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Lippia scaberrima Sond. (Verbenaceae): traditional uses, phytochemical and pharmacological properties

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Abstract
Lippia scaberrima is a woody shrub widely used as traditional medicine throughout its distributional range in southern Africa. This study was aimed at providing a critical review of the traditional uses, phytochemical and pharmacological properties of *L. scaberrima*. Several electronic search engines and specialized reference tools such as Google, Google Scholar, Scopus, Web of Science, scientific literature, publishing sites and electronic databases (Pubmed, Springer, Wiley and Science Direct) were used for data retrieval. The leaves of *L. scaberrima* are mainly used as mosquito repellent and tonic, and traditional medicine for respiratory problems, bronchitis, cough, fever, colds and stomach problems. The flowers, leaves, stems and twigs of *L. scaberrima* contain essential oils, coumarins, flavonoids, phenols, saponins, quinones, tannins and terpenoids. Pharmacological research revealed that the leaf and twig extracts of *L. scaberrima* and compounds isolated from the species have antibacterial, antifungal, antidiabetic and antioxidant activities. There is need for clinical and toxicological evaluations of crude extracts and compounds isolated from the species since *L. scaberrima* contains potentially toxic compounds.

Keywords: Ethnopharmacology, herbal medicine, indigenous pharmacopeia, *Lippia scaberrima*, Verbenaceae

INTRODUCTION

Lippia scaberrima Sond. is an erect and woody shrub belonging to the *Verbena L.* or vervain or Verbenaceae family. The family Verbenaceae consists of approximately 32 genera and 840 tree, shrub and herbaceous species distributed throughout the world, many of which have an aromatic smell.[1-3] The genus *Lippia* L. comprises about 200 species of herbs, shrubs and small trees distributed throughout south and central America and tropical Africa[3] and only 15 species have been recorded in tropical Africa.[4,5] The *Lippia* species are widely used as traditional medicines throughout the world for treating and managing human ailments such as abdominal pain, anxiety, asthma, bronchitis, burns, chest pains, colds, conjunctivitis, coughs, cutaneous diseases, depression, diarrhoea, dysentery, epilepsy, fever, gonorrhoea, headache, hypertension, malaria, pain, respiratory problems, stomach ache, stress, syphilis, ulcers and wounds.[6-19] Some of the *Lippia* species are characterized by antimalarial, antioxidant, antipyretic, antihypertensive, antimicrobial, spasmolitic, sedative, anticancer, antidiabetic, antiplasmodial and anti-inflammatory activities.[17,19-22] *Lippia scaberrima* is one of the valuable medicinal plant species in South Africa, and the species is included in the book “medicinal plants of South Africa,” a photographic guide to the most commonly used herbal medicines in the country, including its botany, major medicinal applications and active phytochemical compounds.[18] Research by Van Wyk[23] showed that the leaves of *L. scaberrima* have commercial potential as sources of health tea, and health products for fever, cough, colds, bronchitis and influenza in South Africa. Similarly, research by Van Wyk[24] showed that *L. scaberrima* is an important dietary supplement and/or functional food in Botswana with its aerial parts used as health tea, tonic and herbal medicine for stomach problems. *Lippia scaberrima* is commercially traded as natural caffeine-free health tea in southern Africa under the brand name “Musukujane tea”.[16,25-31] Research showed that *L. scaberrima* herbal tea has high socio-economic potential in Botswana as local people use the species as herbal tea and income generation.[29] It is within this context that this review was undertaken aimed at reviewing the traditional uses, phytochemical and pharmacological properties of *L. scaberrima* so as to provide the baseline data required in evaluating the therapeutic potential of the species.

Botanical profile of *Lippia scaberrima*

The genus *Lippia* L. is in honour of Augustin Lippi (1678–1705), a French naturalist and botanist with Italian origins.[32] *Lippia scaberrima* is a perennial woody shrub which can grow up to 60 cm in height. Leaves of *L. scaberrima* are strongly aromatic when crushed, opposite, rarely 3-whorled, shortly petiolated and pale green in colour. The leaves are narrowly lanceolate to elliptic in shape, acute at the apex and cuneate at the base with scattered short strigose hairs on the upper surface. The inflorescence spikes are dense and many-flowered, and greenish-yellow in colour. *Lippia scaberrima* has conspicuous leaf-like bracts in the flower heads. *Lippia scaberrima* has been recorded in Botswana and South Africa in Kalahari sand wooded grassland, pan margins and roadsides at an altitude ranging from 765 m to 1800 m above sea level.[33] *Lippia scaberrima* is morphologically similar to *L. javanica* (Burm.f.) Spreng., but the latter is much taller and its bracts are shorter than the flowers, while *L. scaberrima* has many stems arising from ground level and is usually less than 0.6 metres high, and its bracts are not longer than the flowers.[34]

Lippia scaberrima is a common natural coloniser of gold and uranium mine tailings and contaminated soils in the Witwatersrand Basin region in South Africa and this species can be used for tailings stabilisation.[35-39] Previous research by Louw[40] and Wells et al.[41] categorized *L. scaberrima* as an intruder which becomes dominant in overstocked veld, bushland and grasslands. Combrinck et al.[42] argued that *L. scaberrima* is unlikely to be threatened by genetic erosion or over-exploitation as the species is often invasive in overgrazed and disturbed bushland or grassland.[42]

Medicinal uses of *Lippia scaberrima*

The leaves of *L. scaberrima* are mainly used as mosquito repellent and tonic, and traditional medicine for respiratory problems, bronchitis, cough, fever, colds and stomach problems (Table 1; Figure 1). Other minor uses recorded in ethnobotanical literature based on a single report or record include chest ailments,[16] gastro-intestinal problems,[31] haemorrhoids,[43] haemostatic[43] and influenza.[16]

Table 1: Medicinal uses of *Lippia scaberrima*

Medicinal use	References
Bronchitis	Van Wyk and Gercke[16]; Van Wyk[23]; Dlamini[25]; Combrinck et al.[42]; Smith et al.[44]; Hulela and Thobega[45]
Chest ailments	Van Wyk and Gercke[16]
Colds	Van Wyk and Gercke[16]; Van Wyk[23]; Dlamini[25]; Motlhanka and Nthoiwa[46]; Combrinck et al.[42]; Smith et al.[44]; Hulela and Thobega[45]
Cough	Van Wyk and Gercke[16]; Van Wyk[23]; Dlamini[25]; Combrinck et al.[42]; Smith et al.[44]; Hulela and Thobega[45]
Fever	Van Wyk and Gercke[16]; Van Wyk[23]; Dlamini[25]; Motlhanka and Nthoiwa[46]; Combrinck et al.[42]; Smith et al.[44]
Gastro-intestinal problems	Mmopi et al.[31]
Haemorrhoids	Power and Tutin[43]
Haemostatic	Power and Tutin[43]
Influenza	Van Wyk[23]
Mosquito repellent	Watt and Breyer-Brandwijk[47]; Terblanché[48]; Sandasi et al.[49];
Respiratory problems	Mmopi et al.[31]; Watt and Breyer-Brandwijk[47]; Terblanché[48]; Sandasi et al.[49]
Stomach problems	Van Wyk[24]; Mokgalaka et al.[39]; Watt and Breyer-Brandwijk[47]; Terblanché[48]; Sandasi et al.[49]; Neuwinger[50]; Arnold et al.[51]
Tonic	Van Wyk[24]; Mokgalaka et al.[39]; Combrinck et al.[42]; Smith et al.[44]; Neuwinger[50]; Arnold et al.[51]

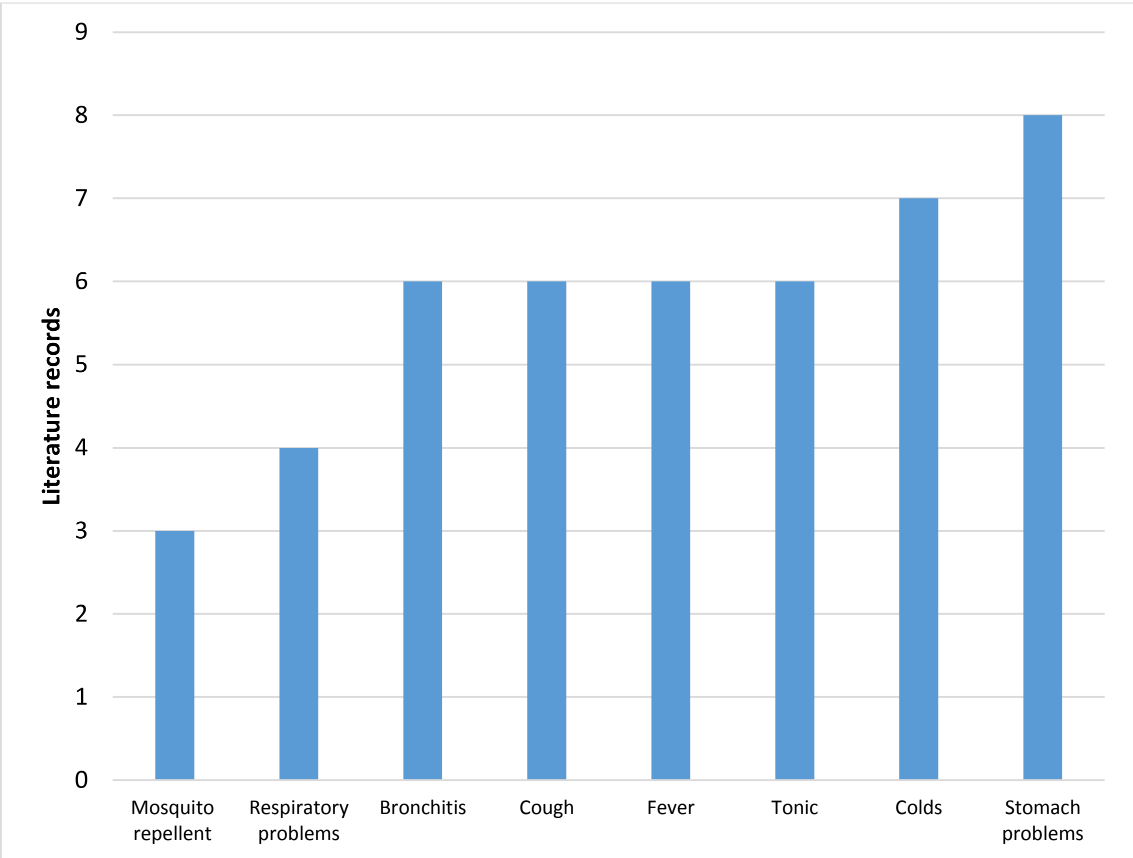

Figure 1. Medicinal applications of *Lippia scaberrima* derived from literature records

Phytochemistry and biological activities of *Lippia scaberrima*

The aerial parts, that is flowers, leaves and twigs of *L. scaberrima* contain essential oils (Table 2) and antibacterial, antifungal and antioxidant activities associated with the species may be attributed to some of these compounds. Other phytochemical compounds that have been identified from the leaves and stems of *L. scaberrima* include coumarins, flavonoids, phenols, saponins, quinones, tannins and terpenoids.[31] The following biological activities have been reported from the leaf and twig extracts of *L. scaberrima* and essential oils isolated from the species: antibacterial,[28,52] antifungal,[52-58] antidiabetic,[31] antioxidant[28,31] activities.

Table 2: Phytochemical compounds and chemical elements identified from the aerial parts of *Lippia scaberrima*

Phytochemical or element	Value	Reference
Arsenic (µg/g)	0.01 – 0.09	Mokgalaka et al.[38];
Borneol (%)	0.8 - 2.0	Combrinck et al.[42]; Regnier et al.[53]
Endo-borneol (%)	0.8 – 4.8	Terblanché et al.[59]
Bornylene (%)	0.1 – 0.4	Terblanché et al.[59]
δ-cadinene (%)	0.2	Terblanché et al.[59]
Calcium (µg/g)	5615 – 15546	Mokgalaka et al.[38]
Camphene (%)	<0.05 – 4.0	Combrinck et al.[42]; Regnier et al.[53]; Terblanché et al.[59]
Camphor (%)	0.1 – 5.8	Combrinck et al.[42]; Regnier et al.[53]; Terblanché et al.[59]
Carveol (%)	0.3	Combrinck et al.[42]
Trans-carveol (%)	<0.05 – 1.3	Terblanché et al.[59]
Carvone (%)	1.0 – 34.0	Mokgalaka et al.[38]; Combrinck et al.[42]; Sandasi et al.[49]; Regnier et al.[53]
β-caryophyllene (%)	<0.05 – 0.4	Combrinck et al.[42]; Terblanché et al.[59]
Chromium (µg/g)	0.32 – 0.96	Mokgalaka et al.[38]
1.8-Cineole (%)	5.0 – 34.1	Combrinck et al.[42]; Regnier et al.[53]; Terblanché et al.[59]
Copper (µg/g)	1.5 – 42.0	Mokgalaka et al.[38]
p-Cymene (%)	3.2 – 4.0	Combrinck et al.[42]; Sandasi et al.[49]; Regnier et al.[53]
Dihydrocarvone (%)	0.4	Combrinck et al.[42]
α-Humulene (%)	<0.05 – 0.8	Combrinck et al.[42]; Terblanché et al.[59]
Iron (µg/g)	0.6 – 161.0	Mokgalaka et al.[38]
Isopiperitone	-	Sandasi et al.[49]
Isoverbascoside	-	Olivier et al.[27]; Shikanga et al.[56]
Limonene (%)	0.2 – 61.0	Mokgalaka et al.[38]; Combrinck et al.[42]; Sandasi et al.[49]; Regnier et al.[53]; Terblanché et al.[59]
Linalool (%)	0.2 – 0.7	Combrinck et al.[42]; Terblanché et al.[59]
Magnesium (µg/g)	947 – 7039	Mokgalaka et al.[38]
Methylpentene (%)	<0.05	Terblanché et al.[59]
Molybdenum (µg/g)	0.01 – 0.07	Mokgalaka et al.[38]
Myrcene (%)	<0.05 – 0.9	Combrinck et al.[42]; Terblanché et al.[59]
Nickel (µg/g)	0.37 – 1.80	Mokgalaka et al.[38]
α-Phellandrene (%)	<0.05 – 2.9	Combrinck et al.[42]; Terblanché et al.[59]
Phosphorus (µg/g)	869 – 2463	Mokgalaka et al.[38]
α-Pinene (%)	<0.05 – 1.9	Combrinck et al.[42]; Terblanché et al.[59]
β-Pinene (%)	<0.05 – 0.8	Combrinck et al.[42]; Terblanché et al.[59]
Piperitenone	-	Sandasi et al.[49]
Potassium (µg/g)	6266 – 18823	Mokgalaka et al.[38]
Sabinene (%)	<0.05 – 2.2	Combrinck et al.[42]; Terblanché et al.[59]
Sulfur (µg/g)	720 – 2202	Mokgalaka et al.[38]
γ-Terpinene (%)	<0.05 – 0.5	Combrinck et al.[42]; Terblanché et al.[59]
α-Terpineol (%)	<0.05 – 2.2	Combrinck et al.[42]; Terblanché et al.[59]
Terpinolene (%)	<0.05 – 0.1	Terblanché et al.[59]
Theviridoside	-	Shikanga et al.[28]
α-Thujene (%)	<0.05 – 0.1	Terblanché et al.[59]
Total soluble phenolic (GAE mg/g)	4.6 – 8.7	Shikanga et al.[28]
Uranium (µg/g)	0.007 – 0.15	Mokgalaka et al.[38]
Verbascoside	-	Olivier et al.[27]; Shikanga et al.[56]
Zinc (µg/g)	0.65 – 10.9	Mokgalaka et al.[38]

Antibacterial activities

Huffman et al.[52] evaluated the antibacterial activities of essential oil isolated from *L. scaberrima* against *Staphylococcus aureus* and *Pseudomonas aeruginosa* using the microdilution method. The essential oil exhibited weak activities against tested pathogens.[52] Shikanga et al.[28] evaluated the antibacterial activities of leaf extract of *L. scaberrima* and the compounds verbascoside and isoverbascoside isolated from the species against *Staphylococcus aureus, Enterococcus faecalis, Escherichia coli* and *Pseudomonas aeruginosa* using the serial microdilution method with gentamycin as a positive control. The extract exhibited weak activities with minimum inhibitory concentration (MIC) values ranging from 0.6 mg/ml to 1.3 mg/ml, while the compounds verbascoside and isoverbascoside exhibited good activities with MIC values ranging from 0.06 mg/ml to 0.25 mg/ml which were comparable to MIC values of 0.02 mg/ml to 0.07mg/ml exhibited by the positive control.[28]

Antifungal activities

Huffman et al.[52] evaluated the antifungal activities of essential oil isolated from *L. scaberrima* against *Candida albicans* and *Cryptococcus neoformans* using the microdilution method. The essential oil exhibited weak activities against tested pathogens.[52] Regnier et al.[53] evaluated the *in vitro* and *in vivo* antifungal activities of essential oils limonene, R-(-)-carvone, S-(+)-carvone and 1,8-cineole isolated from the aerial parts of *L. scaberrima* against *Botryosphaeria parva* and *Colletotrichum gloeosporioides*. The essential oils exhibited activities by inhibiting the growth of the tested pathogens.[53] Combrinck et al.[54] evaluated the antifungal activities of the essential oil isolated from aerial parts of *L. scaberrima* against common commercially important postharvest pathogens of subtropical mango, avocado and citrus fruits. The antifungal activities were evaluated by semi-commercial and commercial trials using fruits treated postharvest with coatings amended with essential oil. The essential oil was found to exhibit strong *in vitro* activities against post-harvest spoilage pathogens of the fruits.[54] Du Plooy et al.[55] evaluated the antifungal activities of essential oil isolated from aerial parts of *L. scaberrima* against *Penicillium digitatum* using *in vitro* antifungal assay and in vivo investigations using inoculated *Citrus sinensis* L., 'Valencia' variety. The authors also evaluated the effectiveness of the essential oil of *L. scaberrima* incorporated into commercial coatings of carnauba tropical®, thiabendazole or imazalil/guazatine (1:1) to improve the postharvest quality of the orange fruit. *In vitro* studies showed that the essential oils were active against *Penicillium digitatum* and excellent disease control was achieved with the amended coatings.[55] Shikanga et al.[56] evaluated the antifungal activities of polar extracts and compounds isoverbascoside, theviridoside and verbascoside isolated from aerial parts of *L. scaberrima* against a Guazatine®-resistant strain of *Penicillium digitatum*. The *in vitro* tests were carried out by incorporating the compounds and plant extracts into malt extract agar at concentrations ranging from 0.2 mg/mL to 1.0 mg/mL and an *in vivo* (curative) assay was conducted using the checker-board technique on *Citrus sinensis* L., 'Valencia' variety. The extract and all the compounds were able to inhibit fungal growth at concentrations above 0.6 mg/mL.[56] Regnier et al.[57] evaluated the antifungal activities of essential oil isolated from aerial parts of *L. scaberrima* against *Colletotrichum gloeosporioides, Lasiodiplodia theobromae* and an *Alternaria* strain using in vitro antifungal assay and in vivo investigations using inoculated avocado (*Persea americana* Mill.) fruit. The authors also evaluated the effectiveness of the essential oil of *L. scaberrima* incorporated into commercial coatings (carnauba tropical® and midseason 865® (MS865) to improve the postharvest quality of avocado fruit. The essential oil inhibited the mycelial growth of all the pathogens when applied at a concentration of 2000 µL/L. Essential oil at a concentration of 1000 µL/L and 2000 µL/L incorporated into the commercial coating inhibited the mycelial growth of the tested pathogens.[57] Manganyi et al.[58] evaluated the antifungal activities of essential oil of *L. scaberrima* against *Fusarium oxysporum* species complex using the toxic medium assay (TMA) at concentrations of 100 µL/L, 250 µL/L, 500 µL/L, 1000 µL/L, 2000 µL/L, 2500 µL/L and 3000 µL/L. At a concentration of 3000 µL/L the essential oil of *L. scaberrima* inhibited 87.0% of fungal growth.[58]

Antidiabetic activities

Mmopi et al.[31] evaluated the antidiabetic activities of 70% methanol of leaf and stem extracts of *L. scaberrima* by evaluating the inhibition of the extracts on α-amylase activity. The extracts exhibited dose-dependent activities with the highest inhibition of 65.0% achieved at a concentration of 20 mg/ml.[31]

Antioxidant activities

Shikanga et al.[28] evaluated the antioxidant activities of leaf extracts of *L. scaberrima* and the compounds verbascoside and isoverbascoside isolated from the species using 2,2-diphenylpycrylhydrazyl (DPPH) free radical scavenging assay with ascorbic acid as a positive control. The extract exhibited weak activities with half maximal effective concentration (EC_{50}) value of 1150 µg/ml, while the compounds verbascoside and isoverbascoside exhibited good activities with EC_{50} values of 89.0 µg/ml and 101.0 µg/ml, respectively which were comparable to EC_{50} value of 75.0 µg/ml exhibited by the positive control.[28] Mmopi et al.[31] evaluated the antioxidant activities of 70% methanol of leaf and stem extracts of *L. scaberrima* using the DPPH, 2,2`-azino-bis(3-ethyl benzothiazoline-6-sulphonic acid) (ABTS) radical scavenging and thiobarbituricacid (TBA) assays with gallic acid, ascorbic acid and butylatehydroxyanisole (BHT) as positive controls. The extracts exhibited activities with the highest ABTS inhibition of 55.0% achieved at a concentration of 25.0 mg/ml. The extracts exhibited activities with the highest DPPH inhibition of 84.0% achieved at a concentration of 0.5 mg/ml. Results from the TBA assay showed that extracts exhibited 45.0% to 55.0% inhibition after 30 minutes.[31]

CONCLUSION

Lippia scaberrima has been implicated in stock losses in South Africa[47,60-62] and therefore, there is need for detailed clinical and toxicological evaluations of crude extracts and compounds isolated from the species. Much work is required on aspects of quality control to ensure safety and ensure that potentially toxic components of *L. scaberrima* herbal products are kept below tolerance levels. Future studies should investigate any side effects and/or toxicity associated with intake of *L. scaberrima* herbal products. Therefore, the use of *L. scaberrima* for the treatment and management of human diseases and ailments should be treated with caution and rigorous toxicological and clinical studies on the different plant parts and compounds isolated from the species are necessary before they are widely prescribed for use as traditional medicines.

Conflict of interest

The author declares that he has no conflict of interest.

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