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A review on the chemistry of some species of genus *Lippia* (Verbenaceae family)

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Abstract

Recently, focus on plant research has increased globally and a large amount of evidence has collected to show great potential of medicinal plants employed in diverse traditional systems. In the customary forms of medicine, plants provided a large number of remedies, which were often useful. *Lippia* genus, which belongs to the family Verbenaceae yields appreciable quantities of metabolites some of which have been shown to have valuable biological activities. Many phytochemical investigations done on this genus have shown the presence of various compounds like triterpenoids, phenols, flavonoids, phenylpropanoids and steroids. This review focuses on ethnopharmacology, phytochemistry and pharmacology of *Lippia* genus to allow the evaluation of the potential for utilization of the largest biomass of *Lippia* genus available.

Keywords: *Lippia*, Triterpenoids, Phenols, Flavonoids, Phytochemistry, Pharmacology.

Introduction

The genus *Lippia* is one of 41 genera of shrubs, herbs or trees which belong to the family Verbenaceae Juss., and is named after the French natural historian and traveler, Augustin Lippi (1678-1701).[1] This genus comprises of approximately 200 species distributed throughout tropical Africa as well as in Central and South America, with Brazil estimated to host 70–75% of the known species.[2] Ethnobotanically, plant species from this genus are used worldwide as food, beverages, seasoning and remedies.[3] The majority of *Lippia* species are used as remedies for gastrointestinal and respiratory complaints[4], lung infections, dysentery and diarrhea[5], analgesic, anti-inflammatory and antipyretic[6], stomach ailments, coughs, colds and asthma.[7] Most phytochemical studies of *Lippia* species have concentrated on the chemistry of the volatile constituents, resulting in limited information being available on the non-volatile secondary metabolites.[8] According to these authors, the most significant non-volatile secondary metabolites produced by *Lippia* species include terpenes (some sesquiterpenes, di- and triterpenes), flavonoids, phenols, iridoid glycosides, phenylpropanoids and naphthoquinones. These compounds may be present in the form of glycosides, in which the compound is attached to one or more sugar moieties.

Medicinal importance and bioactivity of some of the isolated metabolites from *Lippia* species

a) *Lippia nodiflora*

Lippia nodiflora also known as *Phyla nodiflora* is a fast-growing, mat-forming and prostrate perennial plant. When in competition with other species, *L. nodiflora* is capable of growing to a height of between 20 and 30 cm, and overshadow other plants. The leaf and flower extracts of *Lippia nodiflora* have been shown to possess antimicrobial activity against various bacteria such as *Bacillus subtilis, Micrococcus luteus, B. cereus, Staphylococcus aureus, Klebsiella pneumonia, Pseudomonas aeruginosa, K. oxytoca*, and *Escherichia coli*.[9] The methanolic extracts of *L. nodiflora* have been reported to possess antifungal activities against *Aspergillus niger and Candida albicans*[9] as well as antidiabetic and hypolipidaemic properties in streptozotocin-induced diabetic rats.[10] Chloroform and crude extracts also exhibit similar antimicrobial activities. A phytochemical analysis of methanol extract of the aerial parts of *L. nodiflora* led to the isolation a novel triterpenoid referred to as lippiacin (**1**) as well as a benzofuranone rengyolone referred to as halleridone (**2**).[11] Other compounds include essential oils, resins, 6-hydroxyluteolin (**3**), hispidulin (**4**) and stigmasterol (**5**).[9] The methanol extracts of *Lippia nodiflora* were also shown to have antidiabetic and hypolipidaemic properties in streptozotocin-induced diabetic rats (Fig. 1).[10]

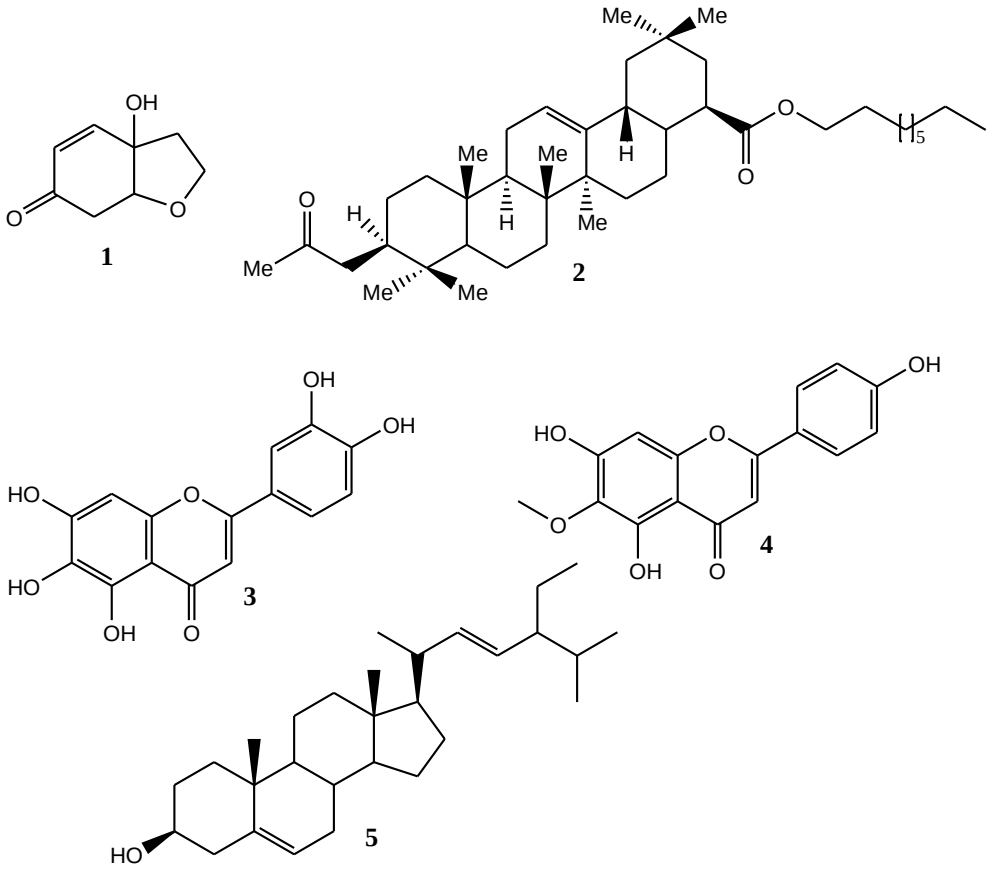

Figure 1: Compounds isolated from *Lippia nodiflora*

b) *Lippia graveolens*

Lippia graveolens, popularly referred to as "oregano" is frequently used in Mexico and the United States as a spice. The apical parts of the plant, when boiled and the fluid taken orally have been found to treat gastrointestinal diseases such as diarrhea, colic and stomach ache. Additionally, the plant has been used to induce abortions in women.[12] The efficacy of the herb against gastrointestinal infections is attributed to the antibacterial properties of the extracts against both Gram-positive and Gram-negative bacteria.[13] The herb also has antifungal activities against *Fusarium sporotrichum, Aspergillus niger, Trichophyton mentagrophytes, Fusarium moniliforme* and *Rhyzoctonia solani*.[14] Extracts from *Lippia graveolens* also have antioxidant activities.[15, 16] Although a lot has been reported on the volatile components of this plant species, the non-volatiles have not been exploited to a greater extent. The essential oils from *Lippia graveolens* have been shown to exhibit larvicidal activity on 10-day-old *R. microplus* tick larvae due to the presence of active compounds such as

thymol (**6**), carvacrol (**7**), p-cymene (**8**), and γ-terpinene (**9**).[17] Carvacrol (**7**), the main compound in *Lippia graveolens* was found to be also effective against human as well as animal viruses such as "acyclovir-resistant herpes simplex virus type 1 (ACVR-HHV-1), acyclovir-sensitive HHV-1, human respiratory syncytial virus (HRSV), bovine herpes virus type 2 (BoHV-2), and bovine viral diarrhoea virus (BVDV)" (Fig. 2).[18]

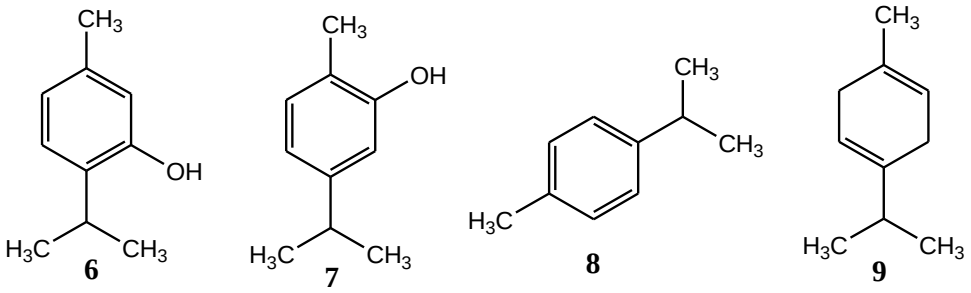

Figure 2: Compounds isolated from *Lippia graveolens*

c) *Lippia citriodora*

Lippia citriodora Kunth is widely spread in tropical, subtropical, central to South America, and in Africa. The plant, which flourishes in loamy soil, is bred from seeds and cuttings. The leaves are used in giving flavor to drinks, desserts, fruit salads and jellies and for spicing up food. A decoction made from the leaves and flowers is given as febrifuge, sedative and anti-flatulent.[19] The plant showed antisplasmodic, antimicrobial properties and is traditionally used to treat *Candida*.[20] From the ethyl acetate leaf extract of *L. citriodora*, three phenolic compounds: dihydrocaffeic acid (**10**), luteolin-7-O-glycoside (**11**) and 4-hydroxycinnamic acid (**12**) were isolated.[21] The three compounds were tested for analgesic, antipyretic, antioxidant and anti-inflammatory activities on both mice and rats and were found to show good activity. In their study to evaluate the elastase inhibition activity of *L. Citriodora* leaves, Venkateswara and co-workers[22] isolated three compounds: Oleanolic acid (**13**), Saccharose (**14**) and Saccharose octaacetae (**15**). Of the three compounds, the triterpenoid, Oleanolic acid showed good elastase activity with IC_{50} value of 15.5µg/ml. *L. citriodora* has also been found to contain phenylpropanoids such as Verbascoside.[23] This compound has been reported to possess antioxidant, antimicrobial, immunosuppressive and antitumour activities (Fig. 3).[24]

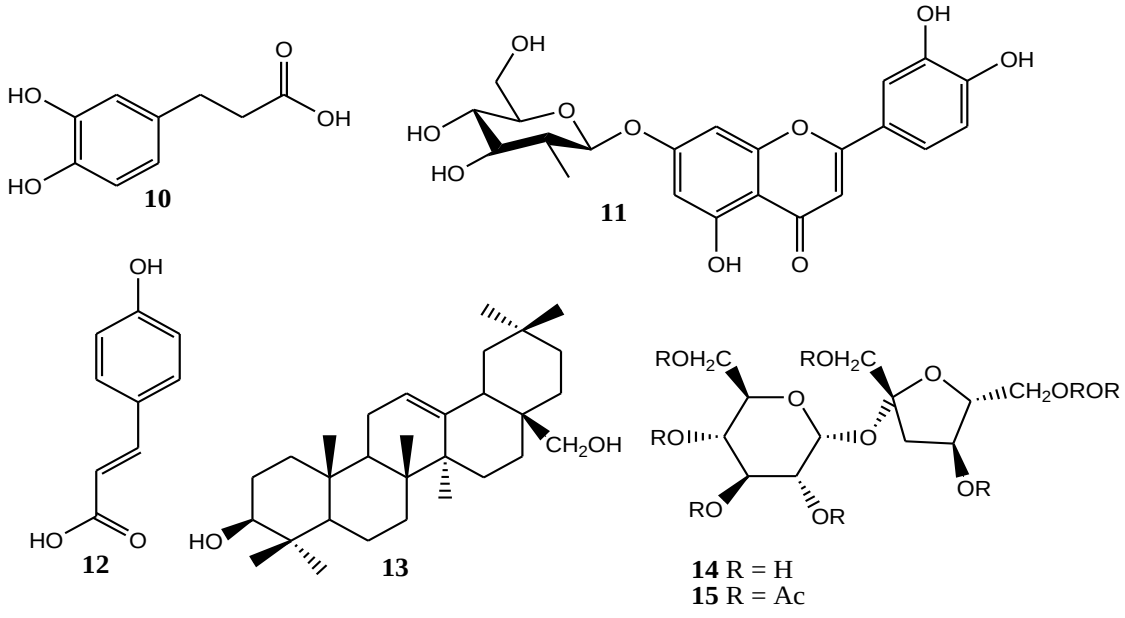

Figure 3: Compounds isolated from *Lippia citriodora*

d) *Lippia alba*

Lippia alba (Mill.) N. E. Brown is a herb that originated from South America whose medicinal attributes have been recognized since 1882.[25, 26] Most of the investigators have studied both the essential oil as well as the non-volatile compounds from the leaves of *L. alba*. In the case of essential oil analysis, the major chemical compounds detected in the essential oil of *L. alba* were geranial and carvenone.[27] In the case of non-volatile compounds investigated, the presence of three iridoids, geniposide (**16**), theveside (**17**) and shanzhizide methyl ester (**18**), was reported.[28, 29] All the three compounds were found again in one study, along with geniposidic acid (**19**), caryoptoside (**20**), 8-epiloganin (**21**) and mussaenoside (**22**).[30] Two biflavonoids (**23**, **24**) were also isolated.[31] Only one work so far has been dedicated to the chemical composition of the roots of *Lippia alba* and led to the characterization of mussaenoside, theviridoside (**25**) and gardoside (**26**) (Fig. 4).[32]

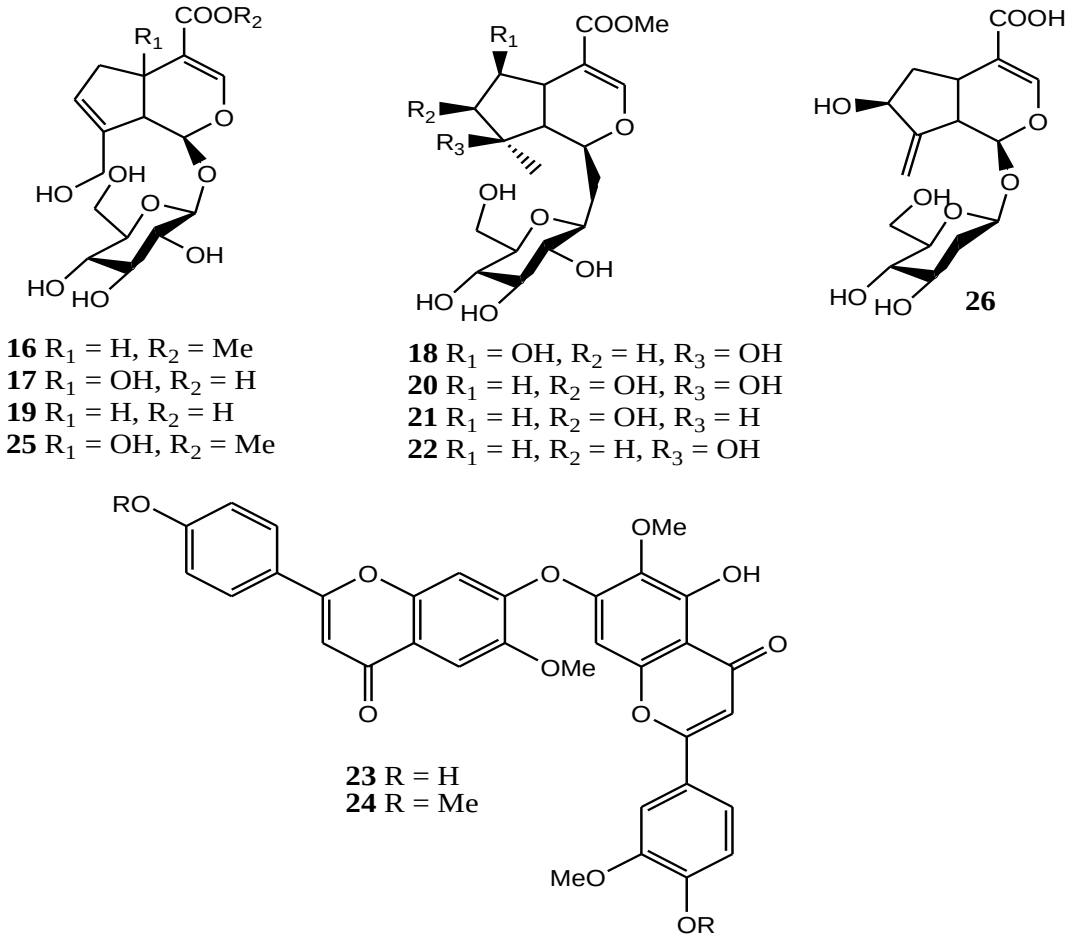

Figure 4: Compounds isolated from *Lippia alba*

e) *Lippia javanica*

Lippia javanica (Burm.f.) Spreng is an erect woody shrub of up to 2m high, with strong aromatic leaves, which gives off a lemon-like fragrance when crushed.[33] Its infusion is commonly used in Africa as a tea against various ailments such as influenza, measles, rashes, malaria, stomach problems, fever, colds, cough, headaches.[34] In such for bioactive compounds with antimicrobial activity against *Mycobacterium tuberculosis* and HIV-1 Reverse transcriptase, Mojovo and co-workers[35] isolated eight compounds from *L. javanica* ethanolic extract. The eight compounds were: 4-ethyl-nonacosane (**27**), three monoterpenes, (E)-2(3)-tagetenone epoxide (**28**), myrcenone (**29**), piperitenone (**30**) and four flavanones, apigenin (**31**), cirsimaritin (**32**), 6-methoxyluteolin 4'-methyl ether (**33**) and 6-methoxyluteolin 3',4',7-trimethyl ether (**34**). Evaluation of these compounds against HIV RT showed that compounds **28** and **30** inhibited the enzyme by 91, 53 and 52% at 100 mg/mL. The results indicated that compound **28** could be of interest as a template in drug discovery research due to the higher activity as compared

to the other compounds. The MIC of compound (**32**) was found to be 200 mg/mL against the H37Rv strain (Fig. 5).

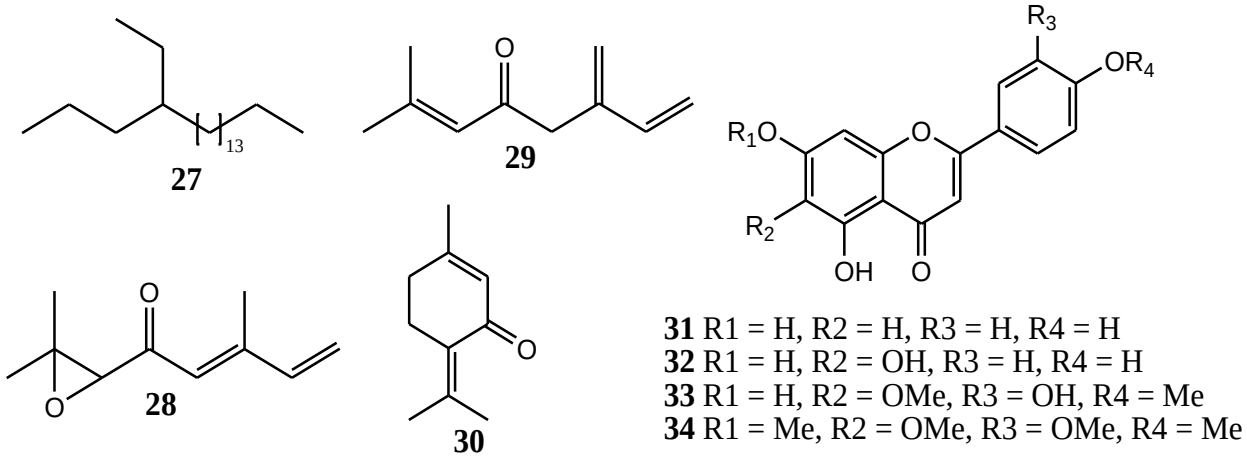

Figure 5: Compounds isolated from *Lippia javanica*

f) *Lippia scaberrima*

Lippia scaberrima is a perennial aromatic shrub that grows to a height of 0.3-0.6 m and occurs at altitudes between 765 and 1800 m above sea level.[36] The plant is still widely used by ethnic groups in many communities. Cloths soaked in a decoction of the plant are applied to alleviate backache. It is also used in the treatment of coughs, colds, fever and bronchial problems.[32] The astringent properties of the extract to make it suitable for the treatment of haemorrhoids.[37] From the leaves of L. scaberrima, four compounds were isolated: 4-O-hexopyranosylhexopyranose (**35**), theviridoside (**36**) and (1S,4aR,7aR) - 4a-hydroxy -7 - (hydroxymethoxyl) – 4 - methyl – 1 , 4a , 5 ,7a-tetrahydrocyclopenta [c] pyyran -1-yl (5, β)-1-glycero-hexopyranoside (**37**). The four compounds were tested for both antimicrobial and antifungal activities and were found to exhibit both antimicrobial and antifungal properties (Fig. 6).

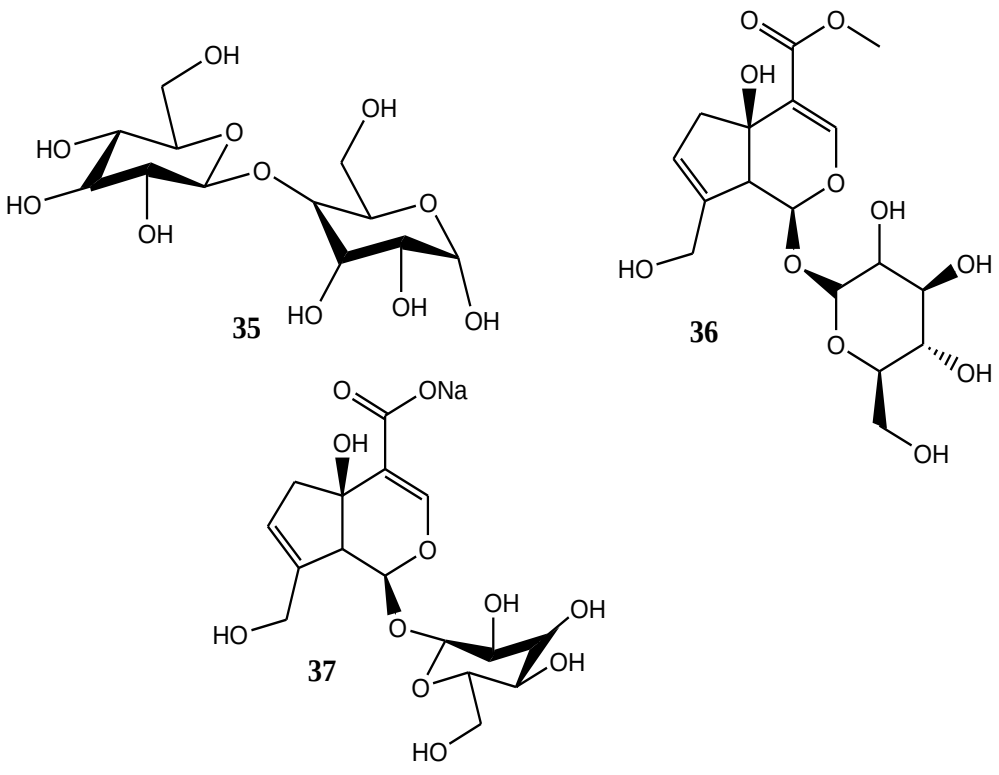

Figure 6: Compounds isolated from *Lippia scaberrima*

Conclusion

Demand for herbal drugs is increasing day by day. Plants contain a number of chemical moieties, with varied pharmacological activities. Many potent and efficacious medicinal principles used for treating dreadful diseases have been isolated from the plant kingdom. So it is very clear that the study of the medicinal plants is important to meet the requirements in effective therapy. Phytochemical studies on the genus *Lippia* have shown that the plant it contains triterpenoids, phenols, flavonoids, phenylpropanoids, iridoid glycosides and steroids all of which have been reported to possess medicinal properties. As a result, *Lippia* plants should be explored further as an alternative source of medicine.

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References

1. Pooley, E.. A field guide to wild flowers: Kwazulu-Natal and the Eastern region. Durban: Natal Flora Publications Trust.1998.

2. Arthur, H., Joubert, E., De Beer, D., Malherbe, C. J., Witthuhn, R. C.. Phenylethanoid glycosides as major antioxidants in *Lippia multiflora* herbal infusion and their stability during steam pasteurization of plant material. Food Chemistry 2011; 127: 581–588.

3. Pascual, M.E., Slowing, K., Carretero, E., Sánchez Mata, D., Villar, A.. Lippia: traditional uses, chemistry and pharmacology: a review. Journal of Ethnopharmacology, 2001a; 76:201-214.

4. Morton, P.. Atlas of medicinal plants of middle America, Springfield, Illinois, USA.1981; 1.

5. Palgrave, M.C., Drummond, R.B., Moll, E.J.. Trees of southern Africa. 3rd Edition, Cape Town: Struik. 2003.

7. Pascual, M.E., Slowing, K., Carretero, E. Villar, A.. Antiulcerogenic activity of *Lippia alba* (Mill.) N.E. Brown (Verbenaceae). Il Farmaco 2001b; 56:501-504.

8. Catalan, C.A.N., De Lampasona, M.E.P.. The chemistry of the genus Lippia (Verbenaceae). In: Kintzios, S.E. (ed.) Oregano: The genera *Origanum* and *Lippia*. 1st ed. London: Taylor & Francis.2002.

9. Zare, Z., Ahmed, M., Sattari, T. N., Iranbakhsh, A., Mehrabian, S. Antimicrobial activity of leaf and flower extracts of *Lippia nodiflora* L. (verbenacea). Journal of Plant Protection Research 2012; 52(4): 401-403.

10. Balamurugan, R., Ignacimuthu, S.. Antidiabetic and Hypolipidemic effect of methanol extract of *Lippia nodiflora* L. in streptozotocin induced diabetic rats. Asian Pacific Journal of Tropical Biomedicine 2011; S30-S36.

11. Siddiqui, B.S., Ahmad, F., Sattar, F.A., Belgum, S.. Chemical Constituents from the Aerial Parts of *Lippia nodiflora* Linn. Arch Pharm Res, 2007; 30(12):1507-1510.

12. Canales, M., Hernandez, T., Caballero, J., de Vivar, A. R., Avila, G., Duran, A., Lira, R.. Informant consensus factor and antibacterial activity of the medicinal plants used by the people of San Rafael Coxcatl´ an, Puebla, Mexico. Journal of Ethnopharmacology 2005; 97:429–439.

13. Hernández, T., Canales, M., Avila, J. G., Duran, A., Caballero, J., de Vivar, A. R., Lira, R.. Ethnobotany and antibacterial activity of some plants used in traditional medicine of Zapotitlán de las Salinas, Puebla (México). Journal of Ethnopharmacology 2003; 88:181–188.

15. Arana-Sa´nchez, A., Estarro ´n-Espinosa, M., Obledo-Va ´zquez, E. N., Padilla-Camberos, E., Silva-Va´zquez, R., and Lugo-Cervantes, E.. Antimicrobial and antioxidant activities of Mexican oregano essential oils (*Lippia graveolens* H. B. K.) with different composition when microencapsulated in β-cyclodextrin. Letters in Applied Microbiology 2010; 50:585–590.

16. Kulisic, T., Radonic, A., Katalinic, V., Milos, M.. Use of different methods for testing antioxidative activity of oregano essential oil. Food Chem 2004; 85:633– 640.

17. Martinez-Velazquez , M., R. Rosario-Cruz ,R., Castillo-Herrera ,G., J. M. Flores-Fernandez ,J.M., A. H. Alvarez , A.H., Lugo-Cervantes, E.. Acaricidal Effect of Essential Oils from *Lippia graveolens* (Lamiales: Verbenaceae), *Rosmarinus officinalis* (Lamiales: Lamiaceae), and *Allium sativum* (Liliales: Liliaceae) Against Rhipicephalus (Boophilus) microplus (Acari: Ixodidae). Journal of Medical Entomology 2011; 48(4):822-827.

18. Pilau, M. R., Alves, S. H., Weiblen, R., Arenhart, S., Cueto, A. P., Lovato, L. T.. Antiviral activity of the *Lippia graveolens* (Mexican oregano) essential oil and its main compound carvacrol against human and animal viruses. Brazilian Journal of Microbiology 2011; 42:1616-1624.

19. The Wealth of India: a dictionary of raw material and industrial products, CSIR, New Delhi, 1995; 4:142.

20. http://www.whitelotusblog.com/2011/06/monograph-verbena-lemon-lippia.html (20 June 2014).

21. El-Hawary, S.S., Miriam F. Yousif, M.F., Abdel Motaal, A.A., Abd-Hameed, L.M.. Bioactivities, phenolic compounds and in-vitro propagation of *Lippia citriodora* Kunth cultivated in Egypt. Bulletin of Faculty of Pharmacy, Cairo University 2012; 50:1–6.

22. Venkateswara, R.G., M. Gopalakrishnan, M., T. Mukhopadhyay, T.. Secondary metabolites from the leaves of *Lippia citriodora* H. B. & K. Der Pharmacia Lettre 2013; 5 (3):492-495.

24. Pieroni, A., Pachaly, P., Huang, Y., Van Poel, B., Vlietinck, A. J.. Studies on anti-complementary activity of isolated flavones from *Ligustrum vulgare* and *Phillyrea latifolia* leaves (Oleaceae). Journal of Ehnopharmacology 2000; 70:213-217.

25. Mors, W.B., Rizzini, C.T., Pereira, N.A., 2000. Medicinal plants of Brazil. In: DeFilipps, R.A. (Ed.), Medicinal Plants of the World. Reference Publications, Inc., Algonac, MI.

26. Hennebelle, T., Sahpaz, S., Joseph, H., Bailleul, F.. Ethnopharmacology of *Lippia alba*. J. Ethnopharmacol. 2008; 116:211–222.

27. Conde, R., Valéria S.C. C., Carmona, F., Contini, S.H.T., Pereira, A.M.S.. Chemical composition and therapeutic effects of *Lippia alba* (Mill.) N. E. Brown leaves hydro-alcoholic extract in patients with migraine. Phytomedicine 2011; 18:1197– 1201.

28. Heinrich, M., Rimpler, H., Barrera, N.A.. Indigenous phytotherapy of gastrointestinal disorders in a lowland Mixe community (Oaxaca, Mexico): ethnopharmacologic evaluation. Journal of Ethnopharmacology 1992; 36:63–80.

29. Von Poser, G.L., Toffoli, M.E., Sobral, M., Henriques, A.T.. Iridoid glucosides substitution patterns in Verbenaceae and their taxonomic implication. Plant Systematics and Evolution 1997; 205:265–287.

30. Hennebelle, T., Sahpaz, S., Joseph, H., Bailleul, F.. Phenolics and iridoids of *Lippia alba*. Natural Product Communications 2006b; 1:727–730.

31. Barbosa, F.G., Lima, M.A.S., Silveira, E.R.. Total NMR assignments of new [C7-OC7]-biflavones from leaves of the limonene-carvone chemotype of *Lippia alba* (Mill) N.E. Brown. Magnetic Resonance in Chemistry 2005; 43:334–338.

32. Sena Filho, J.G., Duringer, J.M., Uchoa, D.E.A., Xavier, H.S., Barbosa Filho, J.M., Braz Filho, R.. Distribution of iridoid glycosides in plants from the genus *Lippia* (Verbenaceae): An investigation of *Lippia alba* (Mill.) N.E. Brown. Natural Product Communications 2007; 2:715–716.

33. Van Wyk, B.E., & Gericke, N.. People's plants. A guide to useful plants of Southern Africa. Pretoria, South Africa: Briza Publications 2000.

34. Hutchings, A., Van Staden, J.. Plants used for stress-related ailments in traditional Zulu, Xhosa and Sotho medicine. Part 1: Plants used for headaches. Journal of Ethnopharmacology 1994; 43:89–124.

35. Mujovo, S.F., Hussein, A.A., Meyer, J.J.M., B. Fourie, B., Muthivhi, T., Namrita, L.. Bioactive compounds from *Lippia javanica* and *Hoslundia opposite*. Natural Product Research: Formerly Natural Product Letters 2008; 22:12, 1047-1054.

36. Retief, E., Herman, P.P.J.. Plants of the northern provinces of South Africa: Keys and diagnostic characters. Pretoria: National Botanical Institute, Strelitzia 6. 1997.

37. Power, B.F., Tutin, F.. Chemical examination of *Lippia scaberrima* Sonder ("Beukess Boss"). American Journal of Pharmacy, 1907; 245:337-350.