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Hyptis suaveolens (L.) poit: A phyto-pharmacological review

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ABSTRACT

The plant *Hyptis suaveolens* (L.) Poit; [Lamiaceae] is reported to possess antifertility, anti-inflammatory, and antiplasmodial properties. Traditionally, the plant extracts were used to cure swellings, abscesses haemorrhoid sand also as memory aid. It has been used as a medicinal tea in many places in asia and as a food and source of essential oil in south america. Parts of the plant were used as analgesic and decongestant, and also to avoid fever and to fuel blood circulation with a sour, minty and sweet-smellingflavour. The English therapeutic journalism shows that it is efficient against bacteria and fungi but there has not been much research yet on its viral effectiveness. *Hyptis suaveolens* is an important source of essential oils, alkaloids, flavonoids, phenols, saponins, terpenes, and sterols, for example diterpenes: suaveolic acid, suaveolol, methyl suaveolate, two steroids: *β*-sitosterol, ursolic acid, two phenolic constituents: rosamarinic acid and methyl rosmarinate along with some other important constituents oleanoic acid, 3*β*-hydroxy lup-12-en-28-oic acid, urs-12-en-3*β*-ol-27-oic acid, 1,19a-dihydroxy-urs-2(3),12-dien-28-oic acid and 3*β*-hydroxyl lup-20(29)-en-27-oic acid. For this reason and pursuant to the, medicinal importance of the plant, this review is an effort to assemble all the information reported on its phyto-pharmacological activities, and information will lend a hand in generating attention towards the plant, and consequently, may be useful in emergent new remedies which may be more effectual and have better curative properties.

Keywords: *Hyptis suaveolens*, Wilaiti tulsi, Lupenoic acid, Oleanoic acid, Podophyllotoxin.

1. INTRODUCTION

Hyptis suaveolens is a very common plant in India. The plant may be collected in large quantities from the wild as well as from those cultured as a crop by the Indians. Indians used to call it "*Chan/Wilaiti tulsi*" and the morning soup made by mixing it with corn is called "*Bate*" meaning memory aid. Its aromatic phyto-constituents are destroyed by gastrointestinal secretions, but the mucilaginous property may be essentially increased. Tea made from the roots of *H. Suaveolens* is used to purify the blood, and it is also used as a remedy for the “diseases” of women. It has been used as a medicinal tea in many places in Asia,[1] and as a food and source of essential oil in South America (Gentry et al 1990).[2]

1.1. Distribution

Hyptis suaveolens(L.) Poit., a member of the *Lamiaceae* or Labiatae family is a common weed of roadsides and waste grounds. The *H. suaveolens*(pignut) is generally described as annual, perennial forb or herb or subshrub or vine. This Dicot (dicotyledonous) is native to tropical America, is an annual herb that occupies roadsides, rail tracks, wastelands, watercourses, pastures and open forests where the soil is well drained. It can form dense thickets in all areas of growth. *Hyptis* is widespread in Australia (northern territory and Queensland), China, Indonesia, Papua New Guinea, Solomon Islands, French Polynesia, Federated States of Micronesia (Chuuk and Yap Islands), Niue Islands, and Guam and the Hawaiian Islands in the USA. It is widespread in West and Central Africa where it is considered an insidious species in some countries. Distribution of *Hyptis* is now thinning out in the tropical dry deciduous forests of the Vindhyan highlands, which lies in North Indian River Plain,between the Gangetic plains and Narmada valley in north India (21°29′ 25°11′ N latitude and 78° 15′ 84°15′ E longitude), Andman and Nicobar.[3, 4]

1.2. Morphology

It is an erect and strappingly aromatic annual herb reproducing by seeds. The stem is woody hairy and bears glandular dots. *Hyptis* is a strong-scented herb, which grows up to 2 m in height, with quadrate hairy stems and ovate to obviate leaves (3-5 cm long and 2-4cm wide). The margins of the leaves are serrulate and the lower surface is densely hairy. The petioles are up to 3 cm long. The flowers grow in small cymes along branch ends with reduced leaves. The calyx is 5 mm long in flower and 10 mm long in fruit and is ribbed; corolla is blue in colour. Nutlets (a small nutlike fruit or seed) are about 1.2-1.5 mm long and slightly notched at the end. Seeds are dispersed through the movement of water, animals, and vehicles. It has a wide range of pollinators and, hence, seed production is enormous. The seed can remain dormant for many years and the plant can sprout vigorously from rootstocks following rains. Morphologicallyits features resembles with *Ocimum* species.[5]

1.3. Common names

Horehound, Pignut, Wild spikenard, Gros baume, Hyptis à odeur (French), Alfavaca-brava, Betônica-brava (Portuguese, Brazil), Chao, Hierba de las muelas, hortela do campo (Spanish), Wilaiti tulsi (Hindi), bhustrena, darp tulas, jungli tulas (Marathi), sirna tulasi (Telugu), bilati tulas (Bengali), Ganga tulasi (Oriya), bhustrena (Sanskrit).[7, 8]

1.4. Traditional values

Hyptis suaveolens has both medicinal individuality as well as insecticidal properties. *Hyptis* literature indicates that leaf extracts cure swellings, abscesses and haemorrhoids. In India the plant is considered to be stimulant, carminative, sudorific and lactogogue. Infusion is used in infections of the uterus; leaf juice is taken in cases of colic and stomach ache.[4] The shoot tops of the plant are edible and also used for flavouring purpose. Leaves are used in the preparation of mint flavoured beverages. Roots are chewed with betel nuts as a stomachic and its decoction is used as an appetizer [6] while some parts of the plant are used for the treatment of headache. Indians used to take it in the morning soup which is made by mixing it with corn. Tea made from the roots of *H. Suaveolens* is used to purify the blood, and is also used as a remedy for the "diseases" of women. In Indonesia, the plant infusion is used to treat catarrhal (inflammation of mucous membranes, especially of the nose and throat) conditions, affections of the uterus, parasitic cutaneous diseases while the leaves are used as stomachic. In Philippines, the leaves are used for the antispasmodic, anti-rheumatic and antisoporific. In West Africa the leaves of *H. suaveolens* are employed as antifertility agent.[3-6]In case of a burning sensation when passing urine (Dysuria) and other urinary complains, dry seeds of *H.suaveolens* are soaked overnight in a glass of water and taken in the morning on an empty stomach along with small amounts of sugar for about a week.[9] The very strong aromatic mint/thyme-like smell leads to the use of the plant as an insectifuge. As its English name bush tea implies, *H. suaveolens* serves in West Africa as an acceptable substitute in infusion for tea. It. is carminative, sudorific (causing or increasing sweat), lactogenic, anti-catarrhal and anti-parasitic.[5] The plant has been reported to possess antifertility, anti-inflammatory and antiplasmodial properties.[4, 24, 32]

2. Ethnobotanical uses

Tumor, Malaria, Head Ache, Cancer, Expectorant, Fever, Stomach Ache, Cold, Yellow Fever, Rheumatism, Analgesic, Spasm, Antispasmodic, Constipation, Urethritis, Liver Stimulant, Antisudorific, Depurative, Stomachic, Apéritifs, Dyspepsia, Menorrhagia, Sudorific, Be´chic (*relieving a cough*), Epistaxis, Nausea, Tea, Bilious, Pacifier, Palsy, Carminative, Flu, Poison(Veterinary), Repellent(Insect) LactogogueCatarrh.

3. Phytoconstituents of *hyptis suaveolens*

Hyptis suaveolens is an important source of essential oils, alkaloids, flavonoids, phenols, saponins, terpenes, and sterols, for example diterpenes: suaveolic acid, suaveolol, methyl suaveolate, two steroids: *β*-sitosterol, *β*- sitosterol glycoside two phenolic constituents: rosamarinic acid and methyl rosmarinate along with some other important constituents, Oleanolic acid or oleanic acid, ursolic acid, 3*β*-hydroxy-lup-12-en-28-oic acid, urs-12-en-3*β*-ol-27-oic acid, 1,19a-dihydroxy-urs-2(3),12-dien-28-oic acid and 3*β*-hydroxyl lup-20(29)-en-27-oic acid.[19, 21, 22, 23]Researchers have done alot of work in the field of phytochemical investigation of the plant. The phytochemical investigation shows that the plant "*Hyptis suaveolens"* contains essential oils as major components mainly in leaves, shoots and seeds. However, the oils from *H. suaveolens* differ in compositions according to geographical origin of plants. *Hyptis suaveolens* contains many diverse phytochemicals like *α*-Phellandrene (*12*), which is a monocyclic terpene with a pleasing aroma, *α* -pinene (*18)* a terpene having very reactive four membered rings,4,11,11-Trimethyl-8-Methylene-Bicyclo{7.2.0}-Undec-4-ene (*16*), *α*-Caryophyllene (*16b*), 3-cyclohexen-1-carboxaldehyde (*17*), 5*α*-androst-2,11-dione (*19*), 5*α*-androst-9(11)-en-12-one (*20*), 4-methyl-1-(1-methylethyl)-3-cyclohexen-1-ol (*22)*, Thujane (*13*), 1 8 cineole

(*14*), 3,7-dimethyl-1,6-octadien-3-ol (*15*), 2,5-dimethyl-3-methylene-1,5-heptadiene (*25*), 1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (*24*),*α*-cymene (*26*), elemene (*21*). Iwu et al identified the presence of thirty two terpenoids with the help of GC-MS analysis. Limonene (*11*); thujane (*13*); *α*-pinene (*18*); *α*-phellandrine(*12*); 4-methyl-l-(l-methylethyl)-3-cyclohexen-l-ol (*22*); 3-cyclohexen-1-carboxyaldehyde (*17*); elemene (*21*); 4, 11, 1 l-trimethyl-8-methylene bicyclo [7.2.0] undec-4-ene (*16*); octahydro-1, 4-dimethylazulene (*23*); 5*α*, 8*β*, h-9*β*, h-10a- labd-14-ene; 5*α*-androst-9(l l)-en-12-one (*20*) and 5*α*-androstan-2,11-dione (*19*) were the major components identified.[10] A further study was done on chemical composition of the essential oil of *Hyptis suaveolens* collected from Darwin (Northern Territory, Australia) in 1997 by Peerzada et al, and they concluded that the presence of 1, 8-cineole (*14*) and *β*-caryophyllene (*1*) as main constituents with minor concentration of *β*-Pinene (*18b*), Sabinene (*6*), Fenchol (*5*), 4-terpinenol (*7*), eugenol (*3*), *α*-copaene (*2*), *β*-elemene, *α*-Humulene (*16b*), *α*-Bergamotene (*8*), aromadenedrene (*9*), γ-cardinene, δ-cadinene, *α* phallandrene (*12*), myrcene (*12b*), linalool (*13b*), *α*-terpinolene, γ -terpinene (*28*). They reported the absence of *α*-Terpinene (*27*), p-Cymene, Limonene (*11*), *α*-terpinene, Cimenenol, δ-Elemene.[11]Previous, preliminary investigation done by Azevedo et al in 2001 reported the presence of sabinene (*6*), limonene (*11),* bicyco-germacrene (49), *β*-phellandrene and 1,8-cineole as the principal constituents. The investigation also indicated geographic variation in essential oil composition, that the sesquiterpenes are mainly produced in the samples grown at lower latitudes.[12]Rivas et al 2002,has reported the presence of 1,8-cineol, fenchone (*51*) and *β*-pinene (*18b*) as most abundant constituents of the oil.[13]Malele et al 2003concluded that *H. suaveolens* originated in Eastern Coast of Tanzaniacontains the sesquiterpene hydrocarbons *β*-caryophyllene (*1*), *β*-elemene (*21b*), trans-*α*-bergamotene (*8*) and bicycle-germacrene (*49*), together with the sesquiterpene alcohol spathulenol (*50*) represented the most abundant components. Of these, only *β*-caryophyllene and trans-*α*-bergamotene have been reported to occur abundantly. Among the monoterpenes, limonene (*11*), camphene (*53*), terpinolene (*52*) and *α*-teipineol were found. Unlike previous reports, sabinene was only found in very small amounts. But the study shows the absence of 1, 8-cineole, germacrene D (*54*) and germacrene B (*55*).[15] In a similar analysis, leaves of *H. suaveolens* have been reported to contain flavonoids 1.90±0.14%, alkaloids 2.80±0.28%, tannins 5.50±0.074%, saponins 6.10±0.42%, while stems has flavonoids 0.30±0.14%, alkaloids 1.60±0.00%, tannins 0.23±0.07%, saponins 10.50±0.79%. cyanogenic glycoside contents were found to be 44.18±1.39 mg $100g^{-1}$ for leaves and 52.04 ± l.39mg $100g^{-1}$ for stems. Proximate analysis of leaves gave protein 0.24±0.01%, fat2.0±0.0%, fibre 5.63±0.53%, ash 11.40±0.57% and carbohydrates 55.72±0.64%, while proximate analysis of stem gave protein 8.75±0.00%, Fat 2.0±0.0, fibre 17.35±1.63%, ash 9.58±0.3% and carbohydrates 38.13±0.53. Calcium oxalate crystals occurred mostly within the ground tissue of the leaves, stems and roots. The presence of crystals within the ground tissue of leaves stems and roots suggest that these crystals might have storage and supportive functions.[16-18] A recent phytochemical analysis of *Hyptis suaveolens* concluded that it contains major mineral elements which are important as human nutrition; the plant contains Potassium (K), Calcium (Ca), Phosphorus (P), Nitrogen (N), Magnassium (Mg), Sodium (Na).[14]Manchard et al and Prawatsri et al isolated three diterpenes: suaveolic acid, suaveolol, methyl suaveolate, two steroids: *β*-sitosterol (*34*), oleanolic acid (*37*), ursolic acid (*36*), two phenolic constituents: rosamarinic acid (*32*) and methyl rosmarinate (*33*) from the plant. Later chemical analysis of the plant also lead to the separation and isolation of the two main diterpenoid compounds which confirms the presence of suaveolic acid(*29*) and suaveolol(*30*).

The same study also reported that sualveolic acid present in leaves and stems of *Hyptis suaveolens* Poit., Lamiaceae, which on further treatment converted to methyl suaveolate (*31*).[19, 25]On the other hand, earlier investigations done by *Mishra* et alresulted in the identification of *β*- setosterol (*34*), oleanoic acid (*37*), 3*β*-hydroxy lup-12-en-28-oic acid (*39a*), urs-12-en-3*β*-ol-27-oic acid (*α*-peltoboykinolic acid, *38*) and3*β*-hydroxyl lup-20(29)-en-27-oic acid (*39*).They alsoreported the isolation of an unidentified pentacyclic triterpene from the roots of *Hyptis suaveolens*. [20, 21]Mukharjee et alfound the presence of a new pentacyclic triterpene established as urs-12-en-3*β*-29-oic acid (*41*).[43] Raja et al[22]isolated hyptadienic acid identified as A(1)-1,19α-dihydroxy-urs-2(3),12-dien-28-oic acid (*44*) from the *Hyptis suaveolens,* while, after the examination of seed-coat mucilage[41] identified a novel highly branched acidic polysaccharide L-fuco-4-*O*-methyl-D-glucurono-D-xylan (*48*). They proposed a structure having a 4-linked *β*-D-xylan back bone carrying side chains of single 4-*O*-methyl-*α*-D-glucuronic acid residues at *O*-2 and 2-*O*-L-fucopyranosyl-D-xylopyranose units at *O*-3. Ziegler et al[23] isolated Dehydroabietinol (*42*)) from *Hyptis suaveolens* (L.) Poit.

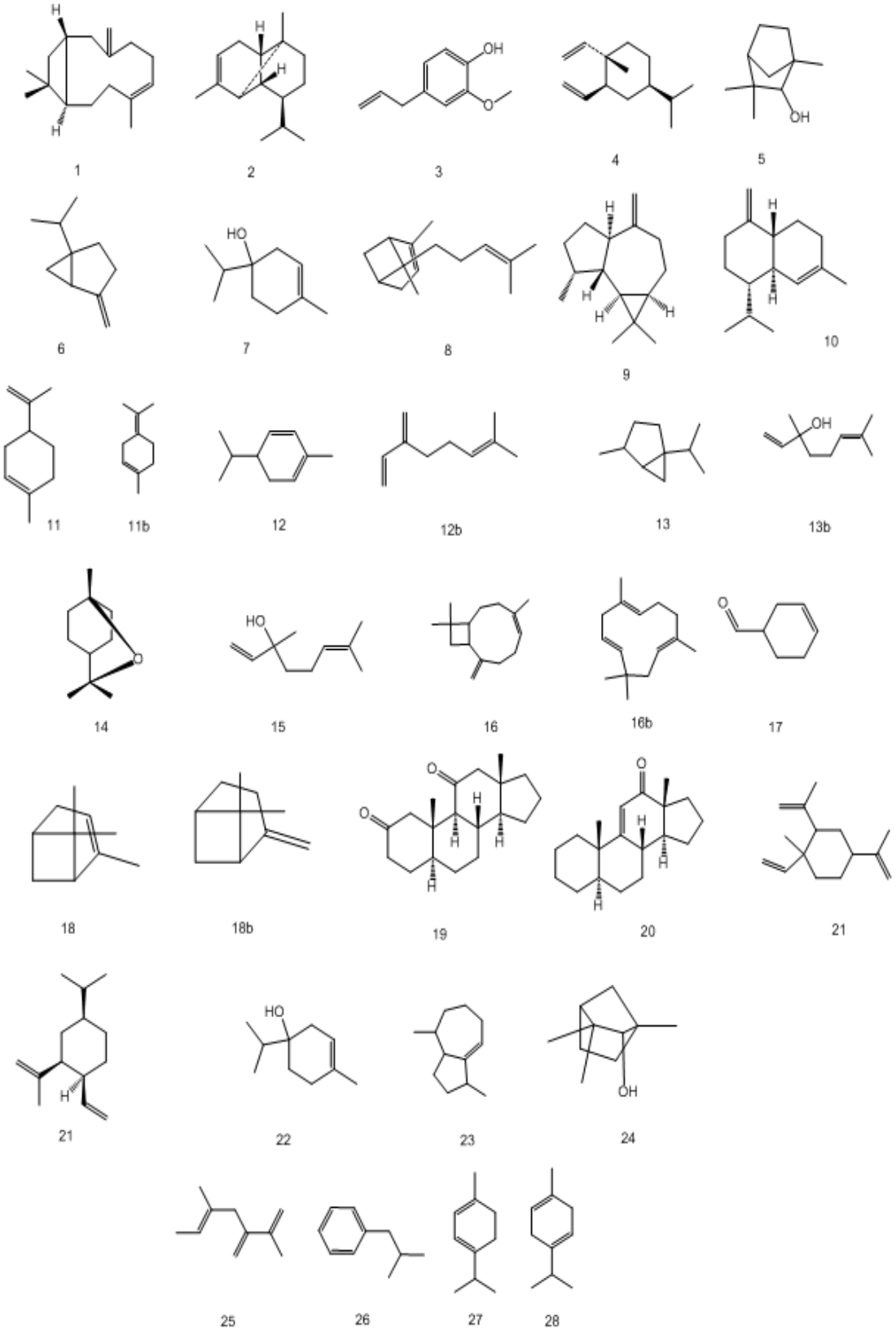

Figure- I: Structures of Phytoconstituents of Hyptis suaveolens (01-28)

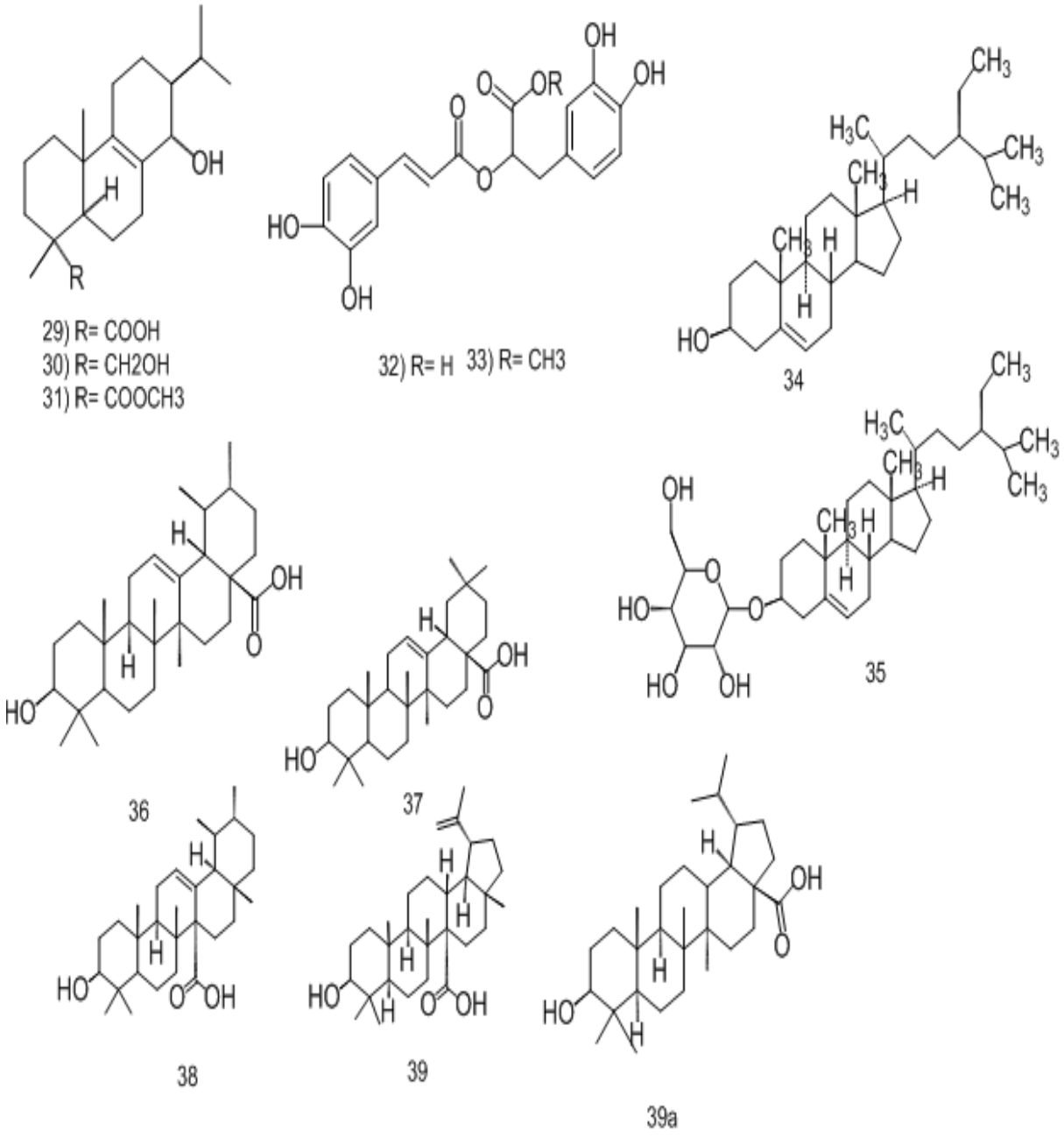

Figure -II: Structures of Phytoconstituents of Hyptis suaveolens (29-39a)

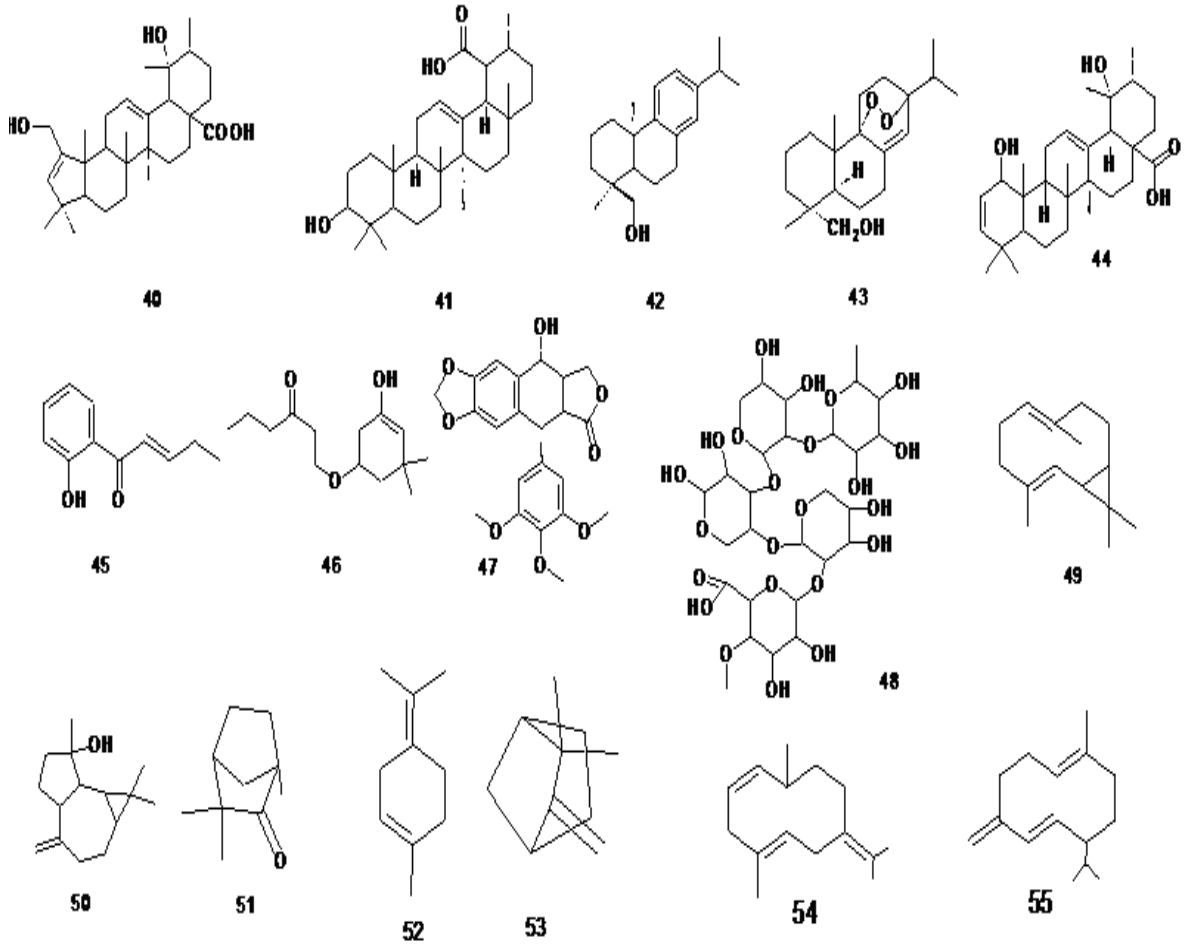

Figure - III: Structures of Phytoconstituents of Hyptis suaveolens (40-55)

In another investigation, Chukwujekwu et al isolated an abietane-type diterpenoid endoperoxide, 13*α-epi*-dioxiabiet-8(14)-en-18-ol (*43*) through bioactivity-guided fractionation of the petroleum ether extract of the leaves of *Hyptis suaveolens* which differs only in the substitution of the endoperoxide group on the aromatic ring of Dehydroabietinol (*42*). [24]During recent investigation (Raja et al, 2005) two novel compounds were isolated from *Hyptis suaveolens* and identified as (2E)-1-(2-Hydroxyphenyl) pent-2-en-1one (*45*) and 1-[(3-Hydroxy-5, 5-dimethyl cyclohex-3en-1yl) oxy] Hexane-3-one (*46*). [42]Very recent systematic study (Lautie et al, 2008) using LC-MS of *H. suaveolens* extract, showed the ion peaks similar to those of podophyllotoxin and ^{1}HNMR spectroscopy signal led to the discovery of podophyllotoxin (*47*).[44]

4. PHARMACOLOGICAL EFFECTS

Although biological attributes of the plant have not been well documented but *Hyptis suaveolens* has good medicinal value due to the presence of essential oils, alkaloids, flavonoids, phenols, saponins, terpenes, and sterols. In traditional System of Medicine, the plant was used as a stimulant, carminative, for wounds, sudorific, lactogogue, in catarrhal condition, infection of uterus, parasitic skin diseases. It was also used as an anthelmintic.[9, 46] The leaves are applied as insectifuge because of its strong aroma especially against mosquitoes. A leaf poultice is applied to cancers and tumours in the America.[55]Leaf sap of *H. suaveolens*with lemon juice is taken in Sierra Leone for stomach ache and the leaf is applied around the head for head ache or topically to maturate boils. [6]

4.1. Antimicrobial activity

The antibacterial activity of *H. suaveolens* volatile oil was tested against various kinds of bacteria and fungi that caused dermatological diseases. It was reported that the volatile oil from *H. suaveolens*inhibits certain bacteria and fungi.[27]

Another study provedthat the essential oil of *Hyptis suaveolens* leaves showed antibacterial activity at 5 mg/ml concentration against two gram-positive and four gram-negative bacteria.[28] Various extracts from *Hyptis suaveolens* leaves were evaluated for their antimicrobial activity in vitro. Steam distillation extract exhibited broad-spectrum antibacterial against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Micrococcus luteus* and antifungal activity against *Fusarium oxysporum*, *Aspergillus niger*, *Helminthosporium oryzae*. It showed highest antifungal and antibacterial activity against *Aspergillus niger* and *Micrococcus luteus*, respectively. Activity indices of *Aspergillus niger* against miconazole (25 µg/ml) and *Micrococcus luteus*against chloramphenicol (10 µg/ml) were 0.89 and 0.67, respectively.[29] Iwu et al observed that essential oil of *H. suaveolens* displayed good antimicrobial activity against yeast, filamentous fungi and showed a mild inhibitory effect on *Candida albicans* and *Aspergillus nigers*.[10] The hydro distilled essential oil of fresh leaves of wild *Hyptis suaveolens* exhibited significant antimicrobial activity against *Mucor* sp. when compared to ketoconazole.[15] However when antimicrobial activity of *H. suaveolens* was compared to *A. galangal*, *H. suaveolens* was found to have the MID values of 1:160, 1:160, 1:80, 1:20, 1:20, 1:80, 1:80 against *Staphylococcus aureus, Streptococcus suis, Erysipelothrix husiopathiac, Pseudomonas aeruginosa, Escherichia coli, Pasteurella multocida and Actinomyce pyogenes*, respectively.[30]Antifungal studies of leaves of *Hyptis sauveolens* Poit. confirms that 95% ethanol extracts (2.39% w/w) were known to have antifungal activity.[31]It was also documented that the antifungal potential of *H. suaveolens* oil was more pronounced than its antibacterial properties. The same study reported that inhibition of fungal growth was dose dependent with a MID value of 1:640. The 20% ethanolic solution of *H. suaveolens* oil had antifungal power similar to 6% boric acid, 2% benzoic acid, or 5% salicylic acid but higher than 4% phenol. The activity decreased when the oil was stored at high temperatures (>40°c). The oil inhibits the growth of all test microorganisms, albeit at different concentrations. By comparison, it was found to have more potent activity in antifungal than antibacterial action. The oil was less active against gram negative bacteria, particularly *P. aeruginosa* and *E. coli*, while it showed good results against gram positive bacteria. This might be due to the protection of the gram negative bacteria by a hydrophilic outer membrane which could suppress the passage of the lipophilic essential oil.[27]

4.2 Analgesic, anti-inflammatory and wound healing activity

The anti-inflammatory activity of the two compounds namely suaveolol and methyl suaveolate was tested for the first time as inhibition of croton oil-induced dermatitis of the mouse ear. These two compounds showed nearly the same dose-dependent topical anti-inflammatory activity; only two to three times lower than that of the reference drug indomethacin. The anti-inflammatory properties of these compounds could contribute to the antiphlogistic (Reducing inflammation or fever) activity of extracts of *Hyptis* species and confirm the rational use of *Hyptis suaveolens* extracts.[32]The ethanolic extract of *Hyptis suaveolens* was tested to study the effects on the inflammatory reaction, using the technique of Carageenan induced paw edema in albino rats. The extract showed significant anti-inflammatory activity comparable to the reference standard Ibuprofen. Antioxidant investigations of the ethanol extract along with its fraction using nitric oxide induced free radical assay methods showed good free radical scavenging activity thereby supporting its anti-inflammatory properties.[31]Shirwaikar et al evaluated *Hyptis suaveolens* for its wound healing activity in ether-anaesthetized Wistar rats at doses of 400 and 800 mg/kg using incision, excision, and dead space wound model. Significant increase in skin breaking strength, granuloma breaking strength, wound contraction, hydroxyproline content, dry granuloma weight and decrease in epithelization period was observed. However the enhanced wound healing activity may be due to free radical scavenging action of the plant and enhanced level of antioxidant enzymes in granuloma tissue. Better collagenation may be because of improved antioxidant studies.[50] Anti-nociceptive property of aqueous extract of *Hyptis suaveolens* leaves was studied using both chemical and thermal models of nociception in mice. After oral administration of aqueous extract (100, 200, and 400 mg/kg) writhing induced by acetic acid decreased licking activity of the early phase in formalin test and increased the reaction time in hot-plate test.[51]

4.3 Anti-oxidant activity

In view of antioxidant activity, a supportive study was done on granuloma tissue to estimate the levels of catalase and superoxide dismutase. Significant increase in the level of these antioxidant enzymes was recorded. Granuloma tissue was subjected to histopathological examination to determine the pattern of lay-down for collagen using Van Gieson and Masson Trichrome stains.[48] The antioxidant activity of the essential oils was determined by

using two complementary methods: 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay and 2, 2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) free radical decolourization assay. Results indicated that the essential oil of *H. suaveolens* have IC_{50} (µg/ml) values of 3721±0.019.[28] The antioxidant activity of aqueous extract the *Hyptis suaveolens* was determined by mean of the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging test. The results were again in favour that *H. Suaveolens* exhibit strong antioxidant radical scavenging activity with IC_{50} value of 100µg/ml. The antioxidant activity of aqueous extract could be due to the presence of flavonoids.[48] Nantitanon et al examined *Hyptis suaveolens* for its antioxidant by means of the DPPH radical scavenging test and ABTS free radical decolourization assay. In both methods the antioxidant activity of *H. suaveolens* was dependent on time and concentration showed IC_{50} value of 3.72 mg/ml whereas the TEAC value determined by the ABTS assay was 65.02 µM/mg.[49] In another study, the antioxidant activity of the methanol extracts of the leaves of *Hyptis suaveolens* Poit. was reported to exhibit strong antioxidant radical scavenging activity with IC_{50} value of 14.04 µg/Las compared to 0.4 and 1.15 μgmL^{-1} for Gallic acid, BHA respectively. This observation of antioxidant potential of methanolic extract expected due to the presence of flavonoids.[52]

4.4. Antiplasmodial activity

Hyptis suaveolens, widely used in traditional medicine for malarial treatment and increased interest ledto the identification of theconstituent responsible for this activity.[56] Dehydroabietinol isolated from *Hyptis suaveolens* (L.) Poit. was found to inhibit growth of chloroquine-sensitive as well as chloroquine-resistant strains of *Plasmodium falciparum* cultivated in erythrocytes *in vitro* (IC_{50} 26 - 27 µM). However, erythrocytes exposed to dehydroabietinol were transformed in a dose-dependent manner towards spherostomatocytic forms with concomitant formation of endovesicles, as disclosed by transmission electron microscopy.[23] Later petroleum ether extract of the leaves of *Hyptis suaveolens* was found to restrain an abietane-type diterpenoid endoperoxide known as 13*α*-epi-dioxiabiet-8(14)-en-18-ol which on further investigation displayed an elevated antiplasmodial activity with an IC_{50} of 0.1µg/ml. The antiplasmodial constituent dehydroabietinol of *Hyptis suaveolens* showed its activity due to transformation of discocytes into stomatocytes.[24]

4.5. Antiulcer activity and Gastroprotective Activity

Antiulcer activity of aqueous (500 mg/kg) and ethanolic extract (500 mg/kg) of the *Hyptis suaveolens* was evaluated on Cysteamine hydrochloride (450 mg/kg) induced gastric and duodenal ulceration. The aqueous extract of the plant *Hyptis suaveolens* showed potent activity than ethanolic extract, concluding that the plant *Hyptis suaveolens* increases healing of duodenal ulceration and prevents the development of experimentally induced duodenal ulceration in rats.[45] Vera-Arzave et al 2012 reported that suaveolol isolated from hexane extract showed gastroprotective activity at doses between 10 and 100 mg/kg.[57]

4.6. Antifertility activity

The anti-fertility effects of the petroleum ether, alcohol, and aqueous extracts of *Hyptis suaveolens* were studied in pregnant rats. The alcoholic extracts of *Hyptis suaveolens* (leaves) showed a 100 % anti-fertility action at doses of 150 mg/kg and 125 mg/kg, respectively. Further research is in progress to determine the stage of gestation at which *Hyptis suaveolens* is most effective.[34]

4.7. Immunomodulatory activity

The alcoholic extract of *H. suaveolens* possesses immunomodulatory as well as anti-oxidant property, and the latter property may be responsible for the amelioration of the immunosuppressant effect of pyrogallol.[35] A recent investigation, done by Jain et al, reported that the dried alcoholic (90%) extract of the aerial parts of *H. suaveolens* not only prevented the pyrogallol induced suppression of Humoral Immune Response (HIR) and Cell mediated Immune Response (CMIR) but also prevented the rise in Lipid peroxidase enzyme (LPO) levels, when administered orally (75 mg/kg for 28 days), to the group of mice with artificially induced immune suppression and oxidative stress using pyrogallol (50 mg/kg for 05 days). However, the immunomodulatory activity of *H. suaveolens* has been attributed to their anti-oxidant properties confirmed by TBARS (Thiobarbiturate Acid Reactive Substance) method.[53]

4.8. Anti-diabetic activity

The anti-diabetic study of the extracts in alloxan-induced diabetic rats, showed significant ($p<0.05$) reduction in the blood glucose concentration and the result tends to suggest that the methanolic extract of *H. suaveolens* leaves possess anti-diabetic activity in alloxan-induced diabetic rats.[54]

4.9. Miscellaneous

A current study showed evidence that the pharmacologically active substance(s) present in ethanolic extract of *Hyptis suaveolens* possess anti-diarrhoeal effect. The effect of plant extract a higher dose of 500 mg/kg was comparable to the effect of standard anti-motility drug loperamide at a dose of 50 mg/kg.[58]Hydro-distillate of *Hyptis suaveolens* leaves was evaluated for its acaricidal potency in ruminants. The essential oil, with strong aroma, was 100% and 98% effective *in vitro* and *in vivo* respectively on single application. Engorged female ticks failed to oviposit upon treatment. The adult and nymphal stages of ticks of *Hyalomma* sp., *Rhipicephalus* sp. and *Haemophysalis* sp. were found to be highly susceptible to the steam distillate, favouring its use as acaricide.**[34, 36]**

5. TOXICITY

The ethanolic extract of *Hyptis suaveolens* was examined for itstoxicity effect on the larvae of the yellow fever mosquito *Aedes aegypti*. Eight graded concentrations of: 0.9 ppm, 0.8 ppm, 0.7 ppm, 0.6 ppm, 0.5 ppm, 0.4 ppm, 0.3ppm and 0.2 ppm of plant extract weretested on the larvae. The mean lethal dose LD_{10} was 0.01ppm while LD_{50} was 0.60 ppm and LD_{90} was 1.45 ppm. LD_{10} for the control was 0.65 ppm, LD_{50} 0.9 ppm and LD_{90} 2.0 ppm. The extract caused high mortality rate on the larvae at concentrations of 0.9ppm (80%) and 0.3ppm (80%).**[35]** Ethanolic extract from whole plants of *Hyptis suaveolens* was screened using the brine shrimp lethality test. The extract was found to possess significant toxicity against brine shrimps with LD_{50} value of 0.914 ppm at 99% confidence level. The result suggests the presence of highly active, bioactive compounds and requires further examination for detection of specific pharmacological properties. Repeated-dose dermal toxicity 28-day study of *H. suaveolens* cream in various concentrations (3%, 10% and 30%) revealed that *H. suaveolens* cream in the concentrations of 3% and 10% produces no toxic effect. Further investigation should be carried out to obtain more information on the effect of 30% cream.**[36]** Preliminary study showed no animal death during acute toxicity test with doses up to 5 g/kg (p.o.).**[51]**

6. CONCLUSION

This review delivers a widespread assessment of indigenousmedical uses, phytochemical components and an insight on its pharmacological expansions for its use as a therapeutic plant. However the plant has been specifically considered for its antimicrobial, analgesic, anti-inflammatory, wound healing activity and antioxidant properties. Due to presence of wide range of phytochemicals viz. alkaloids, flavonoids, phenols, saponins, terpenes, and sterols also it may be further evaluated for other therapeutic potential such as antiviral and chemopreventive use along with its toxicological profile.

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