

## Review Article



# Potential therapeutic uses of *Moringa stenopetala*: a scoping review

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Received: Jun 16, 2020

Accepted: Aug 22, 2020

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### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

### Author Contributions

Conceptualization: Hadis M; Data curation:

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## ABSTRACT

Anecdotal claims about the therapeutic “miracles” of the plant *Moringa stenopetala* to various human diseases are widespread in Ethiopia. However, there are no existing published systematic reviews to support or refute these assertions. This scoping review aimed to systematically examine and summarize the range and nature of the literature on potential and actual therapeutic uses of *M. stenopetala* in order to identify research gaps and inform researchers and policymakers. The scoping review used the methodological framework of Arksey & O'Malley for scoping reviews and recommendations by Levac and colleagues. We searched the Cochrane Library, PubMed, WorldCat, Epistemonikos, and Google Scholar. To ensure the search was as comprehensive as possible, we also searched grey literature sources such as OpenGrey. We included studies that attempted to evaluate the therapeutic value of *M. stenopetala* on any health outcome in any context. We excluded reports about the effects of *M. stenopetala* on non-human health and non-research reports. We screened 2,946 records and included 56 studies. We found antibacterial, antifungal, antiparasitic, antidiabetic, antioxidants, antihypertensive, anti-inflammatory and analgesic, antidyslipidemia, safety (toxicity, and teratogenic effects), anticancer and fertility studies. All except 4 studies reported the potential therapeutic effects of *M. stenopetala* on either one or more infections or ailments. Two studies reported the absence of antibacterial and antiparasitic activities and 2 studies reported safety concerns; 1 reported cytotoxic effect while the other reported the teratogenic effect of the plant at higher doses. No clinical trials were found. The review found that many claims accorded to *M. stenopetala* have scientific bases and that the plant has potential as a possible source of herbal medicinal products. Further studies on the toxicity of the plant, randomized trials, and pre-requisites for randomized trials such as good manufacturing practices should be addressed in the future to tap into the therapeutic potential of the plant.

**Keywords:** Moringa; Cabbage tree; Antihypertensive agents; Antifungal agents; Antioxidants; Phytotherapy

## INTRODUCTION

*Moringa stenopetala* (Bak. f.) Cufod commonly known as Moringa belongs to a single genus of the family *Moringaceae* whose center of endemism is in northeast tropical Africa. The genus has 14 species in the tropics and subtropics.<sup>1</sup> *M. stenopetala* is a tree indigenous to Ethiopia, Kenya, and Somalia.<sup>2</sup> In Ethiopia it is known by different vernacular names: 'Haleko' in *Gofa* and *Wolayta* areas, 'Shelagta' in the *Konso* language, 'Shiferaw' in Amharic.<sup>2</sup> *M. stenopetala* is cultivated in terraced fields, gardens, and small towns in Ethiopia, it also grows naturally in riverine and *Acacia-Commiphora* woodlands.<sup>2,3</sup> It is cultivated mainly for its leaves which are boiled and eaten like cabbage (hence sometimes called 'cabbage tree') and is available for sale in local markets.<sup>2,4</sup>

Traditional claims to the uses of *M. stenopetala* are many and diverse ranging from serving as food for human consumption (cabbage), animal feed, and to a being medicinal plant for a range of human and animal diseases. Over 5 million people depend on *M. stenopetala* as a vegetable source in southern Ethiopia.<sup>5</sup> The *Turkana* (a *Nilotic*) people native to the *Turkana* district in northwest Kenya take an infusion of the leaves orally as a remedy for leprosy. The *Njemps*, a tribe in the Rift Valley province in Kenya, chew the bark to relieve coughs and use bark extracts to accelerate the expulsion of the placenta in both humans and domestic animals. The *Konso* people (an ethnic group in south-central Ethiopia) use it to prevent colds and anemia; the *Dirashe* and *Burji* people in southern Ethiopia use it to relieve indigestion and for treating dysentery.<sup>3,5</sup> Around Arba Minch, a town in southern Ethiopia, the decoction of leaflets and roots of *M. stenopetala* is used for treating malaria, diabetes, hypertension, asthma, common cold, wound, stomach problem, to expel retained placenta.<sup>6</sup> Other uses of the plant among others include soil conservation, providing shade and acting as a windbreaker, fuelwood, fence material, and also serving as an ornamental tree.<sup>2</sup>

As a result of the medicinal and nutritional claims accorded to *M. stenopetala* and due to the positive preliminary results obtained from various scientific experiments the attention given to *M. stenopetala* by entrepreneurs,<sup>7</sup> non-governmental organizations,<sup>8</sup> academia,<sup>9,11</sup> the mass media,<sup>12,14</sup> civil societies,<sup>15</sup> and policy makers<sup>8</sup> has intensified. The Ethiopian government is providing funding for research and development of *M. stenopetala* for therapeutic usage. There are now sachets of *M. stenopetala* powder sold in supermarkets in Ethiopia as a purported treatment for hypertension, hypotension, poor circulation, headaches, excess cholesterol, intestinal parasites, gastritis, lung problems, asthma, and 300 other conditions. A similar claim is made about its sister plant, *Moringa oleifera*, a tree that is indigenous to India.<sup>16</sup> There are now studies that report patients take *M. stenopetala* leaf powder for treating hypertension may be as a result of the attention given to this plant.<sup>17</sup>

To inform the public, donors, academia, policymakers, and other stakeholders and to make effective, judicious use of the available evidence regarding *M. stenopetala* and provide future research direction, the scientific evidence regarding the plant should be summarized, analyzed and presented in an easily accessible format.

## METHODS

The scoping review used the methodological framework of Arksey & O'Malley for scoping reviews<sup>18</sup> and recommendations on the framework by Levac and colleagues.<sup>19</sup> A protocol was developed before the start of the review.

### Ethics approval

Since this review involves collecting, reviewing, and summarizing data that is already in the public domain, it did not require ethics approval from an Institutional Review Board (IRB).

### Identifying relevant studies

The following databases were searched to find relevant studies: the Cochrane Library, PubMed, WorldCat, Epistemonikos, and Google Scholar. To ensure the search is as comprehensive as possible, grey literature sources such as OpenGrey, databases of relevant organizations such as the World Health Organization (WHO), Food and Agricultural Organization (FAO), United Nations International Children's Emergency Fund (UNICEF), and Addis Ababa University electronic library were included. There were no, language, publication type or date limits. A search string broad enough, *M. stenopetala*, was used in all databases not to miss any potentially relevant study. The first search was undertaken on 22nd October 2018; it was updated on 19th May 2020.

### Study selection

Studies that attempt to evaluate the therapeutic potential of *M. stenopetala* on any human health outcome in any context were considered for inclusion. All types of experiments: studies on human subjects, animal models, and *in vitro* studies were included. Any form of plant preparation regardless of the type of extraction, type of solvents, doses, type of plant parts (leaf, root, bark, and wood) were included. All publications lacking scientific design and publications on non-human ailments and infections were excluded.

Two authors (MH and YG) independently screened the titles and abstracts of all search results and determined eligibility as determined by the inclusion criteria mentioned above. Full texts of all potentially eligible were retrieved. The first author did the screening of the full-text articles; the team was consulted whenever there is any doubt regarding the legitimacy of a study.

### Data extraction

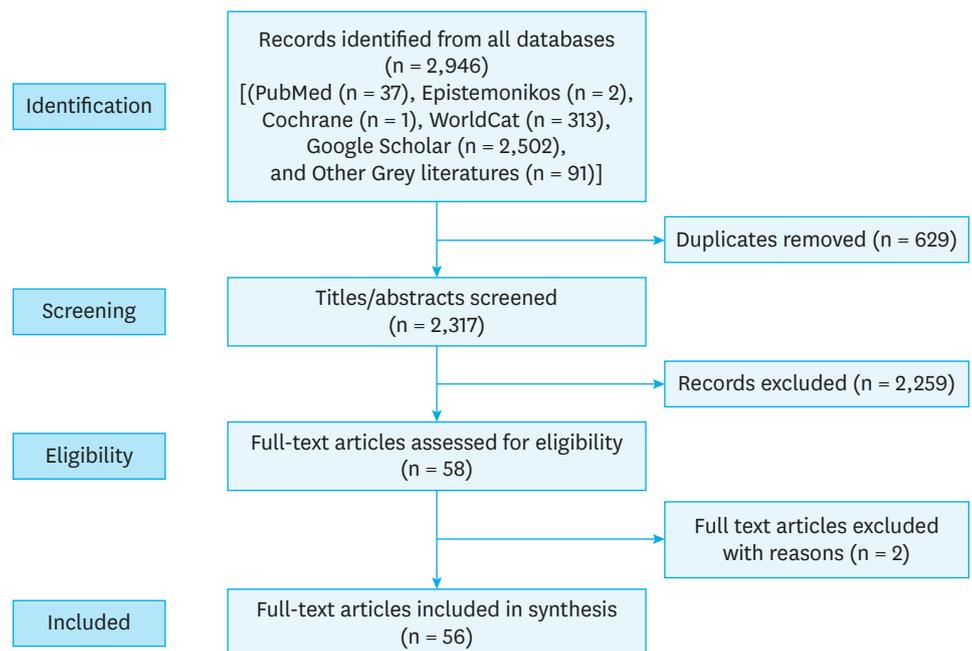
Relevant information from selected studies was extracted using a form developed by the team. The data collection form included the following information: author(s), year of publication, study location, aim(s) of study, study design, type and duration of intervention, type of comparator, study population, clinical setting, study population, and key findings as they relate to the scoping review question. Data were extracted by MH with a consultation with the team.

## RESULTS

The search results and selection process are summarized in **Fig. 1**. The searches from all the databases yielded 2,946 records. After removing duplicates and screening the titles and abstracts we excluded 2,888 studies. Excluded studies comprised more duplicates that escaped the first screening of duplicates due to indexing differences, and studies which are beyond the scope of the scoping review like water clarification of *M. stenopetala* and agronomic studies of the plant. Full articles of 58 potentially eligible studies were retrieved for further screening; out of which 2 studies were excluded. Studies excluded and the reasons for excluding them are summarized in **Table 1**.<sup>20,21</sup>

**Table 1.** Studies excluded and reasons for exclusion

Authors	Year	Aims/objective of the study	Study design	Type of intervention (Moringa preparation)	Key findings	Reasons for exclusion
Meskerem and Boonkaewwan <sup>20</sup>	2013	To assess the protective effects of <i>M. stenopetala</i> leaf supplemented diets on <i>Eimeria tenella</i> infected chickens	<i>In vivo</i> study in chickens	Leaf powder and ethanol extract	These results suggest that <i>M. stenopetala</i> has a protective effect against <i>E. tenella</i> infection in chickens. However, Moringa-supplemented diets did not reduce mortality.	The study was on a zoonotic disease not on a human disease
Assefa et al. <sup>21</sup>	2015	To investigate the effects of thermal treatment of aqueous extracts of <i>M. stenopetala</i> leaves on phenolic and flavonoid content, antioxidant and alpha-amylase inhibition activities	<i>In vitro</i>		Lose of phenolic content, antioxidant, and alpha-amylase inhibition activities at decoction time of 15 minutes. Cooking practice should not exceed 10 minutes!	The study was not about therapeutic uses



**Fig. 1.** PRISMA flow diagram for the scoping review process.

### Description of included studies

All included studies were carried between 1980 and 2020. The interest in *M. stenopetala* research has increased overtime especially since 2011. All studies were preclinical; animal or *in vitro* studies except one which was an observational study on humans. The majority of the studies were conducted on *M. stenopetala* collected from Ethiopia mainly from southern Ethiopia; only a few studies were from Kenya and one from Sudan.

### Scope of included studies

The range of experiments on potential therapeutic uses of *M. stenopetala* includes antibacterial, antifungal, antiparasitic, antidiabetic, antioxidants, antihypertensive (diuretic), anti-inflammatory and analgesic, antidyslipidemia, safety (toxicity), anticancer, teratogenic and fertility studies. The overwhelming majority of studies were conducted on the leaves.

### Studies on antibacterial and antifungal activities

Twelve studies have reported on *in vitro* antimicrobial and antifungal activity of *M. stenopetala* on common human pathogens. Various extracts were used from different parts of the plant.

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**Table 2.** Summary of studies on antibacterial and antifungal activities of *M. stenopetala*

Authors	Year	Extract	Pathogen	Main finding
Walter et al. <sup>22</sup>	2011	Methanol and n-hexane extracts of seeds	<i>S. typhi</i> , <i>V. cholerae</i> , and <i>E. coli</i>	For methanol extract, the highest inhibitions were observed on <i>E. coli</i> , <i>S. typhi</i> , and <i>V. cholerae</i> respectively; while for n-hexane extract, a higher inhibition was seen on <i>S. typhi</i> than on <i>V. cholerae</i> and <i>E. coli</i> .
Biffa <sup>23</sup>	2005	Methanolic and aqueous extracts of bark and leaf	<i>S. aureus</i> , <i>S. agalactiae</i> , and <i>S. dysgalactiae</i>	Both extracts have potent microbial growth inhibition effects.
Mitiku and Yilma <sup>24</sup>	2017	Silver nanoparticles from aqueous extract of leaves	<i>E. coli</i> and <i>S. aureus</i>	Synthesized nanoparticles from aqueous extract have antibacterial activity.
Chekesa and Mekonnen <sup>25</sup>	2015	Leaves, stem bark, root bark and seed extracts of methanol, ethyl acetate, and chloroform	<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>E. coli</i> , and <i>S. boydii</i>	<i>S. aureus</i> was found to be the most susceptible bacteria to crude 80% methanol extract of seeds, chloroform fraction, and ethyl acetate extract of root barks. <i>P. aeruginosa</i> was the most resistant bacteria to all crude extracts.
Eilert et al. <sup>26</sup>	1981	Ethyl acetate fraction of the aqueous extract of seeds	<i>Bacillus</i> spp., <i>Serratia</i> spp., <i>S. aureus</i> , <i>Mycobacterium</i> spp., and fungi spp.	(a-L-Rhamnosyloxy)benzyl isothiocyanate was identified as an active antimicrobial agent form seed of <i>M. oleifera</i> and <i>M. stenopetala</i> . The compound acts on several bacteria and fungi.
Mechesso et al. <sup>27</sup>	2016	Ethanol extract of leaves	<i>S. aureus</i> , <i>B. cereus</i> , and <i>Salmonella</i> spp.	<i>M. stenopetala</i> showed no antimicrobial activity.
Sahilu <sup>28</sup>	2010	Crude water extract of seeds	<i>E. coli</i> , <i>P. aeruginosa</i> , <i>S. boydii</i> , <i>S. aureus</i> , and <i>S. pneumoniae</i>	The crude water extract of <i>M. stenopetala</i> has antibacterial activity.
Tesemma et al. <sup>29</sup>	2013	Crude petroleum ether, chloroform, acetone, methanol, and water extracts of root wood	<i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , and <i>S. typhimurium</i>	<i>M. stenopetala</i> has antibacterial activity; acetone extract being the most active.
Raghavendra et al. <sup>30</sup>	2016	Methanol extract of leaves	<i>S. aureus</i> and <i>Bacillus subtilis</i> , <i>P. aeruginosa</i> , <i>E. coli</i> and <i>Ralstonia solanacearum</i>	<i>M. stenopetala</i> has antimicrobial activity.
Manilal et al. <sup>31</sup>	2020	Diethyl ether, ethyl acetate, methanol, and ethanol extracts of leaves	Methicillin-resistant <i>S. aureus</i>	<i>M. stenopetala</i> exhibited significant antibacterial activity.
Seleshe and Kang <sup>32</sup>	2019	Chloroform, methanol, ethanol and water extract of leaves	<i>K. pneumoniae</i> , <i>B. cereus</i> , <i>S. pneumoniae</i> , <i>S. aureus</i> , <i>L. monocytogenes</i> , <i>E. coli</i> , <i>S. typhimurium</i> , <i>C. albicans</i> , and <i>A. niger</i>	<i>M. stenopetala</i> leaves have great potential in the development of food preservatives and antibiotic drugs.
Adane et al. <sup>33</sup>	2019	Petroleum ether, chloroform, and acetone extracts of root bark. The acetone crude extract was subjected to column chromatographic separation	<i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , and <i>S. typhimurium</i>	Four compounds: stigmasterol, ursolic acid, tasnemoxide, and oleic acid were isolated from acetone extracts of root barks of <i>M. stenopetala</i> . The compounds showed comparable antibacterial activities to each other.

All the studies (except one) have shown activities on target pathogens. **Table 2** summarizes the main aspects of the studies.<sup>22-33</sup>

### Studies on antidiabetic activities

Twelve studies reported on antidiabetic activities of *M. stenopetala* (**Table 3**).<sup>34-45</sup> Ten of them were animal studies on either rabbits, mice, or rats while 2 were *in vitro* studies. All the studies were on leaf extracts, except one which also included seeds using various solvents. All the studies have reported favorable results on reducing blood sugar and other diabetic symptoms (**Table 3**).<sup>34-45</sup>

### Studies on antioxidant activities

Seven *in vitro* studies reported on the antioxidant activity of *M. stenopetala* leaves. Only 1 study has besides evaluated extract of seeds. All the studies have demonstrated that *M. stenopetala* has antioxidant activity (**Table 4**).<sup>24,34,41,46-49</sup>

### Studies on antiparasitic activities

Three *in vivo* studies and 4 *in vitro* studies and 3 both *in vitro* and *in vivo* study reported on the antiparasitic activities of *M. stenopetala* (**Table 5**).<sup>6,9,50-57</sup> Seven of the studies used extracts of

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**Table 3.** Summary of studies on antidiabetic activities of *M. stenopetala*

Authors	Year	Solvent/fractionate	Experimental animal	Main finding
Awoke et al. <sup>34</sup>	2019	Methanol-water extract and ethyl acetate fractionate	Swiss albino mice	Ethyl acetate fraction of <i>M. stenopetala</i> treatment resulted in a significant reduction of fasting blood glucose level.
W/kidan <sup>35</sup>	2017	Aqueous extract	Swiss albino rats	Repeated oral administration of <i>M. stenopetala</i> aqueous extract has beneficial effects on hyperglycemia.
Toma et al. <sup>36</sup>	2015	Aqueous ethanol extract and n-butanol fraction	Swiss albino rats	Both extracts possess antihyperglycemic effects and alleviate streptozotocin-induced pancreatic damage in diabetic rats.
Toma et al. <sup>37</sup>	2014	Hydroalcoholic extract	<i>In vitro</i> study	<i>M. stenopetala</i> has beneficial biochemical effects by inhibiting intestinal $\alpha$ -glucosidase, pancreatic cholesterol esterase, and pancreatic lipase activities. A daily supplement intake of the leaves of <i>M. stenopetala</i> may help in reducing hyperglycemia.
Sileshi et al. <sup>38</sup>	2014	Crude 70% ethanol extract, butanol fraction, dichloroethane fraction, hexane fraction and aqueous residue of a solvent-solvent fraction	Swiss albino mice	The crude ethanol extract and solvent-solvent fractions, as well as chromatographic fractions, have an antihyperglycemic effect.
Nardos et al. <sup>39</sup>	2011	Ethanol extract, aqueous extract, petroleum ether fraction, chloroform fraction, butanol fraction and the aqueous residue	Swiss albino mice	Both extracts and chloroform fraction, butanol fraction and aqueous residue reduced blood glucose levels significantly.
Mussa et al. <sup>40</sup>	2008	The crude aqueous extract, chloroform fraction, n-butanol fraction, and aqueous residue fraction	Swiss albino mice	The crude extracts, as well as the n-butanol and chloroform fractions of the leaves of <i>M. stenopetala</i> , have both hypoglycemic and antihyperglycemic effects.
Habtemariam <sup>41</sup>	2015	Methanol extract, petroleum ether, chloroform, ethyl acetate, n-butanol, and water fractions	<i>In vitro</i> on human pancreatic cell line	<i>M. stenopetala</i> extract and its major active constituent, rutin, can protect the human pancreatic $\beta$ -cells, 1.4E7 cells, from oxidative damage and/or cell death. The study for the first time provided direct evidence into the potential nutritional value and antidiabetic potential of <i>M. stenopetala</i> components.
Asres <sup>42</sup>	1993	Petroleum ether, ether, chloroform, acetone, and methanol extracts	Rabbits	Of all the extracts tested, only acetone extract exhibited significant hypoglycemic effect.
Makonnen et al. <sup>43</sup>	1997	Aqueous extract	Rabbits	The extract lowered blood glucose.
Ghebreselassie et al. <sup>44</sup>	2011	Aqueous extract	Swiss albino mice	Extract reduced serum glucose level.
Toma et al. <sup>45</sup>	2012	Butanol fraction	Mice	Significant reduction of fasting blood sugar.

**Table 4.** Summary of studies on antioxidant activity of *M. stenopetala*

Authors	Year	Extract/fraction	Assays for determining antioxidant activity	Main finding
Mitiku and Yilma <sup>24</sup>	2017	Silver nanoparticles from aqueous extract of leaves	Hydrogen peroxide scavenging assay	Synthesized AgNPs showed better antioxidant activity than standard ascorbic acid.
Dadi et al. <sup>46</sup>	2018	Different drying methods followed by 50% and 70% ethanol extraction; and 100% aqueous extraction of leaves	DPPH and ABTS radical scavenging assays	Freeze drying yielded more bioactive compounds and showed higher antioxidant activity compared to oven drying. The 70% of ethanol extraction gave the highest yield compared to 50% extraction and aqueous extraction.
Habtemariam <sup>41</sup>	2015	Methanol extract of leaves and seeds and petroleum ether, CHCl <sub>3</sub> , ethyl acetate, n-butanol and water fractions	DPPH	Two major antioxidants were identified: rutin and neochlorogenic acid. Both the crude extract and rutin displayed protective activity of human pancreatic $\beta$ -cells from oxidant-induced cell death.
Hagos et al. <sup>47</sup>	2018	Methanolic and aqueous extracts of leaves	Hydrogen peroxide radical scavenging assay	<i>M. stenopetala</i> is a promising source of natural antioxidants.
Kassaw et al. <sup>48</sup>	2016	Methanolic extract of leaves	Hydrogen peroxide radical scavenging assay	Methanolic extract of <i>M. stenopetala</i> has a good scavenging activity.
Tebeka and Libsu <sup>49</sup>	2014	Aqueous methanol extract of leaves	DPPH assay, FRAP, peroxide value, and conjugated diene hydroperoxide assays	<i>M. stenopetala</i> is able to scavenge DPPH radicals, reduce K <sub>3</sub> [Fe(CN) <sub>6</sub> ] to K <sub>4</sub> [Fe(CN) <sub>6</sub> ] (reducing power ability) and inhibit oxidation of sunflower oil.
Awoke et al. <sup>34</sup>	2019	Methanol-water extract and ethyl acetate fractionate of leaves	DPPH assay	The ethyl acetate fraction of <i>M. stenopetala</i> showed the highest total phenolic content and strong free radical scavenging potential.

DPPH, 2,2-diphenyl-1-picrylhydrazyl; ABTS, 2,2'-Azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) diammonium salt; AgNP, green synthesis of silver nanoparticle.

leaves while 2 studies used roots and 1 study used the essential oil of seeds. All the studies reported that *M. stenopetala* has antiparasitic activities except one study which reported that the column fraction of water extract of the root of *M. stenopetala* did not show antiparasitic activity on *Plasmodium berghei* (Table 5).<sup>6,9,50-57</sup>

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**Table 5.** Summary of studies on antiparasitic activities of *M. stenopetala*

Authors	Year	Extract	Parasite	Main finding
Asnake <sup>50</sup>	2004	Water and ethanol extracts of root and leaves	<i>P. berghei</i> in mice	Water extract of the root of <i>M. stenopetala</i> showed significant suppressive effect on <i>P. berghei</i> .
Kifleyohannes et al. <sup>51</sup>	2014	Methanol and water extract of leaves	<i>T. congolense</i> in mice	The extracts have a suppressive effect on parasitemia; the effect was comparable to the commercial drug, diminazene aceturate.
Kinuthia et al. <sup>52</sup>	2015	Water extract of leaves	<i>L. major</i> in mice and <i>in vitro</i>	Crude aqueous extract of <i>M. stenopetala</i> shows antileishmanial activity at low toxicity.
Kinuthia et al. <sup>53</sup>	2014	Crude methanolic extracts of leaves	<i>L. major</i> in mice and <i>in vitro</i>	Lowered the amastigotes burden in the spleens of mice.
Kinuthia et al. <sup>54</sup>	2013	Crude aqueous extracts of leaves	<i>L. major</i> in mice and <i>in vitro</i>	Blends of crude aqueous extracts of <i>M. stenopetala</i> , <i>C. citrinus</i> , and <i>A. sativum</i> possess <i>in vitro</i> and <i>in vivo</i> antileishmanial activity against <i>L. major</i> promastigotes and amastigotes.
Mekonnen and Gessesse <sup>6</sup>	1998	Crude ethanol extract of leaves	<i>L. donovani in vitro</i>	<i>M. stenopetala</i> has antileishmanial activity.
Mekonnen et al. <sup>9</sup>	1999	Acetone and ethanol extracts of leaves and root bark	<i>T. brucei</i> , <i>T. cruzi</i> and <i>L. donovani in vitro</i>	The fresh root wood ethanol extract and the dried leaves acetone extract were found to be active against <i>T. brucei</i> .
Nibret and Wink <sup>55</sup>	2010	The essential oil of seeds	<i>T. brucei in vitro</i>	The oil and its main compound, benzyl isothiocyanate showed potent trypanocidal activities.
T/Mariam <sup>56</sup>	2005	Column fractions of water extract of roots	<i>P. berghei</i> in mice	Fractions did not show a significant effect on parasitemia as compared to the reported activity in its crude form.
Bekele et al. <sup>57</sup>	2013	Petroleum ether:ethyl acetate (50:50) extract of roots	<i>L. aethiopica in vitro</i>	Compounds isolated have promising antileishmanial activities.

**Table 6.** Summary of studies on antihypertensive activities of *M. stenopetala*

Authors	Year	Extract (other preparation of plant)	Lab animal	Main finding
Mengistu et al. <sup>58</sup>	2012	Aqueous crude leaf extract	Guinea pigs for the <i>in vivo</i> study and descending thoracic aorta for the <i>in vitro</i> study	<i>M. stenopetala</i> has blood pressure-lowering effect.
Geleta et al. <sup>11</sup>	2016	Aqueous and 70% ethanol extracts of leaves	Wistar rats	Both extracts prevented blood pressure increment significantly compared to the standard drug.
Fekadu et al. <sup>59</sup>	2017	Aqueous crude extract and hot tea infusion of leaves	Wistar rats	Both the aqueous crude extract as well as the hot tea infusion of the leaves possess significant ( $P < 0.01$ ) diuretic, natriuretic, and kaliuretic effects. The aqueous crude extract (125 mg/kg) and hot tea infusion (2 tsp) displayed the highest diuretic activity (101% and 96%, respectively) comparable to the reference drug, furosemide (10 mg/kg).
Geleta et al. <sup>60</sup>	2016	Aqueous crude, 70% ethanol crude, aqueous fraction of aqueous crude, ethyl acetate fraction of aqueous crude extracts of leaves	<i>In vitro</i> (thoracic aortic ring of a guinea pig)	All extracts showed a relaxant (vasodilatory) effect in pre-contracted isolated whole, spirally cut thoracic aortic strips of guinea pigs in a dose-dependent manner.
Geleta et al. <sup>61</sup>	2015	Hydro-ethanol extract of leaves	Swiss albino mice	The crude hydro-ethanolic extract of <i>M. stenopetala</i> leaves possesses a diuretic activity in mice model of diuresis.

### Studies on antihypertensive activities

Five studies using leaf extracts of different solvents and tea infusion of the leaves have demonstrated the potential of *M. stenopetala* in lowering blood pressure. Four of the studies, 3 were *in vivo* studies one was an *in vitro* study. The mechanisms of lowering blood pressure include a diuretic, natriuretic, kaliuretic, and vasodilatory effects (Table 6).<sup>11,58-61</sup>

### Studies on analgesic and anti-inflammatory activities

Two *in vivo* and one *in vitro* studies on the leaf extract of *M. stenopetala* leaves have shown that the plant has an analgesic and anti-inflammatory potential (Table 7).<sup>62-64</sup>

### Studies on antidiyslipidemia activities

Two *in vivo* and 1 *in vitro* studies (Table 8) have reported on antidiyslipidemia activities of *M. stenopetala* leaf extracts.<sup>11,36,37</sup> All the extracts have shown positive results in improving lipid profiles.

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**Table 7.** Summary of studies on analgesic and anti-inflammatory activities of *M. stenopetala*

Authors	Year	Extract	Laboratory animal	Main finding
Geremew et al. <sup>62</sup>	2015	Methanol leaf extract	Swiss albino mice	The extract showed a dose-dependent significant reduction of pain in analgesia models ( $P < 0.001$ ).
Tamrat et al. <sup>63</sup>	2017	Chloroform, aqueous and methanol fractions of leaves	Swiss albino mice	All the extracts have shown significant central and peripheral analgesic activities and they also significantly reduced carrageenan-induced inflammation.
Mekonnen <sup>64</sup>	1999	Ethanol extract of leaves	<i>In vitro</i> (tissues of albino mice and guinea pigs)	The extract has shown antispasmodic and oxytocic activities.

**Table 8.** Summary of studies on antidyslipidemia activity of *M. stenopetala*

Authors	Year	Extract	Laboratory animals	Main finding(s)
Toma et al. <sup>37</sup>	2014	Hydro-ethanol extract of the leaves	<i>In vitro</i> lab study	The hydro-ethanol extract of the leaves has demonstrated antihyperlipidemic activity.
Toma et al. <sup>36</sup>	2015	The aqueous ethanol extract and n-butanol fraction of leaves	Swiss albino rats	Aqueous ethanol and n-butanol extracts of <i>M. stenopetala</i> leaves have improved lipid profiles (significantly decreased the levels of cholesterol and triglycerides).
Geleta et al. <sup>11</sup>	2016	Aqueous and 70% ethanol extracts of leaves	Wistar rats	The extracts prevented increment of the lipid profile (cholesterol and triglycerides).

### Studies on anticancer activities

There was only one study on the anticancer potential of *M. stenopetala*.<sup>65</sup> The study aimed at identifying potential anticancer agents from the seeds. Water extract of the seeds after defatting by hexane demonstrated cytotoxic activity against the liver hepatocellular HepG2a (human liver cancer cell line) and SH-SY5Y neuroblastoma cells. Subsequent analysis of the extract yielded the principal active constituent glucomoringin isothiocyanate or moringin (4[ $\alpha$ -L-rhamnosyloxy]-benzyl isothiocyanate).

### Studies on thyroid function

A single cross-sectional observational study<sup>66</sup> has evaluated whether consumption of *M. stenopetala* and cassava affect the thyroid function of pregnant women as measured by thyroid-stimulating hormone (TSH), thyroxine (T4), and triiodothyronine (T3). The results did not show any significant difference between the 2 groups.

### Studies on the antifertility activity

The antifertility test was carried using ethanol extract of the leaves in Swiss albino mice showing a 73.3% antifertility effect compared to a control group.<sup>6</sup>

### Safety and toxicity studies

Eight *in vivo* studies and 1 *in vitro* study reported on the safety and toxicity of *M. stenopetala*. Six of the studies were on leaf extracts, and one was on seed and the other one was on leaf, root, and seed of *M. stenopetala*. Two studies have reported safety concerns while the rest of the studies have reported the absence of toxic effects (Table 9).<sup>38,67-74</sup>

## DISCUSSION

Except for 2 experiments which were conducted to see the antibacterial effect of ethanol extract of leaves on pathogenic bacteria<sup>27</sup> and the antiparasitic effect of column fractions of water extract of roots on *P. berghei*<sup>55</sup> which reported no antibacterial and antiparasitic effects and 2 studies<sup>70,74</sup> on the safety of the plant, all the studies have reported that *M. stenopetala* has favorable effects on various pathogens and ailments. Some of the traditional claims<sup>4-6</sup>

## Therapeutic potential of *M. stenopetala*

**Table 9.** Summary of studies on the safety and toxicity of *M. stenopetala*

Authors	Year	Aims/objective of the study	Study design	Type of intervention (Moringa preparation)	Key findings
Sileshi et al. <sup>38</sup>	2014	To evaluate the antihyperglycemic activity and subchronic toxicity of an extract of <i>M. stenopetala</i> leaves in mice.	<i>In vivo</i> study in Swiss albino mice	70% ethanol extract of <i>M. stenopetala</i> leaves	Some effects on the liver of the mice on subchronic administration.
Berger et al. <sup>67</sup>	1984	To assess the toxicological effects of <i>M. stenopetala</i> and <i>M. oleifera</i> seeds.	<i>In vivo</i> study in Sprague Dawley rats	Ground seeds in olive oil	No toxic effects on the gut, heart, and liver were observed.
Geleta et al. <sup>68</sup>	2015	To assess the safety of the extracts and fractions of <i>M. stenopetala</i> leaves.	<i>In vivo</i> study in Wistar rats	Aqueous crude, 70% Ethanol crude, Ethyl acetate fraction and aqueous residue of aqueous crude extracts of leaves	The aqueous leaf extract of <i>M. stenopetala</i> is practically non-toxic to the female Wistar rats when administered orally. Whereas, the repeated oral daily administration has revealed potential damage to the liver in a dose-dependent manner but not to the kidney. Further studies, however, need to be done to confirm this.
Feyissa <sup>69</sup>	2015	To investigate the acute and sub-chronic toxicities of aqueous extracts of leaves of <i>M. stenopetala</i> in rats.	<i>In vivo</i> study in albino rats	Crude aqueous extract of the leaves of <i>M. stenopetala</i>	There was no significant difference in the gross histopathology of the thyroid gland, adrenal gland, and pancreas of the experimental rats as compared to the control group.
Mekonnen et al. <sup>70</sup>	2005	To establish the effect of <i>M. stenopetala</i> extracts on the viability and metabolic integrity of cultured HEPG2 cells.	<i>In vitro</i> study on HEPG2 cells	Water and ethanol extracts of leaves, ethanol extracts of seed and root	The ethanol extract of the leaves and seeds from <i>M. stenopetala</i> show that they contain toxic substances that are extractable with organic solvents or are formed during the process of extraction with these solvents.
Musa et al. <sup>71</sup>	2015	To evaluate the acute toxic effect of butanol fraction of the leaves of <i>M. stenopetala</i> in experimental rats.	<i>In vivo</i> study in rats	Butanol fraction of leaves	Rats treated with up to a dose of 5,000 mg/kg showed no toxic signs on behavior, gross pathology, and body weight, as compared with the controls.
Musa et al. <sup>72</sup>	2016	To investigate the sub-chronic toxic effects of butanol fraction of leaves of <i>M. stenopetala</i> on blood parameters of experimental rats.	<i>In vivo</i> study in rats	Butanol fraction of leaves	Butanol fraction did not produce adverse effects on hematological and biochemical parameters of blood.
Bayu et al. <sup>73</sup>	2020	To investigate the effects of chronic administration of aqueous leaf extract of <i>M. stenopetala</i> .	<i>In vivo</i> study in rats	Crude water extract of leaves	Prolonged administration of extract of <i>Moringa stenopetala</i> at therapeutic doses are safe, but shows sign of mild toxicity as dose increases, with differential effect on male versus female rats.
Teshome <sup>74</sup>	2019	To evaluate the possible teratogenic effects of <i>M. stenopetala</i> leaves in rat embryos and fetuses.	<i>In vivo</i> study in rats	Methanol extract of leaves	Administration of crude extract of <i>M. stenopetala</i> at a higher dose was not safe in pregnant Wistar albino rats; its toxic and teratogenic effects were evidenced by the significant delay in embryonic and fetal development, decrease in maternal weight gain during gestational periods and increase in fetal resorptions and fetal death.

of the medicinal uses of *M. stenopetala* more or less were supported by the studies. The antimalarial,<sup>50,55</sup> anti-diabetic,<sup>34-45</sup> antibacterial (dysentery, wound healing, leprosy, cough,<sup>22-33</sup> and antihypertension<sup>11,58-61</sup> claims were proved in the laboratories. The traditional use of the plant to expel the placenta both in humans and animals is supported by the study whereby the leaf extract showed some oxytocic activity on uterus strips of guinea-pigs and mice.<sup>64</sup> On the other hand, regardless of the favorable reports of the majority of studies, a study<sup>70</sup> has raised concerns on the safety of *M. stenopetala* leaves and seeds when extracted with ethanol which contained toxic substances which may be extractable with organic solvents or formed during the process of extraction. A recent study<sup>74</sup> on methanol extract of the leaves has also signaled the potential teratogenic effect *M. stenopetala* when higher doses are administered in rats. These 2 studies highlight the need for more safety studies on *M. stenopetala*. Besides, this scoping review has shown that all the studies on *M. stenopetala* are preclinical; and the information circulating in the media and on sachets containing powdered *M. stenopetala* in supermarkets in the country that *M. stenopetala* can cure 300 diseases should be taken with great caution as it could mislead the consumer by imparting unwarranted confidence to use the plant substituting prescribed drugs. The concomitant use of the plant with prescribed drugs has already been reported.<sup>17</sup>

From the traditional uses and claims and preclinical evidence, the potential of *M. stenopetala* as a herbal medicine for a variety of infections and ailments is very high. In addition to the favorable results from crude extracts (Tables 2-6), the identification of moringin (4[ $\alpha$ -L-rhamnosyloxy]-benzyl isothiocyanate) from the seeds of the plant,<sup>65</sup> a phytochemical reported to have a chemoprotective effect against cancer, together with the isolation of rutin, a bioflavonoid, with antioxidant and anti-inflammatory properties,<sup>41,75</sup> buttresses the evidence on the potential usefulness of the plant. However, without clinical studies to evaluate the actual benefits and risks, the potential of *M. stenopetala* will remain untapped.

According to United Nations Development Programme (UNDP)/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR),<sup>76</sup> there is a need for clear recommendations regarding data required to support clinical trials in which herbal medicines are evaluated for treatments. Pre-requisites for conducting a clinical trial of a conventional drug involves 4 sets of issues: chemical-manufacturing control (CMC) issues, non-clinical issues, clinical-issues, and ethical issues. Based on these criteria, but adapted to the particular case of traditional medicines clinical trial of herbal products is supported by international organizations.<sup>76</sup> According to the aforementioned reference, a guidance titled 'operational guidance: Information needed to support clinical trials of herbal products',<sup>76</sup> spells out the requirements to be fulfilled to conduct a clinical trial for a herbal product vis-a-vis the requirements for a clinical trial of a conventional drug. Accordingly, a clinical trial of *M. stenopetala* for a particular disease (or diseases) has a long way to go as the studies so far have not generated enough data that are pre-requisites for a clinical trial such as the absence of CMC evidence which is similar for a conventional drug: analysis of 1 or more hypothesized active ingredients for different diseases and ailments (unlike the analysis of the active pharmaceutical ingredients of a conventional drug), specifications, storage conditions, information on 'Good Agricultural Practices', information on Good Manufacturing Practices, etc. Besides, the safety issues raised by studies,<sup>70,74</sup> the pre-requisites for the clinical trial have to be addressed before contemplating clinical trials.

*M. oleifera* indigenous to sub Himalayan regions of India, Pakistan, Asia Minor, Africa, and Arabia and cultivated in many tropical countries is also known for its multipurpose uses including medication for a variety of ailments like that of *M. stenopetala*.<sup>16,41</sup> These similarities of the 2 sister plants further substantiate the potential of *M. stenopetala* as a therapeutic plant.

This review has summarized what is known and what is unknown about *M. stenopetala*, which is getting a great deal of attention as a medicinal plant for many ailments. Though the plant is a very promising candidate as a possible source of therapeutic herbal products the claims on mass media as 'a miracle plant' which could cure 300 diseases is wrong without the evidence from clinical studies. The review has found that traditional claims accorded to *M. stenopetala* have a scientific basis and as a result has shown that the plant has great potential as a possible source of herbal medicinal products. Further studies on the safety of the plant, high-quality evidence studies such as randomized controlled studies, and pre-requisites for clinical trials such as good manufacturing practices should be addressed in the future to tap into the therapeutic potential of the plant. Studies on the plant should be coordinated in such a way that they address the gaps to support clinical trials, instead of repeating random studies. This review could help researchers as a quick reference source. Funding agencies could use this review as a source material to select proposals for funding, which is to support studies that add value to what is already known, not studies which are repetitions. The mass media should try to look for the best available evidence (such as this review) before disseminating

unfounded information. The public should be aware that though *M. stenopetala* has a lot of potential as a therapeutic source for a lot of ailments there is no evidence supported by clinical trials. Without a national coordinating body on the development of *M. stenopetala*, to support its therapeutic, nutritional, and economic potential with scientific evidence the potential of the plant could remain untapped for the foreseeable future. Neighboring countries in the horn of Africa, where *M. stenopetala* is endemic could also benefit from this study.

## ACKNOWLEDGMENTS

The authors are grateful to Dr. Getnet Tizazu and Dr. Worknesh Ayele for helping improve the language when the protocol for the study was being prepared. Dr. Getachew Addis has shared with us his literature from his private collections.

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