Traditional medicinal plants used in the treatment of tuberculosis in Ethiopia: A systematic review

Samuel Getachew a,*, Girmay Medhin b, Abyot Asres c, Gemeda Abebe d, Gobena Amenie e

a Department of Biology, College of Natural and Computational Sciences, Mizan-Tepi University, PO Box 121, Tepi, Ethiopia
b Akilu Lemma Institute of Pathobiology, Addis Ababa University, PO Box 1176, Addis Ababa, Ethiopia
c School of Public Health, College of Health Sciences, Mizan Tepi University, Mizan Amman, Ethiopia
d School of Medical Laboratory Science and Mycobacteriology Research Center, Jimma University, Jimma, Ethiopia
e Department of Veterinary Medicine, College of Agriculture and Veterinary Medicine, United Arab Emirates University, PO Box 15551, Al Ain, United Arab Emirates

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ABSTRACT

Background: Majority of people in Ethiopia heavily rely on traditional medicinal plants to treat a number of diseases including tuberculosis (TB). However, there has been lack of comprehensive evidences on taxonomic distribution of medicinal plant species, methods of preparation of remedies from these plants and how the remedies are administered. This systematic review is designed to examine and synthesize available evidences focusing on medicinal plants that have been used for TB treatment in Ethiopia.

Methods: Research findings related to ethno-botanical and pharmacological approaches of TB remedies were retrieved from databases. Electronic libraries of Ethiopian Universities and relevant church-based religious books were also reviewed as additional sources. Evidences are searched and organized in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.

Result: From a total of 68 research documents that reported use of plants for treatment of TB 98 plant species belonging to 82 genera and 49 families were identified. The most frequently reported plant species belonged to family Lamiaceae (n = 8), Euphorbiaceae (n = 7), Cucurbitaceae (n = 6) and Fabaceae (n = 6). Croton macrostachyus, Allium sativum, and Myrsine Africana were the most often mentioned anti-TB medicinal plants. Shrubs (35.7%) and trees (29.6%) were reported as dominant growth forms while plant roots (31.6%) and leaves (28.6%) were frequently used plant parts for the preparations of the treatment. The most favored administration route was oral (59.1%). About 87% of the preparations were made from fresh plant materials. No experimental/clinical evidence was presented for 79.6% (78/98) of the reported plants to support their anti-mycobacterial activities.

Conclusion: In Ethiopia, the number of herbal remedies is enormous and their use for TB treatment is a common practice. However, majority of them are not yet backed up by evidence generated through scientific experimentation and this warrants further experimental and clinical validations. Moreover, the efficacy, toxicity and safety tests should be initiated and this would help in the rapid identification of new anti-TB regimens, and possibly it would lead to developing more effective new plant-based drugs. This systematic review will serve as a reference for the selection of plants for developing new anti-TB regimens.

1. Introduction

The current modern treatment of TB depends on rifampicin, ethambutol, isoniazid and pyrazinamide, which are less effective (Brigden et al., 2014) and costly with serious side-effects (Bhatcha, 2013; Zazuetta-Beltran et al., 2013; Mohan and Sharma, 2004). An emergence of drug resistant (Gupta et al., 2010; Zazuetta-Beltran et al., 2011) and geographically specific strains of TB etiollogies (Firdessa et al., 2013) has further exacerbated the situation (threat) in TB-burdened developing countries of Africa, and have necessitated a need to search for new treatment regimens that target medicinal plants (Andualem et al., 2014; Hostettmann et al., 2006; Kloos et al., 1978; Kloos, 1976; Askun et al., 2013; Bhatcha, 2013).

The use of medicinal plants remains the primary source of healthcare for majority of people in most of developing countries, it may reach 70-80% among the Africans, and it could be as high as 85% in the sub-
Saharan Africa (Mann et al., 2008c; Mann et al., 2007; WHO, 2002; Zuberi, 2014; Andarge et al., 2015; Abbink, 2002; Obakiro et al., 2020). Medicinal plants may offer a new hope for developing alternative medicines for a number of diseases as they are easily accessible (Zuberi, 2014; Heinrich, 2000) and cheap with a minimum of side effects (Hostettmann et al., 2000; Siddiqui et al., 2014; Abebe, 1996). Plant derived medicines may also help in fighting drug resistance (Bhattacha, 2013; Singh et al., 2015) and combating geographically specific strains of TB etiologies (Gupta et al., 2010). Therefore, effective and alternative anti-TB drugs preferably plant-based ones have to be developed to fight drug resistance and to reduce TB associated mortality and morbidity (Andualem et al., 2014; Amsalu, 2010; Hostettmann et al., 2000; Eneyew et al., 2014; Bishaw, 1991; Gupta et al., 2010).

In Ethiopia there are more than 6,600 vascular plant species (Bekele-Tesemma, 2007). From 70-80% of the Ethiopians still rely on traditional medicinal plants (TMPs) to treat a variety of diseases such as gastrointestinal (Belayneh et al., 2012; Bekalo et al., 2009), respiratory tract and sexually transmitted infections (Abera, 2014; Kewessa et al., 2015), hemorrhoids, rashes (Tesfahuneygn and Gebreegziabher, 2019), hypertension, diabetes (Andarge et al., 2015), malaria (Abbink, 2002; Alemneh, 2021a,b; Agize et al., 2013) and others (FMHO, 2003; Negussie, 1988; Birhan et al., 2011). However, there has been no study that has synthesized existing evidence focusing on documentation of traditional medicinal plants (TMPs) being used in treating TB in Ethiopia. And this has resulted in unavailability of comprehensive data on plant species, methods of preparation and administration of traditional TB remedies. This systematic review was designed to address this gap by documenting existing TMPs that are being used in TB treatments in Ethiopia. In this paper we report synthesis of existing evidence that was obtained from a systematic review of the available literatures on anti-mycobacterial plants with the hope of providing comprehensive data to hasten the research effort on development of novel plant derived drugs against human and bovine TB.

2. Methods

This systematic review and analysis of peer reviewed journal articles, MSc/PhD theses/dissertations, and unpublished documents related to medicinal plants used for the treatment of TB [n = 68] in Ethiopia was conducted over nine month period from November 2020 to July 2021.

2.1. Literature search strategy

Web-based systematic search strategy was employed. Ethnobotanical/ethno-medicinal studies reporting on medicinal plants used for traditional TB treatment in Ethiopia were gathered through two different search modalities for published and unpublished research findings. Google search engine and local university websites were assessed for unpublished MSc/PhD thesis research reports while international scientific databases that include PubMed, Research gate, Science direct, Web of Science, Google Scholar, academia edu, and AJOL were used as sources of published journal articles. The search was done using several key terms: Ethiopia/Ethiopian plants/Ethiopian medicinal plants/anti-tuberculosis plants, anti-lymphadenitis/gland TB plants, traditional knowledge/TMPs, herbal medicine/remedies, indigenous knowledge, folk medicine/remedies, ethno-botany/ethno-botanical, ethno-pharmaceutical/medicines/, ethno-pharmacological/medicines/, ethno-pharmaceutical, cultural medicine following “Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)” guidelines and guidance (Moher et al., 2009a,b).

2.2. Inclusion criteria

Published and unpublished ethnobotanical/medicinal reports including experimental studies about treatments of TB in Ethiopia and reported before May 2021 were included.

2.3. Exclusion criteria

Information from published and unpublished ethno-botanical and ethno-medicinal surveys lacking scientific plant names and not reporting information about anti-TB medicinal plants were excluded from the analysis.

2.4. Screening and criteria

For this systematic review, the title and abstract of identified journal articles/theses/dissertations/reports were downloaded and all those suitable for the purpose were screened out and critically inspected for inclusion.

2.5. Data retrieval

A data collection tool was developed in Microsoft Excel format into which all retrieved data (botanical name, plant family, local name(s), part(s) used, habit of growth, preparation and administration mode, extraction method of each plant used for TB treatment), were entered. Mispelled information in some studies, particularly local name and habit of the plants, geographic locations of the study localities/districts, and misspelled scientific names were retrieved and corrected through direct web-searching.

2.6. Data analysis

All retrieved relevant data about the Ethiopian TMPs were entered into structured Microsoft office Excel format and exported to Statistical Software Packages for Social Science (SPSS, software version 20.0). Descriptive statistical methods, percentage and frequency were used to analyze ethno-botanical data on reported medicinal plants.

3. Results

Peer reviewed journal articles, M.Sc./Ph.D. theses/dissertations research reports representing ten different regional states of Ethiopia and other unpublished documents [n = 68] were included and analyzed in this review (Figure 1).

3.1. Taxonomic distribution of herbal medicines of TB in Ethiopia

A total of 98 different plant species that are used to treat TB traditionally were retrieved from 68 ethno-medicinal study reports recruited for this review. The plants were from 82 genera and 49 families. While taxonomic summary of reported plants is put in Table 1, detailed taxonomic and geographic distribution, habit, parts used, modes of preparation and routes of administration and dosage of herbal remedies of TB is found in Table 2.

3.2. Growth habit of medicinal plants, parts used, condition of preparations and routes of administration

3.2.1. Growth form of plants used for TB treatment

The growth forms of herbal remedies of TB indicated that the shrubs had the highest proportion with 35.7% of the species while trees (29.6%), herbs (22.4%) and climbers (9.2%) made up the second highest proportion. The remaining 3.1% were the bulbs.

3.2.2. Plant parts used for remedy preparation

Many plant parts are utilized in Ethiopia for anti-TB remedy preparation. Most of the preparation of herbal TB medicines involved the use of a single plant part (95.9%). Plant roots (31.6%) occupied the largest proportion followed by the leaves (28.6%). In a few of TM of TB, use of aerial plant parts (n = 4), seeds (n = 4) and barks (n = 4) were also indicated. But in the remaining proportion, different parts of the plants
were mixed together to prepare traditional TB remedies. Flowers, stems and the whole plant parts were reported as very rarely used parts for the preparation. Moreover, majority of the remedies were prepared from freshly harvested parts of medicinal plant species (73.5%) (Table 2).

### 3.2.3. Preparation and routes of administration of herbal recipes for TB treatment

Different formulations and application procedures of medicinal plant preparations were used to treat TB across the regions of Ethiopia. The most commonly used route of administration was oral (59.2%) followed by dermal/topical route (for gland TB), (10.2%). Intranasal application or sniffling is the least reported route of application, (3.1%). But for (16.7%) plant species the administration routes of TB TM have not been reported. The major modes of remedy preparation from medicinal plant materials were crushing (52%) followed by pounding (29.6%) (Table 2).

Out of a total of all reported traditionally used TB remedies 87.7% and 10.4% plant species were described to be used for the treatment of pulmonary TB (PTB) and extra-pulmonary TB (EPTB), respectively, while 5.2% were used for bovine TB (BTB) (Table 2).

3.3. Solvents and additives for preparation of anti-TB herbal medicines

The reported herbal medicines of TB in Ethiopia are prepared by using fresh material, dried form and in some cases either fresh or dried form of the plant parts. During the preparation of most of the TM of TB, water is used as a solvent and in some cases milk and alcohols are added. Milk, cow butter and honey are the commonly used additives to prepare the medicinal plant materials. A few of these TM are also recommended to be taken with hot drinks and ”injera”.

3.4. Geographic distribution and frequency of citations of anti-TB medicinal plants

The largest number of herbal TB treatments were reported from Oromia Regional State (n = 22; 22.4%) followed by Tigray (n = 16; 16.3%) and Amhara, (n = 14; 14.3%). From each of the Southern Nations, Nationalities and Peoples Regional (SNNPR) States and Afar region (n = 13; 13.3%) plant species were described. In the study reports across the country, Croton macrostachyus (n = 7), Allium sativum (n = 5), Myrsine africana (n = 4), Zingiber offfcinale (n = 4) and Allium ursinum (n = 4) are the most frequently reported plant species. The frequency of reports across the regions and distribution in the Ethiopian Flora Region are shown in Table 3.

3.5. Medicinal plants with documented experimental/clinical evidence for anti-mycobacterial activity

Seventy eight (79.6%) plant species reported in this review had no experimental/clinical evidences for their ability to kill the etiologies of TB. Allium ursinum, Dodonea angustifolia (Balcha et al., 2014; Gemechu et al., 2013), Artemisia abyssinica, Croton macrostachys, Eucalyptus camaldulensis, Ocimum basilicum (Gemechu et al., 2013), Otostegia integ- rifolia (Kahaliw, 2016; Enyew et al., 2014), Pterolobium stellatum (Balcha et al., 2014), Carissa edulis, Persea americana, Vernonia amygdalina (Kahaliw, 2016) were some of the plants on which clinical/experimental investigations were carried out in Ethiopian research centers and Universities. Though all the remaining plant extracts show the ability to kill...
| SN | Family Name | Botanical name | Common name(s)/language name/s | Region | Habit | Part used | ROA | Mode of preparation/Types of TB | References |
|----|-------------|----------------|--------------------------------|--------|-------|-----------|-----|--------------------------------|------------|
| 1  | Lamiaceae   | *Artemisia abyssinica* Shc.Bip.ex.A.Rich | Tiroo (Oro) Oro H Lv Or Not specified | Gemechu et al., 2013; Bekalo et al., 2009 |
| 2  | *Artemisia afra* Jacq. ex Willd | Chiqugn (Amh) Oro H Lv Or Not specified | Bekalo et al., 2009; Vineger et al., 2008 |
| 3  | *Clerodendrum myricoides* Hochst. Vatke | Aghbio (kaifi) Kaffa Sh Or Not specified | Abate, 1989 |
| 4  | *Ocimum americanum* L. | Zeka-keba (Amh) SNNP H Fr Not specified | Bekalo et al., 2009 |
| 5  | *Ocimum basilicum* L. | Besobilla (Amh) Amh H Sd Not specified | Gemechu et al., 2013 |
| 6  | *Ocimum lamiifolium* Hochst. ex Benth.... | Demakessie (Oro) Oro T Lv Fresh leaves pounded and juice is drunk | Gizachew et al., 2013; Mesfin et al., 2005; Getahun, 1976 |
| 7  | *Oenanthe procumbens* (H. Wolff) Norman | Bunkaka Hida (Or) Amh Sh Lv Or, Sk Oral/skin EPTB | Amsalu, 2010 |
| 8  | *Otostegia integrifolia* Benth | Tinjute (Amh) Amh Sh Rt Or, Ins Fresh or dried leaf is used as fire fumigation | Kahaliw, 2016; Enyew et al., 2014 |
| 9  | Euphorbiaceae | *Clutia abyssinica* Kaub. & Spach. | Yemar semat (G) SNNP Sh Lv Or Infusion | Teka et al., 2020 |
| 10 | *Croton macrostachyus* Hochst. ex Delile | Masincho (Si) SNPN T Ba Or Boiling leaves of shoots in water and decanting the toxic water, & allowed to dry. Mixing dry fine powder with powder of spices & water, and giving about two syringes per day for a month | Tefera and Kim, 2018; Kewessa et al., 2015; Balcha et al., 2014; Gemechu et al., 2013; Amsalu, 2015; Geyid et al., 2005 |
| 11 | *Euphorbia canadelastrum* Ketsby | Kulkual (Amh) Amh/ Oro T Lq Or Dropping diluted in water (drinking) | Bekele and Reddy, 2014; Mesfin et al., 2013 |
| 12 | *Euphorbia tirucali* L. | Kenchib (Amh) T Lq Not specified | Genene and Hazare, 2017 |
| 13 | *Euphorbia cryptospinosa* Bally | Aananno (Oro) Oro C Rt Or Crushing internal part of the root with the roots of *Solanum incanum* & *Osyris quadripartita*, making s/n & adding honey then drinking as necessary when the patients become thirsty | Fenetahun and Eshetu, 2017; Ashagre et al., 2016 |
| 14 | *Jatropha glauca* Vahl. | Qablis (Af) Afar Sh Rt Or, Ins Making infusion of fresh root and administering intranasal and orally | Seifu, 2004 |
| 15 | *Ricinus communis* L. | Qobbo Oro Sh Lv Or Rubbing fresh warmed leaf with fine on the swelling | Wolditsadik, 2018 |
| 16 | Cucurbitaceae | *Coccinia abyssinica* (Lam.) Cogn | Anchote (Oro) Oro H Rt Or Cooking its root with leaves of *Croton macrostachyus* and eating with ‘injera’ for four days | Birhanu et al., 2015; Davit and Estifanos, 1991; Megerasa et al., 2013; Getahun, 1985; Amare, 1973 |
| 17 | *Cucumis dipssacces* Ehrenb. | Hafaflo (Tig) Tig C Rt Or Not specified | Zenebe et al., 2012 |
| 18 | *Cucumis ficifolius* A.Rich | Yemdir embouy (Amh) SNPN/ Amb/ Tig H Fr Or Mixing its fruit with root of *Gnidia involucrata* and bulb of garlic, crushing and soaking it 7 days in local ‘Tella’ and taking one cup for five days or powdered, mixed with water, drink | Araya et al., 2015; Regassa, 2013; Gebeheywu, 2011 |
| 19 | *Cucumis pastulatus* L. | Qalfoon (Som) Oro C RT Or Chewing the root or crushing the root, making s/n and drinking one coffee cup daily until cured | Ashagre et al., 2016; Balemie et al., 2004 |
| 20 | *Momordica foetida* Schumach | Yubrarre SNPN C Rt Or Crushed/pounded fresh/dry root mixed with *Allium sativum* bulb is taken orally before breakfast for three days. | Mesfin et al., 2009 |
| 21 | *Zehneria scabra* (Linna. E.) Sond. | Haregresa (Amh) Amh H St, Lv SK/ To Not specified | Alemneh, 2021a,b |

(continued on next page)
| SN | Family Name | Botanical name | Common name(s)/language name/s | Region | Habit | Part used | ROA | Mode of preparation/Types of TB | References |
|----|-------------|----------------|--------------------------------|--------|-------|----------|-----|--------------------------------|------------|
| 22 | Fabaceae    | Acacia albizita Del. | Gerbi (Oro) Oro/ SNNP | T | AP | Or | Concoction, crushed | (Temam and Dillo, 2016; Belayneh et al., 2012) |
| 23 | Acacia mellifera (M. Vahl) Benth | Kontir grar (Amh) Oro/F Sh Lv Or | ETPB (fresh leaves consumption) | (Teklehaymanot, 2017) |
| 24 | Acacia oryza (Forsk.) Schweinf | Wanga (Or) Afar Sh Rt Or, Ins | Fresh root consumption | (Teklehaymanot, 2017) |
| 25 | Calpurnia aurea (Alton) Benth | Hittawutse (Tig) Tig | Sh Rt Or | Not specified | (Geneche et al., 2013; Zenebe et al., 2012) |
| 26 | Erythrina brucei Schweinf | Woleko (Sid) SNNP | T | Ba | Or | Not specified (Bovine TB) | (Kewessa et al., 2015) |
| 27 | Pterolobium stellatum (Forsk.) Brenan. | Kentefa (Amh) Oro/ Tig | Sh | Rt | Not specified | (Kahaliw, 2016; Balcha et al., 2014) |
| 28 | Alliaceae | Allium cepa L. | Qey shinkurt (Amh) | Sh | Bu | Or | Fresh chewing | (d’Avigdor et al., 2014; Fulas, 2007; Fulas, 2003) |
| 29 | Allium ursinum L. | Yejib shinkurt (Amh) | T | Fr | Or | Fresh fruits crushed & blended with honey & butter | (Balcha et al., 2014; Geneche et al., 2013; Belayneh et al., 2012; Yirga, 2010) |
| 30 | Allium sativum L. | H Kashari shunkurutta (Oro) Oro/ SNNP/ Tig | B | Bu/ Lv | Or | Taking orally grinded and mixed with honey | (Osman et al., 2020; Belayneh et al., 2012; Mesfin et al., 2009; Wondimu et al., 2007) |
| 31 | Apocynaceae | Carissa edulis Vahl | Agam (Amh) | T | Rt | Or | Not specified | (Kahaliw, 2016) |
| 32 | Carissa spinarum L. | Otilaa (Si) SNNP | Sh | Fr | Or | Not specified | (Kewessa et al., 2015) |
| 33 | Kanahia lani flora (Forssk.) R. Br. | Leehamohcaxa (Af) | Sh | Rt Or | Not specified | (Seifu, 2004) |
| 34 | Asteraceae | Echinops kebericho Mesfin | kebericho (Oro) Oro | H | Rt | Not specified | (d’Avigdor et al., 2014; Abebe et al., 2003) |
| 35 | Lagerra tomentosa (Sch.Bip.ex A.Rich.) Oliv.& Hiern | Kekekez (Amh) Amh | T | LV | Sk/To | Tying fresh pounded leaf on the swelling. | (Woldisadik, 2018) |
| 36 | Vernonia amygdalina Del. | Grawa (Amh) Amh | Sh | Rt | Or | Not specified | (Kahaliw, 2016) |
| 37 | Capparidaceae | Balanites rotundifolia (van Tiegen) Blatter | Alayito (Af) | Sh | Lv | Or, Ins | Making infusion of fresh leaves and administering intranasal and a small amount orally | (Seifu, 2004) |
| 38 | Boscia angustifolia A. Rich | Kermed (Tig) | T | Ba | Or | Crushing together with whole part of Celtis africana homogenize with water and drinking a bottle cup of the solution for 7 consecutive days in the morning | (Gidey et al., 2015) |
| 39 | Cadaba rotundifolia Forssk | Kanshele (Kam) | Sh | Lv | Or, Ins | Bovine TB (fresh leaves consumption) | (Teklehaymanot, 2017) |
| 40 | Malvaceae | Hibiscus cannabinus L. | Dans'a (Dawro) SNNP | Sh | Fl | Or | Chopped, pound | (Agize et al., 2013) |
| 41 | Malva parvi flora L. | Siito (Halaba) SNNP | H | Lv | Or | The leaf is crushed, powder mixed with water drunk | (Regassa et al., 2017) |
| 42 | Sida schimperiana Hochst. ex A. Rich | Cherefeg (Amh) | H | Rt | | Not specified | (Genene and Hazare, 2017) |
| 43 | Eucalyptus spp. | Bahir zaf (Amh) | T | Lv | Not specified | (Birhanu et al., 2015) |
| 44 | Eucalyptus camaldulensis Dehnh | Key bahir zaf (Amh) | T | Lv | Not specified | (Geneche et al., 2013; Birhane et al., 2011) |
| 45 | Syzygium guineense (Willd.) DC. | Duwancho (Sid) SNNP | T | Bk | Or | Not specified (used for both human and bovine TB) | (Kewessa et al., 2015) |
| 46 | Oleaceae | Jasminum abysсинicum Hochst. | Tembelel (Amh) Amh | T | AP | Not specified | (Geyid et al., 2005) |
| 47 | Olea europaea L. | Weira (Amh) | Oreo/ SNNP/ Afar | T | Fr | Or | Not specified | (Legesse et al., 2011; Teklehaymanot and Giday, 2010; Amenu, 2007) |
| 48 | Olea europaea subsp. cuipita (Wall. Ex G.Don.) Gilf | Ejerza (Oro) Oreo | T | Rt | Sk/To | The extracted oil from the roots put on the affected site (Bone TB) ETPB | (Jima and Megersa, 2018; Kewessa et al., 2015) |
| SN | Family Name | Botanical name | Common name(s)/language name(s) | Region | Habit | Part used | ROA Mode of preparation/Types of TB | References |
|---|---|---|---|---|---|---|---|---|
| 49 | Solanaceae | Capsicum annuum L. | Geed case (Som) | Som | H | WP | Or | Grounding the stem and dissolving with water & drinking (Issa, 2015) |
| 50 | Solanaceae | Solanum anguivi Lam. | Ambu (Bench) | SNPN | Sh | Lv | Sk/To | Pounding leaf and apply topically for gland TB (Giday, 2009a; 2009b) |
| 51 | Solanaceae | Solanum marginatum L. f. | Abyiengule(Tig) | Tig | Sh | Sds | Or | Drying seeds, crushng & adding into milk or coffee and solution taking every morning for 21 days (Araya et al., 2015) |
| 52 | Anacardiaceae | Rhus vulgaris Meikle | Kammo (Amh) | Amh | Sh | Fr | Or | Grounding fruits are mixing with honey and one glass is drunk on empty stomach until recovery. (Gebeeyehu, 2011) |
| 53 | Euphorbiaceae | Schinus Molle L. | Kundo berbere (Amh) | Oro | T | Sd | Or | Crushing seeds and mixing with honey and eating (Getaneh and Girma, 2013) |
| 54 | Aizoaceae | Calotropis procera (Ait.) Ait | Ginda (Tig) | Tig | Sh | Rt | Ins | Crushing its roots into powder and mix with pounded bark of Croton macrostachyus and leaves of Ficus pumata & sniffing (Araya et al., 2015) |
| 55 | Rutaceae | Dregae sp. | Geed sare (Sum) | Som | C | Lv | Or | Grinding leaves and boiling with milk and drinking (Issa, 2015) |
| 56 | Combretaceae | Combretum molle G. Don | Xanasuda (Sum) | Som | T | Lv | Or | Grounding the leaves boiling and drinking (Issa, 2015) |
| 57 | Aizoaceae | Kirkia capensis subsp. Africana | Dakagleba (ku) Kunama | Tig | T | Lv | Or | Crushing the leaf, and drink a cup of the juice for three consecutive days (Gidey et al., 2015) |
| 58 | Meliaceae | Trichilia dregeana Sonn. | Anunu (Amh) | Oro | T | Rt | Or | Powdering and taking its 1/2 cup of tea (Itana, 2015) |
| 59 | Myrtaceae | Ekebergia capensis Aiton | Olochcho (Sid) | SNPN | T | Ba | Or | Crushing and pounding mixing with Hot Water/Bovine TB (Tefera and Kim, 2019; Kewensa et al., 2015; Banerjee et al., 2019) |
| 60 | Myristaceae | Embelia schimperi Forst. | Sharrengo (Gedio) | SNPN | Sh | Rt | Or | Crushing fresh root with water and taking that for several days (Mesfin et al., 2009) |
| 61 | Myristaceae | Myristica africana L. | Qacama (Oro) | Oro | Sh | Lv | Or | Leaves crushed and squeezed in fresh form with water. The juice was then indicated to be drunk in very small amount for three days (Gizachew et al., 2013; Vineger and Yewhalaw, 2007; Wolde Gebre-Mariam, 2002; Desina and Binggeli, 2000) |
| 62 | Rubiaceae | Clerodendrum trichophyllum (L.) Rich. | Fiiti (Oro) | Oro | C | Lv | Sk/To | Pounding the leaves, dissolving in water & drinking half of small glass & applying certain amount of the solution into the wound's opening using syringe, and also putting residues on its opening (gland TB) (Fenetashun and Edheten, 2017; Ashaghe et al., 2016; Temam and Dillo, 2016) |
| 63 | Rubiaceae | Clerodendrum xenoxe (L.) Rich. | Azo-hareg (Amh) | SNPN/ Oro | C | AP | Or | Not specified (Temam and Dillo, 2016; Geyid et al., 2005) |
| 64 | Rutaceae | Citrus limon (L.) Burm.f. | Lemin (Tig) | Tig | Sh | Fr | Or | Not specified (Zenebe et al., 2012) |
| 65 | Rutaceae | Clausena antiscus (Willd.) Benth. | Agam (Amh) | Oro | Sh | Lv | Or | Not specified (Gizachew et al., 2013; Vineger and Yewhalaw, 2007) |
| 66 | Rosaceae | Rosa x richardii Rehd. | Tsigereda | Amh | Sh | Fl | Sk/To | As a skin tie (Gland TB) and also for Bone TB (Alemneh, 2021a,b) |
| 67 | Rosaceae | Rubus arcticus L. | Go’ra (Oro) | SNPN | Sh | Rt | Or | The root is pounding root, boiling, and drinking (Tuasha et al., 2018; Gedif and Hahn, 2003) |
| 68 | Rosaceae | Rubus x hygrophilus (S. Watson) Rehd. | Gaale (Amh) | Oro | T | Rt | Or | Not specified (Gemecu et al., 2013; Lulekal et al., 2008) |
| 69 | Rosaceae | Rubia cordifolia L. | Menscherer | Amh | C | Rt | Or | Crushing and smaunng root in water in 3 days then drink (Chokole, 2017) |
| 70 | Amaranthaceae | Indigofera amethystodes Jausch. et Spach | Jeere (Oro) | Oro | H | Rt | Or | Not specified (Gemecu et al., 2013; Lulekal et al., 2008) |
| 71 | Amaranthaceae | Celosia corymbosa Forrak. | Kontoma (Af) | Afar | H | Rt | Or, Ins | Root consumption (Teklehaimanot, 2017) |
| 72 | Amaranthaceae | Celosia argentea Forrak. | Jia Dhaakubinitu (Or) | Amh | H | Rt | Sk/To | Not specified (Alemneh, 2021a,b) |
| 73 | Apiaceae | Anethum graveolens L. (dill) | Exutul (Amh) | Tig | H | AP | Or | Not specified (Balcha et al., 2014) |
| 74 | Apiaceae | Amanthus amariffolius Schott | Amoch (Amh) | Oro | H | Lv | Or | Not specified (Vineger et al., 2008) |
| SN | Family Name | Botanical name | Common name(s)/language name/s | Region | Habit Part used | ROA | Mode of preparation/Types of TB | References |
|----|-------------|----------------|-------------------------------|--------|-----------------|-----|-----------------------------|------------|
| 75 | Asphodelaceae | Aloe species | QUEREYA (AF)/RIET (Amh) | AFAR/Amh | SH | ST/RT | Or | Drinking its infusion mixed with room of Tamarix aphylla and root of Salvadora Persica L. Also, taking orally dried, powdered root buried for 6 months mixed with honey or only Aloe sp root buried for 6 months, dried and powdered then mixed with 1kg of honey and taken orally | (Zewdu et al., 2015; Seifu, 2004) |
| 76 | Balanitaceae | Balanites aegyptiaca (van Tieghem) | UDA (AF) | AFAR | SH | LV | Or, INS | Fresh leaves consumption | (Teklehaymanot, 2017) |
| 77 | Boraginaceae | Buxus arbicularis (Hutch. & E.A. Bruce) | ULAGEITA (AF) | AFAR | SH | FR | Or, INS | Bovine TB (fresh fruit consumption) | (Teklehaymanot, 2017) |
| 78 | Brassicaceae | Lepidium sativum L. | SHUNFAX (Som) | SOM/Oro | H | SD | Or, SK/TO | Swallowing fresh seeds, applying on open swelling or wound, adding small amount of sulphur & covering it with seed paste of L. Sativum & latex of C. Procera (EPTB topical for gland TB) | (Teman and Dillo, 2016; Araya et al., 2015; Irsa, 2015) |
| 79 | Canellaceae | Warburgia ugandensis Sprague | KENIFA/ZOGDOM (Amh) | AMH | T | BK | Not specified | (Giday, 2009a, 2009b; Lulekal et al., 2008; Wube et al., 2005) |
| 80 | Celastraceae | Maytenus senegalensis Lam. | KOMBOLICHA (Oro) | AMH | H | WP | SK/TO | Applying on Skin for Gland TB | (Giday et al., 2007) |
| 81 | Lauraceae | Persea americana Mill | AVOCADO | AMH | T | LV | Not specified | (Kahalib, 2016) |
| 82 | Legianniacae | Buddleja polytopia | ANFAR (Tig) | TIG | T | LV | Or | Not specified | (Balcha et al., 2014) |
| 83 | Loranthaceae | Tapinanthus globiferus (A. Rich.) Tiegh. | Hafa-teketsula (Amh) | AMH | H | WP | SK/TO | Crushing/pounding fresh root mixed with cold water and taking orally | (Mesfin et al., 2009) |
| 84 | Melianitaceae | Bersama abyssinica Fresen | JEJEBBA | SNNP | SH | RT | Or | Crushing its leaves with roots of C. Procera is into powder and mixing with pounded bark of Croton macrostachyus & sniffing | (Araya et al., 2015) |
| 85 | Moraceae | Ficus palmata Forsk | QOTILEBELE-S | TIG | SH | LV | INS | Chewing, infusion with hot drinks, eating together with other foods | (Wondimu et al., 2007) |
| 86 | Olacaceae | Ximenia americana L. | HUDHAA (Oro) | ORO | T | RT | Or | Crushing leaves and skin tie (Gland TB) | (Giday, 2009a, 2009b; Teklehaymanot, 2009) |
| 87 | Plumbaginaceae | Plumbago zeylanica L. | AMIRA (Agew) | AMH | SH | LV | SK/TO | Pounding them to make solution and drinking 1 water glass daily for a month | (Ashagre et al., 2016) |
| 88 | Santalaceae | Ostrya quadrifurctia Decn | WAASUO (Oro) | ORO | SH | LV, RT | Or | The root mixed with the fruit of Cucumis cificolus and bulb of garlic are crushed and soaked 7 days in local “Tella” and one cup is taken for five days | (Gebeeyehu, 2011) |
| 89 | Thymelaeaceae | Gnidia involucrata Steud | BOTO (Amh) | AMH | H | RT | Or | Crushing its leaves with roots of Cucumis cificolus and bulb of garlic are crushed and soaked 7 days in local “Tella” and one cup is taken for five days | (Giday et al., 2007) |
| 90 | Xyloglousaceae | Balanites aegyptiacus (L.) Delile | MEKIE (Tig) | TIG | T | FR | Or | Not specified | (Zenebe et al., 2012) |
| 91 | Polygonaceae | Rumex abyssinicus Jacq. | Mekmoko (Oro) | TIG/Oro | H | RT | SK/TO | Making paste and mixing with cow butter as ointment | (d’Avigdor et al., 2014; Moravec et al., 2014; Zenebe et al., 2012; Gebeeyehu, 2011; Abebe et al., 2002; Gedif and Hahn, 2003) |
| 92 | Salvadoraceae | Salvadora persica L. | QADAYTO (AF) | AFAR | T | RT | Or | Making the infusion of the root, and the leaves of Aloe sp. And administering orally with root of Salvadora persica | (Seifu, 2004) |
| 93 | Sapindaceae | Dodonaea angustifolia L.F. | KIRKITA (Amh) | TIG/SNNP | SH | FR | Or | Powdering dry fruit with water and giving orally | (Balcha et al., 2014; Birhane et al., 2011; Mesfin et al., 2009) |
| 94 | Scrophulariaceae | Sirga hormithica (Del.) Benth | ADIRI Bereka (Tig) | TIG | H | LV | Or | Crushing the leaf, homogenizing with water and drinking | (Giday et al., 2015) |
| 95 | Tamaricaceae | Tamarix aphylla (L.) Karst | SAAGANTO (AF) | AFAR | T | RT | Or, INS | Making infusion of its root with root of Tamarix aphylla and leaves of Aloe app and administer orally with Salvadora persica. | (Seifu, 2004) |

(continued on next page)
mycobacterial species, Carissa edulis, Vernonia amygdalina (Kahaliw, 2016) and Anethum graveolens (Balcha et al., 2014), failed to show any anti-mycobacterial activities. Particularly, Oostega integrifolia (Kahaliw, 2016; Enyew et al., 2014), Persea americana (Kahaliw, 2016), Pterolobium stellatum (Kahaliw, 2016; Balcha et al., 2014) and Jasminum abyssinicum (Geyid et al., 2005) were reported to show significant anti-mycobacterial activities (Table 4).

### 4. Discussion

Ethiopia is endowed with abundant medicinal plant resources and traditional herbal practices. Majority of its people live in rural areas and still relies on TMPs for the treatment of human and livestock ailments including TB (Abebe, 2001; Ashagre, 2011; Banerjee et al., 2014; Genene and Hazare, 2017). However, available research evidences on herbal remedies of TB in the country is highly fragmented.  

In this review, 98 different plant species from 82 genera and 49 families that are used to treat TB traditionally were retrieved but it was found higher than review reports from India (Arya, 2011), South Africa (Semenya and Maroyi, 2013) and Uganda (Bunalema et al., 2014) that reported 48, 21 and 90 plant species, respectively. Higher report of anti-TB herbal medicines indicates the reliability of Ethiopians on TM, and this could be due to the high cost of modern drugs, paucity and inaccessibility of modern health services, and cultural acceptability of herbal medicines (Agize et al., 2013; Banerjee et al., 2014; Gedif and Hahn, 2005; Teklehaymanot and Giday, 2010; Seifu, 2004). Of these plant species, shrubs had the highest proportion (35.7%) of plant species which are followed by trees (29.6%), and herbs (22.9%). This finding is consistent with a number of ethnobotanical studies from Ethiopia (Bhatcha, 2013; Abebe, 2011; Alemneh, 2021a,b; Jima and Megersa, 2018; Gofa et al., 2015) and beyond (Obakiro et al., 2020; Bhatcha, 2013). This may be explained by the fact that shrubs are perennial in the arid or sub-arid environments and may be available for use as MPs.

Plants belonging to family Lamiaceae (8 species), Euphorbiaceae (7 species), Cucurbitaceae (6 species) and Fabaceae (6 species) were found as dominant families from which herbal remedies of TB prepared. Moreover, this review's finding of plant species belonging to Lamiaceae, Euphorbiaceae and Fabaceae is in line with the reports of Obakiro et al. from Eastern African countries that included Kenya, South Sudan Tanzania and Uganda (Obakiro et al., 2020; Tabutfi et al., 2010). Moreover, significant anti-tubercular activity of plants from family Lamiaceae were also reported from Turkey (Askun et al., 2013) and Nigeria (Ibekwea et al., 2014), implying their higher potential as a target of future study. Moreover, plants belonging to the family Fabaceae were experimented to have biosynthetic phytochemicals with effective anti-mycobacterial activity in Ethiopia and Nigeria (Gemechu et al., 2013; Mann et al., 2008c; Ibekwea et al., 2014). However, plants in Hyacinthaceae, Moraceae and Rutaceae families were the most represented ones in a study from Southern Africa (Semenya and Maroyi, 2013).

According to this systematic review, 22(22.4%) of the herbal TB treatments were reported from Oromia Regional State followed by Tigray 16(16.3 %) and Amhara, 14(14.3%). From each of the SNNPR and Afar regional States, 13(13.3%) plant species were described. Of the study reports across the country, Croton macrostachyus, Allium sativum, Myrsine Africana, Zingiber officinalis and Allium ursinum were the most frequently reported plant species with frequencies of 7, 5, 4, 4, and 4, respectively. Similarly, studies that covered countries of Eastern Africa (Obakiro et al., 2020), India (Gupta et al., 2010; Arya, 2011) and others (Mann et al., 2008c) also revealed the potential of anti-tubercular activities of these plants. Therefore, these plant species should be

### Table 3. The most frequently reported herbal medicines used for the treatment of TB in Ethiopia.

| Scientific Name (Family) | Total reports | Areas/regions of reports | References |
|--------------------------|---------------|--------------------------|------------|
| Croton macrostachyus     | 7             | SNNP/Amh/Tig/Addis Ababa  | (Balcha et al., 2014; Geyid et al., 2005; Tekfa and Kim, 2019; Gofa et al., 2015; Kewesa et al., 2015; Amsalu, 2015; Gemechu et al., 2013) |
| Allium sativum           | 5             | Oro/Amh/SNNP             | (Osman et al., 2020; Belayneh et al., 2012; Wondimu et al., 2007; Mesfin et al., 2009; Birhanu et al., 2015) |
| Myrsine africana         | 4             | Oro/Adlis Ababa/Benishangul | (Wolde and Gebre-Mariam, 2002; Desisa, 2006; Vineger and Yewhalaw, 2007; Gizachew et al., 2013) |
| Zingiber officinale      | 4             | Amb/Tig                 | (Teklay et al., 2013; Giday et al., 2007) |
| Allium ursinum           | 4             | Oro/SNNP/Tig            | (Balcha et al., 2014; Gemechu et al., 2013; Belayneh et al., 2012; Yirga, 2010) |
| Ocimum tenuiflorum       | 4             | Oro/SNNP/Tig            | (Getahun, 1976; Gizachew et al., 2013; Mesfin et al., 2005) |
| Cleratia hirsuta         | 3             | Oro/SNNP/Tig            | (Teplan and Dillo, 2016; Esfahian and Ehsami, 2017; Ashaghe et al., 2016) |
| Dodonaea angustifolia    | 3             | SNNP/Tig                | (Balcha et al., 2014; Birhan et al., 2011; Mesfin et al., 2009) |
| Ekebergia capensis       | 3             | SNNP                    | (Tekfa and Kim, 2019; Kewesa et al., 2015; Banerjee et al., 2014) |
considered as prime candidates for further in-depth experimental investigations. As the strains of mycobacteria are emerging and changing with specificities in some localities, these plant species could be used to tackle the challenges in TB control (Dawit and Estifanos, 1991; Worku, 2019; Siddiqi et al., 2014).

It is also disclosed that the use of a single plant part (96.9%) of which, the plant roots (31.6%) occupied the largest proportion followed by the leaves (28.6.1%) is more common. Flowers, stems and the whole plant parts were reported as very rarely used parts for the preparation. These findings are also found to be consistent with other studies (Giday et al., 2010; Lulekal et al., 2008) that reported leaves and roots as dominant parts against TB (Arya, 2011; Singh et al., 2015). But the use of plant roots for remedy preparation could significantly affect the sustainability of these herbal medicines unlike the use of aerial parts (Belayneh et al., 2012; Gedif and Hahn, 2003; Moges et al., 2019).

This review has also described oral and intranasal routes (>75%) as the most commonly used routes of administration, implying the herbal remedies are safe for systemic applications, and this was indicated in other studies from Ethiopia (Tesfahuneygn and Gebregziabher, 2019), Malaysia (Sabran et al., 2016), India (Arya, 2011) and Eastern Africa (Obakiro et al., 2020).

The frequency of reports across the regions and distribution in the Ethiopian Flora are different but available experimental evidences are rare in the country in contrast to a study done in Nigeria (Ibekwea et al., 2014). Seventy eight (79.6%) of the plant species reported in this review had no experimental/clinical evidences for their ability to kill the etiologies of TB. Some evidences on the effectiveness of anti-mycobacterial activities of some herbal remedies of TB were done on Allium ursinum, Artemisia abyssinica, Carissa edulis, Croton macrostachys, Dodonea angustifolia, Eucalyptus camaldulensis, Ocimum basilicum, Otostegia integrifolia, Persea americana, Pterolobium stellatum, Vernonia amygdalina (Kahaliw, 2016) and Anethum graveolens (Balcha et al., 2014). Particularly, Otostegia integriololia (Kahaliw, 2016; Enyew et al., 2014); Persea americana (Giday, 2009a, 2009b; Lulekal et al., 2008; Wube et al., 2005), Croton macrostachys (Giday, 2009a, 2009b; Lulekal et al., 2008; Wube et al., 2005), Eucalyptus camaldulensis (Giday, 2009a, 2009b; Lulekal et al., 2008; Wube et al., 2005) and Anethum graveolens (Balcha et al., 2014). Particularly, Otostegia integriololia (Kahaliw, 2016; Enyew et al., 2014) Persea americana (Kahaliw, 2016), Pterolobium stellatum (Forsk), Brenaon (Kahaliw, 2016; Balcha et al., 2014) and Jasminum abysinicum (Hochst; Geyid et al., 2005) were reported to show significant ability to kill mycobacterial species (Table 3). This was also indicated in other studies. Experimental investigations of available anti-TB TMPs are much important for the purpose of potential identification of new anti-tuberculosis drug regimens that further assist standardization of plant-based anti-TB recipes (Bunalema et al., 2014; Ibekwea et al., 2014; Arya, 2011) but in Ethiopia much remains to be done.  

### 5. Conclusion

In Ethiopia, TB remains one of the most difficult public health concerns and majority of its people across the country still rely on a number

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**Table 4. List of medicinal plants with documented experimental/clinical evidence for anti-mycobacterial activity.**

| Botanical name | Family Name | Parts used | Effectiveness | Solvent/Extraction done by | References |
|----------------|-------------|------------|---------------|---------------------------|------------|
| Allium ursinum | Liliaceae    | Bu         | Reported as effective | Methanolic extract | (Balcha et al., 2014) |
| Anethum graveolens | Apiaceae | AP | Reported as negative | Methanolic extract | (Balcha et al., 2014) |
| Artemisia abyssinica | Lamiaceae | Lv | Reported as effective | 80% methanolic crude extract | (Gemechu et al., 2013) |
| Buddleja polystachia | Loganiaceae | Lv | Reported as negative | Methanolic extract | (Balcha et al., 2014) |
| Calpurnia aurea. | Fabaceae | Rt | Reported as effective | 80% methanolic crude extract | (Gemechu et al., 2013; Zenebe et al., 2012) |
| Carissa edulis Vahl | Apocynaceae | Rt | Failed | Chloroform-maceration | (Kahaliw, 2016) |
| Clasena antisata | Rutaceae | Lv | Reported as effective | Crude aqueous and mesh extracts | (Gizachew et al., 2013; Vineger and Yewhalaw, 2007) |
| Dodonea angustifolia | Sapindaceae | Lv | Reported as effective | Methanolic extract | (Balcha et al., 2014) |
| Eucalyptus camaldulensis | Myrtaceae | Lv | Reported as effective | 80% Methanolic crude extract | (Gemechu et al., 2013; Birhane et al., 2011) |
| Jasminum abysinicum. | Oleaceae | AP | Reported as effective | Crude aqueous and methanolic extract | (Gizachew et al., 2013; Wolde and Gebre-Mariam, 2002; Desissa and Birgogli, 2000; Vineger and Yewhalaw, 2007) |
| Myrrhine africana | Myrrhaceae | Lv | Reported as effective | Crude aqueous and methanolic extract | (Gizachew et al., 2013; Wolde and Gebre-Mariam, 2002; Desissa and Birgogli, 2000; Vineger and Yewhalaw, 2007) |
| Ocimun basilicum | Lamiaceae | Sd | Reported as effective | 80% methanolic crude extract | (Gemechu et al., 2013) |
| Ootostegia integrifolia | Lamiaceae | Rt | Reported as effective with significant Anti-MTB activity | Chloroform-maceration/80% methanol-solvent | (Kahaliw, 2016; Geyid et al., 2005) |
| Persea americana | Lauraceae | Lv | Reported as effective with significant Anti-MTB activity | Acetone/80% methanol | (Kahaliw, 2016) |
| Pterolobium stellatum | Fabaceae | Rt | Reported as effective with significant Anti-mycobacterial activity | Chloroform/80%-maceration methanol-solvent | (Kahaliw, 2016; Balcha et al., 2014) |
| Vernonia amygdalina. | Asteraceae | Rt | Failed | Chloroform-maceration | (Kahaliw, 2016) |
| Warburgia Ugandensis | Canellaceae | Ba | Reported as effective with significant Anti-mycobacterial activity | | (Giday, 2009a, 2009b; Lulekal et al., 2008; Wube et al., 2005) |
| Croton macrostachys | Euphorbiaceae | LV | Reported as effective with significant Anti-mycobacterial activity | Methanolic extract | (Gizachew et al., 2013; Geyid et al., 2005) |
| Cucurbita abyssinica | Cucurbitaceae | Rt | Reported as effective its juice has saponin as an active substance and is used to treat TB | | (Dawit and Estifanos, 1991) |
| Clematis simensis | Ranunculaceae | AP | Reported as effective | Methanolic extract | (Geyid et al., 2005) |
of plants for its treatment. However, majority of these anti-TB plant species used by herbal practitioners are not supported with scientific investigation, and this warrants further experimental and clinical validations of these commonly used TMPs of TB. Moreover, the efficacy, toxicity and safety tests should be initiated and this would help in the rapid identification of new anti-TB regimens, and possibly it will lead to a more effective drug development that could help in combating against the rapidly emerging and changing strains of TB etiologies with specificitities in some localities.

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