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RESEARCH ARTICLE

Health Benefits of the Seeds, Oils, Roots and Leaves of Monodora Tenuifolia

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ABSTRACT

Medicinal plants and their derived products have been used by human beings for centuries in the treatment and prevention of various disease conditions and they continue to play significant role in modern medicine. Interestingly, thousands of studies have been conducted both in developed and developing countries to assess the efficacy of medicinal plants and some of such studies have culminated in the development of plant-based medications. Reports showed that more than 90% of traditional remedies contain medicinal plants. The increasing significance of medicinal plants can be seen from its economic contribution. It has been reported that global trade in herbs is more than USD100 billion per year while India and China medicinal plant trade is USD200 to 500 billion per year. As part of examining the significant contributions that medicinal plants have been making to human health and continued relevance, this review focuses on the antioxidant, antidiabetic, antilipidemic, anti-inflammatory, antimalarial, antimicrobial and antileishmanial activities of Monodora tenuifolia.

INTRODUCTION

Monodora tenuifolia plant belong to the annonacaea family. The family consists of tropical and subtropical plants, widely distributed in countries in Africa, South and Central America and Asia. Viewed as the largest mangnolide families, they are believed to have 40 to 50 genera with 500 to 600 species (Al Kazman et al., 2022). The species in this family provide vital edible fruits while the seeds and oils from the family are source of consumable oils, soap and alcohol making. Various chemicals such as flavonoids and alkanoids have been derived from the fruits, seeds, leaves and bark of plants in this family. The species of the family differ according to origin, location and climate (Ekeanyanwu, 2013). The aromatic flowers are noticed first before the development of other parts of the plants. The seeds are generally large with irregular surface endosperm and small embryo. Also, the species of this family are used traditionally for wound healing, treatment of dysentery, fever and gastrointestinal problems (Attiq et al., 2017). This review focuses on the antioxidant, antidiabetic, antilipidemic, anti-inflammatory, antimalarial, antimicrobialand antileishmanial activities of Monodora tenuifolia. Although there have been reviews on this plant, most have looked at either the roots, or seeds or leaves and have not comprehensively examined the health benefits of the seeds, oils, roots and leaves of Monodora tenuifolia ina single review.

Monodora tenuifolia was first described by George Bentham. It is commonly found in West costal countries such as Cameroon, Gabon, Guinea and Nigeria (Ezenwali et al., 2010). Its spherically shaped fruit is suspended on a long stalk containing several brownish and smooth seeds within a non-edible pulpy mass with the seeds encasing an edible kernel (Ekeanyanwu and Njoku, 2013). The seeds of Monodora tenuifolia form principal ingredients in herbal preparation applied in the treatment of toothache, dysentery, diarrhoea, constipation and post-natal haemorrhage (Njoku et al., 2012). Its root, leaves, oil and bark are used in the treatment of various skin-related conditions (Ekeanyanwu and Njoku 2013; Ogunsina et al., 2016).

Chemical and nutritional composition

Monodora tenuifolia is a seasonal spice in the Annonaceae family and contains fat, oils, minerals and several chemical compounds. It seeds contain 26.2% fat and oils with the oil having an iodine value of 192, a peroxide value of 11.5 and saponification value of 116. It is important to note that these constituents vary according to location and climatic condition (Ajayi, 2008). It has been reported that the volatile oils from the root contain sesquiterpene hydrocarbons and indole derivatives while the flavonoid-rich seeds contain quercetin and coumarin (Ugwuona et al (2017). In a study conducted in Ibadan, Oyo State in Nigeria, Ajayi and Aghanu (2011)reported on the physical and chemical characterization of the seeds of M tenuifolia. Chukwuma and Uzoma (2013) reported on both the chemical and nutritional composition of the seeds and oils of M tenuifolia. The authors documented the presence of alkaloids, cyanogenic glycosides, tannins and flavonoids as well as on the proximate composition such as crude fibre, crude protein, crude fat, ash, moisture and carbohydrates while analysis of the mineral content shows calcium, sodium, iron, zinc, potassium, magnesium, and phosphorus in their various concentrations. Further analysis of the seeds shows that it contains vitamin A, C, E, thiamine, niacin and riboflavin in their various concentrations. Interestingly, the concentrationsof these constituents differ from the seeds reported by Ajayi and Aghanu (2011). While the seeds of M tenuifolia in Ajayi and Aghanu's study were obtained from the western part of Nigeria, that of Chukwuma and Uzoma's were obtained in the eastern part of Nigeria, highlighting the effects of difference in location and climate. Effiong et al (2009); Ekeanyanwu (2013) and Ekeanyanwu et al (2010) have also reported on the chemical and nutritional composition of the seeds and oils of M tenuifolia with some difference in concentrations of the various constituents. According to Oguntimein et al (1989), gas chromatography-mass spectrometry analysis of volatile oil from the roots of M tenuifolia yielded 41 components. The main components were two unidentified sesquiterpene hydrocarbons (15.5%) and three indole derivatives: 3-prenylindole (5.6%), 6-prenylindole (4.1%) and on unidentified indole derivatives (5.6%). The authors also reported that the essential oil was principally sesquiterpene (33.4%). The leaves of M tenuifolia contain alkaloids, flavonoids, tannins, saponins, glycosides, phenolics and essential oils (Akinwunmi et al., 2014).

Figure 1: Tree of Monodora tenuifolia (Njoku et al., 2005)

Figure 2: Leaf of Monodora tenuifolia (Ekeanyanwu & Njoku, 2013).

Figure 3: Seeds of Monodora tenuifolia (Ezenwali et al., 2010).

Antioxidant activity

Phenolics are secondary metabolites that are synthesised by plants in response to biotic and abiotic stressors (Putrussa et al., 2014; Nzekwe et al 2022), known to play significant role in the defence system of plants with important health enhancing benefits specifically due to theinherent antioxidant properties (Akinwunmi et al., 2014). In a study by Akinwunmi et al (2014), the phenolic profile of M tenuifolia was determined and reported to contain phenolics, caffeic acid, cafechin, quercetin, kaempherol, methyl isoeugenol, eugenol, safrole and elemicin. This report clearlyindicatesthat the antioxidant activity of M tenuifolia is related to its phenolic content, hence its ability to serve as antioxidant is linked to the redox properties which is key in absorbing and scavenging reactive oxygenor nitrogen reactive species. In 2024, Nzekwe et al reported on the antioxidant activity of M tenuifolia benth seeds. The study showed that plasma total antioxidant increased significantly in rats fed with flavonoid-rich seeds of M tenuifolia. It concluded that Monodora tenuifolia seeds could improve antioxidant status by ameliorating oxidative stress and enhancing antioxidant enzyme activities. Ugwuona et al (2017) evaluated the antioxidant activity of the seeds of M tenuifolia. The authors reported that the plant extract suppressed lipid peroxidation in beef and pork, reduced ferric iron to ferrous iron, reduced DPPH in a dose-dependent manner and that the antioxidant activity of the extract was concentration-dependent and increased with higher total phenol concentration. In another study, Ugwuona et al (2019) reported that extract of M tenuifolia exhibited significant radical scavenging capacity and its antioxidant properties increased with its concentrations. Njoku et al (2005) has reported on the phenolic content and antioxidant properties of the oil of M tenuifolia.

Antimicrobial activity

Generally, plants have been reported to have antimicrobial properties that inhibit the growth of bacteria, fungi, viruses and protozoa (Ezenwali et al., 2010; Karime et al., 2021). These properties are fundamentally due to the secondary metabolites which are produced by the plants and include alkaloids, tannins and phenolic compounds (Menkem et al., 2016). Reports indicate that these metabolites can alter the metabolism of bacteria, making them more susceptible to antibiotics; they equally interfere with molecular targets in bacteria and can penetrate the cell membranes of pathogens, interacting with intracellular targets. For example, extract of cumin seeds has been reported to be effective against various strains of Gram-positive and Gram-negative bacteria (Njoku et al., 2005). Adeoye and Oguntimein (1986) reported on the antibacterial activity of indole-derived compound (3-dimethhylallylindole) isolated from Monodora tenuifolia. Njoku et al (2005) documented that the seed oil of Monodora tenuifolia displayed marked activities against Bacillus subtilis, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa. Research reports indicate that Shigella spp, Salmonella spp, , E.coli, Klebsiella spp and Staphylococcus aureus are responsible for various bacterial infections. Interestingly, certain plants have been tested and found to be effective in the traditional and clinical management and treatment of these bacterial infections (Ngouana et al (2015). Monodora tenuifolia has been found to be useful in the traditional and clinical

treatment of various bacterial infections (Fiamegos et al., 2011). To further investigate this, Ogarawu et al (1998) tested the potency of Monodora tenuifolia against selected bacterial pathogens. The authors noted that the antibacterial activity of the extract of M tenuifolia was seen by inhibition of growth of tested bacterial species.Drug resistant microbial infections due to microorganisms such as Staphylococcus aureus and Pseudomonas aeruginosa is a growing public health problem affecting various countries across the globe (Fiamegos et al., 2011). To overcome this problem, some scientists have investigated the antimicrobial activity of medicinal plants. Menkem and colleagues (2016) conducted an experiment and observed that antibacterial activity exhibited by the crude extracts (Monodora tenuifolia inclusive) against Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhi and Escherichia coli that are linked to various infectious diseases provides scientific justification in the use of medicinal plants in many developing countries such as Nigeria, South Africa and Cameroon. Karime et al (2021), Ngouana et al (2015) and Njoku et al (2005) have reported on the antifungal activity of Monodora tenuifolia.

The anti-diarrhealproperties of seed extract of *Monodora tenuifolia*was investigated by Ezenwali et al. (2010) usingrodent models of diarrhea. They reported that an oral LD 50 value at 5000 mg/kg is safe. It was concluded that the seeds of *M. tenuifolia* possessanti-diarrheal properties mediated throughinhibition of hyper secretion and gastrointestinalmotility which substantiate the use in thetreatment of diarrhea in traditional medicine.

Anti-inflammatory activity

Monodora tenuifolia is very rich in flavonoids and its anti-inflammatory activity has been reported (Nzekwe et al., 2023, Ekeanyanwu and Njoku 2015; Manach et al., 2005). Various mechanism of actions has been noted for the action of anti-inflammatory activities of flavonoid-rich plants such as Monodora tenuifolia. Flavonoids affect enzymatic activities such as phospholipase, lipoxygenase and nitric oxide producing enzymes and nitric oxide synthase which are useful in metabolising arachidonic acid. It has been reported that the inhibition of these specific enzymes by flavonoids reduces the production of mediators of inflammation, making flavonoids key anti-inflammatory agents (Akinwunmi and Oyedapo, 2015).

Leishmanicidal, trypanocidal and anti-helminthic activities

Helminths and other parasites are of major public health concern especially in developing countries. It is particularly worrying in Africa with millions of people infected due to poor environmental conditions, poor hygiene and poor health facilities (Preston et al., 2017; Karime et al., 2021; Loiseau et al., 2000). The application of plant products as agents of deworming in human and animals has been in practice for many centuries. Anti-helminthic actions of plants are linked to their secondary metabolites (polyphenols, terpenoids, alkanoids and tannins) (Williams et al., 2014). Also, plants and plant-derived products could play a significant role in reducing dependence on anti-helminthic drugs (Charlier et al, 2014).

In a study to investigate the leishmanicidal, trypanocidal and anti-helminthicactivities of Monodora tenuifolia, Karime et al (2021) collected leaves of M tenuifola and following proper identification of the plant, the authors conducted an experiment to assess these activities. The anti-leishmanial activity of the isolated compounds and the extracts were tested in vitro against Leishmania donovani according to previously described method (Mbongo et al., 1997). Trypanocidal activity was studied, using Glasgow Veterany Research 35 strain of T. brucei brucei. Extracts and compounds were evaluated for their activity against bloodstream forms of T. brucei brucei following previously described method (Loiseau et al., 2000). For the anti-helminthic activity, Caenorhabditis elegans strain was used following the method of Barrows et al. (2006). The tests were done in microplate of 24 wells, each well receiving 10-15 parasites in 0.5 mL. After 7 to 20 days of incubation with tested extracts, isolated compounds and mebendazole (standard drug), the optical density of each well was measured and the percentage of motionless worms, considered as dead were determined. The authors reported that the cold extracts of M tenuifolia demonstrated activity against Leishmania donovani and Trypanosoma brucei brucei. However, the isolated compounds from the plant did not demonstrate anti-helminthic activity, implying the synergistic activity of the extract is key in its anthelminthic activity.

Antidiabetic and antilipidemic activity

Diabetes is an endocrine metabolic disorder known to cause severe morbidity and mortality resulting from various complications (Jan et al., 2022; Abu et al., 2024). There are different types of diabetes, however type 2 diabetes is the most prevalent type and accounts for 90% to 95% of diabetic cases (Li et al., 2004; Nzekwe et al., 2023; Nethengwe et al., 2024). Antidiabetic therapies include insulin and others such as biguanides, with many displaying side effects (Patel et al., 2011; Bashkin et al., 2021). These antidiabetic therapies are costly with side effects. This has precipitated the search for more effective and safer antidiabetic agents such as plant and plant-derived products. Medicinal plants have been documented to play important role in the management of diabetes due to their ability to restore pancreatic function and cells by inducing an increase in insulin output or by inhibiting intestinal absorption of glucose or by facilitating metabolites in insulin-dependent processes (Bhushan et al., 2010; Sempore et al., 2021). To investigate the antidiabetic activity of Monodora tenuifolia, Ekeanyanwu and Njoku (2013), conducted a laboratory-based experiment in an animal model. The authors collected fresh seeds of Monodora tenuifolia growing in a university community in Eastern Nigeria. Following proper identification of the plant, the seeds were blended into powdery form.Twenty-four rats, weighing 95 g to 140 g) were selected for the experiment,divided into 4 groups of 6rats in eachgroup and used in the experiment.The authors reported that following feeding of animals for 14 days with flavonoid-rich fraction resulted in a significant increase in serum triacylglycerol levels and very low density lipoprotein in groups administered 100 mg kg−1 (group 2), 200 mg kg−1 (group 3) and 400 mg kg−1 (group 4) of the flavonoid rich fraction while serum high density lipoprotein reduced significantly in groups administered 100 mg kg−1 (group 2), 200 mg kg−1 (group 3) and 400 mg kg−1 (group 4) of the extract. However, there was no significant effect on fasting blood glucose level and lipid and low-density lipoprotein and cholesterol in the groups administered 100 mg kg−1 (group 2), 200 mg kg−1 (group 3) and 400 mg kg−1 (group 4) of the flavonoid rich fraction of Monodora tenuifolia. Interestingly, it was observed that serum triacylglycerol, very low-density lipoprotein and high-density lipoprotein normalised after 28 days of oral administration of the flavonoid rich fraction. Recently, in an experiment to investigate the antidiabetic activity of Monodora tenuifolia, Nzekwe et al (2023), used animal model to assess this property. In this study, the authors assessedthe effect of a flavonoid-rich fraction of Monodora tenuifolia seed extract on bloodselected indices in drug-induced diabetic male rats. The animals were divided into7 groups with 6 animals per group.The findings indicate a significant increase in the levels of triacylglycerol, cholesterol, LDL-cholesterol,VLDL-cholesterolin diabetic rats. However,the administration of the extract significantly improved the observed biochemical indices.In addition, an increased concentration of HDL-cholesterol concentration was observed in the diabeticrats upon treatment with the extract. The findings suggest that the extract could be a potentanti-nephropathy and anti-cardiomyopathy agent in diabetic condition and that it could play a role in ameliorating complications resulting from kidney and cardiacdamage in diabetic state.

Damola et al (2024) assessed the anti-hyperglycaemic activity of selected medicinal plants including Monodora tenuifolia. They performed phytochemical screening and inhibitory activities of key carbohydrate-metabolizing enzymes (alpha-amylase and alpha-glucosidase). Phytochemicals screening of these plants showed the presence of flavonoids, tannin, saponin and alkaloids. The n-hexane and ethyl acetate fractions of M tenuifolia seeds showed inhibition of α-amylase and α-glucosidase activities. The authors concluded that M tenuifolia inhibited carbohydrate-metabolizing enzymes demonstrating potential anti-hyperglycaemic activity.

As a result of underutilisation of selected plant seeds in the recipes for the management of diabetes mellitus, there is need for further investigations. For this reason, Raji (2022), evaluated the chemical constituents and medicinal applications of some locally sourced plant seeds (Monodora tenuifolia inclusive). Seeds of the plants were collected, identified at the herbarium, University of Ibadan, Nigeria. The seeds were processed according to standard procedures and analysed to determine the constituent's elements by atomic absorption spectrophotometry. Extraction was performed using methanol and qualitative and quantitative phytochemical and antioxidant constituents were determined following standard procedures. Various compounds were identified and in vitro screening revealed that all the extracts have antidiabetic activities, while in vivo test showed that it significantly reduced fasting blood glucose.

Wound healing property

Wound can be described as a distortion in the cellular, anatomical, and functional epithelial integrity of the skin consequent to physical, chemical, thermal microbial, or immunological insult; followed by disruption of the structure and function of underlying normal tissue (Mekonnem et al., 2013, Kim et al., 2018; Oguntibeju, 2019). The principal response in wound healing involves a process of connective tissue repair and is known by four phases: haemostasis, inflammation, proliferation, and remodelling in which the repair process involves the coordination of various cells, growth factors and cytokines (Kim et al., 2018).

Because of ethnobotanical survey, several species of plants and herbs with wound healing activities have been identified in Africa and other developing countries. The use of medicinal plants in wound management and care involves disinfection, debridement, and the provision of adequate environment for natural healing process (Firdous and Santya, 2018). Because ingredients present in medicinal plants are believed to be less toxic and have fewer side effects compared with orthodox therapeutic agents; there has been increased and renewed interest in the use and application of medicinal plants in wound healing process in diabetic and non-diabetic conditions (Attah et al., 2016).Monodora tenuifolia plant has beenused by traditional medicine practitioners in Nigeria and other African countries. Report shows that various parts of the planthave some medicinalvalues and are being used in different regions of Nigeria for wound healing. To provide scientific evidence toits wound healing activity, Ajayi et al (2015), conducted an experiment on the seeds of Monodora tenuifolia as this is important in validating record of its medicinal applications and toexpand its use to include its integration into modern medical healthcare systems. In this study, Ajayi et al (2015), using an animal model assessed the wound healing activity of the seeds of Monodora. tenuifoliaby incorporating the extracts into paraffin in concentrations of 5% and 10% w/w. Woundhealing activities of the extracts were studied by determining the wound area (mm2), percentage ofwound closure, period of epithelialisation and histological analysis of the control and test groups.Significant wound healing effect was noticed for *M. tenuifolia* seed extract, indicating that the seed extract of *M. tenuifolia* has a wound healing capacity as shown from the experimental values of the wound closure area,improved tissue regeneration at the wound site observed through the daily monitoring andhistopathological parameters related to the healing of the wound.

Antimalarial activity

Malaria is aprincipal public health problem in West Africa and many other developing countries in the tropics. Although various modern approaches have been applied in the treatment and eradication of malaria; however, it remains a serious public healthchallengedue to expensive anti-malarial drugs and drug-resistant Plasmodium falciparum (Tsaban et al.,2012). Reports show that millions of people are at risk of malaria infection inseveral countriesglobally withovert 1 million people dead annually(Hay et al., 2010) with pregnant women and children <5 years at higher risk of serious morbidity (Mfopa et al., 2017). For centuries, majority of people in developing countries recognize and use the properties of several plants to treat malaria and other diseases (Asase et al., 2010). Report indicates that the Annonaceae (the family which M tenuifolia belong) are gaining relevance and are increasingly being used as antimalarial agents (Boyomet al., 2011). To test the antimalarial activity of Monodora tenuifolia, Tsaban et al (2012) conducted a survey to document indigenous knowledge, usage customsand practices of Annonaceae species in the treatment of malaria in four Cameroonian areas. The authors reported that 7 speciesof Annonaceae were found to be used in the treatment of malaria, while 14 species were used to treat symptoms that were related to malaria.

Mfopa et al (2017) investigated the antimalarial activities of leaves, twigs and stem bark of each M tenuifolia and other plants. The toxicity of the plants was also tested in Swiss rats to determine the safety of the plants. It was observed that oral administration of the extracts of the plants at 500 mg/kg b.w in mice showed no signs of toxicity. The plants exhibited significant suppressive effect against malaria parasite for the duration of the experiment. The findings support the use of the plants in the traditional treatment of malaria and could play a role in the future development of antimalarial drugs. Rolland et al (2021) further assessed the anti-plasmodial activity of 4 medicinal plants that included M tenuifolia used in traditional malaria remedies. The authors applied a standard in vitro method with clinical Plasmodium falciparum isolates and concluded that the 4 extracts showed a good activity on clinical isolate.

Toxicity

Based on research report, Monodora tenuifolia is considered to have a low toxicity profile, with studies showing no significant signs of toxicity at high doses, with an LD50 (lethal dose for 50% of test animals) reported as greater than 5000 mg/kg body weight. However, some authors have expressed concerns because of potential cytotoxic effects due to the presence of myristicin in the plant extract (Saha et al., 2011; Nandy & Datta, 2012). Monodora tenuifolia seed appears to be practically safe (LD50 above 5000 mg kg−1) when administered acutely to mice through the oral route. When administered orally to rats in a14- and 28-day study, some biochemical parameters such as serum triacylglycerol and very low-density lipoprotein were significantly increased after 14 days of administration. However, the parameters normalised after 28 days of administration of the extract (Ekeanyanwu & Njoku, 2014).

Previous reports showed the safety of M. tenuifolia in rodent. Toxicological bioassays were assessed based on biochemical, haematological parameters as well as histopathological observations. Flavonoid rich fraction of M. tenuifolia seeds and other parts were found to be safe and could serve as nutraceuticals (Njoku et al., 2012; Ogbonnia et al., 2010).It has been observed that certain person may experience allergic reactions or sensitivities to Monodora tenuifolia, therefore, it is recommended that an individual intending to use the extract should speak to a health professional.

Future studies

Futurestudies on Monodora tenuifolia are necessary to isolate, identify, and purify active compounds in the plant extracts that are involved in various biological activities linked to the plant. Application of various parts of M tenuifolia as a possible adjuvant in the orthodox treatment of different disease conditions need to be explored for its maximum benefits. Large clinical trials on the use of M tenuifolia in various disease conditions especially in diabetic condition should be carried out.

CONCLUSION

Medicinal plants are vital to both human and animal health. Reports indicate that medicinal plants have been in use for several centuries in the treatment and prevention of different diseases. Medicinal plants act as a natural medium of therapeutic ingredients to manage diseases and providing foundation for modern pharmaceuticals, specifically in settings with limited access to conventional medicines. Medicinal plants are readily available in many developing countries and are culturally relevant to many societies and communities, hence its wide applications in human and animal health. Monodora tenuifolia is one of those medicinal plants that has played significant role in human health. It belongs to the Annonnaceae family. The seeds of Monodora tenuifolia form main ingredients in herbal preparation applied in the treatment of toothache, dysentery, diarrhoea, constipation and post-natal haemorrhage. Its root, leaves, oil and bark are known for the treatment of various skin-related conditions. Its chemical and nutritional composition provides insight into the biological activities of the plant and its applications in the management of many disease conditions.

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