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Ethnomedicinal Uses and Therapeutic Activities of *Piper Guineense:* A Review

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ABSTRACT: The use of medicinal plants in most developing countries as therapeutic agents for the maintenance of good health is a widespread practice. One of such plant products is *Piper guineense*, which is a West African spice used in many folklore medicines and has a number of verified pharmacological activities. Proximate analysis reveals that the plant contains crude protein, fat, carbohydrate, vitamins and minerals while preliminary phytochemical screening and gas chromatography-mass spectrophotoscopy of the methanol leaf and seed extract of *Piper guineense* revealed the presence of several constituents such as alkaloids, glycosides, tannins, flavonoids, terpenes; sesquiterpenoids and monoterpenoids, saponins and secondary metabolites such as Aromadendrene, 1,6,10- Dodecatriene,7,11-dimethyl-3-methylene and piperine, piperidine amongst other secondary metabolites. Studies have revealed that *Piper guineense* possess several pharmacological and therapeutic properties such as anti-oxidant, anti-microbial, aphrodisiac, anti-parasitic, anti-inflammatory, anti-convulsant, molluscicidal, oestrogenic and oxytocic properties. This paper provides a review on the morphology, physicochemical and phytochemical constituents, ethnomedicinal and scientifically proven therapeutic activities of *Piper guineense.*

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Humans have since the commencement of civilization, used medicinal plants for their therapeutic value. Nature has always been a source of medicinal agents and therapeutic relief for thousands of years and a large number of modern drugs have been formulated and isolated from natural plant sources. Many of these formulations and isolations are based on reported uses of the plants in traditional medicine. The plant-based, traditional medicine systems continue to play an essential role in health care, with about 80% of the world's inhabitants relying mainly on traditional medicines for their primary health care (Owolabi *et al.* 2007). In Africa, medicinal plants are of great importance to the health of individuals and communities (Edeoga *et al.* 2005). Many of these indigenous medicinal plants were used as spices and food plants. They were sometimes added to foods meant for pregnant and nursing mothers for medicinal purposes (Okwu 2001, 2005). Based on the World Health Organization (WHO) definition (WHO 1977), a medicinal plant is any plant, which one or more of its organ contains substances that can be used for the therapeutic purposes or which, are precursors for the synthesis of useful drugs. This definition helps to distinguish those plants whose therapeutic properties and constituents have been proven and established scientifically and those plants that are regarded as medicinal but which have not yet been subjected to thorough research and investigation. Also, the WHO, (2001) further defines a medicinal plant as herbal preparations produced by subjecting plant materials to extraction, fractionation, purification, concentration or other physical or biological processes which may be produced for immediate consumption or as a basis for herbal products. Medicinal plants have also been defined as plants containing inherent active ingredients used to cure disease or relieve pain (Okigbo *et al.* 2008). It has been widely observed that traditional medicines and medicinal plants are widely used in most developing countries as therapeutic agents for the maintenance of good health (UNESCO 1998). Most modern drugs are still derived from plants and many others, which are synthetic analogues are built on prototype compounds isolated from plants. Interest in medicinal plants as a re-emerging health aid has been fueled by the rising costs of prescription

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drugs in the maintenance of personal health and wellbeing and the bio-prospecting of new plant-derived drugs (Lucy and Edgar 1999). The ongoing growing recognition of medicinal plants is due to several reasons such as reported toxicity of synthetic drugs, escalating faith in herbal medicine and affordability of most medicinal plants (Kala 2005). Furthermore, the rise in the use of medicinal plants in industrialized societies has been traced to the fact that drugs and chemotherapeutics have been extracted and developed from these plants and these plants have also been used for traditional herbal remedies (UNESCO 1998). The medicinal properties of plants could be based on the antioxidant, antimicrobial antipyretic effects of the phytochemicals in them (Adesokan *et al.* 2008). The World Health Organization advocates that medicinal plants would be the best source to obtain a variety of drugs and 11% of the 252 drugs considered as basic and essential by the World Health Organization are exclusively of plant origin and a significant number are synthetic drugs gotten from natural precursors. Some examples of important drugs obtained from plants are digoxin from *Digitalis species* used for treating heart failure, quinine (antimalarials) and quinidine (antiarrhythmic) from *Cinchona species*, vincristine and vinblastine (anticancer agents) from *Catharanthus roseus*, atropine from *Atropa belladonna* and morphine and codeine from *Papaver somniferum* (Rates 2001). It is estimated that 60% of anti-tumour and anti-infectious drugs already on the market or under clinical trial are of natural origin (Rates 2001). Therefore, medicinal plants have been investigated to better understand their properties, safety and efficacy (Nascimento *et al,*. 2000). Medicinal plants contain bioactive compounds that are responsible for their medicinal properties or purposes. These bioactive compounds either act on the systems of animals (including man) that use them and/or on the systems and metabolism of microbes causing the ailment. Bioactive compounds from medicinal plants play a major role in regulating host-microbe interaction most often in favour of the host. This has informed the identification of bioactive compound in plants, their isolation, purification and characterization of active ingredients in crude extracts by various analytical methods. The objectives of the paper are to highlight the morphology, physicochemical and phytochemical constituents, ethnomedicinal uses and scientific-based therapeutic uses of *Piper guineense*.

Morphology and botanical description of Piper guineense: Piper guineense is a vine plant that belongs to the Kingdom Plantae, Division Magnoliophyta, Class Magnoliopsida and Order Piperales, family Piperaceae and genus Piper. It is commonly used as a spice in West Africa and its common English names include West African Black pepper, Benin pepper, Guinea pepper, Ashanti pepper and false cubeb; it is locally known as: "Soro wisa" by the Ghanaians, "masoro" by Hausa speaking tribes, "iyere" by the Yoruba and "uziza" by Igbo speaking tribes of Nigeria (Attah *et al,*. 2012). The plant is a perennial climber and climbs up to 12m high on trees by means of its adventitious rootlets. It has a corky lower stem, simple leaves which are opposite, ovate, acuminate at the apex and cordate at the base with five principal nerves. Its inflorescence is pedicel flower spikes that are about 4-6cm long. The flowers are greenish-yellow and arranged in a spiral on the spine. The fruit is oval, occurs in clusters are small (5mm in diameter) and red-brown when ripe but black when dry (Okwute and Egharevba 2013).

Fig. 1: *Piper guineense* leaves and seeds (Source: Google)

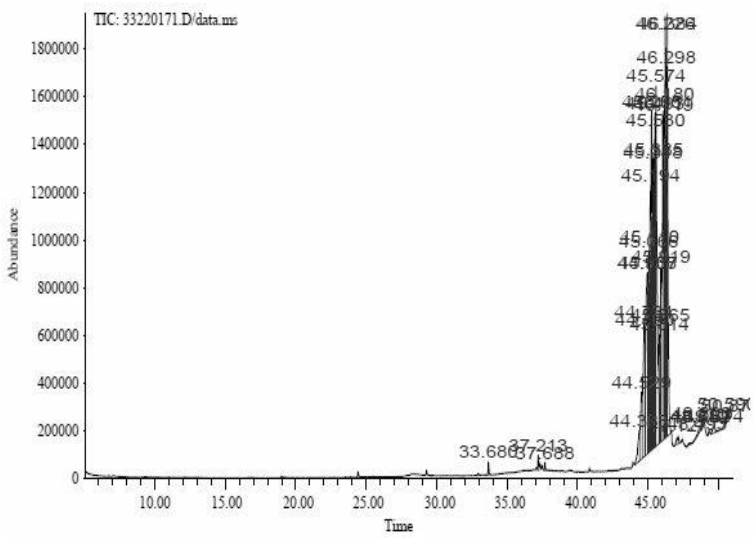
*Origin, habitat and distribution of Piper guineense***:** The plant is widely distributed in the tropical regions of central and western Africa and can be found countries such as Nigeria, Guinea, Ghana and Uganda. It grows in closed forests, forest edges and generally wet places in forests clearings (Burkill *et al.* 1985; Oyemitan 2017).

Ethnomedicinal uses: Piperguineense is used in many folklore medicines and has a number of verified pharmacological activities. Plant parts such as roots, seeds, stem bark and leaves are used in traditional medicine (Busia 2007). In regions of Africa, the fruits and leaves are used as a treatment for vomiting, worms, tonsillitis, rheumatism and stomach aches (Hamill *et al.* 2003; Ndukwe *et al.* 2007). The leaves are also used as an anti-bacterial especially for healing wounds (Martins *et al.* 1998). West African pepper has been indicated to treat different medical conditions such as boils, bronchitis, catarrh, chest pains, coughs, dyspepsia, impotence, insect repellant, lumbago,

rheumatism, uterine fibroid, wounds, stomach aches and discomforts (Ekundayo *et al.* 1988; Busia 2007). The fruits are used also as a tonic, to easy childbirth, for tumours, insecticide and for haemorrhoids (Neuwinger 2000). Traditionally, the herb is prepared in several forms including decoctions, powders or tinctures (Busia 2007). Roots have been also used as an aphrodisiac, treatments for colds, respiratory diseases and caries. It was reported that a mixture of leaves, roots and fruits are incorporated in preparations for the treatment of infectious diseases as an antibacterial agent (Iwu 2014). Leaves are used for abdominal disorders, antihelmintic, chickenpox, bronchitis, cough, headache, lumbar pain, gingivitis, chest complains and diseases, intestinal colic and as antiseptic. In Cameroon, West African pepper leaves are mixed with leaves of *Pentas shimperana* spp. *occidental* to make a yellow soup that is used to treat diarrhea (Focho *et al.* 2009). In Southeast Nigeria, the leaves are used to trigger the contraction of the womb, as a pre-labour stimulation and also to enhance the expulsion of the placenta and other remains from the womb (Udoh 1999; Nwosu 2000). *Piper* species are also used in folk medicine for the treatment of coughs, intestinal diseases, bronchitis, venereal diseases, colds, rheumatism and diarrhoea (Sandberg *et al.* 2005; Iwu 2014).

Physicochemical/ nutritional constituents of Piper guineense: Piper guineense contain nutritional and anti-nutritional factors that confer on it its flavour, aroma and preservative properties. The proximate analysis reveals that the plant contains crude protein, fat, carbohydrate, vitamins and minerals. The moisture content of the leaves has been reported to range from 6.11% - 11.70%, crude protein ranges from 15.17% - 16.67%, crude fibre9.26% - 20.99%, fat content of 1.91% - 2.24%, total ash of 7.73% - 11.98% and a total carbohydrate of 43.86% - 48.21% (Nwankwo *et al.* 2014; Imo *et al.* 2018). The seed has been reported to have a moisture content range of 5.98% - 12.35%, crude protein of 5.86% - 12.99%, crude fibre of 6.95% - 8.79%, fat content of 4.06% - 9.89%, total ash of 4.55% - 6.33% and total carbohydrates of 57.32% - 65.46% (Besong *et al.* 2016; Imo *et al.* 2018). The leaves are rich in vitamins and minerals with a value of 248.37 mg/100 for vitamin C, 32.26 µg/100 for vitamin E, 13.311ppm for magnesium, 47.127ppm for calcium, 0.284ppm for manganese, 0.109ppm for chromium, 0.074ppm for copper, 0.568ppm for zinc, 2.646ppm for iron, 8.570ppm for potassium, 5.270ppm for sodium and 1.290ppm for phosphorus (Nwankwo *et al.* 2014; Imo *et al.* 2018). The seeds are also rich in vitamins and minerals with a value of 7.08 µg/g for vitamin A, 0.029 µg/g for vitamin B_1, 0.16 µg/g for vitamin B_2, 292.62 µg/g for vitamin C, 6.723ppm for magnesium, 11.195ppm for calcium, 0.159ppm for manganese, 0.195ppm for chromium, 0.069ppm for copper, 0.649ppm for zinc, 3.786ppm for iron, 8.870ppm for potassium, 5.370ppm for sodium and 1.560ppm for phosphorus (Besong *et al.* 2016; Imo *et al.* 2018).

Phytochemical constituent of Piper guineense: Plants have an inexhaustible ability to synthesize aromatic substances, most of which are phenols or their oxygen-substituted derivatives (Geissman 1963). Most are secondary metabolites, of which at least 12,000 have been isolated, a number estimated to be less than 10% of the total (Schultes *et al.* 1978). In many cases, these substances serve as plant defence mechanisms against predation by microorganisms, insects, and herbivores due to their biocidal properties. Some metabolites are also involved in defence mechanisms against abiotic stress (e.g., UV-B exposure) and are important in the interaction of plants with other organisms (e.g., the attraction of pollinators) (Rosenthal 1991). Some, such as terpenoids, give plants their odours, others (quinones and tannins) are responsible for plant pigment. Many compounds are responsible for plant flavour (e.g., the terpenoid capsaicin from chilli peppers), and some of the same herbs and spices used by humans to season food yield useful medicinal compounds. It is believed that most of the 100,000 known secondary metabolites are involved in plant chemical defence systems and they appear to have developed as a response of plants to the interactions with predators throughout the millions of years of co-evolution (Wink and Raton 1999). Preliminary phytochemical screening and gas chromatography-mass spectrophotoscopy of the methanol leaf and seed extract of *Piper guineense* revealed the presence of several constituents such as alkaloids, glycosides, tannins, flavonoids, terpenes; sesquiterpenoids and monoterpenoids, saponins and secondary metabolites such as Aromadendrene, Oleic acid, Octadecenoic acid, methyl ester, 9,12-Octadecadienoic acid. Methyl ester (E.E), n-Hexadecanoic acid, 3-[(4-methoxyl-benzoyl)-hydrazono]-N-(1-phenyl-ethyl)-butyramide, 3-[2-(3,4-Dimethoxy-phenyl)-2-oxo-ethyl-3H-[1,3,4]oxadiazol-2-oneamongst other secondary metabolites (Scott *et al.* 2002; Gbadamosi *et al.* 2011; Ejele *et al.* 2012; Udoh *et al.* 2012; Oyemitan *et al.* 2015). These metabolites confer medicinal properties such as antioxidant, anti-inflammatory, anti-tumour, anti-allergic and antiplatelet properties, anti-malarial, antihypertensive, antiarrhythmic and anti-cancer properties (Heikens *et al.* 1995; Adesokan and Akanji 2010; Okoye and Ebeledike 2013).



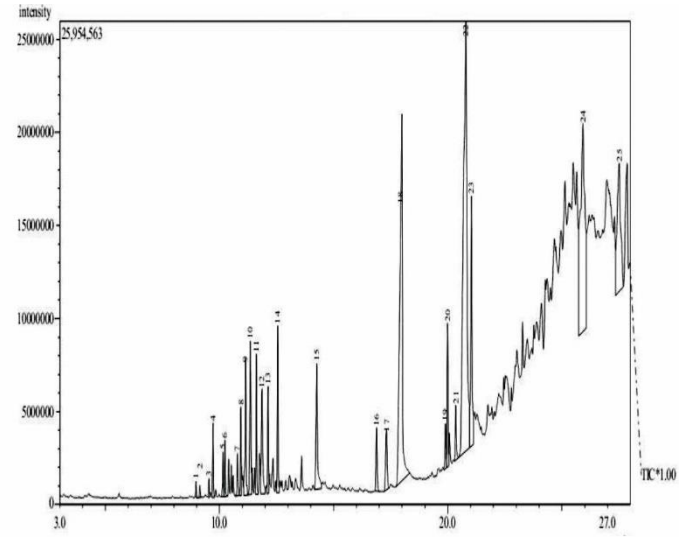
Source: Imo *et al.*, (2018)

Fig. 2: Distribution and concentration of secondary metabolites in the chromatograms of the ethanolic extracts of *Piper guineense* leaves

Table 1: Molecules identified in the chromatograms of ethanolic extracts of *Piper guineense* leaves.

Name of compounds	RI (min)	Area peak (90
Hexadecanoic acid, methyl ester	31680	0.20
Octadecenoic acid methyl estera).	37213	025
Methyl stearate	37688	0.14
1-Naphthalene carboxamide, N-butyl•	44383	1.08
3-Debenzoluranamine	44.731	6.48
Sarcosine, Ninaphthoyll-octyl ester	44.790	122
2-(Octanoyloxy)propane.1,3.thylblsidecanoato	44.938	5.45
1-Naphthaiene carboxamide, N-0-methylpeopyl	45.007	239
Decanoic acid, 1,23-propanetriyi ester	45.066	5.49
2-0XlanoYlowl/fX0Pane-13-dryl bis(decanoale)	45.194	6.71
3iOctanoyloxylpropane-1,2-cltyl bis(decanoate)	45255	12.92
1-Naphthamide.N-bu44•N-txty4	45.348	3.12
•thy141-methylthiazole	45385	181
1-Naphthamide, N-butyl-N-hexyl	45374	9.49
Laurie anhydride	45814	1.41
Fumark acid, hexyl 233-tricttlorophenyl ester	43865	1.14
Fumanc add2-chkrophenyLisohernester	45.919	222
Fumark add, 15-d8lucrophenyl ischexyl ester	46.051	7.62
Fumaric acid, hexyi pent-4-en-2/1 ester	46.119	3.68
Fumark add, 2-fonnytphenyl isohexyl ester	46226	7.88
Fumaric acid, isohexyl 3-nittophenyl ester	46298	5.56
Fumaric acid, 4cyancphenyl isohex-yl ester	46384	1025
5-0,4-Dimethoxypheny0-13-dimethy1-6H-pyrrc4013.4-d1Pyrimidine-2.4-dione	47.127	023
9Octadecencic add (Z)-, 23.drhydroxypropyl ester	48.493	0.05
Oxirane, tetradeefr	48.682	0.19
23•1)ihydroxyprcpyl elaidate	48.751	0.04
6-Octadecenoic add, (Z)-	48800	0.05
9Octadecenoic acid	49.674	033
1-Tricosene	50590	0.30
2-01.PrcOY1)oxybenrslidene acetophenone	50873	0.09

Source: Imo *et al.*, (2018)



Source: (Ojinnaka *et al.* 2016)

Fig. 3: Distribution and concentration of secondary metabolites in the chromatograms of the methanolic extracts of *Piper guineense* seed

Table 2: Molecules identified in the chromatograms of methanolic extracts of *Piper guineense* seeds.

S/N	RETENTION TIME	AREA PEAK	COMPOUND
1	11.858	2.48	Dodecanoic acid
2	14.258	3.26	Tetradecanoic acid
3	17.942	16.28	n-Hexadecanoic acid
4	20.800	26.09	Oleic acid
5	21.042	5.61	Octadecanoic acid
6	16.883	1.28	Pentadecaboic acid, 14-methyl-,methyl ester
7	19.900	0.74	9,12-Octadecadienoic acid. Methyl ester (E.E)
8	19.992	2.26	11-Octadecenoic acid, methyl ester
9	20.350	0.94	Octadecanoic acid, methyl ester
10	11.617	1.90	3,5,7-Cycloheptatriene-1,3-dimethanol
11	8.967	0.17	1,3,6-Hepatriene-2,5,5-trimethyl
12	9.142	0.14	Copaene
13	9.542	0.22	trans-alpha-Bergamotene
14	9.717	1.00	Cyclohexane,1-ethenyl-1-methyi-2,4-bis(1-methylethenyl)
15	10.158	0.62	1,3,6,10-Dodecatraene-3,7,11-trimethyl-(Z.E)
16	10.242	0.72	gamma-Elemene
17	10.783	0.66	Aromadendrene
18	10.933	1.14	Cyclopropane, 1-(2-methylene-3-butenyl)-1-(1-methylenepropyl
19	11.150	2.26	beta-Myrcene
20	11.358	1.43	Cyclohexe,3-(1,5-dimethyl-4-hexenyl)-6-methylene, [S-(R*,S)]
21	17.325	1.59	Cyclohexene, 1-nonyl-
22	12.125	1.48	1-Hydroxyl-1,7-dimethyl-4-isopropyl-2,7-cyclodecadiene
23	12.550	2.36	Pyridine, 3-(5-phenyl-4H-1,2,4-triazol-3-yl
24	25.917	15.94	3-[(4-methoxyl-benzoyl)-hydrazono]-N-(1-phenyl-ethyl)-butyramide
25	27.508	7.88	3-[2-(3,4-Dimethoxy-phenyl)-2-oxo-ethyl-3H-[1,3,4]oxadiazol-2-one

Source: (Ojinnaka *et al.* 2016)

Reported therapeutic activities: Several scientific pieces of research have been carried out to determine the therapeutic and pharmacological potentials of *Piper guineense*.

Anti-oxidant activity: Piper guineense has been reported in several in-vitro and in-vivo studies to possess high reducing power and scavenging abilities and this could be attributed to the presence of polyphenols in the plant (Okon *et al.* 2013; Omodamiro and Ekeleme 2013; Moukette *et al.* 2015; Adeniyi *et al.* 2017). They also inhibited the oxidation of LDL by increasing the time (lag time) for oxidation to take place and as such prevented the collapse of the antioxidant system (Agbor *et al.* 2012).

Anti-microbial activity: The results of a preliminary antimicrobial screening of the methanol extracts of some medicinal plants specifically spices in Ghana reveals that P. *guineense* has antibacterial activity against both Gram +ve and –ve bacteria and also has pronounced antifungal activity (Konning *et al.* 2004). Studies have reported that *Piper guineense* could be an important source of bactericidal compounds against

M. tuberculosis (Tekwu *et al.* 2012). Anyanwu and Nwosu (2014) also studied the antimicrobial activity of aqueous and ethanolic extracts of Piper guineense leaves on some bacterial and fungal organisms and the results showed that the extracts inhibited the growth of all the microbial isolate tested.

Aphrodisiac potentials: Using parameters such as penile erection index, copulatory behaviour and orientation activities towards themselves (genital grooming) and female rats (anogenital sniffing, mounting), aqueous extracts of P. *guineense* modified the sexual behaviour of male rats by increasing sexual arousal (Kamtchouing *et al.* 2002). Memudu *et al.*, (2015) and Ochei *et al.*, (2017) also investigated the aphrodisiac potentials of this plant and obtained results similar to that of Kamtchouing *et al.*, (2002).

Effect on Fertility: Conflicting reports have been generated on the effect of Piper guineense on fertility as it has been reported to improve fertility in male rats by improving sperm motility, sperm functions, testicular steroidogenesis and testicular weight (Memudu *et al.* 2015), however, Umoh *et al.*, (2013) reported that the chronic consumption of Piper guineense seeds caused numerous atrophied and damaged seminiferous tubules distortion, degenerated myoid cells, spermatogenic lining cells degeneration and interstitial fibrosis against the background of connective tissues with marked area of necrosis in the testis. Piper guineense has also been shown to inhibit fertility in female mice and rats as it prevented conception in some studies by inhibiting the maturing of follicles and acted as an abortifacient in other studies (Olatunji-Bello *et al.* 2008; Ekanem *et al.* 2010; Aprioku and Nwogu 2018).

Anti-parasitic potentials: The use of naturally occurring natural plant products (such as oils, powders, extracts) to protect agricultural products against a variety of insect pests is a common practice in many parts of the world. Natural plant products are gaining much attention because of the demand for more natural and organic foods and the use of Piper guineense seeds and leaves extract to protect grains, legumes and other agricultural products against pests and parasites have been well documented.

Piper guineense has been reported to be a very effective grain protecting agent against serious infestation in stored grains as it has been shown to protect grains against *Sitophilus zeamais*, S*itophilus oryzea, Tribolium castaneum, Callosobruchus maculates* and *Oryzaephilus mercator* without affecting seed quality (colour, taste, texture or nutritional composition) (Mbata *et al.* 1995; Okonkwo and Okoye 1996; Lale and Yusuf 2000; Lale and Alaga 2001; Adedire and Akinkurolere 2005; Akumefula *et al.* 2014). Aqueous extracts of Piper guineense has also been reported to protect several vegetable crops such as in brassica crops, aqueous extracts caused a mortality rate of 100% of the larvae of *Plutella xylostella*, in beans (*Vigna unguculata*), it reduced the egg viability of important pests such as *Maruca vitrata* and *Clavigralla tomentosicollis* and in banana and plantain crop, it exhibited repellent properties against the banana weevil (*Cosmopolites sordidus*) (Ekesi 2000; Oparaeke 2007; Ntonifor *et al.* 2010). It has also been reported to be active against *Carassius auratusauratus* and *Pisces cyprinidae* (Goldfish) monogenean parasites (Juliani *et al.* 2013). Pulverized leaves of Piper guineense on smoked catfish during storage inhibited the hatching of eggs and adult emergence of *Dermestes maculatus* (Fasakin and Aberejo 2002).

Anti-inflammatory potentials: Treatment of inflammation with anti-inflammatory agents probably began in ancient Egypt with the use of decoctions or extracts of herbs containing salicylates such as willow leaves or bark when Hippocrates advocated the use of willow bark to relieve the pain of childbirth in 400BC (Brune and Hinz 2004). Piper guineense leaves and seeds have been reported to possess anti-inflammatory potentials both in-vitro and in-vivo (Omodamiro O. D and Jimoh M. A. 2014; Oyemitan *et al.* 2015; Anyasor *et al.* 2018; Akinloye *et al.* 2020) and these anti-inflammatory potentials are attributed to the presence of its phytochemical constituents which have been proven to have anti-inflammatory effects (García-Mediavilla *et al.* 2007; Rathee *et al.* 2009). P. *guineense* happens to be among the top listed plants in an ethnobotanical of plants and plant recipes for the treatment of inflammatory diseases such as rheumatoid- arthritis and asthma (Ogbole *et al.* 2010).
Other therapeutic potentials: Extracts of *P. guineense* have shown a significant molluscicidal effect in *Biomphalaria pfeifferi*, the snail intermediate host of *Schistosoma mansoni*, which causes intestinal schistosomiasis (Ukwandu *et al.* 2011). Following electrical stimulation, the leaf and seed extracts of *Piperguineense* exhibited pharmacological properties, a depolarizing neuromuscular blocking action on the skeletal muscle activity of rats and frogs (Udoh *et al.* 1999). Also, further studies on the uterine muscle of rats indicate the leaf and seed extracts of *Piperguineense* possess oestrogenic and oxytocic properties (Udoh 1999). An aqueous extract of the West African black pepper *Piper guineense* was reported to possess anticonvulsant activity at doses which do not cause significant CNS depression (Abila *et al.* 1993). An ethanolic extract of *P. guineense*

leaves has been reported by Kabiru *et al.*, (2016) to have analgesic, anti-protozoal and anti-plasmodial activities in a dose-dependent manner. Methanolic extracts of *P. guineense* have shown significant hepatoprotective properties against carbon tetrachloride-induced hepatotoxicity (Oyinloye *et al.* 2017).

Conclusion: Piper guineense is an important source of various nutrients and phytochemicals which confer on it several medicinal potentials. Majority of its ethnomedicinal uses have been proven by scientific researches both in-vitro and in-vivo. Also, extensive studies have been carried out to determine the secondary metabolites present in both the seeds and leaves. However, further work needs to be done to determine the specific compounds responsible for each therapeutic activity is has been observed to possess or if a synergy of these compounds is more effective.

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