Efficacy of *Anogeissus leiocarpus* (DC.) as Potential Therapeutic Agent against Trypanosomiasis Diseases: A Review

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Abstract
Infectious diseases such as HIV, malaria, tuberculosis, pneumonia, leishmaniasis, diarrhoea and human African trypanosomiasis are responsible for one in two deaths in developing countries, where poverty, limited access to health care, drug resistance and a changing environment make populations particularly vulnerable. As a consequence, herbal medicines have attracted much attention as potential therapeutic agents in the prevention and/or management of parasitic and infectious diseases, as they can yield potential leads to address emerging infections and resistance. The present review underscores the relevant information concerning the botany, traditional uses, and phytochemicals constituents of Anogeissus leiocarpus as a potent therapeutic agent for counteracting the menace of African trypanosomiasis.

Key words: *Trypanosomiasis, Anogeissus leiocarpus, ethnotherapy.*

1. Introduction

Trypanosomes are haemo-protozoan parasites transmitted by tsetse fly and cause the disease called African trypanosomiasis. The disease causes serious losses in cattle, sheep and goats (Maigari *et al.*, 2015a), and other host animals including pigs, horses, cats, monkeys and camels (Maigari *et al.*, 2015a, b). The economic importance of the disease include high morbidity rates, frequent mortality, lower work efficiency and the high costs of treatment for animal that contract the disease (Bourn *et al.*, 2005). It also reduces the growth rate, milk production, strength of farm animals and most of the time leads to death of the affected animal (Yusuf *et al.*, 2015).

Members of the kingdom *Plantae* are used medicinally in different countries and are sources of many potent and powerful drugs (Kubmarawa *et al*, 2009). Among several factors contributing towards the potential use of phyto-medicine are safety, lack of adverse reactions and minimal side effects which have been mostly found to particularly influence the use of such medicines in developed countries (Renckens and Dorlo, 2013) as most of the developing countries have adopted traditional medical practice as integral part of their culture (Kamboj, 2000). Similarly, herbal preparations represent one of the most important traditional medicine therapies and are still the mainstay of majority of the world populations, mainly in the developing countries, for primary health care.
Anogeissus leiocarpus is a tree widely distributed in northern Nigeria. The bark and seed of the tree is used for the treatment and prevention of worm infestation in equine species

(Ahmad and Wudil, 2013). Traditional healers in the north eastern part of Nigeria also believe that the bark of the plant is very effective in the treatment of African trypanosomiasis (Bizimana, 1994). Recent research findings have confirmed some of the claims of the traditional healers on medicinal plants while some were scientifically disapproved (Wurochekke and Nok, 2004; Wurochekkke *et al.*, 2005 and Shuaibu *et al.*, 2008).
Several reviews on medicinal plants used in treatment of trypanosomiasis have been published (Amina and Mohammad, 2013 and Ogungbe and Setzer, 2009). It is estimated that 66%–85% of the World's population depends directly on plants as medicine and search for drugs derived from plants has accelerated in recent years (Newmann and Cragg, 2012 and Ravi-Kumar *et al*., 2011). Therefore, this paper entails to document several works conducted on the potent prophylaxis ability of *Anogeissus leiocarpus* as trypanocidal agent against both human African trypanosomiasis (HAT) and African Animal Trypanosomosis (AAT) as such will pave way and provide efficient room for further researches on the pharmacological activities and clinical relevance of this plant.

2. Review of Related Literature

2.1. *Plant Taxonomy*

Binomial name: *Anogeissus leiocarpus* (DC.) Guil & Perr
Synonyms*: Anogeissus schimperi* Hochest. Ex Hutch. & Dalz., *Concarpus leiocarpus* DC.
Family: *Combretaceae* (Ahmad, 2014)
English name: African birch, Axle wood tree (Victor *et al*., 2013).
Vernacular names: Fung dialect: Al-Selak, Arabic: EL-Sahab (El Ghazali *et al.,* 2003), Hausa: Marke, Farin gamji, Fulfulde: Kojoli, Nupe: Kukunchi (Victor *et al.,* 2013),
Kanuri: Annum, Yoruba: Ainy, Orin-odon, Igbo: Atara (Aliyu, 2006).

2.2. *Botanical Description*

Anogeissus leiocarpus is a deciduous tree species that can grow up to 15–18 m of height and measure up to 1 m diameter (Ahmad, 2014). Bark greyish and scaly, branches often drooping and slender, leaves alternate, ovate–lanceolate in shape, 2-8 cm long and 1.3-5 cm across (Ouedraogo *et al*., 2013). The leaves are acute at the apex and attenuate at the base, pubescent beneath. Inflorescence globose heads, 2cm across, yellow; the flowers are bisexual, petals absent. Fruits are globose, cone like heads; each fruit is broadly winged, dark grey, 3cm across. It can reproduce by seeds as well as vegetative propagation (Ouedraogo *et al*., 2013; El Ghazali *et al.*, 2003).

2.3. *Geographical Distribution and Habitat*

Anogeissus leiocarpus is typical element of woodlands and savannas of the Sudanian regional centre of endemism (Ahmad, 2014). It has large ecological distribution ranging from the boarders of Sahara up to the out layer humid tropical forests. In West Africa, from Senegal to Nigeria, Cameroon and extends to Ethiopia and East Africa. It grows in dry forests and gallery forests (Ouedraogo *et al*., 2013; Hennenberg, 2005).

2.4. *Traditional Uses*

Many traditional uses have been reported for the plant. In Sudanese traditional medicine the decoction of the barks is used against cough (El Ghazali *et al.,* 2003). Rural populations of Nigeria use sticks for dental hygiene, the end of the sticks are chewed into fibrous brush which is rubbed against teeth and gum (Rotimi, 1988). Ivory Coast traditional practitioners use the plant for parasitic disease such as Malaria, Trypansomiasis, Helminthiasis and dysenteric syndrome (Okpekon, 2004). In Togolese traditional medicine, it is used against fungal infections such as dermatitis and Mycosis, also the decoction of leaves is used against

stomach infections (Batawila *et al*., 2005). The plant is also used for the treatment of diabetic ulcers, general body pain, blood clots, asthma, coughing and tuberculosis (Victor, 2013).

2.5. *Potential Constrains*

The leaves of *Anogeissus leiocarpus* are rich in tannin, they contain ellagic, gallic and gentisic acids, derivatives of gallic and ellagic acids and several flavonoids that are very useful for dyeing (Andary *et al.*, 2005), but that may have deleterious effect on nutritive values. However, no sign of toxicity were observed in growing goats fed with African birch (Yahaya *et al.*, 2000).

2.6. *Phytochemical Constituents*

Already, extensive work has been done on the phytochemical components of *Anogeissus leiocarpus.* The phytochemical analysis of the extracts of *Anogeissus leiocarpus* revealed the presence of alkaloids, glycosides, phenols, steroids, tannins, anthraquinones, saponins and flavonoids (Mann *et al*. 2010 and Kaboré *et al*., 2010). In a similar study conducted by Aliyu and Sani (2011), alkaloids, tannins, saponins, flavonoids and glycosides were found to be present in ethanol and aqueous stem bark extracts of *Anogeissus leiocarpus* while tannins and flavonoids were absent in the chloroform extract of the plant. Moreover, the active compounds isolated from this plant have been shown to be mainly triterpenes and ellagic acid derivatives; flavonoids and phenolic compounds like flavogallonic acid bislactone (Abedo *et al.,* 2013 and Nwude and Ibrahim, 1980). For instance, anogelline and dakaline are obtained from its bark are used as cosmetics with anti-ageing properties (Abedo *et al.* 2013). These phytochemicals have been proven beyond reasonable doubt and established to be the driving force behind pharmacological activities of many medicinal plants (Mann *et al.,* 2008).

3. African Trypanosomiasis

Tsetse transmitted African trypanosomiasis is a parasitic disease caused by a protozoan of the genus *Trypanosoma*. *Trypanosoma vivax, Trypanosoma congolense* and to a lesser extent *Trypanosoma brucei brucei* are the main species responsible for African Animal Trypanosomosis (AAT) in West Africa while *T. b. rhodesiense* and *T. b. gambiense* cause sleeping sickness or Human African Trypanosomiasis (HAT) (Maigari *et al.*, 2015b). The disease is cyclically transmitted by a bite of the vector—tsetse fly (*Glossina* species) (D'Archivio *et al*., 2011).

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 (Ayodele *et al*., 2013; Joshua *et al.*, 1983). In addition to the old Gboko endemic, there have been reports of the disease outbreak in many other communities in Nigeria (Airauhi *et al.*, 2001; Edeghere *et al*., 1998).The prevalence rate in different breeds of animals in Nigeria for the past few years have been studied and ranged from 8.4% to 15.53% (Bauer *et al.*, 1999; Griffin and Allonby, 1979).

In Africa, the annual loss in livestock production and mixed agriculture alone due to the disease is valued at 5 billion US dollars (Nwodo *et al* 2015). 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 (Nwodo *et al* 2015). 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 (Nwodo *et a.l* 2015). 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 (Nwodo *et al.* 2015).

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 (Nwodo *et al.* 2015 and Simarro, 2012). Others such as homidium, isometamidium and diminazene aceturate are used in animal infections. Each of these drugs has one or more of various challenges including very expensive, highly toxic, need parenteral administration and parasites increasing resistance. The Drugs for Neglected Diseases *initiative* (DND*i*) is developing fexinidazole to a new oral drug for HAT with a good chance of success and it has entered Phase II/III clinical study in patients with late-stage sleeping sickness (Nwodo *et al.* 2015).

4. *Anogeissus leiocarpus* (DC.) and Trypanocidal Activity: An over view

Medicinal plants contain pharmacologically active principles which over the years have been exploited in traditional medical practice for the treatment of various ailments (Adebanjo *et al.*, 1983). Several studies were conducted in order to ascertain the trypanocidal activity of this plant against a significant number of trypanosome species. A research to evaluate *in vitro* trypanocidal effect of *Anogeissus leiocarpus* root methanol extract against *T.b. brucei* and *T. congolense* at concentrations of 4mg/ml, 2mg/ml and 0.4mg/ml was carried and immediately caused cessation or reduction in motility of the parasites in extract treated blood compared to that of parasite loaded control blood without extract which is taken as a measure of trypanocidal activity (Atawodi, 2003). It was found that there is only slight reduction in motility in *T. congolense* and drastically reduced motility in *T. brucei* compared to control (Atawodi, 2003). Methanol extract of leaves, roots and stem barks of the plant showed interesting *in vitro* trypanocidal activity (Okpekon, 2004). The aqueous, butanol fractions of the methanol extract of *Anogeissus leiocarpus* were associated with *in vitro* trypanocidal activity against four strains of *Trypanosoma* species. Castalagin isolated from these fractions showed trypanocidal activity on both, the human and domestic animal pathogens causing trypanosomes (Shuaibu, 2008).

Furthermore, as reported by Wurochekke and Anyanwu (2012), the water and methanolic extracts of the bark of the plant made parasites immotile immediately after incubation, as methanol extracts of the leaf and root made parasites immotile 10 minutes after incubation, the aqueous extracts of the leaf and roots gradually reduced motility and 15 minutes after incubation all parasites were immotile. The shorter the time of cessation of motility of the parasite, the more active and efficacious the extract was considered to be (Atawodi *et al*., 2003). Likewise when the stem bark extract of the plant was administered at the concentrations of 100mg/kg/day and 200mg/kg/day against rats infected with *Trypansoma brucei*, the level of parasitaemia increased progressively in all the infected groups to reach a peak seventh day post infection. Treatment did not directly affect the course of parasitaemia (Wurochekke and Anyanwu, 2012). However, the rats treated with 200 mg/kg body weight/day lived longer than those of the infected untreated control group (Wurochekke and Anyanwu, 2012). The pack cell volume (PCV) of the infected control group dropped faster compared to the gradual decrease observed in the treated groups, thus, this suggests that the bark of the plant may have higher concentration of the active component responsible for the activity observed (Wurochekke and Anyanwu, 2012).

The active components in the stem bark of *Anogeissus leiocarpus* and *Terminalia avicennoides* were hydrolysable tannins (Shuaibu *et al*., 2008). It also implies that the active ingredient responsible for the activity observed in this work can easily dissolve in the solvents (methanol and water) used for the extraction (Wurochekke and Anyanwu, 2012). *In vitro* activity shown by the various parts of the plant produce evidence to support the local

use of the plant, since bioactive screening is a useful method for pre-selection of plants for bioassay guided isolation and identification of active principles.

Many works reported the plant to possess a vast number of pharmacological activities including antiplasmodial (Mann *et al*. 2014), antioxidant (Ahmad, 2014), antibacterial (Aliyu and Sani, 2011), antidiabetic (Mann *et al*. 2014), leishmanicidal (Ahmad, 2014), antimalarial (Ahmad, 2014), anthelmintic (Ahmad, 2014), antifungal (Mann *et al*. 2008) and trypanocidal activities among others (Ahmad, 2014; Bizimana, 1994 and Mann *et al*. 2014). In Nigeria, several ethnobotanical studies of Nigerian plants used in the traditional management of trypanosomiasis indicated both significant *in vitro* /*in vivo* antitrypanosomal activity (Shuaibu, 2008 and Abubakar *et al*., 2005). Notable among these plants studied within the Nigerian biosphere were extract of *Anogeissus leiocarpus*, which distinctively exhibited a significant trypanocidal activity. In few cases, metabolites responsible for the associated activity have been isolated and potent bioactive compounds were reported (Mann *et al*., 2004). Moreover, a plant with high *in vitro* trypanocidal activity may have no *in vivo* activity and vice versa, because of peculiarities in the metabolic disposition of the plant's chemical constituents. Therefore, plants found to be active in *in-vitro* investigations must be tested *in vivo* and tested clinically before a definite statement can be made on their trypanocidal potentials (Atawodi *et al.*, 2003).

In a recent research survey conducted to assess the management of trypanosomiasis among Fulani herdsmen in Taraba state using natural plant products, out of 64 respondents interviewed, 67.19% were found to have remedy for animal trypanosomiasis while the remaining 32.81% had no remedy for trypanosomiasis (Salihu *et al*., 2014). The *Caesilpiniaceae* family has the highest frequency of use with 36.36% and *Combretaceae* 27.27% among which is *Anogeissus leiocarpus* in which the stem bark is more utilized and prepare as either decoction, infusion or squeezing of the plants or in pulverized form (Salihu *et al*., 2014). The methanolic root extract of *Anogeissus leiocarpus* also exhibited significant trypanocidal activity as it drastically reduced motility of *T.b. brucei* immediately after 60 minutes of incubation at concentration of 4mg/ml and causes slightly reduced motility against *T. congolenses* at 2mg/ml and 4mg/ml concentrations respectively (Atawodi *et al*., 2003).

5. Conclusion and Recommendations

Plant preparations remain a promising source of traditional medicine for control and management of both humans and animals ailments. Indeed, the discovery of compounds with anti-parasitic and antimicrobial activities from traditional medicinal plant remedies remains a medically and potentially challenging task. This review on *Anogeissus leiocarpus* represents an overview of its potentials in combating trypanosomiasis in humans as well as animals. The review might serve as the scientific baseline information for the use of documented plants as well as a starting point for future studies for the discovery of better trypanocidal agents. Pharmacological efficacy of this plant is shown to be attributed to its phytochemicals constituents such as tannins, alkaloids, flavonoids, saponins etc. Thus, further researches need to be conducted in order to explore the various medicinal properties of our naturally endowed flora.

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