LANNEA ACIDA: A REVIEW OF ITS MEDICINAL USES AND PHYTOCHEMISTRY AND PHARMACOLOGICAL PROPERTIES

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ABSTRACT

Lannea acida is widely used as herbal medicine in West Africa. The present study critically reviewed the medicinal uses and phytochemistry and pharmacological properties of L. acida. The keywords including L. acida, its synonyms, English common names, medicinal uses, and phytochemistry and pharmacological properties of the species were searched using electronic databases such as ISI web of knowledge, ProQuest, ScienceDirect, OATD, Scopus, OpenThesis, PubMed, and Google Scholar. The search for pre-electronic literature such as conference papers, scientific articles, books, book chapters, dissertations, and theses was carried out at the university library. Literature studies revealed that L. acida is mainly used for injuries, inflammation and pain, gastrointestinal problems, fever and malaria, gynecological and pregnancy disorders, ethnoveterinary medicine, hemorrhoids, skin diseases, and infections. Phytochemical compounds identified from the species include alkaloids, cardiac glycosides, flavonoids, phenols, saponins, steroids, tannins, and terpenoids. Pharmacological studies revealed that L. acida extracts have anthelmintic, antibacterial, antidiarrheal, anti-inflammatory, antiviral, antioxidant, estrogenic, fertility, hyaluronidase, phospholipase A2, proteolytic, and vibrioctidal activities. Given the importance of L. acida as herbal medicine, there is a need for detailed studies aimed at establishing the efficacy, clinical relevance, and safety of the plant extracts and compounds.

Keywords: Anacardiaceae, Lannea acida, Traditional medicine, West Africa.

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INTRODUCTION

Lannea acida A. Rich. belongs to the cashew or Anacardiaceae family. The name of the genus, "Lannea," is based on a Latin word “lana” which translates to “wool” in reference to young plant parts which are densely hairy or possibly to the wool on the roots of some Lannea species [1,2]. The synonyms of L. acida are Lannea buettneri Engl., Lannea djalonica A. Chev, Lannea glaucescens Engl, Lannea lagdoensis (Engl and K. Krause) Midd., Lannea oleosa A. Chev, Odnaacida (A. Chev) Walp., and Sorindela lagdoensis Engl. and K. Krause [3-6]. The genus Lannea consists of approximately 40 species which are usually trees, shrubs, or suffrutescent, occupying different habitats in Sub-Saharan Africa, with only one species recorded in Tropical Asia and several species introduced throughout the world [4-6]. L. acida is a multipurpose tree indigenous to Benin, Burkina Faso, Cameroon, Central African Republic, Côte d’Ivoire, Gambia, Ghana, Guinea, Mali, Niger, and Nigeria [3,7-13]. The species has been recorded in wooded savannah, forest edges, bushed grassland, rocky outcrops, and near riverbed sandy soils at an altitude ranging from 0 to 1600 m above sea level [13]. The tree species is widely used by local communities in West Africa as a source of dye, food, medicines, and other commodities. Its berry-like fruits which are about 1 cm across and 1.5 cm long occur in large clusters and are consumed either fresh or dried and can be stored for use months later [14]. The fruits have a slightly acidic and somewhat resinsious, pleasant taste, and both fresh and dried fruits are eaten raw or made into juice, jam, and puddings [14]. The young leaves of L. acida are cooked as leafy vegetables [13]. In clearing land for agricultural purposes, some communities in West Africa do not cut L. acida, thereby ensuring a continued supply of goods and ecosystem services provided by the species [13]. In Senegal, L. acida is regarded as an important herbal medicine, with different plant parts sold on informal herbal medicine markets [13]. Marquet and Jansen [15] identified L. acida as an important useful plant species with domestication potential in West Africa based on its multipurpose uses and popularity as herbal medicine. It is within this context that this review was undertaken aimed to summarize the medicinal uses and phytochemical and pharmacological properties of L. acida so as to provide baseline data required for evaluating the therapeutic potential of the species.

MEDICINAL USES OF L. ACIDA

The major documented diseases and ailments treated by L. acida extracts were grouped and classified following the guidelines provided by Cook [16] and Gruca et al. [17] (Table 1). The major medicinal uses of L. acida (in descending order of importance) include injuries, inflammation and pain, gastrointestinal problems, fever and malaria, gynecological and pregnancy disorders, ethnoveterinary medicine, haemorrhoids, skin diseases, and infections (Fig. 1). In multitherapeutic applications, the bark of L. acida is applied topically for swellings mixed with cloves of Parkia biglobosa (Jacq.). R. Br. ex G. Don, while the leaves of L. acida are mixed with leaves and roots of Alafia barteri Oliv. and Flueggea virosa (Rosch. ex Willd.) Royle and pods of Xylopia aethiopica (Dunal). A. Rich. as herbal medicine for cancer [18]. In Ghana, the leaves of L. acida are mixed with those of Asidricarta indica A. Juss. and Mangifera indica L. as herbal medicine for malaria [19]. The bark of L. acida is mixed with that of Guiera senegalensis J. F. Gmel as herbal medicine for intestinal parasites [20], while bark mixed with different plant parts of Euphorbia unispina N. E. Br. are used against new castle disease [21]. In Benin, the roots of L. acida are mixed with the bark of Detarium microcarpum Guill. and Perr. and Khaya senegalensis (Dess.) A. Juss. and used as ethnoveterinary medicine against foot and mouth [21].

PHYTOCHEMISTRY AND PHARMACOLOGICAL PROPERTIES OF L. ACIDA

Sultana and Ilyas [51] identified a flavanone, 6,7-(2”-2”-dimethyl chromeno)-8,9γ-dimethyl allyl flavanone1 (Fig. 2) from the acetone extract of L. acida leaves using nuclear magnetic resonance (NMR) and ultraviolet-visible spectroscopy. Similarly, Muhaissen [52] identified four flavonoids which included 6,7-(2”-2”-dimethyl chromeno)-8,9γ-dimethyl allyl flavanone 1,
### Table 1: Medicinal uses of *Lannea acida*

| Medicinal use                               | Parts of the plant used                             | Country                                      | References |
|---------------------------------------------|----------------------------------------------------|----------------------------------------------|------------|
| Injuries, inflammation, and pain (abdominal pain, burns, furuncle, gout, rheumatism, swellings, toothache, ulcers, and wounds) | Bark, leaves, roots, and stem bark                  | Benin, Burkina Faso, Côte d’Ivoire, Gambia, Mali, Nigeria, and Senegal | [3,13,22-28] |
| Swellings                                   | Bark mixed with cloves of *Parkia biglobosa* (Jacq.) R. Br. ex G. Don | Benin                                         | [29]       |
| Anemia                                      | Stem bark                                          | Côte d’Ivoire                                | [24]       |
| Blood tonic                                 | Bark                                               | Nigeria                                      | [30]       |
| Cancer                                      | Stem bark                                          | Nigeria                                      | [31]       |
| Cancer                                      | Leaves mixed with leaves and roots of *Alafia barteri* O. & R. Fluegge and *Flueggea virosa* (Roxb. ex Willd.) Royle and pods of *Xylopia aethiopica* (Dunal) A. Rich. | Nigeria | [18] |
| Consciousness loss                          | Bark, leaves, and roots                            | Burkina Faso                                | [32]       |
| Convulsions                                 | Whole plant                                        | Ghana                                        | [33]       |
| Cough                                       | Bark, leaves, and roots                            | Burkina Faso                                | [34]       |
| Diabetes                                    | Whole plant                                        | Guinea                                       | [35]       |
| Gastrointestinal problems (abdominal bloating, constipation, diarrhea, dysentery, and stomach ache) | Bark, leaves, roots, and stem bark                  | Burkina Faso, Cameroun, Côte d’Ivoire, Niger, and Senegal | [24,25,27,28,34,36-41] |
| Epilepsy                                    | Bark, leaves, and roots                            | Burkina Faso                                | [32]       |
| Epistaxis                                   | Stem bark                                          | Burkina Faso                                | [42]       |
| Eye problems                                | Bark                                               | Nigeria                                      | [27]       |
| Gynecological and pregnancy disorders (facilitate labor, infertility, gynecological complaints, and menstrual pain) | Bark and stem bark                   | Burkina Faso, Cameroun, Nigeria, and Senegal | [13,27,41,42] |
| Fever and malaria                           | Bark, leaves, roots, and stem bark                   | Benin, Burkina Faso, and Nigeria              | [3,34,42-44] |
| Malaria                                     | Leaves mixed with those of *Azadirachta indica* A. Juss. and *Mangifera indica* L. | Ghana                                        | [19]       |
| General well-being                          | Bark                                               | Nigeria                                      | [45]       |
| Gonorrhea                                   | Roots and stem bark                                | Côte d’Ivoire                                | [24]       |
| Hemorrhoids                                 | Bark and leaves                                    | Burkina Faso, Niger, and Senegal             | [39,40,46] |
| Hallucination                               | Bark, leaves, and roots                            | Burkina Faso                                | [32]       |
| Headache                                    | Stem bark                                          | Burkina Faso                                | [42]       |
| Intestinal worms                            | Bark and leaves                                    | Nigeria                                      | [40]       |
| Mycosis                                     | Bark                                               | Burkina Faso                                | [39]       |
| Skin diseases and infections                | Bark, leaves, roots, and stem bark                  | Burkina Faso and Nigeria                     | [34,36,42,47] |
| Snakebite                                   | Cortex                                             | Mali                                         | [49]       |
| Ethnoveterinary medicine (internal parasites and new castle) | Bark                                           | Benin and Burkina Faso                       | [49,50]    |
| Intestinal parasites                        | Bark mixed with that of *Guiera senegalensis* J. F Gmel | Cameroon                                     | [20]       |
| Foot and mouth                              | Root mixed with the bark of *Detarium microcarpum* Lannea acida | Benin                                         | [21]       |
| Newcastle                                   | Bark mixed with *Euphorbia unispina* N. E. Parkia   | Benin                                        | [21]       |

3′,4′-Dihydroxy-7,8-(2′,2′-dimethyl chromeno)-6,7-dimethyl allyl flavonol 2, 7-methyltectorigenin 3, and irisolide 4 (Fig. 2) from the bark of *L. acida* using NMR, UV, infrared, and mass spectrometry. Flavonoids are characterized by several pharmacological properties, for example, irisolide 4 is known to possess anti-*.Helicobacter pylori* activities [53], inhibition of prostaglandin E2 production [54], hepatoprotective activities [55,56], cancer chemopreventive activities [57], estrogenic activities [58], inhibitory effect of JC1 virus gene expression [59], anti-inflammatory activities [60,61], and protective properties against hydrogen peroxide (H₂O₂) [62]. Other phytochemical compounds identified from the bark and stem bark of *L. acida* include alkaloids, cardiac glycosides, phenols, saponins, steroids, tannins, and terpenoids [37,41,63-65]. Leung et al. [66] analyzed the calcium, carbohydrates, energy, fat, fiber, phosphorous, and protein content of *L. acida* leaves as a means of estimating the quality of leaves as vegetable sources (Table 2).

The pharmacological activities exhibited by *L. acida* extracts include the following: Anthelmintic [25], antibacterial [24,67], anti-diarrheal [37], anti-inflammatory [64], antimycobacterial [34], antioxidant [65,67], estrogenic [41], fertility [68], hyaluronidase [48,69], phospholipase A₂ [48,69], proteolytic [48,69], and vibriocidal [70] activities.

### Anthelmintic activities

Kone et al. [25] evaluated the anthelmintic activities of ethanol stem bark extract of *L. acida* using the nematode *Haemonchus contortus* Rudolphi as the test species and ivermectin and fenbendazole, commercial anthelmintics as positive controls by determining the number of unhatched eggs and the number of larvae, the developmental stages of larvae, and their mobility. The extract exhibited larvicidal concentration (LC₅₀) value of 0.8 mg/ml, while ivermectin and fenbendazole exhibited LC₅₀ values of 0.001 mg/ml and 0.01 mg/ml.
respectively [25]. The anthelmintic activities exhibited by the species corroborate the traditional usage of the bark and leaves of L. acida against intestinal worms in Niger [40] and as ethnoveterinary medicine against intestinal parasites in Cameroon [20].

**Antidiarrheal activities**

Etuk et al. [37] evaluated the antidiarrheal activities of the aqueous bark extract of L. acida using the castor oil model of diarrhea induction in Wistar rats with diphenoxylate as a standard antidiarrheal agent. The oral administration of 200 mg/kg of the extracts exhibited inhibition against castor oil-induced diarrhea in rats [37]. These results show that L. acida has potential in the management of gastrointestinal problems such as abdominal bloating, constipation, diarrhea, dysentery, and stomach ache [24,25,27,28,34,36-41]. Research by Stark et al. [71] and Maroyi [72] showed that medicinal plants have potential in the treatment of gastrointestinal disorders and the pain that is associated with the disorders.

**Antibacterial activities**

Kone et al. [24] evaluated antibacterial activities of ethanol root extracts of L. acida against Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecalis, Streptococcus pyogenes, and Bacillus subtilis using agar diffusion and microdilution methods with gentamicin and tetracycline as positive controls. The extracts were active against S. aureus, E. faecalis, and S. pyogenes with minimum inhibitory concentration (MIC) values ranging from 23 µg/mL to 1500 µg/mL and half maximal inhibitory concentration (IC₅₀) values ranging from 94 µg/mL to 188 µg/mL. The MIC values exhibited by the two controls ranged from 0.2 µg/mL to >50 µg/mL and IC₅₀ values ranged from 25 µg/mL to 50 µg/mL [24]. Ouattara et al. [67] evaluated antibacterial activities of ethanol bark extracts of L. acida against Bacillus subtilis, Enterobacter aerogenes, E. faecalis, Proteus mirabilis, P. aeruginosa, Salmonella enterica, Salmonella typhimurium, S. aureus, and Staphylococcus camorum using disc diffusion and broth microdilution methods with ciprofloxacin, erythromycin, and tetracycline as positive controls. The extracts exhibited activities against all tested pathogens except E. aerogenes with 11–17 mm zone of inhibition. The extracts were active against most pathogens except S. typhimurium with MIC values ranging from 7.8 to 125.0 µg/mL and minimum bactericidal concentration values ranging from 15.6 to >500.0 µg/mL [67]. These antibacterial activities exhibited by the extracts of L. acida support the traditional usage of the species as remedy for bacterial pathogens causing diarrhea [24,25,27,34,37,39,41], dysentery [25,34,38,40], furuncle [28], gonorrhea [24], microbial infections on burns and wounds [3,22,23], skin infections [36], stomach ache [24,28,36,38,39,40], and toothache [1,3,26].

**Anti-inflammatory activities**

Owusu and Ofori-Amoah [64] evaluated anti-inflammatory activities of aqueous stem bark extract of L. acida using paw edema and writhing test assays in male Sprague Dawley rats. The extract at 30–300 mg/kg reduced prostaglandin E2-induced paw edema in both prophylactic and curative protocols. The extract also significantly inhibited acetic acid-induced abdominal writhing movement in imprint control region mice. In the prophylactic protocol, at 30 mg/kg, the percentage total inhibitory effects of the extract were 68.4%, while in the curative protocol, the percentage maximal inhibitory effects of the extract at 300 mg/kg were 67.1%. The extracts inhibited prostaglandin E2-induced paw edema and acetic acid-induced writhing movements in imprint control group mice and, therefore, are potential remedies for inflammation and pain [64], corroborating the traditional usage of the species against rheumatism [3,22,24], swellings [3,22,29], ulcers [27], and wounds [3,22,23].

**Antimycobacterial activities**

Ouattara et al. [34] evaluated antimycobacterial activities of ethanol-water bark extract of L. acida using the anti-Mycobacterium tuberculosis...
assay against *M. tuberculosis* H37Rv. The percentage of inhibition of *M. tuberculosis* proliferation was 77.6% and 36.8% at 1.2 and 0.6 mg/mL, respectively [34]. These documented antimycobacterial activities of *L. acida* extracts which support the medicinal uses of the species in the treatment of respiratory system disorders including cough in Burkina Faso [34].

**Antioxidant activities**

Ouattara et al. [67] evaluated antioxidant activities of ethanol bark extracts of *L. acida* using the 2,2'-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay with gallic acid and quercetin as positive controls. The extract exhibited IC<sub>50</sub> value of 345.7 µg/mL, while the controls, gallic acid and quercetin exhibited much lower IC<sub>50</sub> values of 0.6 µg/mL and 0.9 µg/mL, respectively [67]. Onosode et al. [65] evaluated the antioxidant activities of ethyl acetate stem bark extracts of *L. acida* using the DPPH free radical scavenging assay with ascorbic acid as control. The extract exhibited the highest percentage scavenging activity of 90% at a concentration of 20 µg/mL which was comparable to scavenging activity exhibited by ascorbic acid, although the scavenging activity of the control was relatively more pronounced than that of the extract at 2.5 mg/mL, 5 mg/mL, and 10 mg/mL [65]. The antioxidant activities exhibited by *L. acida* extracts are probably due to flavonoids and phenolics that have been identified from the species [41,51,52,65,67], and flavonoids and phenolics are known to exhibit antioxidant properties [73-81].

**Estrogenic activities**

Oumarou et al. [41] evaluated the estrogenic activities of bark ethanol extracts of *L. acida* using a 3-day uterine proliferation assay and a 12-week oral treatment in ovariectomized adult female Wistar rats. To evaluate estrogen-like effects of *L. acida* extracts, a simple and sensitive E-screen cell proliferation assay was performed with MCF-7 cells.

The 3-day oral administration of bark extracts induced an increase in uterine wet weight, uterine water content, uterine total protein and glycogen levels, uterine and vaginal epithelial heights, and mammary glands differentiation. At 200 mg/kg, a long-term treatment with the extract prevented body weight gain and loss of bone mass and/or density induced by ovariectomy [41]. *L. acida* extract improved bone microarchitecture and could restore normal bone mineralization by increasing the inorganic phosphorus and calcium level in bone. The *L. acida* ethanol extract induced a significant increase of MCF-7 cells yield at concentrations of 10 µg/mL, 100 µg/mL, and 200 µg/mL as compared to DMSO control [41]. Taken altogether, this finding provides the evidence that *L. acida* is a potential alternative for the prevention of postmenopausal osteoporosis which occurs as a consequence of estrogen decline at menopause [41].

**Fertility activities**

Ahmed et al. [68] evaluated the effect of methanolic stem bark extract of *L. acida* on sperm count, sperm motility, sperm morphology, serum testosterone, and histology of the testes on male Wistar rats. Results of this study showed that the administration of the stem bark extract of *L. acida* increased sperm count, morphology, motility, and serum testosterone levels in Wistar rats [68].

**Hyaluronidase activities**

Molander et al. [48] evaluated the hyaluronidase activities of aqueous and ethanol cortex extracts of *L. acida* using the hyaluronidase assay with arthritogenic acid as a positive control and *Bitis arietans* and *Naja nigricollis* as enzyme sources. The aqueous and ethanol extracts exhibited inhibition of 64% and 11%, respectively, where *B. arietans* was used as an enzyme source and 10% and 136% where *N. nigricollis* was used. Both the extracts exhibited IC<sub>50</sub> values of 0.1 mg/mL. The ethanol extract exhibited an IC<sub>50</sub> value of 0.08 after removal of polyphenols [48]. Molander et al. [69] also evaluated aqueous and ethanol cortex extracts of *L. acida* in an *ex vivo* air-liquid interface model and a wound healing scratch assay as well as for their ability to permeate the skin barrier and inhibit venom-induced cell death. The extracts were not able to lower the cell toxicity of the venom and showed no effect against cell death and tissue damage [69].

**Phospholipase A<sub>2</sub> activities**

Molander et al. [48] evaluated the phospholipase A<sub>2</sub> activity of aqueous and ethanol cortex extracts of *L. acida* using the phospholipase A<sub>2</sub> activity assay with ethylenediaminetetracetic acid (EDTA) as a positive control and *B. arietans* as an enzyme source. The aqueous and ethanol extracts exhibited inhibition of 137% and 122%, respectively, and IC<sub>50</sub> values of 0.2 mg/mL and 0.1 mg/mL. The ethanol extract exhibited an IC<sub>50</sub> value of 0.2 after the removal of polyphenols [48]. Molander et al. [69] also evaluated aqueous and ethanol cortex extracts of *L. acida* in an *ex vivo* air-liquid interface model and a wound healing scratch assay as well as for their ability to permeate the skin barrier and inhibit venom-induced cell death. The extracts were not able to lower the cell toxicity of the venom and showed no effect against cell death and tissue damage [69].

**Proteolytic activities**

Molander et al. [48] evaluated the protease activities of aqueous and ethanol cortex extracts of *L. acida* using casein as substrate according to the method of Satak et al. [82] adjusted to microtiter plates with 4-(2-aminoethyl)benzenesulfonyl fluoride and EDTA as positive controls and *B. arietans* as an enzyme source. The aqueous and ethanol extracts inhibited trypsin activities of 102% and 86%, respectively, while aqueous extract exhibited IC<sub>50</sub> value of 0.2 mg/mL [48]. Molander et al. [69] also evaluated aqueous and ethanol cortex extracts of *L. acida* in an *ex vivo* air-liquid interface model and a wound healing scratch assay as well as for their ability to permeate the skin barrier and inhibit venom-induced cell death. The extracts were not able to lower the cell toxicity of the venom and showed no effect against cell death and tissue damage [69].

**Vibriocidal activities**

Akinsinde and Okuoya [70] evaluated vibriocidal activities of aqueous and ethanol stem extracts of *L. acida* against *Vibrio cholerae* using agar diffusion method with streptomycin as control. The extracts showed moderate activities with a zone of inhibition ranging from 5 to 15 mm [70]. These antibacterial activities exhibited by extracts of *L. acida* support the traditional usage of the plant as a remedy for diarrhea in Cameroon Burkina Faso [34,39, Cameroon [41], Côte d’Ivoire [24,25], and Nigeria [27,37].

**CONCLUSION**

*L. acida* is an important herbal medicine in West Africa, and there are still some research gaps in the phytochemical and pharmacological analyses of the crude extracts of the species as well as compounds isolated from the species. There is a need to correlate the medicinal uses of the species with the chemical compounds and pharmacological properties of the compounds and extracts of the species. Detailed research on pharmacokinetics, *in vivo*, and clinical research involving compounds isolated from *L. acida* and extracts of the species are required. Future research should also focus on the toxicological properties of the compounds isolated from the species as well as its crude extracts. Since *L. acida* is used in combination with other plant species in various herbal concoctions, it is important to evaluate the synergistic effects of the different extracts and their ability to enhance the efficiency of the additive mixtures. Detailed phytochemical, pharmacological, and toxicological studies will enable researchers to evaluate the therapeutical importance of the species in tropical Africa [83,84].

**AUTHORS’ CONTRIBUTIONS**

I declare that this work was done by the author named in this article.

**CONFLICTS OF INTEREST**

No conflicts of interest are associated with this work.

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