Ethnomedicinal uses, phytochemistry and pharmacological properties of the genus, Kirkia

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Abstract

Purpose: To review the phytochemical, ethnopharmacology and traditional uses of the Kirkia species throughout their distributional range.

Methods: The information documented in this article is from scientific journals, books, theses and reports obtained from library collections and electronic search engines such as Google, Google scholar, publishing sites such as Elsevier, ScienceDirect, BioMed Central (BMC), PubMed and other scientific database sites such as ChemSpider and PubChem.

Results: Kirkia species are used as herbal remedies for abdominal pain, cholera, cough, snake bites and toothache in East, Central and Southern Africa. There are similarities in the use of Kirkia species as herbal medicines in Central and Southern Africa in terms of plant parts used, herbal preparation, route of administration and dosage. The chemical composition of Kirkia species is dominated by fatty acids, flavonols, isocoumarin, lignans, neolignans, nor-carotenoids, phenols and tannins isolated from leaves, stem bark and roots. Major biological activities demonstrated by Kirkia species include antimicrobial, antioxidant, antiplasmodial and antiplatelet activities.

Conclusion: Kirkia species are valuable herbal medicines with multiple pharmacological effects. Kirkia extracts and their isolates are potential sources of modern medicines following future detailed studies to elucidate their mechanisms of action, toxicity and clinical trials.

Keywords: Africa, Ethnobotanical, Isocoumarin, Kirkia species, Lignans, Livelihood needs, Neolignans, Traditional medicine

INTRODUCTION

The monotypic genus Kirkia Oliver is a member of the dicotyledonous family Kirkiacae Takhtajan which contains six species [1,2]. The genus Kirkia was named after Dr John Kirk (1832 - 1922), an English doctor and plant collector, who accompanied Livingstone on his Zambezi expedition [3]. Genus Kirkia is distributed in tropical Africa from Ethiopia and Somalia, south to Madagascar, South Africa and Namibia [4,5]. Kirkia acuminata Oliver is the most known and widely distributed species in the genus [4,6]. It is semi-deciduous, monoecious medium-sized tree, drought resistant and generally grows in hot and dry areas of Angola, Botswana, Democratic Republic of Congo (DRC), Malawi, Mozambique, Namibia, Zambia, Zimbabwe and South Africa [7].

Kirkia burgeri Stannard is a shrub or small tree divided into two sub-species, K. burgeri subsp. burgeri growing mainly on limestone slopes in Ethiopia. Kirkia burgeri subsp. burgeri is categorized as vulnerable (VUB2ab) (i,ii,iii,iv) on the IUCN Red List [8], primarily because of...
reduction in population size based on decline in area of occupancy, extent of occurrence and/or quality of habitat. *Kirkia burgeri* subsp. *somalensis* Stannard is confined to gypsum and anhydrite slopes in northern Somalia where it is categorized as near threatened [9]. *Kirkia burgeri* subsp. *somalensis* is generally rare and threatened by habitat degradation, grazing and over-exploitation of the species as a source of construction timber. *Kirkia dewinteri* Merxm. & Heineis a small tree up to 10 m tall endemic to the limestone and dolomite outcrops in the northwestern part of Namibia [4,6,10].

*Kirkia dewinteri* is categorized as vulnerable (VUD2) on the IUCN Red List in Namibia [11] primarily because of habitat destruction. Ecological research done on *K. dewinteri* showed that the species is generally rare in Namibia, characterized by restricted distributional range and in need of protection from human disturbances and wild fires [10]. *Kirkia leandrii* (Capuron) Stannard, is a tree, endemic to dry deciduous forest of Bemaraha, central Madagascar [5]. *Kirkia tenuifolia* is a shrub or small tree which is common or occasional in sandy or stony bushland in Ethiopia, Kenya and Somalia [4]. *Kirkia wilmsii* Engl. is a deciduous tree endemic to South Africa, found on granite and dolomitic soils in dry bushveld areas or on rocky slopes in Gauteng, Limpopo, Mpumalanga and the North West provinces [4,6,12].

*Kirkia species* are characterized by fatty acids, flavonols, isocoumarin, lignans, neolignans, nor-carotenoids, phenols and tannins which are used medicinally. Preliminary chemical and pharmacological studies done so far on *Kirkia* species have shown promising results with the possibility that these phytochemical compounds may be responsible for the medicinal uses and biological activities demonstrated by the species. The genus certainly has a high use value. The present review compiles fragmented information on the phytochemical, ethnomedicinal and traditional uses of the *Kirkia* species, hoping that this information will highlight the ethnomedicinal and traditional uses of the *Kirkia* species, hoping that this information will highlight the ethnomedicinal importance of the genus and will provide baseline information for future researchers intending to do further work on the genus.

**Vernacular names and traditional uses**

*Kirkia* species are known by various vernacular names in different geographical areas in Eastern, Central and Southern Africa (Table 1). Insight into the societal value of *Kirkia* species in East, Central and Southern Africa can be gained by examining these vernacular names. A survey of literature showed at least 39 vernacular names for *K. acuminata* in Southern Africa (Table 1). *Kirkia burgeri* subsp. *burgeri* is known by two vernacular names in Ethiopia (Table 1), while *Kirkia tenuifolia* is known by one vernacular name in Ethiopia (Table 1).

| Vernacular name(s). Language or geographical region in brackets | Country | Reference(s) |
|---------------------------------------------------------------|---------|--------------|
| *Ivomena, modumela, motsemodumo, mozumina, muzumina (Setswana), white syringa (English)* | Botswana | [13,14] |
| *Mtsambu, mtambwi, mzumba, ntungundwa (Nyanja)* | Malawi | [15] |
| *Mtsaange, nt’sun’gundwa (Sena); pokolo pokolo (Tsonga)* | Mozambique | [16] |
| *Mountain kirkia, white syringa (English)* | Namibia | [7,10] |
| *Modumela (Northern Sotho, Tswana); mvumayila (Tsonga); muvumala, muvumela (Venda); umsila-omhlohe, umsilinga (Zulu), white kirkia, white seringa (English), witsering (Afrikaans)* | South Africa | [6,17,18] |
| *Mtsambu (Nyanja); mzumba (Senga, Tumbuka); musanta (Tonga), white syringa (English)* | Zambia | [19] |
| *Bastard marula, white seringa, white syringa (English); mubvumira, mutsakatidze, mutuwa, mutuva (Shona); musanta (Tonga); umvumila, umvumile (Ndebele); vumila (Hlengwe, Shangaan)* | Zimbabwe | [7,20-24] |
| *Kirkia burgeri* Stannard subsp. *burgeri* | Ethiopia | [25,26] |
| *Bisdhopuza (Borana); musdhugaa (Afan Oromo)* | Namaibia | [10] |
| *Kirkia dewinteri* Merxm. & Heineis | Ethiopia | [26] |
| *Kirkia tenuifolia* Engl. | South Africa | [6,17] |
| *Hudhaa sawwaa (Afan Oromo)* | | |
| *Kirkia wilmsii* Engl. | | |
| *Bastard pepper tree, mountain kirkia, mountain seringa, wild pepper tree (English); basterpeperboom, bergsering, slaploot, wildepeperboom (Afrikaans); legaba, modumela (Northern Sotho)* | | |

**Table 1:** Vernacular names of *Kirkia* species
Kirkia dewinteri is known by one vernacular name in Namibia (Table 1), while Kirkia wilmsii is known by nine vernacular names in South Africa (Table 1). Local people rarely name plant species that they do not use. The long list of vernacular names for K. acuminata and K. wilmsii indicates that local people in Central and Southern Africa have an active interest in these species.

The traditional uses of Kirkia species are referred to in many folkloric and ethnobotanical studies done in East, Central and Southern Africa, where the species are still used as primary sources of traditional medicine. A total of 15 human ailments are treated with Kirkia species (Table 2). Abdominal pain, cholera, cough, snake bites and toothache are the most commonly treated human diseases and ailments (Table 2). Many similarities can be recognized when the ethnomedicinal uses of K. acuminata are compared in Central and Southern Africa in terms of plant parts used, herbal preparation, route of administration and dosage strength (Table 2). For example, bark infusion of K. acuminata is taken as a remedy for abdominal pains in South Africa [27] and Zimbabwe [21]. Root decoction is taken as remedy for cough in Botswana [13,14], Mozambique [28], South Africa [27] and Zimbabwe [21]. Fruit juice of K. acuminata is used as a snake bite antidote in Botswana [14] and Zimbabwe [21,23,24]. Such similarities may be ascribed to efficacy of the plant species. This observation is supported by Hossan et al [33] who argued that a plant species is regarded as effective herbal medicine if it is used by many people in different geographical regions for the same disease or ailment.

The most frequently used plant parts are bark (53 %), roots (23 %), fruits and leaves (12 % each) (Figure 1A). It is well recognized by conservationists that medicinal plants primarily valued for their root parts and those which are intensively harvested for their bark often tend to be the most threatened by over-exploitation [30]. There is need for implementing conservation strategies and mechanisms in East, Central and Southern Africa aimed at conserving Kirkia species, given the fact that K. burgeri subsp. burgeri, K. burgeri subsp. somalensis and K. dewinteri are threatened with extinction [8,9,11]. The population decline of Kirkia species is due to habitat degradation and loss [8,9,11], naturally rare and highly localized in distribution [10,11], over-exploitation of the species [9] and medicinal plant trade. According to Moeng and Potgieter [31], K. wilmsii roots were observed in 44 % of the medicinal plant (muthi) markets in the Limpopo province, South Africa. Given the widespread usage of Kirkia species in traditional medicine resulting in negative impacts on wild populations calls for conservation strategies aimed at halting or reducing these negative impacts. Therefore, conservation of Kirkia species and the traditional knowledge associated with their medicinal applications are important for sustainable utilization of the species. It is important to take concrete conservation measures aimed at protecting the species against over-exploitation and habitat loss. Kirkia remedies are often utilized in the form of decoction or infusion (60.9 %), bark powder mixed with food (17.4 %), ointments or paste (13.0 %), body and tooth wash (4.3 %) (Figure 1B). Most (70.6 %) of the preparations are prescribed orally (Table 2). All Kirkia remedies are used as monotherapies (Table 2).

In addition to the medicinal uses, the swollen roots of K. acuminata, K. tenuifolia and K. wilmsii are used as sources of water during drought [5,7,17,20,34]. Leaves, seeds and twigs of K. acuminata and leaves of K. burgeri subsp. burgeri and K. wilmsii are browsed by game and livestock [17,25,45]. The timber or wood of K. acuminata and K. wilmsii are used for construction poles, carving household utensils and furniture [12,40]. Fibre obtained from the bark, young shoots and roots of K. acuminata and K. wilmsii used for weaving [6,7,12,17]. Kirkia acuminata is grown around homestead boundaries as a barrier or hedge or live fence and also as an ornamental and shade tree. In South Africa, Zambia and Zimbabwe, K. acuminata is commonly used as live fence around fields, gardens, homesteads and schools as a form of protection against animals; around enclosures (kraals) for livestock. The poles of K. acuminata take root and grow easily [12] explaining the high proportion of study households (23 %) with the species growing around their homesteads as live fence in Malawi [41].

Phytochemical studies

Over the last 50 years, there have been numerous attempts to scientifically validate the ethnomedicinal uses of Kirkia species. However, most of these studies concentrated on K. acuminata, possibly because of its availability when compared with other Kirkia species which are highly localized with restricted distribution. Some ethnopharmacological studies have also been carried out on K. wilmsii, a South African endemic species. Based on literature records documenting traditional and potential medicinal uses of K. acuminata and K. wilmsii, researchers
have also investigated their phytochemical and pharmacological properties aimed at identifying the compounds responsible for their wide use in traditional medicine. Multiple classes of phytochemicals including tannins [43,46,47], quercetin, caffeic acid, ellagic acid and gallic acid [54], flavonol, lignans, neolignans, nor-carotenoids and isocoumarin [49], phenols, acetic acid, propionic acid, iso butyric acid, butyric acid and valeric acid [50] have been identified from *K. acuminata* and *K. wilmsii* leaves, roots, seeds and twigs.

Fresh leaves and twigs of *K. acuminata* have a wide variety of nutrients such as minerals, fibre, proteins and fat [43,46,47]. *Kirkia acuminata* leaves, seeds and twigs are a good source of minerals such as calcium, copper, iron, magnesium, manganese, phosphorus, sodium and zinc [43,45,47]. According to Aganga and Mosase [43], *K. acuminata* seeds have adequate quantities of phosphorus, calcium, magnesium, potassium, iron and copper required for beef, sheep and goat growth and production, while the content of sodium, manganese and zinc are below the recommended levels required by ruminants for growth and productivity. Some of these nutrients are present in low concentrations, but may have significant impact on animal health as both *K. acuminata* and *K. wilmsii* are important stock feed in southern Africa [17,20,43,46,47].

Nooiteboom [48] isolated quercetin, caffeic acid, ellagic acid and large quantities of gallic acid from hydrolysed leaf extracts of *K. wilmsii* (Figure 2). Similarly, Gemeda and Hassen [50] isolated acetic acid, propionic acid, iso butyric acid, butyric acid and valeric acid from both *K. acuminata* and *K. wilmsii* leaves and young stems. Diakanamwa et al. [51] isolated 3,3′-di-O-methyllellagic acid 4-O-β-D-xylopyranoside from *K. acuminata* roots. From *K. acuminata* hexane stem bark extract, Mulolland et al. [49] isolated (+)-(6S,7E,9R)-blumenol A and (+)-(6S,7E)-dehydrovomifoliol and (+)-de-O-methyllassiodiplodin. The methanol stem bark extract of *K. acuminata* yielded neolignan, (-)-4′,9,9′-trihydroxy-3′-methoxy-3-O.8′,4′,O.7′-neolignan while dichloromethane extract yielded (+)-dihydrodehydrodiconiferyl alcohol, (+)-lyoniresinol and (-)-ent-isolariciresinol [49]. The dichloromethane extract of *K. wilmsii* yielded (+)-(6S,7E,9R)-blumenol A, (+)-(6S,7E)-dihydrovomifoliol, (+)-4-ethanone-3,4-dihydro-6,8-dihydroxy-5-methylisocoumarin and (+)-(2R,3R)-7-O-methylaromadendrin. Although there is a possibility that these phytochemical compounds may be responsible for the medicinal uses and biological activities demonstrated by both *K. acuminata* and *K. wilmsii*, but no studies were found in literature with details of biological activities of these compounds isolated from *Kirkia* species.

**Pharmacological activities**

Some of the pharmacological activities of *K. acuminata* and *K. wilmsii* reported in literature correlate with some of their ethnomedicinal uses listed in Table 2. While some of these pharmacological activities may not relate directly to their ethnomedicinal uses, they may provide some insight into potential therapeutic value and bioactive properties of *K. acuminata* and *K. wilmsii*. The biological activities that have been reported so far include antimicrobial [52-55], antioxidant [56], antiplasmodial [36] and antiplatelet [56] activities.

![Figure 1: Preparation of Kirkia herbal medicines in East, Central and Southern Africa. A: Plant parts used and B: Herbal preparations](image-url)
Table 2: Traditional uses of Kirkia species

| Use                  | Plant part(s) used and preparation                                                                 | Country practised and reference(s)                      |
|----------------------|--------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| **Medicinal uses**   |                                                                                                  |                                                        |
| **K. acuminata**     |                                                                                                  |                                                        |
| Abdominal pain       | Bark infusion taken by mouth                                                                      | South Africa [27], Zimbabwe [21]                        |
| Antiemetic           | Bark infusion taken by mouth                                                                      | Zimbabwe [21]                                          |
| Backache             | Bark infusion taken by mouth                                                                      | Zimbabwe [32]                                          |
| Cholera              | Bark decoction drunk or bark powder mixed with food                                              | Zimbabwe [22,24]                                       |
| Constipation         | Bark decoction drunk or bark powder mixed with food                                              | Zimbabwe [22,24]                                       |
| Cough                | Root decoction taken by mouth                                                                     | Botswana [13,14], Mozambique [28], South Africa [27], Zimbabwe [21] |
| Diarrhea             | Bark decoction drunk or bark powder mixed with food                                              | Zimbabwe [22,24]                                       |
| Dysentery            | Bark decoction drunk or bark powder mixed with food                                              | Zimbabwe [22,24]                                       |
| Fever                | Not specified                                                                                   | Zambia [33]                                            |
| Snake bite antidote  | Fruit juice applied on bitten part                                                               | Botswana [14], Zimbabwe [21,23,24]                     |
| To bring luck        | Powdered inner bark added to bathing water                                                        | Botswana [13]                                          |
| To fatten babies     | Baby washed with root infusion                                                                   | Zimbabwe [21]                                          |
| Toothache            | Tooth washed with decoction of pulverized roots                                                  | Zimbabwe [4,7]                                         |
| Toothache            | Burnt root powder rubbed on painful tooth                                                        | Zambia [20]                                            |
| Vomiting             | Bark infusion is taken by mouth                                                                   | South Africa [27]                                      |
| Wounds               | Fruit juice applied to wounds                                                                   | Zimbabwe [20,23,24]                                    |
| **K. tenuifolia**    |                                                                                                  |                                                        |
| cholera              | Bark decoction is taken by mouth                                                                 | Somalia [34]                                           |
| **K. wilmsii**       |                                                                                                  |                                                        |
| Diabetes mellitus    | Root juice taken orally                                                                          | South Africa [35]                                      |
| Fever                | Leaf decoction                                                                                    | South Africa [36]                                      |
| Hypertension         | Roots eaten raw                                                                                   | South Africa [37,38]                                  |
| Malaria              | Bark/leaf decoction                                                                              | South Africa [36,39]                                  |
| Toothache            | Tooth washed with root decoction                                                                  | South Africa [40]                                      |
| **Other uses**       |                                                                                                  |                                                        |
| **K. acuminata**     |                                                                                                  |                                                        |
| Charcoal             | Wood made into charcoal                                                                           | Malawi [7]                                             |
| Hedge, ornamental,   | Grown and managed as hedge, cattle enclosure, live fence, ornamental, stock shade and shade tree  | Malawi [15,41], South Africa [17], Zambia [20], Zimbabwe [7] |
| shade                | in home gardens                                                                                   |                                                        |
| Religious significance| Often planted in grave-yards in memory of the deceased                                              | Zambia [20]                                            |
| Religious significance| Shona people believe that ancestral spirits live in K. acuminata branches                         | Zambia [42]                                            |
| Source of water      | Swollen roots are used as a source of water during drought                                        | South Africa [17], Zambia [20], Zimbabwe [7]           |
| Stock feed           | Leaves and seeds browsed by game and livestock                                                   | Botswana [43], Zambia [20], Zimbabwe [44]             |
| Timber, wood         | For construction poles; wood for carving and furniture                                            | Botswana [14], Malawi [41], South Africa [17], Zambia [20], Zimbabwe [7] |
| Weaving               | Root bark made into cloth                                                                         | Zambia [19,20], Zimbabwe [4,7]                         |
| **K. burgeri subsp. burgeri** |                                                                                                  |                                                        |
| Source of water      | Swollen roots are used as a source of water during drought                                        | Kenya [5,34]                                           |
| **K. tenuifolia**    |                                                                                                  |                                                        |
| Garden plant         | An excellent garden plant which tolerates mild frost                                              | South Africa [6]                                       |
| Source of water      | Swollen roots are used as a source of water during drought                                        | South Africa [5,17]                                   |
| Stock feed           | Foliage often cut as goat fodder and eaten by other wild animals                                  | South Africa [17]                                      |
| Timber, wood         | Wood used for making household utensils                                                          | South Africa [12,40]                                  |
| Weaving               | Fibre obtained from the bark, young shoots and roots is strong and used for weaving               | South Africa [5,6,12,17]                              |
Figure 2: Chemical structures of compounds isolated from leaves, stem bark and roots of Kirkia species
Antimicrobial activity

One of the most common ethnomedicinal uses of *Kirkia* species, *K. acuminata*, *K. tenuifolia* and *K. wilmsii* is in the treatment of a wide range of infectious diseases caused by microorganisms. Such diseases or ailments include symptoms such as cholera [22,24,34], diarrhoea [22,24], dysentery [22,24], fever and malaria [33,36,39], toothache [4,7,20] and wounds [21,23,24]. Such wide use of *Kirkia* species against microbial infections in traditional medicine prompted Masoko [54] to evaluate antibacterial effects of acetone, dichloromethane, hexane and methanol leaf extracts of *K. acuminata* against *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* with ampicillin as the positive control. In this study, *E. faecalis* was the most sensitive microorganism with average MIC value of 0.1 mg/ml followed by *E. coli* (0.31 mg/mL) while *S. aureus* and *P. aeruginosa* were resistant with MIC values of 0.97 mg/mL and 1.25 mg/ml respectively [54]. Similarly, Mmushi et al [52] evaluated acetone, dichloromethane, hexane and methanol leaf extracts of *K. acuminata* against *Mycobacterium smegmatis* using rifampicin as a positive control. The acetone, dichloromethane, hexane and methanol extracts demonstrated antimycobacterial activity with MIC values ranging between 0.31 to 0.63 mg/mL against *M. smegmatis* [52].

Suleiman et al [53,57] evaluated the hexane, acetone, dichloromethane and methanol extracts of *K. wilmsii* against *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* using the bioautographic procedure and a two-fold serial microdilution method. The authors found 18 inhibition bands against bacteria. Suleiman et al [53,57] also evaluated the hexane, acetone, dichloromethane and methanol extracts of *K. wilmsii* against *Aspergillus fumigatus*, *Candida albicans*, *Cryptococcus neoformans*, *Microsporum canis* and *Sporothrix schenckii* using the bioautographic procedure and a two-fold serial microdilution method. The authors found 11 inhibition bands against fungi. The acetone, dichloromethane, hexane and methanol extracts of *K. wilmsii* had antibacterial and antifungal activities with MIC values ranging from 0.07 to 2.50 mg/mL against the tested bacteria and fungi [53,57]. The leaves of the *K. wilmsii* further showed biological activity against the animal fungal pathogen *Aspergillus fumigatus* and the MIC ranged from 0.17 to 2.11 mg/mL [57]. In another study, Chigayo et al [55] evaluated the antimicrobial activity of aqueous root extracts of *K. wilmsii* using an HPLC gradient elution method with kanamycin as the positive control. The extracts showed antimicrobial activities against *Aeromonas hydrophilia*, *Candida albicans*, *Enterobacter aerogenes*, *Escherichia coli*, *Proteus mirabilis*, *Salmonella typhi*, *Shigella dysenteriae*, *Staphylococcus aureus*, *Vibrio cholerae* with minimum inhibitory concentration (MIC) ranging from 0.08 mg/mL to 3.445 mg/mL. Results of these studies implies that *K. acuminata* and *K. wilmsii* may be used as a broad spectrum antibiotics.

Antiplasmodial activity

Clarkson et al [36] evaluated leaf extracts of *K. wilmsii* against *Plasmodium falciparum* using the parasite lactate dehydrogenase (pLDH) assay. The dichloromethane/methanol (1:1) was highly active and showed promising antiplasmodial activity with IC<sub>50</sub> of 3.7 µg/mL, while water extra showed a weak activity with IC<sub>50</sub> of >100 µg/mL [36]. These pharmacological evaluations are important as the bark and leaf decoctions of *K. wilmsii* are used as herbal medicine for fever and malaria in South Africa [36,39]. Such pharmacological evaluations are also important for future research focusing on control and management of parasites and mosquito vectors in the tropics.

Antioxidant and antiplatelet activities

Extracts of *K. wilmsii* exhibited antioxidant properties in the qualitative assay using DPPH with EC<sub>50</sub> value of 3.57 ± 0.41 µg/mL [56]. In the quantification of antioxidation using ABTS, the extracts of *K. wilmsii* showed low antioxidant activities with respect to TEAC values of 0.67. *Kirkia wilmsii* showed low antiplatelet activity with EC<sub>50</sub> value of 0.22 ± 0.02 µg/mL [56]. The documented antioxidant and antiplatelet activities of *K. wilmsii* may be attributed to the presence of phytochemicals since compounds such as flavonols and phenolics are known to have antioxidant properties [58] and also lower the risk of cancer, heart diseases, hypertension and stroke [59]. Detailed anti-hypertensive studies of *K. wilmsii* are recommended based as ethnopharmacological studies by Semenya and Potgieter [37] revealed that 97 % of traditional healers in the Limpopo province, South Africa use *K. wilmsii* in a similar manner as hypertension remedy in terms of herbal preparation, route of administration and dosage strength.

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Toxicity studies

*Kirkia wilmsii* extracts showed comparably low toxicity when compared with the reference agent berberine (cytotoxic agent) with hemaglutination assay titre value of 0.80 and agglutination value of 1.25 mg/mL [56]. Toxicological evaluations carried out so far on *Kirkia* are preliminary considering their widespread usage as herbal medicines in southern Africa. It is important to ascertain any toxicological effects that can occur as a result of chronic or sub-chronic usage of *Kirkia* species, and the different plant parts should be tested against a wide range of cell lines as well as using other in vitro toxicological assays and in vivo studies.

CONCLUSION

Of the six *Kirkia* species, only *K. acuminata*, *K. wilmsii* and to some extent *K. tenuifolia* have been studied so far under different ethnobotanical and ethnopharmacological aspects. The others are either threatened with extinction or are highly localized, naturally rare and in need of human intervention to save them from extinction. There is therefore need to develop conservation strategies and mechanisms for *Kirkia* species that are threatened with extinction as well develop micropropagation protocols as an alternative and viable means to provide sufficient plants to meet the herbal medicine needs and at the same time protecting the natural populations.

From literature, it is clear that both *K. acuminata* and *K. wilmsii* have been used for centuries in southern Africa as herbal medicines for microbial infections in humans and scientific studies carried out so far have validated some of their traditional antimicrobial uses. Up to now, only a few pharmacological studies directly dealing with the documented traditional uses of *K. acuminata* and *K. wilmsii* have been performed. Phytochemical studies led to the identification of a large number of fatty acids, flavonols, isocoumarin, lignans, neolignans, nor-carotenoids, phenols and tannins. Most of these phytochemicals have not been evaluated, therefore, these compounds must be evaluated biologically in more detail. Further investigations should focus on phytochemical studies of these isolated compounds and try to link such pharmacological properties to documented ethnomedicinal uses.

Concerning toxicological information, no significant data are reported. A weak cytotoxic activity is described only for *K. wilmsii* [56]. Future research should focus on assessing biological and toxicological aspects of the leaves, stem bark and roots of *Kirkia* species used as herbal medicines as well as both their bioactive extracts and isolated compounds. There is no doubt that results presented in this review may provide useful clues to promote further investigations of ethnopharmacological properties as well as potential use of phytochemicals isolated from *Kirkia* species.

DECLARATIONS

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Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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