Research Paper

A review on Ziziphus mucronata Willd (Rhamnaceae) commonly used to treat infections and inflammation-related conditions in southern Africa

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ABSTRACT

In under-resourced areas of developing countries, a significant number of people are heavily reliant on medicinal plants for primary health care needs. Extracts of Ziziphus mucronata are among the widely used ethnomedicine to treat infections and relief pain. The focus of this review is to collect all available information on the ethnomedicinal uses, pharmacology and cytotoxicity of the extracts of Z. mucronata. Information was sourced from online search engines such as Google scholar, Science Direct, PubMed, Web of Science, academic books and published thesis etc. Extracts of the root, bark, leaves and fruits are used to treat microbial infections, type-2 diabetes, malaria, some types of cancer as well as analgesics. Absolutely, extracts of Z. mucronata possess additional medicinal benefits such as anti-inflammatory, anti-microbial, anti-plasmodial and anti-helminthic. The observed pharmacological activities are attributed to the constituent cyclopeptide alkaloids and other phytochemicals present in various parts of the plant. The isolated cyclopeptide alkaloids were found to possess potent anti-microbial properties. The plant species is widely distributed across Africa, and there are no reports of a threat to its existence in the wild. This under-utilised plant species is widely distributed in Africa, and its extracts are used to treat various diseases. Reports on the biological activities of the extracts may partly support its ethnomedicinal uses but other potential biological activities are yet to be explored. Also, the mode of action of the isolated compounds is not fully known. Phyto-compounds with proven biological activities and relatively safe profile could be used as templates for the development of potent drugs.

Key words: Ziziphus mucronata, ethnopharmacology, phytochemistry, ethnomedicinal use, taxonomical description.

INTRODUCTION

Medicinal plants continue to play a significant role in meeting the primary health care needs of people living in resource limited areas of developing countries, such as those in Africa. One of the most important albeit scarcely exploited medicinal plants endemic to Africa is Ziziphus mucronata Willd (Rhamnaceae), but it was not listed among the commercially important medicinal plants of South Africa (Street and Prinsloo, 2013). The Rhamnaceae family consists of forty-nine genera and nine hundred plant species (Simpson, 2006). The genus Ziziphus includes eighty-six species, of which Z. mucronata Willd is among the most common and best-known trees of southern Africa. The members of the taxon are drought tolerant and very resistant to heat, sometimes are found growing in very arid areas (Paroda and Mal, 1989). The ancient Greeks refer to the tree as zizyphon, from the Arabic zizouf, a name for the mythical lotus. This was taken into Latin as zizyphum, or zizypha for the fruits. The species name mucronata is Latin meaning pointed, probably referring to its thorns or the apex of its leaves. Z. mucronata Willd. subsp. mucronata
Willd., also known as buffalo thorn, is a small to medium-sized tree, with a spreading canopy. It is distributed throughout the rainfall areas of sub-Saharan Africa, extending from western Africa across tropical sub-Saharan Africa to Ethiopia and Arabia, then southwards to southern Africa.

There are several known ethnomedicinal uses of various parts of the plant to treat ailments in both humans and for ethnoveterinary applications. Its bark and roots are used medicinally for the treatment of gonorrhoea, rheumatism, gastrointestinal problems and snake bites (Adamu et al., 2005; Tas et al., 1991). Decoctions made of boiled roots and leaves are applied externally to boils, sores and glandular swellings for pain relief while warm bark infusions are used for body pains, expectorants in cough, respiratory infections and chest problems (Amusan et al., 2005; Venter and Venter, 2002). In the northern region of Nigeria, a decoction of the plant is used traditionally to treat type-2 diabetes mellitus (Etuk et al., 2010; Onakpa and Owoleke, 2010).

A recent review of this plant species provided sparse records on ethnomedicinal uses and related pharmacological activities of its extracts (Mokgolodi et al., 2011). This updated review expanded on such report and summarizes recorded ethnomedicinal uses, phytochemistry, pharmacological activities and potential cytotoxicity of extracts of Z. mucronata Willd sub-species mucronata. While several attempts have been made to demonstrate the efficacy of some of the anecdotal claims of its traditional uses using in vitro and in vivo studies, the mode of action of the constituent bioactive compounds is still poorly understood. Furthermore, it is hoped that this information would stimulate further investigations into the mechanisms and basis of action of some of the isolated compounds that could be used as templates for the development of bioactive drugs.

**Taxonomical description**

*Z. mucronata* Willd. subsp. *mucronata* (Rhamnaceae) has several common names including buffalo thorn (English), blinkblaar-wag-'n-bietjie (Afrikaans), umphafa, umlahlankosi, isilaha (isiZulu), umphafa (isiXhosa), umlahlabantu (Swazi); mokgalo (Tswana), mukhalu (Venda), mphasamhala (Tsonga), mokgalô, monoana (Northern Sotho). In northern Nigeria, it is known as magaryankura (Adamu et al, 2005), kangua Kankolokole (Bemba), ngwelulu (Lola), sula (Hemba) by some tribes in the Democratic Republic of Congo (Mبيانa et al, 2008) and omukekete in the Ohangwena and Oshikoto regions of Namibia (Cheikh-Youssef and Embashu, 2013), respectively (Table 1). This plant species is a spiny, small deciduous shrub to medium-sized tree, 3-20 m in height, with a spreading canopy (Figure 1a). The main stem is green and hairy when young with branches in ziz-zag arrangement. The bark is reddish brown or roughly mottled grey, cracked into small rectangular blocks, revealing a red and stringy under the surface (Figure 1b). The thorns are paired along the stems, one facing forward and the other facing backward. Leaves are simple, alternate, ovate or broadly ovate, varying enormously in size from tree to tree. The leaves are tapering or often with mucronate apex, strongly asymmetrical base, cordate to rounded on one side; margin finely serrated, often badly eaten by insects, glossy green above, slightly hairy and paler below; 3- to 5-veined from the base; veins covered with fine hairs when young; petiole up to 20 mm long; stipules, when present, take the form of small thorns at the nodes, one straight and one hooked. Leaves turn golden yellow in autumn (Figure 1d). Flowers are borne in dense clusters in leaf axils; green to yellow; ± 4 mm in diameter; inconspicuous (October-February). The fruit is a smooth, shiny, leathery, spherical drupe, 12-20 mm in diameter, reddish-brown or deep red when ripe, slightly sweet, the pulp is dry (Figure 1e). The fruit sometimes stays on the plant long after the leaves have fallen (March-August), roughly the size of a grape, and ripen into a deep brown-red. The seeds are usually solitary, elliptic and compressed. It can survive in a variety of soil types, occurring in many habitats, mostly open woodlands, often on soils deposited by rivers, and grows frequently on termite mounds.

**Distribution and habitat**

The buffalo thorn is distributed throughout the summer rainfall areas of sub-Saharan Africa, extending from South Africa northwards to most parts of Africa and Arabia.

*Z. mucronata* grows in areas dominated by thorny vegetation in both temperate and tropical climates (Maier et al., 2006). It is also found in a wide range of habitats such as woodlands, open scrubland, on rocky koppies, open grasslands, on a variety of soils along streams, nutrient-rich valley bottoms and forest margins. It reaches its largest size on the margins of scrub forest and on deep, alluvial soils near water. Its presence is said to indicate the presence of underground water. This particular plant can survive a wide variety of soil conditions, heat, cold frost and drought (Maier et al., 2006).

**Conservation status**

This plant species is not considered to be endangered in South Africa as it was not listed among the red-listed plants of the South African National Biodiversity Institute's threatened species programme (SANBI, 2017). There are no records of threats to its existence in South Africa (Mthethwa, 2009; Semenya et al., 2013) or elsewhere in Africa where the trees are well distributed. Factors that
Table 1: The various local names, habitat and ethnomedicinal uses of different tribes in Africa.

<table>
<thead>
<tr>
<th>Culture</th>
<th>Country</th>
<th>Ethnomedicinal uses</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Umphafa, umlahlankosi, isihla</td>
<td>Zulu</td>
<td>Its bark and roots are used to treat rheumatism, gastrointestinal complaints and snake bites. Warm bark infusions are used as expectorants in cough and chest problems while root infusions are popular as a remedy for diarrhoea and dysentery. Decoctions of roots and leaves are applied externally to sores and glandular swellings for pain relief. The leaves and roots are used to treat sores, wound and burns. The fruits are eaten by children. The roots are used to treat gonorrhoea and chlamydia. The roots are used in Limpopo with other plants to treat different kinds of diseases.</td>
<td>Tas et al., 1991. van Wyk et al., 1997</td>
</tr>
<tr>
<td>Umphafa</td>
<td>Xhosa</td>
<td></td>
<td></td>
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<tr>
<td>Mokgalo</td>
<td>Tswana</td>
<td></td>
<td>Van der Merwe, 2000</td>
</tr>
<tr>
<td>Mphasamhala, ncecenyi</td>
<td>Tsonga</td>
<td></td>
<td>Liengme, 1981</td>
</tr>
<tr>
<td>Mokgalô, moomaona</td>
<td>Sepedi</td>
<td></td>
<td>Semenya et al., 2013</td>
</tr>
<tr>
<td>Mutshetshete</td>
<td>Venda</td>
<td></td>
<td>Chauke et al., 2015</td>
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<td></td>
<td></td>
<td></td>
<td>Moteetee and van Wyk, 2006</td>
</tr>
<tr>
<td>Mokhalo</td>
<td>Sesotho</td>
<td>Leaf, roots and bark infusions used for chest complaints, sores, wounds, pain relief, skin infections and syphilis. Edible fruit eaten as porridge and meal. The fruits and seeds can be fermented for beer.</td>
<td>Long, 2005</td>
</tr>
<tr>
<td>Umlahlabantu</td>
<td>Swati</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mabyana-a-mala-a-tupa, moketeke,</td>
<td>Batswana</td>
<td>The leaves are used locally as food and a health drink; the leaf paste can also be used in the treatment of boils. The root of the plant is usually used in the treatment of a wide range of painful conditions. The roots, bark and leaves are used in the treatment of arthritis, chest pains and boils. The sweet fruits of the plant are widely eaten or dried, ground to powder and cooked as porridge.</td>
<td>Setshogo and Venter, 2003, Kwape et al., 2013, Koeven, 2001</td>
</tr>
<tr>
<td>mokgalo</td>
<td></td>
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<tr>
<td>Omuk魄ete</td>
<td>Ovambo</td>
<td>Ethnoveterinary uses of the root extracts to treat diarrhoea in cattle. Extracts of the fruits are used to make wine and medicine. Extracts of the leaves and roots are used to treat skin allergy, sore fingers and rash.</td>
<td>Cheikhyoussef and Embasu, 2013</td>
</tr>
<tr>
<td>Omukaru</td>
<td>Herero</td>
<td></td>
<td>Quattrocchi, 2016</td>
</tr>
<tr>
<td>Muchechete, Mwichechete</td>
<td>Tonga/Tokaleya/Lozi</td>
<td>Root or leaf infusion is taken orally to treat gonorrhoea, syphilis, boils, pneumonia and cough</td>
<td>Chinsembu, 2016</td>
</tr>
<tr>
<td>muChecheni, chiNanga, muPakwe,</td>
<td>Shona</td>
<td>The leaves, roots and fruit are used for wounds, abnormal pains and infertility in women</td>
<td>Maroyi, 2011</td>
</tr>
<tr>
<td>muPasamala, muTsosomva</td>
<td></td>
<td></td>
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<tr>
<td>Umpafa</td>
<td>Ndebele</td>
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</table>
promote the disappearance of plant species from the wild includes unsustainable over-harvesting, habitat degradation due to agricultural practices and urban development or mining. These practices subsequently affect plants’ biodiversity and may result in the extinction of certain plant species from the wild if conservation strategies are not timely implemented.

**MATERIALS AND METHODS**

Online search engines such as Google Scholar, Web of Science, PubMed, PubChem, Scopus, Science direct and academic books, reports, journal and thesis were explored for information. Reports on ethnobotanical uses, ethnom pharmacology and phytochemistry of *Z. mucronata*, including surveys on traditional uses and distribution were sourced. The results obtained were systematically compiled and presented in this report to provide an update on the importance of this plant species in the lives of people living in under-resourced communities.

**RESULTS AND DISCUSSION**

**Ethnomedicinal and supplementary uses**

Extracts of the leaves, stem-bark and root of *Z. mucronata* are used to treat chronic cough, boil, tooth ache, rheumatism and swellings in South Africa (Iwalewa et al., 2007). A decoction of the glutinous roots is commonly administered as a painkiller for all sorts of pains, gastrointestinal problems and dysentery (van Wyk et al., 1997). A concoction of the bark and the leaves is used for respiratory ailments and other septic swellings of the skin. Pastes of the root and leaves can be applied to treat boils, swollen glands, wounds and sores. Steam baths from the bark are used to purify and improve the complexion (Palmer and Pitman, 1972). In East Africa, roots are used for treating snake bites (Hutchings et al., 1996). Most of the ethnopharmacological uses may be attributed to the peptide alkaloids and antifungal principles isolated from the bark and the leaves. The leaves are also edible and can be cooked into spinach. The seeds can be roasted and ground as a substitute for coffee (Heuzé and Tran, 2017). The leaves and fruits are also a valuable source of forage for livestock (Heuzé and Tran, 2017). The berries are edible and are used to make a porridge or as a coffee substitute (Long, 2005; Kwape et al., 2013a). The seeds are
also ground and used as a coffee substitute while the Ovambo people in Namibia use the seeds to distill “ombike”, a traditional beer. The fruit can also make a beer if fermented properly (Cheikhyoussef and Embashu, 2013).

In addition to the ethnomedicinal uses, there are other supplementary uses of this plant species such as in spirituality and construction (Hutchings, 2007; Cheikhyoussef and Embashu, 2013). The African tradition and culture believes in the application of this tree for spiritual beliefs and superstitions (Hutchings, 2007). The Zulus and Swazis of southern African use the buffalo thorn relating to burial rites. The part of the tree was also placed at a Zulu chief’s burial site to signify his resting place (Hutchings, 2007). It is thought that a twig from the tree attracts, carries and accompanies the spirit of the deceased from the place of death to the new resting place. When a
stock owner is dead and buried according to customary beliefs within the cattle or goat kraal, some branches would be placed on the grave so that the animals nibbled on leaves and twigs, and so understood that their master had died (Palmer and Pitman, 1972). In other parts, locals drag a branch around the village to protect them from evil spirits, as it is believed to keep evil spirits away (Hutchings et al., 1996). In Botswana as well as most parts of South Africa, the residents believe that the plant species may provide protection against lightning, such that anyone standing under the tree in a storm would be safe. It is also believed that if it is felled in summer, a drought, hail or lightning will certainly follow. Wood from this tree is used for timber, wagon making and fence posts as it yields a yellow, fine-grained, heavy wood which contains 12.2-15.7% tanning matter (Watt and Brandwijk, 1962). The elasticity of the shoots makes it suitable for bows and whip sticks. Some farmers use the thorny branches to make kraals or hedges to protect their livestock from predators.

Phytochemistry and pharmacological activities

The scientific validation of various parts of *Z. Mucronata* ethnomedical applications have been undertaken, to decipher its ability to treat infections; inflammation-related conditions and pain relief have yielded several cyclopeptide alkaloids. Subsequent to the isolation of some cyclopeptide alkaloids from the bark, Auvin et al. (1997) further isolated abyssenine A and mucronine D from the root bark. This was followed by the isolation of mucronine A-J and frangufoline from the stem and root barks (Figure 2a-g). Cyclopeptide alkaloids are widely distributed in the Rhamnaceae family but they have also been isolated in other plant families such as Asteraceae and Rubiaceae amongst others consisting of 0.01-1% of dried plant materials (Gournelis et al, 1998).

Phytochemistry

In a screening for the phytochemical constituents of the extracts of *Z. mucronata*, the analysis indicated the presence of polyphenols, flavonoids, tannins, alkaloids and saponins. Polyphenols and flavonoids are thought to be responsible for some of the biological activity of the extracts such as antioxidant, anti-inflammatory and antimicrobial activities (Kwape et al., 2013b; Iwalewa et al., 2007; Adewusi and Steenkamp, 2011; McGaw et al., 2007). Olajuyigbe and Afolayan (2011) reported the presence of significant amounts of polyphenols in the ethanol fruit extracts, followed by the acetone and aqueous extracts, respectively. Phenolic compounds either act by inactivating lipid free radicals or by preventing the decomposition of hydroperoxides into free radicals (Maisuthisakul et al., 2007). As such, this prevents oxidation and damage to delicate nuclear molecules such as the DNA.

Flavonoids are a group of natural phenolics with several biological activities such as anti-inflammatory, anti-allergic, anti-microbial, anti-oxidant, anti-neoplastic and anti-inflammatory properties (Adewusi and Steenkamp, 2011; McGaw et al., 2007).

Figure 2: The chemical structures of some of the cyclopeptide alkaloids that have been isolated from the extracts of *Z. mucronata*. (a) mucronine A, (b) mucronine B, (c) mucronine E, (d) sanjoinine-A (Frangufoline A), (e) abyssenine B.
anti-microbial and anti-cancer activities. Olajuyigbe and Afolayan (2007) detected the presence of proanthocyanidins in the bark extracts of Z. mucronata. Although found in minute quantities, proanthocyanidins are most likely implicated in the anti-sickling activity seen in the extracts (Mpiana et al, 2008). Other complex polyphenolic compounds such as tannins have also been studied in the phytochemical profile of extracts of Z. mucronata. The broad spectrum anthelmintic activity of extracts of this plant species is suspected to be due to the presence tannins (Watermann et al., 2010). Alkaloids are natural anti-inflammatory and analgesic compounds synthesized by some plants. The isolated alkaloids, particularly cyclopeptide alkaloids from its extracts are believed to be responsible for the analgesic, anti-inflammatory and anti-plasmodial activities.

**Pharmacology**

The reported biological activities of extracts of Z. mucronata are due to the pharmacological attributes of the constituent compounds. Some of these activities may be linked to the ethnomedicinal uses of extracts of the plant to treat infection, painful symptoms and chronic diseases such as type-2 diabetes mellitus (Table 2). The results in Table 2 suggest that bioactive compounds are extracted more with polar solvents with an exception of the dichloromethane extracts for anti-helmintic activity. This may partly support the anecdotal claims of its efficacy by local users because decoction and infusions made of water are the common mode of preparation and use.

**Antibacterial activities**

Pathogens are constantly evolving and the development of resistance to available medication continues unabated. Therefore, there is always a need for alternative therapeutic strategies to combat this trend. Aqueous extracts of the bark/root of Z. mucronata significantly inhibited the growth of Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus and Escherichia coli in a study by Adamu et al. (2005). Comparable results were also obtained by McGaw et al (2007) using aqueous extracts of the leaf on same bacteria species, as well as Enterococcus faecalis. These results suggest that the extracts contained useful phyto-compounds that could be helpful in treating diseases associated with these organisms. These compounds could be exerting their biological activity either in isolation or in synergy with other compounds present in the extracts.

**Anti-inflammatory and analgesic activities**

Inflammation is a complex biological process designed as a protection against foreign invaders and injury. However, impaired inflammatory process is implicated in the progression of several chronic diseases such as rheumatoid arthritis, obesity, type-2 diabetes mellitus and Alzheimer’s disease. Painful symptom is one of the classical signs of an inflammatory process and it contributes significantly to the severity of a chronic disease. Acetylcholine esterase is a key enzyme involved in the hydrolysis of neurotransmitter, acetylcholine. A deficiency or low levels of this neurotransmitter in the brain is responsible for Alzheimer’s disease. Some traditionally used plants have shown potentials in the inhibition of acetylcholine esterase as a therapy for the disease. Adewunmi and Steenkamp (2011) demonstrated the ability of ethyl acetate root extracts of Z. mucronata to significantly inhibit the activities of acetylcholine esterase.

**Anti-diabetic activities**

Type-2 diabetes mellitus is a chronic disease resulting from insulin resistance and pancreatic β-cell malfunctioning, which is characterised by sustained hyperglycaemia (Salas-Salvado et al., 2011). Because most of the anti-diabetic drugs in current use are associated with adverse effects such as liver problems, diarrhoea and nausea (Fujisawa, 2005), attention has shifted to alternative strategies such as the use of natural products. Decoctions made from the plant is used traditionally in Northern Nigeria to treat type-2 diabetes mellitus (Etuk et al., 2010). This ethnomedicinal uses for type-2 diabetes mellitus was the basis of scientific evaluation in recent studies (Mpiana et al., 2008; Waterman et al., 2010; Adewusi and Steenkamp, 2011). A bioassay guided study resulted in the isolation of a butanol fraction with potent α-glucosidase and α-amylase inhibitory activity (Ibrahim and Islam, 2007). The butanol fraction had significant anti-hyperglycaemic activity at a dose of 300 mg/kg body weight in rats but could not alleviate complications associated with type-2 diabetes (Ibrahim and Islam, 2007). The anti-hyperglycaemic of the extracts of Z. mucronata was further demonstrated by Mousinho (2013) using methanol extracts with the best bioactivity observed at 62.5 µg/mL. However, the mechanism of action of extracts of this plant species was believed to be independent of insulin. The mechanism of hypoglycaemic action was via the inhibition of both α-glucosidase and α-amylase possibly involving the activation of certain receptors without insulin. This could present an alternative therapeutic strategy for treating this type of disease in the future.

**Antioxidant activities**

The fruit extracts of Z. mucronata had a dose-dependent antioxidant activity and in direct correlation with the polarity of the extractant (Kwape et al., 2013b). Significant
Table 2: Some recorded biological activities based on ethnomedicinal uses of extracts of *Z. mucronata*.

<table>
<thead>
<tr>
<th>Plant part</th>
<th>Ethnomedicinal uses</th>
<th>Solvent used</th>
<th>Biological assay</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruits</td>
<td>Extracts of the fruits are used to make wine and medicine. Extracts of the leaves and roots are used to treat skin allergy, sore fingers and rash 11 (Cheikhyoussef and Embashu, 2013)</td>
<td>Water, ethanol, acetone</td>
<td>Free radical scavenging activity</td>
<td>Kwape et al., 2013b; Olajuyigbe and Afolayan, 2011</td>
</tr>
<tr>
<td>Bark/root</td>
<td>Decoctions of the leaves and roots are used to treat sores, wound and burns (van der Merwe, 2000)</td>
<td>Water/ Ethanol</td>
<td>Anti-bacterial activity against <em>Proteus mirabilis</em>, <em>Pseudomonas aeruginosa</em>, <em>Staphylococcus aureus</em> and <em>Escherichia coli</em>, <em>Klebsiella pneumoniae</em></td>
<td>Adamu et al., 2005;</td>
</tr>
<tr>
<td>Root</td>
<td>Decoction of root is used as a remedy for snake bite; Poultice from roots and leaves are applied to boils and skin infection (Quattrocchi, 2016)</td>
<td>Methanol</td>
<td>Anti-fungal activity against <em>Trichophyton rubrum</em>, <em>Trichophyton mentagrophytes</em>, <em>Aspergillus fumigatus</em> and <em>Microsporum gratiss</em></td>
<td>Adamu et al., 2006</td>
</tr>
<tr>
<td>Leaf</td>
<td>Extracts of the leaf used to treat enteric conditions (Kudi and Myint, 1999)</td>
<td>Methanol</td>
<td>Anti-viral activity against poliovirus and astrovirus</td>
<td>Kudi and Myint, 1999</td>
</tr>
<tr>
<td>Root</td>
<td>The roots are macerated in water and used for stomach ache; constipation and muscular pain (Bruschi et al., 2011)</td>
<td>Methanol</td>
<td>Good inhibitory action on acetylcholine esterase activity</td>
<td>Adewusi and Steenkamp, 2011; Kwape et al., 2013a</td>
</tr>
<tr>
<td>Root</td>
<td>Root infusions are popular as a remedy for diarrhoea and dysentery (van Wyk et al., 1997)</td>
<td>Ethanol</td>
<td>Anti-bacterial activity against <em>Escherichia coli</em>, <em>Staphylococcus aureus</em> and <em>E. faecalis</em></td>
<td>Olajuyigbe and Afolayan, 2011</td>
</tr>
<tr>
<td>Stem bark</td>
<td>Used to treat fever (Adamu et al., 2006)</td>
<td>Ethyl acetate</td>
<td>Anti-malarial activity against <em>Plasmodium falciparum</em></td>
<td>Zininga et al., 2017</td>
</tr>
<tr>
<td>Root bark</td>
<td>Used to treat sickle cell anaemia 10 (Mpiana et al., 2007)</td>
<td>Water</td>
<td>Anti-sickling activity on erythrocytes</td>
<td>Mpiana et al., 2008</td>
</tr>
<tr>
<td>Twig/wood/rootbark</td>
<td>Extract of the bark is used as anti-helmintic (Quattrocchi, 2016)</td>
<td>Dichloromethane/methano (1:1) and water</td>
<td>Anti-helmintic activity against <em>Caenorhabditis elegans</em>, <em>Hymenolepis diminuta</em>, <em>Schistosoma mansoni</em></td>
<td>Waremann et al., 2010; Moolgard et al., 2001</td>
</tr>
<tr>
<td>Leaf</td>
<td>Extracts of the leaf are used locally as health drink (Kwape et al., 2013a)</td>
<td>Methanol</td>
<td>Protective effect on liver function</td>
<td>Kwape et al, 2013a</td>
</tr>
<tr>
<td>Bark</td>
<td>A decoction of the plant is also used to treat type-2 diabetes mellitus (Etuk, 2010)</td>
<td>Water/Butanol/methanol</td>
<td>Anti-diabetic</td>
<td>Ibrahim and Islam, 2007; Mousinho, 2013</td>
</tr>
</tbody>
</table>
free radical scavenging activity was observed with the methanol extracts but less activity with the hexane extracts using the 2,2'-azinobis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS) method. Similar results were previously reported by Olajuyigbe and Afolayan (2011) using the ABTS and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity methods. The ethanol extract had the highest antioxidant activity, followed by the acetone extract while the aqueous extract was the least active. The respective IC$_{50}$ values of 0.0306 ± 0.04, 0.0317 ± 0.04 and 0.0429 ± 0.04 mg/mL were obtained using the ABTS methods, while IC$_{50}$ values of 0.0422 ± 0.03, 0.0482 ± 0.02 and 0.0646 ± 0.02 mg/mL were obtained using the DPPH methods for the ethanol, acetone and water extracts of the bark (Olajuyigbe and Afolayan, 2011). These reports indicated the presence of antioxidant compounds in parts of Z. mucronata that could be beneficial in the management of oxidative stress. Oxidative stress has been implicated in the pathogenesis of many chronic diseases, therefore extracts having potential as antioxidants could be useful in the management of such disease.

**Potential anti-viral activity**

An ethnobotanical survey conducted in Zambia listed Z. mucronata among the plant species used to treat HIV/AIDS related diseases (Chisembo, 2016). A previous study on the methanol leaf extracts indicated significant activity on poliovirus and astrovirus (Kudi and Myint, 1999). Although recent breakthroughs in the development of anti-retroviral drugs have been recorded, HIV/AIDS remains a lethal disease, especially in resource limited areas of developing countries. There are no scientific records on the inhibition of HIV virus by Z. mucronata extracts, but the ethnomedicinal uses of its plant extracts for related diseases and the inhibition of the growth of other viruses (Kudi and Myint, 1999) could serve as a motivation for such evaluation.

**Hepato-protective activities**

Oxidative stress is implicated in the pathogenesis and progression of many chronic ailments including liver diseases. Induction of lipid peroxidation by dimethaote can cause oxidative stress, and this hypothesis was tested to determine the capacity of Z. mucronata extracts to protect the liver in a mice model. Treatment with methanol extracts of the leaf of Z. mucronata was found to prevent lipid peroxidation in rats (Kwape et al., 2013a). In addition, the methanol fruit extracts also protected the liver in a similar manner (Kwape et al, 2013b), suggesting that the bioprotective compounds are present in both the leaves and fruits. The methanol fruit extracts further demonstrated good free radical scavenging activity, which suggests that the mode of action of the extracts was via the deactivation of oxidative radicals which could be harmful to hepatic cells.

**Other pharmacological activities**

Methanol extracts of the root of Z. mucronata inhibited the growth of Trichophyton rubrum, Trichophyton mentagrophytes, Aspergillus fumigates and Microsporum gratis (Adamu et al., 2006). These organisms have been implicated in superficial skin infections such as cutaneous mycoses, thus extracts of Z. mucronata may be helpful in the treatment of such disease. Aqueous extracts of the root bark also had good activity against cestodes of Hymenolepis diminuta (Mølgaard et al., 2001), a causative organism of schistosomiasis. In another study to demonstrate anti-sickling activity, aqueous extracts of Z. mucronata actively prevented sickling of erythrocytes (Mpiana et al., 2008). The anthocyanin and tannin contents of the extracts were presumed to be responsible for this bioactivity (Mpiana et al., 2008). The anti-plasmodial activity of ethyl acetate fraction of the stem bark of Z. mucronata was active against Plasmodium falciparum (Zininga et al., 2017).

**Cytotoxicity**

Medicinal plants are usually extracted and administered by traditional healers using water or ethanol as solvents. There are no reports of adverse health effects resulting directly from the consumption of herbal products made of extracts of Z. mucronata. The dichloromethane extracts of the root of Z. Mucronata was reported to have mutagenic effects on strain TA98 in the presence or absence of metabolic activation (Elgorashi et al., 2003). Also, the methanol extracts of the leaf were found to be relatively cytotoxic to HT-29 human colon cancer cells (Kudi and Myint, 1999). However, administration of 300 mg/kg body weight of methanolic extracts of the leaf (Kwape et al., 2013), root and twig (Taylor et al., 2003) did not show any sign of toxicity in rats. It is plausible that organic solvents such as dichloromethane can transform the bio-activity of the constituent of phyto-compounds.

**Conclusions**

Extracts of Z. mucronata are widely used as food, beverages and medicines to treat infections and relieve painful conditions. The observation on these ethnomedicinal uses has led to the isolation of potent compounds with demonstrable biological activities. However, some of the ethnomedicinal uses of extracts of the plant, such as anti-diarrhoea, anti-viral and anti-cancer activities are yet to
evaluated scientifically. Although, the biological activities of the extracts have been attributed to the isolated cyclopeptides alkaloids, proanthocyanidins, tannins and other polyphenols, but the mechanisms of action of these compounds remain unclear.

This plant species is widely available in Africa, and if the ethnomedicinal uses could be proven with scientific data, it may serve as a cheaper alternative source for disease treatment. Also, exploitation and possible exportation of this natural resource to other parts of the World could provide extra income for communities in Africa. Apart from a few in vivo studies on extracts of Z. mucronata (Ibrahim and Islam, 2007; Kwape et al., 2013a; Kwape et al., 2013b), most reports were based on in vitro evaluations.

Much work is required to fully explore and validate the ethnomedicinal uses and potentials of this important plant species. This knowledge would be essential in the development of drugs or at least form part of the templates for the development of potent drugs.

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