

A Review of the Phytochemical and Pharmacological Properties, and Ethnomedicinal Uses of Some Nigerian *Phyllanthus* species-Part 2.

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Abstract

Phyllanthus L. is an important plant genus belonging to the family Phyllanthaceae. The species of the genus are mainly annual or perennial herbs, shrubs, trees, or climbers distributed in tropical and subtropical regions. The members of the genus are used in traditional medicine in the treatment of human ailments like dysentery, cancers, jaundice, wounds, ulcers, malaria, stomach disorders, fever, gonorrhoea etc. The present review elucidates the phytochemical and pharmacological properties and ethno-medicinal applications of four species of genus *Phyllanthus* found in Nigeria. The most important of the compounds reportedly isolated from the species are lignans, tannins, flavonoids, terpenoids, alkaloids, saponins etc. Literature reveals that the plants possess important pharmacological activities such as: anti-cancer, antidiabetic, antimalarial, antiviral, anti-inflammatory, immunomodulatory, antioxidant activities etc. We recommend that further investigations be conducted on the phytochemical and pharmacological properties of the plants to affirm their ethno-medicinal uses and to isolate and characterize the important bioactive compounds which may be utilized in pharmaceutical drug formulation.

Keywords: *Phyllanthus*, phytochemicals, pharmacological, ethno-medicinal, pharmaceutical uses.

Introduction

Plants have been contributing to the livelihood of man since time immemorial. They are used by man as sources of food, medicine, shelter clothing, and so on. The use of plants in traditional medicine is as old as human race. Traditional or herbal medicine signifies the medical practice by local ethnic groups using natural herbs. According to Ukwubile and Nathaniel (2014), about 13,000 species of plants have been used as drugs throughout the world. Traditional medicine has gained great popularity among the greater percentage of the populace particularly in developing countries where orthodox medicine is grossly inefficient, ineffective, and quite expensive. In fact, traditional medicine using plant extracts continue to provide health coverage for over

Traditional medicines are used for the treatment of many health challenges including common ailments like coughs, fevers, asthma, malaria, hypertension, jaundice, eye afflictions, dysentery, diarrhea, gonorrhoea, urinary and intestinal problems (Burkil, 2004; Mao *et al.*, 2016). Traditional medicinal plants also show various biological or pharmacological properties including anti-inflammatory, anti-cancerous, anti-diabetic, anti-hypertensive, antimalarial, anti-cardiovascular, antioxidant, immunomodulatory, anti-lipidemic, anti-protective, anti-hyperglycemic, and anti-hepatotoxic activities (Sarin *et al.*, 2014; Harvey *et al.*, 2015). Medicinal plants have the capacity to cure diseases because they are rich in bioactive substances (drugs). Therefore, the medicinal plants are rich sources of new drug discovery

80% of the world's population, especially in the developing world (Igbinosa *et al.*, 2009). Different regions or nations have their different connotations and patterns of traditional or indigenous or herbal medicine. In Africa, traditional medicine practice is under the generic name African Traditional Medicine Practice (ATMP), by various ethnic nationalities in the African Continent. Also, Ayurveda Medicine (AM) originated from Southeast Asia, Unani Medicine (UM) from Arab countries in the Middle East, and Acupuncture and Traditional Chinese Medicine (TCM) originated from China (Tao *et al.*, 2014), which is also known as Oriental Medicine (Liu *et al.*, 2015). Others are homeopathy which originated from Europe (Smith, 2012), and Naturopathy also from Europe (Kimbal, 2003).

due to some recent drugs that are derived from plant-derived compounds (Harvey *et al.*, 2015). Some of these compounds have been discovered from species of genus *Phyllanthus* some of which are of immense use in traditional medicine. Thus, the present review provides information about some *Phyllanthus* species found in Nigeria including the summary of their phytochemical constituents, pharmacological properties and ethnomedicinal uses.

Genus *Phyllanthus* (L.), is the largest genus in the flowering plant family Phyllanthaceae with varying number of species ranging from 750 to 1200 (Kathriarachchi *et al.*, 2006; Mabberley, 2008). The genus has a remarkable diversity of growth forms including annual and perennial herbs, shrubs, trees, climbers, floating aquatics, and pachycaulous succulents; generally monoecious. *Phyllanthus* are widely distributed in all tropical and subtropical regions of the world including tropical Africa, tropical America, Asia, and Oceania (Mabberley, 2008; Mao *et al.*, 2016). *Phyllanthus* species have been of great use in traditional medicine in different parts of the world for a long time. Many species of *Phyllanthus* are employed in the treatment of various human afflictions such as malaria, asthma, jaundice, ulcer, hepatitis, flu, diabetes, fevers, dropsy, inflammations, and so on. Four species of *Phyllanthus* occurring in Nigeria are reviewed for their phytochemical constituents, pharmacological properties, and ethnomedicinal uses. The *Phyllanthus* species under review are: *P.amarus*, *P.muellerianus*, *P.niruri*, *P.nummulariifolius* (Fig.1).

Phyllanthus amarus Schum.& Thonn.(syn.*P.carolinianus* Blanco), commonly known as sleeping plant or carry-me-go-seed, is a small, erect, annual herb, growing from 10-15 cm tall but usually less than 30 cm. The stem can be branched or unbranched; leaves alternate, elliptic, oblong, distichous, with small leaflets oblong; flowers numerous, monoecious, axillary, pale green, often flushed with red; fruits tiny, smooth capsules containing seeds; seeds with strong parallel and transverseribs (Burkil, 2004; Awomukwu *et al.*, 2015). It is of wide distribution in Nigeria and a popular ingredient in traditional medicine in Nigeria (Ukwubile and Nathaniel,2014).It is a weed of cultivated fields, gardens, open localities, waste places, grassy scrub vegetation, and dry forests, and on humid sandy soils(Burkil,2004).

**A****B****C**

Fig.1:Habit of study plants (A). *P.amarus* (B). *P.muellerianus* (C). *P.niruri*

Phyllanthus muellerianus (Kuntze) Exell. [syn. *P. floribundus* (Baill.) Mull. Arg.], is a deciduous or evergreen, glabrous shrub with numerous, more or less straggling stems from the base and sometimes with a climbing habit, sometimes becoming more tree-like, and can grow up to 12 m tall; leaves relatively large, simple, alternate, ovate to ovate-lanceolate, distichous, 2 mm long; flowers in clusters, unisexual; fruits copious panicles of small red, fleshy, globose, shinning berries, that eventually turn black, 6-seeded; seeds angular (Hyde *et al.*, 2020). According to Mao *et al.* (2016), *P. muellerianus* is the most popular herbal drugs of the genus *Phyllanthus* in Africa. It is often found in riverine vegetations and fringing woodlands, swampy forests, and tall grasslands (Burkil, 2004).

Phyllanthus niruri L. (syn. *P. fraternus* Webster), with the common names Gale of the wind, stone-breaker, or seed-under-leaf, is similar morphologically with *P. amarus*. It is a perennial shrub or herb, growing up to 50-70 cm tall, with ascending herbaceous branches; leaves numerous, distichous, elliptic-oblong, simple; flowers numerous, small, pale green, often flushed with red; fruits tiny, smooth, globose capsules; seeds trigonous (Pankaj, 2002). It grows in wet soils; mature plants tolerate complete flooding, and can grow as epiphytes on leaf axils (Le Bourgeois *et al.*, 2008).

Methodology

The literature used for this review was gathered from various search engines and data bases including WebScience, NCBI Site Search, Research Gate, PubMed, Google Scholar and Science Direct. The literature published prior December 2020 on phytochemicals and pharmacological properties of the extracts and ethnomedicinal uses of the *Phyllanthus* species studies. The search terms "Phyllanthus", "phytochemicals", "pharmacologicals" and "ethnomedicinal uses" were employed for each of the reviewed *Phyllanthus* species with no exact time limit. The appropriate full-texts of the eligible papers were identified and accordingly accessed. All the necessary references were checked for appropriate citations. All articles with titles/abstracts were employed without any language restrictions.

Phytochemical Constituents

Phytochemicals are secondary metabolites or bioactive compounds produced by plants and so they are plant-derived. Therefore, phytochemicals are natural plant products. The bioactive compounds in plants (phytochemicals) are responsible for their pharmacological and medicinal properties. A wide variety of bioactive compounds are produced by plants and this gives them the potential to be utilized as medicinal plants. Various groups of phytochemicals have been isolated and identified from *Phyllanthus* species using various techniques including chromatographic procedures. According to Mao *et al.* (2016), more than 510 compounds have been isolated from the species of *Phyllanthus*, the majority of which are lignans, triterpenoids, flavonoids, alkaloids, tannins, saponins, phenolic compounds, steroids, anthraquinones, and cardiac glycosides. The compounds isolated from each of the study *Phyllanthus* species and their biological or pharmacological properties as well as their ethnomedicinal uses are summarized in Table 1. Among these compounds, lignans and tannins exhibit various activities and are considered the major biologically active compounds of the genus *Phyllanthus* (Geethangili and Ding, 2018).

Pharmacological Properties

The bioactive compounds in medicinal plants (phytochemicals) or drugs show various biological or pharmacological activities. According to Geethangili and Ding (2018), epidemiological and experimental investigations suggest that medicinal plants possess great potential in the management of various types of human afflictions. Consequently, medicinal plant extracts and their purified compounds (bioactive compounds or phytochemicals) have significant growth inhibitory potential against various pathogens such as different types of cancer cells *in vitro* as well as *in vivo* (Harvey *et al.* (2015). The remarkable traditional uses of genus *Phyllanthus* have led to the various researches of their biological activities. Some of the pharmacological activities of the genus *Phyllanthus* include anti-malarial, anti-viral, anti-fungal, anti-bacterial, anti-microbial, antioxidant, anti-diabetic, anti-cancer, anti-inflammatory, anti-hypoglycemic, anti-lipidemic, immunomodulatory, anti-hepatotoxic activities etc. The biological activities and the parts of the study plants used are indicated in Table 1. In the *Phyllanthus* species reviewed, the extracts may be from the roots, stems, stem bark, leaves, fruits, seeds, and whole plants.

Ethnomedicinal Uses

Traditional medicine practice is presently popular particularly in developing countries including Nigeria by the use of many groups of plants. Among these plants are species of genus *Phyllanthus* some of which are used as medicinal plants in Nigeria (Obidike *et al.*, 2010; Okoli *et al.*, 2011; Ofokansi *et al.*, 2013; Ukwubile and Nathaniel, 2014). The traditional application experiences of these plants may have reference value for the traditional treatment of many diseases. Traditionally, the whole plants, roots, stems, fruits, roots, leaves, and seeds of *Phyllanthus* species under review are used in the treatment of various ailments in different regions of the world. Such diseases include malaria, cough, asthma, convulsion, diarrhea, dysentery, skin diseases, wound, intestinal disorders, eye problems, fever, gonorrhoea, and others as depicted in Table 1.

Table 1: Scientific, common and vernacular names, phytochemical constituents, pharmacological properties, and ethnomedicinal uses of some species of Nigerian *Phyllanthus* genus.

S/N	Scientific name	Parts used	Common Name	Vernacular Name	Phytochemical Constituents	Pharmacological Properties	Ethnomedicinal uses
1.	<i>P. amarus</i> <i>L. (P. syn. P. carolinianus)</i>	Roots, stem, leaves, fruits, seeds, sap, whole plant.	Sleeping plant or carry-me-go-seed	Enyi kwonwa (Igbo), Geeron-Tsuntsaa-yee (Hausa), Eyi-olobe (Yoruba)	Lignans (eg. phyllanthin, hypophyllanthin, phylteralin, nirtetralin, niranthin) (Singh <i>et al.</i> , 2009; Taesotikul <i>et al.</i> , 2011), ellagitannins (eg. phyllanthusiin D, amariinic acid, elaeocarpusin, repandusinic acid A, and geraniinic acid B (Gupta and Vaghela, 2019), flavonoids, alkaloids, tannins, sterols, terpenes, phenols, and volatile oils (Meena <i>et al.</i> , 2017)	Diuretic, antioxidant, anticarcinogenic, anti-inflammatory, antibacterial, antipoison, antivom, antifungal, antiviral, antimicrobial, antiseptic, sedative, and astringent properties (Harikumar <i>et al.</i> , 2009; Patel <i>et al.</i> , 2011), antiprotective, antidiabetic, antiproliferative, gastroprotective, cardioprotective, antileptospiral, hepatoprotective (Xavier <i>et al.</i> , 2012), antitumor, cooling, stomachic, and immunomodulatory activities (Islam <i>et al.</i> , 2008; Gupta and Vaghela, 2019); antiarthritic, effects (Mali <i>et al.</i> , 2011), and antiplasmodial activity (Appiah-Opong <i>et al.</i> , 2011), as tonic, febrifuge, cholagogue,	Cough, colic, dysentery, oedema, diabetes, fever, pains, sore throat (Burkil, 2004; Adeneye, 2012), blennorrhoea, oliguria, painful wounds, ventral diseases, haemorrhoids, otitis, tachycardia, female sterility, abscesses, stomach pains, hepatitis B (Huang <i>et al.</i> , 2003; Burkil, 2004), bladder infections, chronic kidney disease, kidney stones, liver diseases, cancers (Londhe <i>et al.</i> , 2012), gonorrhoea, heavy menstrual bleeding, diarrhoea, skin infections, urinary tract infections (Wong, 2020), ophthalmopathy, scabies, ulcers, menorrhagia, diseases of spleen

						vermifuge (Burkil,2004),	and genital afflictions (Ewake and Enogieru, 2011; Ravikumar <i>et al.</i> , 2011), skin ulcers, obesity, jaundice, swellings, tuberculosis and ringworms (Maity <i>et al.</i> , 2013; Gupta and Vaghela, 2019), nephrolithiasis(Boi m <i>et al.</i> , 2011).
2.	<i>P.muellerianus</i> (Kuntze) Exell. (syn. <i>P.floribundus</i> (Baill.) Mull.Arg.)	Leaves, stem bark, young shoots,leafy twigs,leaf sap,stem sap, roots, root bark, flowers.		Ọgu azu or Anya-nunu (Igbo), Majiriya kurumi (Hausa), Arunjeran (Yoruba)	Lignans, tannins, flavonoids, saponins, alkaloids, anthraquinones (Doughari and Sunday, 2008; Burkil, 2004; Cesari <i>et al.</i> , 2015), steroids, triterpenes, cardiac glycosides, and phenols (Brusotti <i>et al.</i> , 2012; Ajibua <i>et al.</i> , 2017).	Antiplasmodial, antifungal, and antimicrobial activities (Brusotti <i>et al.</i> ,2012),tonic,antiseptic, purgative, anthelmintic (Burkil,2004), fabrifuge,decongestant, alterative, aphrodisiac, cooling, aperients, anti-inflammatory, and antibacterial effects(Ofokansi <i>et al.</i> , 2013), immunoboosting, immunosuppressing, and immunomodulatory properties (Agbo,2018)	Intestinal troubles, severe dysentery, chest complains, anaemia, constipation, toothache, dysmenorrhoea, male infertility, malaria, venereal diseases, and eye problems (Burkil, 2004;Zirihi <i>et al.</i> , 2005), fevers, skin eruptions, paralysis, coughs, rheumatism, intercostals pains, rashes, jaundice, stomach problems, diarrhoea, and diabetes(Mao <i>et al.</i> ,2016), colds, wounds, tetanus, abscesses, sore throat, pneumonia, enlarged glands, gonorrhoea, sinusitis, bronchitis (Fowler, 2006;Agyare <i>et al.</i> ,

							2011; Das <i>et al.</i> , 2012).
3.	<i>P. niruri</i> L. (<i>Diasperus niruri</i> (L.) Kuntze)	Leaves, stem, whole plants, fruits	Gale of wind, stone-breaker, or seed-under-leaf.	Enyikwonwa (Igbo), Geeron-Tsuntsaayee (Hausa), Yin-olobe (Yoruba)	Lignans (eg, phyllanthin and hypophyllanthin), flavonoids, triterpenes, steroids, tannins, glycosinoids, and essential oils (Patel <i>et al.</i> , 2011; Zhu <i>et al.</i> , 2011; Wei <i>et al.</i> , 2012), polyphenols, alkaloids, diterpenoids (Hossain and Salenhuddu, 2006), terpenoids, coumarins, saponins, and cardiac glycosides (Samah, 2012; Danladi <i>et al.</i> , 2018; Ishimaru <i>et al.</i> , 2018).	Antimicrobial, antiviral, antibacterial, antioxidant, antidiabetic, antipyretic, diuretic, antiplasmodial, anti-inflammatory, anticancer, astringent, and hepatoprotective effects (Nwanjo <i>et al.</i> , 2007; Okoli <i>et al.</i> , 2011; Watson and Preedy, 2013), hyperlipidemic, hyperuricemic, nephroprotective, antinematodal, radioprotective, analgesic, and kidney-protective activities (Murugaiya and Chan, 2009; Amin <i>et al.</i> , 2013; Danladi <i>et al.</i> , 2018), immunomodulatory, antinociceptive, antitumor, and anticarcinogenic properties (Rajeshkumar <i>et al.</i> , 2002; Obidike <i>et al.</i> , 2010; Giribabu <i>et al.</i> , 2014; Raymond <i>et al.</i> , 2017), vasorelaxant effect (Izuka <i>et al.</i> , 2006).	Jaundice, chronic dysentery, dyspepsia, cough, asthma, malaria, indigestion, diabetes, urinary diseases, skin diseases, ulcers, sores, swellings, hepatitis B, hemorrhagic cystitis (Murugaiya and Chan, 2009; Xia <i>et al.</i> , 2011; Ifeoma <i>et al.</i> , 2013; Liu <i>et al.</i> , 2014), enteritis, wounds, scabies, ringworms, gonorrhoea, gall stone, fever, excess uric acid, kidney disorders, and anoxia (Li <i>et al.</i> , 2007; Narendra <i>et al.</i> , 2012; Venkateshwarlu <i>et al.</i> , 2012), bronchial infections, liver diseases, oedema, sore throat, female sterility, oliguria, and vaginitis (Danladi <i>et al.</i> , 2018), irregular menstruation, tachycardia, itchiness, arthritis, otitis, weakness of male organs, renal calculi, liver infections, viral infections, to

							restore liver activity, to enhance body defense and as blood tonic (Nishuira <i>et al.</i> , 2004; Murugaiya and Chan, 2009), and to treat hemorrhage (Boeira <i>et al.</i> , 2011).
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Conclusion

Three *Phyllanthus* species were reviewed for their phytochemical constituents, pharmacological or biological activities and ethnomedicinal uses. The species showed the presence of a variety of bioactive compounds including lignans, flavonoids, tannins, alkaloids, saponins, phenols, steroids (sterols), glycosides, and a number of other compounds. These phytochemicals isolated from the study plants exhibited a wide range of biological properties including antibacterial, antifungal, antiviral, antioxidant, anti-inflammatory, antidiuretic, antidiabetic, anticancer, antihypertensive, antiplasmodial, antimalarial, hypolipidemic, hepatoprotective stimulant and immunomodulatory properties. The plants investigated possessed numerous medicinal applications including the treatment of malaria, diabetes, jaundice, diarrhea, dysentery, gonorrhoea, fevers, coughs, cancers, asthma, dropsy, convulsions, constipation, pains, eye afflictions, sorethroat, oedema, headache, inflammations, and so on. Consequently, the phytochemical and pharmacological properties of these *Phyllanthus* species may be correlated with their medicinal uses. Further extensive studies of the phytochemical and pharmacological properties of the *Phyllanthus* species should be carried out for subsequent application in pharmaceutical industry.

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