

Review Article

A Review of the Ethnobotany and Pharmacological Importance of *Alstonia boonei* De Wild (Apocynaceae)

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Alstonia boonei De Wild is a herbal medicinal plant of West African origin, popularly known as God's tree or "Onyame dua". Within West Africa, it is considered as sacred in some forest communities; consequently the plant parts are not eaten. The plant parts have been traditionally used for its antimalarial, aphrodisiac, antidiabetic, antimicrobial, and antipyretic activities, which have also been proved scientifically. The plant parts are rich in various bioactive compounds such as echitamidine, $N\alpha$ -formylechitamidine, boonein, loganin, lupeol, ursolic acid, and β -amyryn among which the alkaloids and triterpenoids form a major portion. The present paper aims at investigating the main research undertaken on the plant in order to provide sufficient baseline information for future work and for commercial exploitation.

1. Introduction

Many cultures throughout the world still rely on indigenous medicinal plants for their primary health care needs [1]. To date, 25% of modern medicines are derived from plants that have been used by traditional medical practitioners [2]. It is a fact that traditional systems of medicine have become a topic of global importance. Although modern medicine may be available in many developed countries, people are still turning to alternative or complementary therapies including medicinal herbs. Yet, few plant species that provide medicinal herbs have been scientifically evaluated for their possible medical applications. The safety and efficacy data are available for even fewer herbs, their extracts and active ingredients and the preparation containing them. Tropical and subtropical Africa contains between 40–45,000 species of plant with a potential for development and out of which 5,000 species are used medicinally [3]. Still there is a paradox, in spite of this huge potential and diversity, the African continent has only contributed 83 of the 1100 classic drugs globally [3]. African countries are at a stage where traditional medicine is considered more for its capacity to generate other medicine than for its own sake. In many cases research

undertakings and the commercial use stemming from that research have always relied on information provided by the local communities and, in many instances, have hardly benefited from the research results [4]. In Africa, traditional healers and remedies made from plants play an important role in the health of millions of people. The relative ratios of traditional practitioners and university-trained doctors in relation to the whole population in African countries are revealing. In Ghana, for example, in the Kwahu district, there are 224 people for every traditional practitioner, compared to nearly 21,000 people for one university-trained doctor [4].

Typically, studies on the medicinal plants such as *Alstonia boonei* have focused on the bioactivity of its chemical constituents, ethnobotany, pharmacology, and taxonomy. However, a comprehensive or systematic review on the plant is lacking. Furthermore, in much of the older literature concerning West Africa, the name *Alstonia congensis* has been erroneously used for *Alstonia boonei*. Consequently, this paper synthesizes studies on *Alstonia boonei* (Figure 1). This is necessary to recapitulate the findings on the plant and thereby provide a comprehensive and current repository for references on the plant.



FIGURE 1: Plate showing clockwise order from top right, the leaves, stem, branches, and whole plant of *Alstonia boonei*.

2. Classification, Cultivation, and Ethnobotanical Uses of *Alstonia*

2.1. Classification. *Alstonia* comprises about 40 species and has a pantropical distribution. There are about twelve species of the genus *Alstonia*. *Alstonia boonei* De Wild belongs to the family Apocynaceae. The species are scattered all over the world of which two are indigenous to Africa. The plant is known locally in Ghana as Onyame dua, Osen-nuru, or Sinduro in Twi, Onyame dua in Fante, Sinu or Adawura in Ga-Adangbe, Bakunin, Nyamenlebaka, Emenle, or Emie in Nzema, and Siaketekre, Nyemi dua, or Asi atoe in Ewe [5]. Elsewhere, *Alstonia* is known as Australian fever bush, Australian quinine, Devil tree, Dita bark, fever bark, or palimara [6].

2.2. Cultivation. *Alstonia* grows into a giant tree in most of the evergreen rain forests of tropical West Africa. The plant thrives very well in damp riverbanks. It is well known to all the traditional healers practicing along the west coast of Africa. It occurs in deciduous and fringing forest of Ghana [6]. *Alstonia boonei* De Wild is a deciduous tree up to 35 meters high (Figure 1). It buttresses deep-fluted high and narrow. Its white latexes are copious. The leaves are in whorls at nodes, oblanceolate, apex rounded to acuminate, lateral vein prominent almost at right angle to midrib. The flowers are white with lax terminal cymes. The fruits are paired with slender follicle up to 16 cm long with brown floss at each end.

2.3. Ethnobotanical Uses. The bark of *Alstonia* tree is one of the effective analgesic [7] herbs available in nature. All the

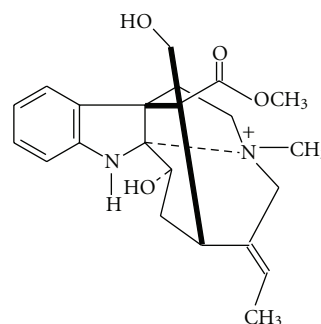
parts of the plant are very useful but the thick bark cut from the matured tree is the part that is most commonly used for therapeutic purposes. The bark of the tree is highly effective when it is used in its fresh form; however, the dried one could equally be used. Therapeutically, the bark has been found to possess antirheumatic [7], anti-inflammatory [7], analgesic/pain-killing, antimalaria/antipyretic, antidiabetic (mild hypoglycaemic), antihelminthic, antimicrobial and antibiotic properties [8–10]. A decoction could be sweetened with pure honey and be taken up to 4 times daily as an effective painkiller for the following conditions.

Painful menstruation (dysmenorrhoea), when associated with uterine fibroid or ovarian cysts in women; lower abdominal and pelvic congestion associated with gynaecological problems such as pelvic inflammatory diseases; to relieve the painful urethritis common with gonococcus or other microbial infections in men. *Alstonia* decoction also exerts a mild antibacterial effect in this case, relieving the aches and pains associated with malaria fever. *Alstonia* is taken in the form of preparations that exhibits antipyrexia and anti-malaria effects, to combat rheumatic and arthritic pains. The decoction of *Alstonia* bark could be taken alone as an effective pain-killing agent. A cold infusion made from the fresh or dried bark of *Alstonia* taken orally two to three times daily exerts a mild hypoglycaemic effect on diabetic patients. The cold infusion is also administered orally for the purpose of expelling round worms, threadworms [7], and other intestinal parasites in children.

The fresh bark of *Alstonia* could be used in preparing herbal tinctures; it is particularly useful as an effective antidote against snake, rat, or scorpion poison. It is also useful in expelling retained products of conception and afterbirth when given to women. Asthma can be treated with a drink prepared from parts of *Trema orientalis* and decoction of the bark of *Alstonia boonei* mixed with the roots and bark of cola and fruits of *Xylopi parviflora* with hard potash [7]. The bark decoction of *Alstonia boonei* is used with other preparations in the treatment of fractures or dislocation [7], jaundice, and for inducing breast milk. Its latex is taken as a purgative. The hardened latex is used for the treatment of yaws. *Alstonia boonei* De Wild is regarded as one of few herbs with potential anti-HIV indicators. In some African countries *Alstonia boonei* is considered a sacred tree and worshipped in the forest and hence human beings in those countries do not eat its parts.

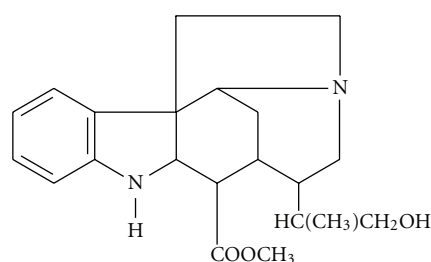
3. Chemical Composition

A wide array of chemical compounds has been isolated from *Alstonia boonei*. These include alkaloids, tannins, iridoids, and triterpenoids [5]. Chromatography of bark extracts of *Alstonia boonei* on silica gel plates with the solvent system AcOEt-MeOH-H₂O (150:26:19) produced 6 separate spots with alkaloid reactions and the alkaloids isolated from the plant include echitamine (1) and echitamidine (Scheme 1), voacangine and akuammidine, N α -formylechitamidine, and N α -formyl-12-methoxyechitamidine [5, 11–13]. Echitamine (1), which is also isolated from the bark of *Alstonia scholaris*,



Echitamine (1) [C₂₂H₂₉N₂O₄]⁺Mwt = 385.48

SCHEME 1



Echitamidine (2)

SCHEME 2

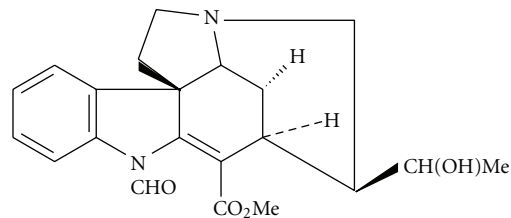
Alstonia cogenesis, and *Alstonia neriifolia*, has been assigned the nomenclature [(3 β , 16R)-3,17-Dihydroxy-16-(methoxycarbonyl)-4-methyl-2-4(14)-cyclo-3, 4-secoakuammilinium. Its structure is as shown in Scheme 1.

Echitamidine (2), on the other hand, has molecular formula of C₂₀H₂₂O₃N₂, with a melting point of 244°C and molecular weight of 338 g/mol. Its structure is as shown in Scheme 2.

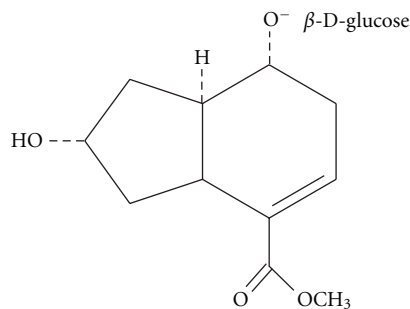
The structure of N-formylechitamidine (3) is as shown in Scheme 3.

These alkaloids, especially echitamine (1), possess a battery of pharmacological and autonomic activities [14, 15] including anticancer activities [16–23]. Alkaloids and related compounds isolated from other *Alstonia* species include the glycosides of venoterpene [24], nareline [25, 26], lagunamine [27], 19-episcolarinine [28], butamine, dobutamine [29, 30], alschomine [31], N α -methylbutylamine, isoalschomine [32], picrinine [33], strictamine [34, 35], rhazimanine [36], vallesamine [37], (20S)-19,20 dihydrocondylocarpine [38], scholarine [39], pseudoakuammigine [40], tetrahydroalstonine [41], akuammicine [42], picralinal [43], rhazine [44], scorlarine-N(4)-oxide, scholaricine [45, 46], and flavone glycosides [47, 48].

Iridoids isolated from *Alstonia boonei* include boonein and loganin. Loganin (Scheme 4) is a key intermediate in the biosynthesis of indole alkaloids. It is a crystal of melting point of 222–223°C [α]_D²⁰ –82.1 (water). It is freely soluble in water, less soluble in 96% alcohol and sparingly soluble in

N α -formylechitamide (3)

SCHEME 3



(4)

Loganin [C₁₇H₂₂O₁₀] Mwt = 390.39

SCHEME 4

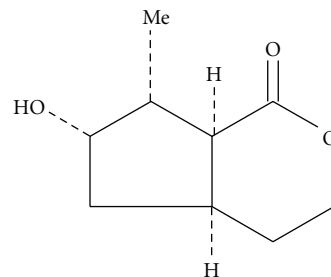
absolute alcohol. It is practically insoluble in ether, pet. Ether, ligroin, ethyl acetate, and chloroform.

Boonein (5) is a C-9 monoterpenoid α -lactone, isolated from the bark of *A. boonei* (Apocynaceae). The structure was established by chemical and spectroscopic methods and by X-ray analysis. Its structure is as shown in Scheme 5. It is a possible precursor in the indole alkaloid biogenesis [49].

The triterpenoids isolated from *Alstonia boonei* include lupeol (6), ursolic acid (7), and β -amyrin (8).

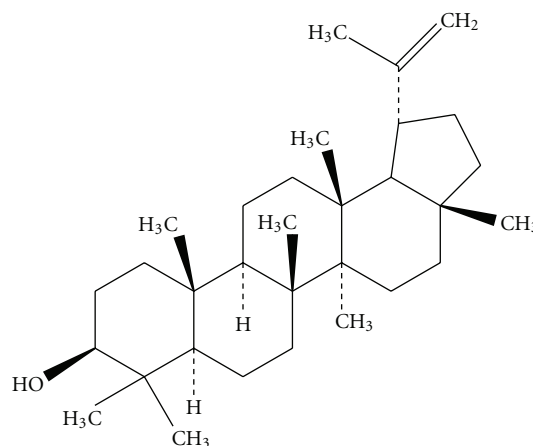
Lupeol is also known as (3 β)-Lup-20(29)-en-3-ol, monogynol B, β -viscol, or fagarasterol. Its structure is as shown in Scheme 6. It has a melting point of 215°C and a molecular weight of 426.73 with a molecular formula of C₃₀H₅₀O. The percentage composition of the various elements is, C = 84.44, H = 11.81, and O = 3.75. Lupeol forms needlelike crystals from alcohol or acetone. It is freely soluble in ether, benzene, pet. ether, and in warm alcohol. It is practically insoluble in water, dilute acids, and alkalis. Its acetate C₃₂H₅₂O₂ forms needlelike crystals from acetone with melting point of 218°C and $[\alpha]_D^{20} +47.3$.

Ursolic acid is also known as urson, prunol micromerol, or malol. Its systematic name is (3 β)-3-hydroxyurs-12-en-28-oic acid. Its structure is as shown in Scheme 7. Its melting point range is 285°C–288°C. One part dissolves in 88 parts of methanol, 178 alcohol (35 boiling alcohol), 140 ether, and 388 chloroform, 1675 carbon disulfide. It is moderately soluble in acetone and soluble in hot glacial acetic acid and in 2% alcoholic NaOH. It is insoluble in water and pet. ether its acetate has a melting point of 289–290°C. Ursolic acid is used as an emulsifying agent in pharmaceuticals and foods.



Boonein (5)

SCHEME 5



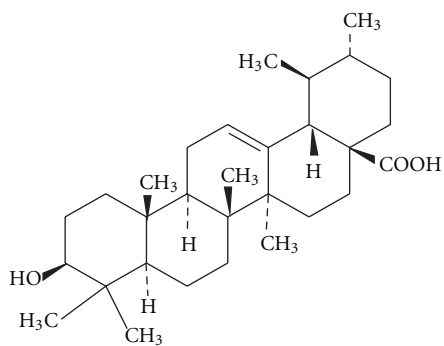
Lupeol (6)

SCHEME 6

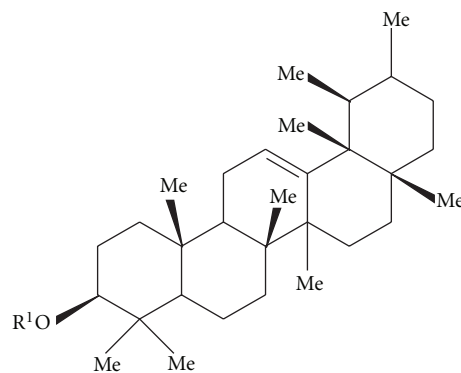
β -amyrin (8) has a molecular formula of C₃₀H₅₀O with a molecular weight of 426.73. Its structure is as shown in Scheme 8. Its melting point is 197–197.5°C. It forms needle-like crystals from pet. ether or alcohol.

For example, five compounds, which are triterpenes and sterols, were isolated from the hexane fraction of the alcohol extract of the leaves of *Alstonia scholaris* R. Br. The compounds are identified as 4 α ,14 α ,24-trimethyl-9 β ,19-cyclo-5 α -cholest-24(29)-en-3 β -ol, stigmaterol, betulin, betulinic acid, and α -amyrin acetate [50]. The structures of the isolated compounds were principally deduced by physiological and chromatographic characters as well as by spectroscopic analyses. The isolated compounds were reported for the first time.

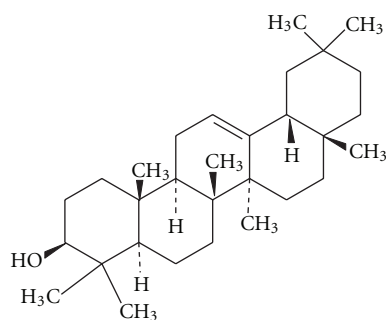
The flowers of *Alstonia scholaris* contain n-hexacosane, lupeol, β -amyrin, palmitic acid, and ursolic acid. The components were extracted with petroleum ether at 60–80°C and separated by chromatographic methods. Mass spectra and spectrographic methods were used for identification. The root and root bark of *Alstonia scholaris* contain α -amyrin, α -amyrin acetate, lupeol acetate, stigmaterol, β -sitosterol, and campesterol and its isomer [50]. The stem bark of *Alstonia scholaris* contains α -amyrin acetate, lupeol acetate, and β -sitosterol [71, 72]. The isolation of α -amyrin acetate and lupeol acetate was done with 96% ethanol on the air-dried bark. The concentrated extract was stored for 2 weeks

Ursolic acid (7) [C₃₀H₄₈O₃] Mwt = 456.71

SCHEME 7

 α -Amyrin palmitate (9)

SCHEME 9

 β -Amyrin (8)

SCHEME 8

and gave a solid, which (on several crystallizations from EtOH) gave colorless needles of melting point of 160°C. This product was chromatographed through a column of alumina (4 × 32 cm) and eluted with pet. ether (b.p. 40–60°C). Rechromatography of the fractions gave 2 products. The first one forms colourless plates in (EtOH-Et₂O) with mpt of 224–5°C, [α]29D 80° (all rotations detected in CHCl₃), with one acetyl group and no active H. The second product colourless needles in (EtOH-Et₂O) with mpt of 215–16°C, [α]28D 40°, containing an acetyl group and no active H. On hydrolysis of the first product with methanolic KOH, a substance with mpt of 184°C, [α]28D 84°, identical with α -amyrin was obtained. This on benzylation gave α -amyrin benzoate which forms prisms in (C₆H₆-EtOH) with mpt of 198°C, [α]28D 92°. Similarly, on hydrolysis the second product gave a substance with mpt 212–13°C, [α]27D 22.6°, identical with lupeol. Benzylation gave lupeol benzoate which forms colourless plates in (C₆H₆-EtOH) with mpt of 259–60°C, [α]27D 60.4°.

4. Pharmacological Properties

Triterpene compounds (R1 = H, C ≥ 10 fatty acid acyl) are useful as anti-inflammatory and antiarthritic agents [73].

α -Amyrin acetate isolated from petroleum ether extract of *Alstonia boonei* root bark was hydrolyzed with NaOH to α -amyrin followed by esterification with palmitoyl chloride to obtain α -amyrin palmitate (9). Rats were injected with 150 μ L of complete Freund's adjuvant containing 10mg/mL *Mycobacterium tuberculosis* in the right hind footpad. Its structure is as shown in Scheme 9. From days 11–19 rats were fed orally with 56 mg I/kg in 1 mL of water. Regression analysis of the rate of the ankle diameter change from days 11–19, postadjuvant injection showed that the diameter of the ankle decreased by 31% in treated animals.

In a similar research work, the triterpenes- α -amyrin acetate, β -amyrin acetate, β -amyrin, and lupeol acetate isolated from the petroleum ether extract of *Alstonia boonei* De Wild, root barks were tested for their anti-inflammatory effects in CFA-induced arthritic rats [74]. When administered orally daily from days 11 to 19 after adjuvant, lupeol acetate and β -amyrin acetate were most effective in preventing further increases in ankle adjuvant swelling. All triterpenes abrogated the increases in WBC count, increased liver and/or kidney weights but only α -amyrin acetate significantly increased serum GOT levels. In the presence of β -amyrin, there was significant neutrophil degeneration. Triterpenes of *Alstonia boonei* root barks were shown to be antiarthritic but the effects on liver and kidney weights raised the possibility of toxicity in antiarthritic therapy.

In another development, lupeol acetate isolated from the petroleum ether fraction of *Alstonia boonei* root barks was tested for its anti-arthritic effect in CFA-induced arthritic rats [75]. It was administered orally every 48 hrs (66 mg/kg body wt.) from days 32 to 40 after adjuvant and assessed on day 60. Lupeol acetate was able to return the increase in spleen weight and the reduction in serum alkyl phosphatase to nonarthritic control values.

The anti-inflammatory triterpenoids are also inhibitors of serine proteases [56]. The lupane triterpenoid lupeol, the ursane triterpenoid α -amyrin, and esters of these compounds present in the bark of roots of *Alstonia boonei* (Apocynaceae) have anti-inflammatory properties. α -Amyrin is a competitive inhibitor of bovine trypsin

TABLE 1: An overview of research work on pharmacological properties of *Alstonia boonei*.

Plant part used	Activity	Reference
Stem bark	Antiplasmodial (anti-malarial/antipyretic)	Bello et al. [51]; Ebiloma et al. [52]; Abel and Busia [53]
Stem bark	Insecticidal	Abel and Busia, [53]; Oigiangbe et al. [54]
Root bark	Anti-inflammatory	Osadebe et al. [55]; Olajide et al. [56]
Stem bark	Analgesic, aphrodisiac, trypanocidal	Kweifio-Okai et al. [57]; Asuzu and Anaga [58]
Stem bark	Sedative	Adesina [59]
Stem bark	Anti-snake venom	Gabriel et al. [60]; Majekodunmi [61]; Olajide et al. [56]
Stem bark	insomnia	Asuzu and Anaga [58]
Leaves	Antidiabetic	Din et al. [62]
Stem bark	Anthelmintic	Wesche et al. [63]
Stem bark, leaves	Antimicrobial	Adomi [64]; Omoregbe et al. [65]
Stem bark	Rheumatic pains	Olajide et al. [56]
Stem bark	Antidiarrhoeal	Amole and Ilori [66]
Stem bark	Spasmolytic and hypotensive	Iwu, [67]; Forster et al. [68]
Stem bark	Abortifacient, astringent, immunostimulant potentials	Taiwo et al. [69]
Stem bark	Antipsychotic	Elisabetsky and Costa-campos [70]

and chymotrypsin (Ki values 29 microM and 18 microM, resp.). Lupeol linoleate, lupeol palmitate, and alpha-amyrin linoleate are noncompetitive inhibitors of trypsin (Ki values 7 microM, 10 microM, and 16 microM, resp.). Alpha-amyrin linoleate is also a non-competitive inhibitor of chymotrypsin (Ki value 28 microM). Lupeol is a competitive inhibitor of both trypsin and chymotrypsin (Ki values 22 and 8 microM, resp.). Alpha-amyrin palmitate is a potent non-competitive inhibitor of chymotrypsin (Ki 6 microM). Lupeol, alpha-amyrin, and the palmitic and linoleic acid esters of these compounds are ineffective or very weak as inhibitors of porcine pancreatic elastase and of *Lucilia cuprina* and *Helicoverpa punctigera* leucine aminopeptidases. These hydrophobic triterpenoids represent further examples of anti-inflammatory triterpenoids that are PKA inhibitors as well as being selective protease inhibitors.

When the methanol extract of the stem bark of *Alstonia boonei* was investigated for anti-inflammatory, analgesic, and antipyretic properties [76], it was found out that the extract caused a significant ($P < 0.05$) inhibition of the carrageenan-induced paw oedema, cotton pellet granuloma, and exhibited an anti-arthritis activity in rats. Vascular permeability induced by acetic acid in the peritoneum of mice was also inhibited. The extract also produced marked analgesic activity by reduction of writhing induced by acetic acid, as well as the early and late phases of paw licking in mice. A significant ($P < 0.05$) reduction in hyperpyrexia in mice was also produced by the extract. This study has established anti-inflammatory, analgesic, and antipyretic activities of the stem bark of *Alstonia boonei*.

The anti-inflammatory activity of a Ghanaian anti-arthritis herbal preparation was also investigated [76]. The herbal preparation is made of a boiling water extract from a powdered sample containing *Alstonia boonei* root bark (90%), *Rauvolfia vomitoria* root bark (5%), and *Elaeis guineensis* nut without pericarp (5%). The herbal preparation was tested intraperitoneally for its anti-inflammatory

activity by measuring rat hind paw oedema induced by the subplantar injection of carrageenin in the presence or absence of arachidonic acid. Arachidonic acid increased swelling during the early phase of carrageenin oedema. The extract suppressed the late phase of carrageenin oedema and both phases in the presence of arachidonic acid. These preliminary results are consistent with a herbal preparation known to be used in the management of rheumatoid arthritis [77].

The extract was again tested for its anti-inflammatory activity by measuring over a period of 17 days the changes in rat ankle diameter caused by subplantar injection of complete Freund's adjuvant [76]. The extract fed in drinking water ad libitum reduced ipsilateral ankle adjuvant swelling by an average of 16% for the period of +4 to +17 days and improved weight gain.

α -Amyrin palmitate, present in the Ghanaian antiarthritic herbal preparation of *Alstonia boonei*, *Elaeis guineensis*, and *Rauvolfia vomitoria*, was synthesized and tested on complete Freund's adjuvant-induced arthritic rats [57]. Administered orally at 56 mg/kg body wt (BW) daily for 8 days from days 11 to 18 after adjuvant (acute) or at 66 mg/kg BW every 48 hours for 5 days from days 32 to 40 (chronic), the drug returned the increases in serum hyaluronate and blood granulocytes towards nonarthritic levels and correct the moderate anemia of adjuvant arthritis. Histological examinations of the proximal interphalangeal foot joints showed reduced synovial proliferation and invasion of joints and reduced leukocyte infiltration of bone marrow and periarticular tissue in treated rats. The results suggest that α -amyrin palmitate contributes to the previously shown antiarthritic effect of the herbal preparation.

Odeku [78] reported the anti-malarial property of the stem bark of *Alstonia boonei*, which could be formulated in tablet form. Odugbemi et al. [79] studied the anti-malarial activities of *Alstonia boonei*. Other important pharmacological properties of the plant are shown in Table 1.

5. Toxicology, Contaminants, and Side Effects

Modern synthetic medicines have undergone various levels of experiments for safety and efficacy unlike some herbal preparations. Large proportion of public assumes that herbal remedies or complementary and alternative medicine (CAM) are inherently safe because it is natural. It is important to remember that the majority of powerful chemicals found in plant, which can be used to treat human diseases, have evolved to serve different purposes in the plant itself. For instance, the chemical is being used to protect the plant from insects. These natural insecticides will soon poison the bugs. In sufficient high doses, it can harm human too. The World Health Assembly has highlighted the need to develop herbal pharmacopoeias and to develop and apply scientific criteria and methods for proof of safety and efficacy of medicinal plant products. However, only few countries have developed national herbal pharmacopoeias; limited plant species that provide medicinal herbs have been scientifically evaluated for their possible medical applications; the safety and efficacy data are available for even fewer herbs. Without well-documented information on the safety, efficacy, and phytochemical characteristics of different compounds, it is difficult for external buyers to assess the likely utility or value of some new raw materials and extracts of African origin. In order to address these lacunae, the Association of African Medicinal Plants Standards is developing an African Herbal Pharmacopeia with trading standards which provide information and technical data on some 50 important medicinal plants.

6. Conclusion

Notwithstanding the potential pharmacological benefits of *Alstonia boonei* in particular and medicinal plants in general, herbal pharmacopeia are largely lacking. The main problem facing the use of traditional medicines is the proof requirement that the active components contained in medicinal plants are useful, safe, and effective. This is required to assure the medical field and the public regarding the use of medicinal plants as drug alternatives. The proofs of pharmacology activity that are available at present are mostly based on empirical experience. The scientific proof then becomes the most important thing, in order to eliminate the concern of using medicinal plants as drugs for alternative treatment. This study attempted to synthesize work on *Alstonia boonei* De Wild, a medicinal plant used in African alternative medicine for its anti-malarial, aphrodisiac, anti-diabetic, antimicrobial, and antipyretic activities. This study shows the potential of the plant that research on dose-dependent safety, side effects, and toxicological issues regarding the use of the plant in alternative medicine are essentially lacking; the situation might limit widespread commercial adoption.

References

[1] N. Farnsworth, A. O. Akerele, A. S. Bingel, D. D. Soejarto, and Z. Guo, "Medicinal plants in therapy," *Bulletin of the World Health Organization*, vol. 63, no. 6, pp. 965–981, 1985.

[2] G. Cragg and D. J. Newman, "Biodiversity: a continuing source of novel drug leads," *Pure and Applied Chemistry*, vol. 77, no. 1, pp. 7–24, 2005.

[3] B.-E. Van Wyk, "A broad review of commercially important Southern African medicinal plants," *Journal of Ethnopharmacology*, vol. 119, no. 3, pp. 342–355, 2008.

[4] E. Rukangira, "Overview on medicinal plants and traditional medicine in Africa," *Qualitative Health Research*, vol. 14, pp. 675–690, 2004.

[5] M. N. B. Ayiku, *Ghana Herbal Pharmacopoeia*, Technology Transfer Centre, 1992.

[6] B. K. Gosse, T. A. Bryson, and T. Gokou, "Study of triterpenoids from *Alstonia boonei*," *Société Ouest-Africaine de Chimie*, vol. 5, no. 8, pp. 123–128, 1999.

[7] D. Abbiw, *Useful Plants of Ghana: West African Uses of Wild and Cultivated Plants*, Intermediate Technology Publications, Royal Botanical Garden, Kew, London, 1990.

[8] S. Hadi and J. B. Bremner, "Initial studies on alkaloids from Lombok medicinal plants," *Molecules*, vol. 6, no. 2, pp. 117–129, 2001.

[9] B. B. Fakae, A. M. Campbell, J. Barrett et al., "Inhibition of glutathione S-transferases (GSTs) from parasitic nematodes by extracts from traditional Nigerian medicinal plants," *Phytotherapy Research*, vol. 14, no. 8, pp. 630–634, 2000.

[10] T. S. Kam, K. T. Nyeoh, K. M. Sim, and K. Yoganathan, "Alkaloids from *Alstonia scholaris*," *Phytochemistry*, vol. 45, no. 6, pp. 1303–1305, 1997.

[11] M. Kucera, V. O. Marquis, and H. Kucerova, "Nigerian medicinal plants. I. TLC thin-layer chromatographic separation and quantitative evaluation of *Alstonia boonei* alkaloids," *Planta Medica*, vol. 21, no. 4, pp. 343–346, 1972.

[12] G. Croquelois, N. Kunesch, M. Debray, and J. Poisson, "*Alstonia boonei* alkaloids," *Medicinal Plants and Phytotherapy*, vol. 6, no. 2, pp. 122–127, 1972.

[13] J. U. Oguakwa, "N α -formylechitimidine, an alkaloid from *Alstonia boonei*," *Phytochemistry*, vol. 23, no. 11, pp. 2708–2709, 1984.

[14] J. A. O. Ojewole, "Studies on the pharmacology of echitamine, an alkaloid from the stem bark of *Alstonia boonei* L. (Apocynaceae)," *International Journal of Crude Drug Research*, vol. 22, no. 3, pp. 121–143, 1984.

[15] J. A. O. Ojewole, "Autonomic pharmacology of echitamine, an alkaloid from *Alstonia boonei* De Wild," *Fitoterapia*, vol. 54, no. 3, pp. 99–113, 1983.

[16] B. Chandrasekaran and B. Nagarajan, "Growth inhibitory effect of echitamine and plumbagin on fibrosarcoma in rats," *Arogya*, vol. 9, no. 1, pp. 60–63, 1983.

[17] V. Saraswathi, A. C. Shyamala, S. Subramanian, and S. Govindasamy, "Studies on the effects of echitamine chloride on serum glycoproteins and lysosomal hydrolases of sarcoma-180 induced mice," *Fitoterapia*, vol. 69, no. 1, pp. 73–75, 1998.

[18] V. Saraswathi, N. Ramamoorthy, S. Subramanian, V. Mathuram, P. Gunasekaran, and S. Govindasamy, "Inhibition of glycolysis and respiration of sarcoma-180 cells by echitamine chloride," *Chemotherapy*, vol. 44, no. 3, pp. 198–205, 1998.

[19] V. Saraswathi, V. Mathuram, S. Subramanian, and S. Govindasamy, "Modulation of the impaired drug metabolism in sarcoma-180 bearing mice by echitamine chloride," *Cancer Biochemistry Biophysics*, vol. 17, no. 1-2, pp. 79–88, 1999.

[20] V. Saraswathi, S. Subramanian, N. Ramamoorthy, V. Mathuram, and S. Govindasamy, "In vitro cytotoxicity of echitamine chloride and adriamycin on Ehrlich ascites carcinoma cell cultures," *Medical Science Research*, vol. 25, no. 3, pp. 167–170, 1997.

- [21] S. Viswanathan, N. Ramamurthy, S. Subramanian, V. Mathuram, and S. Govindasamy, "Enhancement of the cytotoxic effects of Echitamine chloride by vitamin A: an in vitro study on Ehrlich ascites carcinoma cell culture," *Indian Journal of Pharmacology*, vol. 29, no. 4, pp. 244–249, 1997.
- [22] P. Kamarajan, N. Sekar, V. Mathuram, and S. Govindasamy, "Antitumor effect of echitamine chloride on methylcholonthrene induced fibrosarcoma in rats," *Biochemistry International*, vol. 25, no. 3, pp. 491–498, 1991.
- [23] N. Keawpradub, P. J. Houghton, E. Eno-Amooquaye, and P. J. Burke, "Activity of extracts and alkaloids of Thai *Alstonia* species against human lung cancer cell lines," *Planta Medica*, vol. 63, no. 2, pp. 97–101, 1997.
- [24] G. K. Biswas and G. S. Saharia, "A new alkaloidal glycoside from *Alstonia scholaris*," *Indian Journal of Chemistry*, vol. 1, no. 1, pp. 66–67, 1978.
- [25] T. S. Kam, K. T. Nyeoh, K. M. Sim, and K. Yoganathan, "Alkaloids from *Alstonia scholaris*," *Phytochemistry*, vol. 45, no. 6, pp. 1303–1305, 1997.
- [26] Y. Morita, M. Hesse, and H. Schmid, "*Alstonia scholaris*: the structure of the indole alkaloid nareline," *Helvetica Chimica Acta*, vol. 60, no. 4, pp. 1419–1434, 1977.
- [27] T. Yamauchi, F. Abe, W. G. Padolina, and F. M. Dayrit, "Alkaloids from leaves and bark of *Alstonia scholaris* in the Philippines," *Phytochemistry*, vol. 29, no. 10, pp. 3321–3325, 1990.
- [28] T. Yamauchi, F. Abe, R. F. Chen, G. I. Nonaka, T. Santisuk, and W. G. Padolina, "Alkaloids from the leaves of *Alstonia scholaris* in Taiwan, Thailand, Indonesia and the Philippines," *Phytochemistry*, vol. 29, no. 11, pp. 3547–3552, 1990.
- [29] T. Yamauchi and F. Abe, "Regional differences of indole alkaloids in *Alstonia scholaris* and *Alstonia macrophylla*," *International Congress Series*, vol. 1157, pp. 51–58, 1998.
- [30] W. Boonchuay and W. E. Court, "Minor alkaloids of *Alstonia scholaris* root," *Phytochemistry*, vol. 15, no. 5, p. 821, 1976.
- [31] F. Abe, R. F. Chen, T. Yamauchi et al., *Alkaloids From the Leaves of Alstonia scholaris*, vol. 31, Fukuoka University, Fukuoka, Japan, 1989.
- [32] F. Abe, R. F. Chen, T. Yamauchi, N. Marubayashi, and I. Ueda, "Studies on the constituents of *Alstonia scholaris*. Part I. Alschomine and isoalschomine, new alkaloids from the leaves of *Alstonia scholaris*," *Chemical & Pharmaceutical Bulletin*, vol. 37, no. 4, pp. 887–890, 1989.
- [33] R. Ghosh, P. Roychowdhury, D. Chattopadhyay, and Y. Iitaka, "The structure of an alkaloid, picrinine, from *Alstonia scholaris*," *Acta Crystallographica C*, vol. 44, no. 12, pp. 2151–2154, 1988.
- [34] J. Banerji and R. Chakrabarti, "Constituents of *Alstonia scholaris* R.Br.: conversion of picrinine into strictamine and to a pyrrolidinoindolenine system," *Indian Journal of Chemistry B*, vol. 23, no. 5, pp. 453–454, 1984.
- [35] S. K. Bhattacharya, R. Bose, S. C. Dutta, A. B. Ray, and S. R. Guha, "Neuropharmacological studies on strictamine isolated from *Alstonia scholaris*," *Indian Journal of Experimental Biology*, vol. 17, no. 6, pp. 598–600, 1979.
- [36] A. Rahman and K. A. Alvi, "Indole alkaloids from *Alstonia scholaris*," *Phytochemistry*, vol. 26, no. 7, pp. 2139–2142, 1987.
- [37] A. Rahman, K. A. Alvi, S. A. Abbas, and W. Voelter, "Isolation of 19,20-Z-vallesamine and 19,20-E-vallesamine from *Alstonia scholaris*," *Heterocycles*, vol. 26, no. 2, pp. 413–419, 1987.
- [38] A. Rahman, K. A. Alvi, and A. Muzaffar, "Isolation and ¹H/¹³C-NMR studies on 19,20-dihydrocondylocarpine: an alkaloid from the leaves of *Ervatamia coronaria* and *Alstonia scholaris*," *Planta Medica*, vol. 52, no. 4, pp. 325–326, 1986.
- [39] A. Banerji and A. K. Siddhanta, "Scholarine: an indole alkaloid of *Alstonia scholaris*," *Phytochemistry*, vol. 20, no. 3, pp. 540–542, 1981.
- [40] A. Banerji and J. Banerji, "Isolation of pseudoakummine from the leaves of *Alstonia scholaris* R. Br.," *Indian Journal of Chemistry B*, vol. 15, no. 4, pp. 390–391, 1977.
- [41] S. C. Dutta, S. K. Bhattacharya, and A. B. Ray, "Flower alkaloids of *Alstonia scholaris*," *Planta Medica*, vol. 30, no. 1, pp. 86–89, 1976.
- [42] W. Boonchuay and W. E. Court, "Alkaloids of *Alstonia scholaris* from Thailand," *Planta Medica*, vol. 29, no. 4, pp. 380–390, 1976.
- [43] R. C. Rastogi, R. S. Kapil, and S. P. Popli, "Picralinal—A key alkaloid of picralima group from *Alstonia scholaris*," *Experientia*, vol. 26, no. 10, p. 1056, 1970.
- [44] A. Chatterjee, B. Mukherjee, S. Ghosal, and P. K. Banerjee, "Occurrence of rhazine in *Alstonia scholaris*: biogenetic and chemotaxonomic significance of the co-occurrence of several indole alkaloids having a common structural pattern," *Journal of the Indian Chemical Society*, vol. 46, no. 7, pp. 635–638, 1969.
- [45] A. Rahman, M. Asif, M. Ghazala, J. Fatima, and K. A. Alvi, "Scholaricine, an alkaloid from *Alstonia scholaris*," *Phytochemistry*, vol. 24, no. 11, pp. 2771–2773, 1985.
- [46] J. Banerji, R. Mustafi, and D. J. Roy, "(–)-Scholarine and (+)-lochneridine—constituents of *Alstonia scholaris* R.Br. (Apocynaceae)," *Indian Journal of Chemistry B*, vol. 23, no. 5, p. 455, 1984.
- [47] J. S. Chauhan, R. Chaturvedi, and S. Kumar, "Isookanin-7-O-a-L-rhamnopyranoside, a new flavanone glycoside from the roots of *Alstonia scholaris* R. Br.," *Indian Journal of Chemistry B*, vol. 24, no. 2, p. 219, 1985.
- [48] E. K. Desoky, "Flavonoidal contents of *Alstonia scholaris* R.Br," *Bulletin of Pharmaceutical Sciences*, vol. 22, no. 2, pp. 117–121, 1999.
- [49] G. B. Marini-Bettolo, M. Nicoletti, I. Messana et al., "Research on African medicinal plants-IV1 1 Part III: see ref. 1. Boonein, a new C-9 terpenoid lactone from *Alstonia boonei*: a possible precursor in the indole alkaloid biogenesis," *Tetrahedron*, vol. 39, no. 2, pp. 323–329, 1983.
- [50] E. K. Desoky, M. S. Kamel, and D. W. Bishay, "Sterols and triterpenes from *Alstonia scholaris* R.Br.," *Bulletin of Pharmaceutical Sciences*, vol. 23, no. 1, pp. 65–71, 2000.
- [51] I. S. Bello, T. Oduola, O. G. Adeosun, N. O. A. Omisore, G. O. Raheem, and A. A. Ademosun, "Evaluation of antimalarial activity of various fractions of *Morinda lucida* leaf extract and *Alstonia boonei* stem bark," *Global Journal of Pharmacology*, vol. 3, pp. 163–165, 2009.
- [52] G. Ebiloma, E. Amlabu, F. O. Atanu, W. Amlabu, and O. Aminu Rhoda, "Effect of the aqueous extracts of *Alstonia boonei* on the haematological profiles of mice experimentally infected with the chloroquine-sensitive strain of *Plasmodium berghei* NK-65," *Hematologia*, vol. 1, pp. 11–18, 2012.
- [53] C. Abel and K. Busia, "An exploratory ethnobotanical study of the practice of herbal medicine by the Akan peoples of Ghana," *Alternative Medicine Review*, vol. 10, no. 2, pp. 112–122, 2005.
- [54] O. N. Oigiangbe, I. B. Igbinosa, and M. Tamo, "Insecticidal activity of the medicinal plant, *Alstonia boonei* De Wild, against *Sesamia calamistis* Hampson," *Journal of Zhejiang University Science B*, vol. 8, no. 10, pp. 752–755, 2007.
- [55] P. O. Osadebe, G. B. Okide, and I. C. Akabogu, "Study on anti-diabetic activities of crude methanolic extracts of *Loranthus micranthus* (Linn.) sourced from five different host trees,"

- Journal of Ethnopharmacology*, vol. 95, no. 2-3, pp. 133–138, 2004.
- [56] O. A. Olajide, S. O. Awe, J. M. Makinde et al., “Studies on the anti-inflammatory, antipyretic and analgesic properties of *Alstonia boonei* stem bark,” *Journal of Ethnopharmacology*, vol. 71, no. 1-2, pp. 179–186, 2000.
- [57] G. Kweifio-Okai, D. Bird, B. Field et al., “Antiinflammatory activity of a Ghanaian antiarthritic herbal preparation: III,” *Journal of Ethnopharmacology*, vol. 46, no. 1, pp. 7–15, 1995.
- [58] U. Asuzu and A. O. Anaga, “Pharmacological screening of the aqueous extract of *Alstonia boonei* bark,” *Fitoterapia*, vol. 63, no. 5, pp. 411–417, 1991.
- [59] S. K. Adesina, “Studies on a Nigerian herbal anticonvulsant recipe,” *International Journal of Crude Drug Research*, vol. 20, pp. 93–100, 1982.
- [60] O. Gabriel, N. Harrision, O. Okey, and A. Ukoah, “Changes in lipid and haematological profile of aqueous ethanolic extract of *Alstonia boonei* in rats,” *The Internet Journal of Hematology*, vol. 4, no. 1, pp. 1–5, 2008.
- [61] S. O. Majekodunmi, “Formulation of the extract of the stem bark of *Alstonia booneias* tablet dosage form,” *Tropical Journal of Pharmaceutical Research*, vol. 7, no. 2, pp. 987–994, 2008.
- [62] N. Din, S. D. Dibong, E. Mpondo Mpondo, R. J. Priso, N. F. Kwin, and A. Ngoye, “Inventory and identification of plants used in the treatment of diabetes in Douala town (Cameroon),” *European Journal of Medicinal Plants*, vol. 1, no. 3, pp. 60–73, 2011.
- [63] D. Wesche, D. Black, and W. K. Milhous, in *Proceedings of the 39th Annual Meeting of the American Society of Tropical Medicine and Hygiene*, Book of Abstracts, no. 138, New Orleans, LA, USA, 1990.
- [64] P. O. Adomi, “Antibacterial activity of aqueous and ethanol extracts of the stem bark of *Alstonia boonei* and *M. lucida*,” *Scientific Research and Essays*, vol. 1, no. 2, pp. 50–53, 2006.
- [65] R. E. Omoregbe, O. M. Ikuebe, and I. G. Ihimire, “Antimicrobial activity of some medicinal plants extracts on *Escherichia coli*, *Salmonella paratyphi* and *Shigella dysenteriae*,” *African Journal of Medicine and Medical Sciences*, vol. 25, no. 4, pp. 373–375, 1996.
- [66] O. O. Amole and O. O. Ilori, “Antimicrobial activity of the aqueous and ethanolic extracts of the stem bark of *Alstonia boonei*,” *International Journal of Phytopharmacology*, vol. 1, no. 2, pp. 119–123, 2010.
- [67] M. M. Iwu, *Handbook of African Medicinal Plants*, CRC Press, London, UK, 1993.
- [68] H. Forster, H. Niklas, and S. Lutz, “Antispasmodic effects of some medicinal plants,” *Planta Medica*, vol. 40, no. 4, pp. 309–319, 1980.
- [69] O. B. Taiwo, B. H. Kroes, C. J. Beukelman, S. T. A. J. Horsten, J. M. Makinde, and R. P. Labadie, “Activity of the stem bark extract of *Alstonia boonei* de wild (apocynaceae) on human complement and polymorphonuclear leukocytes,” *Journal of Ethnopharmacology*, vol. 17, pp. 13–15, 1998.
- [70] E. Elisabetsky and L. Costa-Campos, “The alkaloid alstonine: a review of its pharmacological properties,” *Evidence-Based Complementary and Alternative Medicine*, vol. 3, no. 1, pp. 39–48, 2006.
- [71] A. Khaleque, K. M. Ismail, and M. Shafullah, “Chemical investigations on *Alstonia scholaris*. Part I: isolation of lupeol acetate, β -sitosterol, one alkaloid and three other non-alkaloidal compounds from the bark,” *Bangladesh Journal of Scientific & Industrial Research*, vol. 26, no. 1–4, pp. 1–7, 1991.
- [72] G. Kweifio-Okai, *Triterpene Compounds Having Antiinflammatory and Antiarthritic Activity*, PCT International, 1993.
- [73] G. Kweifio-Okai and G. Carroll, “Antiarthritic effect of *Alstonia boonei* triterpenes,” *Recent Advances in Toxinology Research*, vol. 10, no. 3, pp. 19–28, 1992.
- [74] G. Kweifio-Okai and A. R. Carroll, “Antiarthritic effect of lupeol acetate,” *Phytotherapy Research*, vol. 7, no. 2, pp. 213–215, 1993.
- [75] A. Rajic, G. Kweifio-Okai, T. Macrides, R. M. Sandeman, D. S. Chandler, and G. M. Polya, “Inhibition of serine proteases by anti-inflammatory triterpenoids,” *Planta Medica*, vol. 66, no. 3, pp. 206–210, 2000.
- [76] G. Kweifio-Okai, “Antiinflammatory activity of a Ghanaian antiarthritic herbal preparation: I,” *Journal of Ethnopharmacology*, vol. 33, no. 3, pp. 263–267, 1991.
- [77] G. Kweifio-Okai, “Antiinflammatory activity of a Ghanaian antiarthritic herbal preparation: II,” *Journal of Ethnopharmacology*, vol. 33, no. 1-2, pp. 129–133, 1991.
- [78] A. Odeku, “Formulation of the extract of the stem bark of *Alstonia boonei*,” *Tropical Journal of Pharmaceutical Research*, vol. 7, no. 2, pp. 987–994, 2008.
- [79] T. O. Odugbemi, O. R. Akinsulire, I. E. Aibinu, and P. O. Fabeku, “Medicinal plants useful for malaria therapy in Okeigbo, Ondo State, Southwest Nigeria,” *African Journal of Traditional, Complementary and Alternative Medicines*, vol. 4, no. 2, pp. 191–198, 2007.