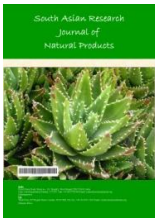

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Literature Review on the Phytochemistry and Pharmaco-Biological, Nutritional and Cosmetic Properties of *Lippia multiflora* and New Research Perspectives

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: *Lippia multiflora* is a wild/spontaneous food plant with numerous pharmaco-therapeutic activities and rich in terpenic and phenolic bioactive compounds whose valorization as nutaceutical can help a better management of chronic diseases.

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Objective: To make an inventory of the current knowledge on the plant in order to direct the future research in the hypothesis that this plant contains chemical groups which would act either individually or in synergy, in order to confer several properties to him of which the anti-sickle cell activity.
Methodology: A non-exhaustive bibliographic search for articles published on the plant was conducted in several electronic databases (Science Direct, PubMed, Web of Science, Scopus, Google scholar, SciELO, etc.) using as search strategy the following keywords: *Lippia multiflora*, phytochemistry, pharmacology and toxicology.
Results and discussion: It appears from this study that the chemical composition of the essential oil is variable within the species *L. multiflora*. These chemical varieties also called chemotypes are endowed with numerous pharmacological properties (antifree radical, antibacterial, antiinflammatory, antiproliferative, hypotensive, antimalarial, antifungal activities, etc.). This plant also contains anti-sickle cell phytomarkers such as ursolic acid (a triterpene acid) and verbascoside (a phenolic compound). *L. multiflora* reduces oxidative stress by increasing the content of reduced glutathione (essential for the protection of erythrocytes) and nitric oxide (vasodilator effect).
Conclusion and perspectives: The results of this literature review show that in addition to its numerous documented biological properties, *L. multiflora* also reduces oxidative stress by increasing the content of glutathione and nitric oxide and can thus relieve sickle cell disease. However, the anti-sickle cell activity of this plant species has not yet been scientifically validated although the plant is used in the treatment of anemia in Traditional Medicine. Therefore, it is desirable that a more thorough study be carried out on *L. multiflora* in order to determine the different chemotypes from the Democratic Republic of Congo (DRC) and then to evaluate the anti-sickling, antihemolytic and anti-radical activities and the effect of these chemotypes on the osmotic fragility of sickle cell erythrocytes.

Keywords: Traditional medicine; scientific evidence; universal health coverage; Lippia multiflora; sickle cell disease; Democratic Republic of the Congo.

1. INTRODUCTION

The demographic explosion and the poverty that engulf the African continent constitute a major difficulty in accessing adequate primary health care treatments. Thus, to alleviate this situation, the use of Traditional Medicine is an appropriate strategy to address the problems posed. Medicinal plants are a vital resource for the majority of people living in Africa and are the main means by which individuals treat themselves [1, 2]. Indeed, according to the World Health Organization (WHO), more than 80% of the population in Africa resort to Traditional Medicine to solve the problem of Primary Health The use of medicinal plants for various health problems is not only a choice, but is also linked to extreme poverty and the high costs of synthetic drugs [3-5].

From the ethnobiological point of view, Africa, with its biological and cultural diversity, constitutes a reservoir of knowledge on medicinal plants. Thus, to perpetuate this ethnomedical knowledge, several works have been carried out on medicinal plants used as alicament in Africa and particularly in the Democratic Republic of Congo. Among these plants, we have in particular Lippia multiflora. Among these works, we can note those of Mutwale et al. [6] who showed that *L. multiflora* is endowed with antioxidant activity. This aromatic plant is consumed as an alicament in the Bandundu province of the Democratic Republic of the Congo (DRC) to treat konzo, a disease caused by oxidative stress. *L. multiflora* is native to Central and West Africa [7]. Phytochemical data show that it contains the various secondary metabolites such as glycosides, phenylethanoids [8], 1,8cineole, sabinene, linaalol, α- terpinol [9] and phenols [10]. Okhale et al. [11] and Pollyana et al., [12] showed that the essential oils of this plant contain chemotypes rich in mycenono, carvone, pipertenone, ipsenone, linanol, citral, carvacrol, thymol, lippiol, and ketone terpenoid.

In addition, several pharmacological data reveal that *L. multiflora* is endowed with various pharmacological properties such as anti-radical [6, 13, 14] and anti-inflammatory activities [13, 15].

In a recent study, it was also reported that this plant is also used in Congolese Traditional

Medicine to treat anemia, one form of which is sickle cell disease, a genetic disease endemic to tropical regions [16].

The aim of this literature review is to make an inventory of the current knowledge on *L. multiflora* in order to orient future research in the hypothesis that this plant contains chemical groups which would act either individually or in synergy, in order to confer several pharmaco-biological properties to it. Thus, Traditional Medicine based on scientific evidence can contribute to universal health coverage (UHC) in Africa in general and in the DRC in particular (access to health services without facing financial difficulties).

2. BOTANICAL DESCRIPTION

Lippia multiflora Moldenke (Verbenaceae) is a perennial plant that can reach 2.7 to 4 m in height. The stems of this wild food plant are angular, pubescent and branched at the ends. They bear large, bluish-green, oblong leaves, whorled in threes or fours, with a long cuneate base, acuminate apex, finely toothed margin and whitish pubescence. The plant *L. multiflora* has inflorescences in ombelliform, globular or cylindrical terminal spikes. The flowers are white and small in short cylindrical glomerules. These are wide (5 to 7 mm), long (5 mm to 2 cm) and are arranged in terminal colymbiform panicles. The fruit of *L. multiflora* has a dark yellow, sweet, edible fleshes in which are sheltered seeds [17].

3. PHYTOGEOGRAPHIC DISTRIBUTION

Soro et al. [7] reported that *Lippia multiflora* is native to Central and West Africa, possessing nutritional and pharmaco-therapeutic properties. Pascual et al. [18] reported in the literature that *L. multiflora* is widely distributed in South America, Central America and tropical Africa. In the DRC, it is found in the savanna ecosystems of Bandundu and Central Kongo.

This plant (Fig. 1) was introduced in the province of North-Ubangi by Professor Koto-te-Nyiwa Ngbolua.

Fig. 1. *Lippia multiflora*: A. A domesticated plant (Photo Ngbolua, 2019); B. A wild plant with flowers [17]

4. ETHNOBOTANICAL DATA

Among the Boo and Peulh peoples of Benin, *L. multiflora* is used in primary health care and as food (sauce, soup and tea). This plant is used in this region in the treatment of several diseases such as gastritis, fever, malaria, toothache, hypertension, injury, and physical weakness of the baby, itching and reduced lactation [19].

In Nigeria, Oladimeji et al. [20] showed that essential oils of *L. multiflora* have pediculocidal and scabicidal properties against body lice, head lice and scabies mites. In addition, the essential oils of *L. multiflora* inhibit scabies.

Okhale et al. [11] showed that the genus *Lippia* has about two hundred species with ethno-pharmacological applications and contain a myriad of biologically active compounds. In Côte d'Ivoire, *Lippia* tea is used as a medicinal tea and then as an insecticide (at low doses). The leaves of this plant are the most commonly used part [21]. Ethnobotanical surveys conducted in western DRC have shown that *L. multiflora* treats erectile dysfunction [22]. In another study conducted in the DRC, it was reported that the leaves stems, inflorescences, barks and roots are used in Kinshasa to treat 18 diseases including asthma, sexual weakness, gastritis, stomach ache, malaria, diabetes, eye pain, generalized pain, hemorrhoids, inflammation, yellow fever, high blood pressure, urinary tract infections, angina, prostatitis, kidney disease, cough and anemia [16].

5. PHYTOCHEMICAL DATA

Lippia multiflora is an aromatic plant with a camphorated odor. The essential oil of the leaves of *L. multiflora* domesticated in different bioclimatic regions of Congo-Brazzaville in Central Africa is rich in mono-terpenes whose major compounds are: (Z)-tagetone **1**; (E)-tagetone **2**, myrcene **3**, p-cymene **4**, thymol **5**, carvacrol **6**, limonene **7**, piperitenone **8**, neral **9**

Fig. 2. Sample of *Lippia multiflora* (bulukutu) sold in a market in Kinshasa city (Photo Ngbolua, 2019)

and geranial **10**. Several chemical compounds such as alpha-pinene **11**, beta-pinene **12**, myrcene **13**, 1,8-cineole **14**, gamma-terpinene **15** alpha-terpineol **16**, carvacrol **17**, trans-caryophyllene **18** as well as an ipsenone **19**, 2-methyl-6-methylene-7-octen-4-one **20** were identified in the essential oil of the dry leaves of *L. multiflora* [17]. Bagora et al. [13], by analyzing the essential oils of *L. multiflora* by gas chromatography coupled with mass spectrometry (GC/MS) and gas chromatography equipped with a flame ionization detector (GC/FID), revealed the presence of p-cymene **4**, b-caryophyllene **21**, thymol **5**, c-terpinene **22** and thymyl acetate **23**. Analysis (GC/FID and GC/MS) of essential oils of *L. multiflora* from Burkina Faso revealed the presence of thymol/p-cymene/thymyl acetate [23].

HPLC-DAD/MS analysis of *L. multiflora* extract revealed the presence of phenylethanoid glycosides with verbascoside as the major product [8]. However, the analysis (capillary GC and GC/MS) of the essential oils of *L. multiflora* leaves revealed thirty-six compounds of which the major constituents are 1,8-cineole **14**, sabinene **24**, linalol **25** and α-terpineol **26** [9].

Analysis of the aqueous extract of *L. multiflora* indicated the presence of the phenolic compounds (nuomioside A **27**, samioside **28**, verbascoside **29**, isoverbascoside **30**, alyssonoside **31**, and leucoseptoside A **32**) and a monoterpene (geniposide **33**) [10].

Okhale et al. [11] showed that the essential oils of this species contain chemotypes rich in myrcenone **34**, carvone **35**, piperitenone **36**, ipsenone **37**, linalol **25**, citral **38**, carvacrol **6** and, thymol **5**.

These essential oils also contain β-caryophyllene **21** and iridoid glycosides (chemotaxonomic marker) [11]. The results of atomic absorption spectrophotometry analysis showed significant mineral content (Potassium, Calcium, Magnesium, Iron, Sodium, Manganese, Zinc, Copper and Cadmium). The literature also reports that this bio-resource is rich in ash and is therefore a good source of minerals and also protein, but is low in fat [7].

Kanko et al. [24] showed that the dried leaf extract of this plant contains ursolic acid **39**, n-tritriacontane **40** and salvigenin **41**. Lamaty et *al*. [25] showed that the chemical composition of essential oils from different biogeographical regions of Congo-Brazzaville differed from those described in the literature, notably the presence of 7-octen-4-one **42**. This terpenoid-ketone is reported for the first time in the literature [25]. Pollyana et al. [12] reported that the leaves of this plant contain the terpenoids, phenylpropanoids, and polyketides while the flavonoids and alkaloids are in trace amounts. Nutritional analysis showed that buds and young leaves of *L. multiflora* are richer than old leaves [26]. Mukungulu et *al.* [27] showed that *L. multiflora* contains the alkaloids, steroids, quinones and polyphenols. The following non-volatile compounds have been identified in this plant : flavonoids, verbascoside **29**, isoverbascoside **30**, carotenoids, caffeic acid **43**, 3,4-dihydroxyphenyl-ethanol ester **44**, sterols, saponosides, peptides and caffeine **45**, tannins, leucoanthocyanins, steroids or terpenoids, actenoside **46**, quercetol **47**, kaempferol **48**, stigmasterol **49** and trtriacontane **50** [17]. Studies by Yehouenou et al. [28] showed that the chemical composition of essential oils of *L. multiflora* varies according to the place of harvest: in two regions of Benin, one of the chemotypes is mainly composed of oxygenated monoterpenes (linalol 91.9%: linalol chemotype) and the other is composed of several oxygenated monoterpenes (1-8 cineole 50% and α-terpinol 13.8%) as well as hydrogenated monoterpenes (sabinene 14.4%): 1-8 cineole, α-terpinol and sabinene chemotype. These results show that the chemical composition of essential oils extracted from the same species is very variable.

Factors such as plant development, organ, plant condition, soil, climate, exposure, season, extraction method, etc. underlie this variability [29-31]. Fig. 3 gives the chemical compounds present in *Lippia multiflora*.

The chemical composition of the essential oil can vary within the same species (here *Lippia multiflora*), these chemical varieties are called chemotypes [29-31].

6. PHARMACO-BIOLOGICAL DATA

Mutwale et al. [6] showed that the phenolic extract of *L. multiflora* leaves possesses antioxidant activity at concentrations of 1-20 µg/mL towards ABTS and DPPH radicals. This activity is due to the presence of verbascoside as a major phenolic compound. The essential oil of *L. multiflora* is active towards ABTS and DPPH radicals [13]. Etou et al. [14] showed that aqueous extract of *L. multiflora* leaves reduces

oxidative stress. The inhibition of catalase activity as well as the increase in glutathione (GSH), nitric oxide (NO) in treated rats and the increase in malondialdehyde/malonic aldehyde (MDA: bio-marker of lipid peroxidation) in control rats is experimental evidence that the aqueous extract of *L. multiflora* leaves has a high antioxidant potential that could contribute to the prevention or treatment of several diseases related to oxidative stress including sickle cell disease.

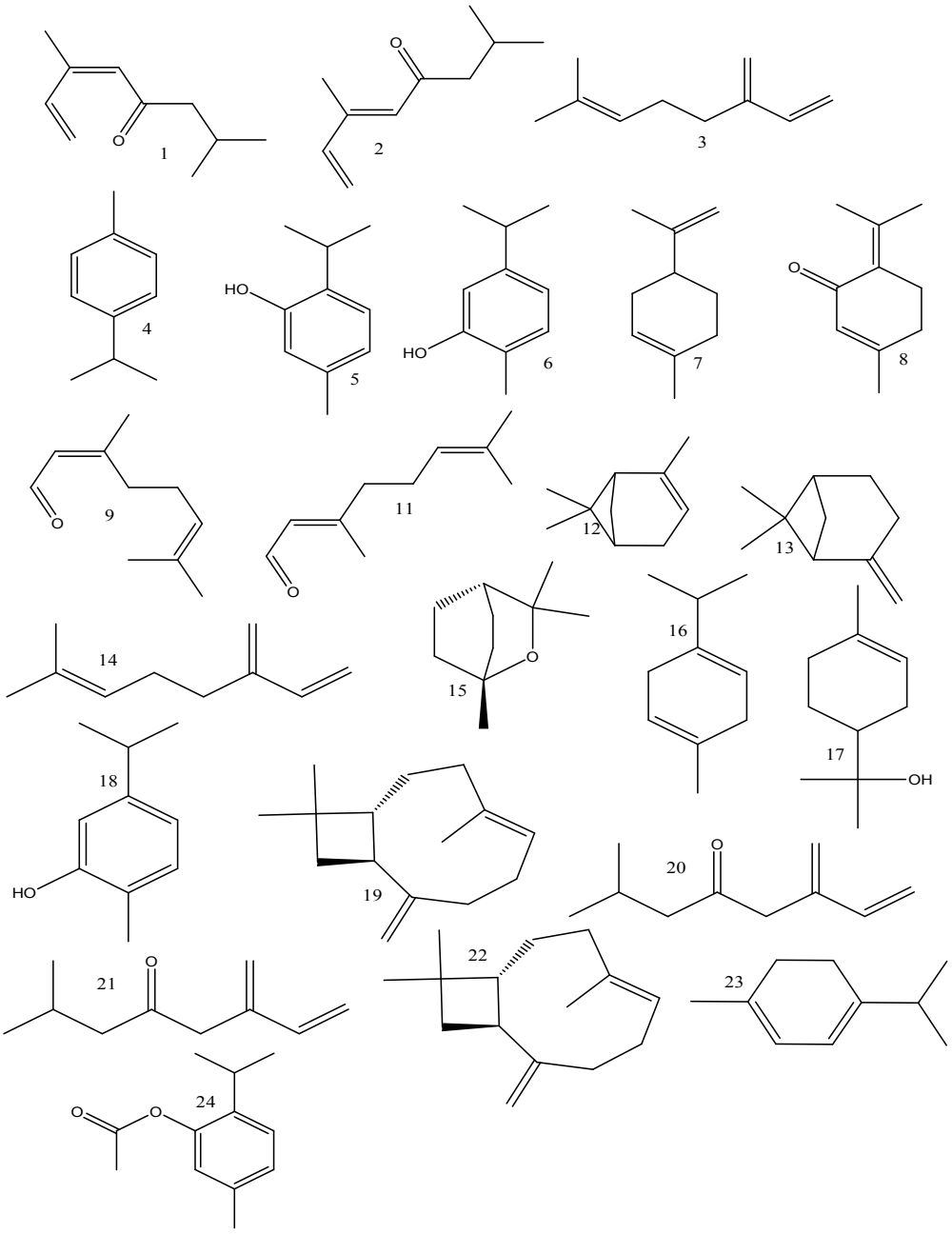

Fig. 3. Chemical compounds present in *Lippia multiflora*:
(Z)-tagetone 1; (E)-tagetone 2, myrcene 3, p-cymene 4, thymol 5, carvacrol 6, limonene 7, piperitenone 8, neral 9, geranial 10, alpha-pinene 11, beta-pinene 12, myrcene 13, 1,8-cineole 14, gamma-terpinene 15, alpha-terpineol 16, carvacrol 17, trans-caryophyllene 18, ipsenone 19, 2-methyl-6-methylene-7-octen-4-one 20, b-caryophyllene 21, c-terpinene 22, thymyl acetate 23, sabinene 24)

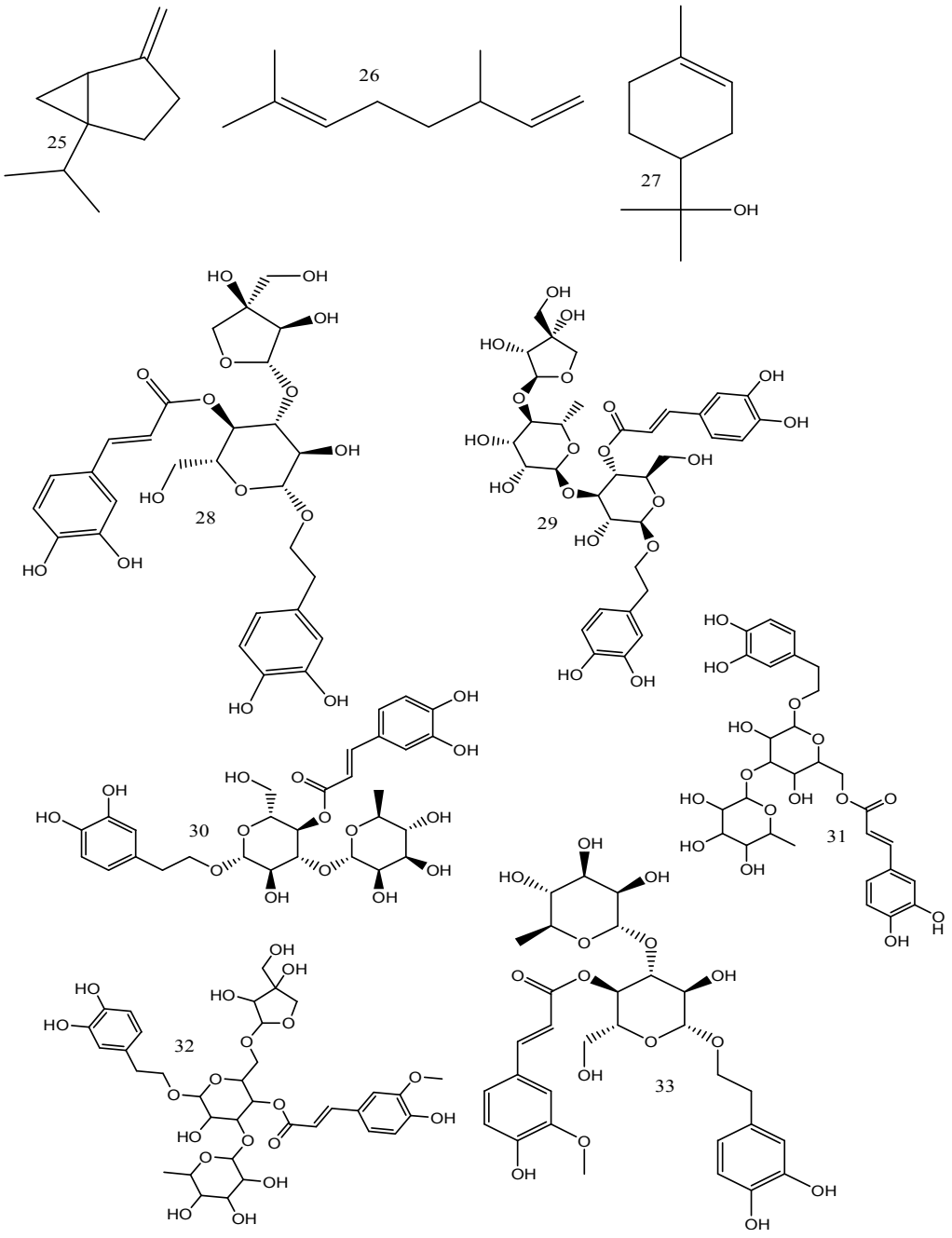

Fig. 3. Chemical compounds present in *Lippia multiflora* (Continued):
*linalol **25**, α-terpineol **26**, nuomioside A **27**, samioside **28**, verbascoside **29**, isoverbascoside **30**, alyssonoside **31**, leucoseptoside A **32**, geniposide **33***

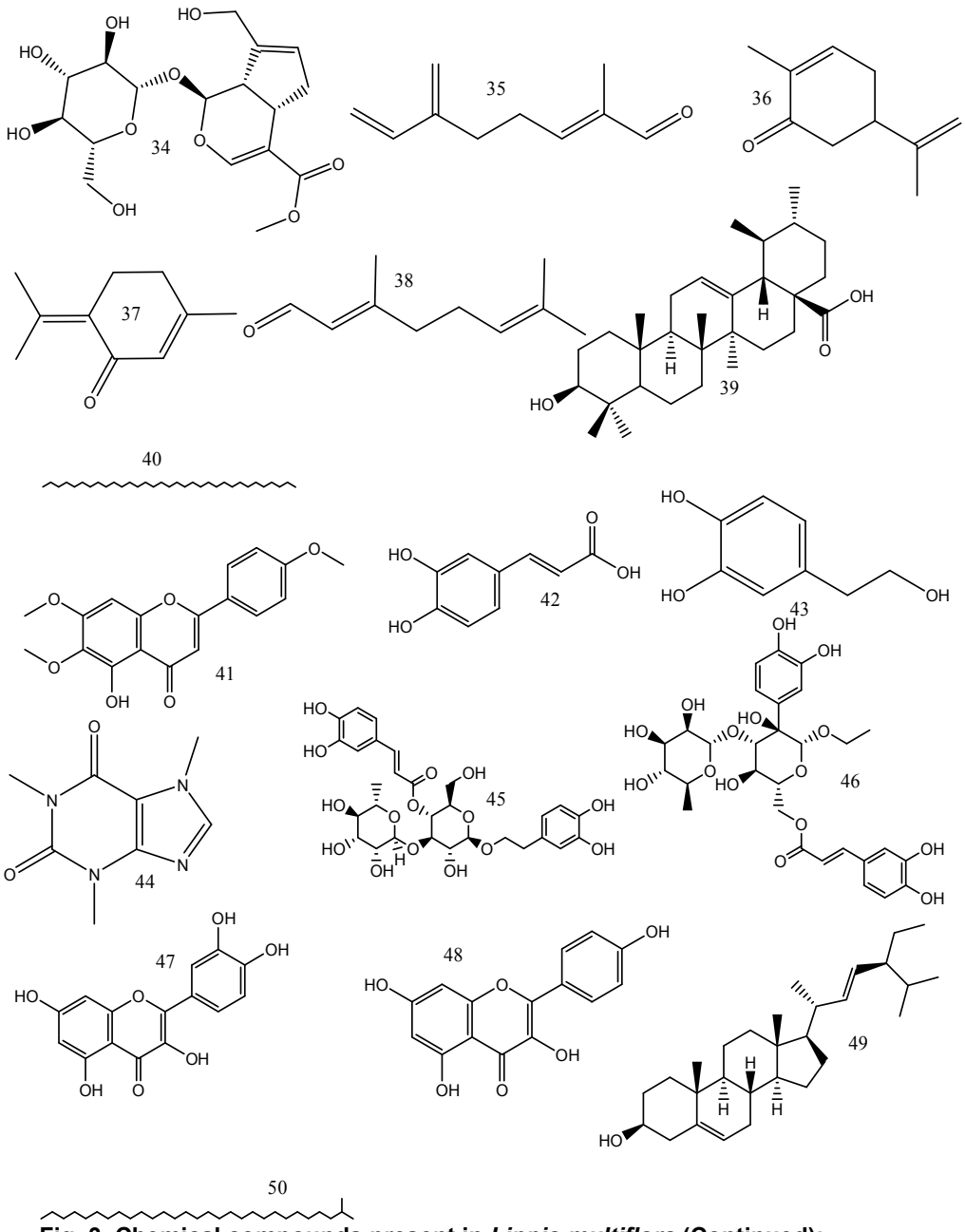

Fig. 3. Chemical compounds present in *Lippia multiflora* (Continued):
*myrcenone **34**, carvone **35**, piperitenone **36**, ipsenone **37**, citral **38,** ursolic acid **39**, n-tritriacontane **40**, salvigenin **41**, 7-octen-4-one **42**, caffeic acid **43**, 3,4-dihydroxyphenyl-ethanol ester **44**, caffeine **45**, actenoside **46**, quercetol **47**, kaempferol **48**, stigmasterol **49**, trtriacontane **50***

The anti-inflammatory activity was evaluated *in vitro* by Bagora et al. [13]. In this study, the authors showed that the essential oils of this plant are endowed with significant anti-inflammatory properties at the dose of 8 mg/mL. Soro et al. [7] showed that this plant is endowed

with anti-inflammatory properties towards macrophages in vitro. This activity depends on the chemotype and the yield of essential oils which are functions of the place of domestication of the plant. The anti-inflammatory activity of *L. multiflora* shows that in regions where access to modern therapeutics is limited or impossible, this medicinal and aromatic plant can be recommended as an alternative in the management of sickle cell disease patients, since inflammation is one of the results of the clinical expression of sickle cell disease [32].

Bagora et al. [13] showed that the essential oils of *L. multiflora* are endowed with antiproliferative properties towards LNCaP, PC-3 and glioblastoma cell lines SF-767).

Bassole et al. [23] reported that the essential oils of *L. multiflora* are active against gram-negative bacteria.

Koïta et al. [10] showed that the aqueous extract of *L. multiflora* has antifungal activity towards the fungi *Phaeoisariopsis personata* and *Puccinia arachidis*. The essential oils of this plant also have fungicidal activity against *Fusarium oxysporum*, *Aspergillus ochraceus* and *A. parasiticus* [28].

Pascual et al. [18] showed that *L. multiflora* has antimalarial properties.

Bouagnon et al. [33] showed that the aqueous extract of *L. multiflora* is endowed with the hepatoprotective properties against ethanol-induced toxicity in Wistar rats.
Pollyana *et al.* [12] reported some species of the genus *Lippia* are responsible for the relief of some central nervous system disorders.

The total phenolic extract of *L. multiflora* inhibits thromboxane A_2 biosynthesis. Verbascoside has been reported as the active ingredient responsible for the hypotensive action of the total phenolic extract of *L. multiflora* [34].

Table 1 gives the synthesis on the pharmaco-biological properties of *L. multiflora* reported in the literature.

Table 1. Pharmacobiological activities of *L. multiflora*

Active ingredients	Pharmaco-biological activity	References
Verbascoside, caffeic acid, chlorogenic acid, luteolin, quercetin and rutin	Anti-free radical activity: o DPPH/ABTS IC_{50} : 7,56-29,1 µg/mL o DCFH-DA IC_{50} : 1-20 µg/mL	[6]
p-cymene, β-caryophyllene, thymol, ɣ-terpinene and thymyl acetate	Anti-free radical activity and cytotoxic activities: o DPPH IC_{50} : 42.23 ± 62.73 µg/mL o ABTS IC_{50} : 1.02 ± 60.02 µg/mL o Lipoxygénase (%I) = 96.96±4.0 o LNCaP IC_{50} = 0.586 ± 0.14 mg/mL o PC-3 IC_{50} = 0.306 ± 0.03 mg/mL o SF-767 IC_{50} = 0.316 ± 0.02 mg/mL o SF-763 v = 0.476 ± 0.14 mg/mL	[13]
Thymol, p-cymene and thymyl acetate	Anti-bacterial activity: o *Bacillus cereus* LMG 13569 (MBC) = 0.5 o *Enterococcus faecalis* CIP 103907 (MBC) = 1 o *Escherichia coli* CIP 105182 (MBC) = 0.25 o *Listeria innocua* LMG 13568 (MBC) = 1 o *Proteus mirabilis* CIP 588104 (MBC) = 0.25 o *Salmonella enterica* CIP 105150 (MBC) = 0.06 o *Shigella dysenteria* CIP 54051 (MBC) = 0.5 o *Staphylococcus aureus* ATCC 25923 (MBC) = 0.06 o *Staphylococcus camorum* LMG 13567	[23]

Active ingredients	Pharmaco-biological activity	References
	(MBC) = 0.5	
Verbascoside, isoverbascoside, nuomyoside A, isonuomyoside A et luteolin-7-O-glucuronide	Anti-free radical activity: o Verbascoside DPPH (IC_{50}) = 0.755 o Isoverbascoside DPPH (IC_{50}) = 0.935 o Nuomioside A DPPH (IC_{50}) = 0.723 o Isonuomioside A DPPH (IC_{50}) = 1.207	[8]
1,8-cineole, sabinene, linalool et *al.* α-terpineol	Anti-free radical activity: IC_{20} = 100 mg/L	[9]
Aqueous extract	Hepato-protective activity: o Protective effect against ethanol-induced toxicity: 300 et 900 mg/kg	[33]
Nuomyoside A, isonuomyoside A, samioside, verbascoside, isoverbascoside, alyssonoside leucoseptoside A et geniposide.	Antifungal activity: o *Phaeoisariopsis personata* et *Puccinia arachidis* (Efficacité %) : 33.33 - 58.33 and 5.56 - 38.89	[10]
Methanolic extract	Cytotoxic activity: 125 µg/mL	[7]
(E,E)-α-farnesene, (E)-β-farnesene and (E,E)-farnesol	Antiviral activity: o Coronavirus 2 (SARS-CoV-2)	[35]
Methanolic extract	Antibacterial activity: o *Staphylococcus aureus, Bacillus subtilis and Escherichia coli* (MIC) *:* 2 mg	[7]
Terpineol, α- and β-pinene	Pedicidal and acaricidal activities: o *Pediculus humani corporis* and *Pediculus humani capitis* (I%) : 20	[20]
Aqueous extract	Analgesic activity: o Rats (Wistar) : 200, 400 and 600 mg/kg	[12]
p-Cymene, Thymol and thymyl acetate	Analgesic activity: o Mice (Swiss) : 2, 4 - 8 mL/kg	[12]
Crude extract: Alkaloids, flavonoids, tannins, saponins, glycosides and volatile oils	Analgesic activity: o Mice (Swiss) : 200-400 mg/kg	[12]
Aqueous extract: Alkaloids, flavonoids, steroids and tannins	Analgesic activity: Strychnine induced Convulsion: o Rats (Wistar) : 400, 800 mg/kg	[12]
Linalool, 1-8 cineole, α-terpinol and sabinene	Antibacterial activity: o *Escherichia coli* ATCC 25922 (CMI) : 640 - 1920 µg/mL and (CMB) : 5120 – 15360 µg/mL o *Staphylococcus aureus* ATCC 25923 : (CMI) : 640 - 1920 µg/mL and (CMB) : 1280 – 3840 µg/mL	[28]
Linalool, 1-8 cineole, α-terpinol and sabinene	Fungicidal activity: o *Fusarium oxysporum, Aspergillus ochraceus* et *A. parasiticus* : 2 µL/mL	[28]
Aqueous extract	Larvicidal activity: o *Anopheles gambiae* : LC_{50} = 2.0, 25.1 et 30.2 mg/L	[27]
Catechic and gallic tannins, flavonoids, anthocyanins, leucoanthocyanins, triterpenoids, mucilage, coumarins and reducing compounds	Toxicity : o Larves des crevettes : LC_{50} = 13.28±1.52 mg/mL (feuilles) ; 0.46±0.05 mg/mL (fleurs)	[36]
Aqueous extract	Myorelaxing properties *:* o 0.25-1.0 g/kg reduced amphetamine	[31]

Active ingredients	Pharmaco-biological activity	References
	induced locomotor activity in mice o 0.5-1.0 mg/mL inhibited contractions of the isolated rat diaphragm in response to the phrenic nerve stimulation	
Aqueous extract	Anti-oxidative activity: o Leucocytes de rats et souris : 5 – 20 mg/mL	[14]

7. TOXICOLOGICAL DATA

The work of Hondi-Assah et al. [37] on sub-acute or sub-chronic toxicity revealed that the aqueous extract of Lippia multiflora causes minor hepatic lesions in rats at a dose of 400 mg/kg. However, in the acute toxicity test, these lesions are not observed at 1200 mg/kg. Moreover, there is no statistically different difference between the hematobiochemical markers (transaminases, alkaline phosphatase and bilirubin) of the treated rats and those of the control rats indicating that this medicinal and aromatic plant is not toxic. *L. multiflora* is well tolerated in rats and does not induce mortality up to a dose of 1200 mg/kg by intraperitoneal administration [38].

8. COSMETIC PROPERTIES OF *L. multiflora*

It has been reported that the essential oil of *L. multiflora* can be used as an adjuvant in human and pet shampoos and contributes to the improvement of hair dyeing and quality [20, 39].

9. NUTRITIONAL PROPERTIES OF *L. multiflora*

The essential oil of *L. multiflora* is used as a spice, meal condiment, and drink flavoring [40]. This aromatic and medicinal plant is therefore a food supplement.

The leaves are also rich in micronutrients (K, Ca, P, Mg, Fe) and contain the proteins and vitamin C [7].

10. TRANSCULTURAL USE OF *Lippia* GENUS ACCORDING TO CHEMO-TAXONOMICAL APPROACH

Although *L. multiflora* is a plant native to Africa and marketed as antimalarial phytomedicine (Malarial inn Republic of Mali and Tetra in Republic of Congo-Brazzaville), other species of the genus *Lippia* are also used in Central and Latin America and in the Indian subcontinent to treat various diseases including helminthiasis and respiratory disorders [18, 41]. In Ayurveda, the plant species like *Lippia nodiflora* is used as aphrodisiac, stomachic and anthelmintic. They are also useful in treatment of cardiovascular diseases, blood, eye; ulcers, wounds, asthma and bronchitis [42].

11. CONCLUSION AND PERSPECTIVES

The present research was carried out with the aim of inventorying the current knowledge on *L. multiflora* in order to guide future research considering the hypothesis that this plant species contains chemical groups which would act either individually or in synergy, in order to confer several pharmaco-biological properties to it. The results of this literature review show that in addition to its numerous documented biological properties, *L. multiflora* also reduces oxidative stress by increasing glutathione and nitric oxide content and can thus relieve sickle cell disease subjects. However, the anti-sickle cell activity of this plant species has not yet been scientifically validated although the plant is used in the treatment of anemia in Traditional Medicine. Therefore, it is desirable that a more thorough study be conducted on *L. multiflora* in order to first determine the different chemotypes from the DRC and then to evaluate the anti-sickling, anti-hemolytic, anti-radical activities and the effect of these chemotypes on the osmotic fragility of sickle cell erythrocytes. These scientific evidences will allow exploiting this plant as a food supplement in sickle cell patients.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products (traditional healers) because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ngbolua KN, Rafatro H, Rakotoarimanana H, Urverg RS, Mudogo V, Mpiana PT, Tshibangu DST. Pharmacological screening of some traditionally-used antimalarial plants from the Democratic Republic of Congo compared to its ecological taxonomic equivalence in Madagascar. International Journal of Biological and Chemical Sciences. 2011;5(5):1797-1804.
2. Ngbolua KN, Rakotoarimanana H, Rafatro H, Urverg RS, Mudogo V, Mpiana PT, Tshibangu DST. Comparative antimalarial and cytotoxic activities of two Vernonia species:V. amygdalina from the Democratic Republic of Congo and V. cinerea subsp vialis endemic to Madagascar. International Journal of Biological and Chemical Sciences. 2011;5(1):345-353.
3. WHO (World Health Organization). Traditional medicine strategy 2002-2005; 2002. Available:http://www.who.int/medicines/library/trmtrateng.pdf.
4. Mongeke MM, Ngbolua KN, Bakola RD, Inkoto CL, Elikandani PN, Mowuli CY. Survey on the plants used in Traditional medicine by Bambenga:Pygmy from Dongo Sector (Territory of Kungu, Province of Sud-Ubangi) in Democratic Republic of the Congo. Revue Marocaine des Sciences Agronomiques et Vétérinaires. 2018;6(4):469-475.
5. Ngbolua KN, Inkoto CL, Mongo NL, Ashande CM, Masens YB, Mpiana PT. Ethnobotanical and floristic study of some medicinal plants marketed in Kinshasa, Democratic Republic of Congo. Moroccan Journal of Agronomic and Veterinary Sciences. 2019;7(1):118-128.
6. Mutwale PK, Mbombo PM, Thierry F, Mouithys-Mickalad A, Mumba DN, Dibungi PTK, HEKabamba NN, Serteyn D, Tits M, Frédérich M, Muyembe J-JT. Antioxidant potentiality of three herbal teas consumed in Bandundu rural areas of Congo. Natural Product Research. 2017;31(16):1940–1943.
7. Soro LC. Biochemical characterization and biological activities of the leaves of *Lippia multiflora* (Verbenaceae) "savannah tea tree" grown in forest and savannah environments of Côte d'Ivoire. Abidjan,. PhD thesis: Nutrition and food security: Université Nangui Abrogoua. 2016;204.
8. Arthur H, Joubert E, De Beer D, Malherbe CJ, Witthuhn RC. Phenylethanoid glycosides as major antioxidants in *Lippia multiflora* herbal infusion and their stability during steam pasteurisation of plant material. Food Chemistry. 2011; 127(2):581-588 DOI:10.1016/j.foodchem.2011.01.044 PMID:23140703.
9. Avlessi F, Alitonou G, Sohounhloue DK, Menut C, Bessiere JM. Aromatic plants of tropical West Africa. Part XIV:Chemical and biological investigation of the essential oil of *Lippia multiflora* Mold. from Benin. Journal of Essential Oil Research. 2011; 17:405-407.
10. Koïta K, Baissac Y, Sanon E, Campa C, Sankara P. Phenolics from *Lippia multiflora* Moldenke as potential bioactive agents against peanut pathogens. Agricultural Science Research Journal. 2017;7(9):267-276.
11. Okhale SE, Nwanosike EM, FatokunOT, Kunle UF. Phytochemistry and ethnopharmacology of *Lippia g*enus with a statement on chemotaxonomy and essential oil chemotypes. International Journal of Pharmacognosy. 2016;3(5):201-211. DOI:10.13040/IJPSR.0975-8232.IJP.3(5).201-211.
12. Pollyana S. Siqueira-Lima, Fabiolla R.S. Passos, Angélica M. Lucchese, Irwin R.A. Menezes, Henrique D.M. Coutinho, Adley A.N. Lima, Gokhan Zengin, Jullyana S.S. Quintans, Lucindo J. Quintans-Júnior. Central nervous system and analgesic profiles of Lippia genus. Revista Brasileira de Farmacognosia. 2019;29(1):125-135. DOI:https://doi.org/10.1016/j.bjp.2018.11.006.
13. Bagora B, Bassole IHN, Gnoula C, Nebie R, Yonli A, Morel L, Figueredo G, Nikiema J-B, Lobaccaro J-MA, Simpore J. Chemical composition, antioxidant, anti-inflammatory and anti-proliferative activities of essential oils of plants from Burkina Faso. PLoS ONE. 2014;9(3):e92122. DOI:10.1371/journ*al*.pone.0092122.

14. Etou Ossibi AW, Morabandza CJ, Nsonde Ntandou GF, Tsala D, Elion Itou RDG, Ouamba JM, Abena AA. Anti-oxidative stress potentiality of the aqueous extract of *Lippia multiflora* Moldenke leaves (Verbenaceae). Journal of Pharmacognosy and Phytochemistry. 2016;5(6):254-258.
15. Soro LC, Munier S, Pelissier Y, Grosmaire L, Yada R, Kitts D, Atchibri ALO, Guzman C, Boudard F, Menut C, Robinson JC, Poucheret P. Influence of geography, seasons and pedology on the chemical composition and anti-inflammatory activities of essential oils from *Lippia multiflora* Mold. leaves. Journal of Ethnopharmacology. 2016;194:587-594. DOI:http://dx.doi.org/10.1016/j.jep.2016.10.047
16. Masengo CA, Bongo NG, Robijaona B, Ilumbe GB, Ngbolua KN, Mpiana PT. Quantitative ethnobotanical study and sociocultural value of *Lippia multiflora* Moldenke (Verbenaceae) in Kinshasa, Democratic Republic of Congo. Moroccan Journal of Agronomic and Veterinary Sciences. 2021;9(1):93-101.
17. Abena AA, Etou Ossibi AW, Gouolally T, Okemy AN, Ouamba JM. Étude monographique de *Lippia multiflora* Moldenke (Verbenaceae). Phytothérapie. 2016;1-6. DOI 10.1007/s10298-016-1025-8.
18. Pascual ME, Slowing K, Carretero E, Sa´nchez Mata D, Villar A. Lippia:traditional uses, chemistry and pharmacology:a review. Journal of Ethnopharmacology. 2001;6:201–214.
19. Atanasso JA, Chadare FJ, Padonou EA, Ahouansinkpo E, Koura K, Houehanou T, Assogbadjo A E, Glele Kakaï R, Sinsin B. Habitats and uses of *Lippia multiflora* Moldenke:local perception of four ethnic groups in Benin (West Africa). Agronomie Africaine. 2017;29(2):111-120.
20. Oladimeji FA, Orafidiya OO, Ogunniyi TAB, Adewunmi TA. Pediculocidal and scabicidal properties of *Lippia multiflora* essential oil. Journal of Ethnopharmacology. 2000;72:305–311.
21. Ekissi AC, Yao-Kouame A, Konan AG, Alui KA, Agbo NG, Kati-Coulibaly S. Manufacturing process and various uses of savannah tea (*Lippia multiflora*) in Ivory Coast. Asian Journal of Agriculture and Rural Development. 2013;3(8):597-608.
22. Ndongo IE, Inkoto CL, Bongo NG, Mulenga CM, Ilinga BL, Shetonde MO, Mbala MB, Tshilanda DD, Mvingu KB, Kayembe SJ, Mpiana PT, Ngbolua KN. Ethno-botanical survey and ecological study of medicinal plants traditionally used against erectile dysfunction in Democratic Republic of the Congo. Bioscience and Bioengineering. 2018;4(4):85-91.
23. Bassole IHN, Ouattara AS, Nebieb R, Ouattara CAT, Kabore ZI, Traore SA. Chemical composition and antibacterial activities of essential oils of Lippia chevalieri and *Lippia multiflora* from Burkina Faso. Phytochemistry. 2003; 62:209-212.
24. Kanko C, Koukoua G, N'Guessana YT, Fournier J, Pradère JPl, Toupet L. Contribution to the phytochemical study of *Lippia multiflora* (Verbenaceae). Chemistry Reports. 2004;7:1029-1032.
25. Lamaty G, Menut C, Bessiere JM, Ouamba JA, Silou T. 2-Methyl Gmethylene-7-cten4-One, a constituent of *Lippia multiflora* essential oil. Phytochemistry. 1990; 29(2):521-522.
26. Ekissi AC, Konan AG, Yao-Kouamé A, Bassirou B, Kati-Coulibaly S. Evaluation of chemical constituents of savannah tea leaves (*Lippia multiflora*). Journal of Applied Biosciences. 2011;42:2854-2858.
27. Mukungulu GT, Tshilanda DD, Tshibangu DST, Tshiwew EM , Vulama AS, N'sita NN, Kitambala AK, Mafuta SM, Musibono DE, Mpiana PT. Larvicidal Activity of Some Congolese Plant Extracts against *Anopheles Gambiae*. Journal of Advancement in Medical and Life Sciences. 2015;3(2):1-4. DOI:10.5281/zenodo.999687.
28. Yehouenou B, Sessou P, Dahouenon-Ahoussi E, Koudoro Y, Alitonou GA, Sohounhloue D. Chemical composition and antimicrobial activities of volatile extracts from fresh leaves of *Lippia multiflora* Moldenke against pathogenic and adulterated microorganisms isolated from foods sold near roads in Benin Republic. EC Microbiology. 2020;16(3):01-09.
29. Soro LC, Munier S, Atchibri ALOA, Grosmaire L, Menut C, Malan KA, Pelissier Y. Chemical composition of leaf essential oils of *Lippia multiflora* Mold. grown in savannah and forest area in the Ivory Coast. Journal of Essential Oil Bearing Plants. 2015;18:1:154-160. DOI:10.1080/0972060X.2014.977571.

30. Ngbolua KN. Quantitative ethnobotany: Methodological approaches for the evaluation and valorization of endogenous knowledge in tropical regions. European University Publishing, Riga: Latvia; 2020. ISBN:978-613-9-53635-1.
31. Masunda AT, Inkoto C, Masengo CA, Bongili S B, Basilua JP K, Legbiye EM, Ngbolua KN, Mpiana PT. Traditional uses, physical properties, phytochemistry and bioactivity of *Lippia multiflra* Moldenke (Verbenaceae):A mini-review. Discovery Phytomedicine. 2020;7(1):19-26.
32. Wembonyama SO. Moringa oleifera, a boon in the management of major sickle cell syndrome? Journal of Medicine, Public Health and Policy Research. 2021;1(1):31-35.
33. Bouagnon R, Yeo D, Kouass K, Beugre K, Djaman JA, Nguessan JD. Hepatoprotective effect of aqueous extract of *Lippia multiflora* Leaves against ethanol-induced toxicity in Wistar rats European Journal of Medicinal Plants. 2015;7(3):146-155.
34. Chanh PH, Chanh APH. Comparative effects on TXA2 biosynthesis of products extracted from *Lippia muttiflora* Moldenke leaves. Prostaglandines, Leukotrienes & Essential Fatty Acids. 1988;34(2):83-88.
35. da Silva JKR, Figueiredo PLB, Byler KG, Setzer WN. Essential oils as antiviral agents, potential of essential oils to treat SARS-CoV-2 infection:An in-silico investigation. International Journal of Molecular Sciences. 2020;21(10):3426. https://doi.org/10.3390/ijms21103426.
36. Djengue HW, Dansi A, Assogba MF, Ahissou H, Adjatin A, Dansi M, Gbénou DJ. Phytochemical screening and toxicity of *Lippia multiflora* Moldenke, a minor aromatic leaf vegetable consumed in Benin. International review of current research in biosciences and plant biology. 2017;4(5):77-84.
37. Hondi-Assah C, Abena AA, Kokolo J, Badila C, Diatewa M. Hepatoprotective effects of *Lippia multiflora* and a Congolese phytomedicine. Phytotherapy. 2003;1(5):135-140.
38. Abena AA, Ngondzo-Kombeti GR, Bioka D. Psychopharmacological properties of *Lippia multiflora*. Encéphale. 1998;24:449-54.
39. Yang YC, Lee SH, Clark JM, Abn YJ. Insecticidal activity of plant essential oils against *Pediculus humanus capitis* (Anoplura:Pediculidae). Journal of Medical Entomology. 2004;41:699-704.
40. Kanko C, Sawaliho BEH, Kone S, Koukoua G, N'Guessan YT. Study of the physico-chemical properties of essential oils of *Lippia multiflora*, *Cymbopogon citratus*, *Cymbopogon nardus*, *Cymbopogon giganteus*. Chemistry Reports. 2004;(7): 1039 -1042.
41. Maroyi A. *Lippia javanica* (Burm.f.) Spreng.: Traditional and commercial uses and phytochemical and pharmacological significance in the African and Indian subcontinent. Evidence-Based Complementary and Alternative Medicine; 2017 DOI:https://doi.org/10.1155/2017/6746071.
42. Venu S. A mini review on medicinally important plant *Lippia nodiflora*. Asian Journal of Research in Chemistry. 2018;11(1):176-178.

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