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To,

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Natural Antioxidants from Plant Source: A Comprehensive Review of *Vernonia amygdalina*

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Abstract

Bitter leaf, also known as *Vernonia amygdalina* has been a staple plant in traditional medicine for centuries. Recent studies have expounded on its incredible antioxidant properties, making it a promising natural remedy for various health issues. For its richness in flavonoids, phenols, and ascorbic acid, bitter leaf has been shown to inhibit free radicals, mitigate oxidative stress, and protect against cell damage. Its antimicrobial properties make it an effective agent against a broad spectrum of infections, while its antioxidant properties mitigate harmful free radicals, and tissue damage. Research has shown that bitter leaf has the potential of managing cancer, diabetes, and liver disease, as well as the benefits to impact reproductive and gut health. However, some of the challenges to the use of this plant are toxicity and haematological changes. Despite these challenges, the overall reports suggest that *V amygdalina* is a valuable plant with numerous health benefits, warranting further research and consideration for its possible therapeutic applications. The aim of this study is to provide a comprehensive review of the antioxidant properties of *V amygdalina*, exploring its potential as a natural remedy for various health issues, and evading the potential limitation.

Keywords: Bitter leaf, Free radicals, Oxidative stress, Antioxidants, Therapeutic applications.

Introduction

The significance of antioxidants in both food preservation and dietary supplementation cannot be overstated. These compounds serve as guardians against the detrimental effects of oxidation, and combating oxidative stress in the human body (Shahidi, 2015). Categorized by their mechanisms, antioxidants manifest as primary agents, intercepting free radicals; secondary antioxidants, which impede chain initiation; and tertiary antioxidants, which are involved in bio-molecule repair (Daramola and Adegoke, 2011). Plants are reservoirs of various antioxidants that are essential for mitigating diseases associated with free radicals (Lawal *et al*., 2016). Phytochemicals, often referred to as 'plant-chemicals', constitute the non-nutritive components of plants, offering an array of health benefits and disease-preventive properties (Ahmed *et al*., 2014). In livestock, the correlation between disease onset and diminished antioxidant levels is well-established

(Lykkesfeldt and Svendsen, 2017). Oxidative stress emerges as a pivotal factor in pathological conditions affecting animal health, welfare, and productivity (Buchet *et al*., 2017). Recent studies have explored the efficacy of plant-derived additives as natural substitutes for synthetic antioxidants, highlighting the potency of natural extracts, essential oils, and plant by-products in bolstering oxidative stability and extending shelf life across various livestock species (Tsiplakou *et al*., 2021; Righi *et al*., 2021; Pitino *et al*., 2021)

Antioxidant properties of *V. amygdalina*

Bitter leaf contains flavonoids, including luteolin, luteolin 7-O-β-glucuronoside, and luteolin 7-O-β-glucoside which have been identified for their antioxidant properties against radicals (Farombi and Owoeye, 2011). Among these flavones, luteolin exhibited superior antioxidant activity compared to the others. In diabetic rats, the aqueous extracts of bitter leaf effectively reduced serum levels of malondialdehyde, indicating antioxidant potential (Owolabi *et al*., 2008). Additionally, ethanolic extracts of bitter leaf displayed robust antioxidant properties by inhibiting β-carotene bleaching, linoleic acid oxidation, and Fe^{2+}/ascorbate-induced lipid peroxidation in rat liver microsomes (Chist´e *et al*., 2014). *V amygdalina* leaf also contained notable phenol, flavonoid, and ascorbic acid contents, contributing to its antioxidative activities. These compounds act as potent free radical scavengers, with the leaf extract demonstrating significant reducing power, evidenced by a reduction in the Fe^{3+} ferricyanide complex to its ferrous form (Lou *et al*., 2006). Studies on diabetic rats revealed that aqueous extracts of *V. amygdalina* reduced serum malondialdehyde levels, indicative of antioxidant effects (Nwanjo, 2005). Similar findings by Iwalokun *et al*. (2006) and Adaramoye *et al*. (2008) further supported the antioxidant properties of bitter leaf. Moreover, Owolabi *et al*. (2008) demonstrated that both ethanolic and aqueous

extracts of bitter leaf effectively inhibited β-carotene bleaching, linoleic acid oxidation, and Fe^{2+}/ascorbate-induced lipid peroxidation in rat liver microsomes.

Importance of antioxidant properties of *V amygdalina*

Vernonia amygdalina holds a longstanding traditional usage as a remedy for various ailments, including diarrhea, fungal and bacterial infections, inflammation, cancer, and diabetes. Additionally, its juice finds application in wound healing (Ugbogu *et al*., 2021). Notably, bitter leaf has exceptional biodegradable, biocompatible, nontoxic, and non-immunogenic properties, and prolongs drug release within the gastrointestinal tract. Chitosan, a novel source of polysaccharides with these same properties, derived from marine fish scales and shells of crustacean including crabs, shrimps, and lobsters (Hashem and Ali, 2024), also offers potential in similar regard (Inneke *et al*., 2020). The antimicrobial properties of bitter leaf make it a viable candidate for combating a broad spectrum of infections, as evident in its inhibitory actions against bacteria, fungi, and viruses (Ugbogu *et al*., 2021). Its antioxidant constituents effectively neutralize harmful free radicals, thereby mitigating tissue damage (Edo *et al*., 2023). Moreover, organic extracts from bitter leaf demonstrate cytotoxic effects on human nasopharyngeal cancer cells, suggesting its potential utility in cancer treatment, diabetes management, and liver disease therapy (Makhaik *et al*., 2021; Hussain *et al*., 2022;). Chimpanzees in the wild were investigated to consume bitter leaf during parasite infections, indicating its natural medicinal properties (McLennan *et al*., 2017). These benefits extend to reproductive health, with studies demonstrating its ability to increase sperm count and improve semen quality in men, as well as regulate menstrual cycles in women, and alleviate their premenstrual syndrome symptoms (Trendafilova *et al*., 2020; Owheruo *et al*., 2023). Additionally, bitter leaf contains quercetin, known for its efficacy in alleviating inflammatory bowel disease and reducing gut inflammation, contributing to improved

gut health and reduced stomach discomfort (Ighodaro *et al*., 2017; Ugbogu *et al*., 2021). Furthermore, its anti-inflammatory properties and fibre content also make it beneficial for overall gut health (Edo, 2022). Bitter leaf is also known to be rich in chemical constituents such as steroid glycosides, specifically vernonioside B1, and it exhibits potent anti-parasitic, anti-tumour, and bactericidal effects. Its usage extends to treatment of schistosomiasis, diarrhea, and general physical malaise (Ogbonda *et al*., 2013). Overall, bitter leaf emerges as a crucial protective food, essential for maintaining health, preventing disease and treating various illnesses.

Potential challenges to the use *V amygdalina*

In a sub-acute toxicity study conducted by Rachmaini *et al*., (2024), reported that mice exposed to *V amygdalina* leaf aqueous fraction (VALAF) showed no signs of mortality, morbidity, or alterations in general behavior. Notably, VALAF did not elicit severe toxicity resulting in hematological changes, indicating its tolerability up to a dosage of 1000 mg/kg body weight. This suggests the potential of VALAF as a safe pharmaceutical candidate. Similarly, Zakaria *et al*. (2016) administered *V amygdalina* aqueous extract to female Sprague Dawley rats at increased doses up to 5000 mg/kg body weight and observed no toxicity signs or mortality. Liver function tests revealed a slight increase in aspartate aminotransferase (AST) and globulin levels, while other parameters remained within normal ranges. Based on statistical analysis, *V amygdalina* toxicity was determined to exceed 5000 mg/kg body weight. Abdulmalik and Oladapo (2020) reported that a high cholesterol diet administered to rabbits for twelve weeks resulted in increased relative liver weight, aspartate transaminase levels, superoxide dismutase levels, and hepatic microvesicular steatosis. However, treatment with 200 mg/kg of aqueous extract of *V. amygdalina* ameliorated superoxide dismutase levels without affecting malondialdehyde levels, liver enzymes, or liver histology. On the other hand, Chike *et al*. (2018) concluded that the ethanolic leaf extract of *V.*

amygdalina may induce anemia, especially upon prolonged exposure, as evidenced by changes in body weights and hematological parameters observed in animals.

Igile *et al*. (2023) note that bioactive compounds like sesquiterpene lactones and flavonoids in bitter leaf contribute to its potential in culinary and medicinal applications but limit consumer acceptability due to bitterness. Extensive processing is needed to reduce this bitterness, which may degrade bioactive compounds and reduce their potency. Additionally, Igile *et al*. (2023) highlight the presence of anti-nutritional factors such as oxalates, phytates, tannins, and cyanogenic glycosides, which can pose health risks if consumed in large amounts without proper preparation. These compounds may interfere with nutrient absorption or cause toxicity, requiring careful processing and dosage control.

Despite promising preclinical results for diabetes management, Erukainure *et al*. (2023) noted that limited human trials have been conducted to validate the therapeutic efficacy and safety of bitter leaf, hindering its integration into mainstream medicine.

Conclusion

Vernonia amygdalina has been extensively studied, and its potential as a natural remedy for various health issues, due to its richness in phytochemicals that enables it to inhibit free radicals, mitigate oxidative stress, and protect cell damage, has been expounded.

Its antioxidants play a significant role in combating oxidative stress and mitigating diseases associated with free radicals. It also showed therapeutic application in preventing and treating various ailments such as cancer, diabetes, and liver disease. Its antimicrobial properties also make it effective against a broad spectrum of infections. Concerns have been raised over its latent toxicity. However, studies have generally reported low toxicity levels.

Overall, the benefits of bitter leaf outweigh the risk concerns, thus, the advocacy for it as a natural remedy for healthy diet and combatting various health issues, is widely supported. Moderate consumption and further research are recommended to fully explore its benefits.

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