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Mini-Review

NUTRITIVE AND MEDICINAL VALUE OF *GONGRONEMA LATIFOLIUM* BENTH. (ASCLEPIADACEAE).

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Keywords

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Abstract

Background

The tropical rainforest plant *Gongronema latifolium* Benth. (Asclepiadaceae) is popular for its nutritive and medicinal value across many African nations. It is commonly used as a vegetable in soups, salad or as a spice in other food preparations. The rich phytochemistry of this plant may explain its ethnopharmacological uses in diabetes, malaria, hepatitis, stomachache, anorexia and cough.

Aims

To cover details about the origin, botanical features, ethnopharmacological uses, indigenous rights, phytochemical profile and pharmacological properties of *G. latifolium*.

Methods

PubMed and Google Scholar databases were searched for the name "*Gongronema latifolium*".

Results & Conclusion

This short review tried to establish the ethnomedical importance of *G. latifolium*. It is enriched with varities of flavonoids, saponins, alkaloids and steroidal phytochemicals which exhibit prominent pharmacological actions such as hypoglycaemic, hypolipidemic, cytotoxic, antioxidant, and antimicrobial *in-vitro* and *in-vivo*. One of the bioactive compounds, iloneoside, showed potent antileukemic activity. It should be evaluated against other cancer cell lines. Lastly, further research is required to understand the true potential of this African plant.

Keywords: *Gongronema latifolium*, Ethnopharmacological, Phytochemistry, Ileonoside, cancer

INTRODUCTION

The rich floral diversity of the tropical rainforests is blessed with an enormous amount of natural plant products known for their high dietary benefits and medicinal value (Dalziel et al.1937). One such plant is *Gongronema latifolium* Benth. of the family Asclepiadaceae, formerly known as *Marsdenia latifolia* (Okafor 1975). *G. latifolium* is grown locally in West Africa and addressed with different names such as “Utasi” by the Ibibios, Quas and Efiks ethnic groups; “Utazi” by the Igbos and “Arokeke” by the Yorubas (Hutchinson 1973; Edim et al. 2012). The popularity of *G. latifolium* further extends to Ghana and Senegal where it is known as “Akan-Asante aborode” and “Server gasule” respectively (Hutchinson 1973). This edible, highly nutritious plant has a sharp, bitter and slightly sweet characteristic taste when consumed fresh. Moreover, the plant has green leaves, yellow colored flowers and produces white latex on the incision (Balogun et al. 2016).

The leaves of *G. latifolium* are rich in fats, proteins, vitamins, minerals and many essential amino acids collectively contributing to its high nutritional value (Eleyinmi 2007). “Utazi” is commonly used as a vegetable in soup and salad preparations or as a spice in dried powdered form (Dalziel et al.1937; Okafor 1975 and Morebise et al. 2002). Medicinally, the sliced plant is boiled with lime juice or infused in water for at least three days to produce liquor, which is taken as a purgative against intestinal worms and for colic and stomach pain (Okafor 1975; Onike 2010). The main aim of this mini-review is to provide a detailed description of the origin and geographical distribution, botanical characteristics, ethnopharmacological use, phytochemical profile, and pharmacological properties of *G. latifolium.*

ORIGIN AND GEOGRAPHICAL DISTRIBUTION

G. latifolium plant originates from the West of Africa. It is grown widely throughout the tropical and sub-tropical countries such as Nigeria, Guinea-Bissau, Western Cameroon, Ghana, Senegal, Côte d'Ivoire, and Sierra Leone, and can be propagated easily using seed or stem cuttings. It is also found in America, Northern and Southeastern Asia. *G. latifolium* is present in the wild African forest and is also cultivated in family farms due to its medicinal and nutritional importance (Nelson 1965; Okafor 1975; Agbo et al. 2005; Owu et al. 2012).

BOTANICAL CHARACTERISTICS

G. latifolium is a climbing perennial shrub capable of twining around vertical support, as well it can grow horizontally on the ground up to 5 metres long. The soft woody stem produces adventitious roots in contact with soil (Osuagwu et al. 2013). The stem of the plant is hollow, soft, and hairy in texture and contains white latex which is released on incision or injury. The base of the stem is hard and woody to provide rigid support. It has simple, opposite, decussate, and occasionally whorled green leaves with an entire margin and long petiole (Osuagwu et al. 2013). The leaf blade is broadly ovate to almost circular with a deep cordate base and an acuminate apex (Balogun et al. 2016).

The flowers of *G. latifolium* are small, fragrant, bisexual, star-shaped (actinomorphic) and pale yellow in color with axillary cymes type of inflorescence (Osuagwu et al. 2013). The calyx lobes are elliptical to rounded shaped and hairy at apex. The corolla is long, tubular and campanulate at the apex; the corona has five fleshy and creamy lobes with a brown base (Hutchinson and Dalziel, 1931). Anthers are erect with membranous apical appendages. There are two pollinia per pollinarium; the ovary is superior (Balogun et al. 2016; Osuagwu et al. 2013 and Mosango 2022). In Nigeria, *G. latifolium* plant flowers in July and August annually (Mosango 2022).

The fruit of *G. latifolium* is green initially and turns dark brown to black on maturity. It is a dehiscent seed pod called a follicle which is oblong-lanceolate (Osuagwu et al. 2013). At maturity, the fruit splits open lengthwise releasing flat seeds which are attached to a white silky tuft (pappus) which aids dispersal for pollination (Balogun et al. 2016; Osuagwu et al. 2013). The seeds are small, comma-shaped about 0.5 cm in length (Osuagwu et al. 2013).

The plant, when grown from stem cuttings, matures in 12 months. It usually requires a hot climate of 32º to 37.5º C. Flowers are pollinated by insects due to their attractive color and fragrance. Fruits develop very

slowly and often the mature old fruits meet the new flowers on the plant. The seeds of *G. latifolium* germinate in 1 to 2 weeks at 27º C with a 67% germination rate (Osuagwu et al. 2013).

As per recent anatomical characterisation by Aderiran et al. (2022), *G. latifolium* microscopically shows anomocytic stomata, rosette-shaped calcium oxalate crystal and non-glandular, uniseriate multicellular trichome. Moreover, the stomatal number and index were found to be 8.25 ± 0.52 and 17.60 ± 0.95, respectively.

ETHNOPHARMACOLOGICAL USES

The medicinal properties of all parts of *G. latifolium* have been exploited by different ethnic groups for different ethnomedical indications (Table 1). *G. latifolium* leaves are used traditionally by the Ikales of Ondo State of Nigeria to treat malaria, nausea, and anorexia (Morebise and Fafunso 1998; Morebise et al. 2006). As per the reports by Owu et al. (2012) and Mosango et al. (2022), some communities in West Africa use *G. latifolium* in the treatment of cough, intestinal worms, dysentery, dyspepsia, and malaria. Moreover, the people of Sierra Leone use stems of *G. latifolium* to prepare an infusion or decoction with lime juice which is consumed orally to treat colic and stomach pain (Oliver-Bever 1986). The utility of *G. latifolium* is different in Senegal and Ghana, where the leaves are rubbed topically on body joints of children to help them walk while the boiled extract of the fruit is used as a laxative (Mosango 2022). Edet et al. (2011) describe the use of leaf extract by Efik and Quas tribes belonging to the Cross River state of Nigeria to treat diabetes, malaria, hypertension, and constipation.

Table 1: Ethnomedicinal uses of different parts of *G. latifolium* plant

Part of the Plant	Ethnomedicinal uses	Method of extraction	References
Leaf	Dysentery, antihelmintic, catarrh, congested chest, running nose, cough, viral hepatitis, bilharzias, malaria, hypertension, diabetes, asthma, constipation, nausea, and anorexia	Maceration/Chewing	(Oliver-Bever 1986; Essien et al. 2007; Juliani et al. 2009; Edet et al. 2011; Owu et al. 2012; Chioma 2014; Mosango 2022; Ihesie 2022)
Root	Root Sickle cell anemia, relieve wheezing associated with asthma	Decoction	(Balogun et al. 2016)
Stem	Purgative, hypertension and diabetes	Decoction	(Farombi, 2003)
Fruit	Laxative, stomachache, malaria	Chewing	(Osuagwu et al. 2013)
Latex	Dental caries	Incision & collection	(Osuagwu et al. 2013)

It is widely used for the treatment of cough in Nigeria (Essien et al., 2007). Additionally, fresh leaves are chewed by asthmatic patients to relieve wheezing while oral cold macerated preparation of roots of *G. latifolium* is prescribed for the treatment of asthma (Essien et al. 2007; Mosango 2022). A few communities in Africa also use this plant in the treatment of viral hepatitis, bilharzia, and other microbial infections (Mosango 2022). One of the famous polyherbal preparations for hepatitis and malaria is a decoction of *G. latifolium*, *Mormodica charantia* or *Veronica amygdalina* and *Ocimum gratissimum* given to help cleanse the liver (Ihesie 2022). The extract of *G. latifolium* is consumed widely across Nigeria for the maintenance of blood glucose level (diabetes) and as a cleansing purge by Muslims during Ramadan, respectively (Juliani et al. 2009; Chioma 2014). Fruits of *G. latifolium* are consumed orally with or without seeds for stomachache, malaria and as a laxative (Osuagwu et al. 2013). The leaves are also added to foods such

as soups, porridges, and popular Ibo stews such as the *Nkwobi* (cow leg pepper soup) and *Isi ewu* (Goat head pepper soup). These leaves a bitter taste impart, sweet aroma and stimulate the appetite (Adelaja and Fasidi 2009; Osuagwu et al. 2013).

PHYTOCHEMISTRY OF *GONGRONEMA LATIFOLIUM*

The ethnomedicinal and nutritional value of *G. latifolium* in the African communities attracted many phytochemists to investigate the composition of this herb. There is a wealth of studies on the distribution and occurrence of major classes of secondary metabolites in different parts of the plant summarized in Table 2. The dried leaves of *G. latifolium* contain a high concentration of saponins (18.11%), tannins (16.23%), cyanides (14.32%), flavonoids (11.13%) and phenols (11.11%) with scarce quantity of alkaloids (0.12%) (Offor et al., 2015). Another phytochemical investigation on fresh leaves by Osuagwu et al. (2013) reported high alkaloid content (10%) in comparison to the dried sample. Egbung et al. (2011) also observed higher concentration of flavonoids, alkaloids, hydrogen cyanide and tannins in root extract of *G. latifolium* than stem.

Table 2: Presence of major classes of phytoconstituents in the different plant parts of *G. latifolium*.

	Leaves	Root	Fruit	Stem
Alkaloids	X	X	X	X
Anthraquinones	X			
Cardiac glycosides	X			
Coumarins	X			
Cyanogenic glycoside	X	X	X	X
Essential oil	X			
Fats and oil	X			
Flavonoids	X	X	X	X
Glycosides	X	X		
Iridoids	X			
Organic acids	X			
Oxalate	X			
Resins	X			
Saponins	X	X	X	X
Steroids	X			
Tannins	X	X	X	X
Terpenoids	X			

(Ekundayo 1980; Schneider et al. 1993; Antai et al. 2009; Aka et al., 2011; Egbung et al. 2011; Osuagwu et al. 2013; Enemor et al. 2014; Ezekwe et al. 2014; Offor and Uchenwoke 2015; Gyebi et al. 2017; Ugada and Ibiam 2014 and Beschel et al. 2020).

The active principle(s) of this plant is not fully established although Iwu et al. (1998) reported flavones and sterols as the most likely active constituents. The claim was strengthened when Morebise and Fafunso et al. (1998) examined the antimicrobial activity of a methanolic extract containing saponins and flavonoids. The presence of tannins (polyphenolic compounds) in the leaves was also confirmed by Eze and Nwanguma (2013), who proposed the potential of *G. latifolium* extract as a food preservative. The results by Osuagwu et al. (2013) showed that the fruits of *G. latifolium* are more potent than leaves as believed by the local tribes due to a higher concentration of alkaloids, saponins and phenols. A recent comparative phytochemical analysis showed that *G. latifolium* leaf extract contains higher quantity of alkaloids, glycosides, saponins, tannins and reducing sugars than bitter leaf, African basil and African black pepper, respectively (Mgbeje et al. 2019).

More detailed phytochemical investigations isolated a number of secondary metabolites suumarised in Table 3. Of note, the 80% methanolic extract of *G. latifolium* dried leaves by Gyebi et al. (2017) revealed the presence of iloneoside (Figure 1), a new ditigloylated pregnane glycoside with potent antileukemic activity

Table 3. Isolated and Identified compound in *G. latifolium*.

CLASS Subclass	Compound	Reference
PHENOLICS		
Flavonoids		
	Rutin	Beschel et al. (2020)
	Kaempferol	Beschel et al. (2020)
Coumarins		
	Scopoline	Beschel et al. (2020)
	Esculetin	Beschel et al. (2020)
TERPENES		
	14-Methyl-8-hexadecenol	Ugadu and Ibiam (2014)
	Ester-9-octadecanoic acid	Ugadu and Ibiam (2014)
Iridoids		
	Ebuloside	Beschel et al. (2020)
	Valerenic acid	Beschel et al. (2020)
Triterpenes and Steroids		
	3-β-Acetate lup-20(29)-en-3-ol	Ugadu and Ibiam (2014)
	Acetate-19-cyclolanost-24-en-3-ol	Ugadu and Ibiam (2014)
	Cholestane-3-5,-dichloro-6-nitro-(3β, 5α, 6β)	Morah and Inaku (2021).
	Oleic acid	Ugadu and Ibiam (2014)
	β-Sitosterol	Schneider et al. (1993)
	Lupenyl cinnamate	Schneider et al. (1993)
	Lupenyl acetate	Schneider et al. (1993)
	Lupeol	Schneider et al. (1993)
	Lycopene	Morah and Inaku (2021).
Saponins	Oleananesaponin	Beschel et al. (2020)
	Timosaponin B II	Beschel et al. (2020)
	Metasaponin 1 and 2	Beschel et al. (2020)
Pregnane glycosides	Ileoneoside	Gyebi et al. (2017)
	Marsectohexol	Schneider et al. (1993)
	Ajugoside	Schneider et al. (1993)
	Marsdenin derivative 1	Schneider et al. (1993)
	Marsdenin derivative 2	Schneider et al. (1993)
Cardiac glycosides		
	digoxigenin	Morah and Inaku (2021)
Essential Oil		
	aromadendrene hydrate (9.8%)	Chioma et al. (2014).
	linalool (19.5%)	Chioma et al. (2014).
	(E)-phytol (15.3%)	Chioma et al. (2014).

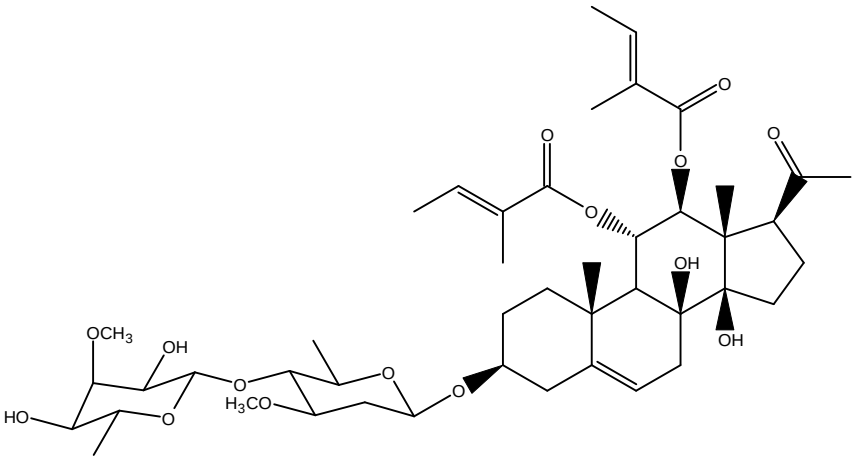

Figure 1: Structure of iloneoside

The investigation on primary metabolites -carried out on leaves by Offor and Uchenwoke (2015) and Mensah et al. (2008) to determine the nutritive composition of *G. latifolium*- showed high amounts of carbohydrates (38.55%) and proteins (33.60%) followed by moisture content (11.13%), ash content (9.11%), crude fibre (4.22%) and fat (3.41%). Eleyinmi (2007) reported almost similar composition along with the presence of significant amounts of leucine, valine, phenylalanine, aspartic acid, glutamic acid and glycine amino acids and minerals such as potassium, iron, magnesium, manganese, sodium, calcium, copper and zinc (Offor and Uchenwoke 2015). Moreover, Enemor et al. (2014) concluded the presence of vitamin A, C, E and B_3 in the leaves of *G. latifolium.*

PHARMACOLOGICAL PROPERTIES OF *GONGRONEMA LATIFOLIUM*

G. latifolium exhibits multiple pharmacological actions due to the presence of a diverse class of phytochemicals. The exact mechanism of action behind each pharmacological response is not known. However, the high ethnopharmacological importance of *G. latifolium* continues to attract researchers for various *in-vitro* and *in-vivo* evaluations of this herb.

Hypoglycemic activity

Akah et al. (2011) reported a significant antidiabetic effect of intraperitoneal administration of the aqueous and methanolic extract of *G. latifolium* in alloxan-induced diabetic rats. However, the potency of methanolic extract was highest with a LD_{50} value of 900mg/kg. Adebajo et al. (2012) investigated *in-vitro* insulin stimulating activity using INS-1 cells and *in-vivo* hypoglycemic activity in glucose-loaded rats of methanolic extract of *G. latifolium* roots and stems. The *in-vitro* and *in-vivo* test results showed significant antihyperglycemic activity similar to glibenclamide drug confirming insulin as an unreported mechanism of action of the plant. An experiment by Ezekwe et al. (2014) strengthens the fact that an intact pancreas is required for the hypoglycemic action of *G. latifolium* which follows similar mechanism of action like sulfonylureas. Studies by Saidu and Okorocha (2013) and Udo et al. (2013) also reported the *in-vivo* hypoglycemic activity of ethanolic and aqueous extracts in rats. The flavonoids of *G. latifolium* are believed to be responsible for the hypoglycemic effect (Ezekwe et al., 2014; Saidu and Okorocha, 2013).

Several *in-vivo* investigations on flavonoid rich *G. latifolium* extract showed management of blood sugar levels via fetuin-A and tumour necrosis factor-alpha, inhibition of inflammatory cytokines with redox imbalance and increasing levels of insulin, respectively (Ajiboye et al. 2022; Ojo et al. 2020 and Oyinloye 2022). However, marsectohexol, a pregnane phytochemical isolated from *G. latifolium* leaf showed much potent in-vitro α-amylase inhibition with IC_{50} = 3.712 µg/mL than reference inhibitor acarbose (IC_{50}= 15.418 µg/mL). As per molecular docking analysis, marsectohexol exhibited the highest binding affinity (-8.8 kcal/mol) to human pancreatic α-amylase than acarbose (-8.1 kcal/mol). Hence, this pregnane active compound may be responsible for antihyperglycaemic effects (Ogunyemi et al., 2020). While another *in-silico* study identified eleven compounds (mainly flavonoids) such as apigenin, baicalin, chicoric acid, genistein, gallocatechin, quercetin, kaempferol, naringenin, luteonin, robinetin, and rosmaric acid which

formed stable complexes with antidiabetic protein targets along with moderate toxicity and drug-drug interaction and good G.I absorption (Ajiboye et al., 2022).

Anticancer activity

Emeka et al. (2015) reported potent *in-vitro* cytotoxic activity of a dichloromethane leaf extract of *G. latifolium* against A-549 human lung carcinoma and MCF-7 breast cancer cell lines with IC_{50} of 9.57µg/mL and 6.51µg/mL, respectively. Moreover, a recent update by Gyebi et al. (2017) discovered iloneoside from methanolic leaf extract of *G. latifolium*, which was found to be a potent inhibitor of human leukaemia cell line *in-vitro*. They further strengthen their claim using molecular docking analysis where iloneoside could accommodate within the hot spots of anti-apoptotic protein Bcl-2. An *in-vivo* investigation of aqueous extract of *G. latifolium* on tumour necrosis factor-α and transforming growth factor-β was carried out in rabbits. The extract exhibited significant inhibition of both cytokines with the greatest inhibition at a dose of 400 mg/kg (Rowaiye et al. 2021).

Antioxidant activity

Experiments on streptozotocin-induced diabetic rats showed a significant increase in superoxide dismutase, glutathione reductase, glutathione peroxidase and glucose-6-phosphate dehydrogenase activities while a decrease in lipid peroxidation, suggesting the antioxidant action of aqueous and ethanolic extract of *G. latifolium*, respectively (Ugochukwu and Babady, 2002) and Ugochukwu et al., 2003). *In-vitro* free radical scavenging activity against 1,1-diphenyl-2-picrylhydrazyl (DPPH) was also reported by Emeka et al. (2015).

A similar result was achieved by Adegbenro et al. (2021) who used a blanched and unblanched *G. latifolium* supplemented diet on fat-induced hyperlipidemic rats. Interestingly, the group receiving blanched *G. latifolium* showed better antioxidant activity than the animals receiving unblanched leaves due to the higher content of flavonoids. Another *in-vivo* investigation on male Wistar rats exhibited the antioxidant potential of ethanolic extract of *G. latifolium* by reducing liver, kidney and heart malondialdehyde levels and increase in antioxidant enzyme levels (Analike et al. 2022). Okeke et al. (2022) reported the radioprotective potential of ethanolic extracts of *G. latifolium* against radiation-induced oxidative stress in Wistar albino rats due to the presence of antioxidants like flavonoids and polyphenols which can scavenge free radicals and regulate endogenous enzymes.

Antimicrobial activity

As per the in-vitro antibacterial evaluation carried out by Eleyinmi (2007), the methanolic extract showed activity against *S. enteritidis*, *S. cholerasius* ser *typhimurium, L. monocytogenes* and *P. aeruginosa* while the aqueous extracts were active only against *E. coli* and *P. aeruginosa.* According to Nwinyi et al. (2008) the ethanolic leaf extract was nearly 4 times more potent than the aqueous leaf extract of *G. latifolium* against *E. coli* and *S. aureus.* Dose-dependent inhibition of *Staphylococcus aureus, S. pneumonia, E. coli, P. mirabilis* and *P. aeruginosa* by ethanolic leaf extract was also reported by Omodamiro and Ekeleme (2013).

However, this disagrees with recent works which suggest poor activity against *S. aureus* and *E. coli* and no statistical difference in antibacterial activity between aqueous and ethanolic extracts, respectively (Akani et al. 2020; Ndubueze et al. 2020). An *in-vivo* study exploring the anti-malarial activity of *G. latifolium* extract against *P. berghei* infected mice showed chemo-suppressive and prophylactic effects, but the standard drug chloroquine performed way better (Orumwensodia and Uadia 2022). Adenayo et al. (2022) investigated the anti-plasmodial activity of pregnane glycosides previously isolated from *G. latifolium*. Iloneoside showed significant activity *in-vitro* and was able to potentiate the activity of chloroquine by 3200% against drug resistant strain of *P. falciparum* at dose higher than 0.625 µg/mL. As per *in-silico* analysis, iloneoside bonded with similar binding pattern and tendency to the selected P*f* proteins as chloroquine, suggesting similar mechanism of action.

Anti-inflammatory activity

Morebise et al. (2002) tested the *in-vivo* anti-inflammatory activity of aqueous extract of *G. latifolium* in rats. The extract successfully inhibited carrageenan-induced rat paw oedema, carrageen-induced leucocyte migration in the animal and dye leakage induced by intraperitoneal injection of acetic acid. Another *in-vivo* study of methanolic leaf extract by Morebise et al. (2005) reported the inhibition of nystatin-induced rat paw oedema and stabilization of erythrocyte membrane subjected to lysis by heat and hypotonic solution.

Immunomodulatory effect

The *in-vivo* immunostimulatory effect of the methanolic extract in Wistar albino rats was reported by Simeon et al. (2014). They observed a significant increase in interferon-γ, delayed type hypersensitivity, primary and secondary antibody titer along with non-significant increase in tumour necrosis factor-α and interleukin-2. As per the *in-vivo* experiment by Akpan and Effiong (2015), administration of *G. latifolium* leaves in streptozotocin-induced diabetic rats resulted in a decrease in the level of CD_4^+ cell count, WBC, platelets, monocyte, neutrophil and a significant increase in RBC, hemoglobin and lymphocyte count as compared to the diabetic control.

Hypolipidemic activity

The ethanolic root extract, when administered in diabetic rats, showed a reduction in serum glucose, triacylglycerol, total cholesterol, and very low-density lipoprotein with an increase in high-density lipoprotein. However, no significant change was seen in serum low-density lipoprotein (Robert et al. 2013). This is in agreement with two recent in-vivo investigations in rats, which recorded an improvement in lipid profile and increase in activity of antioxidant enzymes reducing metabolic and cardiovascular risks (Uchendu et al. 2021; Beschel et al. 2019). Furthermore, Adebayo et al. (2022) investigated the cardiovascular effects of marsdenin derivative isolated from *G. latifolium* in albino mice. The results revealed hypolipidemic effects along with reduction in heart and plasma creatine kinase activities and heart Calcium-Magnesium-ATPase activity. Hence, marsdenin derivative may not predispose subjects to atherosclerosis but may cause problems due to interference with cardiac muscle contraction and relaxation at high doses.

Haematological effects

Aqueous leaf extract given to female albino rats showed a decrease in mean haemoglobin concentration, packed cell volume, platelet count, total white blood cell count, mean bleeding and clotting time (Oguwike et al. 2013).

Renal effects

Onuoha and Chinaka (2013) and Ndodim et al. (2014) reported a reduction in urea and creatinine levels in rats induced with carbon tetrachloride and chloroquine respectively, on the administration of aqueous leaf extract of *G. latifolium*. However, this is in disagreement with a recent *in-vivo* study in rats where ethanolic extract recorded an increase in serum urea and a decrease in serum triglycerides and creatinine levels suggesting mild renal disturbances/injury (Sulaiman et al. 2022).

Effects on the nervous system

In-vitro analysis on alkaloids isolated from *G. latifolium* revealed concentration-dependent inhibition of acetylcholinesterase, butyrylcholinesterase and monoamine oxidase with IC_{50} 87.39 µg/ml, 118.65 µg/ml and 61.37 µg/ml respectively. Moreover, GC-FID analysis showed the abundance of choline in the extract (Nwanna et al. 2019). Interestingly, an *in-silico* analysis of flavonoids isolated from *G. latifolium* showed inhibition of leucine-rich repeat kinase 2, glycogen kinase 3β and mitogen-activated protein kinase 14 with moderate pIC_{50} values. All three protein kinases are associated with the pathogenesis of Alzheimer's and Parkinson's disease. Additionally, flavonoids such as catechin, gallocatechin, butein and isorhamnetin exhibited drug-likeness characteristics with low drug-drug interaction and high GI absorption (Oyinloye et al. 2021). An *in-vivo* experiment in Swiss albino mice by Ujong et al. (2022) reported that ethanolic extract of *G. latifolium* improved visio-spatial learning and cognitive memory in mice.

Effects on the reproductive system

An animal study of the ethanolic extract of *G. latifolium* on male Wistar rats exhibited an increase in serum concentration of testosterone, follicle stimulating hormone and luteinizing hormone at doses 100 mg/kg and 200 mg/kg body weight whereas, decreased in progesterone levels. Surprisingly, at a higher dose (200 mg/kg body weight) slightly greater progesterone levels (15 mg/dl) were recorded as compared to the level 13 mg/dl at a dosage of 100 mg/kg body weight, while the normal group showed 19 mg/dl. Moreover, the authors did not attempt to discuss this (Dasofunjo et al. 2020).

Another *in-vivo* investigation on male wistar albino rat showed significant increase in serum concentrations of male reproductive hormones and aphrodisiac effects (Effiong et al. 2022). Effects of methanolic extract of *G. latifolium* on lactating Wistar albino rats showed a dose-dependent increase in serum prolactin level

and milk production whereas, oxytocin levels remain unchanged (Ogbonna et al. 2022). This may be due to the presence of saponins and flavonoids which have phytoestrogenic effects (Wina et al. 2005; Das et al. 2012; Di Gioia and Petropoulos 2019).

Hepatoprotective activity

Omodale et al. (2017) investigated the hepatoprotective potential of aqueous root extract of *Gongronema latifolium* against paracetamol-induced hepatotoxicity in adult albino rats. The results of this study showed a dose-dependent decrease in the serum liver enzymes. However, at high doses and prolonged usage, alcoholic extract of *G. latifolium* may cause hepatotoxicity as per two in-vivo studies (Al-Hindi et al. 2019; Omodamiro et al. 2021). Moreover, aqueous leaf extract in lactating dams exhibited increase in liver and pancreatic weight index with slight inflammation cells but no hepatotoxicity (Katchy et al. 2020). Lastly, another in-vivo experiment confirms hepatoprotective effect of *G. latifolium* by decreasing activities of alanine aminotransferase, aspartate aminotransferase, creatine kinase and lactate dehydrogenase enzymes along with absence of pathological lesion at 15% inclusion of the herb (Adeyemi-Doro et al. 2021).

CONCLUSION

The research studies highlighted in this essay tried to demonstratethe ethnomedical importance of *G. latifolium*. The plant, *G. latifolium* truly requires further research on isolation and characterization of the pharmacologically active compound(s), along with a complete understanding of the mechanism of action at the molecular level, sustainability, variation among botanical species and safety profile in man It would be interesting to find out is iloneoside and other pregnane glycosides fulfils their anticancer potential in future investigations.

Conflicts of Interest

The authors declare no personal or financial conflict of interest related to this work.

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