Ethnobotany, ethnopharmacology, and phytochemistry of traditional medicinal plants used in the management of symptoms of tuberculosis in East Africa: a systematic review

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Abstract

Objective: Many studies on the treatment of tuberculosis (TB) using herbal medicines have been undertaken in recent decades in East Africa. The details, however, are highly fragmented. The purpose of this study was to provide a comprehensive overview of the reported medicinal plants used to manage TB symptoms, and to analyze scientific reports on their effectiveness and safety.

Method: A comprehensive literature search was performed in the major electronic databases regarding medicinal plants used in the management of TB in East Africa. A total of 44 reports were retrieved, and data were collected on various aspects of the medicinal plants such as botanical name, family, local names, part(s) used, method of preparation, efficacy, toxicity, and phytochemistry. The data were summarized into percentages and frequencies which were presented as tables and graphs.

Results: A total of 195 species of plants belonging to 68 families and 144 genera were identified. Most encountered species were from Fabaceae (42.6%), Lamiaceae (19.1%), Asteraceae (16.2%), and Euphorbiaceae (14.7%) families. Only 36 medicinal plants (18.5%) have been screened for antimycobacterial activity. Out of these, 31 (86.1%) were reported to be bioactive with minimum inhibitory concentrations ranging from 47 to 12,500 μg/ml. Most tested plant extracts were found to have acceptable acute toxicity profiles with cytotoxic concentrations on normal mammalian cells greater than 200 μg/ml. The most commonly reported phytochemicals were flavonoids, terpenoids, alkaloids, saponins, cardiac glycosides, and phenols. Only Tetradenia riparia, Warburgia ugandensis, and Zanthoxylum leprieurii have further undergone isolation and characterization of the pure bioactive compounds.

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Conclusion: East Africa has a rich diversity of medicinal plants that have been reported to be effective in the management of symptoms of TB. More validation studies are required to promote the discovery of antitubercular drugs and to provide evidence for standardization of herbal medicine use.

Keywords: Antimycobacterial, Antitubercular, Medicinal plants, Herbal medicine, Phytochemicals, Mycobacterium tuberculosis

Background
Tuberculosis (TB) is a chronic infectious bacterial disease caused by Mycobacterium tuberculosis (Mtb). It affects mainly the respiratory system but may also affect other organs of the body causing pulmonary and extrapulmonary TB respectively. The World Health Organization (WHO) estimated that a quarter of the world’s population is infected with Mtb and thus at a risk of developing TB [1]. Although TB affects all people, those living with HIV/AIDS are at a higher risk of developing active TB [2]. The burden of TB is still high as it is ranked among the ten diseases of global concern [3]. In 2018, a total of 10 million new cases and 1.49 million deaths due to TB were reported worldwide. In East Africa, 378,000 new cases and 91,000 deaths (24%) occurred. In East Africa, Kenya and Tanzania are still ranked among the 30 countries with a high burden of TB in the world [1].

Treatment of TB remains a challenge due to the emergence of multidrug-resistant Mtb strains and extensively drug-resistant TB cases which poorly respond to the first line antitubercular drugs (rifampicin, isoniazid, pyrazinamide, and ethambutol). These drugs also have side effects and a high potential to interact with antiretroviral drugs resulting in increased toxicity, poor compliance, and treatment failure [4–6]. As a result, many TB patients have resorted to using alternative and complementary medicines with herbal remedies being the most widely used in the management of tuberculosis [7]. Due to limited access to health services and chronic poverty in East Africa, many people not only believe that herbal medicines are efficacious and safe but also affordable, available, and culturally acceptable [8–10]. Thus, there is widespread use of herbal remedies by many people in the East Africa to manage symptoms of TB [7–13]. The WHO also reported that approximately 60% of the world’s population depend on non-conventional therapies for primary health care [14].

The search to discover new effective drugs against Mtb has intensified globally in the last decade as the current therapies become less effective and in an attempt to have a world free of TB by 2035 [1]. With natural products being the leading sources of novel drugs, ethnobotanical surveys and scientific validation studies have been conducted on East African flora in the past decades [7–10]. Several plant species have been documented and some of their extracts, fractions, and isolated pure compounds have been tested for efficacy and safety [15–18]. However, this information is highly fragmented.

Comprehensive data on medicinal plants used in the management of TB is important for the conservation of these species as some of them are either rare or endangered. It also provides more evidence that increases the confidence in the utilization of these herbal remedies for primary health care as well as their regulation by relevant authorities in case of ineffectiveness and toxicity [19, 20]. The analysis and synthesis of the results may also help in identifying existing gaps and challenges in the current research and stimulates future research opportunities. This can lead to identification of novel molecules that can be developed into new antitubercular drugs with better efficacy and safety profiles [21]. This review was therefore undertaken to compile a comprehensive report on the ethnobotany, ethnopharmacology, and phytochemistry of medicinal plants used in management of symptoms of TB in the East African region so as to generate knowledge on the current status and future opportunities for drug discovery against TB.

Methods

Reporting and protocol registration
This systematic review was reported according to the Preferred Reporting Items for the Systematic Reviews and Meta-Analyses (PRISMA) guidelines [22]. The protocol used in this study was registered with the International Prospective Register of Systematic Reviews (PROSPERO) and can be accessed at their website (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=187098) with the registration number CRD42020187098.

Literature search strategy
Relevant literature pertaining the ethnobotany, phytochemistry, efficacy and safety of medicinal plants utilized in management of symptoms of TB in Uganda, Kenya, Tanzania, Rwanda, Burundi and South Sudan were re-
retrieved from Scopus, Web of Science Core Collection, PubMed, Science Direct and Google Scholar [23–25]. Key search words such as tuberculosis, *mycobacteria*, tuberculosis symptoms, tuberculosis treatment, vegetal, antituberculosis, antitubercular, antimycobacterial, cough, traditional medicine, ethnobotany, alternative medicine, and ethnopharmacology combined with either Uganda, Kenya, Tanzania, Rwanda, Burundi, or South Sudan were used. All publishing years were considered, and reports in the returned results were carefully scrutinized. More searches were carried out at the Google search engine using more general search terms, such as *mycobacteria*, tuberculosis, antituberculosis, antimycobacterial, cough, vegetal species, vegetal extract, traditional medicine, alternative medicine, plants, plant extract, vegetal, herbal, complementary therapy, natural medicine, ethnopharmacology, ethnobotany, herbal medicine, herb, herbs, decoction, infusion, macerate, and concoction combined with either Uganda, Kenya, Tanzania, Rwanda, Burundi, or South Sudan. The searches were done independently by the authors for each country and the outputs were saved where possible.

Data collection
A data collection tool was designed in Microsoft Excel (Microsoft Corporation, USA) to capture data on different aspects of medicinal plant species used in TB management. This included botanical name, plant family, local name(s), part(s) used, growth habit, mode of preparation and administration, method of extraction, efficacy, toxicity and phytochemical screening of crude extracts, isolated pure compounds, and efficacy and toxicity. Careful review of the articles was done, and data were captured using the tool. The collected data were checked for completeness, processed independently for each country by the authors and later analyzed.

Data analysis
Missing information in some studies (local names and growth habit of the plants), and misspelled botanical names were retrieved from the Google search engine and botanical databases (The Plant List, International Plant Names Index, NCBI taxonomy browser, and Tropicos) respectively.

Results and discussion
Ethnobotanical studies
With the current antitubercular drugs becoming less effective in the management of multidrug-resistant Mtb strains, medicinal plants can provide the novel molecules for development of new efficacious and safe drugs [26, 27]. From the electronic survey in multidisciplinary databases, 44 reports on medicinal plants used for management of symptoms of TB in East Africa were retrieved. A total of 195 species of plants belonging to 68 families and 144 genera were identified (Table 1). Some of these documented plant species have also been reported in other regions across the world for management of TB. For example, *Psidium guajava*, *Catha edulis*, *Carica papaya*, *Citrus limon*, *Lantana camara*, *Aloe vera*, *Biden pilosa*, *Piliostigma thonningii*, *Tamarindus indica*, *Ficus platyphylla*, and *Vernonia cinerea* in Nigeria, South Africa, Ethiopia, India, and Mexico [60–64]. This implies that plants continue to occupy a critical niche in the environment due to their rich possession of secondary metabolites (phytochemicals) that have potential to be used as medicines for several ailments that affect man. Therefore, the use of herbal medicines in the provision of primary health care remains an integral component of all health systems globally [14].

Most encountered species were from the family Fabaceae (42.6%), Lamiaceae (19.1%), Asteraceae (16.2%), Euphorbiaceae (14.7%), Moraceae (10.3%), Rubiaceae (10.3%), Rutaceae (8.8%), Burseraceae (7.4%), and Cucurbitaceae (7.4%) (Fig. 1). Fabaceae, Asteraceae, and Lamiaceae were also reported to provide the largest number of plants species used for TB management in South Africa, Ghana, Nigeria, Ethiopia, and India [64–72]. From these families, 15 species were the most cited in East Africa (Fig. 2). These families were reported from at least four countries of East Africa. This could probably be attributed to the abundant distribution of the analogue active substances among species from these families [23, 24]. The family Fabaceae has biosynthetic
| Botanical name                  | Family           | Local Names          | Habit   | Part used            | Country    | Author(s) |
|--------------------------------|------------------|----------------------|---------|----------------------|------------|-----------|
| *Acacia ataxacantha* DC        | Fabaceae         | Not reported         | Tree    | Roots                | Kenya      | [28]      |
| *Acacia hockii* De Wild.       | Fabaceae         | Kasana (Luganda), Kashiono | Tree    | Leaves, Stem bark    | Uganda     | [7, 10]   |
| *Acacia horrida* (L.)          | Fabaceae         | Leri (Samburu)       | Tree    | Stem bark            | Kenya      | [29]      |
| *Acacia mearnsii* De Wild.     | Fabaceae         | Burikoti             | Tree    | Stem bark            | Uganda     | [10]      |
| *Acacia nilotica* (L.)         | Fabaceae         | Sunut                | Tree    | Fruit                | South Sudan | [30]      |
| *Acacia polyacantha* Wild.     | Fabaceae         | Egirigirioi          | Tree    | Stem bark            | Uganda     | [10]      |
| *Acacia senegal*               | Fabaceae         | Lderekesi (Samburu)  | Tree    | Stem bark            | Kenya      | [29]      |
| *Acacia spectabilis* A. Cunn. Ex Benth. | Fabaceae    | Gasiya (Luganda)     | Tree    | Leaves               | Uganda     | [7]       |
| *Acanthus pubescens* (Thomson ex Oliv.) Engl. | Acanthaceae     | Matovu, Itojo        | Herb    | Roots                | Uganda, Kenya | [10, 12] |
| *Achyranthes aspera* L.        | Amaranthaceae    | Muhruru              | Herb    | Flower               | Uganda     | [10]      |
| *Achyrospermum carvalhoi* Gürke | Lamiaceae       | Kanyarafundo         | Shrub   | Leaves               | Uganda     | [10]      |
| *Acakanthera frisorum*         | Apocynaceae      | Chipilikwa (Samburu) | Tree    | Leaves               | Kenya      | [29]      |
| *Adenia gummifera*             | Passifloraceae   | Chepnyalidet (Nandi) | Climber | Roots                | Kenya      | [31]      |
| *Adhatoda engleriana* Lindau C.B. Clarke | Acanthaceae | Iringoringo (Chagga) | Herb    | Roots                | Tanzania   | [32]      |
| *Ageratum coryoides* L.        | Astaraceae       | Namirembe (Luganda)  | Herb    | Whole plant          | Uganda     | [7]       |
| *Allangium chinense* (Lour.) Harms | Coraceae     | Omusisita (Luganda)  | Herb    | Stem bark            | Uganda     | [7]       |
| *Albizia anthelmatica*         | Fabaceae         | Lamuntana (Samburu)  | Tree    | Stem bark            | Kenya      | [29]      |
| *Albizia coriaria* Welw. Ex Oliv. | Fabaceae     | Mugavu (Luganda), Etek (Lango), Musita (Lusoga), Omusesa (Rungangkore), Omubele (Wanga) | Tree    | Stem bark            | Uganda, Kenya | [7–10, 12, 33] |
| *Albizia species*              | Fabaceae         | Enningono (Luganda)  | Tree    | Stem bark            | Uganda     | [7]       |
| *Albizia versicolor*           | Fabaceae         | Not reported         | Tree    | Leaves               | Uganda     | [12]      |
| *Albizia zygia* (DC.) Macbr.   | Fabaceae         | Ekegonchori (Kuria)  | Tree    | Roots                | Kenya      | [12]      |
| *Allium sativum* L.            | Alliaceae        | Kitungu saumu (Luo), Garlic (Luganda) | Herb    | Leaves               | Uganda, Kenya | [10, 12] |
| *Aloe vera* (L.) Burm. f.      | Asphodelaceae    | Kigaji (Luganda)     | Herb    | Leaves               | Uganda     | [7]       |
| *Aloe secundiflora* Engl.      | Aloaceae         | Sukuroi (Samburu), Osukuroi (Masai), Kiluma (Kamba) | Herb    | Leaves               | Kenya      | [12, 34] |
| *Amaranthus spinosus*          | Amaranthaceae    | Kidodo (Luganda)     | Herb    | Leaves               | Uganda     | [10]      |
| *Amoitis usietopscarpus* (DC) Guill. & Perr. | Combretaceae | Sahab                  | Tree    | Stem bark            | South Sudan | [30, 35] |
| *Antiaris toxicaria* Lesch.    | Moraceae         | Kirundu (Luganda)    | Tree    | Stem bark            | Uganda     | [7]       |
| *Asparagus africanus* Lam.     | Asparagaceae     | Mukira givango (Luganda) | Tree    | Stem bark            | Uganda     | [10]      |
| *Aspilia africana* (Pers.) C.D. Adams | Asteraceae | Makaayi (Luganda) Emaruoit | Herb    | Root bark, Leaves    | Uganda     | [7, 10]   |
| *Aspilia plurigeta* Schweinf.  | Asteraceae       | Rirangera            | Herb    | Roots                | Kenya      | [28]      |
| *Azadirachta indica* L.        | Meliaceae        | Muarubaini (Kamba)   | Tree    | Seeds                | Kenya      | [12]      |
| *Azadirachta indica* A. Juss.  | Meliaceae        | Neem tree (Luganda)  | Tree    | Leaves, stem bark    | Uganda     | [7, 10]   |
| Botanical name          | Family                  | Local Names                                      | Habit     | Part used       | Country                  | Author(s) |
|------------------------|-------------------------|--------------------------------------------------|-----------|-----------------|--------------------------|-----------|
| *Balanites aegyptiaca* (L.) Delile | Zygophyllaceae   | Ongosua (Maasai), Ekorete                        | Shrub     | Stem bark       | Tanzania, Kenya, Uganda  | [10, 12] |
| *Bersama abyssinica* Fres.          | Melianthaceae       | Kipsigiet (Sabaot), Kibuirimetiet (Nandi)        | Tree      | Leaves          | Kenya                    | [36]      |
| *Bidens pilosa* L.                                            | Asteraceae          | Sere, Labika (Luganda), Kalala (Lusoga), orionot (Lango) | Herb      | Flowers, Leaves | Uganda, Rwanda, Burundi  | [7, 10, 37, 38] |
| *Blighia unijugata* Baker Sapindaceae                  | Tree                | Enikuza nyana (Luganda)                          | [7]       | Stem bark       | Uganda                    | [7]       |
| *Boscia senegalensis* (Pers.) Lam.                           | Capparaceae         | Kursan; Mukheit                                  | Shrub     | Not reported    | South Sudan               | [35]      |
| *Bridelia micrantha* (Hochst.) Baill.                           | Euphorbiaceae       | Katazamitti (Luganda), Umugimbu,                | Tree      | Stem bark, Root  | Uganda, Burundi           | [7, 38]  |
| *Brillantaisa owariensis* P. Beauv.                             | Aranthaceae         | Icuga                                            | Herb      | Leaves          | Uganda                    | [10]      |
| *Cadaba farinosa* Forsk                                          | Capparaceae         | Lumuriai (Samburu), Akado marateng (Luo)        | Shrub     | Not reported    | Kenya                     | [39]      |
| *Callistemon citrinus* (Curitis) Skeels                       | Myrtaceae           | Mwalabalutonya (Luganda)                         | Shrub     | Leaves, Stem bark | Uganda                    | [7, 9, 10] |
| *Canarium schweinfurthi* Engl.                                 | Burseraceae         | Muwafu (Luganda), Mubafu (Lusoga, Rutoro)       | Tree      | Stem bark, roots | Uganda, Kenya              | [7, 9, 12] |
| *Canephora pierre ex A. Froehner*                             | Rubiaceae           | Emwanyi (Luganda)                                | Shrub     | Stem bark       | Uganda                    | [7]       |
| *Capparis erythrocarpos* Isert                                 | Capparaceae         | Muzingani omwelu, Kitunku ekitono                | Shrub     | Roots           | Uganda                    | [10]      |
| *Capparis tomentosa* L.                                        | Capparaceae         | Muzingani omwelu, Kitunku ekitono                | Shrub     | Roots           | Uganda                    | [10]      |
| *Carica papaya* L.                                              | Caricaceae           | Amapapali, Paapali essajja (Luganda), Mupapali omusalza (Lusoga), Apapalu (Lango) | Shrub     | Leaves, Stem   | Uganda                    | [7, 9, 10] |
| *Carissa edulis* (Forsk.) Vahl                                 | Apocynaceae         | Muyonza, Ekamuriei (Ateso)                       | Shrub     | Roots           | Uganda                    | [10]      |
| *Cassine buchananii* Loes.                                      | Celastraceae        | Mbaluka (Luganda)                                | Tree      | Stem bark, Leaves | Uganda                    | [8]       |
| *Catha edulis* Forsk                                             | Celastraceae        | Chemgangoi (Sabaot)                              | Shrub     | Stem bark       | Kenya                     | [36]      |
| *Celosia trigyna* L.                                            | Amaranthaceae       | Kakubaggiri (Luganda)                            | Herb      | Leaves          | Uganda                    | [7]       |
| *Chaetacme arista* Planch.                                      | Ulmaceae            | Embutami (Luganda)                               | Tree      | Leaves          | Uganda                    | [7]       |
| *Cinnamomum zeylanicum* Blume                                   | Lauraceae           | Mudalasini (Luganda)                             | Tree      | Stem bark       | Uganda                    | [7]       |
| *Cissampelos pereira* L.                                       | Menispermaeae       | Karigi munana                                    | Shrub     | Roots           | Kenya                     | [28]      |
| *Cissus quinquangularis* L.                                     | Vitaceae            | Sukurtuti                                       | Herb      | Roots           | Kenya                     | [12, 34] |
| *Citrus limon* (L.) Osbeck                                     | Rutaceae            | Nimawa                                           | Tree      | Fruit           | Uganda                    | [9]       |
| *Combretum molle* RBr. ex. G. Don.                              | Combretaceae        | Ndagi, Loro (Lango)                              | Tree      | Stem bark       | Uganda                    | [7, 8, 10] |
| *Commiphora species* Burseraceae                               | Burseraceae         | Oltemuai (Sabaot)                                | Shrub     | Not reported    | Kenya                     | [40]      |
| *Commiphora edulis* (Klotzsch)                                  | Burseraceae         | Not reported                                     | Shrub     | Stem bark, Leaves | Kenya                    | [12, 26] |
| *Commiphora ellenbeckii* Engl.                                  | Burseraceae         | Not reported                                     | Shrub     | Stem bark, roots | Kenya                     | [26]      |
| *Commiphora mildbraedii* Engl.                                  | Burseraceae         | Not reported                                     | Shrub     | Stem bark, Roots | Kenya                     | [26]      |
| *Cordia africana* Lam.                                         | Boraginaceae        | Not reported                                     | Tree      | Roots           | Tanzania, Kenya           | [12]      |
| *Crassoscelum vitellinum*                                       | Apiaceae            | Akyangubira                                      | Herb      | Leaves          | Burundi                   | [38]      |
| *Crossopteryx febrifuga*                                        | Rubiaceae           | Not reported                                     | Tree      | Roots           | Tanzania, Kenya           | [12]      |
| Botanical name                  | Family            | Local Names                                      | Habit  | Part used     | Country           | Author(s) |
|--------------------------------|-------------------|--------------------------------------------------|--------|---------------|--------------------|-----------|
| Croton dichogamus              | Euphorbiaceae     | Olioiborrbenek (Massai)                          | Shrub  | Roots         | Tanzania, Kenya    | [12]      |
| Croton macrostachyus           | Euphorbiaceae     | Omutsiwitswi (Wanga), Mukinduri (Kikuyu)         | Tree   | Leaves, Roots | Kenya              | [33]      |
| Croton sylvaticus              | Euphorbiaceae     | Not reported                                     | Tree   | Roots         | Tanzania           | [41]      |
| Croton zambesicus              | Euphorbiaceae     | Um-Gilagla                                       | Tree   | Fruit         | South Sudan, Kenya | [42, 43] |
| Cryptolepis sanguinolenta      | Apocynaceae       | Kafulu (Luganda)                                 | Shrub  | Roots         | Kenya, Uganda      | [12, 44] |
| Cymbopogon citratus            | Poaceae           | Kisuhi (Luganda), Akisube (Ateso), Lum cai (Lango)| Herb   | Leaves        | Uganda             | [7]       |
| Cyperus rotundus               | Cyperaceae        | Ekekeriaut                                       | Herb   | Roots         | Uganda             | [10]      |
| Cyperus rotundus L.            | Cyperaceae        | Ekekeriaut                                       | Herb   | Roots         | Uganda             | [10]      |
| Cryptostemma adenocaula        | Vitaceae          | Lordo (Samburu)                                  | Herb   | Not reported  | Kenya              | [34]      |
| Dalbergia melanoxylon          | Fabaceae          | Not reported                                     | Tree   | Stem bark     | Kenya              | [28]      |
| Datura stramonium              | Solanaceae        | Not reported                                     | Herb   | Leaves        | Rwanda              | [45]      |
| Desmodium salicifolium         | Fabaceae          | Enkolimbo (Luganda)                              | Herb   | Leaves        | Uganda             | [7]       |
| Desmodium repandum             | Papilionaceae     | Ituza                                            | Herb   | Leaves        | Uganda             | [10]      |
| Dichrostachys cinerea          | Fabaceae          | Chinjiri (Digo)                                  | Tree   | Roots         | Kenya              | [28]      |
| Dodonaea angustifolia          | Sapindaceae       | Musambya (Luganda)                               | Shrub  | Leaves        | Uganda             | [10]      |
| Dracaena steudneri             | Asparagaceae      | Kajjolyenjovu (Luganda)                          | Tree   | Stem bark     | Uganda, Kenya      | [7, 9, 10, 12] |
| Dychrostachys glomerata        | Fabaceae          | Not reported                                     | Tree   | Leaves, Roots | Uganda, Kenya, Tanzania | [10, 12, 29] |
| Embelia schimperi              | Myrsinaceae       | Sachuonet (Ogiek)                                | Tree   | Stem bark     | Kenya              | [46]      |
| Entada abyssinica A. Rich.     | Fabaceae          | Laginaria (Luo) Mwolola (Luganda)                 | Shrub  | Roots, Stem bark, Leaves | Uganda, Kenya, Tanzania | [7, 10, 12, 29] |
| Euphorbia ingens               | Ebenaceae         | Emus, Kasalagala/Muda (Lusoga)                    | Shrub  | Roots         | Uganda             | [28]      |
| Euphorbia schimperi Screeley   | Euphorbiaceae     | Kazagamira (Luganda)                             | Tree   | Leaves        | Uganda              | [7]       |
| Faidherbia albida              | Fabaceae          | Haraz                                            | Tree   | Leaves        | South Sudan        | [42]      |
| Ficus glumosa Delile           | Moraceae          | Muwo (Luganda)                                   | Shrub  | Stem bark     | Uganda              | [7]       |
| Ficus natalensis              | Moraceae          | Omutubu (Luganda), Mugaire (Lusoga)              | Tree   | Stem bark     | Uganda              | [7]       |
| Ficus platypylla              | Moraceae          | Mudodwe                                          | Shrub  | Stem bark     | Uganda              | [10]      |
| Ficus saussureana             | Moraceae          | Omuwo (Luganda)                                  | Shrub  | Stem bark     | Uganda              | [8]       |
| Fleurya aestuans              | Urticaceae        | Munyango (Luganda)                               | Herb   | Leaves        | Uganda              | [7]       |
| Botanical name                  | Family              | Local Names                  | Habit     | Part used                  | Country                  | Author(s) |
|--------------------------------|---------------------|------------------------------|-----------|---------------------------|--------------------------|-----------|
| Garcinia buchananii Baker      | Clusiaceae          | Musaali (Luganda)            | Tree      | Stem bark, Root bark      | Uganda, Kenya, Tanzania  | [7, 10, 12]|
| Gnaphalium purpureum L.        | Asteraceae          | Omuya (Luganda)              | Herb      | Leaves                    | Uganda                   | [7]       |
| Gridia buchananii Gilg         | Thymelaeaceae       | Not reported                 | Herb      | Roots                     | Kenya                    | [49]      |
| Gomphocarpus physocarpus E. Mey.| Apocynaceae         | Gashaho                      | Herb      | Leaves                    | Uganda                   | [10]      |
| Guttenbergia cordifolia Benth. ex Oliv. | Aste     | Eloutapem                    | Herb      | Roots, Leaves             | Uganda                   | [10]      |
| Harrisonia abyssinica          | Simaroubaceae       | Mutagataga (Meru), Osito (Luo), Orongoriwe (Kuria), Lushaike | Shrub      | Stem bark                 | Uganda, Kenya            | [10, 50, 51]|
| Harungana madagascariensis Lam.ex Pior | Hypericaceae | Mukabiransiko (Luganda)      | Tree      | Stem bark, Leaves         | Uganda                   | [8]       |
| Helichrysum odoratissimum (L.) | Asteraceae          | Lweza (luganda)              | Herb      | Leaves                    | Uganda                   | [10]      |
| Heterotis canescens            | Melastomataceae     | Usmusomawa’-bungere,         | Herb      | Leaves                    | Burundi                  | [38]      |
| Hibiscus fusca Garcke          | Malvaceae           | Lusaala (Luganda)            | Herb      | Leaves                    | Uganda                   | [7]       |
| Hoslundia opposita Vahl        | Lamiaceae           | Cherononit, Cherungut (Nandi), Nfodo (Lusoga) | Shrub      | Leaves, Uganda            | Kenya                    | [10, 31]  |
| Hypericum revolutum Vahl       | Clusiaceae          | Mushungwa                    | Tree      | Leaves                    | Uganda                   | [10]      |
| Hypoestes verticillaris (L.) Sol. | Acanthaceae        | Narubat (Ogiek)              | Herb      | Roots                     | Kenya                    | [46]      |
| Iboza multiflora (Benth.) E. A. Bruce | Lamiaceae  | Iseja                        | Shrub      | Leaves                    | Uganda                   | [10]      |
| Iboza riparia (Hoehst.) N. E. Br. | Lamiaceae          | Muravumba                    | Shrub      | Leaves                    | Uganda                   | [10]      |
| Indigofera emarginella Steud. ex A. Rich. | Fabaceae    | Olutunga msonzi (Luganda)    | Shrub      | Leaves, Stem bark         | Uganda                   | [7]       |
| Indigofera lupatana Baker F    | Fabaceae            | Not reported                 | Shrub      | Roots                     | Kenya                    | [28]      |
| Kalanchoe gaucescens Planch. ex Benth. | Crassulaceae   | Ekyondo ekyeru (Luganda)     | Herb      | Leaves                    | Uganda                   | [7, 9]    |
| Kalanchoe integrar             | Crassulaceae       | Not reported                 | Shrub      | Leaves                    | Rwanda                   | [48]      |
| Khaya senegalensis             | Meliaceae           | Not reported                 | Tree       | Leaves, Stem bark         | South Sudan              | [52]      |
| Lagenaria sphaerica (Sond.) Naudin | Cucurbitaceae    | Mutanga                      | Herb      | Leaves                    | Uganda                   | [10]      |
| Lantana camara L.              | Verbenaceae         | Kayukiyuki (Luganda), Owinyiblo (Lango), Kanpanga (Ateso) | Shrub      | Leaves                    | Uganda                   | [7, 10, 53]|
| Lantana trifolia               | Verbenaceae         | Not reported                 | Shrub      | Leaves                    | Rwanda                   | [48]      |
| Leonotis nepenthila (L.) R. Br. | Lamiaceae           | Susunig                      | Shrub      | Leaves                    | Uganda                   | [10]      |
| Leucas calostachys Oliv.       | Lamiaceae           | Kakuba musulo (Luganda)      | Shrub      | Leaves, Whole plant       | Uganda                   | [8]       |
| Lippia grandifolia Hochst. ex A. Rich. | Verbenaceae | Olugumaguma (Luganda)        | Herb      | Leaves                    | Uganda                   | [7]       |
| Lonchocarpus eriocalyx Harms   | Fabaceae            | Not reported                 | Tree       | Stem bark                 | Kenya                    | [11, 28]  |
| Maesa lanceolata Forsk.         | Myrsinaceae         | Muhanga                      | Tree       | Roots                     | Uganda                   | [10]      |
| Mangifera indica L.            | Anacardiaceae       | Muyembe (Luganda), Aeme (Lango) | Tree       | Stem bark                 | Uganda, Kenya            | [7, 9, 10, 12, 47]|
| Maytenus senegalensis          | Celastraceae        | Naligwallimu (Luganda), Muwaiswa, Eterka, Ite reka | Shrub      | Root bark                 | Uganda                   | [7, 10]   |
| Botanical name                                      | Family           | Local Names                                     | Habit | Part used      | Country         | Author(s) |
|----------------------------------------------------|------------------|-------------------------------------------------|-------|----------------|-----------------|-----------|
| Microglossa pyrifolia (Lam.)                       | Asteraceae       | Kabilli akatono (Luganda)                       | Shrub | Roots          | Uganda          | [10]      |
| Microgramma lycopodioides (L.) Copel              | Polypodiaceae    | Kukumba (Luganda)                              | Herb  | Roots, Leaves  | Uganda          | [8]       |
| Milicia excelsa (Welw.) C.C. Berg                 | Moraceae         | Muvule (Luganda)                               | Tree   | Leaves         | Uganda          | [7]       |
| Momordica foetida Schumach.                       | Cucurbitaceae    | Bombo (Luganda), Luiwula/Mwishwa               | Herb  | Leaves         | Uganda, Rwanda  | [7, 10, 45]|
| Momordica rostrata A. Zimm.                       | Cucurbitaceae    | Chepkologolio (Ogiek)                          | Herb  | Roots          | Kenya           | [46]      |
| Morella kandtiana (Engl.) Verdc. & Polhill        | Myricaceae       | Mukikimbo (Luganda)                            | Herb  | Roots, Leaves, Whole plant | Uganda          | [8]       |
| Morinda lucida Benth.                             | Rubiaceae        | Kabaja nsayi (Luganda)                         | Tree   | Stem bark      | Uganda          | [7]       |
| Moringa oleifera Lam.                             | Moringaceae      | Moringa (Luganda)                              | Tree   | Fruit, Stem    | Uganda          | [7, 10]   |
| Mucuna pruriens (L.) DC.                          | Papilionaceae    | Lugenyu (Luganda)                              | Vine   | Leaves         | Uganda          | [10]      |
| Myrica kandtiana Engl.                            | Myricaceae       | Enkikimbo (Luganda)                            | Tree   | Fruit, Leaves, Stem bark, Root bark | Uganda          | [7]       |
| Mynine africana L.                                | Myrsinaceae      | Seketeti (Samburu)                             | Shrub  | Not reported   | Kenya           | [34]      |
| Nauclea latifolia Sm                              | Rubiaceae        | Karmadoda                                      | Tree   | Fruit          | South Sudan     | [54]      |
| Ocimum basilicum                                  | Lamiaceae        | Ususurra                                      | Herb   | Leaves         | Burundi         | [38]      |
| Ocimum suave Willd.                               | Lamiaceae        | Muhumuzanganda (Luganda)                       | Herb   | Leaves         | Uganda          | [10]      |
| Olea capensis L.                                  | Oleaceae         | Pekeriondet (Sabaot)                           | Tree   | Stem bark      | Kenya           | [36]      |
| Olinia rochetiana                                 | Penaeaceae       | Kaptolongit (Sabaot)                           | Tree   | Roots          | Kenya           | [36]      |
| Ornecarpum trichocarpum (Taub.) Harms             | Papilionaceae    | Eseperuea                                      | Tree   | Roots          | Uganda          | [10]      |
| Pappea capensis (Spreng) Eckl. & Zeyh.            | Sapindaceae      | Muba (Kikuyu), Enkorirri, Oltimigomi (Maasai)  | Shrub  | Stem bark, Root bark | Kenya           | [55, 56] |
| Panire curatellifolia Planch. ex Benth.           | Chrysobalanaceae | Umunazi                                        | Tree   | Stem bark, roots | Burundi         | [38]      |
| Pavetta crassipes K. Schum.                       | Rubiaceae        | Not reported                                   | Shrub  | Roots          | Tanzania, Kenya | [12]      |
| Pentas longiflora Oliv.                           | Rubiaceae        | Isagara                                        | Herb   | Roots          | Rwanda          | [37]      |
| Persea americana Mill.                            | Lauraceae        | Ovacado (Luganda)                              | Tree   | Stem bark      | Uganda          | [7, 9]    |
| Phaseolus lunatus L.                              | Fabaceae         | Kayindiyindi (Luganda)                         | Herb   | Leaves         | Uganda          | [7]       |
| Phaseolus vulgaris L.                             | Fabaceae         | Bijanjaro (Luganda)                            | Herb   | Husks          | Uganda          | [7]       |
| Phyllanthus reticulatus Poir.                     | Phyllanthaceae   | Mutulika (Luganda)                             | Shrub  | Leaves         | Uganda          | [7]       |
| Pilostigma thomningii                             | Fabaceae         | Chebutiandet (Sabaot)                          | Tree   | Leaves         | Kenya           | [36]      |
| Piptadeniustrum africana                          | Fabaceae         | Mpewere (Luganda)                              | Tree   | Stem bark      | Uganda          | [7, 9, 10]|
|PECTRANTHUS BARBATUS Andrews                       | Lamiaceae        | Ekibankulata (Luganda), Ebiriririmutano (Ateso) | Shrub  | Leaves         | Uganda          | [7, 10]   |
| PLECTRANTHUS HADIENSIS                            | Lamiaceae        | Kibwankulanta (Luganda)                        | Shrub  | Whole plant, Leaves | Uganda          | [8]       |
| Plumbago dawei                                    | Plumbaginaceae   | Lkiarianthus (Samburu)                         | Herb   | Stem bark      | Kenya           | [29]      |
| Plumbago zeylanica L.                             | Plumbaginaceae   | Musaijabanda (Luganda), Mukya (Kamba)          | Herb   | Leaves         | Uganda, Kenya   | [7, 34, 57]|
| Podocarpus usambarensis Plbg.                     | Podocarpaceae    | Kamusenene (Luganda)                           | Tree   | Leaves         | Uganda          | [7]       |
| Prunus africana (Hookf) Kalkman                   | Rosaceae         | Ntaseesa, Ngwabuzito (Luganda, Rutoro),Sirumandu (Lugisu) | Tree   | Stem bark      | Uganda          | [7]       |
Table 1 Medicinal plants used in treatment of symptoms of TB in East Africa (Continued)

| Botanical name                      | Family               | Local Names          | Habit     | Part used                  | Country            | Author(s) |
|-------------------------------------|----------------------|----------------------|-----------|----------------------------|--------------------|-----------|
| *Pseudospondia microcarpa* (A. Rich.) Engl. | Anacardiaceae         | Muziru (Luganda)     | Tree      | Stem bark                  | Uganda             | [7]       |
| *Psidium guajava* L.                | Myrtaceae            | Mpera (Chagga)       | Tree      | Fruit, Leaves, Stem bark, Root bark | Uganda, Kenya, | [7, 12]  |
| *Pycnostachys ericifolia* Reh.      | Lamiaceae            | Musindikwa (Luganda) | Shrub     | Leaves                    | Uganda             | [10]      |
| *Rhamnus prinoides* L’Herit.        | Rhamnaceae           | Munanira (Luganda)   | Shrub     | Leaves                    | Uganda             | [10]      |
| *Rhoicissus tridentata* (L.) Wild. & R.B.D. Drumm. | Vitaceae             | Mumara (Luganda)     | Shrub     | Leaves                    | Uganda             | [10]      |
| *Rhus natalensis* Bernh. ex Krauss  | Anacardiaceae         | Lmisigiyoi, Muthigiu (Kikuyu) | Tree      | Roots, Leaves             | Kenya              | [51]      |
| *Rhus vulgaris* Meikle              | Anacardiaceae         | Kakwansokwanso (Luganda) | Herb     | Stem bark                  | Uganda             | [7]       |
| *Ribes uva-crispa* L.               | Grossulariaceae       | Entuntunu (Luganda)  | Shrub     | Leaves                    | Uganda             | [7]       |
| *Rosmarinus officinalis* L.         | Lamiaceae            | Not reported         | Herb      | Leaves                    | South Sudan        | [52]      |
| *Rubia cordifolia* L.               | Rubiaceae            | Kasalabakesi (Luganda) Urumunwa (Kuria) | Tree     | Leaves, Whole plant | Uganda, Kenya, Tanzania | [7, 9, 10, 12, 16] |
| *Rumex abyssinicus* Jacq.           | Polygonaceae          | Not reported         | Herb      | Leaves                    | Rwanda             | [48]      |
| *Sapium ellipticum* (Hoehst.) Pax   | Euphorbiaceae         | Omusasa (Luganda)    | Shrub     | Stem bark                  | Uganda             | [7]       |
| *Securidaca longipedunculata* Fresen. | Polygalaceae         | Mukondwa, Awee illa (Lango), Mukondwa (Lusoga), Ellici (Ateso) | Tree     | Roots                       | Uganda             | [8, 10]  |
| *Senna siamea* (Lam.) Irwin & Barneby | Fabaceae             | Gasiya seed          | Tree      | Stem bark                  | Uganda             | [10]      |
| *Sesamum calycinum* Pedaliaceae    | Pedaliaceae          | Lutungotungo (Luganda) | Herb     | Leaves, Whole plant | Uganda             | [8]       |
| *Solamnum aculeastrum* Dunal        | Solanaceae           | Mutura (Kikuyu), Ekitengo (Luganda) | Shrub     | Fruit, Roots, Leaves      | Uganda, Kenya     | [7, 8, 12] |
| *Solamnum incanum* L.              | Solanaceae           | Entengotengo Ennene (Luganda), Ocokocok (Lango), Ntonka (Lusoga), Mutongu (Kamba),Entulelei (Maasai) | Shrub     | Fruit                       | Uganda, Kenya     | [7, 12]  |
| *Solamnum mauense* Bitter           | Solanaceae           | Ng’onyyoyiek (Ogiek) | Shrub     | Seeds                      | Kenya              | [46]      |
| *Spathodea campanulata* P. Beauv.   | Bignoniaceae         | Kifabakazi (Luganda) | Tree      | Stem bark                  | Uganda             | [7]       |
| *Syzygium cumini* (L.) Skeels       | Myrtaceae            | Jambula (Luganda)    | Tree      | Stem bark                  | Uganda             | [7, 9]    |
| *Tamarindus indica* L.              | Fabaceae             | Mukogete (Luganda), Cwao (Lango) | Tree      | Leaves                     | Uganda             | [10]      |
| *Teclia nobilis* Del.               | Rutaceae             | Luzo                 | Shrub     | Leaves                     | Uganda             | [10]      |
| *Tetradenia riparia* (Hoehst.) Codd | Lamiaceae            | Ekyewamala (Luganda) | Herb     | Leaves                     | Uganda, Rwanda     | [7, 37]  |
| *Terminalia laxiflora* Engl. & Diels | Combretaceae         | Darout               | Tree      | Stem bark                  | South Sudan        | [30]      |
| *Tithonia diversifolia* (Hems.) A. Gray | Asteraceae          | Ekimyula, Okelokelo (Lango) | Shrub     | Stem bark                  | Uganda             | [7]       |
| *Toddalia asiatica* (L.) Lam       | Rutaceae             | Simborichet (Sabact), Mururue (Kikuyu), Oleppamunyo (Maasai), Kawule (Luganda) | Shrub     | Roots, Leaves              | Uganda, Kenya     | [7, 8, 10, 36] |
| *Tragia brevipes* Pax               | Euphorbiaceae        | Nakeapian            | Climber   | Roots                      | Uganda             | [10]      |
| *Tragia subsessilis* Pax            | Euphorbiaceae        | Totoananyia         | Herb      | Roots                      | Uganda             | [10]      |
| *Trichilia dregeana* Sond.          | Meliaceae            | Sekoba (Luganda)     | Tree      | Stem bark                  | Uganda             | [7]       |
pathways that produce majorly flavonoids, terpenoids, and alkaloids as secondary metabolites [73–75]. It is these phytochemicals that are responsible for the antimycobacterial activity against different mycobacterial strains [67, 70, 76, 77]. Other families reported in East Africa to house medicinal plants for management of TB and have also been reported in other countries in clude Acanthaceae, Apocynaceae, Cariaceae, Combretaceae, Malvaceae, Moraceae, Myrtaeae, Rhamnaceae, Rubiaceae, Solanaceae, and Zingiberaceae [64, 72, 78–81].

Geographically, none of the documented plant species was reported to be used in the management of TB across all the East African countries. However, two plant species (Erythrina abyssinica and Eucalyptus species) are used by at least 4 countries. A total of 30 plant species were reported to be used by at least two countries. Uganda had the highest number of species mentioned followed by Kenya and then Tanzania (Table 1). The differences in species utilization could be attributed to the differences in soil chemistry, rainfall, topography, and climate that results into differences in phytochemical composition of the same species growing in different geographical areas [82]. Additionally, it could also be due to differences in knowledge and experiences as result of different social and cultural backgrounds that exists across the countries. Uganda had many ethnobotanical surveys conducted to document medicinal plants used in the management of tuberculosis as compared to other countries. Most of these medicinal plants were growing as trees (40.0%), herbs (29.7%), shrubs (27.7%), and rarely as climbers, vines, or lianas (Fig. 3).

Analysis of ethnomedicinal recipes revealed that mainly leaves (38.6%), stem bark (28.4%), and roots (18.6%) were used for preparing herbal remedies. Root bark, whole plants, fruits, flowers, seeds, and husks were rarely used (Fig. 4). Harvesting of leaves and stem bark allows sustainable utilization of the plants hence promoting their conservation as opposed to use of roots and whole plants. Additionally, leaves are the primary sites for secondary metabolic pathways in plants while stem barks act as major concentration areas (deposition sites) for the synthesized metabolites [9, 57].

Most articles reviewed reported that traditional herbal medicine practitioners usually combined different plant species while preparing herbal medicines. However, they did not report how the herbal medicine from individual plant species can be prepared. Decoction was by far the commonest method of herbal medicine preparation cited. Others included cold infusions, drying and pounding into a powder, burning into ash, chewing, and steaming. Use of more than one plant in combination is more effective than single plant perhaps due to the synergistic interactions that occur among the different phytochemicals that result into increased bioactivity (efficacy). But also, the benefit of phytochemicals from

| Botanical name | Family | Local Names | Habit | Part used | Country | Author(s) |
|---------------|--------|-------------|-------|-----------|---------|-----------|
| *Triumfetta flavescens* Hochst. ex A. Rich. | Malvaceae | Luwugula (Luganda) | Shrub | Stem | Uganda | [7] |
| *Vachellia drepanolobium* (Harms ex Sjostedt) P.J.H. Huter | Fabaceae | Oluai (Maasai) | Tree | Stem bark, Root bark | Kenya | [55] |
| *Vernonia cinerea* (L.) Less. | Asteraceae | Kayayana, Lukohe (Luganda), Yat Kwong (Lango) | Herb | Leaves | Uganda | [7] |
| *Vernonia amygdalina* Del. | Asteraceae | Mululuzu (Luganda) Lubilli | Shrub | Leaves | Uganda | [7, 10] |
| *Warburgia ugandensis* Sprague | Canellaceae | Abaki, Sokoni (Samburu), Muthiga (Kikuyu) | Tree | Stem bark | Uganda, Kenya, Tanzania | [7–10, 12, 57–59] |
| *Zanthoxylum chalybeum* Engl. | Rutaceae | Ntale ya ddungu (Luganda), Eusuk (Ateso), Agodaman (Lango), Öloisuki (Maasai), Rukuts (Karimojong), Outiku (Lugbara) | Tree | Stem bark | Uganda, Kenya, Tanzania | [5, 8–10, 12] |
| *Zanthoxylum gillettii* (De Wild.) P.G. Waterman | Rutaceae | Sagawatiet, Shihumba/Shikuma | Tree | Stem bark | Kenya | [31] |
| *Zanthoxylum leprieurii* | Rutaceae | Not reported | Tree | Stem bark | Uganda | [5] |
| *Zehneria scabra* | Cucurbitaceae | Umushishiro, | Herb | Leaves | Burundi | [38] |
| *Zingiber officinale* | Zingiberaceae | Tangawizi (Luo), Ntangawuzi (Luganda) | Herb | Stem | Uganda, Kenya | [7, 9, 10, 12] |

Languages: Ateso, Lango, Luganda, Lugbara, Lugisu, Lusoga, Karimojong, and Rutoro (Uganda); Digo, Kamba, Kikuyu, Kisii, Kuria, Luo, Maasai, Meru, Nandi, Ogiek, Sabaot, Samburu, and Wangi (Kenya); and Chagga (Tanzania). Local names with language(s) not indicated were not specified by the authors.
one species counteracting the toxicity of another species could be another explanation.

The major route of administration was oral (via the mouth) although sometimes inhalation and topical application were also reported depending on the preparation method used and the toxicity of the plant(s). Cups, bottles, and tablespoons were the most commonly used for determining the posology of herbal remedies [7, 10, 12].

**Efficacy and safety studies**

Some ethnobotanical studies reported that herbal medicine preparations were effective in the treatment of TB, while some were used in the management of multidrug-resistant tuberculosis [7, 12, 47]. This could be due to the synergistic interaction between the various phytochemicals present in the herbal preparations [27, 83]. However, as much as these herbal medicines might have genuine bioactivity, sometimes they are used concurrently with conventional therapies as supplements and at times adulterated. Therefore, it is important to scientifically validate the claimed efficacy and safety of both the herbal preparations and the individual medicinal plants. Out of the 195 species documented, only 36 plant species (18.5%) have been studied for their antimycobacterial activity. A WHO report [14] indicated that only approximately 10% of the world’s flora have been studied as regards their medicinal potential. This has greatly hindered the discovery of potential lead compounds that could be developed into new antitubercular drugs.
Fig. 2  The most cited plant species used for treatment of TB and its symptoms in East Africa.

Fig. 3  Growth habit of the plants used for preparation of antitubercular remedies in East Africa.
Out of the 36 screened medicinal plants, 31 species (86.1%) were reported to be bioactive with some species exhibiting quite considerable antimycobacterial activity although the current standard drugs had superior bioactivity (Table 2). This is comparable to India where 70% of 365 plants which were studied showed antimycobacterial activity [87]. Among the promising plant species (with minimum inhibitory concentration less than 0.5 mg/ml) were *Erythrina abyssinica*, *Entada abyssinica*, *Bidens pilosa*, *Callistemon citrinus*, *Khaya senegalensis*, *Lantana camara*, *Piptadenistrum africana*, *Rosmarinus officinalis*, *Tetradenia riparia*, and *Zanthoxylum leprieurii*. Isolated pure compounds from three of the promising plant species had much higher activity against Mtb than the crude extracts and fractions. Indeed, some of the compounds from *Zanthoxylum leprieurii* had minimum inhibitory concentrations lower than those of standard antitubercular drugs (Table 3). Crude extracts and fractions usually have less pharmacological activity than standard drugs because of the interference from other inactive substances in the matrix that reduce the overall concentration of the active molecules in the tested dose. This explains why isolation of pure compounds is a critical step in natural product drug discovery process. The five documented medicinal plants that were found to be inactive are *Acacia ataxacantha*, *Dalbergia melanoxylon*, *Indigofera lapatana*, *Lonchocarpus eriocalyx*, and *Solanum incanum*. This could probably be attributed to the absence of inherent bioactive phytochemicals against Mtb in the plant species. This could be brought about by absence or impaired biosynthetic metabolic pathways due to unfavorable growth conditions in the habitat from where the plants grow. This implies that herbal remedies for TB containing each of these plants singly may not be effective. Therefore, other benefits provided by these species in the concoctions of TB such as detoxification of other toxic phytochemicals, preservation of the herbal medicine, or potentiation of the pharmacological activity of other phytochemicals could be investigated.

All toxicity studies reviewed evaluated only the acute toxicity profiles of the medicinal plants either in vitro or in vivo but not both. Of the bioactive extracts screened, less than half of them were tested for their acute toxicity. Selectivity index (SI) is used as the best estimate of the relative toxicity of a compound to normal mammalian cells as compared to the pathogen and hence its suitability for being a drug candidate. According to the SI criterion, compounds with higher SI are regarded to have better toxicity profiles than those with lower SI [88]. From the retrieved data, only two plant species (*Khaya senegalensis* and *Rosmarinus officinalis*) had acceptable selectivity indices to warrant drug discovery from them.

In this study, the SI of only five plant species could be
| Plant                  | Extraction method (solvent) | MIC (μg/ml) on H37Rv strain | MIC (μg/ml) on TMC-331 strain | Toxicity of crude extracts (μg/ml) | Class of compounds                                                                 | Author(s) |
|-----------------------|----------------------------|-----------------------------|------------------------------|-----------------------------------|-----------------------------------------------------------------------------------|-----------|
| Acacia ataxacantha    | Maceration (methanol)      | Not active                  | Not tested                   | IC_{50} = 90.39                  | Phenols, terpenoids                                                              | [28]      |
| Acacia horrida        | Soxhlet (methanol)         | < 1000 (Iso < 500)          | Not tested                   | Not tested                        | Alkaloids, cardiac glycosides, tannins, saponins, terpenoids                      | [29]      |
| Acacia senegal        | Soxhlet (methanol)         | < 1000 (Iso < 500)          | Not tested                   | Not tested                        | Cardiac glycosides, tannins, saponins, terpenoids, flavonoids                    | [29]      |
| Acokanthera friesiorum| Soxhlet (methanol)         | Not tested                  | Not tested                   | Not tested                        | Cardiac glycosides, tannins, saponins, terpenoids, flavonoids                    | [29]      |
| Albizia anthelmitica  | Maceration (methanol)      | Active at 1 g/ml (MIC not determined) | Not tested                   | IC_{50} = 24.51                  | Phenol, terpenoids, flavonoids, saponins                                         | [28]      |
| Bidens pilosa         | Maceration (ethanol)       | 100                         | Not tested                   | Not tested                        | Not tested                                                                        | [37]      |
| Callistemon citrinus  | Maceration (methanol, chloroform) | 325 (methanol), 48 (chloroform) (Iso = 4.0; R = 2.0) | 78 (methanol), 158 (chloroform), Iso = 4.0 | Not tested                        | Flavonoids, alkaloids, triterpenoids, saponins                                    | [15]      |
| Cissampelos pareira   | Maceration (methanol)      | Active at 1 g/ml (MIC not determined) | Not tested                   | IC_{50} = 179                    | Anthraquinones, phenols, terpenoids, flavonoids                                  | [28]      |
| Commiphora edulis     | Maceration (ethanol acetate, DCM, water) | 6250 (Ethyl acetate), 780 (methanol), Not active (water) | Not tested                   | IC_{50} = 393 (DCM), 1734 (ethyl acetate) | Flavonoids, terpenoids                                                             | [26]      |
| Commiphora ellenbeckii| Maceration (ethyl acetate, methanol, water) | 12500 (Ethyl acetate), 3125 (methanol), 780 (water), 15 (Rif) | Not tested                   | IC_{50} = 608 (methanol), 1509 (water) | Alkaloids, saponins, tannins, phenols, flavonoids, terpenoids                    | [26]      |
| Commiphora mildbraedii| Maceration (ethyl acetate, methanol, water) | 6250–9250 (Ethyl acetate), 390–780 (methanol), not active (water), 15 (Rif) | Not tested                   | IC_{50} = 339 (ethyl acetate), 452 (methanol) | Alkaloids, saponins, tannins, phenols, flavonoids, terpenoids                    | [26]      |
| Cordia sinensis       | Soxhlet (methanol)         | < 500 (Iso < 500)           | Not tested                   | Not tested                        | Saponins, flavonoids, terpenoids, tannins                                         | [29]      |
| Cryptolepis sanguinolenta| Methanol chloroform       | 1170 (methanol) (Iso = 0.25; R = 0.25) | 1580 (methanol) (Iso = 0.25) | LD_{50} = 758 mg/kg | Alkaloids, tannins, flavonoids                                                   | [84]      |
| Dalbergia melanoxylon | Maceration (methanol)      | Not active                  | Not tested                   | IC_{50} = 120.04                  | Phenols, terpenoids                                                              | [28]      |
| Dichrostachys cinerea | Maceration (methanol)      | Active at 1 g/ml (MIC not determined) | Not tested                   | IC_{50} = 201.22                  | Phenols, terpenoids                                                              | [28]      |
| Entada abyssinica     | Maceration (methanol)      | 500 (Iso = 0.25)            | Not tested                   | Not tested                        | Flavonoid, alkaloids, saponins, tannins                                         | [12, 29] |
| Erythrina abyssinica  | Maceration (methanol)      | 390 (Rif = 0.25; Iso = 0.25) | 2350 (Iso = 9.38) | LD_{50} = 7762 mg/kg | Flavonoids, alkaloids, tannins                                                   | [44]      |
| Euphorbia ingens      | Maceration (methanol)      | Active at 1 g/ml (MIC not determined) | Not tested                   | IC_{50} = 105.55                  | Phenols, terpenoids                                                              | [28]      |
| Euphorbia scarlatica  | Soxhlet (methanol)         | < 500 (Iso < 500)           | Not tested                   | Not tested                        | Alkaloids, cardiac glycosides, terpenoids, flavonoids                            | [29]      |
| Gnidia buchananii     | Maceration (methanol)      | Active at 1 g/ml (MIC not determined) | Not tested                   | IC_{50} = 76.24                  | Phenols, terpenoids                                                              | [28]      |
| Indigofera lupatana   | Maceration (methanol)      | Not active                  | Not tested                   | IC_{50} = 60.37                   | Phenols, terpenoids                                                              | [28]      |
| Khaya senegalensis    | Maceration (ethyl acetate, chloroform) | 6.25 | Not tested | IC_{50} = 1000 | Not tested | Alkaloids, cardiac glycosides, terpenoids, flavonoids | [52] |
calculated (Table 4) because they were the only plant species with both the inhibitory concentration on Mtb and cytotoxic concentration on normal mammalian cell lines (IC\textsubscript{50}) reported. Hence, there is need to emphasize dual testing of both toxicity and efficacy of natural products for drug development purposes.

Two other systems of acute toxicity classification: The National Cancer Institute (NCI) and Organization for Economic cooperation and development (OECD) guidelines 423 were used to assess the toxicity profiles of the different extracts [89, 90]. There was no single plant species among those tested for acute toxicity that was reported to be highly toxic (with IC\textsubscript{50} less than 20 \(\mu\)g/ml). All the plant species with promising bioactivity that were tested for toxicity had acceptable acute toxicity profiles. These included *Rosmarinus officinalis*, *Lantana camara*, *Khaya senegalensis*, and *Erythrina abyssinica* (Table 2).

| Plant                  | Extractation method (solvent) | MIC (\(\mu\)g/ml) on H37Rv strain | MIC (\(\mu\)g/ml) on TMC-331 strain | Toxicity of crude extracts (\(\mu\)g/ml) | Class of compounds | Author(s) |
|------------------------|-------------------------------|-----------------------------------|-----------------------------------|------------------------------------------|--------------------|-----------|
| Lantana camara         | Maceration (methanol, chloroform) | 20 (Rif = 1)                       | 15 (Iso = 0.25)                  | LD\textsubscript{50} > 500 mg/kg         | Not reported       | [53]      |
| Lonchocarpus eniocalyx | Maceration (methanol)          | Not active                         | Not tested                        | IC\textsubscript{50} = 201.87            | Terpenoids, phenols, flavonoids | [28]      |
| Loranthus acaciae      | Soxhlet (methanol)             | < 1000 (Iso < 500)                 | Not tested                        | Not tested                               | Alkaloids, cardiac glycosides, saponins, flavonoids | [29]      |
| Mangifera indica       | Methanol                       | 3130 (methanol) (Iso = 0.25; R = 0.25) | 590 (methanol) (Iso = 0.25)       | Not tested                               | Phenols, terpenoids | [16]      |
| Pentos longiflora      | Maceration (ethanol)           | 1000                               | Not tested                        | Not tested                               | Not tested         | [37]      |
| Piptadenistrom africana| Maceration (chloroform)        | 395 (chloroform)                   | 395 (chloroform)                  | Not tested                               | Flavonoids, tannins | [15]      |
| Plumbago dawei         | Soxhlet (methanol)             | < 1000 (Iso < 500)                 | Not tested                        | Not tested                               | Cardiac glycosides, tannins, terpenoids, flavonoids | [29]      |
| Rosmarinus officinalis | Maceration (chloroform)        | 6.25                               | Not tested                        | IC\textsubscript{50} = 100               | Not tested         | [52]      |
| Salvadora persica      | Soxhlet (methanol)             | < 500 (Iso < 500)                  | Not tested                        | Not tested                               | Alkaloids, cardiac glycosides, terpenoids, flavonoids | [29]      |
| Solanum incanum        | Methanol chloroform            | Not active                         | Not active                        | Not tested                               | Not tested         | [16]      |
| Tetradenia riparia     | Maceration (ethanol)           | 500                                | Not tested                        | Not tested                               | Not tested         | [37]      |
| Warburgia ugamensis    | Methanol chloroform            | 4690 (methanol), 2350 (chloroform) (Iso = 0.25; R = 0.25) | 2350 (methanol), 590 (chloroform) (Iso = 0.25) | Not tested                               | Flavonoids, tannins, terpenoids | [85, 86] |
| Zanthoxyllum leprieurii| Methanol                       | 47.5 (Iso = 4.0; R = 2.0)           | 75.3 (Iso = 4.0)                  | Not tested                               | Alkaloids          | [5]       |

IC\textsubscript{50} median cytotoxic concentration, LD\textsubscript{50} median lethal dose, Iso isoniazid, Rif rifampicin, H37Rv pan sensitive Mtb strain, TMC331 rifampicin-resistant Mtb strain, MIC minimum inhibitory concentration. Extracts in [26] were tested against *Mycobacteria smegmatis*.

### Table 3 Isolation and characterization studies on medicinal plants used for management of TB in East Africa

| Plant                  | Pure compounds with antitubercular activity | Chemical class | MIC of pure compounds (\(\mu\)g/ml) | Author(s) |
|------------------------|---------------------------------------------|----------------|------------------------------------|-----------|
| Zanthoxyllum leprieurii| 2-hydroxy-1, 3-dimethoxy-10-methyl-9-acridone (1), 1-hydroxy-3-methoxy-10-methyl-9-acridone (2), 3-hydroxy-1, 5, 6-trimethoxy-9-acridone (3) | Acridone alkaloids | 1.5 (1), 0.2 (2), 0.4 (3); tested against H37Rv | [5]       |
| Warburgia ugamensis    | Muzigadial (4), muzigadiolide (5), linoleic acid (6) | Sesquiterpenes | 64 (4), 128 (5), 16 (6); tested against *M. smegmatis* | [58, 85] |
| Tetradenia riparia     | 15- santaracopimaradiene-7a, 18-dio1 (7)      | Diterpenediol  | 25–100                             | [37]      |

MIC minimum inhibitory concentration. No toxicity studies of the pure compounds were conducted.
guidelines, Lantana camara, Erythrina abyssinica, and Cryptolepis sanguinolenta had slight toxicity as their median lethal doses (LD₅₀) were above 500 mg/kg. These results justify the general public belief that traditional medicines are relatively safer as compared to the current conventional therapies. However, toxicity testing should be done on all potential medicinal plants and their phytochemicals before concluding that they are safe for human treatment [91–94]. This is because toxicity of herbal medicines may be due to presence of inherent poisonous chemicals in the plant species, misidentification of the plant species, adulteration or contamination during harvesting, preparation, and storage [95, 96]. Acute toxicity tests determine a single high dose that kills 50% of the cells or animals in a population. They may not be evident enough to depict the real toxicity situation for herbal remedies taken for a longer time in chronic conditions like TB [18, 97]. Therefore, this may necessitate sub-chronic and chronic toxicity tests to be carried out on a medicinal plant species with a potential lead compound [95].

**Phytochemistry of the reported plants**

Phytochemical investigation reveals the chemical nature of the pure compounds that are responsible for the pharmacological activity as well as the toxicity of medicinal plants [19, 64, 98–101]. Chromatographic and spectroscopic techniques are used to identify and elucidate the chemical structures of compounds [102–107]. In this study, maceration was the commonly used method of extraction as compared to Soxhlet. Majority of the hexane extracts were reported to be inactive against mycobacterial strains while almost all methanolic extracts were active. Methanol being a polar solvent extracts polar phytochemical while hexane (a non-polar solvent) extracts non-polar compounds. It is reasonable to assert that the antimycobacterial activity of the extracts is largely due to polar phytochemicals. There were variations in bioactivity of different parts of the same plant with no specific patterns. This could be due to differences in their rate of accumulating the bioactive substances.

The phytochemicals that were frequently screened for have been alkaloids, saponins, cardiac glycosides, flavonoids, terpenoids, and phenols. All these secondary metabolites were reported to be present in different bioactive extracts. The most commonly reported phytochemicals were flavonoids, terpenoids, and alkaloids [15, 17, 26, 29, 70, 106, 108]. Flavonoids and alkaloids were reported to be absent in three out of the five inactive plants (Table 2). Out of the 31 bioactive plant species, only three (Tetradenia riparia, Warburgia ugandensis, and Zanthoxylum leprieurii) have been further characterized to identify the pure compounds responsible for their antimycobacterial activity [5, 37, 58, 85] (Table 3). This is attributed to the complexity and the rigorous nature of the process that require extraction, screening, isolation, and characterization [100, 109, 110]. Low extraction yield, compound instability, high costs, low technology especially in developing countries, limited access to advanced chromatographic, and spectroscopic equipment and inadequate funding have made it difficult to undertake herbal medicine research [21, 111, 112]. This is further complicated by the microbiological nature of the Mtb that require bioassays to be conducted in biosafety level 3 laboratories that are not readily available in East Africa [60, 113]. More robust and effective techniques are required to fasten the drug discovery process against TB [3, 77, 92, 114].

A total of seven pure compounds have been isolated and characterized with bioactivity against Mtb (Fig. 5). These are 2-hydroxy-1,3-dimethoxy-10-methyl-9-acridone (1), 1-hydroxy-3-methoxy-10-methyl-9-acridone (2), 3-hydroxy-1, 5, 6-trimethoxy-9-acridone (3), 4-chloro-3-hydroxy-6-methoxy-9-acridone (4), 2-hydroxy-6-methoxy-9-acridone (5), 3-hydroxy-5,6-dimethoxy-9-acridone (6), and 4-hydroxy-3,6-dimethoxy-9-acridone (7). These pure compounds are promising lead candidates for development of new anti-TB drugs.

### Table 4: Selectivity indices of some antitubercular plant species reported in East Africa

| Plant                  | Solvent              | MIC on Mtb strain (µg/ml) | IC₅₀ (µg/ml) | Selectivity index (SI) | Comment                                      |
|------------------------|----------------------|--------------------------|-------------|------------------------|----------------------------------------------|
| Commiphora edulis      | Dichloromethane      | 1560                     | 393         | 0.25                   | More toxic to human cells than the Mtb; not useful |
|                        | Ethyl acetate        | 3125                     | 1734        | 0.55                   | More toxic to human cells than the Mtb; not useful |
| Commiphora ellenbeckii | Water                | 780                      | 1509        | 1.93                   | More toxic to Mtb than human cells but the SI is low. May be optimized for lead candidate identification |
|                        | Methanol             | 3125                     | 608         | 0.19                   | More toxic to human cells than the Mtb; not useful |
| Commiphora mildbraedii | Methanol             | 390                      | 452         | 1.16                   | More toxic to Mtb than human cells but the SI is close to 1. No practical application |
|                        | Ethyl acetate        | 6250                     | 339         | 0.054                  | More toxic to human cells than the Mtb; not very useful |
| Khaya senegalensis     | Chloroform           | 6.25                     | 1000        | 160                    | More toxic to Mtb than human cells with high SI. Promising for development of lead candidate |
| Rosmarinus officinalis | Chloroform           | 6.25                     | 100         | 16                     | More toxic to Mtb than human cells with high SI. Promising for development of lead candidate |

IC₅₀: cytotoxic concentration normal cells; SI: selectivity index
muzigadial (4), muzigadiolide (5), linoleic acid (6), and 15-sandaracopimaradiene-7α, 18-diol (7). Compounds 1, 2, and 3 are acridone alkaloids; 4, 5, and 6 are sesquiterpenes, while 7 is a diterpenediol [5, 37, 85]. In Asia and America, several studies have reported pure compounds isolated from medicinal plants to have promising antimycobacterial activity [78, 115–117]. For example, Bisbenzylisoquinoline alkaloids from *Tiliacora triandra* (tiliacorinine, tiliacorine and 2′-nortiliacorinine) were found to have comparable antimycobacterial activity (MIC = 0.7–6.2 μg/ml) to the standard first line drugs against sensitive and resistant Mtb strains [108]. Rukachaisirikul et al. [118] reported that 5-hydroxysophorone (an isoflavone from *Erythrina stricta*) had promising antimycobacterial activity (MIC = 12.5 μg/ml) against Mtb H37Ra. Vasicine acetate and 2-acetyl benzylamine isolated from hexane extract of *Adhatoda vasica* Ness. (Acanthaceae) inhibited one sensitive and multidrug-resistant strain at 50 and 200 μg/ml respectively [119]. Since flavonoids and alkaloids were reported to be absent in three out of the five inactive plants [28] and majority of the isolated bioactive pure compounds belong to the class of alkaloids, terpenoids, and flavonoids [5, 85, 118], it implies that these classes of phytochemicals are the ones most likely to be responsible for the observed antimycobacterial activity.

**Conclusion**

East Africa has a rich diversity of medicinal plants that have been reported to be effective in the management of symptoms of TB. Most of the plants are from the family Fabaceae, Lamiaceae, and Asteraceae. A large proportion of the documented plants have not been scientifically validated for their efficacy and safety. Although the standard drugs had superior activity, majority of the validated plants were found to possess acceptable acute toxicity profile on animal cells and considerable bioactivity with isolated pure compounds showing promising efficacy against Mtb. We recommend more scientific validation studies to be conducted on the remaining plants in order to standardize herbal medicine use and also promote drug discovery and development against TB. More
isolation and characterization studies will enrich the chemical diversity of both the natural product and synthetic chemical libraries from which possible lead candidates could be developed. Currently, we are working on isolation and characterization of bioactive compounds from selected medicinal plants from family Fabaceae identified from this study. These include *Erythrina abyssinica*, *Albizia coriaria*, and *Entada abyssinica*.

**Supplementary information**

Supplementary information accompanies this paper at https://doi.org/10.1186/s41182-020-00256-1.

**Additional file 1: Figure S1.** PRISMA flow diagram used for the review.

**Abbreviations**

IC₅₀: Median cytotoxic concentration; LD₅₀: Median lethal dose; Iso: Isoniazid; MIC: Minimum inhibitory concentration; Rif: Rifampicin; H37Rv: Pan sensitive Mtb strain; TMC331: Rifampicin-resistant Mtb strain; SI: Selectivity Index; TB: Tuberculosis; WHO: World Health Organization

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**Authors’ contributions**

SBO, AK, IK, EK, MPO, TO, and LB designed the study. SBO, IK, EK, MPO, TO, and LB performed literature search for medicinal plants in Uganda, Burundi, Rwanda, Kenya, Tanzania, and South Sudan, respectively. SBO and TO analyzed the collected data. TO, MPO, and LB verified the plant names in botanical databases and local languages. SBO, MPO, TO, and LB wrote the first draft of the manuscript. AK, IK, and EK reviewed the draft manuscript. All authors revised and approved the final manuscript.

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**Ethics approval and consent to participate**

Not applicable

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Not applicable

**Competing interests**

The authors declare that there is no conflict of interest regarding the publication of this paper.

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