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Review

A review on the botanical aspects, phytochemical contents and pharmacological activities of *Warburgia ugandensis*

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Warburgia ugandensis **Sprague (Family Canellacea) commonly known as Ugandan greenheart or pepper bark tree, is a highly valued medicinal plant in traditional medicine with a broad spectrum of antimicrobial activity whose parts especially the leaves and stem bark have for long been used in the treatment and management of many diseases and health conditions such as stomachache, cough, toothache, fever, malaria, oral thrush, measles and diarrhea in African communities where the plant occurs. This review focused on the phytochemical contents, medicinal uses and antimicrobial activities of *W. ugandensis* based on published peer reviewed articles. This review established that the high therapeutic value of *W. ugandensis* is attributed to the abundance of drimane sesquiterpenes in its stem bark and leaves. These chemicals have also made the plant to have potent antibacterial and antifungal activities. However, more pre-clinical and clinical trials need to be done to further validate the traditional medicine applications of *W. ugandensis* for possible drug discovery. Due to its high demand, *W. ugandensis* has been over exploited and hence its population is in drastic decline. Consequently, there is need for development of advanced and more rapid propagation techniques to increase its population and distribution in its natural environment to meet the ever-increasing demand.**

Key words: Antimicrobial, Canellaceae, medicinal uses, phytochemicals, *Warburgia ugandensis.*

INTRODUCTION

Warburgia ugandensis Sprague (Family Canellaceae) is a plant with immense medicinal values with restricted distribution in tropical Africa (Muller et al., 2015). It is commonly known as the “Uganda Green Heart Tree”

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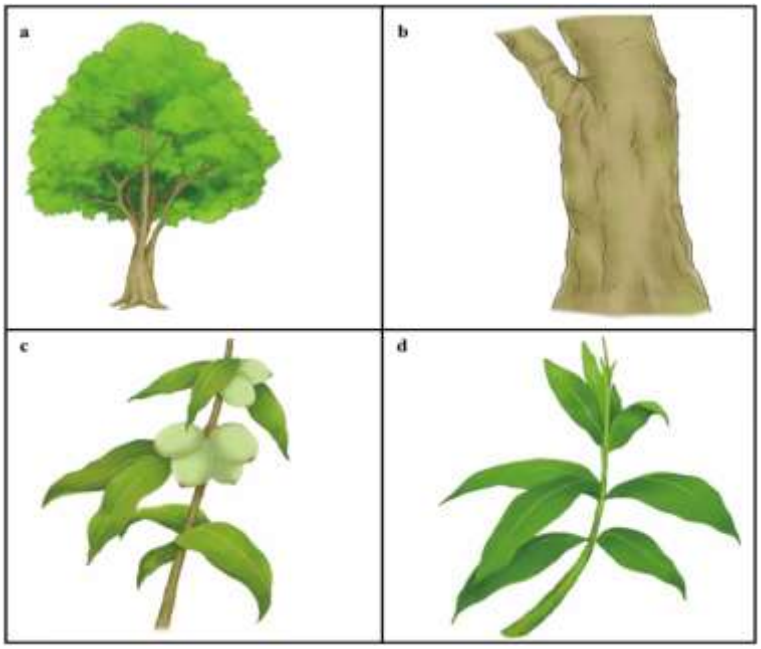

Figure 1. Morphology illustration of the main features of *W*. *ugandensis*: **a)** Whole plant of *W. ugandensis;* **b)** Stems of *W. ugandensis;* **c)** Fruits of *W. ugandensis;* **d)** Leaves of *W. ugandensis*. Source: Natural Chemotherapeutics Research Institute, Uganda.

or the “Pepper bark tree” with a unique characteristic bitter-peppery taste (Njire et al., 2014). Owing to its antimicrobial activities, *W. ugandensis* have been widely used throughout its distribution range to treat and manage myriad of diseases and disorders since time immemorial including cough, toothache, common cold, bronchial infections, parasitic infections, stomachache, fever, malaria, oral thrush, muscle pain, cystitis, constipation, weak joints, measles, and diarrhea among others (Lovett et al., 2006; Henke, 1994; Kiringe, 2006; Kokwaro, 2009; Wamalwa et al., 2006). Indeed, *W. ugandensis* is a highly valued plant species in African traditional health systems especially within the communities where it naturally grows (Were et al., 2015). In fact, due to the increasing demand for chemical diversity in screening programs, and seeking therapeutic drugs from natural products, interest particularly, in medicinal plants throughout the world has significantly grown (Were et al., 2015). This tree species has a high pharmaceutical value with potent antimicrobial activity (Olila et al., 2001).

Scientific studies showed that stem bark and leaves of *W. ugandensis* contain a number of essential phytochemicals such as drimane sesquiterpenes including ugandensidial, polygodial, warburganal, and isopolygodial (Were et al., 2015). Consequently, the medicinal efficacy of this plant could be due to the presence of some of these phytochemicals (Kuglerova et al., 2011). The stem bark of *W. ugandensis* accumulates higher amounts of the medicinally active phytochemical compounds explaining its preference for medicinal use compared to other plant parts (Grieb et al., 2011). Unfortunately, the stripping off of the tree bark injures or kills the tree (Botha et al., 2004). And with the increasing demand in the global market, the wild population of *W. ugandensis* has been greatly exploited raising concerns regarding conservation and the sustainability of utilization (WHO, 2002).

The nature of bioactive compounds in medicinal plants and their activities are influenced by genetic and environmental factors including geographical locations (Ullah et al., 2012; Soureshjan and Heidari, 2014; Arya et al., 2010; Muchugi et al., 2012). Abuto et al. (2016) observed that the antimicrobial activities varied among *W. ugandensis* populations across the Kenya rift valley due to possibly genetic diversity. This therefore, implies that the medicinal efficacy of the same species of plants from different populations may vary. The fruit is inedible, all plant parts have a hot peppery taste, leaves and seeds are used to add flavour to curries (Dharani, 2011). The wood of *W. ugandensis* produces fragrance that persists over 4 years of storage. The tree also produces resin that is used locally in Uganda as glue to fix tool handles (Orwa, 2009).

Botany and distribution of *W. ugandensis*

W. ugandensis is an evergreen plant with a spreading rounded crown (Figure 1a). It grows to about 4.5 to 40 m

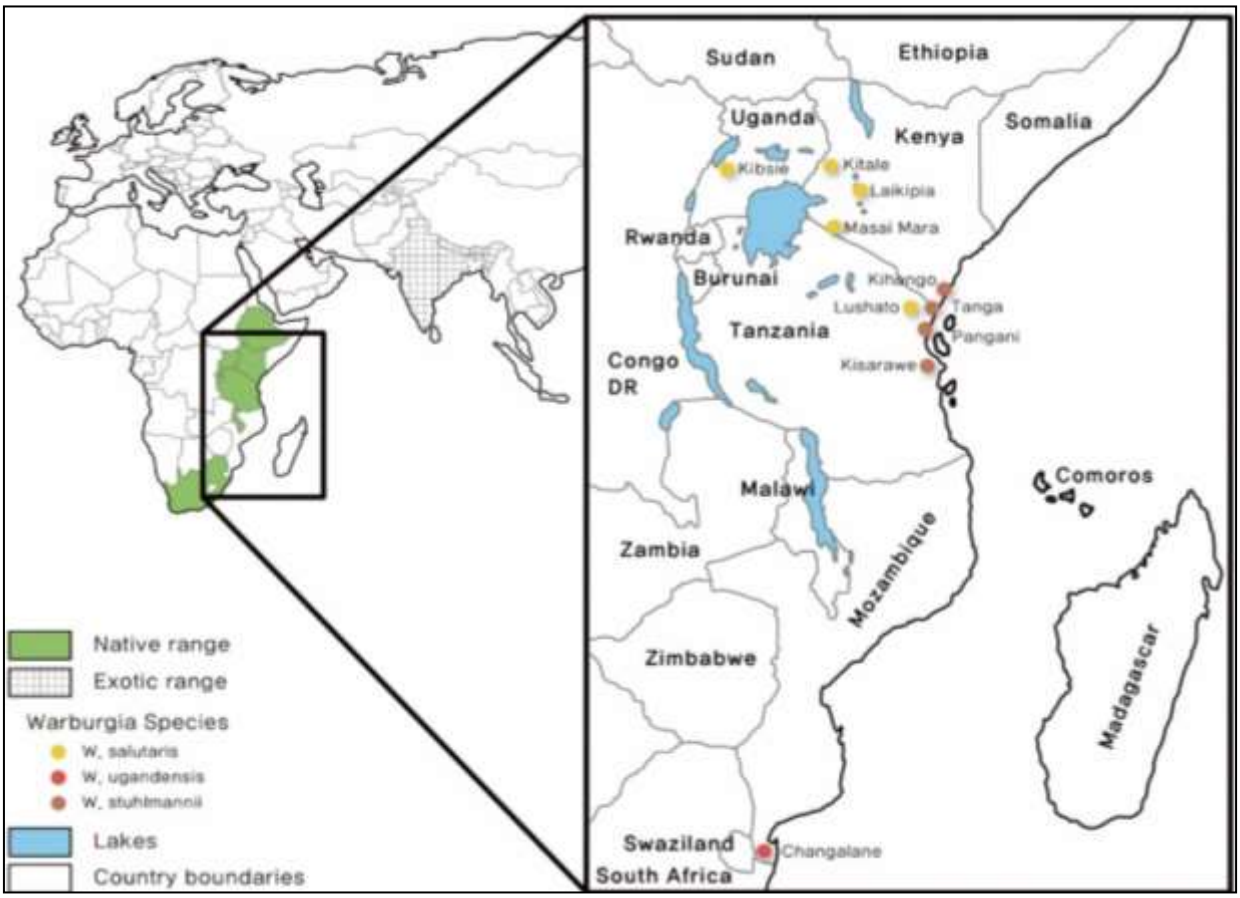

Figure 2. The distribution range of *W. ugandensis* and other related species (Muchugi et al., 2008).

in height and diameter of about 70 cm at breast height (Figure 1a) with a smooth or scaly, pale green or brown stem bark (Orwa, 2009) (Figure 1b); leaves are simple, alternate, stalked, glossy, short, with a presence of dotted glands (Figure 1d); flowers are solitary or in small 3-4 flowered cymes, axillary, regular and bisexual (Leonard and Viljoen, 2015). The fruit is a berry, at first green and ellipsoidal, later sub-spherical and turning purplish on maturation (Figure 1c); seeds are compressed and more or less cordate, yellow-brown in colour (Beentje et al., 1994). In fact, *W. ugandensis* is a hermaphroditic plant.

Ecologically, *W. ugandensis* occurs in lowland rainforests, upland dry evergreen forests, secondary bush and grasslands and on termitaria in swamp forests (Orwa, 2009). *W. ugandensis* and other related species are native to Northeast Tropical Africa: Ethiopia; East Tropical Africa: Uganda, Tanzania and Kenya; Central Africa: Democratic republic of Congo and South Tropical Africa: Malawi, South Africa and Swaziland (Orwa, 2009) (Figure 2).

Traditional medicinal uses of *W. ugandensis*

W. ugandensis has gained a lot of popularity due to the high demand for the medicinal extracts from its bark, roots and leaves for use by traditional healers (Wamalwa et al., 2006; Olila et al., 2001). *W. ugandensis* is one of the priority species for herbal medicine in Kenya (Hamilton, 2008). Herbal medicine extracted from bark, roots, young twigs, leaves and fruits are used by the traditional healers (Maroyi, 2013). *W. ugandensis* is actually considered an integral part of African traditional medicine by very many herbalists and traditional healers across the continent. All plant parts of *W. ugandensis* are used by herbalists and traditional healers to treat a wide range of diseases. Most herbalists/traditional healers use the bark of the herbal plant for various herbal formulations but the leaves and roots are as well highly medicinal. Various plant parts are used to cure or alleviate ailments such as stomachache, malaria, toothache, erectile dysfunction, measles, candidiasis, weak joints among others (Table 1). The mode of common use is by chewing and swallowing the juice from the bark of *W. ugandensis* (Kubo et al., 1976); powdered form is also known to be very effective in the treatment of the same diseases (Githinji et al., 2010). The skills and knowledge about the traditional herbal medicines are normally passed on orally from generation to generation

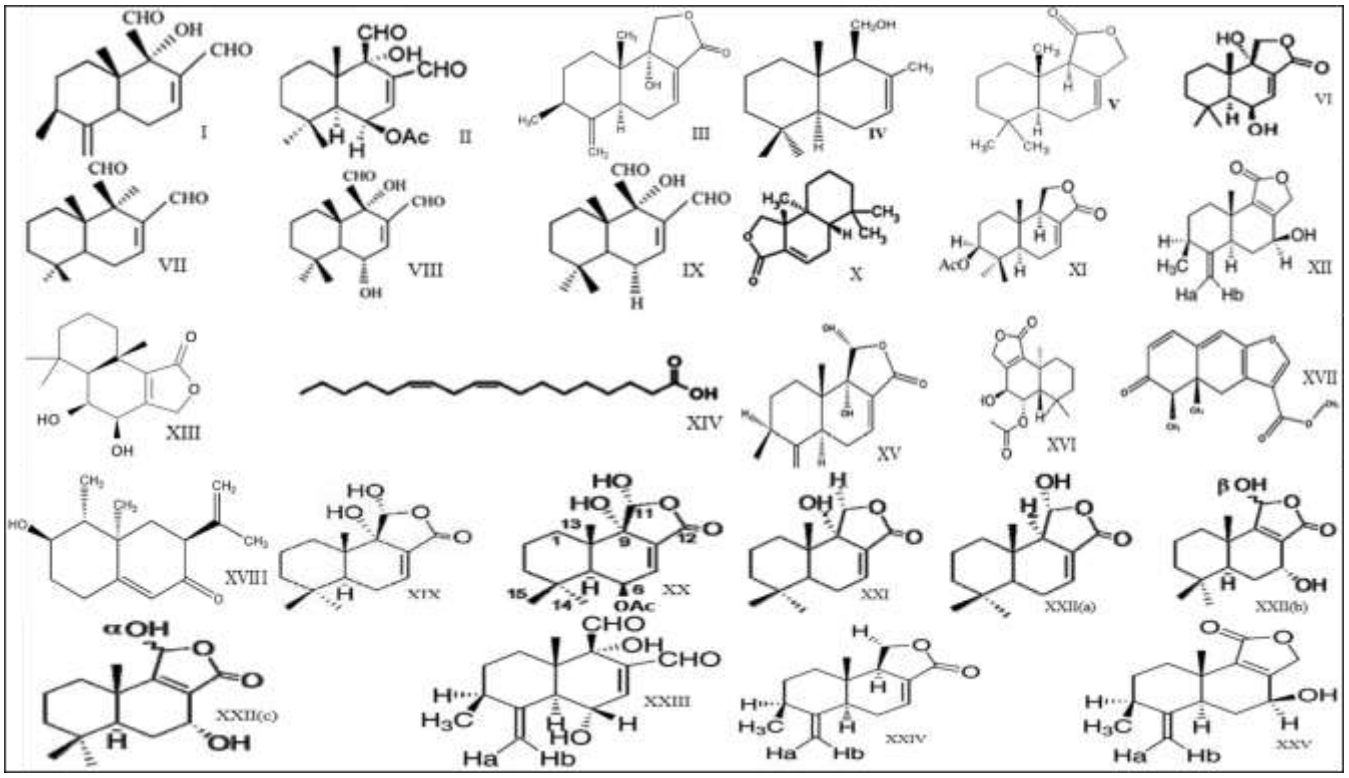

Figure 3. Molecular structures of compounds (I-XXV) in *W. Ugandensis* (Victor, 2013).

(Kassaye et al., 2006).

The knowledge passed on include what each herbal plant treats, and how the plant part is harvested, which plant part to use and the mode of its administration.

Toxicity of *W. ugandensis*

Acute toxicity tests for extracts of *W. ugandensis* showed that the plant is not toxic at acute exposure to test organisms (Ahmad et al., 2017; Karani, 2013). Administration of single doses of varied concentrations of *W. ugandensis* to mice, no mortality was observed even at highest concentrations tested. *W. ugandensis* was classified as relatively harmless based on the scale of Loomis and Hayes (1996) with LD_{50}>5000 mg/kg body weight (Karani, 2013). In another study, *W. ugandensis* was showed to be non-toxic to *Drosophila melanogaster* at acute exposure but toxic at chronic exposure (Ahmad et al., 2017). *W. ugandensis* as well has been used as a medicinal plant whose bark extracts, leaves and young shoots have been used for ages with no adverse effects (Henke, 1994; Kokwaro, 1976; Mbuya et al., 1994). *W. ugandensis* stem bark extracts have been established to be non-toxic to BALB/c macrophages (Githinji et al., 2010). Consequently, it can be concluded that the use of *W. ugandensis* as a medicinal plant is indeed safe although further studies especially clinical studies on its safety still need to be conducted.

Phytochemistry of *W. ugandensis*

The high therapeutic values of *W. ugandensis* is attributed to the abundance of phytochemical compounds in it including drimane sesquiterpenes (Haraguchi, 1998; Frum et al., 2005; Frum and Viljoen, 2006; Jansen and De Groot, 1991; Kioy, 1990) and tannins and mannitol (Van Wyk and Gericke, 2000). Studies on this plant have indicated the presence of the following compounds (Figure 3) muzigadial (I), ugandensidial (II), muzigadiolide (III) (Mashimbye, 1999) drimenol (IV), drimenin (V) (Mohanlall and Odhav, 2009), pereniporin B (VI) and polygodial (VII) (Taniguchi and Kubo, 1993), mukaadial (VIII), warburganal (IX), cinnamolide (X), cinnamolide-3β-acetate (XI), deacetylugandensolide (XIII), 7α-hydroxy-8-drimen-11,12-olide (XII), linoleic acid (XIV), and 11α-hydroxy muzigadiolide (XV) in the stem bark (Kioy, 1990) and Ugandensolide (XVI), warburgin (XVII), warburgiadione (XVIII) (Mohanlall and Odhav, 2009). In addition, sesquiterpenes such as ugandenial A (XIX) (Xu et al., 2009), 9α-11α-dihydroxy,6ß-acetyl-cinnamolide (XX), 9α-hydroxycinnamolide (XXI) and dendocarbins A (XXII) (a), L (b) and M (c) were present (Wube et al., 2005). Coloratane sesquiterpenes 6α,9α-dihydroxy-4(13), 7-coloratadien-11,12-dial (XXIII), 4(13),7-coloratadien-

Table 1. Traditional medicinal uses of *W. ugandensis.*

Disease/Ailment	Plant part	Mode of preparation/administration	References
Cough	Bark	Dried chewed and swallowed.	(Kiringe, 2006; Kokwaro, 2009)
Constipation	Bark	Dried chewed and swallowed.	(Kokwaro, 2009)
Chest pains	Bark	Dried chewed and swallowed.	(Kiringe, 2006; Wamalwa et al., 2006)
Diarrhea	Bark, roots	Dried chewed and swallowed; fresh roots boiled and mixed with soup.	(Lovett et al., 2006)
Malaria	Bark, leaves, roots	Boiled in water and decoction drunk	(Lovett et al., 2006; Kokwaro, 2009; Wamalwa et al., 2006)
Fever	Bark	Dried chewed and swallowed.	(Kokwaro, 2009;Lovett et al., 2006)
Stomachache	Bark	Dried chewed and swallowed.	(Henke, 1994; Kiringe, 2006; Kokwaro, 2009)
Toothache	Bark	Dried chewed and swallowed, dried bark powder can be applied	(Kokwaro, 2009; Lovett et al., 2006)
Hernia	Bark	Dried chewed and swallowed.	(Lovett et al., 2006)
General body pains	Bark	Dried chewed and swallowed.	(Kokwaro, 2009; Lovett et al., 2006)
Fatigue	Bark	Dried chewed and swallowed.	(Lovett et al., 2006)
HIV-related opportunistic Infections	Bark	Dried chewed and swallowed.	(Mbwambo et al., 2009)
Loss of appetite	Bark	Dried chewed and swallowed.	(Kiringe, 2006)
Measles	Bark	Not specified	(Olila, 1993)
Muscle pains	Bark	Dried chewed and swallowed.	(Kokwaro, 2009)
Skin diseases	Leaves	Bath decoctions	(Wamalwa et al., 2006)
Common cold	Bark	Not specified	(Lovett et al., 2006)
Sinuses	Bark	Dried and ground to a snuff	
Throat infections	Bark	Bark decoction or bark mixed with animal fat	(Kiringe, 2006)
Tuberculosis	Bark	Not specified Ethiopia	(Wube et al., 2005)
Ulcers	Bark	Dried chewed and swallowed.	(Kiringe, 2006)
Weak joints	Bark	Weak joints	(Kokwaro, 2009)
Chest pain/Complaints	Bark	Dried chewed and swallowed Or Smoke from burning bark inhaled	(Kiringe, 2006; Wamalwa et al., 2006)
Yellow fever	Bark	Not specified	(Kuglerova et al., 2011)
Visceral leishmaniasis	Bark	Bark boiled in water/soup and taken orally	(Ngure et al., 2009)
Emetic	Bark, leaves	Hot decoction of bark or leaves	(Nanyingi, 2008)
Lung problems	Bark	Bark decoction	(Kiringe, 2006)
Snake bite	Bark	Not specified	(Olila, 1993)
Intestinal Worms	Bark	Not specified	(Lovett et al., 2006)

12,11-olide (XXIV), and 7b-hydroxy-4(13),8-coloratadien-11,12-olide (XXV) are present in stem bark of *W. ugandensis* (Wube et al., 2005) Monoterpenes (Kioy, 1990) and flavonol glycosides in the leaves (Manguro et al., 2003) (Figure 3).

Antimicrobial activities

Many pharmacological studies have confirmed antimicrobial activities of *W. ugandensis* extracts (Were et al., 2015; Kuglerova et al., 2011; Ahmed et al., 2013). The curative efficacy of extracts of *W. ugandensis* is attributed to the potent antifungal and antibacterial activities of the synergistic effects of the different bioactive phytochemical compounds in the plant (Olila et al., 2001; Haraguchi, 1998; Jansen and De Groot, 1991; Mashimbye, 1999; Taniguchi and Kubo, 1993). The pattern of antimicrobial inhibition of the various extracts of *W. ugandensis* varied with the solvents used for extraction and the part of the plant used as well as the regions where the samples were collected. It was observed that the DCM solvent extracts exhibited the highest antimicrobial activity than the MeOH solvent extracts regardless of the plant part analyzed.

Antibacterial and antimycobacterial activities

W. ugandensis showed antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli* in the agar well diffusion assay (Olila et al., 2001). This effect, however, was not demonstrable in the paper disc assay. Kuglerova et al. (2011) also showed that *W. ugandensis* stem bark exhibited antibacterial activity with a minimum inhibitory concentration (MIC) of 256 µg/ml against *S. aureus* and 512 µg/ml against *Enterococcus faecalis*. Similarly in Kitale and Rumuruti in Kenya, dichloromethane stem bark extracts of *W. ugandensis* exhibited inhibitory activity against *S. aureus* and *C. albicans* with mean zones of inhibitions both of 19.75 mm (Abuto et al., 2016). The preliminary bioassay results showed that *S. aureus* and *C. albicans* were the most susceptible microorganisms while *E. coli* was resistant to *W. ugandensis* extracts (Abuto et al., 2016). S*. aureus* was more sensitive than *E. coli* to *W. ugandensis* extracts (agar well assay). Since *S. aureus* is more often associated with secondary bacterial infections in measles than *E. coli* it may explain the value of the plant in measles therapy (Olila et al., 2001). The compound muzigadial has been found to be very active against *S*. *aureus* (Abuto et al., 2016). Antimycobacterial activity of *W. ugandensis* against *Mycobacterium aurum*, *M. fortuitum*, *M. phlei* and *M. smegmatis* were demonstrated using dichloromethane extract of the stem bark of *W. ugandensis* (Wube et al., 2005). Wube et al. (2005) further showed that the active constituents of *W. ugandensis* gave MIC values ranging from 4 to 128 mg/ml, compared to the antibiotic drugs ethambutol and isoniazid with MIC ranging from 0.5 to 8 mg/ml and 1 to 4 mg/ml respectively. Furthermore, muzigadial and muzigadiolide were found to have antimycobacterial activities against *M. fortuitum* (MIC of 16 µg/ml) and *M. phlei* (MIC of 64 µg/ml) respectively (Wube et al., 2005).

Antifungal activity

In a study conducted by Olila et al. (2001), they observed that the ethanolic extracts of the stem bark of *W. ugandensis* showed significant antifungal activity against *Candida albicans*. Similarly, warburganal which is one of the major phytochemicals contained in *W. ugandensis* exhibited a broad-spectrum antifungal activity against yeasts and filamentous fungi especially against *Saccharomyces cerevisiae*, *C. utilis,* and *Sclerotinia libertiana* (Kubo, 1995). Kuglerova et al. (2011) also observed that extracts from stem bark of *W. ugandensis* showed strong antifungal activity with a MIC of 256 µg/ml against *C. albicans* due to the presence of the muzigadial compound in the plant. Furthermore, *W. ugandensis* stem bark and leaves extracts were found to exhibit antifungal activity against *C. utilis* (Mbwambo et al., 2009; Ahmed et al., 2013; Taniguchi et al., 1983).

Antiplasmodial activity

W. ugandensis stem bark extract has showed potent activity against *Plasmodium knowlesi* and *P. Berghei* (Taniguchi et al., 1978). In fact, in an *in vitro* experiment, the methanol extracts from various parts of *W. ugandensis* exhibited antiplasmodial activity with an IC_{50} value of less than 5 mg/ml against both chloroquine-sensitive and chloroquine resistant strains of *P. falciparum* (Taniguchi et al., 1978). This result sets a basis upon which future antimalarial drugs could be developed and typically explained the continuous use of the plant in traditional medicine for the treatment and management of malaria throughout its distribution range.

Other activities

Beside the activities discussed above, the presence of drimane sesquiterpenoids in *W. ugandensis* makes the plant a vital insect pest controlling agent (Olila et al., 2001; Frum et al., 2005; Xu et al., 2009; Nanyingi et al., 2010; Kubo et al., 1977). Similarly, warburganal and muzigadial showed strong inhibitory effects on the feeding of larvae of the monophagous *Spodoptera exempta* and the polyphagous *Spodoptera littoralis* at a concentration of 0.1 ppm in a regular leaf disk method (Nanyingi et al., 2010). *W. ugandensis* also exhibited

antifeedant activity against *S. frugiperda*, *Heliothis armigera* and *H. virescens* (Kubo et al., 1977).

Drimane sesquiterpenoids in *W. ugandensis* are known to have cytotoxic activities that is, toxic effects at cellular level (Frum et al., 2005; Taniguchi and Kubo, 1993; Nanyingi et al., 2010; Meinwald et al., 1978). For example, ethanolic leaf extracts of *W. ugandensis* exhibited cytotoxic activity (95% CI), against brine shrimp larvae with reference to cyclophosphamide, a standard anticancer drug (Mbwambo et al., 2009). In an *in vitro* study, *W. ugandensis* bark exhibited potent cytotoxic activity on KB cell line with 99% and 64% inhibition at 10 and 1 mg/ml, respectively (Xu et al., 2009).

The hexane extract of *W. ugandensis* was strongly antileishmanial against *Leishmania major* and *Leishmania donovani* with IC_{50} value of 9.95 and 8.65 respectively (Ngure et al., 2009). *W. ugandensis* demonstrated trypanocidal activity against *Trypanosoma brucei in vitro* (Olila et al., 2001). A cytotoxic sesquiterpene characterized as muzigadial was isolated from *W. ugandensis* and used to treat trypanosomiasis and other parasitic diseases in animals (Meinwald et al., 1978; Kioy, 1990). Rugutt et al. (2006) in Kenya, showed *W. ugandensis* activity against soil pathogens namely *Fusarium oxysporum*, *Alternaria passiflorae* and *Aspergillus niger.* All these activities clearly justify the continued use of *W. ugandensis* in traditional medicine to treat and manage myriad of diseases and disorders.

CONCLUSION

In all the communities where *W. ugandensis* occurs and particularly across Africa, it is medicinally highly valued and used by the local populations to treat and manage wide range of ailments and health conditions indicating that the species is a very vital source of ethnomedicine. Besides, there have not been records of its toxicity in populations where its leaves and bark have been used as vital sources of medicine. Several pharmacological studies have been carried out on *W. ugandensis* extracts leading to the identification and isolation of highly medicinal compounds backing up some of its documented traditional use in treatment of disease across Africa. There is no much documentation providing evidence of proprietary medicinal product development from *W. ugandensis* yet it has been proven through many studies of its potent therapeutic values. The need for clinical research on the extracts of *W. ugandensis* could be the research gap needed to make these products attractive for further pharmaceutical product development. Further research is therefore important on *W. ugandensis* to develop products with highly valued medicinal contents. In all or most of the areas, the local people use the raw extracts directly in the treatment and management of various ailments without precise standardized dosage across the discipline. Therefore, further preclinical and clinical studies ought to be done to standardize the use of this plant in treatment and management of a number of disease conditions. It is also important to note that the ever-increasing use of *W. ugandensis* in the treatment and management of various ailments has led to over exploitation hence decreasing its population drastically. Consequently, there is need for advanced and rapid propagation techniques to increase the population and distribution of *W. ugandensis*

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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REFERENCES

Abuto JO, Muchugi A, Mburu D, Machocho AK, Karau GM (2016). Variation in antimicrobial activity of warburgia ugandensis extracts from different populations across the Kenyan Rift Valley. Journal of Microbiology Research 6(3):55-64.

Ahmed M, Laing M, Nsahlai IV (2013). *In vitro* antihelmintic activity of crude extracts of selected medicinal plants against Haemonchus contortus from sheep. Journal of Helminthology 87(2):174-179.

Arya V, Yadav S, Kumar S, Yadav JP (2010). Antimicrobial activity of Cassia occidentalis L. (leaf) against various human pathogenic microbes. Life Sciences and Medicine Research 9(1):1-10.

Beentje H, Adamson J, Bhanderi D (1994). Kenya trees, shrubs, and lianas. National Museums of Kenya.

Botha J, Witkowski ETF, Shackleton CM (2004). The impact of commercial harvesting on Warburgia salutaris (‘pepper-bark tree’) in Mpumalanga, South Africa. Biodiversity & Conservation 13(9):1675-1698.

Dharani N (2002). Field guide to common trees & shrubs of East Africa. Penguin Random House South Africa.

Frum Y, Viljoen AM (2006). *In vitro* 5-lipoxygenase and anti-oxidant activities of South African medicinal plants commonly used topically for skin diseases. Skin Pharmacology and Physiology 19(6):329-335.

Frum Y, Viljoen AM, Drewes SE (2005). *In vitro* 5-lipoxygenase and antioxidant activities of Warburgia salutaris and drimane sesquiterpenoids. South African Journal of Botany 71(3-4): 447-449.

Githinji EK, Irungu LW, Tonui WK (2010). *In vitro* effects of Warburgia ugandensis, Psiadia punctulata and Chasmanthera dependens on Leishmania major promastigotes. African Journal of Traditional, Complementary and Alternative Medicines 7(3).

Grieb B, Gebauer J, Mwangi PN (2011). Warburgia ugandensis-Bioassay of different plant parts concerning the antimicrobial activity. Tropentag 2011-Development on the margin-Book of abstracts 418.

Hamilton AC (2008). Medicinal plants in conservation and development

case studies and lessons learnt.
Haraguchi H (1998). Mode of action of antimicrobial substances in plants. Recent Research Development in Agriculture and Food Chemistry 2:259-268.
Henke B (1994). Kenya Trees: Shrubs and Lianas. Nairobi, Kenya: National museums of Kenya.
Jansen BMJ, de Groot A (1991). The occurrence and biological activity of drimane sesquiterpenoids. Natural Product Reports 8(3):309-318.
Kassaye K, Amberbir A, Getachew B, Mussema Y (2006). A historical overview of traditional medicine practices and policy in Ethiopia. Ethiopian Journal of Health Development 20:127-134
Kioy D, Gray AL, Waterman PG (1990). A comparative study of the stem bark drimane sesquiterpenes and leaf volatile oils of Warburgia ugandensis and W. stuhlmanii. Phytochemistry, 29(1):3535–8.
Kiringe JW (2006). A survey of traditional health remedies used by the Maasai of southern Kajiado District, Kenya. Ethnobotany Research and Applications 4:061-074
Kokwaro JO (2009). Medicinal Plants of East Africa. Nairobi, Kenya: East African Literature Bureau.
Kubo I (1995). Antifungal sesquiterpene dialdehyde from the Warburgia plants and their synergists. Studies in natural products chemistry 17:233-233.
Kubo I, Lee YW, Pettei MJ (1976). Potent army worm antifeedants from the East African Warburgia plants. Journal of the Chemical Society, Chemical Communications (24):1013-1014.
Kubo I, Miura I, Pettei MJ (1977). Muzigadial and warbuganal: Potent antifungal, antiyeast and African army worm antifeedant agents. Tetrahedron Letters 18(52):4553-4556.
Kubo I, Nakanishi K (1977). Insect antifeedants and repellents from African plants. In ACS Symposium Series-American Chemical Society (USA).
Kuglerova M, Tesarova H, Grade TJ, Halamova K, Wanyana-Maganyi O, Damme van P (2011). Antimicrobial and antioxidant effects of Ugandan medicinal barks. African Journal of Biotechnology 10(18): 3628-3632.
Loomis TA, Hayes AW (1996). Loomis's essentials of toxicology, 4th edition. Academic press, California.
Lovett JC, Ruffo CK, Gereau RE, Taplin JRD (2006). Lovett, J. C., Ruffo, C. K., Gereau, R. E., & Taplin, J. R. (2006). Field guide to the moist forest trees of Tanzania. London, UK: Society for Environmental Exploration.
Manguro LOA, Ugi I, Hermann R, Lemmen P (2003). Flavonol and drimane-type sesquiterpene glycosides of Warburgia stuhlmannii leaves. Phytochemistry 63(4):497–502.
Maroyi A (2013). The genus Warburgia: A review of its traditional uses and pharmacology. Pharmaceutical Biology 52(3):378-391.
Mashimbye MJ, Maumela MC, Drewes SE (1999). Novel and bioactive metabolites of Warburgia salutaris indigenous to the Northern Province, South Africa. Nigerian Journal of Natural Products and Medicine 3(1):28-30
Leonard CM, Viljoen AM (2015). Warburgia: A comprehensive review of the botany, traditional uses and phytochemistry. Journal of Ethnopharmacology 165:260-285.
Mbwambo ZH, Erasto P, Innocent E, Masimba PJ (2009). Antimicrobial and cytotoxic activities of fresh leaf extracts of Warburgia ugandensis. Tanzania Journal of Health Research 11(2).
Meinwald J, Prestwich GD, Nakanishi K, Kubo I (1978). Chemical ecology: Studies from east Africa. Science 199:1167–73.
Mohanlall V, Odhav B (2009). Furans and furanones with antimycotoxigenic activity isolated from Warburgia salutaris (Canellaceae). Journal of Medicinal Plants Research 3(4):231-240.
Muchugi A, Kindt R, Muluvi GM, Muge E, Kipruto H, Jamnadass RH (2012). Genetic variation of Kenyan populations of Warburgia ugandensis, an important East African highlands medicinal tree species. Journal of Life Sciences, 4: 97-105.
Muchugi A, Muluvi GM, Kindt R, Kadu CAC, Simons AJ, Jamnadass RH (2008). Genetic structuring of important medicinal species of genus Warburgia as revealed by AFLP analysis. Tree Genetics & Genomes 4(4):785-795.
Muller S, Salomo K, Salazar J, Naumann J, Jaramillo MA, Neinhuis C 2015). Intercontinental long-distance dispersal of Canellaceae from the New to Old world revealed by a nuclear single copy gene and (chloroplast loci. Molecular Phylogenetics and Evolution 84:205-219.
Nanyingi M, Mbaria J, Lanyasunya A (2008). Ethnopharmacological survey of Samburu district, Kenya. Journal of Ethnobiology and Ethnomedicine 4(1):14.
Nanyingi MO, Kipsengeret KB, Wagate CG (2010). *In vitro* and *in vivo* antiplasmodial activity of Kenyan medicinal plants. Ethnic Groups 16:17
Ngure PK, Tonui WK, Ingonga J, Mutai C, Kigondu E, Ngrsquo Z, Kimutai A (2009). *In vitro* antileishmanial activity of extracts of Warburgia ugandensis (Canellaceae), a Kenyan medicinal plant. Journal of Medicinal Plants Research 3(2):061-066.
Njire MM, Budambula NLM, Kiiru J (2014). Antimicrobial activity of Warburgia ugandensis against Gram-negative multi-drug resistant bacteria. Journal of Agriculture, Science and Technology, 16: 45-57.
Olila D (1993). A study of the antimicrobial activities of Zanthoxylum chalybeum and Warburgia ugandensis–Ugandan medicinal plants. Uganda [Thesis] Makerere University, Uganda.
Olila D, Olwa-Odyek A, Opudo A (2002). Screening extracts of Zanthoxylum chalybeum and Warburgia ugandensis for activity against measles virus (Swartz and Edmonston strains) *in vitro.* African health sciences 2(1):2-10.
Olila D, Opuda AJ, Olwa-Odyek (2001). Bioassay-guided studies on the cytotoxic and in vitro trypanocidal activities of sesquiterpene (muzigadial) derived from a Ugandan medicinal plant (Warburgia ugandensis). African Health Sciences 1(1):121-15.
Orwa C, Mutua A, Kindt R (2009). Agroforestree database: A tree reference and selection guide version 4.0. (Online). Available from: http://www.worldagroforestry.org.
Rugutt JK, Ngigi AN, Ndalut PK (2006). Native Kenyan plants as alternatives to methyl bromide in soil fumigation. Phytomedicine 13(8):576–83.
Soureshjan EH, Heidari M (2014). *In vitro* variation in antibacterial activity plant extracts on Glaucium elegens and Saffron (Crocus sativus). Bangladesh Journal of Pharmacology 9(3):275-278.
Taniguchi M, Adachi T, Haraguchi H (1983). Physiological activity of warburganal and its reactivity with sulfhydryl groups. The Journal of Biochemistry 94(1).
Taniguchi M, Chapya A, Kubo I, Nakanishi K (1978). Screening of East African plants for antimicrobial activity 1. Chemical and Pharmaceutical Bulletin 26(9):2910-2913.
Taniguchi M, Kubo I (1993). Ethnobotanical drug discovery based on medicine men's trials in African savanna: Screening of east African plants for antimicrobial activity II. Journal of Natural Products 56(9):1539-1546.
Ullah N, Muhammad K, Muhammad UA, Taj AK, Sahibzada UK, Farhat AK (2012). Impact of geographical locations on Mentha spicata antibacterial activities. Journal of Medicinal Plants Research 6(7):1201-1206.
Van Wyk B-E, Gericke N (2000). People's Plants: A Guide toUseful Plants of Southern Africa. Pretoria, South Africa: Briza Publications.
Victor K (2013). Medical Plant Research in Africa: Pharmacology and Chemistry. 32 Jameston Road, London NW17BY, UK.
Wamalwa NL, Oballa P, Gicheru J (2006). Genetic variation of Warburgia ugandensis in Kenya and implications for its cultivation. Kenya Forestry Research Institution (KEFRI), Nairobi.
Were PS, Kinyanjui P, Gicheru MM (2010). Prophylactic and curative activities of extracts from Warburgia ugandensis Sprague (Canellaceae) and Zanthoxylum usambarense (Engl.) Kokwaro (Rutaceae) against Plasmodium knowlesi and Plasmodium berghei. Journal of ethnopharmacology, 130(1), 158-162. Not Cited
Were PS, Waudo W, Ozwara HS, Kutima HL (2015). Phytochemical analysis of Warburgia ugandensis Sprague using Fourier Transform Infra-Red (FT-IR) Spectroscopy. International Journal of
Pharmacognosy and Phytochemical Research 7: 201-205.
World Health Organisation (2002). Traditional Medicine Strategy 2002–2005. From www.who.int/ medicines/library/trm/trm_strat_eng.pdf.
Wube AA, Bucar F, Gibbons S, Asves K (2005). Sequitereones from Warburgia ugandensis and their antimycobacterial activity. Phytochemistry 66(19):2309-2315.
Xu M, Litaudon M, Krief S, et al (2009). Ugandenial A, a new drimanetype sesquiterpenoid from Warburgia ugandensis. Molecules 14(10):3844–50.