Clinical Phytoscience

REVIEW Open Access

Efficacy, safety and phytochemistry of medicinal plants used for the management of diabetes mellitus in Ethiopia: a systematic review

Serawit Deyno[1,2*], Kassahun Eneyew[3], Sisay Seyfe[3] and Elias Wondim[4]

Abstract

Background: Despite tremendous developments in synthetic medicine, medicinal plants are still commonly used for the management of diabetes mellitus. This study synthesized scientific evidence on commonly used medicinal plants for the management of diabetes mellitus (DM) in Ethiopia.

Methods: Databases (PubMed, Cochrane, CINAHL and Google Scholar) have been thoroughly sought and evidence was synthesized.

Results: Thirty studies conducted anti-diabetic activities studies on 19 medicinal plants in Ethiopia. Most of the studies were in vivo studies (25). Others include; clinical study (1), in vitro studies (2), and both in vivo and in vitro study (2). *Trigonella foenum-graecum L.*, clinical study, showed an improved lipid profile in type II diabetic patients. Comparable blood sugar level (BSL) lowering effect to glibenclimide was observed with *Persea Americana* and *Moringa stenopetala*. Noteworthy in vitro half maximal inhibitory concentration (IC 50) of Aloe *megalacantha B* and *Aloe monticola R* were observed. Animal model studies demonstrated the relative safety of the plants extract and phytochemistry studies showed various components.

Conclusion: Medicinal plants used for management of diabetes mellitus in Ethiopia are worthy for further study for pharmacologically active ingredients and clinical evaluation.

Keywords: Medicinal plants, Hypoglycemic, α-Amylase, In vitro, In vivo, Ethiopia

Background

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia due to impaired insulin secretion, defective insulin action or both. Chronic hyperglycemia is associated with long term microvascular complications affecting the cardiovascular, eyes, kidneys, and nerves [1]. The complications include nephropathy, retinopathy, nephropathy, peripheral vascular disease and coronary heart diseases [2]. The complications cause major impact on the lives and well-being of individuals, families and societies.

No successful cure for DM has yet been found but can be managed using insulin, diet modification and oral anti-diabetic agents. Herbal medicines could provide an alternative management. Compromised effectiveness, cost, accessibility, affordability, and tolerability are some of the limitations of current conventional anti-diabetic medicine. African medicinal plants are commonly used in the management of DM and provide an alternative therapy. Research is required on different indigenous plant and herbal formulations. The research will shed

* Correspondence: dserawit@gmail.com; dserawit@std.must.ac.ug
[1]Pharm-BioTechnology and Traditional Medicine Center of Excellence (PHARMBIOTRAC), Mbarara University of Science and Technology, P.O. Box 1410, Mbarara, Uganda
[2]School of Pharmacy, Faculty of Medicine, College of Medicine and Health Sciences, Hawassa University, P. O. Box 1560,, Hawassa, Ethiopia
Full list of author information is available at the end of the article

light on effectiveness and safety of herbal medicines. The findings will help to discover novel drugs and/or optimize the traditional use.

In Ethiopia, there are numerous medicinal plants used for DM and a number of these were assayed for their anti-diabetic activity. An estimated 80 to 90% of Ethiopians use herbal medicine as a primary form of health care [3] and many rural communities continue to depend on it [4]. There are preliminary studies on the scientific evidence of commonly used medicinal plants in Ethiopia though evidences were not synthesized. With a lack of critical appraisal on the currently evidence studies, this study aimed at reviewing information on the reported scientific evidence for effectiveness of medicinal plans used in Ethiopia in the management of DM.

Methods 1

Study design

This systematic review and meta-Analysis was conducted using databases searches and the reporting adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis [5]. PRISMA checklist was included as additional file (see Supplementary file 1).

Search strategy

Databases, PubMed, CINAHL, the Cochrane Central Register of Controlled Trials and clinical trial.gov and Google scholar, were searched from inception to May 25, 2020. The reference lists of all identified articles were searched for additional studies. Flow diagram was used to summarize the number of studies identified, screened, excluded and finally included in the study. Key words used in the search include (Diabetes mellitus OR T1DM OR type I diabetes mellitus OR T2DM OR type 2 diabetes mellitus) AND (Plant* OR herb* OR dietary supplement* OR traditional medicine*) AND (Ethiopia).

Study selection and data extraction

Three reviewers (SS, KE and EW) independently carried out a literature search and examined relevant studies and sequentially screened their titles and abstracts for eligibility. The full texts of potentially eligible studies were retrieved. Disagreements were resolved on discussion with the fourth author (SD). A screening guide was used to ensure that all review authors reliably apply the selection criteria. Human, animal and in-vitro studies which were conducted to examine anti-diabetic effect of medicinal plants in Ethiopia were included. Data extraction was performed using a pre-designed format. Extracted data include first author, study area, scientific, family and local name, study model used, the animal type used, extraction method used, a component of the extract used, duration of treatment, and change in BSL (from diabetic control, from normal control and standard control). A study is included if the effect on diabetic control is reported, otherwise it is excluded.

Definition of terms

Diabetic control refers animals with DM but no standard or experimental treatment is given which could refer a

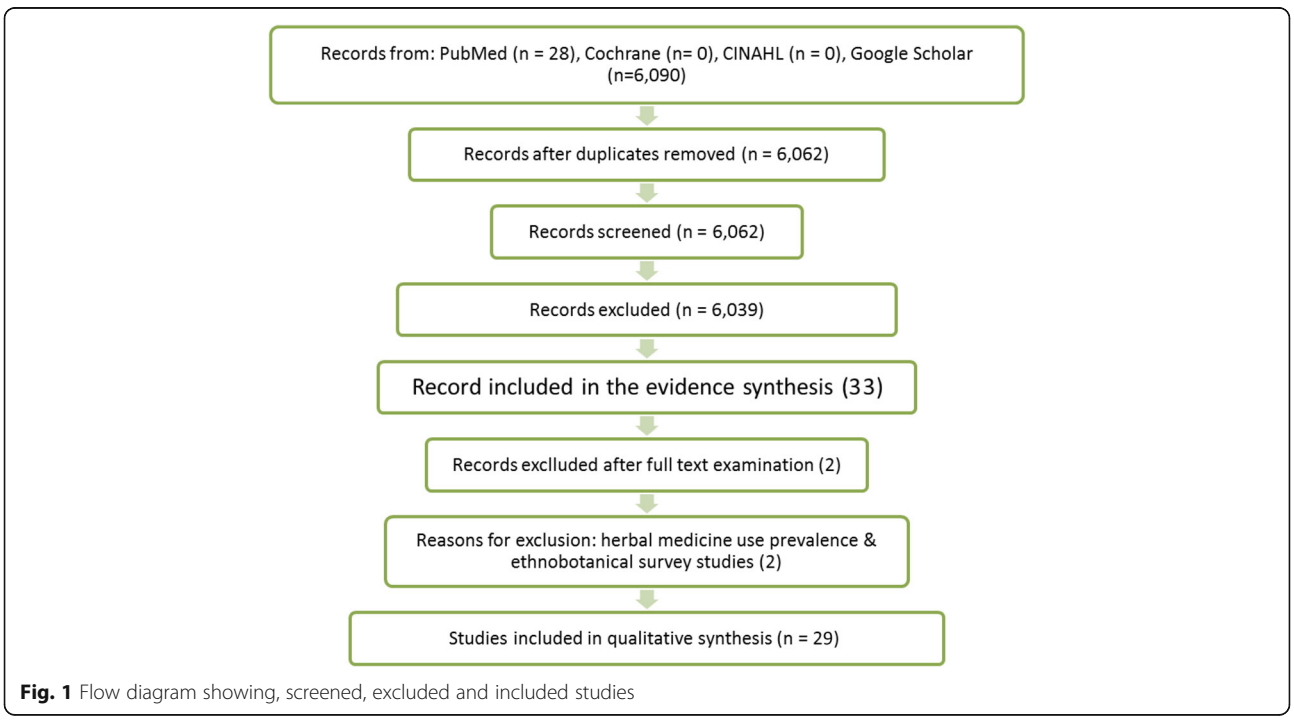

Fig. 1 Flow diagram showing, screened, excluded and included studies

Table 1 Characteristics of included studies

No	Study	Study area	Name of plant (Scientific, family, local)	Model
1.	**Amare** et al., 2020 [35]	Fiche, oromia region	*Aloe pulcherrima* Gilbert and Sebsebe (Aloaceae)	Male Swiss albino mice
2.	**Alema** et al., 2020 [10]	Abiy Addi, Northwest Tigray	*Terminalia brownie Fresen, Combretaceae, Abaloweyba (Am)*	in vitro and STZ-induced mice
3.	**Belayneh e**t al., 2018 [22]	South Gondar zone	*Calpurnia aurea, Fabaceae, digita (Am)*	STZ-induced albino mice
4.	**Belayneh** et al., 2019 [12]	Gondar town	*Datura stramonium L. solanaceae, atefaris (Am)*	STZ-induced diabetic mice
5.	**Birru** et al., 2015 [21]	Lake Tana	*Indigofera spicata Forssk, Fabaceae, yeayitmisir (Am)*	Alloxan-induced albino mice &wistar rats
6.	**Gebremeskel** et al., 2019 [6]	Mekelle	*Trigonellafoenum-graecum*, *Fenugreek, Abish (Am)*	T2DM
7.	**Hammeso** et al., 2019 [14]	SehartiSamre, Mekelle	*Aloe megalacantha* B, Aloaceae, Eret (Am)	STZ -induced mice
8.	**Kifle & Eneyew**, 2020 [34]	South Gondar	Bersama abyssinica Fresen, tena adam (Am)	Male Swiss albino mice
9.	**Kifle et al., 2020** [32]	South Gondar	Bersama abyssinica Fresen	Male Swiss albino mice
10.	**Makonnen** et al., 1997 [17]	Arbaminch area	*Moringa stenopetala, Moringaceae, shiferaw (Am), aleko (Welaytegna)*	Albino rabbits
11.	**Melaku and Amare** et al., 2020 [35]	Wollo, Amhara region	Datura stramonium Linn (Solanaceae)	Male Swiss albino mice
12.	**Mussa** et al., 2008 [11]	Arba Minch	*Moringas stenopetalla*	Alloxan-induced mice
13.	**Nardos**, et al., 2011 [23]	Arbaminch town	*Moringa stenopetala, Moringaceae*,Shiferaw (AM)/Haleko (GM)	Alloxan-induced mice
14.	**Rao** and **Adinew** 2011 [33]	Tepi,	*Persea Americana,* Laurel, Avocado	STZ induced rats
15.	**Seifu** et al., 2017 [27]	Southern, Ethiopia	*Melia azedarach*linn, *Meliaceae*, Laylak (milya)	Ob/obmice and Rats
16.	**Shewamene** et al., 2015 [16]	Ayimba, Gondar, Ethiopia	*Otostegia integrifolia, Lamiaceae*, Tunzut	STZinduced Rat or mice
17.	**Shewasinad** et al., 2019 [26]	Gudoberet, North Shoa	*Thymus schimperi*, Lamiaceae, Tosign	STZ induced mice
18.	**Sileshi et al 2014** [7]	*Arbaminch town*	*Moringa Stenopetala,Moringaceae* "Shiferaw (Am), Halekko (Wolita/gammo)."	Alloxan-induced *Swiss albino mice*
19.	**Tafesse**, etal 2017 [20]	Addis Ababa	*Ajuga remota, Lamiaceae*, Akorarach	Alloxan-induced mice
20.	**Tamiru** et al. 2012 [28]	Dirre, way from Bishoftu to Ziquala	*Caylusea abyssinica* (fresen.) fisch. &Mey. *Resedaceae*	STZ induced Swiss albino mice and Wistar rats
21.	**Taye** et al., 2020 [29]	Suluta, Oromia Region	Thymus schimperi (Lamiaceae)	Swiss albino mice
22.	**Tefera** et al., 2020 [30]	Woreta, Amhara region	*L. culinaris*	Swiss albino mice
23.	**Tekulu** et al. 2019 [25]	Tigray	*Aloe megalacantha B.,Asphodelaceae, Aloe monticola R., Asphodelaceae*"yedega ret. (Am)"	in vitro
24.	**Tesfaye** et al., 2016 [13]	Wolayta soddo, SNNPR	*Justicia Schimperia naacanthaceae*" Sensel or Simiza"	Normal andSTZ-induced mice
25.	**Toma** et al., 2012 [19]	Wolaitta zone, SNNPR	*Moringa Stenopetala*, *Moringaceae* "shiferaw Am" "HalekkoWo."	Alloxan Induced mice
26.	**Toma** et al., 2014 [8]	GamoGofa Zone, SNNPR	*Moringa Stenopetala,*	in vitro
27.	**Toma** et al., 2015 [9]	GamoGofa Zone, SNNPR	*Moringa Stenopetala*	STZ-induced rats
28.	**Tsegaye** et al., 2008 [18]	Semen Mazegaja, Addis Ababa	*UrticasimensisHochst.* ex. A. Rich, "Samma"	STZ-induced mice
29.	**Yibru** et al., 2015 [15]	Addis Ababa	*Coriandrum sativum*, "dembellal"	STZ-induced mice

Where; *STZ* streptozotocin, *T2DM* Type 2 Diabetes mellitus, *Ob/ob* obese mouse

Table 2 In vitro anti-diabetic activity of medicinal plants in Ethiopia

Study	Scientific name	Parts used	Extraction method	Assay method	Active cpd, Fraction / extraction	IC50
Alema et al. 2020 [10]	*Terminalia brownii Fresen*	stem bark	methanolic extract & solvent fractions	α-Amylase Inhibition (chromogenic DNSA method)	aqueous fraction	> *100* μg/ml
					Butanol fraction	84.69 μg/ml
					chloroform fraction	63.41 μg/ml
					ethyl acetate fraction	> *100* μg/ml
					crude extract	> *100* μg/ml
					Acarbose	~ 12.5 μg/ml
Kifle and Eneyew., 2020 [34]	*Bersama abyssinica*	leaf	Methanolic Extraction	α-Amylase Inhibition (chromogenic DNSA method)	Chloroform fraction	30.97 + 0.84
					Ethyl acetate fraction	20.34 + 0.67
					Aqueous fraction	13.33 + 0.57
					Crude extract	6.57 + 0.74
					Acarbose	2.26 + 0.53
Toma et al. 2014 [8]	*Moringa Stenopetala*	powdered leaves	ethanol extract	Pancreatic α-amylase	ethanol extract	> 5 mg/ml
				Maltase		> 5 mg/ml
				Pancreatic C. esterase		> 5 mg/ml
				Pancreatic lipase		> 5 mg/ml
				Sucrase		1.47 ± 0.19 mg/ml
Tekulu et al. 2019 [25]	*Aloe megalacantha B Aloe monticola R*	leaf	Methanol extract	α-Amylase Inhibition (chromogenic DNSA method)	TLC fraction from A. megalacantha coded as AM1	37.83 ± 3.31 μg/mL
					Leaf latex ofA. megalacantha	74.76 ± 1.98 μg/mL
					TLC fraction from A. megalacantha coded as AM2	96.75 ± 1.98 μg/mL
					Leaf latex ofA. monticola	78.10 ± 1.88 μg/mL
					TLC fraction from A. monticola, AG1	56.95 ± 1.88 μg/mL
					TLC fraction from A. monticola, AG2	64.03 ± 3.60 μg/mL
					Acarbose	16.49 ± 1.91 μg/mL

placebo control. Whereas standard controls are animals with induced DM and treated with standard treatment most commonly glibenclamide. Normal controls are animal being followed and managed in the same was as experimental conduction but no induction of Dm or treatment is given.

Results

Characteristics of included studies

A total of 17,954 articles were identified through the electronic database search. De-duplication reduced the total number of articles to 6, 090. After titles and abstracts screening, 33 articles remained and further screening left 29 articles for inclusion [6–28], Fig 1. Among the studies twenty-four were in vivo studies [7, 9, 11–24, 26–32, 33], two were in vitro studies [8, 25] and three was both in vivo and in vitro study [10, 34, 35]. Reasons for exclusion include: herbal medicine use prevalence and ethnobotanical survey studies [36, 37]. Ten of the total studies were conducted in the southern nation nationalities region, 9 in Amhara, four in Tigra, 3 in Addis Abab, 3 in Oromia. Seven studies were done in *Moringa Stenopetala* [7–9, 11, 17, 19, 23], 2 in *Aloe megalacantha* B [14, 25], 2 in *Bersama abyssinica* Fresen [32, 34], 2 in *Datura stramonium* [12, 31], 2 in *Thymus schimperi* [26, 29], and 14 in different plants.

Table 3 In vivo anti-diabetic activity of medicinal plat in Ethiopia

Study	Plant	Animal type	Extraction method/ component	Duration of treatment	From diabetic Control	From standard control
Amare et al., 2020 [35]	*Terminalia brownii Fresen*	Normoglycemic Mice	Methanol E	14 Days	–	200 mg/kg = 16.74 ± 2.57 400 mg/kg = 6.9 ± 2.33 600 mg/kg = 5.36 ± 2.20
		Mice Loaded with Oral Glucose				200 mg/kg = 16.30 ± 1.11 400 mg/kg = 7.14 ± 0.46 600 mg/kg = 3.25 ± 0.96
		STZ -induced Mice			200 mg/kg = − 22.48 ± 4.66 400 mg/kg = − 26.6 ± 5.89 600 mg/kg = − 29.54 ± 4.29	200 mg/kg = 7.94 ± 2.72 400 mg/kg = 3.82 ± 4.51 600 mg/kg = 0.88 ± 2.02
Alema et al., 2020 [10]	*Terminalia brownii Fresen*	Normoglycemic Mice	Methanolic E.	15 days	–	250 mg/kg = − 43.5 ± 6.21500 mg/kg = − 41 ± 7.12 750 mg/kg = − 32.5 ± 9.37
		Mice Loaded with Oral Glucose	Methanolic E.		–	250 mg/kg = − 40 ± 7.3 500 mg/kg = − 46.5 ± 7.67 750 mg/kg = − 44.67 ± 8.38
		STZ -induced Mice	Methanolic E.		250 mg/kg = 151.5 ± 59.14 500 mg/kg = 196.5 ± 61.86 750 mg/kg = 264.33 ± 53.5	250 mg/kg = − 123.67 ± 43.02 500 mg/kg = − 78.67 ± 46.61 750 mg/kg = − 11. 5 ± 34.84
			aqueous F.		500 mg/kg = 324.84 ± 40.14	500 mg/kg = − 11.16 ± 30.22
			Ethyl acetate F.		500 mg/kg = 278.5 ± 51.65	500 mg/kg = − 57.5 ± 37.85
			Butanol F.		500 mg/kg = 68.67 ± 62.71	500 mg/kg = − 267.33 ± 51.93
Belayneh et al., 2018 [22]	*Calpurnia aurea*	Normoglycemic Mice Loaded with Oral Glucose	Methanol E	14 Days	*100* mg/kg = 4.06 ± 8.88 200 mg/kg = 11.73 ± *9.38* 400 mg/kg = 0.67 ± 10.36	100 mg/kg = − 26.33 ± 4.56 200 mg/kg = − 18.66 ± 5.47 400 mg/kg = − 29.72 ± 7.03
					100 mg/kg = 28.12 ± 14.9 200 mg/kg = 18.95 ± 14.5 400 mg/kg = 30.51 ± 13.93	100 mg/kg = − 22.55 ± 11.04 200 mg/kg = − 31.72 ± 10.47 400 mg/kg = − 20.16 ± 9.55
		STZ -induced Mice			100 mg/kg = 144.94 ± 52.94 200 mg/kg = 153.11 ± 60.64 400 mg/kg = 134.89 ± 23.25	100 mg/kg = − 98.95 ± 50.04 200 mg/kg = − 90.78 ± 58.12 400 mg/kg = − 109 ± 58.48
Belaynehet al., 2019 [12]	*Datura stramonium L.*	Normoglycemic mice	Ethanol E	14 days	100 mg/kg = 16.72 ± 7.87 200 mg/kg = 20.11 ± 5.76 400 mg/kg = 15.39 ± 5.30	100 mg/kg = − 23.39 ± 8.10 200 mg/kg = − 20 ± 6.08 400 mg/kg = − 24.72 ± 5.66
		Diabetic mice			100 mg/kg = 38.12 ± 11.30 200 mg/kg = 38.62 ± 11.25 400 mg/kg = 42.89 ± 11.35	100 mg/kg = − 23 .71 ± 2.75 200 mg/kg = − 23.27 ± 2.51 400 mg/kg = − 19 ± 5.30
Birru et al., 2015 [21]	*Indigofera spicata Forssk*	Normoglycemic rat	Methanol E	10 h	100 mg/kg = − 6.66 ± 7.67 200 mg/kg = 10.48 ± 7.11 400 mg/kg = − 2.5 ± 6.45	*100 mg/kg = − 17* ± 6.85 *200 mg/kg = 0.5* ± 6.22 *400 mg/kg = − 12.48* ± 5.51

Table 3 In vivo anti-diabetic activity of medicinal plat in Ethiopia *(Continued)*

Study	Plant	Animal type	Extraction method/ component	Duration of treatment	From diabetic Control	From standard control
		Normoglycemic rat Loaded with Oral Glucose			100 mg/kg = 3.17 ± 10.08 200 mg/kg = 5.5 ± 8.17 400 mg/kg = 10.17 ± 6.73	100 mg/kg = − 26.67 ± 10.22 200 mg/kg = − 24.83 ± 8.33 400 mg/kg = − 20.17 ± 6.93
		alloxan induced mice			100 mg/kg = 179.67 ± 30.71 200 mg/kg = 196 ± 26.86 400 mg/kg = 196.67 ± 24.73	100 mg/kg = − 30.33 ± 23.22 200 mg/kg = − 14 ± 17.80 400 mg/kg = − 13.33 ± 14.41
Hammeso, et al., 2019 [14]	*Aloe megalacantha* B.	Normoglycemic mice	Aqueous E	14 days	100 mg/kg = 55.53 ± 12.65 200 mg/kg = 55.66 ± 13.98 400 mg/kg = 57.61 ± 13.32	100 mg/kg = − 20.16 ± 8.18 200 mg/kg = − 20 ± 10.13 400 mg/kg = − 18.05 ± 9.19
		Postprandial Normoglycemic mice			100 mg/kg = 32.05 ± 8.49 200 mg/kg = 39.83 ± 5.60 400 mg/kg = 30.83 ± 5.54	100 mg/kg = − 8.11 ± 8.07 200 mg/kg = − 0.33 ± 4.94 400 mg/kg = − 9.33 ± 4.87
		STZ-induced diabetic mice			100 mg/kg = 65 ± 5.57 200 mg/kg = 64.83 ± 5.42 400 mg/kg = 66.83 ± 5.39	100 mg/kg = − 12.16 ± 2.83 200 mg/kg = − 12.33 ± 2.52 400 mg/kg = − 10.33 ± 2.46
Kifle and Eneyew., 2020 [34]	*Bersama abyssinica Fresen*	Normoglycemic Mice	Methanolic E.	8 h		100 mg/kg = 25.67 ± 3.07 200 mg/kg = 14.17 ± 2.39 400 mg/kg = 8.83 ± 3.43
		Mice Loaded with Oral Glucose				100 mg/kg = 14.34 ± 10.30 200 mg/kg = 10.17 ± 6.38 *400 mg/kg = 2.50* ± 2.65
		STZ -induced Diabetic Mice	Methanolic E.			400 mg/kg = 21.17 ± 12.47
			chloroform F.			400 mg/kg = 104.0 ± 11.07
			Ethyl acetate F.			400 mg/kg = 69.67 ± 15.32
			aqueous F.			400 mg/kg = 54.5 ± 9.51
Kifle, et al., 2020 [32]	*Abyssinica Fresen.*	Normoglycemic mice	Aqueous F	14 days		100 mg/kg = 26.67 ± 2.28 200 mg/kg = 15.17 ± 2.72 400 mg/kg = 11. 5 ± 5.47
			Ethyl acetate F			100 mg/kg = 29.5 ± 6.28 200 mg/kg = 18.00 ± 3.13 400 mg/kg = 16.33 ± 2.31
		Mice Loaded with Oral Glucose	Aqueous F			100 mg/kg = 21.5 ± 6.24 200 mg/kg = 13.67 ± 6.11 400 mg/kg = 5.67 ± 6.67
			Ethyl acetate F			100 mg/kg = 19.5 ± 7.33 200 mg/kg = 14.67 ± 6.83 400 mg/kg = 9.5 ± 6.31
		STZ-induced mice	Aqueous F		100 mg/kg = − 119.5 ± 14.22 200 mg/kg = − 142.83 ± 16.98 400 mg/kg = − 180.0 ± 12.56	100 mg/kg = 95.33 ± 11.82 200 mg/kg = 72.0 ± 15.02 400 mg/kg = 34.83 ± 9.75
Makonnenet al., 1997 [17]	*Moringa stenopetala,*	Albino rabbits	Aqueous E	6 h	10 g/kg = 5.5 ± 1.48 15 g/kg = 9.8 ± 1.04	10 g/kg = − 37.7 ± 1.48 15 g/kg = − 33.4 ± 1.04
Melaku and Amare et al., 2020 [35]	*Datura stramonium Linn*	Normoglycemic mice	Methanolic E	14 days		100 mg/kg = 17.64 ± *2.13* 200 mg/kg = 17.11 ± 2.91 400 mg/kg = 15.66 ± 3.40
		Diabetic Mice				100 mg/kg = 10.04 ± 1.66 200 mg/kg = 8.37 ± 1.94 400 mg/kg = 6.99 ± 1.65

Table 3 In vivo anti-diabetic activity of medicinal plat in Ethiopia *(Continued)*

Study	Plant	Animal type	Extraction method/ component	Duration of treatment	From diabetic Control	From standard control
Mussa. et al., 2008 [11]	*Moringa stenopetalla,*	Non-diabetic Mice	Aqueous E.	6 h	20.10 ± 10.02	– 23.60 ± 8.13
			Chloroform F.		21.50 ± 10.70	–22.20 ± 8.96
			Butanol F.		15.50 ± 8.39	– 28.20 ± 5.98
			Aqueous R.		12.50 ± 10.38	– 31.20 ± 8.58
		Alloxan-induced mice	Aqueous E.		12.60 ± 10.16	–44.70 ± 9.24
			Chloroform F.		16.00 ± 7.71	–41.30 ± 6.44
			Butanol F.		41.40 ± 10.56	–15.90 ± 9.67
			Aqueous R.		37.80 ± 7.29	–19.50 ± 5.94
Nardos, et al., 2011 [23]	*Moringa stenopetala*	Alloxan-induced diabetic mice (Repeated doses)	Aqueous E	8 days	55.4 ± 4.55	–8.6 ± 4.78
			Ethanol E		59.2 ± 3.26	–4.8 ± 3.58
			Chloroform F		47.9 ± 2.26	–16.1 ± 2.70
			Butanol F		46 ± 3.53	–18 ± 3.82
		Normoglycemic mice (Effects of a single dose)	Aqueous E		23.2 ± 7.53	–14.8 ± 5.50
			Ethanol E		24.8 ± 8.8	–13.2 ± 7.14
			Petroleum F		2.2 ± 7.49	–35.8 ± 5.46
			Chloroform F		20.6 ± 7.75	–17.4 ± 5.79
			Butanol F		24.4 ± 7.78	–13.6 ± 5.85
			Aqueous R		13.2 ± 7.83	–24.6 ± 5.90
		Alloxan induced mice (single dose)	Aqueous E		50.8 ± 4.48	–27.4 ± 4.3
			Ethanol E		54.2 ± 6.08	–24 ± 5.95
			Petroleum F		5.2 ± 3.44	–73 ± 3.20
			Chloroform F		59.2 ± 6.26	–19 ± 6.13
			Butanol F		55.2 ± 4.10	–23 ± 3.90
			Aqueous R		18.8 ± 3.33	–59.4 ± 3.08
Rao and **Adinew** 2011 [33]	*Persea Americaca*	STZ-induced rats	Ethanol E	30 days	145.18 ± 18.89	–6.84 ± 7.14
Seifu, et al., 2017 [27]	Melia azedarach Lin,	Ob/ob mice and rat	Aqueous E	20 days	Decreased at 200mgg/ kg and 400 mg/kg	Similar at 200mgg/kg and 400 mg/kg
Shewamene, et al., 2015 [16]	*Otostegiainte grifolia,*	Normoglycemic mice	Methanol E	4 h	At 100 mg/kg = 25.61 ± 5.76 At 200 mg/kg = 33.77 ± 4.44 At 400 mg/kg = 1.48 ± 7.03	100 mg/kg = – 9.16 ± 4.18 200 mg/kg = – 1.00 ± 2.06 400 mg/kg = – 36.25 ± 5.81
		Streptozotocin induced mice	Methanol E		100 mg/kg =183.67 ± 51.36 200 mg/kg =215.67 ± 74.96 400 mg/kg = 168 ± 50.20	100 mg/kg = – 52.45 ± 47.08 200 mg/kg = – 20.45 ± 71. 400 mg/kg = – 67.62 ± 45.84
		Oral Glucose Tolerance Test in rats	Methanol E	4 h	100 mg/kg = 33.39 ± 5.02 200 mg/dl = 50.39 ± 4.37 400 mg/kg = – 22.19 ± 15.82	100 mg/kg = – 40.11 ± 6.64 200 mg/kg = – 23.11 ± 3.93 400 mg/kg = – 95.69 ± 15.71
Shewasinad, et al., 2019 [26]	*Thymus schimperi*	Normoglycemic mice or rat	Methanol E	Day 15	250 mg/kg = –11.8 ± 8.93 500 mg/kg = – 19.6 ± 7.49750 mg/kg = 1.6 ± 8.48	250 mg/kg = – 75.0 ± 7.16 500 mg/kg = – 82.8 ± 5.26 750 mg/kg = – 61.6 ± 6.60
		Streptozotocin induced rat or mice	Methanol E	Day 15	250 mg/kg = 109.83 ± 11.42 500 mg/kg = 125.27 ± 51.21 750 mg/kg =146.17 ±	250 mg/kg = – 112.84 ± 35.52 500 mg/kg = – 97.4 ± 50.81 750 mg/kg = – 76.5 ± 45.08

Table 3 In vivo anti-diabetic activity of medicinal plat in Ethiopia *(Continued)*

Study	Plant	Animal type	Extraction method/ component	Duration of treatment	From diabetic Control	From standard control
					45.45	
			Ethyl acetate F	Day 15	250 mg/kg = 69 ± 35.29 500 mg/kg = 67 ± 32.80	250 mg/kg = − 167.6 ± 23.83 500 mg/kg = − 169.6 ± 19.99
			n-butanol F	Day 15	250 mg/kg = 132 ± 31.57 500 mg/kg = 143.8 ± 40.38	250 mg/kg = − 104.6 ± 17.91 500 mg/kg = − 92.8 ± 30.91
			Aqueous F	Day 15	250 mg/kg = 104.8 ± 33.16 500 mg/kg = 109 ± 33.46	250 mg/kg = − 131.8 ± 20.58 500 mg/kg = − 127.6 ± 21.06
		In glucose loaded mice	Methanol E	Day 15	250 mg/kg = 80.2 ± 17.6 500 mg/kg = 61.2 ± 16.74 750 mg/kg = 54.4 ± 14.54	250 mg/kg = − 31.8 ± 11.17500 mg/kg = − 51.4 ± 71 At 750 mg/kg = − 60.2 ± 6. 67
Sileshi et al., **2014** [7]	*Moringa Stenopetala,*	Alloxan induced swiss albino mice	Ethanol E	6 h	− 14.29 ± 6.65	34.77 ± 7.54
			Hexane F	6 h	− 25.50 ± 6.32	23.56 ± 7.24
			Dichloromethane F	6 h	−36.56 ± 7.91	12.50 ± 8.67
			Butanol F	6 h	− 22.76 ± 12.17	26.30 ± 12.68
			Aqueous R	6 h	− 23.31 ± 7.82	25.30 ± 8.41
Tafesse et al., 2017 [20]	*Ajuga remota,*	Alloxan-induced mice	Aqueous E	14 days	300 mg/kg = − 18.73 ± 3.32 500 mg/kg = − 29.88 ± 1.64	300 mg/kg = 23.27 ± 4.18 500 mg/kg = 12.12 ± 3.03
			Ethanol E	14 days	300 mg/kg = − 18.84 ± 2.44 500 mg/kg = − 19.16 ± 2.36	300 mg/kg = 23.16 ± 3.52 500 mg/kg = 22.84 ± 3.45
Tamiru et al., 2012 [28]	*Caylusea abyssinica* (fresen.) fisch. &Mey.	normalmice	Methanolic E	4 h	100 mg/kg = 9 ± 5.33 200 mg/kg = 8 ± 4.25 300 mg/kg = 10 ± 4.30	100 mg/kg = 11 ± 7.62 200 mg/kg =10 ± 6.91 300 mg/kg =12 ± 6.94
		streptozotocin induced mice			100 mg/kg = 111.67 ± 53.44 200 mg/kg = 149 ± 41.58 300 mg/kg = 105.78 ± 51.61	100 mg/kg = − 33.7 ± 43.36200 mg/kg = 3.56 ± 27.45 300 mg/kg = − 39.66 ± 41.89
		Oral glucose loaded rat			100 mg/kg = 3.83 ± 6.14 200 mg/kg = 8.17 ± 4.86 300 mg/kg = − 9.5 ± 12.18	100 mg/kg = − 14 ± 10.54 200 mg/kg = − 9.66 ± 9.85 300 mg/kg = − 27.33 ± 14.89
Taye et al., 2020 [29]	*Thymus schimperi*	alloxan induced diabetic mice	Aqueous E	4 h	250 mg/kg = − 128.6 ± 60.97 500 mg/kg = − 155 ± 35.71	250 mg/kg = 76.4 ± 65.45 500 mg/kg = 49.8 ± 42.4
			Methanol E		250 mg/kg = − 145.6 ± 56.11 500 mg/kg = − 171.2 ± 28.91	250 mg/kg = 59.2 ± 60.59 500 mg/kg = 33.6 ± 36.86
Tefera et al., 2020 [30]	*L. culinaris*	Diabetic mice	Methanol E	21 days	100 mg/kg = − 61.34 ± 4.24 200 mg/kg = − 71.34 ± 4.79 400 mg/kg = − 82.25 ± 4.17	100 mg/kg = 49.66 ± 2.17 200 mg/kg = 39.66 ± 3.11 400 mg/kg = 28.75 ± 2.03
Tesfaye et al., 2016 [13]	*Justicia Schimperiana*	Normal mice	Aqueous extract	4 h	200 mg/kg = − 1 ± 3.81 400 mg/kg = 10.17 ± 2.74	200 mg/kg = − 13.33 ± 4.19 400 mg/kg = − 2.16 ± 3.26

Table 3 In vivo anti-diabetic activity of medicinal plat in Ethiopia *(Continued)*

Study	Plant	Animal type	Extraction method/ component	Duration of treatment	From diabetic Control	From standard control
		Streptozocin-induced mice			200 mg/kg = 2.5 ± 11.70 400 mg/kg = 39 ± 11.13	200 mg/kg = − 46.66 ± 9.33 400 mg/kg = − 10.16 ± 8.60
Toma et al., 2012 [19]	*Moringa Stenopetala*	Normal	*Butanol f. of Ethanol extract*	28 days		500 mg/kg = − 2 ± 18.9
		Alloxan Induced Mice	*Butanol f. of Ethanol extract*		500 mg/kg = 77.6 ± 24.11	500 mg/kg = −2 ± 18.9
Tomaet al., 2015 [9]	*Moringa Stenopetala*	streptozocin-induced rats	Ethanol fraction	14 days	at 500 mg/kg = 15.77 ± 3.66	at 500 mg/kg = − 2.5 ± 3.77
			Butanol fraction		at 500 mg/kg = 13.1 ± 3.18	at 500 mg/kg = − 5.17 ± 3.61
Tsegayeet al., 2008 [18]	*Urtica simensis Hochst.* ex. A. Rich At 300 mg/kg Unit mg/dl	STZ-induced diabetic mice	Methanol E	4 h	152 ± 8.36	−131 ± 19.5
			Aqueous E		147.9 ± 33.94	− 135.6 ± 38.33
			Petroleum ether F.		10.5 ± 9.19	− 273 ± 20.05
			Chloroform F.		−14.1 ± 13.95	− 297.6 ± 22.63
			Acetone F.		13.7 ± 21.72	− 269.8 ± 28.09
			Methanol F.		105.5 ± 19.56	− 178 ± 26.31
			Aqueous R		201.7 ± 40.03	−81.8 ± 44.75
Yibruet al., 2015 [15]	*Coriandrum Sativum*	STZI nduced T2DM Mice	Ethanol	21 days	Increased at 300, 400 and 500 mg/kg	Decreased at 300, 400 and 500 mg/kg

Three in vitro studies were conducted on four plants (*Terminalia brownie Fresen, Moringa Stenopetala, Aloe megalacantha B,* and *Aloe monticola R.)* (Table 1).

In vitro studies

In vitro half-maximal carbohydrate digestive enzyme inhibitory concentration (IC 50) of Aloe *megalacantha B, Aloe monticola R, Moringa Stenopetala,* and *Terminalia brownie Fresen* were evaluated. The IC50 was less than*100* μg/ml except ethanolic extract of *Moringa Stenopetala* and aqueous extract of *Terminalia brownie Fresen.* All extract and fractions showed less effect compared to a standard control (acarbose), Table 2.

In vivo studies

There was a significant difference in duration of treatment among in vivo studies, ranges from 4h to 30 days. Fifteen studies used mice, three used rats, and two studies used both rats and mice. In eight of the studies the plant was extracted using methanol, in six ethanol extract and in other six aqueous extract was used, Table 3.

Noteworthy glycemic control was observed with *Terminalia brownie Fresen* for 14 days, better BSL control compared to a diabetic control. Three studies [22, 24, 26] also showed better reductions in BSL compared to a diabetic control. These studies were conducted respectively for 30, 14 and 15 days in *Persea Americana, Calpurnia aurea,* and *Thymus schimperi*. Comparable effect to a standard control (glibenclimide) was observed in *Persea Americana* and *Moringa stenopetala* [9, 19, 23, 24]. Better acute glycaemia control was observed in *Indigofera spicata Forssk, Thymus schimperi* and *Urtica simensis Hochst.*ex. A. Rich [16, 18, 21].

Clinical studies

Trigonella foenum-graecum L. showed noteworthy effect on lipid profile of newly diagnosed type II diabetic patients [6]. Out of 114, 95 completed the study, 49 in the treatment group and 46 in the control group. Both treatment and control groups had abnormal FBG (≥180 mg/dL) and abnormal lipid profile (TC, TG, HDL-C, and LDL-C) at baseline. *Trigonella foenum-graecum* administered (25 mg seed powder solution for 30 consecutive days) showed a significant reduction (13.6%) in serum TC level as compared to baseline TC level. Yet, no significant difference in TC level in the control group. The treatment group showed a statistically significant decrease (23.53%) in serum TG level compared to baseline TG level but the control group had no significant difference in TG level. HDL-C level was significantly increased in the treatment group by 21.7% as compared to the baseline HDL-C level within the group. LDL-C level had a significantly reduced by 23.4% as compared to the baseline LDL-C level. *Trigonella foenum-graecum* produced a significant reduction in TC, TG, and LDL-C levels and an increase in HDL-C level compared to baseline.

Table 4 Preliminary qualitative phytochemical screening of the studied plants

Test	Alema et al., 2020 [10]	*Belayneh* et al *2019* [12]	*Birru* et al *2015* [21]	*Hammeso* et al *2015*	*Shewamene et al 2015* [16]	*Tafesse et al 2017* [20]	*Tamiru et al 2012* [28]	*Tekulu et al 2019* [25]	*Toma et al 2014* [8]	*Amare* et al., *2020* [35]	*Melaku and Amare* et al., *2020* [35]
Plant	*Terminalia brownii Fresen*	*Datura stramonium L*	*Indigofera spicata Forssk*	*Aloe megalacantha Baker*	*Otostegia integrifolia Benth*	*Ajuga remota Benth*	*Caylusea abyssinica*	*Aloe megalacanta and Aloe monticola*	*Moringa stenopetala*	*Aloe pulcherrima*	*Datura stramonium Linn*
Flavonoids	+	+	+	+	+	+	+		+	+	+
Phenols	+	+	–	+	+	+	+		+	+	+
Tannins	+	+	+	+	–	+	+		+	+	+
Saponins	+	[a]	+	+	+	+	+		[a]	+	+
Alkaloids	[a]	+	+	+	–	–	+		[a]	+	+
Terpenoids	+	–	+	+	[a]	[a]	[a]		[a]	[a]	+
Glycosides	[a]	+	+	+	[a]	[a]	+		[a]	+	+
Steroids	+	+	+	–	–	+	+		[a]	–	+
Anthraquinones	[a]	+	[a]	+	[a]	–	–		[a]	+	–

Abbreviations: +, present; –, absent; [a] not tested

Toxicology

Acute toxicity studies in animal model demonstrated the relative safety of the plants extract. Seven plants, *Terminalia brownie, Calpurnia aurea, Datura stramonium, Indigofera spicata Forssk, Aloe megalacantha, Thymus schimperi, Caylusea abyssinica, Justicia Schimperiana*, and *Coriandrum Sativum,* showed LD_{50} greater than 2000 mg/kg [10, 12–15, 21, 22, 26, 28]. Other plants showed LD_{50} greater than 5000 mg/kg [11, 16, 19, 20, 23]. The LD50 of *Moringa stenopetalla* were 50.6 g/kg [11] and 50 g/kg [23]. The LD_{50} of *Persea Americana* was greater 1000 mg/kg [23]. The sub-chronic toxicity of *Moringa Stenopetala* showed normal hematological, significantly higher platelet counts compared to controls, significant changes were observed in the clinical chemistry parameters (urea, creatinine, CA125, TSH, FT3, ALT, TGs, and cholesterol), FT4 significantly reduced, and AST were significantly higher in the mice received the treatment [7].

Phytochemistry

Preliminary phytochemical investigation were given in Table 4 and Tekulu et al, 2019 [25] further studied TLC isolates, AM1 and AG1, separated from leaves latexes of *A. megalacantha* and *A. monticola* respectively. AM1 and AG1are considered to be more polar compounds than AM2 and AG2 as they have small Rf values during isolation using silica gel coated TLC plate with chloroform: methanol (80:20) solvent system [25]. They could be assigned as glycosides of anthraquinones or its derivatives as they have similar R*f* with previously isolated anthraquinone glycosides from leaf latex and root extracts of different Aloe species [38–40].

Discussion

This study reviewed twenty three articles on plants with anti-diabetic activity. Most of the studies (20) were conducted in an animal model, in vitro studies (2) and both in vitro and in vivo study (1). Noteworthy glycemic control was observed with *T. brownie Fresen* compared to a diabetic control. Carbohydrate digestion inhibitory effect was demonstrated in in vitro studies. The possible mechanism for hypoglycemic effect could be decreasing the absorption of ingested sugars as shown in in vitro *α*-amylase/*α*-glucosidase inhibitory activity. The human study was primarily focused on the effect of body weight and lipid profile in patients with type 2 diabetes mellitus [6]. Numbers of studies conducted on anti-diabetic activity of Ethiopian medicinal plants were lower compared to studies conducted in many African countries. For example, a systematic review in Nigeria showed 103 plants have experimental evaluation of their blood sugar reducing effects, either in vivo or in vitro [41].

Several medicinal plants are being used traditionally for treatment of diabetes mellitus in Ethiopia for a long period of time but the number of plants studied is limited. This review summarized studies conducted so far and highlighting the need for further studies. *Moringa stenopetala* is the most commonly studied plant and other plants remain scantly studied. Inhibition of α-amylase, a potential target to control diabetes mellitus for more than 30 years is considered a strategy for the treatment of diabetes mellitus [42].

The effect exerted by *Moringa stenopetala* could most probably be carbohydrate absorption inhibition resulting in hypoglycemia which could give an insight into the mechanism of the hypoglycemic activity of the anti-diabetic plants. Herbal medicines are often complex mixtures of various phytochemicals that work synergistically to achieve a desired therapeutic outcome [43] and therefore several mechanisms of action could be expected including protecting and repairing cells. The mechanism of lowering BSL could also be stimulating insulin secretion and action.

Natural products are promising lead candidates for discovering and also easily available, affordable and tolerable [44, 45]. Plants provide a rich source of bioactive molecules and possess diverse pharmacological actions including anti-diabetic activity. The activity is attributed to either a single component or mixture of phytochemicals. The phytochemicals responsible for anti-diabetic properties could mainly be alkaloids, phenolics, flavonoids, glycosides, saponins, polysaccharides, stilbenes, and tannins [46] and phytochemical investigation of current study showed the presence of this component in most studied plants. Several animal studies reported a wide variation in composition between the extraction methods. Phytochemical compositions are also highly dependent on several endogenous and exogenous factors, environment, genetics, and plant part used, growing, drying, and storing conditions [47].

Investigations of phytochemicals responsible for the anti-diabetic activity have progressed in the last few decades and treating diabetes mellitus with plant-derived compound seems highly attractive as they are accessible and do not require laborious pharmaceutical synthesis.

Strengths and limitation of the studies

The evidence synthesized from in vitro/ in vivo studies will have paramount for further studies in human studies. It will show directions of further the studies and promote the traditional use. The limitation of this study arises from the limitation of the included primary studies. The methods used for the induction of diabetic mellitus were streptozotocin or alloxan which mostly

induces type 1 diabetes mellitus. The methodological challenge in an animal model study is as induction method mostly induces type 2 diabetes mellitus. With its limitation this study provides preliminary activity assay showed further study direction in other plants, identification and isolation of most active components that could join the adventure of modern drug discovery.

It is also worth noting that only one plant has been studied for efficacy in humans in Ethiopia. No clinical trials were conducted and also no clearly defined preparation for clinical trials in Ethiopia. Furthermore, majority of studies did not report the composition of the formulation, standardization protocols and preparation procedures.

Conclusion

This review demonstrated medicinal plants used for management of diabetes mellitus in Ethiopia are worthy for further investigation of pharmacologically active ingredients and clinical study. Further in vitro, in vivo *and clinical* studies are warranted to confirm the claimed activity of commonly used medicinal plant species. Studies should also focus on the identification of the active ingredient(s) of potent plant species for the development of modern medicine. The present review provides useful information to researchers, students, health professionals, policymakers and, traditional medicine practitioners.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40816-021-00251-x.

Additional file 1.

Abbreviations

BSl: Blood sugar level; TC: Total cholesterol; TG: Total glyceraldehydes; LDL-C: Low density lipoprotein cholesterol; HDL-C: High density lipoprotein cholesterol; T1DM: Type 1 diabetes mellitus; T2DM: Type 2 diabetes mellitus; STZ: Streptozotocin; CI: Confidence interval; Rf: Retention factor; LD_{50}: Median lethal dose

Acknowledgments

Not applicable.

Authors' contributions

SD conceived the idea and designed the study. KE, SS and EW searched literature extracted data and drafted manuscript. SD drafted the manuscript. All authors reviewed and approved the final manuscript.

Funding

No funding.

Availability of data and materials

The data supporting the conclusions of this article are included within the article and its supplementary files.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Pharm-BioTechnology and Traditional Medicine Center of Excellence (PHARMBIOTRAC), Mbarara University of Science and Technology, P.O. Box 1410, Mbarara, Uganda. [2]School of Pharmacy, Faculty of Medicine, College of Medicine and Health Sciences, Hawassa University, P. O. Box 1560,, Hawassa, Ethiopia. [3]Department of Biochemistry, Faculty of Medicine, College of Medicine and Health Sciences, Hawassa University, P. O. Box 1560,, Hawassa, Ethiopia. [4]Department of Anatomy, Faculty of Medicine, College of Medicine and Health Sciences, Hawassa University, P. O. Box 1560,, Hawassa, Ethiopia.

Received: 23 July 2020 Accepted: 11 January 2021
Published online: 02 February 2021

References

1. Goldenberg R, Punthakee Z. Definition, classification and diagnosis of diabetes, prediabetes and metabolic syndrome. Can J Diabetes. 2013;37:S8–11.
2. Fowler MJ. Microvascular and macrovascular complications of diabetes. Clin Diabetes. 2011;29:116–22.
3. Organization WH. WHO congress on traditional medicine 2008: Beijing declaration 2011.
4. Belayneh A, Asfaw Z, Demissew S, Bussa NF. Medicinal plants potential and use by pastoral and agro-pastoral communities in Erer Valley of Babile Wereda, Eastern Ethiopia. J Ethnobiol Ethnomed. 2012;8:42.
5. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010;8:336–41.
6. Geberemeskel GA, Debebe YG, Nguse NA. Antidiabetic Effect of Fenugreek Seed Powder Solution (*Trigonella foenum-graecum* L.) on Hyperlipidemia in Diabetic Patients. J Diabetes Res. 2019. https://doi.org/10.1155/2019/8507453.
7. Sileshi T, Makonnen E, Debella A, Tesfaye B. Antihyperglycemic and subchronic toxicity study of Moringa stenopetala leaves in mice. J Coast Life Med. 2014;2:214–21.
8. Toma A, Makonnen E, Mekonnen Y, Debella A, Addisakwattana S. Intestinal α-glucosidase and some pancreatic enzymes inhibitory effect of hydroalcholic extract of *Moringa stenopetala* leaves. BMC Complement Altern Med. 2014;14:1–5. https://doi.org/10.1186/1472-6882-14-180.
9. Toma A, Makonnen E, Mekonnen Y, Debella A, Adisakwattana S. Antidiabetic activities of aqueous ethanol and n-butanol fraction of *Moringa stenopetala* leaves in streptozotocin-induced diabetic rats. BMC Complement Altern Med. 2015;15:1–8. https://doi.org/10.1186/s12906-015-0779-0.
10. Alema NM, Periasamy G, Sibhat GG, Tekulu GH, Hiben MG. Antidiabetic activity of extracts of *Terminalia brownii* fresen. Stem bark in mice. J Exp Pharmacol. 2020;12:61–71.
11. Mussa A, Makonnen E, Urga K. Effects of the crude aqueous extract and isolated fraction of *Moringa stenopetala* leaves in normal and diabetic mice. Pharmacologyonline. 2008;3:1049–55.
12. Belayneh YM, Birhanu Z, Birru EM, Getenet G. Evaluation of in vivo antidiabetic, antidyslipidemic, and in vitro antioxidant activities of hydromethanolic root extract of *Datura stramonium* L. (Solanaceae). J Exp Pharmacol. 2019;11:29–38.
13. Tesfaye A, Makonnen E, Gedamu S. Hypoglycemic and antihyperglycemic activity of aqueous extract of *Justicia Schimperiana* leaves in normal and streptozotocin-induced diabetic mice. Int J Pharma Sci Res. 2016;7:107–13.
14. Hammeso WW, Emiru YK, Getahun KA, Kahaliw W. Antidiabetic and antihyperlipidemic activities of the leaf latex extract of *Aloe megalacantha* baker (Aloaceae) in Streptozotocin-induced diabetic model. Evidence-based Complement Altern Med. 2019. https://doi.org/10.1155/2019/8263786.
15. Yibru E, CMenon MK, Belayneh Y, Seyifu D. The effect of *Coriandrum Sativum* seed extract on hyperglycemia, lipid profile and renal function in streptozotocin induced type- 2 diabetic Swiss albino mice. Int J Heal Sci Res. 2015;5:166–77.

16. Shewamene Z, Abdelwuhab M, Birhanu Z. Methanolic leaf exctract of *Otostegia integrifolia* Benth reduces blood glucose levels in diabetic, glucose loaded and normal rodents. BMC Complement Altern Med. 2015;15:1–7. https://doi.org/10.1186/s12906-015-0535-5.
17. Makonnen E, Hunde A, Damecha G. Hypoglycaemic effect of *Moringa stenopetala* aqueous extract in rabbits. Phyther Res. 1997;11:147–8.
18. Tsegaye W, Urga K, Asres K. Antidiabetic activity of Samma (*Urtica simensis* Hochst. Ex. A. Rich.) in streptozotocin-induced diabetic mice. Ethiop Pharm J. 2008;27:75–82.
19. Toma A, Makonnen E, Debella A, Tesfaye B. Antihyperglycemic effect on chronic administration of butanol fraction of ethanol extract of *Moringa Stenopetala* leaves in alloxan induced diabetic mice. Asian Pac J Trop Biomed. 2012. https://doi.org/10.1016/S2221-1691(12)60461-4.
20. Tafesse TB, Hymete A, Mekonnen Y, Tadesse M. Antidiabetic activity and phytochemical screening of extracts of the leaves of *Ajuga remota* Benth on alloxan-induced diabetic mice. BMC Complement Altern Med. 2017;17:1–9.
21. Birru EM, Abdelwuhab M, Shewamene Z. Effect of hydroalcoholic leaves extract of *Indigofera spicata* Forssk. On blood glucose level of normal, glucose loaded and diabetic rodents. BMC Complement Altern Med. 2015; 15:1–8. https://doi.org/10.1186/s12906-015-0852-8.
22. Belayneh YM, Birru EM. Antidiabetic activities of hydromethanolic leaf extract of *Calpurnia aurea* (Ait.) benth. Subspecies aurea (Fabaceae) in mice. Evidence-based Complement Altern Med. 2018. https://doi.org/10.1155/2018/3509073.
23. Nardos A, Makonnen E, Debella A. Effects of crude extracts and fractions of *Moringa stenopetala* (baker f) cufodontis leaves in normoglycemic and alloxan-induced diabetic mice. African J Pharm Pharmacol. 2011;5:2220–5.
24. Mahadeva Rao US, Adinew B. Remnant B-cell-stimulative and anti-oxidative effects of *Persea Americana* fruit extract studied in rats introduced into streptozotocin - induced hyperglycaemic state. African J Tradit Complement Altern Med. 2011;8:210–7.
25. Tekulu GH, Araya EM, Mengesha HG. In vitro α-amylase inhibitory effect of TLC isolates of *Aloe megalacantha* baker and Aloe monticola Reynolds. BMC Complement Altern Med. 2019;19:1–7.
26. Shewasinad A, Bhoumik D, Hishe HZ, Masresha B. Antidiabetic activity of methanol extract and fractions of *Thymus schimperi* Ronniger leaves in Normal and Streptozotocin induce diabetic mice. Iran J Pharmacol Ther. 2019;16:1.
27. Seifu D, Gustafsson LE, Chawla R, Genet S, Debella A, Holst M, et al. Antidiabetic and gastric emptying inhibitory effect of herbal Melia azedarach leaf extract in rodent models of diabetes type 2 mellitus. J Exp Pharmacol. 2017;9:23.
28. Tamiru W, Engidawork E, Asres K. Evaluation of the effects of 80% methanolic leaf extract of Caylusea abyssinica (fresen.) fisch. & Mey. on glucose handling in normal, glucose loaded and diabetic rodents. BMC Complement Altern Med. 2012;12:1. https://doi.org/10.1186/1472-6882-12-151.
29. Taye GM, Bule M, Gadisa DA, Teka F, Abula T. *In vivo* antidiabetic activity evaluation of aqueous and 80% methanolic extracts of leaves of thymus schimperi (Lamiaceae) in alloxan-induced diabetic mice. Diabetes, Metab Syndr Obes Targets Ther; 2020. https://doi.org/10.2147/DMSO.S268689.
30. Tefera MM, Masresha Altaye B, Yimer EM, Berhe DF, Bekele ST. Antidiabetic effect of germinated lens culinaris medik seed extract in streptozotocin-induced diabetic mice. J Exp Pharmacol. 2020. https://doi.org/10.2147/JEP.S228834.
31. Melaku BC, Amare GG. Evaluation of antidiabetic and antioxidant potential of hydromethanolic seed extract of *Datura stramonium* Linn (Solanaceae). J Exp Pharmacol. 2020. https://doi.org/10.2147/JEP.S258522.
32. Kifle ZD, Anteneh DA, Atnafie SA. Hypoglycemic, anti-hyperglycemic and anti-hyperlipidemic effects of *Bersama abyssinica Fresen* (Melianthaceae) leaves' solvent fractions in normoglycemic and streptozotocin-induced diabetic mice. J Exp Pharmacol. 2020. https://doi.org/10.2147/JEP.S273959.
33. Mahadeva RUS, Adinew B. Hypolipidemic effect of dichloromethane as well as methanolic fruit and leaf extract of Ethiopian alligator pear (*persea americana* mill.) on tyloxapol-induced hyperlipidemic experimental rat. Asian J Res Chem. 2011;4(4):574-8.
34. Kifle ZD, Enyew EF. Evaluation of *in vivo* antidiabetic, *in vitro* α-amylase inhibitory, and *in vitro* antioxidant activity of leaves crude extract and solvent fractions of *Bersama abyssinica Fresen* (Melianthaceae). J Evidence-Based Integr Med. 2020. https://doi.org/10.1177/2515690X20935827.
35. Amare GG, Meharie BG, Belayneh YM. Evaluation of antidiabetic activity of the leaf latex of *Aloe pulcherrima* Gilbert and Sebsebe (Aloaceae). Evidence-Based Complement Altern Med. 2020. https://doi.org/10.1155/2020/8899743.
36. Mekuria AB, Belachew SA, Tegegn HG, Ali DS, Netere AK, Lemlemu E, et al. Prevalence and correlates of herbal medicine use among type 2 diabetic patients in teaching Hospital in Ethiopia: a cross-sectional study. BMC Complement Altern Med. 2018;18:1–8. https://doi.org/10.1186/s12906-018-2147-3.
37. Abdulkadir J. Intake of traditional taenicidal drugs among diabetics and non-diabetics. Ethiop Med J. 1979;17(3):75–80.
38. Cock IE. The Genus Aloe: Phytochemistry and Therapeutic Uses Including Treatments for Gastrointestinal Conditions and Chronic Inflammation. In: Rainsford K, Powanda M, Whitehouse M, editors. Novel Natural Products: Therapeutic Effects in Pain, Arthritis and Gastro-intestinal Diseases. Progress in Drug Research, vol 70. Basel: Springer; 2015. https://doi.org/10.1007/978-3-0348-0927-6_6
39. Abdissa N, Gohlke S, Frese M, Sewald N. Cytotoxic compounds from aloe megalacantha. Molecules. 2017;22:1136.
40. Geremedhin G, Bisrat D, Asres K. Isolation, characterization and in vivo antimalarial evaluation of anthrones from the leaf latex of Aloe percrassa Todaro. J Nat Remedies. 2014;14:119–25.
41. Ezuruike UF, Prieto JM. The use of plants in the traditional management of diabetes in Nigeria: pharmacological and toxicological considerations. J Ethnopharmacol. 2014;155:857–924. https://doi.org/10.1016/j.jep.2014.05.055.
42. Sales PM, Souza PM, Simeoni LA, Magalhães PO. Silveira D α-amylase inhibitors: a review of raw material and isolated compounds from plant source. J Pharm Sci. 2012;15:141–83.
43. Joan IA, Campbell-Tofte PM. Kaj Winther Harnessing potential clinical use medicinal Plants as anti-diabetic agents Botanicals. Targets Ther. 2012. https://doi.org/10.2147/BTAT.S17302.
44. Nwaka S, Hudson A. Innovative lead discovery strategies for tropical diseases. Nat Rev Drug Discov. 2006;5:941–55.
45. Lee K-H. Current developments in the discovery and design of new drug candidates from plant natural product leads. J Nat Prod. 2004;67:273–83.
46. Vinayagam R, Xiao J, Xu B. An insight into anti-diabetic properties of dietary phytochemicals. Phytochem Rev. 2017;16:535–53.
47. Akula R, Ravishankar GA. Influence of abiotic stress signals on secondary metabolites in plants. Plant Signal Behav. 2011;6:1720–31.

Publisher's Note