# A Review of Medicinal Uses, Phytochemistry and Biological Activities of *Markhamia tomentosa*

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**Abstract:** *Markhamia tomentosa* (Benth.) K. Schum. ex Engl. is a shrub or small tree widely used as traditional medicine throughout its distributional range in west Africa. This study was aimed at providing a critical review of medicinal uses, phytochemistry and biological activities of *M. tomentosa*. Documented information on medicinal uses, phytochemistry and biological activities of *M. tomentosa* was collected from several online sources such as Scopus, Google Scholar, PubMed and Science Direct, and pre-electronic sources such as book chapters, books, journal articles and scientific publications obtained from the University library. This study revealed that the bark, leaf, root and stem bark decoction and/or infusion of *M. tomentosa* are mainly used as traditional medicine for elephantiasis, infertility, skin infections, rheumatism, eye problems, pain, diabetes and fever. Phytochemical compounds identified from the species include alkaloids, anthraquinones, cardiac glycosides, flavonoids, phenolics, saponins, sterols, tannins and triterpenoids. *Markhamia tomentosa* crude extracts and compounds isolated from the species exhibited analgesic, acetylcholinesterase and butyrylcholinesterase inhibitory, anti-amnesic, antibacterial, antifungal, antifeedant, anti-inflammatory, antioxidant, antiplasmodial, antitrypanosomal, antiulcer, larvicidal, leishmanicidal and cytotoxicity activities. *Markhamia tomentosa* should be subjected to detailed phytochemical, pharmacological and toxicological evaluations aimed at correlating its medicinal uses with its phytochemistry and pharmacological activities.

**Keywords:** Bignoniaceae, indigenous knowledge, *Markhamia tomentosa*, traditional medicine, tropical Africa.

## INTRODUCTION

*Markhamia tomentosa* (Benth.) K. Schum. ex Engl. 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 [1]. Research by Ibrahim *et al*. [2] revealed that *M. tomentosa* is among five *Markhamia* Seem. ex Baill. species widely used by several cultures in tropical Africa and southeast Asia as traditional medicines against human and animal diseases and ailments. These five *Markhamia* species include *M. lutea* (Benth.) K. Schum., *M. obtusifolia* (Baker) Sprague, *M. stipulata* (Wall.) Seem, *M. tomentosa* and *M. zanzibarica* (Bojer ex DC.) K. Schum. These species are characterized by phytochemical compounds such as flavonoids, phenylpropanoid glycosides, phytosterols, quinones, terpenoids and lignans [2]. The genus *Markhamia* consists of ten species, eight of these have been recorded in tropical Africa while two species have been recorded in southeast Asia [1]. The genus name *Markhamia* is in honour of Sir Clements Robert Markham (1830-1916), an English geographer, writer, traveller and explorer [3]. The species name "*tomentosa*" is a Latin word meaning "covered in hairs" [4]. The synonyms of *M. tomentosa* include *Dolichandrone tomentosa* (Benth.) Benth. & Hook. f. ex B.D. Jacks., *M. sessillis* Sprague, *Muenteria tomentosa* (Benth.) Seem. and *Spathodea tomentosa* Benth. [5-7]. *Markhamia tomentosa* is a shrub or tree growing up to 15 metres in height [8]. The leaves of *M. tomentosa* are pinnately compound with obovate leaflets. The flowers are large and yellow in colour, occurring in terminal or axillary racemes. The fruit is a slender, pendulous capsule, splitting into two halves. *Markhamia tomentosa* has been recorded in deep sand and riverine fringes in woodlands, dry evergreen savanna forests and forest margins. *Markhamia tomentosa* has been recorded in the Democratic Republic of Congo (DRC), Angola, Togo, Benin, Siera Leone, Burkina Faso, Senegal, Cameroon, Nigeria, Central African Republic, Côte d'Ivoire, Congo, Guinea-Bissau, Gabon, Guinea and Ghana [5-7,9]. Therefore, this extensive review was undertaken to evaluate the medicinal uses, phytochemistry and biological activities of *M. tomentosa.*

## 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. tomentosa*. The keywords such as *Markhamia tomentosa,* its synonyms, biological activities, phytochemistry, ethnopharmacology, toxicity, botany and ethnobotany

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were used separately and in combination within the electronic databases of ScienceDirect, Scopus, PubMed, Web of Science and Google Scholar.

## RESULTS AND DISCUSSION

### Medicinal Uses of *Markhamia tomentosa*

The bark, leaf, root and stem bark decoction and/or infusion of *M. tomentosa* are mainly used as traditional medicine for elephantiasis, infertility, skin infections, rheumatism, eye problems, pain, diabetes and fever (Table **1**; Figure **1**). Other medicinal applications of *M. tomentosa* supported by at least two literature reports include the use of the bark, leaf, root and stem bark decoction and/or infusion as traditional medicine for backache [2,10]), headache [2,10], malaria [10,11], oedema [11,12], respiratory infections [8,13], sexually transmitted infections [14,15], snakebite [2,16] and sores [8,17].

### Phytochemistry of *Markhamia tomentosa*

Some researchers identified several phytochemical compounds from the bark, leaves and stem bark of *M. tomentosa* (Table **2**) which include alkaloids, anthraquinones, carbohydrates, cardiac glycosides, flavonoids, phenolics, proteins, resins, saponins, sterols, tannins and triterpenoids [12,27-37]. Some of these phytochemical compounds may be responsible for the biological activities of the species.

### Pharmacological Properties of *Markhamia tomentosa*

The following pharmacological activities have been documented from the leaf, root bark and stem bark of *M. tomentosa* and compounds isolated from the

**Table 1: Medicinal Uses of *Markhamia tomentosa***

| Medicinal use | Part used | Country | Reference |
|---|---|---|---|
| Anaemia | Leaves | Nigeria | [18] |
| Backache | Bark and leaves | Nigeria | [2,10] |
| Diabetes | Roots and stem bark | Guinea and Nigeria | [19,20] |
| Diuretic | Leaves | Ghana | [13] |
| Elephantiasis | Leaves | Nigeria | [2,11,16] |
| Eye problems | Leaves | Angola and Nigeria | [2,10,16,21] |
| Fever | Leaves | Ghana and Nigeria | [8,10,11,13] |
| Gastric ulcers | Bark and roots | Nigeria | [22] |
| Headache | Bark and leaves | Nigeria | [2,10] |
| Heart pain | Leaves | Nigeria | [16] |
| Impotency | Bark | Cameroon | [23] |
| Infertility | Bark and leaves | Angola, Cameroon and Nigeria | [18,21,24,25] |
| Laxative | Bark and leaves | Nigeria | [10] |
| Malaria | Leaves | Nigeria | [2,11] |
| Misfortune | Leaves | Angola | [21] |
| Pain | Bark and leaves | Nigeria and Senegal | [2,8,10] |
| Oedema | Leaves | Nigeria | [11,12] |
| Respiratory infections | Leaves | Ghana | [8,13] |
| Rheumatoid arthritis and pain | Leaves | Nigeria | [2,8,11,12] |
| Sexually transmitted infections | Leaves | Guinea | [14,15] |
| Skin infections | Bark and leaves | Côte d'Ivoire | [8,10,17] |
| Snake bite | Leaves | Nigeria | [2,16] |
| Sores | Leaves | Côte d'Ivoire | [8,17] |
| Thrush | Leaves | Nigeria | [11] |
| Typhoid fever | Bark and leaves | Cameroon | [26] |

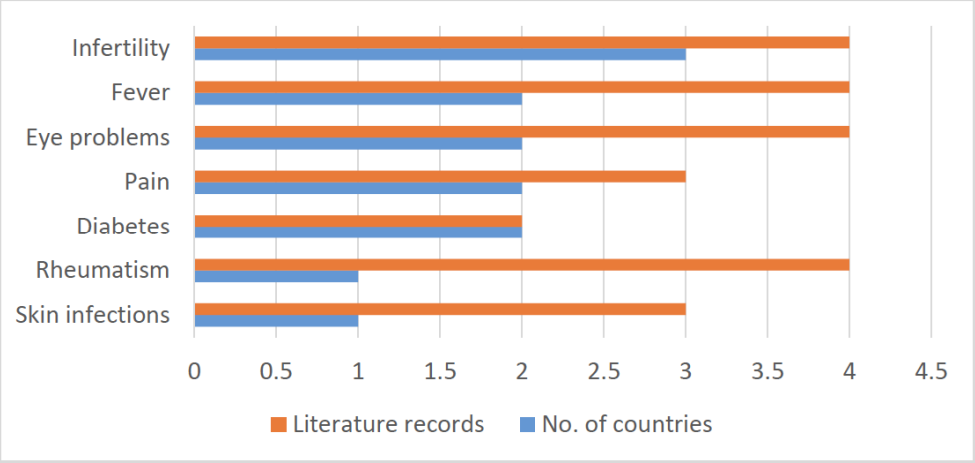


**Figure 1:** Medicinal applications of *Markhamia tomentosa* derived from literature records.

**Table 2: Phytochemical Composition of *Markhamia tomentosa***

| Phytochemical compound | Value | Plant part | Reference |
|---|---|---|---|
| 2-acetylnaphtho[2,3-b]furan-4,9-dione | - | Stem bark | [27] |
| 2-acetyl-6-methoxynaphtho[2,3-b]furan-4,9-dione | - | Stem bark | [27] |
| 3-acetylpomolic acid | - | Stem bark | [27] |
| Acteoside | - | Leaves | [31,32] |
| Ajugol | - | Leaves | [31,32] |
| Alkaloids (mg/g) | 6.5 – 10.7 | Leaves | [33,34] |
| Carnosol | - | Leaves | [31,32] |
| (+)-catechin (µg/mg) | 11.4 | Stem bark | [35] |
| Cyanidin trimmers (µg/mg) | 14.7 | Stem bark | [35] |
| Dilapachone | - | Leaves | [31,32] |
| (−)-epicatechin (µg/mg) | 42.5 | Stem bark | [35] |
| Flavonoids (mg/g) | 3.4 – 4.4 | Leaves | [33,34] |
| Luteolin | - | Leaves | [31,32] |
| Luteolin-3' ,7-di-O-glucoside | - | Leaves | [31,32] |
| Luteolin-7-rutinoside | - | Leaves | [31,32] |
| Mollic acid | - | Leaves | [37] |
| Oleanolic acid | - | Leaves and stem bark | [27,37] |
| oxo-pomolic acid | - | Leaves | [31,32] |
| Phenolics (mg/g) | 21.4 – 22.7 | Leaves | [33,34] |
| Phytol | - | Leaves | [37] |
| Pomolic acid | - | Stem bark | [27] |
| Procyanidin dimer (µg/mg) | 15.9 | Stem bark | [35] |
| Rosmarinic acid (µg/mg) | 541.5 | Stem bark | [35] |
| Saponins (mg/g) | 8.1 – 9.0 | Leaves | [33,34] |
| β-sitosterol | - | Leaves and stem bark | [27,37] |
| β-sitosterol-3-O-β-D-glucopyranoside | - | Stem bark | [27] |
| Tannins (mg/g) | 19.5 – 29.2 | Leaves | [33,34] |
| Tormentic acid | - | Leaves and stem bark | [27,31,32] |
| Total flavonoid content (mg QE/g) | 312.5 | Leaves | [12] |
| Total phenolic content (mg GAE/g) | 422.2 | Leaves | [12] |

species: analgesic [30], acetylcholinesterase and butyrylcholinesterase inhibitory [38], anti-amnesic [35], antibacterial [15,16,28,36], antifungal [16,28,39], antifeedant [39], anti-inflammatory [12,30,40], antioxidant [16], antiplasmodial [27,33], antitrypanosomal [27], antiulcer [31,32], larvicidal [41,42], leishmanicidal [27] and cytotoxicity [27,37,39,43,44] activities.

**Analgesic Activities**

Temdie *et al*. [30] evaluated the analgesic activities of aqueous, hexane, dichloromethane, ethyl acetate, methanol and aqueous residue leaf extract of *M. tomentosa* using writhing and formalin tests in experimental animal models at doses of 50.0 mg/kg, 100.0 mg/kg and 200.0 mg/kg. The extracts exhibited activities by reducing the licking time and writhing responses induced in mice [30].

**Acetylcholinesterase and Butyrylcholinesterase Inhibitory Activities**

Elufioye *et al*. [38] evaluated the acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) inhibitory activities of leaves, root bark and stem bark of *M. tomentosa* using the *in vitro* Ellman's spectrophotometric and *in situ* bioautographic methods with physostigmine as the standard drug. The stem bark and root bark showed the highest activities to the two enzymes, exhibiting 40.6% and 78.5% on AChE and BuChE, respectively [38].

**Anti-Amnesic Activities**

Ionita *et al*. [35] evaluated the anti-amnesic activities of aqueous extracts of *M. tomentosa* stem bark in scopolamine-induced cognitive impaired rats, pretreated with doses of 50.0 mg/kg and 200.0 mg/kg, p.o. for 10 days and a single injection of scopolamine at 0.7 mg/kg i.p. The extracts improved memory in behavioural tests and decreased oxidative stress in the rat hippocampus [35].

**Antibacterial Activities**

Aladesanmi *et al*. [16] evaluated the antibacterial activities of n-hexane, chloroform, ethyl acetate, aqueous and methanol leaf extracts of *M. tomentosa* against *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus* and *Bacillus subtilis* using agar dilution and disc diffusion methods with chloramphenicol as positive control. The extract exhibited weak activities against tested pathogens with the diameter of zone of inhibition ranging from 1.0 mm to 16.0 mm and minimum inhibitory concentration (MIC) values ranged from 0.3 mg/ml to >5.0 mg/ml [16]. Ugbade *et al*. [28] evaluated the antibacterial activities of hexane, ethyl acetate, methanol and aqueous extracts of *M. tomentosa* leaves against *Pseudomonas aeruginosa, Escherichia coli, Bacillus subtilis, Staphylococcus aureus* and *Salmonella typhi* using agar dilution streak technique. The hexane, ethyl acetate and methanol extracts exhibited activities against all tested pathogens with the exception of *Pseudomonas aeruginosa* [28]. Samba *et al*. [15] evaluated the antibacterial activities of methanol leaf extracts of *M. tomentosa* against *Bacillus cereus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus* and *Salmonella typhimurium* using microdilution method. The extract exhibited activities against the tested pathogens with MIC values ranging from 62.5 µg/ml to >1000.0 µg/ml [15]. Voukeng *et al*. [36] evaluated the antibacterial activities of methanol leaf extracts of *M. tomentosa* against *Escherichia coli, Enterobacter aerogenes, Enterobacter cloacae, Klebsiella pneumoniae, Providencia stuartii, Pseudomonas aeruginosa* and *Staphylococcus aureus* using broth micro-dilution method with chloramphenicol and ciprofloxacin as positive controls. The extracts exhibited activities against tested pathogens with MIC values ranging from 128.0 µg/mL to 1024.0 µg/mL [36].

**Antifungal Activities**

Aladesanmi *et al*. [16] evaluated the antifungal activities of n-hexane, chloroform, ethyl acetate, aqueous and methanol leaf extracts of *M. tomentosa* against *Candida albicans, Candida pseudotropicalis* and *Trichophyton rubrum* using agar dilution and disc diffusion methods with acriflavin as positive control. The extract exhibited weak activities against *Candida pseudotropicalis* with the diameter of zone of inhibition of 3.0 mm [16]. Ugbade *et al*. [28] evaluated the antifungal activities of hexane, ethyl acetate, methanol and aqueous extracts of *M. tomentosa* leaves against *Candida albicans* using agar dilution streak technique. The hexane, ethyl acetate and methanol extract exhibited activities against the tested pathogen [28]. Ibrahim *et al*. [39] evaluated the antifungal activities of ethyl acetate, methanol and hexane extracts of endophytic fungi *Trichoderma longibrachiatum* and *Syncephalastrum racemosum* isolated from the leaves of *M. tomentosa* against *Fusarium oxysporum, Sclerotinia sclerotiorium, Rhizoctonia solani* and *Botrytis cinerea* using the dual culture assay and

poisoning food assay. The isolated endophytic fungi and solvent extracts exhibited activities with MIC value of 1000.0 µg/mL against the tested pathogenic fungi in the dual culture and poisoning food assays [39].

**Antifeedant Activities**

Ibrahim *et al*. [39] evaluated the antifeedant activities of ethyl acetate, methanol and hexane extracts of endophytic fungi *Trichoderma longibrachiatum* and *Syncephalastrum racemosum* isolated from the leaves of *M. tomentosa* against the *Spodoptera litura* larvae using the leaf disc choice test method at concentrations of 250.0 µg/mL, 500.0 µg/mL and 1000.0 µg/mL. The extracts exhibited minimal feeding deterrent activities [39].

**Anti-Inflammatory Activities**

Temdie *et al*. [30] evaluated the anti-inflammatory activities of aqueous, hexane, dichloromethane, ethyl acetate, methanol and aqueous residue leaf extract of *M. tomentosa* against carrageenan-induced acute inflammation in experimental animal models at doses of 50.0 mg/kg, 100.0 mg/kg and 200.0 mg/kg. The extracts exhibited anti-inflammatory activities [30]. Temdie *et al*. [40] evaluated the anti-inflammatory activities of methanol leaf extracts of *M. tomentosa* on xylene-induced ear oedema in mice, histamine, serotonin and formalin-induced rats' paws oedema and on cotton pellet-induced granuloma formation in rats at doses of 100.0 mg/kg and 200.0 mg/kg body weight. The extracts exhibited activities on both acute and chronic inflammation [40]. Sowemimo *et al*. [12] evaluated the anti-inflammatory activities of ethanolic extracts of *M. tomentosa* leaves using the carrageenan-induced paw oedema in rats, xylene-induced and formalin-induced oedema in mice at doses of 50.0 mg/kg, 100.0 mg/kg and 200.0 mg/kg p.o. The extract produced dose-dependent inhibition in carrageenan-induced, xylene-induced and the formalin tests, exhibiting inhibition of 54.6% and 42.1% in 90 minutes in the histamine-induced and serotonin-induced rat paw oedema models, respectively [12].

**Antioxidant Activities**

Aladesanmi *et al*. [16] evaluated the antioxidant activities of n-hexane, chloroform, ethyl acetate, aqueous and methanol leaf extracts of *M. tomentosa* using 1,1-dipheyl-2-picry-hydrazyl (DPPH) free radical scavenging assay with ascorbic acid as positive control. The extract exhibited activities with half maximal effective concentration ($EC_{50}$) value of 16.5 µg/ml [16].

**Antiplasmodial Activities**

Tantangmo *et al*. [27] evaluated the antiplasmodial activities of hexane, ethyl acetate and methanol extracts of *M. tomentosa* stem bark and the compounds 2-acetylnaphtho[2,3-b]furan-4,9-dione, 2-acetyl-6-methoxynaphtho[2,3-b]furan-4,9-dione, pomolic acid and 3-acetylpomolic acid isolated from the stem bark against the chloroquine-resistant strains of *Plasmodium falciparum* (K1 and W2) using the [$^3$H]-hypoxanthine incorporation assay with chloroquine as positive control. Both the extracts and the compounds exhibited activities against the tested strains with the median inhibitory concentration ($IC_{50}$) values ranging from 0.1 µg/ml to >5.0 µg/ml [27]. Bankole *et al*. [33] evaluated the antiplasmodial activities of aqueous leaf extract of *M. tomentosa* using a modified Peter's four-day suppressive test in a mouse model of chloroquine-resistant *Plasmodium berghei* ANKA strain using doses of 250.0 mg/kg, 500.0 mg/kg and 800.0 mg/kg. The extract showed the chemosuppression of parasites of 73.0% at day four in comparison to chemosuppression of 90.0% exhibited by the standard reference drug, chloroquine diphosphate [33].

**Antitrypanosomal Activities**

Tantangmo *et al*. [27] evaluated the antitrypanosomal activities of hexane, ethyl acetate and methanol extracts of *M. tomentosa* stem bark and the compounds 2-acetylnaphtho[2,3-b]furan-4,9-dione, 2-acetyl-6-methoxynaphtho[2,3-b]furan-4,9-dione, pomolic acid and 3-acetylpomolic acid isolated from the stem bark against *Trypanosoma brucei rhodesiense* using the microtitre plate dilution method with melarsoprol as positive control. Both the extracts and the compounds exhibited activities with the $IC_{50}$ values ranging from 0.2 µg/ml to >5.0 µg/ml [27].

**Antiulcer Activities**

Sofidiya *et al*. [31] and Sofidiya *et al*. [32] evaluated the antiulcer activities of the crude ethanolic extract of *M. tomentosa* leaves in indomethacin-induced and pylorus ligation rat models at doses of 50.0 mg/kg, 100.0 mg/kg and 150.0 mg/kg, p.o. The extract exhibited dose-dependent activities by producing 72.0% and 92.0% inhibition of indomethacin and pylorus-induced ulcer at a dose of 150.0 mg/kg, respectively [31,32].

### Larvicidal Activities

Adebago *et al*. [41] and Adebajo *et al*. [42] evaluated the larvicidal activities of methanolic stem bark extracts of *M. tomentosa* against the 4$^{th}$ instar larvae of *Aedes aegypti* with endosulphan, a commercial insecticide as a positive control. The extract exhibited activities with median lethal concentration ($LC_{50}$) value of 8.0 mg/ml in comparison to $LC_{50}$ value of 0.9 mg/ml exhibited by the positive control [41,42].

### Leishmanicidal Activities

Tantangmo *et al*. [27] evaluated the leishmanicidal activities of hexane, ethyl acetate and methanol extracts of *M. tomentosa* stem bark and the compounds 2-acetylnaphtho[2,3-b]furan-4,9-dione, 2-acetyl-6-methoxynaphtho[2,3-b]furan-4,9-dione, pomolic acid and 3-acetylpomolic acid isolated from the stem bark against *Leishmania donovani* using *in vitro* assay with miltefosine as positive control. The extracts exhibited weak activities with $IC_{50}$ value of >5.0 µg/ml while the $IC_{50}$ values exhibited by the compounds ranged from 0.1 µg/ml to 3.4 µg/ml [27].

### Cytotoxicity Activities

Tantangmo *et al*. [27] evaluated the cytotoxicity activities of hexane, ethyl acetate and methanol extracts of *M. tomentosa* stem bark and the compounds 2-acetylnaphtho[2,3-b]furan-4,9-dione, 2-acetyl-6-methoxynaphtho[2,3-b]furan-4,9-dione, pomolic acid and 3-acetylpomolic acid isolated from the stem bark against L-6 cell line (of rat skeletal-muscle myoblasts) using fluorimetric assay with podophyllotoxin as positive control. The extracts exhibited $IC_{50}$ values ranging from 83.0 µg/ml to >90.0 µg/ml while the compounds exhibited $IC_{50}$ values ranging from 0.1 µg/ml to 16.3 µg/ml [27]. Ibrahim *et al*. [43] evaluated the cytotoxicity activities of ethanolic extract of *M. tomentosa* leaves against HeLa, MCF-7 and Vero cell lines using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay with melphalan (40.0 µM) as positive control. The extract exhibited activities against HeLa cells with $IC_{50}$ value of 189.1 µg/ml after 24 hours of post treatment [43]. Ibrahim *et al*. [43] also evaluated the cytotoxic activities of ethanolic extract of *M. tomentosa* leaves using the brine shrimp lethality test. The extract exhibited activities with median lethal dose ($LD_{50}$) value of 31.6 µg/ml [43]. Ibrahim *et al*. [44] evaluated the sub-acute and chronic toxicity activities of aqueous extracts of *M. tomentosa* leaves in rats treated daily with doses of 40.0 mg/kg, 200.0 mg/kg and 1000.0 mg/kg orally for 28 days and 90 days. The extract showed non-toxic effect in the liver and kidney function of the tested rats [44]. Ibrahim *et al*. [39] evaluated the cytotoxicity activities of ethyl acetate, methanol and hexane extracts of endophytic fungi *Trichoderma longibrachiatum* and *Syncephalastrum racemosum* isolated from the leaves of *M. tomentosa* against HeLa cancer cell line using the MTT assay. The methanol fraction of *Syncephalastrum racemosum* exhibited the best activity with $IC_{50}$ value of 43.6 µg/mL [39]. Ibrahim *et al*. [37] evaluated the cytotoxicity activities of crude, hexane, n-butanol, ethanolic, dichloromethane and ethyl acetate extracts of *M. tomentosa* leaves and the compounds sitosterol, mollic acid, phytol and oleanolic acid isolated from the leaves of the species against HeLa cells using MTT assay with melphalan as positive control. The dichloromethane and the compound mollic acid exhibited the best activities with $IC_{50}$ values of 83.3 µg/ml and 34.7 µg/ml, respectively [37]. These findings call for further toxicological evaluations.

## CONCLUSION

Research on *M. tomentosa* over the past decades showed that the species is an important traditional medicine in west Africa. The diverse biological activities exhibited by the crude extracts and compounds isolated from the species imply that the species is directly or indirectly involved in a range of physiological processes which offers protection against both free radicals and growth of undesirable microbes. Therefore, future research should aim at correlating the medicinal uses of the species with its phytochemistry and pharmacological activities.

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