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POTENTIALS OF *Parkia biglobosa* AND *Annona senegalensis* as ANTIDOTE TO SNAKE SPECIES COMMON IN NORTHWESTERN NIGERIA: REVIEW

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ABSTRACT
Snakebite is a neglected public health problem in tropical countries, especially in rural areas of Northwest Nigeria. However, despite the high rate of snake bites in this region, it's still one of the most poorly documented health concerns because it often occurs to farmers in rural areas where traditional therapists are cherry-picked for emergency treatment. The venom is secreted by the oral snake glands and injected via the fangs into the victim's hands, feet, arms, or legs. The most common snakebite cases in Northwestern Nigeria are Echis ocellatus (African carpet viper), Naja nigricolis (Spitting cobra), and Bitis arietans (Puff adder), with high mortality and morbidity rates in the region. Immunotherapy is the only known snake antivenom, but the limitations and side effects associated with the therapy, such as serum sickness, pyrogen and geographical inter-specific venom variation, has led to the search for another means to treat snake bites. Medicinal plants were the first-line investigations for the snakebite antidote. Recent ethnopharmacological studies revealed several medicinal plants with promising potentials to treat snakebites in Northern Nigeria. This review aimed to document and compile the recent scientific works carried out on the potentials of Parkia biglobosa and Annona senegalensis against snake venom common in Northwest Nigeria. The methodology used in literature synthesis is the qualitative description and content analysis of recent studies onplants with potential activities against snake venoms. The result showed that the potency of methanol extracts of the bark of P. biglobosa and root bark of A. senegalensis have significant potentials to detoxify (in vitro) venom from N. nigrocollis, E. ocellatus and B. arietans found in Northwest. The authors suggested proper documentations of snake bites incidences especially in rural areas where access to effective medications isvery limited.
Keywords: Antivenom, Echis ocellatus, Naja nigricolis, and Bitis arietans, Northwestern Nigeria, Medicinal Plants

INTRODUCTION

Snakebite is a severe health problem, especially to the farmers whose livelihood depends on farming, fishing, and hunting (Babo *et al.,* 2019; Yusuf *et al.,* 2021). Thus, cases associatedwith snakebites are morefrequent in rural areas than in urban; however, the poor documentary of snake incidences in these areas led to high mortality rates, amputations, and other permanent disabilities (Kumar and Devang, 2011; Ameen *et al.,* 2015; Yusuf*et al.,* 2021;). Snake poisoning, commonly known as envenomation, has posed a serious threat to public health in Nigeria. According to the Nigerian Minister of State for Health (MoS-4H), more than 100,000 people die each year of snake poisons, and approximate 5 million cases of snake incidence has been documented worldwide (Premium Times, 2021). Nigeria has experienced an increased death from snake envenomation, even though there are poor documentation about the snake incidence, but "more than 20,000 cases and 2000 deaths from snakebites" are said to be recorded in Nigeria from January to September, 2021 (Premium Times, 2021).

According to Ameen *et al.,* (2015) findings, snakebites are more common among farmers, cattle rearers, hunters in the Northern part of Nigeria.

The incidence, however, occurs often while the victims are farming, walking, or herding (Ismaila and Adamu, 2012). Ameen *et al.,* (2015) identified the three most dangerous snakes accountable for the majority of bites in Northern Nigeria and seen everywhere in Northwest states *viz*: carpet viper (*Echi socellatus*), black-necked spitting cobra (*Naja nigricollis*), and puff adder (*Bitis arietans*). Notwithstanding, the high incidence of snakebites in Nigeria, there has been a very significant shortages of antiserum in the region, which is the only conventional therapeutics against snake venom. This led people living in this region to take victims to the traditional therapists for emergency local treatment.

The use of herbal or medicinal plants for the cure of several infectious diseases is as old as human existence, which is the reason why plants became a bright light towards the development of snake antidote. Majority of world populations today are still rely on traditional and or medicinal plants to treat various ailments, including snakebites (Habib *et al.,* 2001, Hassan *et al.,* 2020). However, the safety, and efficacy of these plants for local treatments of snakebites have been an area of interest in the scientific community. Recent phytochemical screening of these plants shows the presence of very active compounds against the poisonous venom of several snake species (Rizzini *et al.,* 1988; Adzu *et al.,* 2004 and Yusuf*et al.,* 2021). The bioactive components of these plants bind to the venom proteins of carpet viper (*E. ocellatus*), black-necked spitting cobra (*N. nigricollis*), and puff adder (*B. arietans*), thereby detoxifying the effect of their venoms (Adzu *et al.,* 2004). There are several plants with the potentials for snake antivenom. The present review X-rayed the recent scientific works carried out on *P. biglobosa* and *A. senegalensis* the antidotes to common Northwest Nigerian snake species.

Symptoms and Clinical Spectrums of Snake Venoms

Snake venoms are known to be a complicated mixture of toxic, and enzymatic proteins such as the "phospholipase A2 (PLA2s), myotoxins, hemorrhagic metalloproteinases and other proteolytic enzymes, coagulant components, cardiotoxins, cytotoxins, neurotoxins, etc., (Kumar and Devang, 2011). Venom from carpet viper (*E. ocellatus*), black-necked spitting cobra (*N. nigricollis*), and puff adder (*B. arietans*), causes different physical symptoms on the body of the victims. These symptoms, and clinical spectrum of these snakes according to Kumar and Devang (2011); Warrel (2003) and Ameen *et al.,* (2015) are summarized table 1 below:

Table 1: Symptoms and clinical spectrum caused by carpet viper (*E. ocellatus*), black-necked spitting cobra (*N. nigricollis*), and puff adder (*B. arietans*)

SNAKE SPECIES	SYMPTOMS	CLINICAL SPECTRUM
E. ocellatus	Swelling, blistering, necrosis, and hemorrhages primarily due to metalloproteases and ecarin, i.e., an enzyme that activates prothrombin.	1. *Haemotoxin*-is a snake toxins found mainly in,*E. ocellatus* 2. *Phospholipases A2*: clog the electron transfer at cytochrome C level and cedes mitochondrial-bound enzymes soluble; it causes the damages of red blood cells. Phospholipase A2 is present in the venom of all families of poisonous snakes.
N. nigricollis	Envenomation caused by this snake could result in an unusual necrosis, hemorrhage, complement depletion, and respiratory arrest or paralysis.	1. *Cardiotoxins & Haemotoxin*-They are group toxins found mainly in,*E. ocellatus*, and *N. nigricollis* 2. Phospholipase A2 3. *Fasciculins:* toxins that attack the cholinergic neurons thereby destroying acetylcholinesterase; acetylcholine (ACH), they induce numbness and flaccid paralysisas well as tetany, which could lead to death. An example of a snake with this poison is black mambas, *N. nigricollis*
B.arietans	Poison from this snake could lead to a severe loss of tissue damage which may eventually results to amputation of the affected limb, as well as hemorrhage, proteolysis, myonecrosis, and edema.	1. Phospholipase A2 2 α-neurotoxin

Figure 1: L-R: *E. ocellatus, N. nigricollis, B. arietans*

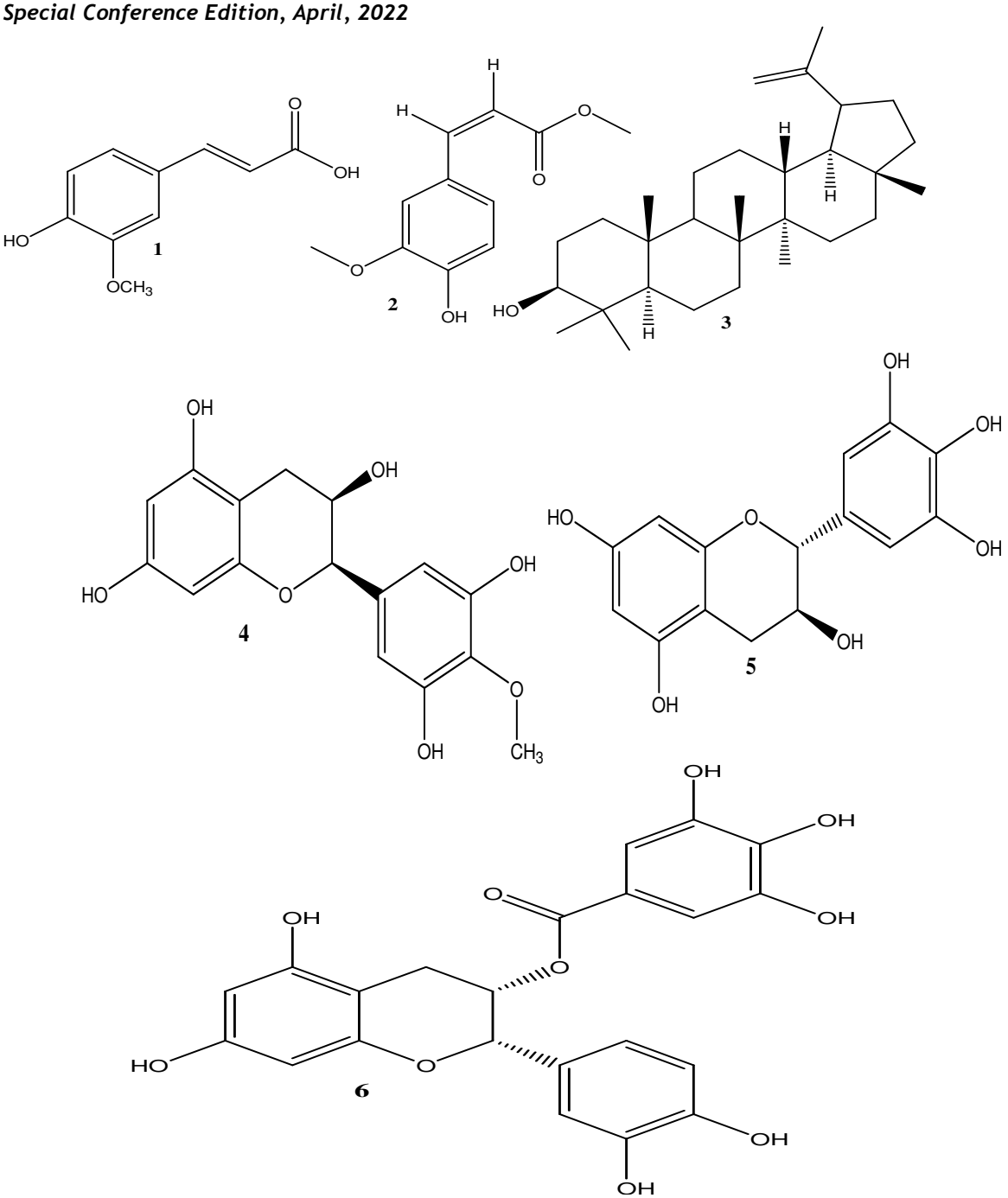
Detoxification Potentials of *P. biglobosa*and *A. senegalensis* against Snake Venoms

P. biglobosa

The name *Parkia* was derived from a Scottish scientist, 'Mungo Park' who reported to have drowned in January, 1805 in the Niger River, Nigeria. It is belonging to the *Leguminosae* family and known by different names, such as African Locust Bean Tree, Doruwa (Hausa), and Naree-hi (Fulani) (Ameen *et al.,* 2015). *P. Biglobosa* tree can be found everywhere in the Northwest and other part of Nigeria which is not usually cultivated. It is a long growing tree with an approximate height of 7 to 20 metre (Das, 2009) with bark dark grey brown, thick fissured (Alabi *et al.,* 2005; Das, 2009;).

Plate 2: *P. Biglobosa*

The stem bark of *P.biglobosa* was traditionally used to treat *E. Ocellatus* and *N. Nigricolli* (Asuzu and Harvey, 2003; Das, 2009; Ameen*et al.,* 2015; Yusuf *et al.,* 2021). Das (2009) reported that, the stem bark of *P. biglobosa* is found helpful for the treatment of many ailments such as violent stomach aches, diarrhoea, pneumonia, bronchitis, severe cough, wounds, dental caries, conjunctivitis, dermatosis and sexually transmitted diseases (STD)". Phytochemical screenings of the stem bark of *P. biglobosa* shows the presence of long-chain esters mixture of "trans-ferulic acid **1** and cis-ferulates**2**, lupeol**3**, 4-O-methyl-epi-gallocatechin **4**, epi-gallocatechin**5**, epi-catechin 3-O-gallate **6** (Alabi *et al.,* 2005; Gbolade, 2021).



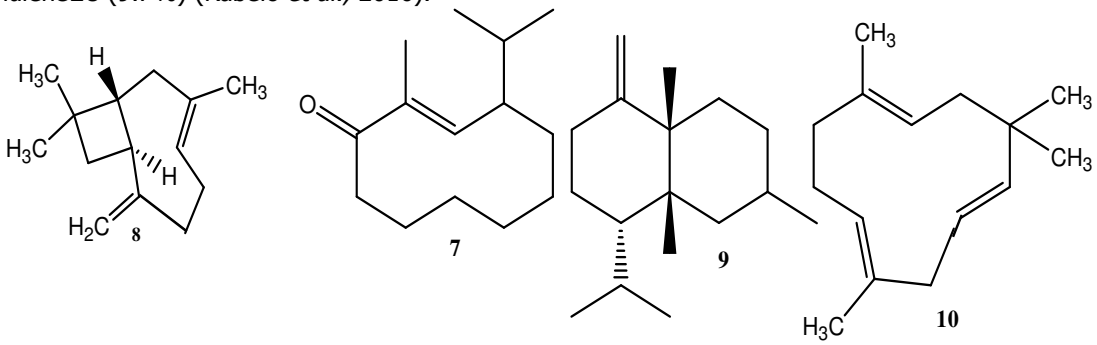
Recent studies conducted on *P. biglobosa* show that, water and methanol extracts of the stem bark show significant ($p<0.001$) protection against *N. nigricollis* venom and slow down the loss of responses to acetylcholine (ACH), carbachol and potassium chloride (KCl), which are usually blocked by *N. nigricollis* venom (Das, 2009; Gbolade, 2021). Furthermore, the methanol extract *P. biglobosa* (75, 150, and 300 µg/ml) significantly ($p<0.05$) protects murine muscle cells in culture against the cytotoxic effects of *N. nigricollis* and *E. ocellatus* venoms (Asuzu and Harvey, 2003). According to Yusuf *et al.,* (2021) 400 mg/kg methanolic extract of *P. biglobosa,* show 40% protection to mice.

A. senegalensis

A. senegalensis (*Annonaceae*), is a shrub-like plant with an estimated height range of 1 to 2 metres (Rabelo *et al.,* 2016), it has a large leaf, oval, and fragrance once they are crunched (Adzu*et al.,* 2005; Rabelo *et al.,* 2016). *A. senegalensis* is called 'Gwadandaji' (Hausa), 'Dukuuhi' (Fulani) and 'Abo' (Yoruba). It is a wild shrub plant that grows in tropical Afrcia with pulpy fruits, solid but orange at maturity (Ameen *et al.,* 2015).

Plate 3: *A. senegalensis*

Different parts of *A. senegalensis* are used as traditional medicine to treat wide variety of infections such as respiratory problems, eye, skin diseases, diarrhea, blood pressure, dysentery, and most commonly is it usage as antidote to snake and scorpion venoms (Rabelo *et al.,* 2016). According to Adzu *et al.,* (2005), the leaves of *A. senegalensis* are used to treatchest pain, coughs, anemia, urinary tract infection while Graham *et al.,* (2000) also reported that cancer treatment of the leaves. The GC and GC-MS analysis on the essential oil obtained from the leaves of *A. senegalensis* show the presence of germacrene D **7** (19.2%), β-caryophyllene **8** (19.1%), γ- cadinene **9** (11.1%) and α-humulene**10** (9.7%) (Rabelo *et al.,* 2016).



Recent *in vivo and in vitro* studies of the stem bark (100 mg/kg) (Yusuf *et al.,* 2021), leaves, and roots (Ameen *et al.,* 2015; Gbolade, 2021) on *A. senegalensis* extracts against *N. nigricolli* (46.3%), *B. arietans* (19.5%) and *E. Ocellatus* (14.6%) venoms show significant detoxification activity. The root bark of *A. senegalensis* was found to have a very significant ($p<0.05$) activity in the group that received 100 and 200 mg/kg of the extract when compared to the saline control group (Adzu *et al.,* 2005).

CONCLUSION

Indigenous plants are used for local treatment of all forms of snakebites in Nigeria, especially in the North. People living in the rural areas of this region seldom treat snakebite in the hospital due to the cost and limitation of antiserum, which is the only known immunotherapy available as an antidote to snake poisons. Traditional therapists used several medicinal plants including, *P. biglobosa* and *A. senegalensis,* against *E. ocellatus* (African carpet viper), *N. nigricolis* (Spitting cobra), and *B. arietans* (Puff adder) envenomation. Meanwhile, scientific studies on these plants, proved their pharmacological potentials against snakebites. Methanol extracts of *P. biglobosa* and *A. senegalensis* administered to mice at different dosages shows appreciable protection against neurotoxic, haemo-toxic, and cytotoxic effects of common Northwest snakes species. Finally, the authors of this mini-review suggested that:

- Proper documentation of snake bites incidences, especially in rural areas where access to effective medications is very minimal should be encouraged.
- More studies should be conducted on the efficacy and toxicity of *P. biglobosa*and *A. senegalensis.*
- Traditional therapists engaged in the local treatment of snakebites should be consulted to explore more plants.
- Government and international organizations should fund researches towards the development of effective medication against snake venom.

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