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Sustainable Use of Plant Products in Ethnomedicine as a Promising Panacea to Effective Control of Trypanosomiasis: A Review

A., Aminu[1*], A. K., Maigari[1], I. H., Hamza[1], I. C., Asongo[2], K. I., Nadada[3]

[1]Nigerian Institute for Trypanosomiasis and Onchocerciasis Research Kano State Liaison Office France Road
[2]Human African Trypanosomiasis research department, NITR Kaduna
[3]Department of Biological Science Faculty of life Science Bayero University Kano

Corresponding author: halifaone@gmail.com, +234-8032076327

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Abstract- Trypanosomiasis is a vector-borne parasitic disease causing serious risksto the lives of about 60 million people and 48 million cattle globally. The current chemotherapy of trypanosomiasis relies on some of the drugs such as (suramin, pentamidine, melarsoprol, eflorinithine, arsobal and mel B) to mention but few which were developed more than 30 years ago. Others such as homidium, isometamidium and diminazene aceturate are used in animal infections. Each of these drugs has one or more of the following challenges: expensive, highly toxicity, parenteral administration and parasitic increasing resistance. Nigerian medicinal plants are known to contain a large variety of phytochemical components in the search for potential new drugs against the illness. Some of the plant extracts have been screened for anti-trypanosomes and they are classified based on their family and the specific part used against each parasite.

***Keywords*:** phytoconstituents, phytochemical, *Trypanosomiasis*,

I. INTRODUCTION

African trypanosomiasis is a parasitic disease caused by a protozoan of the genus *Trypanosoma*. *Trypanosoma vivax* (*T. vivax*), *Trypanosoma congolense* (*T. congolense*) and to a lesser extent *Trypanosoma brucei brucei* (*T. b. brucei*) are the main species responsible for African animal trypanosomosis (AAT) called nagana in West Africa while *T. b. rhodesiense* and *T. b. gambiense* cause sleeping sickness (human African trypanosomiasis, HAT). Surra and Dourine are caused by the other trypanosome species *T. evansi* and *T. equiperdum* respectively. The disease is transmitted by abite of the vector—tsetse fly (*Glossina* species) [1]. In Nigeria, trypanosomiasis seems to be re-emerging as an important livestock disease, assuming major clinical importance in small ruminants and extending to previously designated tsetse-free zones [2,3]. Apart from the old Gboko endemic focus remaining active, there have been reports of the disease outbreak in many other communities in Nigeria [4,5].The prevalence rate in different breed of animals in Nigeria for the past few years have been studied and ranged from 8.4% to 15.53% [6,7]. In Africa, the annual loss in livestock production and mixed agriculture alone due to the disease is valued at 5 billion US dollars. In 1995, WHO Expert Committee estimated that 60 million people were at risk with an estimated 300,000 new cases per year in Africa, with fewer than 30,000 cases diagnosed and treated. In 2004, the number of new reported cases fell to 17,616 and WHO considered in that due to increased control, estimated cumulative rate to be between 50,000 and 70,000 cases. In 2009, the number of new cases reported dropped below 10,000 (9878) for the first time in 50 years and the estimated number of actual cases is currently 30,000. This trend has been maintained in 2012, with 7216 cases reported [8–10]. The current chemotherapy of HAT relies on only six drugs (suramin, pentamidine, melarsoprol, eflorinithine, arsobal and mel B), five of which were developed more than 30 years ago. Others such as homidium, isometamidium and diminazene aceturate are used in animal infections. Each of these drugs has one or more of these challenges: expensive, highly toxic, need parenteral administration and parasites increasing resistance.

II. MEDICINAL PLANTS WITH ANTI-TRYPANOSOMAL ACTIVITIES

II.1 Family *Acanthaceae, Amaryllidaceae, Anacardiaceae, Annonaceae, Apocynaceae, Araceae, Asclepiadaceae, Asteraceae and Burseraceae*

Peristrophe bicalyculata (Acanthaceae) is found almost throughout India, Afghanistan and Africa. The herb is used against tuberculosis, snake poison, in bone fracture, sprain, fever, cold, and cough treatments [34]. 50 mg/kg of Cold water whole plant extract of *P. bicalyculata* immobilized 90% of *T. b. brucei in vitro* after one hour of incubation, while the methanol extract of the plant showed a dose-dependent suppressive property in mice infected with *T. evansi* [35,36]. Nok and Williams described that the extract obtained from *Allium sativum* (Amaryllidaceae) completely eliminated trypanosomes in mice on administering 120 mg/kg live weight at 4 days post-treatment. *A. sativum* is thought to have caused cell death in trypanosomes by inhibiting the synthesis of membrane lipids of the cell [37,38]. The aqueous methanol root extracts of *Lannea kerstingii* and *Mangifera indica* from Anacardiaceae and petroleum ether root extract of *Annona senegalensis* (Annonaceae) at 4 mg/mL, stopped motility of *T. brucei in vitro* within an hour of incubation [39]. In another study, Adeiza *et al.* tested *in vitro* trypanocidal activity of *A. senegalensis* and found that the crude extract immobilized *T. evansi* at 10 mg/mL [40,41]. A fraction obtained from an aqueous leaf extract of *Holarrhena Africana* (Apocynaceae) completely cleared *T. b. rhodesiense* at a dose of 40 mg/kg bw i.p. in infected mice for5 days post treatment [42].

The leaf extract of *Lannea welwistchii* showed trypanocidal activity (MIC = 6.3 mg/mL) against *T. b. brucei* [44]. *Haematostaphis barteri* is used by traditional medical practitioners in the north-eastern Nigeria to treat and manage trypanosomiasis [45]. Using short assay duration of 30 min, 0.5 mg/mL of *H. barteri* aqueous extract immobilize *T. b. brucei* and *T. congolense* [46]. *Carissa spinarum*, also known as the conkerberry or bush plum, is a large shrub that belongs to the Apocynaceae. Its ethanol root extract has been shown to have *in vivo* activity against *T. b. brucei* at ≥100 mg/kg body weight in infected mice [47]. Using a one hour exposure time, methanol extracts of *Adenium obesum* stem bark (Apocynaceae) and *Anchomanes difformis* rhizome (Araceae) stopped 50% of the motility of *T. b. brucei in vitro* at 4 mg/mL [39,48]. *In vivo* trypanocidal activity of *Carrisaedulis* (Apocynaceae) against *T. congolence* infection in rats was investigated using a methanol root extract. Oral treatment at different doses did not significantly clear the parasitemia, however, animals treated with 100 mg/kg/day survived longer than those treated with 200 mg/kg/day and the infected control group [49]. *Saba florida* (Apocynaceae) is traditionally eaten as an antidote against vomiting, diarrhoea and food poisoning [50]. *S. florida* aqueous methanol leaf extract (400 mg/kg) exhibited *in vivo* activity by clearing *T. b. brucei* in infected rats after 7 days [51]. *Gongronema latifolium* (Asclepiadaceae) has been reported to stop motility of *T. congolense* after about 10 min of *in vitro* treatment using 400 mg/kg of the whole plant's methanol extract [52]. The ethyl acetate and methanol extracts of *Tridax procumbens* (Asteraceae), in contrast to extracts obtained with other solvents, were trypanocidal towards *T. b. brucei* at 200 mg/kg [53]. Further investigation of the ethyl acetate extract of *T. procumbens* led to the isolation of four flavonoids; 3-hydroxyflavone (**a**), quercetin (**b**),7,8-dihydroxyflavone (**c**) and catechin (**d**). Compounds **b** and **c** were described to exhibit trypanocidal activity *in vitro* and *in vivo* as pure compounds without affecting normal human cell [54–56]. *In vitro* studies showed *T. b. brucei* was immobilized by 0.4 mg/mL of *Artemisia maritime* (Asteraceae) chloroform and petroleum ether extracts using short assay duration of less than one hour [57]. *Boswellia dalzielii* (Burseraceae), a tree of the Savannah forest of Nigeria, is used for the treatment of wound, diarrhoea, syphilis and to induce vomiting [58,59]. Freiburghaus *et al.* found that the trypanocidal activity of *B. dalzielii* varies according to extraction medium and part of plant used. Based on this, Atawodi *et al.* tested activities of extracts of different parts of *B. dalzielii* against *T. b. brucei*. His results revealed that methanol leaf, stem and root bark extracts of the plant at 10 mg/mL significantly immobilized the trypanosome [60, 61].

II.2 Family *Capparaceae, Celastraceae, Clusiaceae, Combretaceae, Cucurbitaceae, Ebenaceae and Euphorbiaceae*

Leaves of *Crateva adansonii* (Capparaceae) are used to treat ear infections while its root is employed to treat syphilis, jaundice and yellow fevers [62]. The ethyl acetate and hexane crude extract of the plant demonstrated moderate *in vitro* activity (MIC 12.5 µg/mL) against *T. b. brucei* [63]. Two phytoconstituents (oleanolic acid and 4-epi-hederagenin), which were not tested for activity, had also been isolated from *C. adansonii* and could account for the activity of the plant. The seed extract of *Bucholzia coriacea* (Capparaceae) is locally used in treatment of feverish conditions in Eastern Nigeria [64]. *T. b. brucei* was cleared in infected mice after administering 1000 mg/kg of aqueous and methanol seed extracts of *B. coriacea* i.p. for five consecutive days [65-66]. MIC of 0.625 µg/mL has been reported for both compoundsisolated from the hexane-ethyl acetate fraction of *Maytenus laevis* (Celastraceae) root [44, 67]. The highest *in vivo* trypanocidal activity of *Garcinia kola* (Clusiaceae) seeds was observed in the alkaloid fraction which brought about 92.25% reduction in parasitaemia at 100 mg/kg in *T. b. brucei* infected rats. The antitrypanosomal property of the alkaloids from *G. kola* has been suggested to be due to DNA intercalation in combination with protein biosynthesis inhibition [68]. *Anogeissus leiocarpus* (Combretaceae) is a tree widely distributed in northern Nigeria. The aqueous methanol bark extract of *A. leiocarpus* had the highest *in vitro* antitrypanosomal activity out of all the other parts of the plant. 200 mg/kg of the extract made *T. b. brucei* immotile after 10 min incubation. Furthermore, the extract (200 mg/kg) was analyzed *in vivo* using *T. b. brucei* infected rats. Although it did not clear parasitemia in experimental rats after seven days, the rats survived longer than the infected control group [69]. The hexane-ethyl acetate extract of *Terminalia avicennioides* (Combretaceae) bark inhibited *T. b. brucei* activity *in vitro* with MIC of 2.5 µg/mL [43,70,71]. Methanol extracts of *Terminalia superba* (Combretaceae) root and stem were effective with MIC value of 3.1 mg/mL each

against *T. b. brucei in vitro* [44]. Using a short assay duration of about an hour revealed that 10 mg/mL of both *Momordica balsamina* (Cucurbitaceae) and *Diospyros Mespiliformis* (Ebenaceae) methanol extract drastically reduced motility of *T. b. brucei* [39,48]. Two plants of Euphorbiaceae family whose crude extracts showed antitrypanosomal activity, yielded two active compounds; (*Euphorbia poisonii*) and (*Alchornea cordifolia*). These two Compoundshad activity with (MIC of 1.56 μg/mL and < 0.2 μg/mL respectively) against *T. b. brucei* [43].

III. CONCLUSIONS

This review, on antitrypanosomal medicinal plants from the Nigerian flora, represents an overview of the potentials of these plants in combating the disease. However among the family of the plants sample listed above when extracted with the polar and nonpolar solvent revels one or more of the phytochemical components which is responsible for converting the trypanosomes. For effectiveness of the plant extract it's recommended the usage of different chemical constituents during the extraction process so that the maximum number of the phytochemicals can be obtained due to the variation of the trypanosomes.

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