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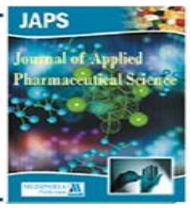

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Essential oil of *Lippia multiflora* Moldenke: A review

Kunle Oluyemisi Folashade and Egharevba Henry Omoregie

ABSTRACT

Lippia multiflora Moldenke is a tropical to subtropical herbaceous aromatic plant widely distributed throughout tropical Africa, South and Central American countries. It has been traditionally used in various communities for different purposes ranging from therapeutic febrifuge in form of tea and fumigants to non-therapeutic drink for relaxation and sedation, and as well as condiments. Of most economic and scientific importance is the essential oil in the aerial part of the plant, the "lippia oil". The therapeutic properties of the plant are largely attributed by researchers to the oil. This review is aimed at collating all the scientific data available on the oil and drawing attention to its chemical components, pharmacological activities and resources for industrial exploration and exploitation.

Keywords: *Lippia multiflora,* **essential oil, monoterpenes, sesquiterpenes.**

Kunle Oluyemisi Folashade and Egharevba Henry Omoregie
National Institute for Pharmaceutical Research and Development (NIPRD), Abuja, Nigeria.

For Correspondence
Kunle O.F.
National Institute for Pharmaceutical Research and Development (NIPRD), Abuja, Nigeria.
Tel. +234-803-314-5116

INTRODUCTION

Lippia multiflora Moldenke also known as *Lippia adoensis* Hochst is a herbaceous plant of the genus *Lippia.* It belongs to the family Verbanaceae, which is composed of 41 genera with approximately 220 species of herbs, shrubs and small trees (Evans, 1989; Jigam *et al.,* 2009; Owolabi *et al*., 2009). *L. multiflora* is a stout woody, perennial and aromatic shrub mainly distributed throughout tropical Africa, South and Central American countries (Pascual *et al*., 2001). It occurs in a wide ecological range throughout West Africa. In undisturbed sites, the plant can grow to a height of 2.7 to 4.0 m bearing large oblong-lanceolate bluish-green leaves (Ameyaw, 2009). The plant flowers from September to November and fruits in January. It possesses white, sweet-scented flowers stalked on cone-like heads in a terminal panicle nearly 120 mm long (Irvine, 1961; Acquaye *et al.*, 2001; Munir, 1993; Kunle, 2000). In Northern Nigeria, *L. multiflora* is commonly found along river beds. It is called bush tea, healer herb, Bunsurun fadama or 'godon kada' (Hausa) (Kunle, 2000). The Yoruba names are 'Efinrin gogoro', 'Efinrin odan' or 'Efinrin Ajase' according to the specific area (Adjanohoun *et al*., 1991; Owolabi *et al*., 2009). The distribution range of *Lippia multiflora* has its major concentrations in Guinea Savannah, Forest Savannah and Transitional and Coastal Savannah zones (Acquaye *et al*, 2001). This plant is commonly known as Lippia tea and commercially known as "Gambian Tea Bush" "Bush Tea", and "Healer Herb" (Irvine, 1961; Acquaye *et al*, 2001). Other species of Lippia which have been worked on include *L. turbinata* and *L. polystachya* from Argentina (Gleiser *et al*., 2007), *L. javanica (*Manenzhe *et al*., 2004), *L. origanoides* HB&K., known in Brazil as "Salva-de-Marajó" (Oliveira *et al*., 2007), *L. chevalieri* Moldenke (Mevy *et al*., 2007). *L. sidoides* Cham popularly

known as "*Alecrim-pimenta*" in Brazil (Botelho *et al.*, 2007), *L. americana*, *L. rugosa* A. Chev, *L. savoryi* Meikle, *L. citriodora* HB&K., *L. nodiflora* Rich, *L. micromera* Schauer, *L. junelliana*, *L. turbinate* (Hutchinson and Dalziel, 1963), *L. scaberrina* Sond (Watt and Breyer-Brandwijk, 1962). *L. grata*, *L. alba* (Mill.) N. E. Brown (Hennbelle *et al*., 2006), *L. glandulosa* schauer (Maia *et al*., 2005), *L. graveolens* from Mexico. Though, most of *Lippia multiflora* is collected from the wild, it is still being cultivated using the seeds and stem cuttings. A recent study has shown that the stem and root cutting mode of cultivation is more effective than using the apical meristem in the presence of exogenous hormones which are growth regulator hormones (Ameyaw, 2009). Estimated fresh leaf yield varies from 5 to 15 metric tons/hectare, corresponding to dry yield of 1.5 to 4.5 tons/hectare (Acquaye *et al*., 2001). Hence, a reliable supply of the product can be maintained with the cultivation of the plant and good management of the existing wild populations. Drying techniques are handled in a similar manner as with other aromatic plants, with care for the leaves not to touch the ground to minimize microbial contamination (UNIDO-ICS-MAP, Acquaye *et al.*, 2001).

Ethno-medicinal uses of *L. multiflora*

The *Lippia* species have a long history of traditional medicinal application some of which have scientific validation. They are mostly used in the treatment of respiratory and gastro-intestinal disorders. Additionally, they exhibit anti-malarial, spasmolitic, sedative, hypotensive and anti-inflammatory activities (Chanh *et al*., 1988a, 1988b; Abena *et al*., 1998; Jigam *et al*., 2009). *L. multiflora* has been used in many traditional and herbal medicines to treat bronchial inflammation, malaria fever, conjunctivitis, gastro-intestinal disturbance, enteritis, coughs and colds (Pascual *et al*., 2001), and possesses hypotensive, fatigue-relieving, and diuretic properties (Kanco *et al*., 2004). Some rural dwellers cook the herbs and use it to relieve stress and enhance sleep (Etou-Ossibi *et al*., 2005). Traditionally, *L. multiflora* has been used as a substitute for tea and as a mouth disinfectant (Menut *et al*., 1993). The leaves are used by different tribes as a hot beverage. Tea-like infusions are used as remedy against malaria fever, stress, hypertension, conjunctivitis, veneral diseases and as a laxative. In Nigeria, the leaves are used for constipation and as a febrifuge (antipyretic). *L. multiflora* tea is commonly consumed in Northern Nigeria as remedy for malaria fever. In Ghana an infusion of sun-dried leaves is consumed as tea with sugar or honey for stomach ailments (Irvine, 1961; Oladimeji *et al*., 2000; Acquaye *et al*., 2001). Villagers in West African rural communities drink Lippia tea after a day's hard work to relax and enhance sleep while in urban areas the tea is drunk in the mornings to relieve stress and relax for the upcoming day. The tea is also used traditionally against hypertension, conjunctivitis, treating venereal diseases and as a laxative (Acquaye *et al*, 2001). The leaves, boiled with palm nut and then made into a drink, help evacuate post-delivery placenta. It is a common children's remedy for fever and constipation accompanied by a light purge and is also used for common colds and chest complaints. The leaf infusion is used as a sudorific (diaphoretic) febrifuge. It forms part of various complex plant recipes for the treatments of sleeping sickness especially for severe jaundice. A leaf decoction is used in Guinea for fumigation and bathing and as a hot application for ear troubles (Irvine, 1961). In Gambia, local beehives are smoked with this fragrant plant to attract settling of bees (Kunle, 2000).

The root ashes are occasionally used as kitchen salt in upper Ubangi (Irvine, 1961). The medicinal property of this plant is believed to be mainly due to the presence of an oil of mint and camphor which yields levogyric camphor. Like many other oil-yielding plants, it is used for rhino-pharyngeal, mouth, and eye-troubles, the leaf juice being applied in eye or nasal drops as required (Irvine, 1961). Most of these effects have been attributed to the glycosides, essential oils and other phytochemical components of *Lippia* (Valentin *et al*., 1995; Terblanche and Korneliies, 1996; Taubi *et al*., 1997). It is however worthy of note that there are several reports in literature corroborating some of these claims in ethno-medicinal use.

Secondary metabolites of *L. multiflora*

Some researchers have reported several known compounds and secondary metabolites in the plant. Such metabolites which are known to belong to special classes of organic compounds that possess potent pharmacological activities and have been reported in literature include, essential oils, lignins, cellulose, tannins, starch, oxalates, flavonoids, saponin glycosides, peptides, caffeine, terpenes and alkaloids (Kunle *et al.*, 2002; Kunle *et al.*, 2003; Jigam *et al*., 2009). However, very few of these compounds have been isolated and characterised from the plant.

THE ESSENTIAL OIL OF *LIPPIA MULTIFLORA*

L. multiflora has long been known as an essential oil yielding plant (Irvine, 1961). Phytochemical studies by several researchers have shown the presence of essential or volatile oil in the aerial part of *L. Multiflora*, which has been extracted and characterized by some workers using instrumental methods like hydrodistillation and Gas Chromatography-Mass Spectrometry (GCMS). Others have also used traditional classical methods of maceration in organic solvents to isolate the oil or components of the oil and then characterize by using GCMS and other spectrometric methods like Nuclear Magnetic Resonance (NMR) and Infra Red spectrometry (Oladimeji *et al*, 2000; Kunle, 2000; Owolabi *et al*., 2009; Jigam *et al*., 2009). The oil which is believed traditionally to possess some pharmaco-therapeutic activities has been widely studied by investigators in the field. Some of these pharmacological activities have been confirmed while others are still ongoing due to conflicting results by different researchers. However, it is widely reported that the lippia oil vary greatly in chemical composition and also to an extent in physical properties like refractive index and density, probably due to geographic factors and genetic makeup (Owolabi *et al*., 2009). The extent of the influence of these two factors on the physicochemical composition of the oil is yet to be scientifically investigated.

Physical properties

Report on the physical properties of the oil in literature is limited and vary widely. The variability is thought to be as a result of variation in chemical component due to geographical cultivation and other environmental and genetic factors (Owolabi *et al.*, 2009). However, the work of Oladimeji and co-workers, and Juliani and co-workers, in 2004 and 2008 respectively is encouraging. The two researchers worked on oils from Nigeria and Ghana respectively (Oladimeji *et al*., 2004; Juliani *et al*., 2008). The two researchers reported a widely varied yield for the oil. In a study of the seasonal variability of the oil yield from the plant in the authors' laboratory, it was revealed that the plant exhibits seasonal variability in its oil content between January and June with the highest yield of 1.57% in June (Kunle, 2000). Reports of physical parameters of the oil by various researchers in the field are shown in Table 1.

Chemical compositions

The essential oil of *L. multiflora* Moldenke which is typically yellow has been extracted and characterized by various workers. This may have been motivated by the very wide traditional use of the oil for both therapeutic and non-therapeutic purposes. The most exploited mode of oil extraction and characterization is hydrodistillation and GCMS respectively. Reports of studies from literature show that there exists a great degree of variability in the chemical composition of the oil which may have been due to a number of interacting factors such as ecological origin, environmental factors like stress (soil type, humidity, mechanical damage and cultures) as well as genetic factors (Owolabi *et al.*, 2009). This wide variability in the chemical composition of the oil calls for caution in the therapeutic and non-therapeutic (cosmetic, nutritive) application of the oil. Table 2 shows the composition of the essential oil of *L. multiflora* from the tropical regions of Africa as reported by some researchers.

Chemotypology

The lippia oil varies widely in components and composition although fairly stable in physical parameters like refractive index and density. The chemical composition has necessitated the classification of the oil into different chemotypes to guide its identification and application. Some chemotypes could clearly be seen along the monoterpenoid (rich in thymol and its derivatives, *ρ-cymene* and carvacrol) and sesquiterpenoid (rich in ipsdienone and ocimenone isomers) divide (Agnaniet *et al*., 2004). Another classification by Juliani and co-workers in 2008 put the analysed samples into five chemotypes namely, linalool(29%) and germacrene D(28%) rich oil, 1,8-cineole (43-47%) and sabinene (12-15%) rich oil, high farnesol (camphoraceous) rich oil, high sesquiterpenes (45-70%) rich oil and high monoterpenes rich oil (*ρ-cymene* 14-19%, thymol 30-40%, thymol acetate 14-17%) (Juliani *et al*., 2008). It is clear that the variation in chemical composition could be due to factors bordering on environmental stress and genetics. Other reports of classification based on chemotypes are shown in Table 3. It is recommended that researchers should explore the resolution of this chemotype variation from genetic constitution. A gene mapping of the geographical or regional species may be necessary to elucidate the chemical variation of the various chemotypes. However the wide variation in chemotype from within a close geographical area as reported in Ghana by Juliani and co-worker is a major challenge. A thorough chemotyping or standard identification criteria is necessary for industrial exploitation. Researchers could look at ratios of mono- to sesquiterpenoids, or 1,8-cineole or thymol to other major components like linalool or germacrene D. This review has attempted to create a chemotyping based on the level of major and frequently occurring components like 1,8-cineole, thymol, and farnesyl or sesquiterpenoids, etc, (Table 4). Only three chemotypes could be authenticated from the various reports.

Table.. 1: Physical Properties Of The Essential Oil Of Lippia Multiflora.

Parameters	**Country**			**Comments**
	Nigeria	**Ghana**	**Others notspecified**	
Colour	Yellow	light yellow, yellow, dark yellow, dark orange-yellow		Colour variation in Ghanaian species was according to product geo-source.
Yield	0.9-1.57%	ND	0.6%, 0.16% (dried plant material), 1.15%	Yield obtained by hydrodistillation
Weight/ml (g/ml)	0.8762 (at 28 °C), 0.914 (at 20 °C)	0.893 – 0.934		
Refractive index	1.468, 1.508	1.4695- 1.5043,	1.5010 at 28° C	
Optical rotation range	+46.55° to +57.60°			
Residue on evaporation	3.85 ± 0.96%			
pH	4.75, 4.60			
Kinematic viscosity	5.46 ± 0.02 cSt			
Surface tension	29.20 ± 0.04 dyn/cm at 28 °C.			
Solubility	80% ethanol.			
Volatility:	The oil is highly volatile above 37.7 °C.			
Freezing Point	ND			
Flash Point	ND			
Boiling Point	90-258 °C			
Acid value	4.63			
Ester value	1.4			
Ester value after acetylation	46.3			
Phenol content	25			

ND= Not determined

Table. 2: Chemical Composition Of The Essential Oil Of *Lippia Multiflora.*

COMPOUNDS	% COMPOSITION			
	1	**2**	**3**	**4**
1,8-cineole	38.7, 60.5	43-47	n	
Sabinene	16.9	12-15	n	
α-pinene	4.7, 4.4			1.2-7.8
β-pinene	13, t			
Linalool		29	n	0.9-5.0
α-terpineol	5.7, 14.1		n	
Terpinolene	t			
Thymol		30-40	41.9, n	27.4, 18.5, 46.3-78.1, 56.7
(Z)- tagetone			11.3, n	
(E)- tagetone			30.2, n	
Myrcene	3.6, 8.9, 1.9		n	
epoxymyrcene			70, n	
Myrtenol				
Limonene	0.7		n	
γ-terpinene	3.3, t		n	
Carvacrol	4.2		7.2	38.6, 16.7
trans-caryophylene	2.5			
(Z)-ocimenone			20.3, n	
(E)- ocimenone			n	
ipsdienone			54.6, n	
geranial			n	
Neral			n	
thymyl acetate		14-17	21.2, n	
ρ-cymene	t	14-19	9.8, n	21.1, 5.1-7.2
α-phellandrene			n	
Ipsenone			n	
Nerolidol			n	0.7-23.6
Geraniol			n	
(*E*)-caryophyllene	0.6		n	
β-caryophyllene			4.6	27, 30, 4.1-9.2, 17.3-59.4, n
Caryophyllene oxide				9, 1.9-6.0
β- farnesene	0.5		7.4, n	
Farnesol		↑		
germacrene D		28		15
γ-Muurolene	t			
Elemol				22
3-methyl-6-(1-methylethylidene)-cyclohex-2-en-1-one				n
2-phenyl-ethyl propionate				12.6
Elemene				33
Ethyl cinnamate				30.3
Amorphene				12.4
Carvone				n
α-thujone				n
verbascoside				n
isoverbascoside				n
α-humulene				2.6-6, n
trans-α-bergamotene				19.3
α-alaskene				3.4-16

1= Nigeria, 2= Ghana, 3= Other African Countries, 4= from other *Lippia spp*., ↑= high, n= reported present, t= trace.

Table. 3: Reported Chemotypes Of *L. Multiflora* Oil.

OIL CHEMOTYPE	DESCRIPTION OF COMPOSITION	SAMPLE SOURCE
Germacrene D rich	linalool (29%) and germacrene D (28%) rich oil	Ghana
1,8-cineole	1,8-cineole (43-47%) and sabinene (12-15%) rich oil	,,
Farnesol rich	high farnesol (camphoraceous) rich oil	,,
Farnesene	high sesquiterpenes (45-70%) rich oil	,,
Thymol	high monoterpenes rich oil (*ρ-cymene* 14-19%, thymol 30-40%, thymol acetate 14-17%)	,,
1,8-cineole rich	1,8-cineole (60.5%), sabinene (16.9%) ,α -terpineol (14.1%), α-pinene (4.4%)	Nigeria
Thymol dominated		,,
Geranial/neral rich		,,
Oil rich in farnesene		,,
Tagetone rich		,,
Epoxymyrcene		,,
Linalool		,,
Nerolidol		,,
ρ-cymene		,,
Myrtenol		,,
Farnesol		,,
Germacrene D		,,
Geraniol		,,
Geranial /neral-type		Togo
Thymol-type		,,
1,8-cineole-type	dominated by 1,8-cineole (63.2%) and Sabinene (13.3%)	,,

Neral/geranial-type		Ivory Coast
1,8-cineole/neral/geranial-type		,,
1,8-cineole-type	1,8-cineole (44.9-51.1%), sabinene (8-12.3%) and α-terpineol (3.1-9.2%)	,,
Linalool-type		,,

Table. 4: Harmonised Chemotypology Table.

Chemotypes	Description
1,8-cineole /sabinene rich	1,8-cineole (>40%), sabinene (>10%)
Thymol /ρ-cymene rich	Thymol + thymyl acetate (>30%), ρ-cymene (>14%)
Farnesol/Sesquiterpene rich	Farnesol + derivatives or total sesquiterpenes (caryophyllene, germacrene-D, humulene, elemene, etc) (>50%)

Pharmacological activities

It is widely believed by researchers that the therapeutic uses of *L. multiflora* plant is largely due to the essential oil contained in the plant (Pascual *et al*., 2001). Again, the traditional uses of the plant as tea or drink and scents to attract bees may have redirected research focus to the essential oil of the aerial part. Many researchers have reported various pharmacological properties of the plant extract and its essential oil. These reports have confirmed some of the traditional therapeutic uses of the plant. Some authors of these reports have also traced these pharmacological activities to some specific chemical constituents of the essential oil (Abena *et al*., 2001).

Safety studies

Various workers have reported some safety data on the leaf extract and oil of *L. multiflora*. A particular study showed that the leaf extract had a high safety level of LD_{50} = 3000 mg/kg body weight. A clinical toxicity study by the WHO-Collaborating Centre for Scientific Research into Plant Medicine (CSRPM), Mali, showed that there were no side effects or any toxicity in fifty people who had consumed the Lippia tea for over 25 years. However, it was reported that an overdose of the trial drug, 'Malarial', used for clinical trials in Mali gave a convulsive activity. 'Malarial' is made up of three herbs namely, *Cassia occidentalis, Lippia chevalieri*, and *Spilanthes oleracea*. 'Malarial' and its components have been shown to have antiplasmodial activity and used to treat the symptoms of malaria such as fever (Acquaye *et al*., 2001; ALNAP database, 2010; ICS-UNIDO-MAPs, 2010). A safety study conducted in rats also showed that the essential oil was not toxic at doses of ≤ 1 g/kg (Pelissier *et al*., 1994). A study of *Lippia multiflora* aqueous extract at different doses 200, 400, 600, 800, 1,000 and 1,200 mg/kg dissolved in 1 ml of NaCl 0.9%, administered by intraperitoneal or oral route, did not show any mortality in rats (Abena *et al*., 1998). It is interesting however to note that there have been no reported cases of adverse effects on the *L. multiflora* oil.

Analgesic and antipyretic properties

The analgesic and antipyretic properties of crude extract and essential oil of *L. multiflora* was reported by Abena and co-workers in 2001. Using classical methods, the workers were able to demonstrate that the crude extract and essential oil do not modify a spontaneous motor activity in wistar rats but caused a reduction of abdominal cramps induced by acetic acid. The results of their psychopharmacological work confirmed the tranquillizing and analgesic activities of *L. multiflora.* The work also suggested that the essential oil exhibited more analgesic activity than the crude extract while the crude extract was more effective as a muscle relaxant (Abena *et al*., 2001). In another study in 2003, Abena and co-worker again demonstrated the analgesic and anti-pyretic properties of the essential oil of *L. multiflora.* In this study, the essential oil produced by hydrodistillation was analyzed and studied for analgesic and antipyretic properties in rats and mice. The results showed significant dose-dependent analgesic effect on acetic acid-induced writhing in mice and antagonized hyperemia induced by brewer's yeast (Abena *et al*., 2003). This finding supports its traditional use as muscle relaxant, for fatigue and stress relieving and as a febrifuge.

Pediculocidal and Scabicidal properties

Oladimeji *et al*. (2000) reported the pediculocidal and scabicidal properties of the essential oil of *L. multiflora*. The essential oil from the leaves was tested for its pediculocidal and scabicidal activities against bodylice, headlice and scabies' mites. The 'knockdown' times obtained for bodylice and headlice using lippia oil preparations were comparatively shorter than those obtained using benzyl benzoate and Delvap Super®, a brand of dichlorvos. The lethal effect of the lippia oil on headlice was increased when applied in an enclosed system that prevented volatilization of the oil while allowing maximum contact of the vapour with the headlice. A 20% v/v preparation of lippia oil applied to scabietic subjects for 5 consecutive days gave 100% cure compared with 87.5% cure obtained for benzyl benzoate preparation of the same concentration. The lippia preparation also caused less skin irritation. These activities were attributed to the presence of terpineol and α- and β-pinene. These volatile components are known to be lethal to body and headlice (Oladimeji *et al*., 2000). In another study by Oladimeji *et al*. (2005), *L. multiflora oil* was demonstrated to be a more effective and safer scabicidal agent than benzyl benzoate. The researchers used two topical emulsion formulations (*Lippia* oil emulsions A and B), each containing 20% w/w of essential oil of *Lippia multiflora* (*Lippia* oil), and compared with benzyl benzoate emulsion BP using a randomized, double blind and group parallel studies. The percentage cure obtained for the *Lippia* oil emulsions (A and B) were about 50%, 80% and 80% on application for 3, 5

and 7 days, respectively, compared with 30%, 60% and 70% obtained for benzyl benzoate emulsion BP for the same treatment period. The study also reported six adverse effects for the *Lippia* oil emulsions, while 10 adverse effects were reported for benzyl benzoate emulsion BP. Essential oils have been known to be effective on skin problems including those indicative of deeper conditions like toxins infection, hormonal imbalance, nervous and emotional turbulence as well as infestation with lice, fleas, ticks, ants, mosquitoes, scabies and moths. Most infestations have been repelled by compounds found in essential oils such as terpenes, eugenol, camphor, methol, etc. (Lawless, 1995; Pearlstine, 2006). Hence the studies support the traditional use of the plant as a fumigant.

Antimicrobial properties

L. multiflora has been traditionally used to treat disease conditions like bronchial inflammation, veneral disease, malaria, conjunctivitis, gastro-intestinal disturbance, enteritis, etc., because of the perceived antimicrobial properties. Recent scientific investigations revealed that essential oil hydrodistilled from leaves of *L. multiflora* possess antimicrobial properties. In a study by Oladimeji *et al*. (2004), it was revealed that fungi were more susceptible to the lippia oil than bacteria, and Gram-positive bacteria were more susceptible than Gram-negative bacteria, with clinical isolates showing more resistance than type strains. This was in contrast to the findings of Bassole *et al.* (2003), who worked on 9 strains and reported that the Gram-negative bacteria were more susceptible. In another study commissioned in France and Côte d'Ivoire, the essential oil was reported to be highly active against isolated microorganisms (bacteria and fungi) of the buccal flora and thus supporting its traditional use in mouthwash in some communities (Pelissier *et al*., 1994). The antimicrobial activity of carvacrol and thymol, which were the major components of the oil has also been reported (Kunle *et al*., 2003; Botelho *et al*., 2007). In the work of Mevy *et al*. (2006), the oil exhibited strong inhibitory effect on the growth of *Staphylococcus aureus* and *Enterococcus hirae*, and a moderate effect was observed for *Candida albicans* and *Saccharomyces cerevisiae*. The report went further to suggest elemol, 1,8-cineole, camphor and *para*-cymene as the principal antimicrobial components of this oil.

Anti-inflammatory, anti-cancer and radical scavenging properties

Studies on anti-inflammatory activity of the oil showed that it did not have any effect on granuloma formation in rats and mice, but antagonized brewer's yeast induced hyperexia at a dose of 8 ml/kg (Abena *et al* 2003). However, the oil has been reported to have antioxidant and radical scavenging activity largely attributable to its phenolic components. The activity was significantly low for some chemotype and higher for others when compared to reference compounds like butylated hydroxyl toluene (BHT), α-tocopherol, thymol and carvacrol (Agnaniet *et al*., 2004; Avlessi *et al*., 2005; Mevy *et al*., 2006). A study of the leaf extract of the plant showed a significant antioxidant activity comparable to Trolox (a prologue of vitamin E). The study also demonstrated that the antioxidant activity of one gram of *Lippia multiflora* leaf is equivalent to 2.7-12.4 g of Trolox (Juliani *et al.*, 2006). In another study on the effect of *L. multiflora* leaf extract in egg albumin-induced paw oedema in rats, the oedema was found to be greatly suppressed irrespective of the dose level of extract used and was comparable to the standard acetyl salicylic acid (ASA) treatment (Jigam *et al.*, 2009).

Antimalarial properties

In an in vitro antimalarial study by Valentin *et al.* (1995), the oil of *L. multiflora* was found to be active against cultures of *Plasmodium falciparum* (FcB1-Columbia chloroquine-resistant strain and F32-Tanzania chloroquine-sensitive strain) parasite. The dilutions inhibiting the *in vitro* growth of the parasite by 50%, 24 and 72 hr after administration of the essential oil to the parasite culture were 1/12000 and 1/21000, respectively. When tested on a highly synchronized culture, the essential oil inhibited growth mostly at the trophozoite-schizont step, indicating a potential effect on the first nuclear division of the parasite (Valentin *et al*., 1995). The oil from Burkina Faso has also been shown to exhibit larvicidal and viscidal activities against eggs of *Anopheles gambiae* and *Anopheles aegypti* larvae. In the study, *L. multiflora* oil was found to be more active than the oils obtained from *Cymbopogum proximus* and *Ocimum canum* (Bassole *et al*., 2003). Though these research findings tend to support its ethnomedicinal use as an antimalarial, its use as an antimalarial therapeutic drug has not been successful on clinical trial studies. There have been two clinical trials conducted on the efficacy of 'Malarial', in Mali. In the first trial, the higher levels of *Plasmodium* spp. dropped to low levels after day 3, but then increased in the following week and did not drop again. In the second clinical trial, levels of *Plasmodium* spp. dropped to very low levels after day 3, then increased slightly, but remained considerably lower than initial values for the remaining 21 days of the study. Research is still being conducted to understand why the Plasmodium levels rise (UNIDO-ICS-MAP and Diallo *et al*., 2004).

Hypotensive property

The traditional use of *L. multiflora* as a hypotensive and muscle relaxant agent, and the vascular properties of its aqueous extract have been confirmed by researchers (Noamesi, 1977, Noamesi *et al*., 1985a and b; Chanh *et al*., 1988a; Mwangi, 1990 and Mwangi *et al*., 1992). In a particular study, the effects of the total phenolic extract from *L. multiflora* leaves (TPLi) and of its second main component (Verbascoside) called (Lil) on TXA2 biosynthesis were investigated. The total phenolic extract and Lil both inhibited TXA2 biosynthesis. Their action was dose-related, Lil being more potent. The study of regression curves representing the hypotensive action and the anti-thromboxane synthetase activity versus log (dose) of TPLi and Lil suggested that Lil may likely be responsible for the TPLi hypotensive action. Its antithromboxane synthetase activity could be considered as a major contributor to the mechanism of this effect (Chanh *et al*., 1988b).

RESOURCE AND PROSPECTS

More than 42 volatile components have been characterized as constituents of *L. multiflora* oil and over 126 volatile components from the *Lippia* specie (Maia *et al*., 2005). Most of these compounds are basically mono- and sesquiterpenoids. Monoterpene and sesquiterpene hydrocarbons and some oxygenated monoterpenes like 1,8-cineole and linalool are every typical of essential oils (Ekundayo, 1989).

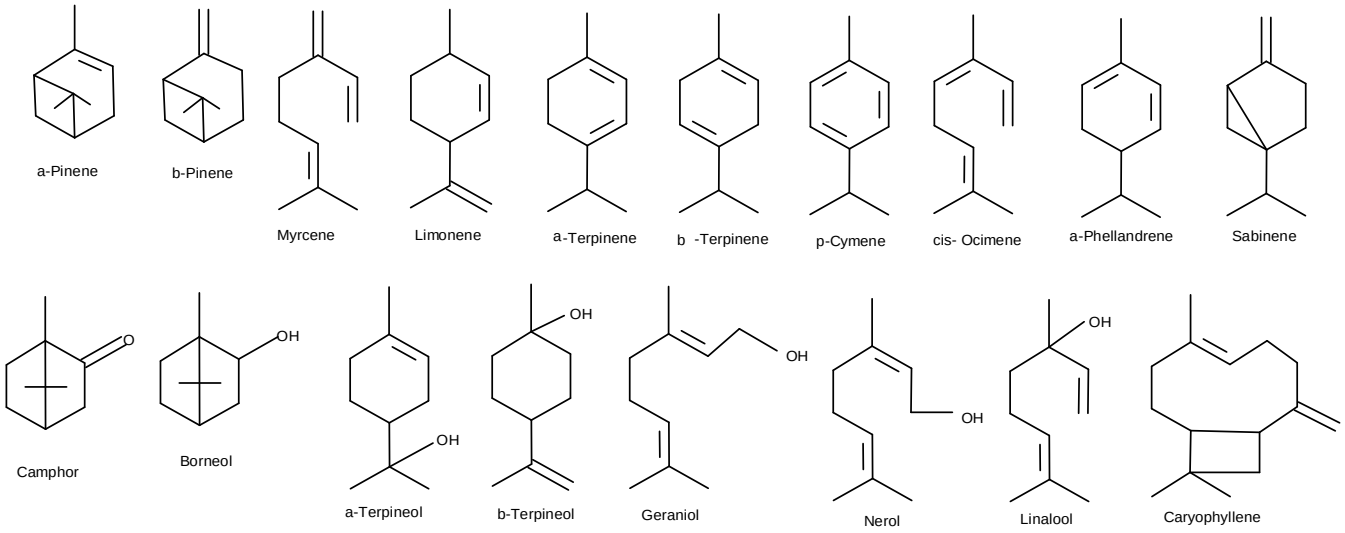
Although the plant leaf is being packaged in Mali, as 'Malarial', and also widely used traditionally as febrifuge and tea, there seems to be no reported case of commercial or economic exploitation of the lippia oil itself. An oil yield of between 0.16 to 1.15% from the aerial part of *L. multiflora* has been reported in literature. A study from the author' laboratory shows a seasonal variation of yield ranging from 0.9-1.57% between January and June (Kunle, 2000). Though the yield is generally less than the approximate 2% obtainable for most essential oil yielding plants, it could still be exploited for economic gains through process optimization as some useful chemical components have been reported in high yield in this oil (Kunle 2000, Owolabi *et al*., 2009; Evan, 2002). The predominantly thymol-containing oil can be a substitute for thymol oil from thyme plant, *Thymus vulgaris*, while the predominatly cineole-rich oil can be a substitute for oil from *Eucalyptus globulus.* The oil can also be a source of pinene which could be used for the production of camphor. The plant's traditional use to smoke beehive in order to attract bees must be due to its fragrance from the essential oil components. It is well known that most organoleptic properties of essential oils are usually due to the oxygenated components which are high in some of the chemotypes of lippia oil. Hence this oil may be ideal material for odour or fragrance fixture in toiletries, perfumery and ointments (Ekundayo, 1988; Evans, 2002). Lippia oil could be a good pharmaceutical raw material for fumigants, disinfectants, antiseptics and expectorants, due to the presence of monoterpenes like thymol, cineole, pinene, myrcene, cymene, etc, in considerable amount in the oil.

These components are known to possess potent antimicrobial and antispasmodic activities (Mwangi *et al*., 1992; Addea-Mensah, 1992). The economic prospect of the exploitation of lippia oil appears largely viable if well investigated and optimized. More work should be done in standardizing the chemotyping criteria and processes. Most of the studies currently ongoing are on wild variant of the plant and efforts should be made at developing cultivated species to improve yield of selected chemical components in order to effectively undertake economic scale cultivation.

CONCLUSION

A lot still needs to be done in the area of investigating the pharmacologic activities of the oil. There is the need to identify the active compound(s) in the extracted oil responsible for the various pharmacologic activities exhibited. This will help in specific therapeutic application of the oil. There is also the need for exhaustive characterization of all the compounds in a given oil extract as this will help in a more accurate chemotyping. Chemotyping could be more meaningful and accurate if the sample size and geographical coverage are enlarged while also noting the ecosystem (including soil type, climate/weather condition, season, etc) and time of collection of cultivated or wild growth. There is the need to also match the various chemotypes with the level and type of pharmacologic activities displayed. For instance, oil richer in carvacrol may display more antimicrobial activity than oil low in carvacrol. Finally, the oil presents great potential as an alternative or good source of some of the monoterpenes and sesquiterpenes of industrial importance. Such terpenoids like carvacrol, thymol and its derivatives, linalool, germacrene D, farnesol, cineol, pinenes, etc, could be extracted in commercial quantity from the oil if the process is optimized. Lippia oil is indeed an under-exploited economic resource that scientists and industrialists could take advantage of as alternative source of raw material.

COMPOUNDS FROM ESSENTAIL OILS OF LIPPIA SPECIES



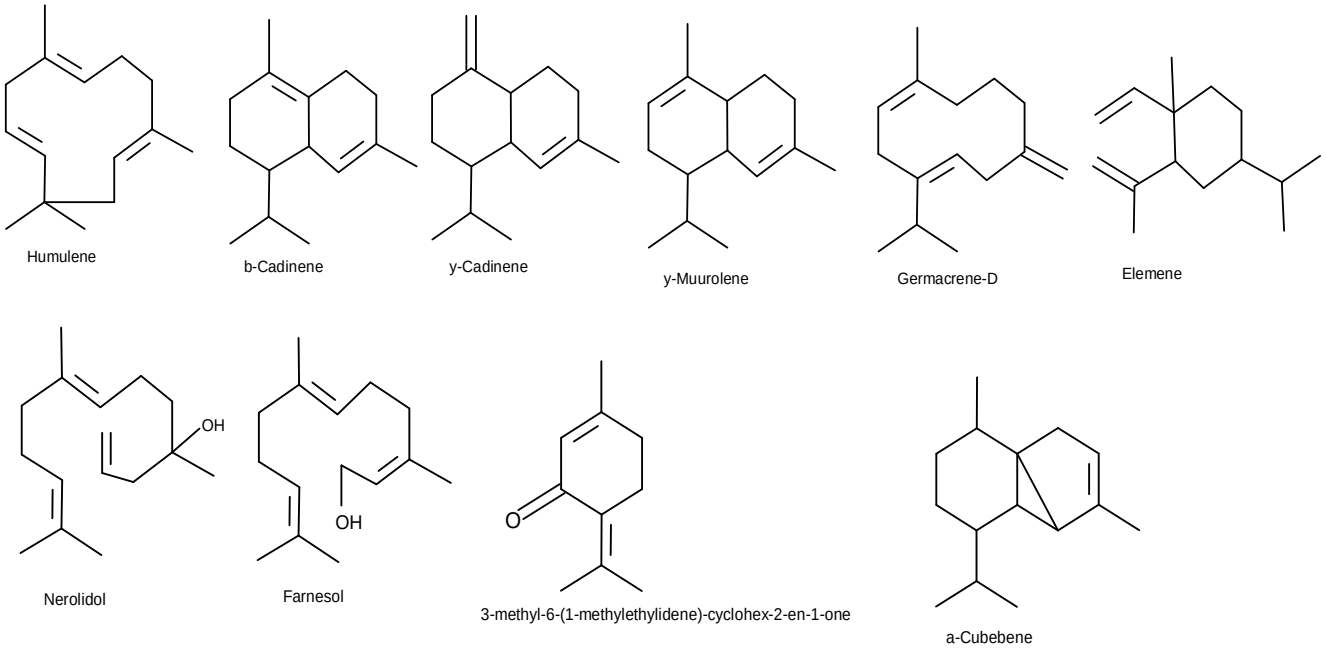


Fig. 1: Selected Compounds from the essential oils of some Lippia species.

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