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REVIEW ARTICLE

Pharmacotherapeutic Properties of *Telfairia occidentalis* Hook F.: A Systematic Review

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ABSTRACT

Globally, there has been a growing interest in medicinal plants by researchers. *Telfairia occidentalis* Hook F. (Fluted pumpkin) is cucurbitaceous vegetable grown in West Africa, particularly in Nigeria for its leaves and seeds. The curative properties of fluted pumpkin are popular in Nigerian folklore medicine, and several investigators have validated these therapeutic effects using animal models. The aim of this work therefore, was to review publicly available literature on the pharmacotherapeutic activities of *T. occidentalis*. Searches were performed on PubMed, Scopus, ScienceDirect, and Google Scholar for related studies, with search dates set between 1990 and 2018. A total of 499 articles were retrieved and analyzed, with 38 studies ultimately retained. Studies contained in this review were carried out in Nigeria, across different locations. 13 categories of pharmacological activities for fluted pumpkin were documented after analyzing full texts of the articles retained. *T. occidentalis* offers myriad of healing properties that can be explored by pharmaceutical industries. As the search for potent drugs from botanical sources continues, there is need for future investigations to isolate and characterize pharmacologically active agents that confer medicinal properties on fluted pumpkin, as well as elucidate the structures of these agents and pathways by which they exert their healing properties.

Key words: Fluted pumpkin, medicinal plant, pharmacological, *Telfairia occidentalis*, therapeutic

INTRODUCTION

Plants are utilized by man as a source of food, medicine, energy, shelter, fodder and other forestry products.[1,2] They are being studied and engineered particularly to produce recombinant pharmaceuticals, genetically modified foods, industrial proteins, and other secondary metabolites.[3] Many pharmaceutical products of modern times can be attributed to insights derived from local knowledge and utilization of medicinal plant resources.[4] The use of botanicals as remedies for the treatment of ailments is popular in sub-Saharan Africa, where traditional medicine is flourishing.[5] In Nigeria, over 50,000 species of plant have been reported to be used for medicinal purposes.[6]

Telfairia occidentalis Hook F. (fluted pumpkin) is a member of the *Cucurbitaceae* family. It is native to West Africa and predominantly grown in Sierra Leone, Ghana, and Nigeria.[7] *T. occidentalis* is one of the main vegetable crops cultivated in the Southern part of Nigeria,[8] where it is known by different names such as "iroko" or "apiroko" in Yoruba, "ubong" in Efik, "ugu" in Igbo, "umeke" in Edo, and "umee" in Urhobo.[7] It is thought to have originated from the Southeastern region of Nigeria and spread by the Igbos, who have cultivated this crop since prehistoric times. Probably, *T. occidentalis* was initially wild throughout its current range; however, wild plants may have been harvested to local extinction and are now substituted with cultivated types.[9,10] *T. occidentalis* is a dioecious, perennial, tropical vine grown for its leaves and edible seeds.[11] It is a creeping herbaceous vegetable with lobed leaves and twisted tendrils that extends over the soil.[12] Fluted pumpkin can be grown on mounds or on flatlands. In domestic gardens, it is often cultivated beside fences or adjacent to a tree, thus enabling the suspension of the fruit from a branch.[13] It may also be cultivated along trellis of different kinds including bamboo.[7] *T. occidentalis* leaves possess high curative, industrial, and nutritional values. According to Akanbi *et al.*[8] the leaves are abundant in fat (18%), protein (29%), and minerals and vitamins (20%). The leaves are also a rich source of phosphorus, calcium, zinc, iron, and copper.[14] Phytochemical screening of fluted pumpkin leaf extracts by Oyewale and Abalaka[15] confirmed the presence of saponins, alkaloids, tannins, and phenolics. Seeds of *T. occidentalis* can be ground and added to soups or roasted, cooked, and eaten. The seeds contain 45% fat, 23% carbohydrates, 20.5% protein, 2.2% fibers, and 4.8% total ash.[8] In addition, the seeds contain phospholipid, glycolipid, and neutral lipid contents of 58%, 26%, and 15%, respectively. Fluted pumpkin seed oil contains 61% unsaturated fatty acids.[14] The healing properties of *T. occidentalis* are popular in Nigerian folklore medicine, and these curative properties have been evaluated by a number investigators. The present study was aimed at reviewing systematically, existing publicly available literature on the pharmacological properties of *T. occidentalis*.

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METHODS

Search strategy

To identify keywords and subject headings, an initial scoping task was performed, after which an ultimate search procedure was carried out. Relevant literature searches were conducted on January 19, 2018 on PubMed, ScienceDirect, and Scopus, with search dates set from 1990 to 2018. To identify more studies, hand searching of articles was performed for originally considered papers from reference list of articles and Google Scholar. Search terms used to query the four databases are presented in Table 1.

Selection criteria

We broadly searched for studies on the pharmacological activities of *T. occidentalis*. We specifically included studies that reported medicinal or curative or therapeutic properties of fluted pumpkin. Studies that were editorials, reviews, or viewpoints were screened out. Only studies that were written in English were reviewed.

Case definitions

According to Sofowora *et al.*,[16] a medicinal plant is any plant whose organs contain active principles which can be employed for curative (pharmacological or therapeutic) purposes or used as precursors for drug synthesis.

Quality criteria

For every full text evaluated, we made sure that the pharmacological properties of *T. occidentalis* were explicitly defined to meet the case definitions stated. Studies with ambiguous investigations and results were excluded from the study.

Data extraction

Three reviewers (OSA, OAB, and JOP) independently conducted a simultaneous search and selection of studies. To resolve any disagreement between the three reviewers over the selection of articles, a re-evaluation was conducted by a fourth reviewer, OOO. From each article, data were retrieved on country (location), specific investigation, findings, and pharmacological property. Data were double extracted by three parallel reviewers (OSA, OAB, and JOP). All data were sorted, compiled, and stored in Microsoft Excel 2013.

Table 1: Search terms on PubMed

#	Searches*
1	Pharmacological properties
2	Therapeutic properties
3	Medicinal properties
4	Curative properties
5	Pharmacological activities
6	Therapeutic activities
7	Medicinal activities
8	Curative activities
9	Pharmacological values
10	Therapeutic values
11	Medicinal values
12	Curative values
13	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14	*T. occidentalis*
15	Fluted pumpkin
16	14 or 15
17	13 and 16

*Searches on Scopus, ScienceDirect, and Google Scholar followed the same pattern. *T. occidentalis*=*Telfairia occidentalis*

RESULTS

Systematic search

Our search returned a total of 477 articles from the databases, with PubMed, ScienceDirect, and Scopus recording 19, 40, and 418 articles respectively. 22 supplementary articles were retrieved from Google Scholar and hand searched reference lists of chosen articles. 46 duplicate articles were eliminated. Totally, 453 studies were scrutinized for connectedness, with 364 articles excluded from the study (24 articles that were editorials, reviews, or viewpoints and 340 studies that were not related to *T. occidentalis*). From the 89 papers left, 51 articles were excluded upon evaluation of their abstracts owing to nonrelatedness of studies to the pharmacological activities of fluted pumpkin. 38 articles were ultimately retained for this review [Figure 1].

Study characteristics

In this review, there are 38 studies conducted in 13 different locations across Nigeria [Figure 2]. 8 studies were retrieved from Ibadan (representing ~ 19% of studies retained), 6 each from Uyo and Lagos (~16% each), 3 each from Akure and Ilorin (~8% each), 2 each from Ado Ekiti, Minna, Nsukka, and Benin (~5% each), and 1 each from Jos, Ogbomosho, Nnewi, and Zaria (~3% each). All included studies were conducted between 1990 and 2018. A summary of the study characteristics is presented in Table 2.

DISCUSSION

The utilization of plants for the treatment of ailments is as old as human existence.[53] In many resource-poor countries, a huge segment of the populace depends on herb doctors and medicinal plants to meet their healthcare exigencies.[54] Herbal medicines are beginning to gain widespread acceptance in the global herbal drug market[55] which is estimated to worth a whooping USD 60 billion.[56] *T. occidentalis* have been reported in several scientific literature to possess therapeutic effects which local communities take advantage of.[47] Based on the studies retained [Table 2], we have grouped the therapeutic properties of *T. occidentalis* into 13 categories [Table 3].

Hypocholesterolemic activity

Hyperlipidemia is a health condition characterized by abnormally high levels of lipid in the blood. This condition which is also referred to as hypercholesterolemia or hyperlipoproteinemia has been listed as one of the leading risk factors that contribute to the incidence and severity of cardiovascular disease.[57] Globally, there is an increasing demand for plant-derived natural products as health supplements[58] for the prevention of heart diseases. The hypolipidermic activities of fluted pumpkin have been documented in some scientific literature. Studies have revealed that cholesterol-induced heart enlargement was significantly reduced in Wistar rats fed with *T. occidentalis* supplemented diets.[17] Adaramoye *et al.*[17] further documented a dose-dependent decrease in lipid peroxidation levels and lowering of postmitochondrial supernatant fraction (PMS) and plasma cholesterol levels in rats administered fluted pumpkin-supplemented diets. Nwozo *et al.*[18] in their study documented the cholesterol and triglyceride-lowering effects of the methanolic extract of *T. occidentalis*. According to Eseyin *et al.*,[28] the ethanolic extract of fluted pumpkin significantly reduced blood cholesterol levels, which gives credence to the utilization of the leaf extract in the management of cholesterolemia. The hypocholesterolemic activity of fluted pumpkin may be due to the presence of flavonoids which significantly reduce blood plasma cholesterol and triglycerides.[59]

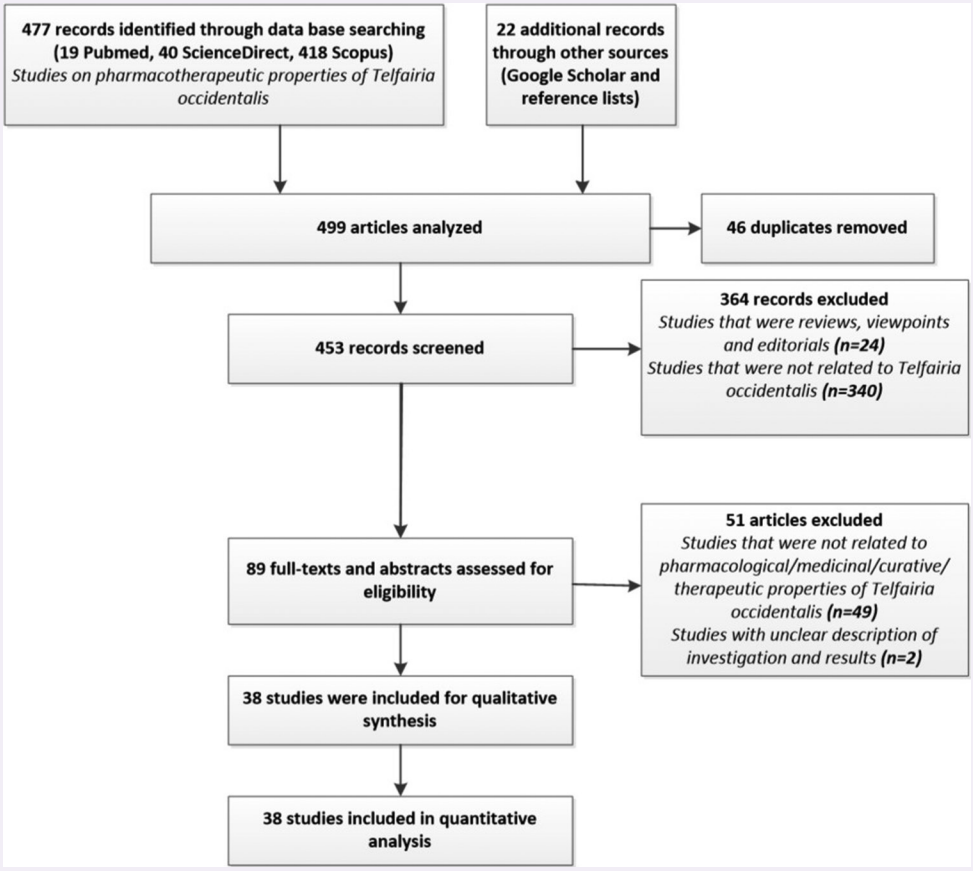

Figure 1: Flowchart for the selection and screening of articles

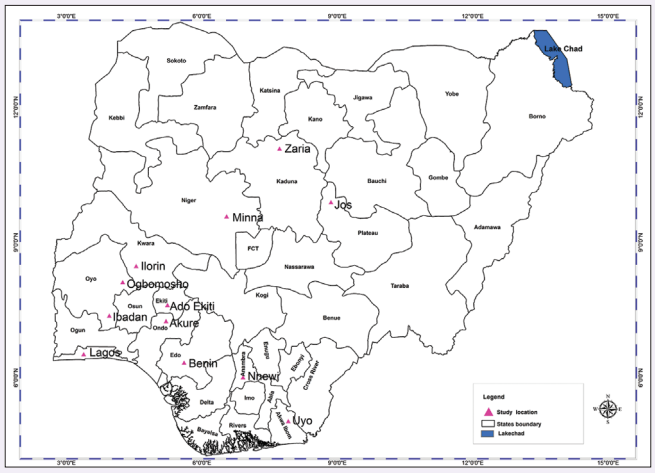

Figure 2: Data map showing locations across Nigeria where investigations were conducted

Antidiabetic activity

Diabetes mellitus (DM) is a metabolic disorder marked by high blood glucose levels and disturbance in carbohydrate, protein, and fat metabolism.[60] In 2014, global estimates revealed that 422 million adults were living with diabetes.[61] Since 1980, there has been a nearly two-fold increase in the global incidence of diabetes, rising from 4.5% to 8.5% in the adult populace. In 2012, the mortality rate from diabetes was reported to be 1.5 million. Some of the complications of diabetes include stroke, cardiac arrest, kidney failure, amputation of lower limb, vision loss, nerve damage,[61] and erectile dysfunction.[62] Poorly managed diabetes in pregnant women could increase the risk of fetal death and other complications.[61] Based on several reports, it is evident that in years to come, diabetes will be one of the world's major disease.[63] Medical treatment for diabetes includes both oral glucose-lowering drugs and insulin.[64] Owing to the side effects linked with oral hypoglycemic drugs for DM treatment, attention has been shifted toward herbal remedies for its management.[65] A number of researchers have confirmed the antidiabetic properties of *T. occidentalis* in rat models. According to Nwozo *et al.*,[18] methanolic extract of fluted pumpkin showed a depressing effect on plasma glucose levels. Eseyin *et al.*[14] in their work, documented that ethanolic seed extract of fluted pumpkin significantly repressed blood glucose levels. Aderibigbe *et al.*[27] and Salman *et al.*[29] observed the hypoglycemic effect of fluted pumpkin leaves in streptozotocin (STZ)-induced diabetic mice and male albino rats respectively. Eseyin *et al.*[31] reported that the ethanolic leaf extract of fluted pumpkin significantly lowered blood glucose levels. The phenolic extract also inhibited activities of α-glucosidase and α-amylase (enzymes associated with type-II diabetes) in adult Wistar rats in a concentration-dependent manner.[20]

Profertility activity

Infertility is a vital aspect of reproductive health that is often neglected.[66] It is a disease that affects the reproductive system and is marked by the inability to achieve a clinical pregnancy following a year or more of constant unprotected sexual intercourse.[67] Couples worldwide, are affected by the

Table 2: Characteristics of included studies on pharmacological properties of *Telfairia occidentalis*

Author	Country (location)	Specific investigation	Findings	Pharmacological property
Adaramoye *et al.*[17]	Nigeria (Ibadan)	Hypolipidemic activity of *T. occidentalis* on Wistar strain of albino rats fed with dietary cholesterol	The study demonstrated that *T. occidentalis*-supplemented diet significantly reduced cardiac enlargement induced by cholesterol in Wistar rats. Rats administered diet fortified with fluted pumpkin showed reduced PMS and plasma cholesterol levels in a dose-dependent manner. Repression of lipid peroxidation levels was also reported	Hypocholesterolemic
Nwozo *et al.*[18]	Nigeria (Ibadan)	Antidiabetic and hypolipidemic effects of methanolic extract of *T. occidentalis* in alloxan-induced diabetic rabbits	Methanolic extract exhibited a depressing effect on plasma glucose, cholesterol, creatinine, and triglyceride levels in diabetic rabbits. The extract was effective in reducing polydipsia to normal in untreated diabetic rats	Antidiabetic and hypocholesterolemic
Eseyin *et al.*[14]	Nigeria (Uyo)	Hypoglycemic effect of ethanolic seed extract of *T. occidentalis* on alloxan-induced diabetic Wistar albino rats	Blood glucose levels was significantly reduced by ethanolic seed extract	Antidiabetic
Saalu *et al.*[19]	Nigeria (Lagos)	Dose-dependent testiculo protective and testiculotoxic potentials of *T. occidentalis* leaf extract in Sprague Dawley rats	At lower doses, leaf extract exhibited testiculoprotective activity. However, testiculotoxicity was observed when higher doses were administered	Profertility
Jimoh[20]	Nigeria (Ado Ekiti)	Enzyme inhibitory and radical scavenging potentials of phenolic extract of *M. oleifera* and *T. occidentalis* leaves on enzymes (α-amylase and α-glucosidase) linked with Type-II diabetes	Phenolic extracts of *M. oleifera* and *T. occidentalis* inhibited α-glucosidase and α-amylase activities in a dose-dependent manner. The phenolic extracts of both plants arrested progression of lipid peroxidation by reducing MDA levels of pancreatic tissues in a concentration-dependent manner. The extracts were also capable of scavenging DPPH in a concentration-dependent manner. In furtherance, phenolic extracts of *M. oleifera and T. occid*entalis *chelated* $Fe^{2+}$and Cu^{2+}in a concentration-dependent manner	Antidiabetic and antioxidant
Okokon *et al.*[21]	Nigeria (Uyo)	Investigation of *in vivo* antimalarial activity of seed and leaf extracts of *T. occidentalis* in mice infected with *P. berghei berghei*	Significant antiplasmodial activities were observed with seed and leaf extracts during early and established infections. In addition, likely schizontocidal activity was observed with seed extract in early and established infections	Antiplasmodial
Oboh[22]	Nigeria (Uyo)	Hepatoprotective activity of ethanolic and aqueous extracts of fluted pumpkin leaves against garlic-induced oxidative stress in Wistar strain albino rats	From the investigation, both aqueous and ethanolic extracts possessed hepatoprotective properties. However, aqueous extract compared to ethanolic extract was more efficacious in protecting liver hepatocytes	Hepatoprotective
Oboh *et al.*[23]	Nigeria (Akure)	Antioxidant and antimicrobial activities of ethanolic and aqueous extracts of *T. occidentalis* leaf	With ethanolic extract, inhibitory effect was observed on some *Enterobacteriaceae* (*E. coli, P. aeruginosa and Proteus* sp.). Aqueous extract suppressed the growth of *S. typhii*. The study also showed that aqueous extract of fluted pumpkin leaves possessed significantly higher free radical scavenging potentials, reducing power, and total phenols	Antioxidant and antimicrobial
Oluwole *et al.*[24]	Nigeria (Ibadan)	Antiinflammatory effect of methanolic extracts *T. occidentalis* leaf and stem in carrageenan-induced paw edema albino rats	Stem and leaf extracts showed significant antinflammatory activities	Antiinflammatory
Alada[25]	Nigeria (Ilorin)	Effect of dietary preparation of *T. occidentalis* on some hematological indices: Hb concentration, PCV, WBC count and RBC counts	Hb concentration, PCV, RBC as well as WBC was significantly increased by dietary preparations of fluted pumpkin	Hematological
Dina *et al.*[26]	Nigeria (Ibadan)	Effect of *T. occidentalis* on experimentally induced anemia in domestic rabbit (*O. cuniculi*)	Hematinic activity comparable to that of standard hemantinic (hematophan B12) was observed	Antianemic

Contd...

Table 2: Contd...

Author	Country (location)	Specific investigation	Findings	Pharmacological property
Aderibigbe *et al.*[27]	Nigeria (Ilorin)	Antihyperglycemic effect of *T. occidentalis* leaves in normoglycemic, glucose and STZ-induced diabetic mice	Blood glucose lowering effect indicative of antidiabetic activity was observed in STZ-induced diabetic and glucose-induced hyperglycemic mice respectively	Antidiabetic
Eseyin *et al.*[28]	Nigeria (Uyo)	Effect of ethanolic extract of *T. occidentalis* leaves on some biochemical indices in Wistar rats	The result of the study revealed a decrease in cholesterol levels, ALT and AST, β-globulin, albumin, albumin/globulin quotient. Increased levels of total protein, α-globulin and γ-globulins were observed	Hypocholesterolemic
Salman *et al.*[29]	Nigeria (Ilorin)	Effects of aqueous leaf extract of *T. occidentalis* on some hematological indices, sperm parameters and blood glucose in male albino rats	Hematological indices increased within 7 days of administration of aqueous leaf extract. Sperm quality was also improved. Extract was capable of lowering blood glucose levels	Hematological improvement, profertility and antidiabetic
Iweala and Obidoa[30]	Nigeria (Nsukka)	Some biochemical, hematological and histological responses to long term administration of *T. occidentalis*-fortified diets in albino rats	Results demonstrated that *T. occidentalis*-fortified diets induced significant increases in Hb and weight. In addition, lipid peroxidation was significantly reduced. No significant changes were observed in ALT, AST, and GST activities	Hematological improvement and antioxidant
Eseyin *et al.*[31]	Nigeria (Uyo)	Comparative hypoglycemic effect of aqueous and ethanolic extracts of leaf and seed of *T. occidentalis* in alloxan-induced white albino male rats	Aqueous leaf and seed extracts had no depressing effect on blood glucose concentration. However, ethanolic leaf extract significantly reduced blood glucose levels whereas ethanolic seed extract did not	Antidiabetic
Okokon *et al.*[32]	Nigeria (Uyo)	Immunomodulatory, anticancer, and antiinflammatory properties of seed extract and fractions of fluted pumpkin on HeLa cells (cervix cancer cells)	Extract was observed to possess prooxidant activity at lower concentrations but mild antioxidant activity at higher concentrations. Oxidative burst activity in whole blood, isolated MNCs and PMCs was inhibited, when serum opsonizing zymosan was used to activate phagocytosis. Hexane fraction of fluted pumpkin seed extract significantly inhibited the proliferation of HeLa cancer cell lines. Significant antiinflammatory activity against xylene- and egg albumin-induced edema in mice were also observed	Anticancer and antiinflammatory
Ejike and Ezeanyika[33]	Nigeria (Nsukka)	Potential of *T. occidentalis* seeds in the inhibition of experimentally induced (hormone-induced) BPH in Wistar rats	Results from the study demonstrated that diet supplemented with 15% fluted pumpkin seed may repress the proliferation of aberrant prostatic cells by raising testosterone: estradiol ratio in rats	Anticancer
Nwanna and Oboh[34]	Nigeria (Akure)	Hepatoprotective and antioxidant activities of free soluble and bound phenolic extract of *T. occidentalis* leaves on acetaminophen-induced liver damage in Wistar strain albino rats	From the study, it was concluded that both bound and soluble-free phenolic extracts of fluted pumpkin leaves protected hepatocytes against oxidative stress but via different pathways. Soluble-free phenolic extract exhibited significantly higher hepatoprotective and antioxidant activity compared to bound phenolic extract	Antioxidant and hepatoprotective
Ogbe *et al.*[35]	Nigeria (Jos)	Antianemic activity of some plant extracts in phenyl hydrazine-induced anemia in rabbits (*O. cuniculi*)	Oral daily dose of *T. occidentalis* leaf extract showed significant antianemic effect	Antianemic
Christopher *et al.*[36]	Nigeria (Benin)	Profertility effects of the aqueous leaf extract of fluted pumpkin on testicular histology, sperm characteristics, and male hormone profile of adult male Wistar rats	Results revealed that aqueous leaf extract of *T. occidentalis* preserved histological architecture of seminiferous tubules and epididymis. The extract also enhanced spermatogenesis. Increased sperm count, motility, and livability were observed with increasing doses and duration of treatment. Studies on hormones showed significant increases in testosterone and testosterone: estrogen ratio among the treated rats with associated increase in the levels of gonadotropic hormones, LH and FSH	Profertility

Contd...

Table 2: Contd...

Author	Country (location)	Specific investigation	Findings	Pharmacological property
Adegbolagun *et al.*[37]	Nigeria (Ibadan)	Synergistic effect of coadministration of aqueous extract of *T. occidentalis* leaves and artesunate in *P. berghei berghei*-infected albino mice	Aqueous extract of fluted pumpkin and *Artesunate* alone or in combination showed 72%, 70% and 85% parasitemia reduction respectively after 48 h. Hematological parameters were significantly improved within 48 h of administration. By the 10th day of administration, all treatments gave 100% clearance	Antiplasmodial
Adetutu and Tijani[38]	Nigeria (Ogbomoso)	Chemopreventive effect of *T. occidentalis* leaf extract on the frequency of mPCE in bone marrow of mice treated with SA	Results showed that fluted pumpkin leaf extract possessed anticlastogenic property. Leaf extract was capable of repressing SA-induced micronuclei formation in polychromatic erythrocytes in mice bone marrow	Anticancer
Ajao and Akindele[39]	Nigeria (Lagos)	Anxiolytic and sedative properties of hydroethanolic leaf extract of the *T. occidentalis* in Swiss mice	*T. occidentalis* hydroethanolic leaf extract exhibited sedative activity at higher concentrations (200 and 400 mg/kg) and anxiolytic activity at lower concentrations (50 and 100 mg/kg)	Anxiolytic and sedative
Akang *et al.*[40]	Nigeria (Lagos)	Testiculoprotective effect of *T. occidentalis* against alcohol-induced damage in Sprague-Dawley rats	*T. occidentalis* inhibited alcohol-induced testicular damage, improved serum testosterone, luteinizing hormone levels, and semen quality	Profertility
Akang *et al.*[41]	Nigeria (Lagos)	Effects of aqueous leaf extract of fluted pumpkin on alcohol-induced cytoarchitectural changes in the testes of adult male Sprague-Dawley rats	This study demonstrated that *T. occidentalis* increased testicular antioxidant enzymes levels and decreased MDA levels when administered alone. When administered with alcohol, leaf extract inhibited the deleterious effects of alcohol on sperm motility, sperm count, and testicular antioxidant enzymes	Antioxidant and profertility
Akindele *et al.*[42]	Nigeria (Lagos)	Effect of hydroethanolic leaf extract of *T. occidentalis* in mouse models of convulsion, muscle relaxation and depression	Fluted pumpkin significantly delayed the onset and reduced the duration of convulsion in Strychnine test. Time of death was also delayed in isoniazid model. Results demonstrated that fluted pumpkin hydroethanolic extract possessed anticonvulsant property	Anticonvulsant
Akindele *et al.*[43]	Nigeria (Lagos)	Antinociceptive and antiinflammatory activities of the hydroethanolic leaf extract of *T. occidentalis* in albino mice and rats	*T. occidentalis* extract in a dose-dependent manner, inhibited acetic acid-induced writhing. Significant peripherally mediated antinociceptive activity was observed. In addition, *T. occidentalis* significantly inhibited rat paw edema development in the three stages of carrageenan test. Antiinflammatory activity was most apparent in the third stage	Antinociceptive and antiinflammatory
Atabo *et al.*[44]	Nigeria (Zaria)	Effect of methanolic and aqueous extracts of *T. occidentalis* leaves, seeds and stems on metHb formation in the blood of SCD patients	Results showed that the leaves, seeds and stem extracts possessed the capacity to improve Fe^{2+}/Fe^{3+} ratio by reducing endogenous metHb concentration. The study also revealed that at 0.8% w/v, methanolic leaf extract induced a high conversion level of metHb	Hematological improvement
Daramola *et al.*[45]	Nigeria (Benin)	Effects of methanol extract of *T. occidentalis* seed on serum hormone concentration, ovary antioxidant activity, and histology in reproductive system of female Wistar rats	Increase in SOD levels, decrease in MDA levels. No significant differences were observed in serum concentrations of estrogen, LH and FSH. Histoarchitecture of ovaries was preserved. Results from the investigation showed that methanolic extract of *T. occidentalis* seed possessed antioxidant activity, thus protecting against cell damage and lipid peroxidation in tissue of rat ovaries	Antioxidant
Kayode *et al.*[46]	Nigeria (Ibadan)	Antioxidative effects of *T. occidentalis* in ameliorating PEM-induced oxidative stress in the brain of Winling albino rats	Results showed that PEM-induced lipid peroxidation was inhibited when fluted pumpkin leaves were coadministered with protein. Increase in SOD and CAT activities were also observed	Antioxidant

Contd...

Table 2: Contd...

Author	Country (location)	Specific investigation	Findings	Pharmacological property
Lawal *et al.*[47]	Nigeria (Minna)	Effects of prolonged administration of the methanolic extract of fluted pumpkin leaves on hematological parameters of Swiss albino rats	Consequent on administration of extract, significant increases in HCT, RBC, Hb, MCHC, and RCD width-SD were observed, suggestive of erythropoiesis stimulation. In addition, WBC and LY count were significantly elevated. Although extract stimulated erythropoietin and leukopoietin release, it however had a depressing effect on thrombopoiesis at higher doses	Hematological improvement
Maduka *et al.*[48]	Nigeria (Nnewi)	Effect of aqueous leaf extract of *T. occidentalis* on gentamycin-induced kidney damage in Wistar albino rats	Histological report from the investigation showed that extract was capable of reversing renal damage induced by gentamycin when coadministered with gentamycin	Renal protection
Oyewole and Abalaka[15]	Nigeria (Minna)	Antimicrobial activities of ethanolic extract of fluted pumpkin leaf on some selected intestinal microorganisms	The result of the investigation demonstrated that a MBC of 0.5 mg/ml and 50 mg/ml inhibited growth of *S. typhi* and *E. coli* respectively. However, extracts of *T. occidentalis* at 500 mg/ml, 50 mg/ml and 5.0 mg/ml had no bactericidal activity on *S. faecalis*	Antimicrobial
Odede *et al.*[49]	Nigeria (Ibadan)	Effect of fluted pumpkin leaf on RBC parameters of albino rats (Wistar strain) after acute blood loss	*T. occidentalis* significantly increased erythrocyte count of treated bled rats compared to bled control. Erythrocyte osmofragility was also significantly repressed in the bled control	Hematological improvement
Oboh *et al.*[50]	Nigeria (Akure)	Suppression of α-amylase and α-glucosidase activities by ethanolic leaf extract of *T. occidentalis*	Unprocessed leaf extract significantly inhibited the activities of α-glucosidase and α-amylase	Antidiabetic
Osukoya *et al.*[51]	Nigeria (Ado Ekiti)	Antinociceptive and antioxidant activities of the methanolic extract of *T. occidentalis*	*T. occidentalis* methanolic seed extract significantly inhibited licking time in both inflammatory and neurogenic stages of formalin-induced paw licking assays in rats. Methanolic extract of fluted pumpkin seed produced significant radical scavenging activity in a dose-dependent manner in DPPH radical scavenging assay	Antinociceptive and antioxidant
Kayode *et al.*[52]	Nigeria (Ibadan)	Healing effect of *T. occidentalis* on liver damage induced by protein malnutrition	Coadministration of protein and fluted pumpkin significantly repressed PEM-induced lipid peroxidation. Coadministration of the diet significantly increased hepatic GSH levels, SOD, and CAT activities. *T. occidentalis*-fortified diet was capable of reversing liver damage	Antioxidant

T. occidentalis=Telfairia occidentalis, M. oleifera=Moringa oleifera, P. berghei berghei=Plasmodium berghei berghei, E. coli=Escherichia coli, P aeruginosa=Pseudomonas aeruginosa, S. typhii=Salmonella typhii, S. faecalis=Streptococcus faecalis, PMS=postmitochondrial supernatant fraction, MDA=Malondialdehyde, DPPH=2,2-diphenyl-1-picrylhydrazyl, Hb=Hemoglobin, metHb=methemoglobin, PCV=Packed cell volume, WBC=White blood cell, RBC=Red blood cell, STZ=Streptozotocin, ALT=Alanine transaminase, AST=Aspartate transaminase, GST=Glutathione-S-transferase, MNCs=Mononuclear cells, PMCs=Polymorphonuclear cells, BPH=Benign prostastic hyperplasia, LH=Luteinizing hormone, FSH=Follicle stimulating hormone, mPCE=Micronucleated polychromatic erythrocytes, SA=Sodium arsenite, SCD=Sickle cell disease, SOD=Superoxide dismutase, PEM=Protein energy malnutrition, CAT=Catalase, HCT=Hematocrit, MCHC=Mean corpuscular hemoglobin concentration, LY=Lymphocyte, MBC=Minimum bactericidal concentration, GSH=Glutathione, RCD=Red cell distribution, SD=Standard deviation, *O. cuniculi=Oryctolagus cuniculi,* Fe^{2+}=Iron, Cu^{2+}=Copper

incapacity to bear children, thus resulting in psychological and emotional uneasiness in both men and women.[66] Numerous treatment options for male infertility are emerging globally. Modern-day treatments such as assisted reproductive methods are expensive with minimal success rates of only 10%–30%. Nonetheless, the traditional medicines are attracting increasing attention as an alternative curative intervention for male infertility.[68] The findings of Christopher *et al.*[36] showed that *T. occidentalis* leaf extract preserved the histological architecture of seminiferous tubules and epididymis, improved spermatogenesis, increased sperm count, motility and livability with increasing concentration, and duration of treatment in Wistar rats. Hormonal studies also showed significant increases in testosterone and testosterone: estrogen ratio. Akang *et al.*[40] in their investigation, documented the prophylactic activity of fluted pumpkin on alcohol-induced testicular damage. They further reported that *T. occidentalis* improved semen quality, serum testosterone, and luteinizing hormone levels. In another study, Akang *et al.*[41] showed that fluted pumpkin leaf extract increased testicular antioxidant enzyme levels and decreased malondialdehyde (MDA) levels levels when administered alone in adult male Sprague-Dawley rats. The leaf extract was also efficacious in ameliorating the harmful effects of alcohol on sperm count, sperm motility, and testicular antioxidant enzymes. The testiculoprotective activity of fluted pumpkin was reported by Saalu *et al.*[19] Salman *et al.*[29] documented that the aqueous leaf extract of *T. occidentalis* improved sperm quality in male albino rats. The pharmacotherapeutic effect of fluted pumpkin on male infertility may be due to its antioxidant components. Antioxidants such as vitamins A, C, and E which are present in fluted pumpkin have been demonstrated to exhibit protective activities on the testes of rat models.[41]

Table 3: Categorization of the pharmacological properties of *Telfairia occidentalis* based on studies retained

Category of pharmacological activity	Disease/biological condition	Author
Hypocholesterolemic	Hyperlipidemia	Adaramoye *et al.*;[17] Nwozo *et al.*;[18] Eseyin *et al.*[28]
Antidiabetic	Hyperglycemia Type-II diabetes	Eseyin *et al.*;[31] Aderibigbe *et al.*;[27] Jimoh;[20] Eseyin *et al.*;[14] Nwozo *et al.*;[18] Oboh *et al.*[50]
Profertility	Oligospermia, reduced sperm motility and testicular antioxidant activity, alcohol-induced testicular damage, low sperm quality and imbalance in gonadotropic hormones	Saalu *et al.*;[19] Salman *et al.*;[29] Christopher *et al.*;[36] Akang *et al.*;[40] Akang *et al.*[41]
Free radical scavenging and antioxidant	Free radical- and ROS-induced tissue damage	Osukoya *et al.*;[51] Kayode *et al.*;[46] Daramola *et al.*;[45] Akang *et al.*;[41] Nwanna and Oboh[34]; Iweala and Obidoa[30]; Oboh *et al.*[23]; Jimoh[20]; Kayode *et al.*[52]
Antiplasmodial	Malaria	Okokon *et al.*[21]; Adegbolagun *et al.*[37]
Hepatoprotective	Liver damage	Oboh;[22] Nwanna and Oboh[34]
Antimicrobial	Diseases caused by certain bacterial infections (*S. typhi, E. coli*, *P. aeroginosa and Proteus* spp.)	Oboh *et al.*;[23] Oyewole and Abalaka[15]
Antinociceptive and antiinflammatory	Pain and inflammation	Oluwole *et al.*;[24] Okokon *et al.*;[32] Akindele *et al.*[43]
Antianemic and hematological improvement	Anemia and hematological anormalies	Lawal *et al.*;[47] Atabo *et al.*;[44] Ogbe *et al.*;[35] Iweala and Obidoa;[30] Dina *et al.*;[26] Alada;[25] Odede *et al.*;[49] Oboh *et al.*[50]
Anticancer	Tumourigenesis (malignant and benign)	Adetutu and Tijani;[38] Ejike and Ezeanyika;[33] Okokon *et al.*[32]
Anxiolytic and sedative	Anxiety and depression	Ajao and Akindele[39]
Anticonvulsant	Convulsion	Akindele *et al.*[42]
Renal protection	Kidney damage	Maduka *et al.*[48]

ROS=Reactive oxygen species

Antioxidant and free radical scavenging activity

It has been established that cellular damage resulting from reactive oxygen species or free radicals is a fundamental mechanism that underpins inflammation, many human neurodegenerative disorders, diabetes, autoimmune pathologies, viral infections, and digestive system disorders.[69] Antioxidative defense pathway is one of the most effective mechanisms to reduce and eliminate free radical-induced oxidative stress. Antioxidants are substances which possess free radical chain reaction-termination activity.[70] A number of diverse, naturally occurring antioxidants with different composition, sites of activity, and physical and chemical properties occur in plants.[71] In recent times, interest in the pharmacotherapeutic potentials of botanicals as antioxidants in inhibiting oxidative stress-induced tissue damage has been on the rise.[72] Jimoh[20] reported the free radical scavenging and antioxidant properties of the phenolic extract *T. occidentalis*. According to Oboh *et al.*,[23] the aqueous leaf extract of fluted pumpkin compared to its ethanolic extract, possessed a significantly higher free radical scavenging capacity, total phenolic content, and reducing power. The antioxidant activity of the leaf extract has also been validated by the work of Nwanna and Oboh,[34] Akang *et al.*,[41] Kayode *et al.*,[46] and Daramola *et al.*[45] who documented the antioxidant activity of fluted pumpkin against lipid peroxidation and tissue damage in the ovaries of female Wistar rats. Iweala and Obidoa[30] in their study, reported significant reduction in lipid peroxidation in albino rats administered *T. occidentalis*-fortified diet. Increase in testicular antioxidant enzyme was observed when leaf extract of fluted pumpkin was administered alone in Sprague Dawley rats.[41] According to Kayode *et al.*,[52] coadministration of *T. occidentalis* and protein inhibited PMS-induced lipid peroxidation, elevated glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) activities. In the same study, it was also observed that fluted pumpkin diet was capable of reversing liver damage. The therapeutic activities of vegetables such as *T. occidentalis* have been linked primarily to the presence of antioxidant vitamins such as α-tocopherol, ascorbic acid, phenolics, and β-carotene.[73]

Antiplasmodial activity

Malaria is a lethal disease caused by Plasmodium parasites (with *Plasmodium vivax* and *Plasmodium falciparum* being the most common and *P. falciparum* the most precarious). The disease is transmitted from person to person through bites of infected female anopheles mosquitoes that act as vectors. Malaria is preventable and treatable.[74] In 2016, almost half of the world's populace were at risk of malaria. The majority of mortality and malaria cases are reported in sub-Saharan Africa. Based on the World Malaria Report published in November 2017, 216 million cases of malaria were reported in 2016, as opposed to 211 million cases in the previous year. An estimated 445,000 deaths from malaria was reported in 2016.[75] Medicinal plants have been employed in the treatment of malaria for many years and are the source of the two main categories (quinine and artemisinin derivatives) of recent antimalarial drugs. Medicinal plants are an important and sustainable source for malaria treatment, particularly in areas where accessibility to and affordability of antimalarial drugs are a problem.[76] Okokon *et al.*[21] reported significant antiplasmodial activity with the seed and leaf extracts of *T. occidentalis* during early and established infections. The seed extract exhibited schizontocidal activity. Antiplasmodic activity of fluted pumpkin was also validated by Adegbolagun *et al.*[37] who documented a reduction in parasitemia within 48 hours, when *Plasmodium berghei berghei*-infected albino mice were administered aqueous extract of *T. occidentalis* alone or in combination with artesunate.

Hepatoprotective activity

Being one of the largest organs in the human body,[77] the liver plays a key role in the regulation of variegated processes which include metabolism, storage, secretion, and detoxification of endogenous and exogenous compounds.[78] Hepatocytes are the functional cells of the liver.[79] Globally, liver disorders are a major problem. Orthodox drugs employed in the treatment of liver diseases are sometimes ineffective and can have grave untoward effects.[80] In addition, the treatment interventions are usually too expensive for resource-poor countries. Herbal medicines

constitute a group of therapeutic agents with low-side effect profile. In recent times, researchers are paying more attention to plant-derived medicines for the treatment of liver diseases.[81] Some researchers have established the hepatoprotective potency of *T. occidentalis*. According to Oboh,[22] the aqueous extract of fluted pumpkin was more effective than the ethanolic extract in protecting hepatocytes against garlic-induced oxidative stress. Nwanna and Oboh[34] in their work found that both soluble-free and bound phenolic extracts of the leaves protected hepatocytes from oxidative stress. However, soluble-free phenolic extract showed significantly higher hepatoprotective activity compared to bound phenolic extract. The hepatoprotective property of fluted pumpkin may be attributed to its rich phenolic content as reported by Oboh *et al.*[23]

Antimicrobial activity

Resistant or multi-resistant strains of microorganisms are constantly emerging despite the existence of potent antibiotics, thus imposing the need for the development of novel drugs with superior antimicrobial action. Therapeutic agents from plants serve as templates for the development of more efficacious drugs with reduced toxicity.[82] The investigation of Oyewole and Abalaka[15] showed that the ethanolic extract of *T. occidentalis* leaves were bactericidal against *Escherichia coli* and *Salmonella typhii*. Oboh *et al.*[23] documented the inhibitory action of fluted pumpkin leaf extract on some members of the Enterobacteriaceae family (*E. coli, Pseudomonas aeroginosa*, *and Proteus sp.*). In furtherance, the work of Oboh *et al*.[23] demonstrated that the aqueous leaf extract inhibited the growth of *Salmonella typhii.*

Antinociceptive and antiinflammatory activity

Pain is a complex sensory episode associated with avoidance motor reflexes and autonomic output alterations.[83] It could be nociceptive, inflammatory, neuropathic, and functional, generated by different neurobiological pathways.[83] Globally, antiinflammatory drugs that are nonsteroidal in origin are used for the treatment of pain, inflammation, and fever, as well as for heart and blood vessel protection. Nevertheless, they are often associated with significant side effects, which include renal damage, gastric ulcer, bronchospasm, and cardiac abnormalities, consequently limiting their usage.[84] Since antiquity, medicinal plants have been utilized as safe antiinflammatory remedies.[85] Plant-derived antiinflammatory agents explored for their curative properties include compounds belonging to different groups of phytochemicals such as glycosides, terpenoids, alkaloids, polysaccharides, flavonoids, cannabinoids, phenolics, and steroids.[86] The antiinflammatory and antinociceptive properties of *T. occidentalis* have been validated by several researchers. The findings of Oluwole *et al.*[24] revealed that carrageenan-induced edema in the subplantar hind paw of adult male albino rats was significantly repressed by the methanolic extract of fluted pumpkin. Fractions and seed extract of *T. occidentalis* have also been reported to exhibit significant antiinflammatory action against xylene- and egg albumin-induced edema in mice ear.[32] According to Akindele *at al.*,[43] fluted pumpkin hydroethanolic leaf extract inhibited acetic acid-induced writhing in a dose-dependent manner. In the same investigation, Akindele *et al.*[43] demonstrated that the extract significantly repressed the development rat paw edema in the three phases of carrageenan test, with antiinflammatory activity most apparent in the third phase. *T. occidentalis* contains nonsteroidal molecules. Such nonsteroidal compounds are favoured as antiinflammatory agents compared to their steroidal counterparts which are known to cause various contraindications like atherosclerosis, hypertension, and osteoporosis.[24]

Antianemic and hematological improvement activity

Anemia is common blood disorder that affects people of all age groups.[35] It is marked by reduced red blood cell (RBC) count or packed cell volume (PCV) and hemoglobin (Hb) levels.[87] Iron deficiency-induced anemia negatively affects motor and cognitive development, thus results in fatigue, and low productivity. During parturition, it may be linked with reduced birth weight and increased risk of maternal and perinatal death.[88,89] In 2013, iron deficiency anemia accounted for approximately 90,000 deaths in both sexes of all age groups in developing nations.[90] Anemia is one of the several maladies asserted to have been successfully treated with plant principles by herb doctors.[35] In recent past, an assortment of natural compounds from plant extracts has been studied by different researchers[91] for their antianemic activities. It was reported that consequent upon administration, the methanolic leaf extract of *T. occidentalis* stimulated significant erythropoietin and leukopoietin in mice.[47] Atabo *et al.*[44] demonstrated that leaf, seed, and stem extracts of fluted pumpkin have the capacity to lower endogenous methemoglobin (metHb) concentration by converting metHb to Hb at a high rate. Ogbe *et al.*[35] found that oral daily dose of *T. occidentalis* showed significant antianemic activity in phenylhydrazine-induced anemia in rabbits. Significant increase in Hb was also reported by Iweala and Obidoa.[30] Dina *et al.*[26] documented the hematinic activity of the aqueous crude extract. According to the findings of Alada,[25] preparations of fluted pumpkin significantly increased PCV, Hb concentrations, RBC, and white blood cell (WBC) counts. The antianemic property of *T. occidentalis* extracts validates its use in folklore medicine for the treatment of anemia.[35] Fluted pumpkin has also been reported to significantly increase erythrocyte count and repress erythrocyte osmofragility in albino rats.[49] Oboh *et al.*[50] in their work, documented that unprocessed leaf extract of fluted pumpkin significantly suppressed the activities of enzymes associated with type-II diabetes.

Anticancer activity

Cancer is a general term for a vast group of diseases that can affect any organ of the body. The term cancer is used interchangeably with malignant tumors and neoplasms. It is characterized by rapid proliferation of aberrant cells that grow uncontrollably and can spread to invade nearby organs (A process known as metastasis). Mortality from tumors is mainly due to metastasis. As one of the leading causes of death worldwide, cancer was responsible for 8.8 million deaths in 2015.[92] Inadequate consumption of fruits and vegetables, high body mass index, lack of physical activities, alcohol, and tobacco use have been implicated as the five leading dietary and behavioural risks that cause cancer.[92] The utilization of herbal medicines in chemoprevention is considered as an ideal treatment that is efficacious with few side effects compared to orthodox drugs.[93] Tropical plants are known to be potential sources for the screening of anticancer compounds.[94] Adetutu and Tijani, 2013[38] reported the anticlastogenic property of the leaf extract of *T. occidentalis* in bone marrow of mice exposed to sodium arsenite. Ejike and Ezeanyika, 2011[33] studied the benign prostatic hyperplasia-inhibiting potential of the seed extract of fluted pumpkin. From their study, it was observed that diet fortified with *T. occidentalis* seeds repressed growth of abnormal prostatic cells. Okokon *et al.*[32] in their findings, demonstrated that the seed extract and fractions of fluted pumpkin exhibited significant antitumor activity against HeLa cell lines. *T. occidentalis* is rich in polyphenols and flavonoids which have both been documented to possess anticancer properties.[95]

Anxiolytic and sedative

Anxiety disorders are a group of mental disorders associated with feelings of fear and anxiety. Symptoms may vary from mild to severe. Anxiety disorder is more a chronic than an episodic disorder due to the duration of symptoms experienced by people.[96] Benzodiazepines are presently the most largely prescribed drugs for anxiety disorder. Nevertheless, contraindications such as psychomotor impairment, potentiation of other central depressant drugs and dependence liability have been reported with the medical use of benzodiazepines. Medicinal plants are potential sources of novel remedies for anxiety disorders.[97] The hydroethanolic extract of *T. occidentalis* has been reported to possess anxiolytic activity at lower concentrations and sedative activity at higher concentrations.[39]

Renal protection activity

Over one-fifth of individuals between the ages of 65 and 74 years are living with chronic kidney disease.[98] Oxidative stress has been implicated as a key factor that contributes to renal damage.[98] Antioxidants from medicinal plants have the capacity to mitigate oxidative stress-induced kidney damage by enhancing the free radical scavenging activity of antioxidant defense systems and reducing lipid peroxidation.[98] The work of Maduka *et al.*[48] showed that the aqueous leaf extract of *T. occidentalis* was capable of reversing gentamycin-induced renal damage in Wistar rats when administered concomitantly with gentamycin.

Anticonvulsant activity

Seizures are caused by excessive electrical impulses in a group of cells located in different parts of the brain. It can range from brief lapses of attention or muscle jerks to prolonged and severe convulsions.[99] From time immemorial, medicinal plants have been used for the treatment of epilepsy and convulsive disorders.[100] Albeit different kinds of anticonvulsant drugs are available for the treatment of convulsion, they are not suitable due to their side effects and interactions. Several medicinal plants have been investigated for their anticonvulsant activity.[101] According to Akindele *et al.*,[42] fluted pumpkin ethanolic leaf extract exhibited anticonvulsant and muscle relaxation properties in mouse models.

CONCLUSION

African indigenous leafy vegetables possess a reservoir of healing properties that sick and recuperating persons can take advantage of.[102] Currently, the use of herbal remedies for the treatment of diseases is gaining popularity. Drugs obtained from botanical sources have been demonstrated to be efficacious, with low side effect profiles compared to their synthetic analogs. This review has highlighted the many potentials that *T. occidentalis* has to offer as a medicinal plant. As the search for potent medicines from herbal sources continues to attract growing interests, future prospects would be to identify, isolate, and elucidate the structure of pharmaceutical principles responsible for the curative properties of fluted pumpkin. Furthermore, the mechanisms by which these compounds exert their therapeutic effects is another area of research that would be worth investigating.

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Conflicts of interest

There are no conflicts of interest.

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