



The Phytochemistry, Ethnomedicinal and Pharmacology Uses of *Justicia carnea* Lindl Used in Traditional medicine in Nigeria- A Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aim: *Justicia carnea* has been used in traditional medicine in Nigeria in the treatment and management of various diseases which include inflammation, cancer, malaria, sickle cell disease, gastrointestinal infections, anemia, HIV, diabetes, diarrhea, typhoid, liver diseases, hepatitis, cough, etc. This review is aimed at checking the relationship between the ethnomedicinal uses, the phytochemistry and pharmacological activities of *Justicia carnea* so as to unveil opportunities for future research.

Methods: A search for relevant information on *Justicia carnea* was performed on scientific databases (Scopus, Google Scholar, Pubmed, SciFinder, PubChem, Web of Science, and other web sources such as The Plant List, Kew Botanical Garden, and PROTA) and books.

Results: Extracts of the *J. carnea* have been reported to have been used in various traditional medicines in treating various diseases. Preliminary phytochemical analyses of extracts of the plant revealed the presence of various secondary metabolites such as flavonoids, tannins, saponins, alkaloids, phenols, terpenoids. The presence of these metabolites was responsible for the anti-anemic, anti-cancer, anti-diabetic, and antioxidant properties shown by the plant. The aqueous leaf

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extract of *J. carnea* having high phenolic and flavonoids contents was able to show antioxidant capacity and also inhibited α -amylase activity (IC₅₀, 671.43±1.88 µg/mL). Also, both methanol and ethanol leaf extracts showed significant *in vivo* reduction in blood glucose levels. The ethanol leaf extract at 500 mg/kg and 1000 mg/kg showed a significant increase in Packed Cell Volume, Red blood cell (RBC), Hemoglobin (Hb) and white blood cell (WBC) counts. Aqueous and ethanol leaf extracts of *J. carnea* have been reported to be relatively safe, though the methanol leaf extract was said to distort both the kidney and liver by showing infiltration of interstitial tissue with inflammatory cells and the portal vein were congested with blood cells, microvesicular steatosis and cytoplasm were replaced with fatty cells with the nuclei being centrally placed respectively.

Conclusion: *J. carnea* is a potential anti anemic, antioxidant, antidiabetic, hepatoprotective agent, which confirmed its uses in treating hepatitis, sickle cell disease, diabetes etc. Further research on isolation and determination of the activities of the metabolites *in vivo and in vitro*, establishing their mechanisms of action is necessary.

Keywords: *Justicia carnea*; phytochemistry; ethnomedicinal; metabolites; anti-sickling; antidiabetic; antioxidant; hepatoprotective.

ABBREVIATIONS

WBC = White blood cell
 RBC = Red blood cell
 Hb = Hemoglobin
 PVC = Packed Cell Volume
 DPPH = Diphenylpicrylhydrazyl
 EC₅₀ = Effective concentration at 50%
 LD₅₀ = Lethal dosage 50
 AST = Aspartate transaminase
 ALT = Alanine transaminase
 ALP = Alkaline phosphatase
 LDL = Low density lipoprotein
 HDL = High density lipoprotein
 FRAP = Ferric reducing antioxidant power
 SOD = Superoxide dismutase
 CAT = Catalase
 GSH = Glutathione
 MDA = Malondialdehyde

1. INTRODUCTION

Plants have been used in traditional medicines since time immemorial. It has been estimated that 70-80% of world population relies on herbal medicine for their primary healthcare needs [1]. Medicinal plants such as *Justicia carnea* have been used against various diseases for thousands of years, and 80% of the worldwide population still depends on herbal medicines [2-3]. *Justicia* is the largest genus of Acanthaceae family, having about six hundred species [4-5]. *Justicia* is a creeping annual or perennial herb growing up to 1.5 or 2 metres tall. This is one of the most appreciated of the sweet green vegetables of Africa. It is cultivated in home gardens in West and Central Africa, especially in Nigeria, Guinea, Ghana, Togo, Benin, Sierra Leone, Cameroon and DR Congo [6-7]. Many

species of *Justicia* have been used traditionally in treating respiratory tract infection, inflammation, gastrointestinal disorders [8-12], fever, diabetes [8,11], liver diseases, diarrhea [8,11,12], arthritis, rheumatism [5,8,10,11,12], anaemia [13], cancer, HIV and diabetes [5]. In DR Congo, species of *Justicia* have also been reported to be used in treating various illnesses such as cancers, arthritis, eye disease, diabetes, gastrointestinal disease, HIV, fever, vaginal discharge, epilepsy, dyspepsia, mental disorder, headache, inflammation [4,14]. They are also used as analgesics, sedatives, hallucinogens, depressors and somniferous agent [4,5,10,15]. Also many metabolites have been reported present in the genus *Justicia*, which include flavonoids, alkaloids, diterpenoids, vitamins, triterpenoids, iridoids, steroids, coumarin, lignans and triterpenoidal glycosides [16]. Lignans have been reported to be major components of most extracts of species of *Justicia* and have shown some pharmacological actions such as anti-inflammatory, anti-tumoral, anti-platelet aggregation, hepatoprotective, male contraceptive, hallucinogenic, superoxide anion radical scavenging, nephroprotective, haematinic, antimicrobial, anti sickling, immunomodulatory, antihypertensive and antiviral activities [6,11,12,14,17].

Though there are many reported ethnomedicinal uses of the *J. carnea*, there are not many scientific researches to support those claims.

2. CLASSIFICATION

The genus *Justicia* named after Scottish Gardner James Justice in the 18th century, established by Linnaeus in 1753 [10,18-20] are scandent or

erect annual or perennial subshrubs or herbs. The leaves are petiolate with an entire leaf margin. They are known by their spicate inflorescences which could be compound or simple, two stamens with asymmetrical anthers each, 3 lobed anterior lip, 2 lobed posterior lip, bilabial corolla, four seeded capsules and a basal sterile portion [4-5,20]. *Justicia*, a tribe of Ruellieae and subtribe of Justiciinae is the largest genus of the Acanthaceae family, having about 600 species [4-5,20], contrarily to the seven hundred species reported by House, 2015 and Daniel, 2011 [20-21]. *Justicia* possess 695 species with scientific names, out of which 376 are accepted species names and 32 scientific names of intraspecific. *Justicia* species are reported to occur in tropical to warm temperate regions of the America, India, Indonesia, Southeast Asia, Malaysia, Pakistan and Africa [14]. *Justicia* comprises of 700 species and is predominantly pantropical, while many still occur in subtropical and temperate regions [21].

Justicia carnea is an evergreen erect perennial shrub or herb that grows up to 4 feet, it has petiolate leaves with an entire leaf margin. It is known for its bilabial corolla, 2-lobed posterior lip, 3-lobed anterior lip, two stamens, four seeded capsules and pinkish flowers. The plant grows well in loamy soil with dappled sunlight [22].

2.1 Ethnomedicinal Uses

Justicia carnea commonly known in Nigeria as: "blood root" [23], "hospital too far" [18], "ogwu obara" in Igbo [11,24], 'Oso-afia in Ogba/Egbema/Ndoni [23]. In Cameroon as: "Ewolamajia" in Bakweri [25], in Ghana as: "Ntumunum" in Bosomtwe and Sekyere East. Also known in Brazil and South America as: "Jacobinia", "Pink jacobinia" Cardinal's guard", "Brazilian plume", "Pine-bur begonia" and flamingo flower" [26]. In Nigeria, the root is used in treating menstrual pain [23], the decoction of the leaf as a blood supplement and the management of anemia [8,11,18,19,26-28]. The plant has also been used as hallucinogens, sedatives [22], ornamental [26], and in treating HIV, cancer, diabetes, whooping cough, epilepsy, bronchitis cold [22], respiratory tract diseases, gastrointestinal infections, inflammation [19,22,26], sickle cell disease, hepatitis, typhoid, [18], malaria [18-19,29], rheumatism, liver disease, arthritis and diarrhea [19]. The plant has also exhibited hypocholesterolemic, anti-microbial, anti-cancer,

[26], antioxidant [19,26], anti-tumor, anti-allergy, anti-inflammatory, and analgesic properties [19].

2.2 Chemical Constituents

The preliminary phytochemical analysis of aqueous leaf extract of *J. carnea* revealed that terpenoids, tannins, alkaloids, carbohydrates, flavonoids, saponins, phenols, reduced sugar, and glycosides. Phenols and flavonoids were found in high concentrations which could be responsible for the anticancer and antioxidant activities exhibited by the plant [26]. The presence of terpenoids and carbohydrates in the aqueous leaf extract of the plant was against the findings of Anigboro et al. [24], who reported their absence in aqueous leaf extract of the same plant. Also present in the aqueous leaf extract are vitamin A, B1, B12, B6, B9, B2, C and E containing the highest concentration of vitamin C, and high concentration of iron and calcium while magnesium, zinc and copper were present in low concentrations [26]. Similarly, Onyeabo et al. [11] in their work had already reported that phenols, alkaloids, tannins, flavonoids, terpenoids, saponins and steroids were present in the ethanol leaf extract of *J. carnea*, with high percentage of terpenoids, alkaloids and saponins. Also present in the extracts were vitamins C, E and A. Proximate analysis of the extract revealed the presence of high percentage of carbohydrate and protein, also present were moisture, crude fibre, ash and low percentage of fat. Igbinaduwa et al. [27] in their work also reported the presence of alkaloids, flavonoids, tannins, phenols and saponins in the methanol leaf extract of *J. carnea*. The result of proximate analysis revealed carbohydrates (30%), protein (24.31%), crude fibre (18.71%), Fe, Zn, K, Ca, and Pb were also found in the extract. In another research, flavonoids, alkaloids, phenols, tannins, carbohydrates, glycosides, gum, protein, fixed oils and fat were reported to be present in methanol leaf extract of *J. carnea*. While alkaloids, fixed oils were absent in the root extract of *J. carnea*, sterols, gum was reported in both stem and root extracts [30]. The absence of saponins in the methanol leaf extract of *J. carnea* was against the report of Igbinaduwa et al. [27] who in their work reported the presence of saponins. The presence of vitamin B12, vitamin C, Ca, Zinc, tannins and iron found in various extracts of *J. carnea* lends credence to the ethnomedicinal use of the plant in treating anaemia [31]. The presence of vitamins A, C and E which are antioxidants in the extract was attributed to a reduction in the oxidative stress

caused by the phenylhydrazine and thereby reversing the anemic condition in the rats. Saponins and alkaloids have been reported to have anti anemic potentials. Phenolics were found in all the extracts of *J. carnea*, with the largest quantity found in the leaf, the phenolics have been attributed to the antioxidant property of leaf of the plant. The use of *J. carnea* in the treatment of cancer, anaemia and diabetes could be attributed to the presence of alkaloids, saponins, flavonoids and phenols. In another work, the ethanol leaf extract of *J. carnea* was said to have contained six compounds- 2,2,3,3,4,4,5,5,5- Nonafluoropentanoic acid methyl ester, Palmitic acid, Phosphorodithioic acid, Diphenyl, Isonicotinic acid N-oxide, 7H-Purine, 7-benzyl-2,6-dichloro- and 9,12,15-octadecatrien-1-ol using GC-MS [10]. While Anigboro et al, [24] in their work identified 2-cyclopenten-1-one, 3-ethyl-2-hydroxy-, 2-methoxy-4-vinylphenol, Formic acid, 2,6-dimethoxyphenyl ester, 9-undecen-2-one, 6,10-dimethyl-, oleic acid, 5-cyclohexadecen-1-one, 2-heptadecenal, 7,11-Hexadecadienal in aqueous leaf extract using also GC-MS. These compounds were similar to compounds in the NIST library software

2.3 Pharmacological Uses

2.3.1 Anti-diabetic / hypoglycemic activity

The fasting blood sugar, the liver, and kidney function tests, as well as the lipid profile of ethanol leaf extract of *J. carnea* on alloxan-induced albino rats, were analyzed, the results revealed that the extract caused an *in vivo* reduction of blood glucose level at both 100mg/kg and 200mg/kg. It was also reported that there was a significant reduction ($p < 0.05$) of serum levels of ALT, creatinine, and AST, while there was a significant increase in serum levels of total protein, urea, and ALP, and a non-significant decrease in serum levels of chloride, sodium, bicarbonate, and potassium. At 200mg/kg, serum levels of TC, TG, LDL, and VLDL were also significantly reduced [8]. Similarly, the methanol leaf extract of *J. carnea* also showed a significant *in vivo* reduction in blood glucose levels in alloxan-induced rats treated with 200, 500 and 1000mg/kg body weight of *J. carnea* [32]. Also, the antidiabetic potential of aqueous leaf extract of *Justicia carnea* was investigated using α -amylase inhibition model from the linear plot of extract concentration ($\mu\text{g/mL}$) against percentage α -amylase inhibition, the extract significantly

($p < 0.05$) decreased α -amylase activity with increasing concentrations of the extract [24]. The results confirmed the folkloric use of *J. carnea* in treating diabetes [22].

2.4 Antioxidant Activity

Meanwhile, the antioxidant activity of methanol leaf extract of *J. carnea* on CCl_4 - induced oxidative stress in female albino rats showed that the extract at 200, 500 and 100mg/kg bw significantly increased the concentrations of CAT, GSH and SOD, but also decreased the serum MDA at the same concentrations [12]. Since reactive oxygen could be produced by CCl_4 , which could also lead to lipid peroxidation, the concentration of MDA which was a secondary product of such peroxidation was increased by CCl_4 which was due to increased lipid peroxidation. Aqueous leaf extract of the plant also exhibited high scavenging activities against DPPH and nitric oxide radicals, with significantly increased ($p < 0.05$) ferric reducing antioxidant power (FRAP) and total antioxidant capacity (TAOC) values in a dose-dependent manner [24]. Phenols and flavonoids present in the leaf of *J. carnea* were attributed to the antioxidant property of the extract [12]. Similarly, the *in vitro* antioxidant activity of ethanol leaf extract of *J. carnea* using DPPH scavenging assay, total phenols, total ascorbic acid, total β -carotene, total lycopene, total flavonoids assays, showed that the extract showed both scavenging and reducing power to both DPPH and Ferric ion with EC_{50} of 200 $\mu\text{g/mL}$ and 40 $\mu\text{g/mL}$ respectively. The extract was also contained high concentration of the content of, total phenols, total ascorbic acid, total β -carotene, total lycopene, total flavonoids [18], which justified its antioxidant property. Flavonoids are potent antioxidants, and act as free radical scavengers so can exhibit antioxidant activity [33]. Phenolic compounds have been shown to exhibit antioxidant properties [34-36], polyphenols are antioxidants that induce cytoprotective proteins which act in a variety of antioxidant actions from the reduction of oxidants to the production of endogenous direct antioxidants [37], flavonoids prevent diseases related to oxidative stress in living systems [38], terpenoids exhibit antioxidant activity in their interactions with free radicals [39], flavonoids are strong polyphenolic antioxidants which reduce oxidative stress by acting as free radical scavengers, they inhibit the aggregation of plasma platelet which participate in the pathogenesis of the cardiovascular disease [26,40]. So the use of the plant in the treatment

of high blood pressure is attributed to the presence of flavonoids. Similarly, terpenoids such as lycopene and β - carotenes containing conjugated double bonds have been reported to have both singlet oxygen and free radical quenching abilities, protect cellular components from oxidative damage, and inhibit lipid peroxidation by scavenging peroxy radicals produced by the peroxidation reaction, and therefore are strong antioxidants [41-52].

2.5 Hepatoprotective Activity

Anti hepatotoxicity assay of methanol leaf extract of *J. carnea* was conducted on CCl₄-induced albino rats. The result indicated that at 200, 500 and 1000mg/kg, the leaf extract showed a significant decrease ($p < 0.05$) in bilirubin, ALP, AST and ALT content. It was reported that there was the better liver framework and in better necrosis of the tested liver from a histopathological survey by the extract, when compared with the liver from CCl₄- induced rat only, showing that the extract exhibited hepatoprotective activity [19]. The result lends credence to the use of the plant in treating hepatitis [18].

2.6 Anti Hyperlipidaemic Activity

The ethanol leaf extract of *J. carnea* was reported to have shown anti hyperlipidaemic activity through significantly reducing serum cholesterol, LDL, VLDL, triacylglycerol concentrations and increasing the HDL concentration in phenylhydrazine –induced anemic rats with respect to anemic and non anemic rats. The decrease in the serum cholesterol concentration was attributed to the presence of steroids- which was said to contain phytosterols that could reduce plasma cholesterol concentration and saponins that has been said to be anti hyperlipidaemic by reducing the uptake of cholesterol in the gut in the extract [11]. Methanol leaf extract of *J. carnea* also showed anti hyperlipidaemic by significantly reducing VLDL, LDL, serum cholesterol and triacylglycerol and increased the HDL [32], which is in line with the report of Onyeabo et al, [11] on ethanol leaf extract. The reduction of triacylglycerol was also attributed to the presence of some metabolites such as saponins in the extract. An increase in HDL and decrease in the LDL by extract would in general reduce cholesterol and reduce the risk of heart attack, cardiovascular diseases, atherosclerosis and stroke [11].

2.7 Anti-Anaemic and Anti-sickling Activities

In a work, the hematological assay of ethanol leaf extract of *J. carnea* on phenylhydrazine-induced anemic rats showed that the extract at 500mg/kg and 1000mg/kg exhibited a significant increase in Packed Cell Volume, RBC, Hb, and WBC counts. The increase in RBC was attributed to the presence of some metabolites such as alkaloids, saponins, and flavonoids. The increase in the hematological parameters reversed the anemic condition of phenylhydrazine-induced anemic rats from 14-day treatment [11]. Confirming the report of Onyeabo et al, Igbinaduwa et al, [27] revealed that methanol leaf extract of *J. carnea* also reversed the phenylhydrazine-induced anaemia by increasing the reduced RBC, WBC, Hb, PCV, platelet, monocytes, lymphocytes, and neutrophil levels 100-1000mg/kg body weight of the extract. The level of monocytes decreased on the administration of higher concentrations of the extract and was attributed to the absence of anaemia at those concentrations. The increase in the RBC and Hb was understandably due to the high concentration of iron present in the extract. In line with their findings, Nji et al, [25] in their work confirmed the haematinic activity of *J. carnea*, when they reported that the leaf powder of the plant also significantly increased the same parameters including platelet counts. Saponins and alkaloids found in the extract have been reported to also have an anti-anemic activity which could have caused the increment in the levels of the hematological parameters. These works validated the use of *J. carnea* as blood tonic and in treating anaemia [8,12,18,26].

2.8 Toxicity Studies

Generally, the leaf extract of *J. carnea* was reported to be nontoxic and could be used in traditional medicine [11], which is in line with the findings of Akintimehin et al, [28] that the LD₅₀ of ethanol extract of *J. carnea* was greater than 5000 mg/kg body weight. Higher doses (> 500 mg/kg) of extract significantly ($p < 0.05$) increased RBC, hemoglobin, and platelet compared to the control. Liver superoxide dismutase (SOD) activity was significantly ($p < 0.05$) increased at 1200 mg/kg while other tested doses caused no detrimental effect on glutathione, catalase, SOD and malondialdehyde level in the liver and kidney. Histopathological examination of liver and kidney showed mild to severe pathological lesion in a dose-dependent

manner. They concluded that the extract of *J. carnea* is relatively safe, could be beneficial in alleviating hematology-related abnormalities without causing adverse effects on endogenous antioxidant system. Contrarily to the report of Onyeabo et al. [11] and Akintimehin et al [28], the photomicrographs of processed kidney liver tissues showed that kidney tissue from animals treated with 100 and 200mg/kg of methanol leaf extract of *J. carnea* showed lobulation of glomerular tuft and collapsed tubules, and there was the infiltration of interstitial tissue with inflammatory cells which indicated distorted kidney, while in the liver, the portal vein was congested with blood cells, micro vesicular steatosis and cytoplasm were replaced with fatty cells, and the nuclei were centrally placed, which indicated that there was a distortion in the liver. The toxicity of the extract could be attributed to the presence of Pb, which had been shown to cause histological changes in the kidney and hydropic degeneration in the liver of dog, diminution and even depletion of total proteins in the kidney and liver of *Oreochromis mossambicus*, caused dramatic changes in the subcellular distribution and expression of rat kidney glutathione S-transferase, caused vacuolation, fatty degeneration, congestion within central veins, hemorrhage and infiltration of inflammatory cells in the liver of rats [53-56]. The results of the toxicity study of methanol leaf extract of *J. carnea* on the liver and kidney would have called to question the safety of decoctions of the leaf used in traditional medicine, but the result of the toxicity study of aqueous leaf extract gave credence to the safety of the decoctions, since most of the decoctions are prepared with water.

3. CONCLUSION

J. carnea is a potential anti anemic, antioxidant, antidiabetic, hepatoprotective agent, which confirmed its uses in treating hepatitis, sickle cell disease, diabetes, etc. Further research on isolation and determination of the activities of the metabolites *in vivo* and *in vitro*, establishing their mechanisms of action is necessary.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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