A synthesis and review of medicinal uses, phytochemistry and biological activities of Markhamia zanzibarica

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**ABSTRACT**

*Markhamia zanzibarica* (Bojer ex DC.) K. Schum. has been used in herbal medicine in tropical Africa since ancient times. *Markhamia zanzibarica* is indigenous to central, eastern and southern Africa. This extensive literature review synthesizes the information currently available on the medicinal uses, phytochemistry and biological activities of *M. zanzibarica*. The University library and electronic search engines Google Scholar, Scopus, Web of Science, ScienceDirect and PubMed were searched for pertinent information on the medicinal uses, phytochemistry and biological activities of *M. zanzibarica*. Traditionally, the species has been used as anthelmintic, and traditional medicine for backache, female reproductive problems, sexually transmitted infections, respiratory infections and gastro-intestinal problems. *In vitro* studies have confirmed the biological activities of *M. zanzibarica* which include antibacterial, antitubercular, antioxidant and cytotoxicity. Various phytochemicals such as alkaloids, anthraquinones, fatty acids, flavonoids, glycosides, phenolics, saponins, sterols, tannins and triterpenes have been isolated from *M. zanzibarica*. Documentation of the medicinal uses, phytochemistry and pharmacological properties of *M. zanzibarica* is essential as this information provides baseline data required for future research and development of health-promoting and pharmaceutical products. However, further pharmacological studies including phytochemical, toxicological, *in vitro* and *in vivo* experiments are needed to provide evidence for the clinical effectiveness of remedies prepared from the species.

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**INTRODUCTION**

*Markhamia zanzibarica* (Bojer ex DC. K. Schum), is a shrub or small tree in the family Bignoniaceae. The family Bignoniaceae consists of 104 genera and 860 plant species which are usually trees, shrubs or lianas and rarely herbs (Fischer et al., 2004). The family *Markhamia*, consists of ten species, eight of these have been recorded in tropical Africa while two species have been recorded in southeast Asia (Fischer et al., 2004). The genus name *Markhamia* is in honour of Sir Clements Robert Markham (1830-1916), an English geographer, writer, traveller and explorer (Palmer and Pitman, 1972). The species name “zanzibarica” means from Zanzibar (Bruschi et al., 2011), an island regarded as a region of Tanzania. The synonyms of *M. zanzibarica* include *Dolichandrone hirsuta* Baker, *D. Latifolia* Baker, *M. acuminata* (Klotzsch) K. Schum., *M. Puberula* (Klotzsch) K. Schum., *M. Stenocarpa* (Baker) K. Schum., *M. Stenocarpa* (Baker) K. Schum., *M. Stenocarpa* (Seem.), *M. zanzibarica* (Bojer ex DC.) Seem., *Spathodea acuminata* Klotzsch, S. puberula
| Medicinal use                  | Part used                                                                 | Country                        | Reference                                                                 |
|-------------------------------|---------------------------------------------------------------------------|--------------------------------|--------------------------------------------------------------------------|
| Abdominal pain                | Bark and root decoction taken orally                                      | Kenya and Tanzania              | (Chhabra et al., 1987; Kigen et al., 2016)                                |
| Anthelmintic                  | Roots decoction taken orally                                              | Kenya and Tanzania              | (Kokwaro, 2009; Louppe et al., 2012)                                     |
| Aphrodisiac                   | Roots mixed with those of Uvaria acuminata Oliv.                          | Kenya                           | (Kaingu et al., 2013a; Kaingu, 2016)                                     |
| Backache                      | Root infusion taken orally                                                | Malawi and South Africa         | (Morris, 1996; Palgrave and Keith, 2002)                                 |
| Breast cancer                 | Root infusion taken orally                                                | Kenya                           | (Kaingu et al., 2014; Kaingu, 2016)                                     |
| Constipation                  | Roots mixed with those of Albizia anthelmintica Brongn., Byrsocarpus bovinianus (Baill.) Baill., Carpolobia goetzei Güerke and Clausena anisata (Willd.) Hook. f. ex Benth. | Tanzania                         | (Chhabra et al., 1987)                                                  |
| Excessive bleeding during child birth | Bark and root infusion taken orally                                      | Kenya                           | (Pakia et al., 2003; Kigen et al., 2016)                                 |
| Female reproductive problems (abortifacient, contraceptive, bleeding during child birth, fibroids, infertility, menstrual problems and retained placenta) | Roots mixed with those of Salvadora persica L. and Uvaria acuminata | Kenya                           | (Kaingu et al., 2013b; Kaingu, 2016)                                     |
| Gastro-intestinal problems (diarrhoea, dysentery and stomach problems) | Bark, leaf and root decoction taken orally                               | Botswana, South Africa and Tanzania | (Arnold and Gulumian, 1984; Hedberg and Staugård, 1989)                  |
| General pains                 | Root decoction taken orally                                               | Mozambique                      | (Watt and Breyer-Brandwijk, 1962; Bruschi et al., 2011)                   |

*Continued on next page*
| Medicinal use                          | Part used                          | Country                  | Reference                                                   |
|---------------------------------------|------------------------------------|--------------------------|-------------------------------------------------------------|
| Headache                              | Leaf infusion applied topically    | South Africa             | (Watt and Breyer-Brandwijk, 1962; Semenya and Maroyi, 2018) |
| Hernia                                | Root decoction taken orally        | Tanzania                 | (Chhabra et al., 1987)                                     |
| Oedema                                | Bark infusion taken orally          | Kenya                    | (Kigen et al., 2016)                                       |
| Oxyuriasis                            | Root decoction taken orally         | Tanzania                 | (Chhabra et al., 1987)                                     |
| Protective charm (against evil spirits)| Leaves                            | Tanzania                 | (Hilonga et al., 2019)                                     |
| Psychiatric problems                  | Root decoction taken orally        | Tanzania                 | (Chhabra et al., 1987)                                     |
| Respiratory infections (cough, expectorant and pneumonia) | Bark and root infusion or decoction taken orally | Kenya, South Africa and Tanzania | (Arnold and Gulumian, 1984; Kokwaro, 2009) |
| Rheumatic fever                       | Roots mixed with those of Phyllanthus ovalifolius Forssk. | Malawi                  | (Morris, 1996)                                             |
| Snake bite                            | Leaf and root decoction applied topically | Kenya                  | (Pakia et al., 2003; Dharani, 2019)                        |
| Sexually transmitted infections (syphilis and venereal diseases) | Bark decoction taken orally       | Kenya and Tanzania       | (Chhabra et al., 1987; Kokwaro, 2009)                      |
| Toothache                             | Bark decoction applied topically   | Tanzania                 | (Watt and Breyer-Brandwijk, 1962; Kokwaro, 2009)           |
| Uterus prolapse                       | Roots mixed with those of Vangueria infausta Burch. ssp. rotundata (Robyns) Verdc. | Tanzania                 | (Chhabra et al., 1991)                                     |
| Yellow fever                          | Stem bark is mixed with that of Mangifera indica L., Maesopsis eminii Engl. and Erythrina abyssinica DC. | Tanzania                 | (Moshi et al., 2009)                                       |
Table 2: Nutritional and phytochemical composition of *Markhamia zanzibarica*

| Nutritional or phytochemical component | Value          | Plant part | Reference                           |
|---------------------------------------|----------------|------------|-------------------------------------|
| **Nutritional component**             |                |            |                                     |
| Acid detergent fibre (%)              | 19.3–51.1      | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Acid detergent bound protein (%)      | 1.8–2.0        | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Ash (%)                               | 4.8–10.8       | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Calcium (%)                           | 1.6            | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Copper (µg/g)                         | 11.0           | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Crude protein (%)                     | 9.0–16.3       | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Iron (µg/g)                           | 215.0          | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Magnesium (%)                         | 0.7            | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Manganese (µg/g)                      | 160.0          | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Neutral detergent fibre (%)           | 38.2–66.9      | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Phosphorus (%)                        | 0.1            | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Potassium (%)                         | 0.8            | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Sodium (%)                            | 0.005          | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Sulfuric acid lignin (%)              | 7.5–18.3       | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| α-tocopherols (µg/g)                  | 13.5–94.1      | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| γ-tocopherols (µg/g)                  | 1.0–1.7        | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Water (%)                             | 39.2–46.0      | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| Zinc (µg/g)                           | 17.3           | Leaves     | and (Dierenfeld *et al.*, 1995)     |
| **Phytochemical component**           |                |            |                                     |
| 3',4',5,7-tetrahydroxy-5'-methoxy-flavanone | -        | Leaves     | (Gormann *et al.*, 2006)            |
| 5,7,3',5'tetrahydroxy flavanone       | -              | Aerial parts| (El-Kersh *et al.*, 2016)           |
| Apigenin                              | -              | Leaves     | (Gormann *et al.*, 2006)            |
| Apigenin 5-O-α-L-rhamnopyranosyl-7-O-ß-D-glucopyranoside | - | Leaves     | (Gormann *et al.*, 2006)            |

*Continued on next page*
| Nutritional or phytochemical component | Value | Plant part | Reference |
|---------------------------------------|-------|------------|-----------|
| Apigenin-7-O-rutinoside               | -     | Aerial parts | (El-Kersh et al., 2016) |
| Campesterol (%)                       | 0.003 | Stem bark | (Khan and Mlungwana, 1999) |
| Eriocitrin                            | -     | Leaves | (Gormann et al., 2006) |
| Hederagenin (%)                       | 0.01  | Leaves | (Gormann et al., 2004) |
| Hentriacontane (%)                    | 2.9   | Leaves | (Gormann et al., 2004) |
| Hexacosanoic (%)                      | 0.1   | Leaves | (Gormann et al., 2004) |
| Hexadecanoic (%)                      | 0.2   | Leaves | (Gormann et al., 2004) |
| Luteolin                              | -     | Aerial parts and leaves | (Gormann et al., 2006; El-Kersh et al., 2016) |
| Luteolin-7-rutinosid                 | -     | Leaves | (Gormann et al., 2006) |
| Luteolin-7-O-D-glucoside              | -     | Aerial parts | (El-Kersh et al., 2016) |
| Naringenin                            | -     | Leaves | (Gormann et al., 2006) |
| Naringenin-7-rutinosid               | -     | Leaves | (Gormann et al., 2006) |
| Nigaichigoside F2                     | -     | Aerial parts | (El-Kersh et al., 2016) |
| Nonacosane (%)                        | 0.6   | Leaves | (Gormann et al., 2004) |
| Octacosanol (%)                       | 0.1   | Leaves | (Gormann et al., 2004) |
| Octadecanoic (%)                      | 0.1   | Leaves | (Gormann et al., 2004) |
| Oleanolic acid (%)                    | 23.1  | Aerial parts and leaves | (Gormann et al., 2004; El-Kersh et al., 2016) |
| Oleic acid (%)                        | 35.8  | Aerial parts | El-Kersh et al. (2016) |
| Palmitic acid (%)                     | 29.5  | Aerial parts | El-Kersh et al. (2016) |
| Pentacosane (%)                       | 23.2  | Aerial parts | El-Kersh et al. (2016) |
| Phytol (%)                            | 2.2   | Aerial parts | El-Kersh et al. (2016) |
| Quadrangularic acid L                 | -     | Aerial parts | El-Kersh et al. (2016) |
| Quadrangularic acid K                 | -     | Aerial parts | El-Kersh et al. (2016) |
| β-Sitosterol (%)                      | 0.01–12.8 | Aerial parts and leaves | (Gormann et al., 2004; El-Kersh et al., 2016) |
| γ-Sitosterol (%)                      | 0.004-14.0 | Aerial parts and root wood | (Khan and Mlungwana, 1999; El-Kersh et al., 2016) |
| Squalene (%)                          | 32.6  | Aerial parts | El-Kersh et al. (2016) |
| Stigmasterol (%)                      | 0.01–0.9 | Aerial parts and leaves | (Gormann et al., 2004; El-Kersh et al., 2016) |
| Total flavonoid content (mg LE/g)    | 14.4  | Aerial parts | El-Kersh et al. (2016) |
| Total phenolic content (mg GAE/g)     | 177.4 | Aerial parts | El-Kersh et al. (2016) |
| Tritriacontane (%)                    | 0.009–3.2 | Leaves | (Khan and Mlungwana, 1999; Gormann et al., 2004) |
| Ursolic acid (%)                      | 36.6  | Aerial parts and leaves | (Gormann et al., 2004; El-Kersh et al., 2016) |
| Verbascoside                          | -     | Aerial parts | El-Kersh et al. (2016) |
| Isoverbascoside                       | -     | Aerial parts | El-Kersh et al. (2016) |
Klotzsch, S. tenuifolia Bojer and S. zanzibarica Bojer ex DC. The English common names of M. zanzibarica include “bean tree”, “bell bean”, "golden bean tree” and “maroon bell-bean”. Markhamia zanzibarica is a slender, much-branched and sometimes straggling shrub or small tree with crooked branches growing up to 10 metres in height (Lovett et al., 2007). The bark is grey, smooth to rough, vertically and narrowly flaky and young branches with conspicuous lenticels. The leaves of M. zanzibarica are pinately compound with obovate leaflets. The leaf margins are smooth or toothed with attenuate apex and broadly tapering to rounded base. The flowers of M. zanzibarica vary from yellow densely flecked with maroon to dark maroon inside and paler outside, occurring in terminal or axillary racemes.

The fruit is a slender, pendulous capsule, hairless with pale dots or lenticils, splitting into two halves. Markhamia zanzibarica has been recorded in deep sand, rocky ridges, hill slopes and riverine fringes in dry evergreen coastal forest, dry lowland forest, woodland, bushveld, grassland, secondary bush at sea level to 1500 m above sea level (Diniz and Bignoniaceae, 1988; Bidgood et al., 2006). Markhamia zanzibarica is indigenous to Zimbabwe, Angola, Somalia, Botswana, Malawi, the Democratic Republic of Congo (DRC), Zambia, Kenya, Mozambique, Tanzania and Namibia (Diniz and Bignoniaceae, 1988; Bidgood et al., 2006). Markhamia zanzibarica is used as a non-alcoholic beverage or famine food in Namibia and South Africa (Fox and Young, 1982; Koenen, 2001). The leaves of M. zanzibarica are browsed by game and livestock (Komwihangilo et al., 1995; Mtengeti and Mhelela, 2006). The leaves of M. zanzibarica are sold as traditional medicines in informal herbal medicine markets in Tanzania (Hilonga et al., 2019). Therefore, this extensive review was undertaken to evaluate the medicinal uses, phytochemistry and biological activities of M. zanzibarica.

**MATERIALS AND METHODS**

The University library and electronic search engines Google Scholar, Scopus, Web of Science, ScienceDirect and PubMed were searched for pertinent information on the medicinal uses, phytochemistry and biological activities of M. zanzibarica. The keywords such as *Markhamia zanzibarica*, its synonyms, biological activities, phytochemistry, ethnopharmacology, toxicity, botany and ethnobotany were used separately and in combination used within the electronic databases of ScienceDirect, Scopus, PubMed, Web of Science and Google Scholar.

**RESULTS AND DISCUSSION**

**Medicinal uses of Markhamia zanzibarica**

The bark, leaf and root decoction or infusion of *M. zanzibarica* are mainly used as anthelmintic, and traditional medicine against backache, female reproductive problems, sexually transmitted infections, respiratory infections and gastro-intestinal problems (Table 1Figure 1). Other medicinal applications of *M. zanzibarica* supported by at least two literature reports include the use of the bark, leaf and root infusion or decoction as an aphrodisiac (Kaingu et al., 2013a; Kaingu, 2016), and traditional medicine for abdominal pains (Chhabra et al., 1987; Kigen et al., 2016), breast cancer (Kaingu et al., 2014; Kaingu, 2016), general body pains (Watt and Breyer-Brandwijk, 1962; Bruschi et al., 2011), headache (Watt and Breyer-Brandwijk, 1962; Semenya and Maroyi, 2018) and snakebite (Pakia et al., 2003; Dharani, 2019).

**Nutritional and phytochemical composition of Markhamia zanzibarica**

(Dierenfeld et al., 1995) investigated the nutritional properties of the leaves and twigs of *M. zanzibarica* (Table 2). Some health-promoting nutrients such as calcium, copper, crude fibre, iron, magnesium, manganese, phosphorus, potassium, proteins, sodium and zinc have been identified from the species, and these reports corroborate the utilization of *M. zanzibarica* as fodder for both game and livestock in tropical Africa (Komwihangilo et al., 1995; Mtengeti and Mhelela, 2006). Phytochemical compounds identified from the aerial parts, leaves, roots and root wood of *M. zanzibarica* include alkaloids, anthraquinones, fatty acids, flavonoids, glycosides, phenolics, saponins, sterols, tannins and triterpenes.

**Pharmacological properties of Markhamia zanzibarica**

(Mayekiso et al., 2009) evaluated the antibacterial activities of acetone leaf extracts of *M. zanzibarica* against *Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecalis* and *Enterococcus coli* using the following microdilution method. The extract exhibited activities against the tested pathogens with minimum inhibitory concentration (MIC) values as low as 0.02 mg/ml. (Mayekiso et al., 2009) also evaluated the antimycobacterial activities of acetone leaf extracts of *M. zanzibarica* against *Mycobacterium fortuitum* and *Mycobacterium smegmatis* using the serial microdilution method. The extract exhibited activities against the tested pathogens with MIC values as low as 0.02 mg/ml (Mayekiso et al., 2009).

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(El-Kersh et al., 2016) evaluated the antioxidant activities of n-hexane, ethyl acetate, butanol, chloroform and ethanol extracts of the aerial parts of M. zanzibarica using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging assay with ascorbic acid as standard. The ethyl acetate extract exhibited the highest activities with half-maximal inhibitory concentration (IC\textsubscript{50}) value of 154.6 μg/ml (El-Kersh et al., 2016).

(Khan and Mlungwana, 1999) evaluated the cytotoxicity activities of the compounds γ-sitosterol, campesterol and tritriacontane isolated from M. zanzibarica using the brine shrimp (Artemia salina) assay with lapachol as reference drug. The compound γ-sitosterol exhibited activities with the median lethal concentration (LC\textsubscript{50}) value of 4.0 ppm, which was lower than the LC\textsubscript{50} value of 5.0 ppm (Khan and Mlungwana, 1999). (McGaw et al., 2010) evaluated the cytotoxicity activities of acetone extracts of M. zanzibarica leaves against Vero kidney cells and bovine dermis cells. The extract exhibited activities with LC\textsubscript{50} values of less than 50.0 μg/ml against both cell types (McGaw et al., 2010; El-Kersh et al., 2016) evaluated the cytotoxicity activities of n-hexane, ethyl acetate, butanol, chloroform and ethanol extracts of the aerial parts of M. zanzibarica against the human cervical adenocarcinoma cell line (HeLa) using the sulforhodamine B colourimetric assay with doxorubicin as a positive control. The extracts exhibited activities with IC\textsubscript{50} values ranging from 9.2 μg/ml to 49.6 μg/ml in comparison to IC\textsubscript{50} value of 7.3 μg/ml exhibited by the positive control (El-Kersh et al., 2016). Similarly, (El-Kersh et al., 2016) evaluated the cytotoxicity activities of n-hexane, ethyl acetate, butanol, chloroform and ethanol extracts of the aerial parts of M. zanzibarica against the HeLa, MCF-7, HEPG2, PC3 and A549 using the sulforhodamine B colourimetric assay with doxorubicin as a positive control. The extracts exhibited activities with the best activities against the cancer cells exhibiting IC\textsubscript{50} values ranging from 8.5 μg/ml to 18.4 μg/ml (El-Kersh et al., 2016).

CONCLUSIONS

This study reviewed the medicinal uses, phytochemistry and biological activities of M. zanzibarica. The current pharmacological studies indicate the potential biological activities of the phytoconstituents and crude extracts of M. zanzibarica, indicating the merit for more attention in future studies. More pharmacological studies including phytochemical, toxicological, \textit{in vitro} and \textit{in vivo} experiments are needed to provide evidence for the clinical effectiveness of remedies prepared from the species.
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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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