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South Africa's Best BARK Medicines Prescribed at the Johannesburg Muthi Markets for Skin, Gut, and Lung Infections: MIC's and Brine Shrimp Lethality

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Abstract: Indigenous trade of medicinal plants in South Africa is a multi-million-rand industry and is still highly relevant in terms of primary health care. The purpose of this study was to identify today's most traded medicinal barks, traditionally and contemporaneously used for dermatological, gastrointestinal, and respiratory tract infections; then, to investigate the antimicrobial activity and toxicity of the respective extracts and interpret outcomes in light of pharmacokinetics. Thirty-one popularly traded medicinal barks were purchased from the Faraday and Kwa Mai-Mai markets in Johannesburg, South Africa. Information on the medicinal uses of bark-based medicines in modern commerce was recorded from randomly selected traders. The minimum inhibitory concentration (MIC) method was used for antimicrobial screening, and brine shrimp lethality was used to determine toxicity. New medicinal uses were recorded for 14 bark species. Plants demonstrating some broad-spectrum activities against tested bacteria include *Elaeodendron transvaalense*, *Erythrina lysistemon*, *Garcinia livingstonei*, *Pterocelastrus rostratus*, *Rapanea melanophloeos*, *Schotia brachypetala*, *Sclerocarya birrea*, and *Ziziphus mucronata*. The lowest MIC value of 0.004 mg/mL was observed against *Staphylococcus epidermidis* for a dichloromethane bark extract of *E. lysistemon*. The tested medicinal barks were shown to be non-toxic against the *Artemia nauplii* (brine shrimp) bioassay, except for a methanol extract from *Trichilia emetica* (69.52% mortality). Bacterial inhibition of bark extracts with minimal associated toxicity is consistent with the safety and valuable use of medicinal barks for local muthi market customers. Antimicrobial outcomes against skin and gastrointestinal pathogens are feasible because mere contact-inhibition is required *in vivo*; however, MIC values against respiratory pathogens require further explaining from a pharmacokinetics or pharmacodynamics perspective, particularly for ingested rather than smoked therapies.

Keywords: bark; antibacterial; traditional medicine; Zulu; brine shrimp lethality

1. Introduction

Bark is the outer protective layer of woody plants. It consists of all tissues outside the vascular cambium, an actively dividing layer of cells responsible for the production of xylem and phloem tissues [1,2]. Bark contains a high mass of polyphenols with medicinal applications [3,4]. Biological studies of medical bark remain scarce, which has led to it being undervalued as a suitable organ [3]. The use of bark in traditional medicine is also common in other parts of the world outside of Africa. A study by Pagliosa et al. [5] conducted in Brazil reported potent antioxidant activity from the methanol extract of bark from *Ilex paraguariensis* A. St. Hil. Furthermore, medicinal bark of different plant species from the British Moracin family were reported to contain bioactive benzofuran derivatives [6]. From south and southeast Asian countries, species from the genus *Dillenia*

87. Mulholland, D.A.; Mwangi, E.M.; Dlova, N.C.; Plant, N.; Crouch, N.R.; Coombes, P.H. Non-toxic melanin production inhibitors from *Garcinia livingstonei* (clusiaceae). *J. Ethnopharmacol.* **2013**, *149*, 570–579. [[CrossRef](#)] [[PubMed](#)]
88. Chinsembu, K.C.; Hjarunguru, A.; Mbangi, A. Ethnomedicinal plants used by traditional healers in the management of hiv/aids opportunistic diseases in Rundu, Kavango East Region, Namibia. *S. Afr. J. Bot.* **2015**, *100*, 33–42. [[CrossRef](#)]
89. Chinsembu, K.C. Study of medicinal flora utilised by traditional healers in the management of sexually transmitted infections in Sesheke District, Western Province, Zambia. *Rev. Bras. Farmacogn.* **2016**, *26*, 268–274. [[CrossRef](#)]
90. Madikizela, B.; McGaw, L.J. *Pittosporum viridiflorum* Sims (Pittosporaceae): A review on a useful medicinal plant native to South Africa and tropical Africa. *J. Ethnopharmacol.* **2017**, *205*, 217–230. [[CrossRef](#)]
91. Bodeker, G.; Van't Klooster, C.; Weisbord, E. *Prunus africana* (hook.F.) kalkman: The overexploitation of a medicinal plant species and its legal context. *J. Altern. Complementary Med.* **2014**, *20*, 810–822. [[CrossRef](#)]
92. Otang, W.M.; Grierson, D.S.; Ndip, R.N. Phytochemical studies and antioxidant activity of two South African medicinal plants traditionally used for the management of opportunistic fungal infections in HIV/AIDS patients. *BMC Complementary Altern. Med.* **2012**, *12*, 43. [[CrossRef](#)]
93. Maroyi, A. Traditional use of medicinal plants in south-central Zimbabwe: Review and perspectives. *J. Ethnobiol. Ethnomed.* **2013**, *9*, 31–49. [[CrossRef](#)] [[PubMed](#)]
94. McGaw, L.J.; Jäger, A.K.; van Staden, J. Variation in antibacterial activity of *Schotia* species. *S. Afr. J. Bot.* **2002**, *68*, 41–46. [[CrossRef](#)]
95. Eloff, J.N. A sensitive and quick microplate method to determine the minimal inhibitory concentration of plant extracts for bacteria. *Planta Med.* **1998**, *64*, 711–713. [[CrossRef](#)]
96. Muthee, J.K.; Gakuya, D.W.; Mbaria, J.M.; Mulei, C.M. Phytochemical screening and toxicity of selected plants used as anthelmintics in Loitoktok Sub-County, Kenya. *J. Phytopharm.* **2016**, *5*, 15–19.
97. Njume, C.; Afolayan, A.J.; Green, E.; Ndip, R.N. Volatile compounds in the stem bark of *Sclerocarya birrea* (anacardaceae) possess antimicrobial activity against drug-resistant strain of *Helicobacter pylori*. *Int. J. Antimicrob. Agents* **2011**, *38*, 319–324. [[CrossRef](#)] [[PubMed](#)]
98. Moyo, M.; Finnie, J.F.; van Staden, J. Antimicrobial and cyclooxygenase enzyme inhibitory activities of *Sclerocarya birrea* and *Harpephyllum caffrum* (anacardiaceae) plant extracts. *J. Ethnopharmacol.* **2011**, *105*, 286–293. [[CrossRef](#)]
99. Amenya, H.Z.; Gathumbi, P.K.; Mbaria, J.M.; Thaiyah, A.G.; Thoithi, G.N. Sub-acute toxicity of the chloroformic extract of *Rapanea melanophloeos* (L.) mez in rats. *J. Ethnopharmacol.* **2014**, *154*, 593–599. [[CrossRef](#)]
100. Khumalo, G.P.; Sadgrove, N.J.; Van Vuuren, S.F.; Van Wyk, B.-E. Antimicrobial activity of volatile and non-volatile isolated compounds and extracts from the bark and leaves of *Warburgia salutaris* (canellaceae) against skin and respiratory pathogens. *S. Afr. J. Bot.* **2019**, *122*, 547–550. [[CrossRef](#)]
101. Sadgrove, N.J.; Jones, G.L. From petri dish to patient: Bioavailability estimation and mechanism of action for antimicrobial and immunomodulatory natural products. *Front. Microbiol.* **2019**, *10*, 2470. [[CrossRef](#)] [[PubMed](#)]
102. Bussmann, R.W.; Malca, G.; Glenn, A.; Sharon, D.; Nilsen, B.; Parris, B.; Dubose, D.; Ruiz, D.; Saleda, J.; Martinez, M.; et al. Toxicity of medicinal plants used in traditional medicine in northern Peru. *J. Ethnopharmacol.* **2011**, *137*, 121–140. [[CrossRef](#)]
103. Oryema, C.; Ziraba, R.B.; Odyek, O.; Omagor, N.; Opio, A. Phytochemical properties and toxicity to brine shrimp of medicinal plants in Erute County, Lira District, Uganda. *J. Med. Plants Res.* **2011**, *5*, 5450–5457.
104. Komane, B.M.; Olivier, E.I.; Viljoen, A.M. *Trichilia emetica* (meliaceae)—A review of traditional uses, biological activities and phytochemistry. *Phytochem. Lett.* **2011**, *4*, 1–9. [[CrossRef](#)]
105. Prozesky, E.A.M.; Meyer, J.J.; Louw, A.I. In vitro antiplasmodial activity and cytotoxicity of ethnobotanically selected South African plants. *J. Ethnopharmacol.* **2001**, *76*, 239–245. [[CrossRef](#)]
106. Germano, M.P.; D'Angelo, V.; Sanogo, R.; Catania, S.; Alma, R.; De Pascual, R.; Bisignano, G. Hepatoprotective and antibacterial effects of extracts from *Trichilia emetica* vahl. *J. Ethnopharmacol.* **2005**, *96*, 227–232. [[CrossRef](#)]
107. Gerstner, J. Some factors affecting the perpetuation of our indigenous silva. *J. S. Afr. For. Assoc.* **1946**, *13*, 4–11. [[CrossRef](#)]
108. Lewis, G.E. Testing the toxicity of extracts of southern African plants using brine shrimp (*Artemia salina*). *S. Afr. J. Sci.* **1995**, *9*, 382–384.
109. Williams, V.L.; Whiting, M.J. A picture of health? Animal use and the faraday traditional medicine market, South Africa. *J. Ethnopharmacol.* **2016**, *179*, 265–273. [[CrossRef](#)] [[PubMed](#)]
110. Meyer, B.N.; Ferrigni, N.R.; Putnam, J.E.; Jacobsen, L.B.; Nichols, D.E.; McLaughlin, J.L. Brine shrimp: A convenient general bioassay for active plant constituents. *Planta Med.* **1982**, *45*, 31–34. [[CrossRef](#)] [[PubMed](#)]
111. Sadgrove, N.J.; Simmonds, M.S.J. Topical and nutricosmetic products for healthy hair and dermal anti-aging using 'dual-acting' (2 for 1) plant-based peptides, hormones, and cannabinoids. *FASEB BioAdvances* **2021**. [[CrossRef](#)]