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Therapeutic uses of *Amaranthus caudatus* L.

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Abstract. The use of plants as therapy is not alien to man. Among plants that could offer novel choice to the limited therapeutic alternatives is *Amaranthus caudatus*. It is typically rich in bioactive compounds such as phenolic acids, lycopene, polyphenols, unsaturated fatty acids, glucosinolates, proteins, soluble peptides, flavonoids, squalene and beta-carotene to say the least. As widely reported in the literature, its various capacities to fight diseases when ingested as food or medicine may not be unconnected to these bioactive compounds available in high concentrations. This current review, therefore, harmonized reports from scientific investigations that validated the use of *A. caudatus* for the treatment of various ailments such as Diabetes mellitus, cancer, malaria, hypercholesterolemia, atherosclerosis, helminthic and bacterial infections, inflammation, hepatic diseases and cardiovascular complications. With this, we hope to put in perspective, the key therapeutic options available in the plant.

INTRODUCTION

From time immemorial, raw extracts from plants have been used for the treatment of various diseases. In the recent time, extracts from different plant parts are being used to complement conventional medicine by using diagnostic and therapeutic strategies outside orthodox medicine in the treatment of various ailments (WHO, 2002; Zollman and Vickers, 1999). This involves different mechanisms such as immune regulation, antiplatelet activity, antioxidant activity, inhibition of leukotriene B4 which causes inflammation (Triantafyllidi *et al.*, 2015). Of great note is the rising concern on safety and side effects of the use of synthetic drugs compared to drugs from natural sources in the management of chronic diseases (WHO, 2002). Endorsement of plant materials globally as viable alternatives has therefore made imperative, large-scale clinical studies on the assessment of natural substances in plants. As for the developed countries, the use of herbal medicine for chronic diseases is encouraged because there is concern about the adverse effects of chemical drugs; and treatments using medicines of natural origin appears to offer more gentle means of managing such diseases (WHO, 2002).

Information on traditional use of plants as medicine has played a key role in the discovery of novel products from plants as people transfer information from one generation to another in a successive manner (Agra *et al.*, 2007; Almeida *et al.*, 2001; Barbosa-Filho *et al.*, 2006; Rocha *et al.*, 2005). Globally, different parts of amaranths are processed into various decoctions, concoction and as soup served to patient as part of traditional medicine, especially in Latin America, India and Africa where the indigenous therapeutic system is prevalent.

Apart from being an important crop for over two-thirds of towns that constituted the Aztec empire, extracts from *Amaranthus* species have been used in different ways by inhabitants of ancient Japanese Peninsula, Nepal, Thailand and in traditional Chinese medicine to treat various diseases such as diabetes, urinary failure, cardiovascular complications, gynaecological disorders, pulmonary problems, jaundice and other infections (Caselato-Sousa and Amaya-Farfan, 2012).

Available information on medicinal uses of *Amaranthus* spp. in pharmaceutical industries suggests more attention should be focused on separation and characterization of bioactive compounds having medicinal properties (Rastogi and Shukla, 2011). Thus, *A. caudatus* can be a future crop for various purposes and can solve the problem of malnutrition, especially in developed countries where the plant is being under-utilized (Jimoh *et al.*, 2018). *A. caudatus* was a very important crop in the pre-Columbian era in South America for years. The Incas placed much value on it like other cereals and potatoes. This was probably due to its huge genetic variability, phenotypic plasticity, high yield and adaptation to marginal environments (Repo-Carrasco-Valencia *et al.*, 2010).

Bioactive compounds in *A. caudatus*

Amaranthus species have been widely reported to contain bioactive compounds such as phenolic acids, lycopene, polyphenols, unsaturated fatty acids, glucosinolates, proteins, soluble peptides, flavonoids, squalene and beta-carotene in typically high concentration which are capable of curing diseases like constipation, diarrhoea, hyperlipidaemia (De la Rosa *et al.*, 2009; Paśko *et al.*, 2008;). Also reported as the main component of amaranth shoots and seeds were ferulic, caffeic and p-coumaric acids; betalains, amaranthin and its isomers; quercetin, amaricin, amaranthoside, carotenoids and flavonoids such as nicotiflorin, isoquercitrin and rutin (De la Rosa *et al.*, 2009; Martirosyan *et al.*, 2004; Oboh *et al.*, 2008; Paśko *et al.*, 2008). The contents and concentration of all these were shown to have been influenced by many factors such as climate, genotype, environment, experimental locations and method of extraction (Steffensen, 2011).

Various concentrations of individual phenolic compounds such as gallic acid, protocatechuic acid, salicylic acids, chlorogenic acid, gentistic acid, 2,4-dihydroxybenzoic acid, ferulic acid, quercetin, rutin, kaempferol-3-rutinoside and ellagic acid have been reported in different parts of *A. caudatus* (Li *et al.*, 2015). Depending on the method of analysis employed, a number of variations have been reported in types and concentrations of flavonoids found in *A. caudatus* (Jimoh *et al.*, 2019). This accounts for the reason why different flavonoids were reported by Repo-Carrasco-Valencia *et al.* (2010) and Klimczak *et al.* (2002) for the same plant. While vanillic and sinapinic acids were not reported by Klimczak *et al.* (2002); p-coumaric acid, ferulic acid, caffeic acid, and protocatechuic acids were not found in quantifiable amount in another study conducted by Repo-Carrasco-Valencia *et al.* (2010).

Although they were first extracted from Beta vulgaris, the deep red coloured pigments; betalains are also found in *A. caudatus* where they form the major part of the drooping inflorescence but sparingly in leaf and stem (Salisbury 1991; Strack *et al.*, 2003). Unlike anthocyanin, betalains contain nitrogen and this made them differ structurally and chemically from anthocyanins although the two have never been reported to coexist in a plant except when the plant is genetically modified (Brockington *et al.*, 2011; Harris *et al.*, 2012; Robinson, 1963; Stafford, 1994).

The biosynthesis of amaranthin, a component of betalain in *A. caudatus* reduces the amount of cellulose, protein, and lignins in the leaves (Gins *et al.*, 2002). Amaranthin occurs both in light and dark periods although more yields are gotten under the influence of white light; the presence of gibberellic acid may inhibit its synthesis in the presence or absence of light (Bianco-Colomas, 1980; Rast *et al.*, 1972; Woodhead and Swain, 1974). Betalains have been recognized for their antioxidant properties and their activities in preventing oxidation of low-density lipoprotein. For this purpose, they are important in the commercial production of natural dye for food and pharmaceutical industries (Escribano, 1998; Li *et al.*, 2015; Tesoriere *et al.*, 2004).

Oxidative stress and degenerative diseases

Many chronic diseases such as cancer, diabetes, heart failure, atherosclerosis, ageing, immunosuppression, neuro-degeneration and other degenerative diseases are consequences of free radicals induced damage to tissues and cells (Young and Woodside, 2001). In biological systems such as cells and tissue, these radicals (mostly oxygen derivatives) are very reactive; they bind easily with pathogenic transition metals (copper and iron) in the body system by either donating or accepting electrons in a systemic oxidative or reductive reaction (Halliwell, 1989; Stohs and Bagchi, 1995). The need to protect cellular apparatus from reactive radical-induced damages makes the presence of both endogenous and exogenous anti-oxidants compelling (Young and Woodside, 2001).

The mechanisms of manifestations of oxidative stress have been described in many chronic diseases such as cancer, ageing, atherosclerosis, and inflammations; conditions which may lead to damages or eventual death of the affected cells (Ashok & Ali, 1999; Hecht, 1999; Rosenfeld, 1998; Young & Woodside, 2001). Antioxidant molecules, therefore, protect cells from damages by creating a defence mechanism that stops adverse effects of free radicals. These molecules are abundant in flowers and leaves of *Amaranthus* species due to the presence of betalains and flavonoids in appreciable concentrations (Kraujalis *et al.*, 2013; Peter and Gandhi, 2017; Strack *et al.*, 2003).

Antioxidant activity of *Amaranthus caudatus*

Evidence from clinical and epidemiological studies have proven that antioxidants mainly flavonoids derived from vegetables are key contributing factors to the reduced occurrences of chronic diseases (Greenwell and Rahman, 2015; Hertog *et al.*, 1993; Rimm *et al.*, 1996; Shahidi, 2000). A number of researchers have investigated antioxidant properties of *A. caudatus*. Conforti *et al.*, (2005) investigated antioxidant potency of two varieties of *A. caudatus*' extracts using different media and reported that ethyl acetate extracts of both varieties showed a high antioxidant activity; although compounds responsible for the activity seem unclear. It was suggested in the same work that *A. caudatus* has a rich source of squalene making it a cheap substitute for marine animals.

Compared to other cereals, *A. caudatus* has high radical scavenging activity (Awika *et al.*, 2003; Repo-Carrasco-Valencia, 2010). After cooking, there was a drastic reduction in antioxidant activity of two varieties of *A. caudatus* between 16-56% and 29-58% of the raw value, suggesting that cooking causes loss of antioxidant property (Repo-Carrasco-Valencia, 2010). The same was observed when different varieties of corns were processed into chips (Pozo-Insfran *et al.*, 2007). This implies that cooking has depleting effects on the antioxidant potency of amaranth's extract.

In addition to the above, amaranth extract was shown to have induced a regression in serum lipids and oxidative stress which has been touted to be important in the physiopathology of common chronic diseases such as diabetes, renal failure, and atherosclerosis (Young and Woodside, 2001). This and other reports on bioefficacy of *A. caudatus* extract have presented this species as a natural antioxidant reserve capable of safeguarding body cells against oxidative stress and supplementing nutrient deficiencies which may lead to chronic dysfunction of the entire body system if left unattended (Jimoh *et al.*, 2019).

Antidiabetic properties

The hallmark of diabetes is the impairment of metabolic engine of the body due to high concentrations of glucose in the blood. The body system is pushed to glucose intolerance level and when this is attained, insulin production becomes impaired thereby leading to poor utilization or assimilation of nutrients (the WHO, 1991; WHO, 2008). Over the years, several hypoglycaemic drugs have been synthesized as remedies for diabetes but they pose grave side effects particularly to pregnant women. This has made pertinent, the search for medicinal plants that contain safer compounds of high hypoglycaemic potency as a cheap but viable alternative to combating diabetes considering that about 800 plants with potential antidiabetic properties have been reported in ethnobotanical surveys (Alarcon-Aguilara *et al.*, 1998; Conforti *et al.*, 2005; Odhav *et al.*, 2013; the WHO, 1980; WHO, 2002).

Reports from independent investigations of antidiabetic activities of some medicinal plants have revealed that extracts derived from *Amaranthus* spp. showed high activity against α-amylase (Clemente and Desai, 2011; Pandhare *et al.*, 2012; Peter and Gandhi, 2017; Sasikumar *et al.*, 2015). Also, Conforti *et al.* (2005) reported high inhibitory effects of hexane, methanolic and ethyl acetate extracts of two varieties of *A. caudatus* on α-amylase; and in that work, squalene isolated from the plant extract was recognised as the major component of hexane extracts and its antidiabetic properties was found to be higher than synthetic squalene.

A dosage of 400mg/kg of the methanolic extract of *A. caudatus* was found to show high antidiabetic activity when administered to normal and streptozotocin-induced diabetic rats over a period of twenty-one days (Girija *et al.*, 2011). This was investigated alongside other two amaranth species; *A. spinosus* and *A. viridis* where the same effects were observed. Also, Zambrana *et al.* (2018) reported that hydro-ethanolic extract of *A. caudatus* improves glucose tolerance in Goto-Kakizaki Rats and Wister rats by increasing serum insulin levels. In this model for Diabetes Mellitus Type 2, an oral administration of 2000 mg of the extract per kg body weight was examined to have improved glucose tolerance in both rats. In the long run, a lower dosage of the extract (1000 mg/kg body weight) was also seen to influence glucose tolerance over a long period of time (21 days). From these reports, it could be concluded that *A. caudatus* is beneficial to diabetic patients as it plays a key role in inhibiting α-amylase effects, coupled with dietary benefits (Girija *et al.*, 2011; Kaur *et al.*, 2010; Odhav *et al.*, 2013).

Anthelminthic activity

Helminthic infections have been reported to have affected two billion people in the world (Hotez *et al.*, 2008; Kumar *et al.*, 2010). The adverse effects of these parasitic worms have led to impairment of cognitive fitness, physical strength, and stunting growth, especially in school-aged children. Such disabling effects have resulted in recurring adversity among populations found in impoverished populations of the world (Crompton and Nesheim, 2002).

Despite their high prevalence and the medical burden helminths have constituted, the number of anthelminthic drugs available is remarkably low considering that human helminths are the most common infections in the world (Hotez *et al.*, 2008; Idris *et al.*, 2017). In addition, there is dearth of knowledge on characteristic mechanisms by which these parasitic worms escape host immune system, defeat body defences, and institute infections by making the body susceptible to killer diseases (Crompton and Nesheim, 2002).

The use of some plant extracts has been found to be potent worm expellers than many synthetic drugs. This became necessary due to high cost and attendant side effects of drugs. Herbal remedies for the treatment of parasitic worms have been proven to have a broad spectrum of activity, easily accessible and very affordable (Mali and Mehta, 2008). Typical examples of such plants are *Xylopia aethiopica*, *Anacardium occidentalis*, *Piliostigma thonningii*, *Piper longum*, *Carica papaya*, *Gynandropsis* *gynandra*, *Nigella sativa*, *Nicotiana tabaccum*, *Trachyspermum ammi*, *Artemisia capillaries*, *Cannabis sativa*, *Allium sativum*, *Rumex crispus*, *Manihot esculentus* and a host of others (Agarwal *et al.*, 1979; Ajaiyeoba *et al.*, 2001; Badar *et al.*, 2017; Idris *et al.*, 2017; Iqbal *et al.*, 2006; Roy & Tandon, 2010).

Apart from plants listed above, folk claims on the wormicidal activity of amaranth species have been validated in various research works (Athanasiadou *et al.*, 2007; Baral *et al.*, 2010; Kumar *et al.*, 2011; Reyad-ul-Ferdous, 2015). It has also been established in literature that *A. caudatus* has potent vermifugal property. Kumar *et al.* (2010) compared the wormicidal effect of methanolic extract of *A. caudatus* with a renowned worm expeller, piperazine and observed that unlike piperazine that has the only paralytic effect on worms, the plant extract was able to kill an adult *Pheretima posthuma* (which is structurally similar to human annelids) after paralyzing it. In the experiment, methanolic extract of the plant was observed to have shown a progressive dose-dependent anthelminthic effect from the loss of motility to paralysis and to the eventual death of the Indian worm (Kumar *et al.*, 2010). The significant vermifugal effect may be attributed to the presence of polyphenolic compounds in the plant as reported severally in its phytochemical evaluations (Jimoh *et al.*, 2019; Manach *et al.*, 2004; Repo-Carrasco-Valencia *et al.*, 2010).

Anticancer potency

Undoubtedly, cancer has become a life-threatening disease in developing and advanced countries being the second leading cause of death throughout the world. Nearly 1 out of every 6 death cases recorded globally is due to cancer (WHO, 2017). In 2012, 8.2 million cancer-related deaths were recorded worldwide while in 2015, 8.8 million deaths were recorded due to cancer and in the next two decades, it has been projected that new cases of cancer will rise to 22 million affecting majorly, South and Central America, Asia and Africa (Siegel *et al.*, 2018; WHO, 2017).

Over the years, a lot of progress has been recorded in the diagnosis and cure of cancer through chemotherapy, surgery, hormonal therapy, radiation therapy and synthetic lethality depending on level or position of a tumour. However, these treatments do not offer complete solution desired. This is evident in the reversion of tumour cells into regenerated and differentiated progenies (Bandhavkar, 2016). Therefore, the demand for an alternative cure for cancer keeps growing.

Naturally occurring anticancer agents are embedded in the plant tissues. These compounds occur as secondary metabolites and there is rising interest in their exploitation for the development of drugs of plant origin as a safe, effective and cheap alternative to reigning chemotherapy (Greenwell & Rahman, 2015; Ren *et al.*, 2003). Findings from pharmacological evaluation of some plant species have aided development of plant-made drugs as alternative treatment for cancer owing to their antiproliferative activities on cancer cell growth without causing harm to non-targeted cells (Ariga & Seki, 2006; Jung *et al.*, 2011; Malíková *et al.*, 2008; Ochwang'i *et al.*, 2014; Sivaraj *et al.*, 2014; Sultana *et al.*, 2014; Thomson & Ali, 2003).

Amaranths have been evaluated to be rich in these bioactive compounds capable of inhibiting proliferation of cancer cells (Martirosyan *et al.*, 2004; Venskutonis *et al.*, 2013). Silva-Sánchez *et al.* (2008) characterized and investigated the anticarcinogenic activity of peptide lunasin found in *Amaranthus hypochondriacus* seeds. Also, a dosage of 50µg/ml of galactosyldiacylglycerols, a compound extracted from *Amaranthus tricolor* has been reported to have shown high activity against proliferative tendencies of cancer cell lines in cyclooxygenase inhibitory assay (Jayaprakasam *et al.*, 2004). In addition, Sreelatha *et al.* (2012) reported the protective effect of ethanolic leaf extract of *Amaranthus paniculatus* administered on Ehrlich's ascites carcinoma (EAC) treated mice at different doses. It was found that the extract initiated a significant reduction in the number, volume, and weight of tumour cells, thereby improving the well-being of the EAC induced mice.

In another series of experiments, Quiroga *et al.* (2015) examined inhibition of tumour cell proliferation by lectin derived from *A. caudatus* which showed high activity with an IC_{50}=0.08 mg/ml and concluded that the amaranth lectin was five times stronger than the refined lectin. The outcome of this research profiled lectins obtained from plants as prospective solutions to cancer at both clinical and preclinical trials (Ernst *et al.*, 2003; Lam & Ng, 2011; Rinderle *et al.*, 1989).

Antimalarial and antibacterial activity

A. caudatus is a vital constituent used in the formulation of SAABMAL®, a polyherbal medicine reputed for antiplasmodial activity (Obidike *et al.*, 2015). In dose-dependent assays, SAABMAL® caused curative, prophylactic and suppressive effects on malaria parasites relatively to the untreated control group. For prophylactic antimalarial activity, a 400 mg dose of SAABMAL®/kg was observed to be similar to that of pyrimethamine, previously used for malaria treatment while for curative activity, 100 and 200 mg/kg dosage was found more effective than the control-treated chloroquine. For suppressive effect on plasmodium parasite, a 400 mg/kg dose of SAABMAL® significantly suppressed malaria in a manner comparable to chloroquine. *A. caudatus*, therefore, plays a synergistic effect with other medicinal plants that constitute a polyherbal remedy (Obidike *et al.*, 2015).

Broekaert *et al.* (1992) also isolated and characterized two antimicrobial peptides (Ac-AMP1 and Ac-AMP2) derived from *A. caudatus* and compared them with glycine/cysteine-rich domain of chitin- binding proteins using their biological and physico-chemical activity. The study reported that both peptides were able to inhibit growth of fungi at much lower doses than other recognised antifungal chitin-binding proteins. Also, the antibacterial effect of ethanolic extract of the plant has been reported to be more effective than the one derived from chloroform and petroleum ether solvents when it was screened for antibacterial activity using three Gram-negative and three Gram-positive bacteria (Maiyo *et al.*, 2010).

Anticholesteromic, antihypercholestromic and atherosclerotic regression activity

Plate and Areas (2002) and Kabiri *et al.* (2011) examined the low-density lipoprotein cholesterol-depressing activity of extruded *A. caudatus* leaves in hypercholesteraemic rabbits and they concluded that eating extruded amaranth lowers cholesterol level and prevents atherosclerosis and other associated heart infections. In addition, the potency of *A. caudatus* extract was said to be more effective compared with lovastatin, a drug used for lowering cholesterol level in hypercholesteraemic individuals. When both (amaranth extract and lovastatin) were administered to rabbits, *A. caudatus* caused a significant reduction in cholesterol, lesion severity and atherosclerotic risks (Kabiri *et al.*, 2010).

From other investigations, anti-cholesterolemic activity of extruded amaranth has been attributed to different components of the plant such as fibres (Qureshi *et al.*, 1996); squalene (Becker *et al.*, 1981); tocopherols and toco-trienols (Lehmann *et al.*, 1994); proteins (West *et al.*, 1984); and unsaturated fatty acids (Plate and Areas 2002).

A similar evaluation of the hypo-cholesterolemic effect of amaranth protein in experimental hypercholesterolemia hamsters proposed that an intake of amaranth protein could result in a remarkable drop in low-density lipoprotein-cholesterol due to its high digestibility, leading to the synthesis of bioactive peptides that affects cholesterol absorption (Mendonça *et al.*, 2009). It could be inferred from the above that amaranth protein could either be used to complement or replace diet in hypercholesteraemic hamsters.

In a related research, Chávez-Jáuregui *et al.* (2010) investigated the effects of snacks fortified with defatted *A. caudatus* on plasma lipids in patients suffering from moderate hypercholesterolemia and observed a significant reduction in highdensity lipoprotein (HDL) plasma levels due to amaranth consumption. It was also observed that cholesterol level reduced in patients that were fed with amaranth snacks for 60 days although the reduction was not so significant. In addition, a daily consumption of 1-3grams of the plant can reduce blood cholesterol by 10% in human when complemented with a rich diet; an indication that the plant could create a panacea for a significant relief in patients with hypercholesteraemic concerns (Villacrés *et al.*, 2013). Based on this, further findings are recommended to establish the effect of amaranth consumption on lipid metabolism in humans.

Cardiovascular protection

Oxidative stress has been reported to contribute largely to the development of cardiovascular diseases. The degree of oxidative stress and antioxidant defence capacity determine the susceptibility of vascular cells to oxidative tension (Higashi *et al.*, 2009). Cardiovascular disorder is a leading cause of disability and death globally (Reddy and Katan, 2004). It was projected that by year 2030, cardiovascular diseases would have resulted in 23.3 million deaths globally, particularly in developing countries (Mathers & Loncar, 2006).

Vegetables are a rich source of dietary flavonoids and other phytochemicals that promote the body's defence mechanism. They protect the epithelial layers of cardiovascular organs from stroke and other tension that may arise from dysfunction due to an inverse relationship between these polyphenolic antioxidants and cardiac arrest (Caselato-Sousa and Amaya-Farfan, 2012; Higashi *et al.*, 2009; Reddy and Katan, 2004). Also, the bioavailability of dietary nutrients such as calcium, magnesium and potassium has been assumed to have protective effects on cardiovascular organs (Ferreira and Arêas, 2010; Krishna *et al.*, 1989; Reddy and Katan, 2004; Young *et al.*, 1995). This is achievable through daily consumption of vegetables and fruits. For example, an intake of potassium at concentrations of 70-80mol/day could be achieved through adequate consumption of vegetables and this will help in maintaining the sodium-potassium balance at an acceptable level as a higher amount of potassium could trigger cardiovascular tension (Reddy and Katan, 2004).

Hepatoprotective function

The liver is an important organ that regulates a number of physiological activities in the body. It plays a major role in processes such as synthesis, secretion (bile), storage (vitamins), metabolism (carbohydrate and fats) and detoxification of both exogenous and endogenous wastes (Ahsan *et al.*, 2009; Madrigal-Santillán *et al.*, 2014). Hepatic cells are contractile cells located in the perisinusoidal region of the liver. The diagnostic state of the hepatic cells plays a major role in the pathophysiology of the liver (Eng and Friedman, 2000). Because of the central function of the liver in the biochemical mechanisms of the body, any damage to the hepatic cells caused by autoimmune diseases and other biological agents such as parasites, bacteria and virus; and undoubtedly, indiscriminate intake of alcohol results in malfunctioning of the liver (Deshwal *et al.*, 2011).

Hepatic diseases, therefore, constitute a major risk to public wellbeing and globally, a concerted effort is being made to address the threat. In spite of this, modern therapy has not been able to offer a definite solution to ways of rejuvenating hepatic cells or protecting the liver itself due to side effects induced by some synthetic drugs that may trigger another danger to the liver (Chattopadhyay, 2003; Madrigal-Santillán *et al.*, 2014). Hence, it is imperative to source an alternative but more effective remedy from herbs and other medicinal plants that are rich in phytochemicals capable of curing liver diseases.

The use of plants for protection of the liver and cure of hepatic diseases is an important interest of phytomedicine. (Adewusi and Afolayan, 2010) had reported hepatoprotective potency of some 107 plant species from 47 families whose extracts have been found helpful in the treatment of liver diseases. In a report compiled on 170 medicinal plants used for the treatment of liver diseases, Govind (2011) reported that *Amaranthus* spp. promote resistance against infections from disease agents by rejuvenating host immune system of the liver (Domitrović and Potočnjak, 2016; Kumar *et al*., 2010; Rahmatullahi *et al*., 2013; Rjeibi *et al*., 2016; Singh *et al*., 2013; Zeashan *et al*., 2008).

Also, methanolic extract of *A. caudatus* was reported for its high hepatoprotective activity when administered on Wister rats with paracetamol-induced liver damages at 200 and 400mg/kg doses (Kumar *et al*., 2011). In addition, amaranthin, a lectin found in *A. caudatus* is an important component of *A. caudatus* agglutinin (ACA), an identifier for both NeuAcα2–3Galβ1–3GalNAcα-O- and Galβ1–3GalNAcα-O-; important glycoprotein conjugates which have been reported as pancarcinoma antigens that detect and prevent the recurrence of hepatocellular carcinoma in man (Cao *et al*., 1999; Chachadi *et al*., 2011; Kumar *et al*., 2011; Rinderle *et al*., 1989).

CONCLUSION

The nutraceutical properties of *A. caudatus* have repositioned it as a staple source of phytonutrients needed for a healthy living. It is equally important to note that the plant offers alternative remedies to various diseases affecting man (Table 1) and despite this potential; it is being underexploited as a source of food and medicine in Africa and other parts of the world. This has necessitated further research into the influence of environment which includes soil types on the qualitative and quantitative differences in the active metabolites in the species. This review, therefore, highlighted the use of the plant from therapeutic standpoints and proposes a detailed investigation of the effects of soil types on medicinal properties or the mineral load of these metabolites, having not been well defined in the literature.

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Table 1. Summary of therapeutic use of *Amaranthus caudatus*

S/N	Therapeutic use	Media of extraction	Plant parts	Model	Pharmacological effect	Dosage	References
1	Antidiabetics	Hexane	Seeds	Wister rat	Plant extract's squalene is higher than synthetic squalene.		Conforti *et al.*, 2005
		Hydro-ethanolic	Seeds	Wister rat		2000mg/kg	Zambrana *et al.*, 2018
		Methanol	Seeds, leaves	Wister rat	High activity on streptozotocin-induced diabetic rats	400mg/kg	Conforti *et al.*, 2005; Girija *et al.*, 2011
		Ethyl acetate	Seeds	Wister rat			Conforti *et al.*, 2005
2	Helminthic infections	Methanol	Whole plant	Pheretima posthuma	Higher activity than Piperazine		Kumar *et al.*, 2010
3	Anticancer	Commercial *A. caudatus* lectin		Tumor cells	Cell apoptosis	0.1 mg/ml & 0.08 mg/ml	Quiroga *et al.*, 2015
4	Antimalarial	Polyherbal	Whole plant	SAABMAL® polyherbal	Polyherbal remedy	100 and 200 mg/kg	Obidike *et al.*, 2015
5	Antibacterial, antimicrobial & antifungal	Chitin binding proteins	Seeds	Fast atom bombardment mass spectroscopy	Inhibition of pathogenic fungi and activity against gram +ve bacteria		Broekaert *et al.*, 1992; Das & Kumar, 2013; Verheyden *et al.*,1995
6	Antihypercholestromic		Leaf		significant reduction in cholesterol	Artherosclerotic regression	Plate and Areas, 2002; Mendonça *et al.*, 2009 and Kabir *et al.*, 2011.
7	Hepatoprotective function	Paracetamol-induced liver damages	Leaf	Wister rats	Hepatogenic activity	200 and 400mg/kg	Kumar *et al.*, 2011
8	Cardiovascular protection	hydroalcoholic	Plant shoot	Rabbits	Regression of fatty lesions in aorta	150 mg/kg day	Kabiri *et al.*, 2011
9	Biotin deficiency	Consumption of 25g amaranth/day	Leaf and stem	Paediatric patient	Correction of biotin deficiency	10mg biotin/day	Guzmán-Maldonado & Paredes-López, 1998

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