

# *Amaranthus dubius* L.: Ethnomedicinal Significance, Phytochemical Profile, and Therapeutic Potential: A Review

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## ABSTRACT

*Amaranthus dubius*, also known as red spinach, is widely recognized for its therapeutic potential in traditional medicine, particularly across tropical and subtropical regions. This review compiles and analyses ethnomedicinal, phytochemical, and pharmacological data on *A. dubius*, underlining its applications in managing various ailments and its potential for development into modern therapeutics. Traditionally, *A. dubius* has been used to treat conditions such as anaemia, inflammation, digestive disorders, and fever, with high nutritional value reinforcing its role in health maintenance. Phytochemical investigations highlight a spectrum of bioactive compounds, including betacyanins, phenolic acids (e.g., Gallic and Vanillic acids), flavonoids (like quercetin, luteolin, and naringenin), and phytosterols, which are responsible for its broad therapeutic activities. Pharmacological studies have demonstrated that *A. dubius* possesses potent antioxidant, anti-inflammatory, hepatoprotective, antiviral, and antianemic properties. The antioxidant effects, primarily from its phenolic and flavonoid constituents, protect against oxidative damage, while anti-inflammatory properties aid in modulating immune responses. Recent research indicates that betacyanins from *A. dubius* exhibit antiviral effects against Dengue Virus Type 2 (DENV-2), and its antianemic activity is supported by evidence showing enhanced haemoglobin levels. Collectively, these findings position *A. dubius* as a promising source of bioactive compounds for managing chronic diseases, infectious conditions, and inflammation, warranting further research into its mechanisms of action and therapeutic efficacy in clinical settings.

**Keywords:** *Amaranthus dubius*, Bioactive Compounds, Pharmacological activities.

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**Received:** 09-04-2025;

**Revised:** 14-06-2025;

**Accepted:** 25-08-2025.

## INTRODUCTION

The *Amaranthus* genus comprises approximately 60 species, some cultivated as food grains, leafy vegetables, or ornamentals.<sup>[1]</sup> In the Caribbean, vegetable amaranth, particularly *Amaranthus dubius*, Mart. ex Thell. (Amaranthaceae) is a widely cultivated leafy vegetable in tropical and subtropical regions, particularly in Africa, Asia, and Latin.<sup>[2]</sup> Commonly referred to as "pira dulce," "bledo," or "bleo," it is extensively utilized in both culinary and medicinal practices.<sup>[3]</sup> Although frequently consumed in Venezuela, it is often considered a weed in rice fields. Due to its high nutritional value, it has been suggested for industrial applications, including flour production, protein concentrates, and hydrolysates. However, its high moisture content results in a

short postharvest shelf life, leading to rapid wilting under tropical conditions.<sup>[4]</sup> The plant is rich in bioactive compounds, making it significant in traditional medicine. Different parts of *A. dubius* are used due to their high protein content, essential minerals, and phytochemicals with pharmacological properties.<sup>[5,6]</sup>

## ETHNOMEDICINAL USES

*Amaranthus dubius* has been extensively used in traditional medicine across various cultures. In Africa and Asia, its leaves are commonly consumed as a leafy vegetable, often cooked with other greens such as *Solanum* spp., *Cleome gynandra*, and *Launaea cornuta*.<sup>[7,8]</sup> In Kenya, it is combined with other traditional vegetables, whereas in Benin, it is usually prepared alone. The leaves of *A. dubius* are recommended as a medicinal food for young children, lactating mothers, and patients suffering from fever, hemorrhage, anemia, constipation, or kidney-related disorders.<sup>[9]</sup> In Tanzania, the whole plant is used to treat stomach ailments. Ugandan communities incorporate *A. dubius* in the



DOI: 10.5530/pres.20252187

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preparation of potash, while Taiwanese aboriginal groups use the leaves and stems as a potherb. Beyond its dietary and medicinal applications, dried *Amaranthus* crops have been burned in Benin for potash preparation. In Senegal, the root is boiled with honey to act as a laxative for infants. In Ghana, macerated *Amaranthus* water is used as a wash for limb pain.<sup>[7]</sup> In Ethiopia, *A. cruentus*, a close relative of *A. dubius*, has been traditionally used as a tapeworm expellant. In Sudan and Gabon, ash derived from *Amaranthus* stems has been applied for wound dressing.<sup>[7]</sup> Additionally, *Amaranthus* is believed to assist individuals with low red blood cell counts, making it beneficial for anaemic patients. The plant is also classified among diuretics due to its ability to promote increased urine production (Grubben, 2004).<sup>[7,8]</sup> Several pharmacological activities have been attributed to *Amaranthus dubius*. It exhibits hepatoprotective, antioxidant, antiviral, antibacterial, anti-inflammatory, and antimalarial properties. The water extract of the plant has been shown to have significant immune-stimulating activity, and it has been used internally to treat excessive menstruation, diarrhea, and internal bleeding. Furthermore, *A. dubius* has been noted for its skincare benefits, helping to hydrate, detoxify, and improve skin elasticity, potentially reducing wrinkle. Due to its rich nutritional profile, including high protein content and bioactive compounds, *Amaranthus dubius* holds potential in both traditional medicine and modern nutritional applications. Further research into its protein identification and validation is needed to fully explore its industrial and pharmacological applications.<sup>[8]</sup>

### Phytochemical Profile of *A. dubius*

*Amaranthus dubius* is a rich source of bioactive compounds, though its profile is not yet fully explored. It contains essential vitamins such as B<sub>6</sub>, K, C, A, folate, and riboflavin, as well as significant levels of phenols, flavonoids, and alkaloids. Research on *Amaranthus* species has identified bioactive flavonoids and phenolic compounds, including rutin, kaempferol, isoquercetin, quercetin, catechin, apigenin, naringenin, and myricetin. These compounds exhibit potent antioxidant properties that mitigate oxidative stress, supporting cellular defense mechanisms and reducing the risk of chronic diseases. The presence of these bioactives highlights the potential of *A. dubius* as a functional food with therapeutic applications. In addition to vitamins and phenolics, *A. dubius* is enriched with secondary metabolites that confer diverse pharmacological benefits, primarily through antioxidant, anti-inflammatory, and anti-Acetylcholinesterase (AChE) activities. Key compounds like gallic acid, vanillic acid, and ellagic acid exhibit robust antioxidant effects by neutralizing free radicals, protecting cells from oxidative stress, and slowing disease progression. These activities are particularly beneficial in managing chronic conditions such as cardiovascular disease, diabetes, and cancer, as well as slowing cellular aging.<sup>[10-14]</sup>

Flavonoids such as quercetin, luteolin, and naringenin amplify the plant's therapeutic potential.<sup>[15]</sup> Their AChE-inhibitory

effects help maintain neurotransmitter balance by preventing the breakdown of acetylcholine, essential for cognitive health, muscle function, and digestion.<sup>[16]</sup> Quercetin and luteolin also reduce lipid peroxidation, which generates harmful by-products often associated with inflammatory diseases such as arthritis and liver disorders.<sup>[17]</sup> These actions make *A. dubius* supportive of organ health, particularly in the liver and cardiovascular system. Moreover, *A. dubius* contains fatty acids and phytosterols, including  $\beta$ -sitosterol, campesterol, and stigmasterol, which exhibit anti-inflammatory and cholesterol-lowering effects.<sup>[18]</sup> These compounds reduce harmful cholesterol levels, protect blood vessels from oxidative damage, and lower the risk of atherosclerosis and other cardiovascular conditions. By addressing both cholesterol management and inflammation, *A. dubius* contributes significantly to cardiovascular health.<sup>[19]</sup> The anti-inflammatory properties of *A. dubius* extends to conditions such as arthritis, asthma, and gastrointestinal disorders. By modulating inflammatory pathways, the plant helps alleviate pain and enhances immune function, offering therapeutic relief for a variety of inflammatory ailments. These benefits are supported by the synergistic activity of its phytochemicals, which include antioxidants like gallic acid, anti-inflammatory agents such as vanillic and ellagic acids, and AChE inhibitors like quercetin and luteolin.

## THERAPEUTIC POTENTIAL

### Hyperlipidemic and Hyperglycaemic

The study demonstrated that bread enriched with *A. dubius* flour at 100 g/kg and 200 g/kg showed beneficial effects on blood lipid and glucose levels in hyperlipidemic and hyperglycemic Sprague Dawley rats. Rats consuming these amaranth-based diets exhibited significant reductions in serum glucose, Triglycerides (TG), Total Cholesterol (TC), and Very Low-Density Lipoprotein Cholesterol (VLDL-C) levels, while showing an increase in High-Density Lipoprotein Cholesterol (HDL-C). Additionally, the abdominal circumference decreased significantly, indicating a reduction in visceral fat, which lowers the risk of metabolic syndrome. The hypolipidemic effect is likely attributed to the high dietary fiber content of *A. dubius*, especially insoluble fiber, which is known to aid in cholesterol reduction and improve intestinal health. The modest hypoglycemic effect observed may result from *A. dubius* components enhancing insulin synthesis or peripheral glucose utilization. These effects suggest that *A. dubius* could serve as a valuable dietary supplement for managing blood lipid and glucose levels, potentially reducing the risk of metabolic and cardiovascular diseases. Further research could determine the optimal concentration of *A. dubius* flour for maximum therapeutic benefit.<sup>[20,21]</sup>

### Anti-Inflammatory Activity

*Amaranthus dubius* leaves demonstrate significant anti-inflammatory activity, positioning the plant as a promising

candidate for managing inflammation-related conditions. Recent studies highlight *A. dubius* as a potent inhibitor of TNF- $\alpha$  release, a key mediator of inflammation, suggesting its potential in addressing chronic inflammatory diseases such as arthritis and inflammatory bowel disease. Its anti-inflammatory properties are closely linked to its antioxidant activity, which neutralizes free radicals and mitigates oxidative stress, a major contributor to inflammatory responses. The anti-inflammatory effects of *A. dubius* are supported by its role in traditional medicine, where it has been used to manage various ailments. The plant's ability to inhibit pro-inflammatory pathways provides a natural and accessible therapeutic option, especially in regions where it is commonly consumed as part of the local diet. Given the increasing demand for plant-based alternatives to synthetic drugs, *A. dubius* holds potential as a safe and effective natural remedy. Its integration into traditional diets and established ethnomedicinal use underscores its relevance as an anti-inflammatory agent. These findings open new opportunities for developing *A. dubius*-based therapies to address inflammation-related conditions, offering a sustainable and cost-effective solution, particularly for communities with limited access to conventional pharmaceuticals.<sup>[22]</sup>

### Antioxidant activity

This study examined the effects of cooking on the antioxidant activity of *A. dubius* commonly consumed in Western Uganda. Cooking methods like steaming and boiling significantly reduced the antioxidant potential of *A. dubius* due to the degradation of heat-sensitive compounds, particularly vitamins A and C, and the leaching of water-soluble antioxidants into the cooking water. However, despite this reduction, *A. dubius* retained a notable level of antioxidant activity, suggesting that its health benefits stem from more resilient compounds, including phenolics, flavonoids, and tannins. These compounds are less susceptible to thermal degradation and continue to contribute to the antioxidant capacity even after cooking. Antioxidant activity in *A. dubius* involves mechanisms such as the reduction of ferric to ferrous iron, indicating the presence of electron-donating compounds that mitigate oxidative stress by neutralizing harmful radicals. Cooking did decrease the reducing power of *A. dubius*, highlighting a loss in certain antioxidants. However, the vegetable still provides protective effects due to the presence of polyphenolic compounds. These bioactive compounds, particularly flavonoids, play a crucial role in stabilizing cell membranes and inhibiting oxidative damage to red blood cells, which is beneficial in preventing cellular oxidative stress. Thus, *A. dubius* remains a valuable source of dietary antioxidants even after cooking, offering health benefits despite some loss in potency. This finding is especially relevant in regions where the vegetable is often cooked before consumption, as it continues to deliver antioxidant protection even after typical culinary preparation.<sup>[23,24]</sup>

### Neuroprotective activity

This study underscores the neuroprotective potential of *A. dubius* protein extracts in addressing Alzheimer's Disease (AD)-related toxicity, particularly the cytotoxicity induced by beta-amyloid (A $\beta$ 1-40) aggregation. The protein extracts exhibited chaperone-like activity, effectively preventing the formation of A $\beta$ 1-40 fibrils, as confirmed by thioflavin T fluorescence and Dynamic Light Scattering (DLS) assays. Among the tested plant extracts, *A. dubius* showed the highest efficacy in inhibiting fibril formation, likely due to its superior chaperone activity. Furthermore, at non-toxic concentrations, *A. dubius* protein extracts protected SH-SY5Y neuroblastoma cells from A $\beta$ 1-40-induced toxicity, demonstrating their neuroprotective effects. These results highlight the potential of *A. dubius* as a promising natural approach to inhibit beta-amyloid aggregation, a key feature of AD pathology, with minimal side effects compared to conventional treatments.<sup>[27]</sup> In addition to its anti-aggregation properties, *A. dubius* was also shown to enhance cognitive function in a ketamine-induced AD-like dementia model in mice. The extract-treated mice exhibited significantly increased step-through latencies in the Passive Avoidance Task (PAT), suggesting a reversal of ketamine-induced cognitive decline. This improvement in cognition may be attributed to the inhibition of Acetylcholinesterase (AChE) activity, a hallmark of AD pathogenesis. AChE inhibition, which is the target of many AD treatments, supports the potential of *A. dubius* in alleviating cholinergic dysfunction and cognitive symptoms associated with AD. Moreover, *A. dubius* extract exhibited antioxidant properties, reducing oxidative stress in the brains of ketamine-treated mice, as indicated by lowered Malondialdehyde (MDA) levels. This suggests that the extract may protect neurons from oxidative damage, a significant contributor to cognitive decline in neurodegenerative disorders such as AD. The cognitive-enhancing effects observed were likely due to the synergistic action of various bioactive compounds, including flavonoids, phenols, and fatty acids, which possess antioxidant, anti-inflammatory, and AChE inhibitory activities. These findings position *A. dubius* as a potential therapeutic agent for managing cognitive dysfunction and neurodegenerative disorders like AD.<sup>[25-27]</sup>

### Anticancer activity

*A. dubius* has demonstrated notable anticancer potential, particularly in the MCF-7 breast cancer cell line. The aqueous extract of *A. dubius* exhibited the strongest cytotoxic activity, with an IC<sub>50</sub> value of 48.22 $\pm$ 3.65 mg/mL. In comparison, other extracts (*A. spinosus*, *A. caudatus*, and *A. viridis*) showed less potent effects, with IC<sub>50</sub> values of 64.90 $\pm$ 3.91, 96.12 $\pm$ 6.20, and 72.34 $\pm$ 4.88 mg/mL, respectively. This increased cytotoxicity in *A. dubius* may be attributed to its higher flavonoid content, which plays a key role in its anticancer effects. Furthermore, *A. dubius* demonstrated significant antioxidant activity, including hydroxyl radical scavenging and ferric reducing power, which are



essential mechanisms for protecting cells from oxidative damage. The higher flavonoid content in *A. dubius* likely contributes to both its antioxidant and anticancer activities, suggesting that the plant may not only reduce oxidative stress but also inhibit cancer cell proliferation. These findings highlight the potential of *A. dubius* as a valuable source of natural compounds for developing anticancer therapies.<sup>[28,29]</sup>

### Anti-Aging Properties

The study investigated the anti-aging properties of *A. dubius* leaves in the context of oxidative stress and cellular senescence, which are key contributors to Age-Related Diseases (ARDs). The phytochemical composition of the A.D. extract was analyzed using GC-MS, and its antioxidant properties, ability to scavenge free radicals and Hydrogen Peroxide ( $H_2O_2$ ), and potential for DNA damage protection were assessed. The results demonstrated that *A. dubius* extract exhibited strong antioxidant activity and was effective at scavenging  $H_2O_2$ , offering protection against DNA damage. Additionally, the extract showed potential in preventing cellular senescence, although it was not restorative. In terms of cytotoxicity, *A. dubius* appeared to be non-toxic to Human Dermal Fibroblast cells (HDF-a) after a 24-hr treatment. These findings suggest that *A. dubius* possesses promising anti-aging properties, primarily through its antioxidant and senescence-preventive effects, making it a potential candidate for developing supplements aimed at mitigating the risk of ARDs.<sup>[30]</sup>

### Anti-bacterial activity

The anti-bacterial activity of *A. dubius* was evaluated through the screening of its aqueous and ethanol leaf extracts against common pathogens, including *Staphylococcus aureus*, *Pseudomonas spp.*, and *Escherichia coli*. The *in vitro* antibacterial activity was assessed using the agar disc diffusion method. Both aqueous and ethanol extracts of *A. dubius* exhibited significant antimicrobial effects, with the highest activity observed against *E. coli*, followed by *S. aureus* and *Pseudomonas spp.* These findings support the traditional use of *A. dubius* in folk medicine as an effective antimicrobial agent. The results suggest that *A. dubius* contains bioactive compounds that could potentially be developed into novel antibacterial formulations for the treatment of infectious diseases. Furthermore, the observed antibacterial properties of *A. dubius*, alongside its traditional applications, warrant further pharmacological studies to evaluate its therapeutic potential and to explore its active components. These promising results highlight the plant's potential as a natural alternative for combating bacterial infections, especially those caused by common pathogens like *E. coli* and *S. aureus*.<sup>[31]</sup>

### Anti-obesity

The study found that *A. dubius* exhibits significant anti-obesity activity, particularly at a dose of 400 mg/kg body weight in progesterone-induced obese mice. When administered at this

higher dose, the extract produced a substantial reduction in BMI throughout the experiment. This effect contrasts with the 200 mg/kg dose, where mice showed an increase in BMI, indicating a dose-dependent anti-obesity response. The anti-obesity properties of *A. dubius* are attributed to its diverse phytochemical composition, including flavonoids, alkaloids, saponins, steroids, and phenols. These compounds are known for their roles in reducing adiposity by mechanisms such as activating  $\beta$ -adrenergic receptors, which promote fat burning, and inhibiting adipogenesis by modulating the activity of PPAR- $\gamma$ , a key regulator in fat cell differentiation. Flavonoids and phenols in *A. dubius* also serve as antioxidants, reducing oxidative stress that can contribute to obesity-related metabolic issues. Furthermore, alkaloids present in the extract are believed to downregulate genes associated with fat accumulation, contributing to its anti-obesity effects. The study suggests that *A. dubius* could be a beneficial natural remedy in managing obesity.<sup>[14]</sup>

### Hepatoprotective activity

The hepatoprotective activity of *A. dubius* leaf extract was assessed in a  $CCl_4$ -induced hepatotoxicity model in mice. In this study, mice were pre-treated with ethanolic extracts of *A. dubius* for seven days before being exposed to hepatic injury. The results demonstrated that *A. dubius* significantly mitigated liver damage by improving body weight, food, and water intake, which were adversely affected in untreated mice. Additionally, liver weight was reduced in the treatment group compared to the negative control, indicating a reduction in hepatic inflammation and damage. Histopathological analysis further supported these findings: while the negative control group exhibited disrupted liver architecture typical of hepatotoxicity, liver tissue in *A. dubius*-treated mice showed considerable restoration toward normal structure. This improvement suggests a protective effect against  $CCl_4$ -induced cellular injury in the liver.

In complementary *in silico* docking studies, stigmastane derivatives from *A. dubius* demonstrated a strong binding affinity to the Pregnane X Receptor (PXR), a receptor involved in liver detoxification pathways. The binding interactions with key amino acids within the receptor's pocket further indicate that the stigmastane compounds in *A. dubius* may play a role in its hepatoprotective mechanism by enhancing detoxification processes. This study provides evidence for the potential of *A. dubius* as a natural hepatoprotective agent.<sup>[32]</sup>

### Anti-anaemic activity

The anti-anemic activity of *A. dubius* has been demonstrated through its impact on haemoglobin levels. Herbal formulations derived from *A. dubius* were administered to patients, with pre- and post-treatment hemoglobin levels measured using a hemocytometer. Results showed a significant increase in hemoglobin levels, supporting the plant's potential in managing nutritional deficiency anaemia. This effect is attributed to the

plant's rich profile of bioactive compounds, such as 2-ethylbutyric acid and phytol, which are thought to play a role in improving blood health. In addition to its antianemic properties, the plant's antioxidants may offer further health benefits in managing conditions like hypertension and heart disease. *A. dubius* thus presents a valuable natural option in addressing anaemia within traditional healthcare systems.<sup>[33]</sup>

### Anti-viral activity

This study explored the antiviral activity of betacyanin from *Amaranthus dubius* (red spinach) against dengue virus type 2 (DENV-2). Betacyanin was extracted from red spinach leaves using methanol, followed by purification through Amberlite XAD16N column chromatography. The cytotoxicity of the betacyanin extract on Vero cells indicated a half-maximal cytotoxic concentration ( $CC_{50}$ ) of 2.287 mg/mL. The antiviral efficacy was assessed by determining the half-maximal inhibitory concentration ( $IC_{50}$ ), with *A. dubius* betacyanin showing a potent  $IC_{50}$  of 14.62 µg/mL and a high selectivity index (SI) of 28.51, indicating effective DENV-2 inhibition relative to cytotoxicity. Additionally, a virucidal assay using the maximum non-toxic concentration revealed an  $IC_{50}$  of 106.8 µg/mL, achieving 65.9% virus inhibition. These results suggest that betacyanin from *A. dubius* holds strong potential as an antiviral agent against DENV-2, showing higher efficacy than many natural compounds, warranting further investigation into its mechanism and *in vivo* effectiveness.<sup>[34]</sup>

### CONCLUSION

*Amaranthus dubius* stands out as a nutritionally rich and therapeutically versatile plant, deeply rooted in traditional medicine across tropical and subtropical regions. Its ethnomedicinal applications, supported by scientific investigations, highlight its potential in managing a wide array of conditions, including anaemia, inflammation, digestive disorders, and fever. The plant's bioactive compounds, such as betacyanins, phenolic acids, flavonoids, and phytosterols, contribute significantly to its antioxidant, anti-inflammatory, hepatoprotective, antiviral, and antianemic properties.

### CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

### ABBREVIATIONS

**DENV-2:** Dengue Virus type 2; **AChE:** Anti-Acetylcholinesterase (AChE); **TG:** Triglycerides; **TC:** Total cholesterol; **VLDL-C:** Very Low-Density Lipoprotein Cholesterol; **HDL-C:** High-Density Lipoprotein Cholesterol; **BMI:** Body Mass Index; **PPAR-γ:** Peroxisome Proliferator-Activated Receptor Gamma; **CCl<sub>4</sub>:** Carbon Tetra Chloride; **PXR:** Pregnane X Receptor; **IC<sub>50</sub>:** Inhibitory Concentration; **SI:** Selectivity Index.

### SUMMARY

*Amaranthus dubius*, commonly known as red spinach, is widely used in traditional medicine for treating anemia, inflammation, digestive disorders, and fever. Rich in bioactive compounds like betacyanins, flavonoids, phenolic acids, and phytosterols, it exhibits strong antioxidant, anti-inflammatory, hepatoprotective, antiviral, and antianemic properties. Notably, its betacyanins show antiviral activity against Dengue Virus Type 2 (DENV-2), while its antianemic effects enhance hemoglobin levels. These findings highlight *A. dubius* as a promising candidate for therapeutic applications, necessitating further research on its clinical efficacy and mechanisms of action.

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**Cite this article:** Kumar BSA, Disha NS, Khalid M. *Amaranthus dubius* L.: Ethnomedicinal Significance, Phytochemical Profile, and Therapeutic Potential-A Review. Pharmacog Res. 2025;17(4):1098-103.