et al.</i> ^[85]
<i>Ocimum basilicum</i>	Sweet basil	Chavibetol	Nepalese	Gang <i>et al.</i> ^[86]
<i>Foeniculum vulgare</i>	Bitter fennel	Estragole	Meetha	Afifi <i>et al.</i> ^[87]

<i>Elettaria cardamomum</i>	Cardamom	Terpinyl acetate	Kapoori	Vaiciulyte <i>et al.</i> ^[88]
<i>Cannabis sativa</i>	Cannabis	β-caryophyllene	Panama	Fiorenzani <i>et al.</i> ^[89]
<i>Calendula officinalis</i>	Calendula	Cadinol, δ-cadinene	Nepalese betel	Satyal <i>et al.</i> ^[45]
<i>Pogostemon cablin</i>	Patchouli	Trans-caryophyllene	Meetha	Basak <i>et al.</i> ^[90]
<i>Lavandula officinalis</i>	Lavender	Geraniol	Tamluk Mitha	Basak <i>et al.</i> ^[90]
<i>Piper nigrum</i>	Pepper	Sabinene	Siguramani I	Periyanayagam <i>et al.</i> ^[13]
<i>Elettaria cardamomum</i>	Cardamom	Alpha-terpineol	South Indian betel	Ashokkumar <i>et al.</i> and Nayaka <i>et al.</i> ^[91,92]

CONCLUSION

In *P. betle* the epigenetic and epigenomic studies could provide insight into the qualitative and quantitative variation in betel leaf constituent. The precise study of epigenetic regulation could substantiate the recovery of more essential oil, aroma compounds in the form of secondary metabolites. This review highlighted the value of understanding the morpho-anatomical variation, seasonal influence, sexual or ploidy analysis, ecological diversity in the exploitation of this high value plant for need based essential oil extraction. The plant could act as a bio-factory for domestic and export market of medicinal and therapeutic natural products. As the plant is vegetatively propagated through stem cutting in Indian subcontinent in semi-*in vitro* condition, a slight modification of agronomic techniques could alter the composition of essential oil in different cultivars. These modification could be exerted by natural or chemical alterations. These epigenetic variants as taxonomic cultivars could replace the expensive transgenic production or tissue culture based metabolic engineering. The epigenetics of BLEO is essential for understanding the industrial niche of the promising creeper.

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Conflict of interests:

The authors declare no conflict of interests.

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