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

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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
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

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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 et 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 Forsk, Fabaceae, yeayitimisir (Am) | Alloxan-induced albino mice &wistar rats |
| 6. | Gebremikael et al., 2019 [6] | Mekelle | Trigonellafoenum-graecum, Fenugreek, Abish (Am) | T2DM |
| 7. | Hammeso et al., 2019 [14] | SehartSamre, 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, Armha 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 | Mela azedtachchlinn, Meliaeace, Laylak (milya) | Ob/obmice and Rats |
| 16. | Shewamene et al, 2015 [16] | Ayimba, Gondar, Ethiopia | Orostegia integinifolia, Lamiaceae, Tenzut | STZ induced Rat or mice |
| 17. | Shewasind 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, Akoarach | Alloxan-induced mice |
| 20. | Tamiru et al. 2012 [28] | Dirre, way from Bishoftu to Ziquala | Caylusea abyssinica (fresen.) fich. B 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, Armha region | L. culinaris | Swiss albino mice |
| 23. | Tekulu et al. 2019 [25] | Tigray | Aloe megalacantha B,Asphodelaceae, Aloe monticola R, “yeedega ret. (Am)” | in vitro |
| 24. | Tesfaye et al., 2016 [13] | Wolayta soddio, SNPR | Justicia Schimperia naacanthaceae Sensel or Simiza” | Normal andSTZ-induced mice |
| 25. | Toma et al, 2012 [19] | Wolaitta zone, SNPR | Moringa Stenopetala, Moringaceae “shiferaw Am” “HalekkoWo,” | Alloxan Induced mice |
| 26. | Toma et al., 2014 [8] | GamoGofa Zone, SNPR | Moringa Stenopetala, | in vitro |
| 27. | Toma et al., 2015 [9] | GamoGofa Zone, SNPR | 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
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 way 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 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 2 In vitro anti-diabetic activity of medicinal plants in Ethiopia

| Study                  | Scientific name                  | Parts used | Extraction method                  | Assay method                              | Active cpd, Fraction / extraction |
|------------------------|----------------------------------|------------|------------------------------------|-------------------------------------------|---------------------------------|
| 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 |
|                        |                                  |            |                                    | Maltaise: > 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              | leaf       | Methanol extract | α-Amylase Inhibition (chromogenic DNSA method) | TLC fraction from A. megalacantha coded as AM1: 37.83 ± 3.31 μg/mL |
|                        | Aloe monticola R                 |            |                                    | Leaf latex of A. megalacantha: 74.76 ± 1.98 μg/mL |
|                        |                                  |            |                                    | TLC fraction from A. megalacantha coded as AM2: 96.75 ± 1.98 μg/mL |
|                        |                                  |            |                                    | Leaf latex of A. 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               |
| 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 | 200 mg/kg = 7.94 ± 2.72 400 mg/kg = 3.82 ± 4.51 600 mg/kg = 0.88 ± 2.02 |
| | | 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 | |
| Alema et al., 2020 [10] | *Terminalia brownii* Fresen | Normoglycemic Mice | Methanolic E | 15 days | 250 mg/kg = −43.5 ± 6.26 500 mg/kg = −41.0 ± 7.12 750 mg/kg = −32.5 ± 9.37 | 250 mg/kg = −78.67 ± 46.61 500 mg/kg = −46.5 ± 7.67 750 mg/kg = −11.5 ± 34.84 |
| | | Mice Loaded with Oral Glucose | | | 250 mg/kg = −40 ± 7.3 500 mg/kg = −46.5 ± 7.67 750 mg/kg = −44.67 ± 8.38 | |
| | | STZ -induced Mice | | | 250 mg/kg = −123.67 ± 43.02 500 mg/kg = −128.0 ± 47.88 750 mg/kg = −12.5 ± 34.84 | |
| | | aqueous F. | | | 500 mg/kg = 324.84 ± 40.14 750 mg/kg = 264.33 ± 53.5 | |
| | | Ethyl acetate F. | | | 500 mg/kg = 278.5 ± 51.65 750 mg/kg = 264.33 ± 53.5 | |
| | | Butanol F. | | | 500 mg/kg = 68.67 ± 62.71 750 mg/kg = 264.33 ± 53.5 | |
| Belalneh et al., 2018 [22] | *Calpurnia aurea* | Normoglycemic Mice | Methanol E | 14 Days | 100 mg/kg = 4.06 ± 8.88 200 mg/kg = 11.73 ± 9.38 400 mg/kg = 29.72 ± 7.03 | 100 mg/kg = −22.55 ± 11.04 200 mg/kg = −31.72 ± 10.47 400 mg/kg = −20.16 ± 9.55 |
| | | Loaded with Oral Glucose | | | 100 mg/kg = 28.12 ± 14.9 200 mg/kg = 18.95 ± 14.5 400 mg/kg = 30.51 ± 13.93 | |
| | | STZ -induced Mice | | | 100 mg/kg = 144.94 ± 52.94 200 mg/kg = 153.11 ± 60.64 400 mg/kg = 134.89 ± 23.25 | |
| Belalneh et 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 | |
| Bieru et al., 2015 [21] | *Indigofera spicata* Forsk | 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 plants 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 | Methanolic E | 8 h | 100 mg/kg = 5.5 ± 0.75 200 mg/kg = 7.0 ± 0.85 400 mg/kg = 10.0 ± 0.85 | 101 mg/kg = − 10.0 ± 0.57 200 mg/kg = − 12.0 ± 0.68 400 mg/kg = − 16.0 ± 0.79 | 101 mg/kg = − 20.0 ± 0.57 200 mg/kg = − 22.0 ± 0.68 400 mg/kg = − 24.0 ± 0.79 |
| Hammes, et al., Aloe megalacantha B. | Normoglycemic mice | Aqueous E | 14 days | 100 mg/kg = 17.67 ± 8.17 200 mg/kg = 31.33 ± 12.47 400 mg/kg = 55.0 ± 19.20 | 100 mg/kg = − 20.0 ± 0.57 200 mg/kg = − 24.0 ± 0.68 400 mg/kg = − 30.0 ± 0.79 |
| Kifle and Eneyew, Bersama abyssinica Fresen | Normoglycemic Mice | Methanolic E | 8 h | 100 mg/kg = 25.67 ± 1.48 200 mg/kg = 29.5 ± 2.00 400 mg/kg = 34.8 ± 2.52 | 100 mg/kg = − 119.5 ± 13.50 200 mg/kg = − 142.8 ± 16.80 400 mg/kg = − 180.0 ± 19.10 |
| Kifle, et al., Abyssinica Fresen | Normoglycemic mice | Aqueous F | 14 days | 100 mg/kg = 5.5 ± 0.75 200 mg/kg = 7.0 ± 0.85 400 mg/kg = 10.0 ± 0.85 | 101 mg/kg = − 20.0 ± 0.57 200 mg/kg = − 24.0 ± 0.68 400 mg/kg = − 28.0 ± 0.80 |
| Melaku and Amare, Datura stramonium Linn | Normoglycemic mice | Methanolic E | 14 days | 100 mg/kg = 7.0 ± 1.00 200 mg/kg = 14.0 ± 2.00 400 mg/kg = 21.0 ± 3.00 | 100 mg/kg = − 119.5 ± 13.50 200 mg/kg = − 142.8 ± 16.80 400 mg/kg = − 180.0 ± 19.10 |
Table 3 In vivo anti-diabetic activity of medicinal plant 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 stenopetala | 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         |
| Mussa. et al., 2008 [11] | Moringa stenopetala | 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         |
| Mussa. et al., 2008 [11] | Moringa stenopetala | Alloxan-induced diabetic mice (Repeated doses)   | Aqueous E                    | 8 days                | 55.4 ± 4.55            | −86.4 ± 4.78          |
|                  |                        |                                                  | Ethanol E                    |                       | 59.2 ± 3.26            | −48.8 ± 3.58          |
|                  |                        |                                                  | Chloroform F                 |                       | 47.9 ± 2.26            | −16.1 ± 2.70          |
|                  |                        |                                                  | Butanol F                    |                       | 46 ± 3.55              | −18.6 ± 3.82          |
| Nardos. et al., 2011 [23] | Moringa stenopetala | Alloxan-induced diabetic mice (Repeated doses)   | Aqueous E                    | 8 days                | 55.4 ± 4.55            | −86.4 ± 4.78          |
|                  |                        |                                                  | Ethanol E                    |                       | 59.2 ± 3.26            | −48.8 ± 3.58          |
|                  |                        |                                                  | Chloroform F                 |                       | 47.9 ± 2.26            | −16.1 ± 2.70          |
|                  |                        |                                                  | Butanol F                    |                       | 46 ± 3.55              | −18.6 ± 3.82          |
| Seifu, et al., 2017 [27] | Melia azedarach Lin, | Ob/ob mice and rat                               | Aqueous E                    | 20 days               | Decreased at 200mg/kg and 400 mg/kg | Similar at 200mg/kg and 400 mg/kg |
|                  |                        |                                                  | Ethanol E                    |                       | 100 mg/kg = −9.16 ± 4.18 | 200 mg/kg = −1.00 ± 2.06 |
|                  |                        |                                                  | Chloroform F                 |                       | 100 mg/kg = −36.25 ± 5.81 | 200 mg/kg = −36.25 ± 5.81 |
|                  |                        |                                                  | Butanol F                    |                       | 100 mg/kg = −75.0 ± 7.16 | 200 mg/kg = −75.0 ± 7.16 |
| Shewamene, et al, 2015 [16] | Osostegia inte grifolia | Normoglycemic mice                               | Methanol E                   | 4 h                   | At 100 mg/kg = 25.61 ± 5.76 | 200 mg/kg = 33.77 ± 4.44 |
|                  |                        |                                                  |                              |                       | At 200 mg/kg = 33.77 ± 4.44 | 400 mg/kg = 1.48 ± 7.03 |
|                  |                        |                                                  |                              |                       | 100 mg/kg = 183.67 ± 51.36 | 200 mg/kg = 215.67 ± 74.96 |
|                  |                        |                                                  |                              |                       | 400 mg/kg = 168 ± 50.20 | 400 mg/kg = −112 ± 18.82 |
|                  |                        |                                                  |                              |                       | 100 mg/kg = −52.45 ± 47.08 | 200 mg/kg = −20.45 ± 71.71 |
|                  |                        |                                                  |                              |                       | 400 mg/kg = −67.62 ± 45.84 | 400 mg/kg = −95.69 ± 15.71 |
| Seifu, et al., 2017 [27] | Persea Americaca | STZ-induced rats                                 | Ethanol E                    | 30 days               | 145.18 ± 18.89          | −6.84 ± 7.14          |
|                  |                        |                                                  |                              |                       | 100 mg/kg = −9.16 ± 4.18 | 200 mg/kg = −1.00 ± 2.06 |
|                  |                        |                                                  |                              |                       | 400 mg/kg = −36.25 ± 5.81 | 200 mg/kg = −36.25 ± 5.81 |
|                |                        |                                                  |                              |                       | 100 mg/kg = −75.0 ± 7.16 | 200 mg/kg = −75.0 ± 7.16 |
| Seifu, et al., 2017 [27] | Moringa stenopetala | Normoglycemic mice                               | Methanol E                   | 4 h                   | 33.39 ± 5.02            | 50.39 ± 4.37          |
|                  |                        |                                                  |                              |                       | 200 mg/dl = 50.39 ± 4.37 | 200 mg/dl = 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 | 400 mg/kg = −95.69 ± 15.71 |
| Shewasined, et al, 2019 [26] | Thymus schimperi | Normoglycemic mice                               | Methanol E                   | Day 15                | 200 mg/kg = −11.8 ± 8.93 | 749.750 mg/kg = 1.6 ± 8.48 |
|                  |                        |                                                  |                              |                       | 500 mg/kg = −19.6 ± 7.49 | 750 mg/kg = −61.6 ± 6.60 |
|                  |                        |                                                  |                              |                       | 750 mg/kg = −76.5 ± 45.08 | 750 mg/kg = −76.5 ± 45.08 |
| Shewamene, et al, 2015 [16] | Osostegia inte grifolia | Normoglycemic mice                               | Methanol E                   | Day 15                | 200 mg/kg = −11.8 ± 8.93 | 749.750 mg/kg = 1.6 ± 8.48 |
|                  |                        |                                                  |                              |                       | 500 mg/kg = −19.6 ± 7.49 | 750 mg/kg = −61.6 ± 6.60 |
|                  |                        |                                                  |                              |                       | 750 mg/kg = −76.5 ± 45.08 | 750 mg/kg = −76.5 ± 45.08 |
## Table 3: In vivo anti-diabetic activity of medicinal plants in Ethiopia (Continued)

| Study | Plant | Animal type | Extraction method/ component | Duration of treatment | From diabetic Control | From standard control |
|-------|-------|-------------|-------------------------------|----------------------|-----------------------|-----------------------|
|       |       |             | Ethyl acetate F                | Day 15               | 250 mg/kg = 69 ± 35.29 | 250 mg/kg = − 167.6 ± 23.83 |
|       |       |             |                               |                      | 500 mg/kg = 67 ± 32.80 | 500 mg/kg = − 169.6 ± 19.99 |
|       |       |             | n-butanol F                   | Day 15               | 250 mg/kg = 132 ± 31.57 | 250 mg/kg = − 104.6 ± 17.91 |
|       |       |             |                               |                      | 500 mg/kg = 143.8 ± 40.38 | 500 mg/kg = − 92.8 ± 30.91 |
|       |       |             | Aqueous F                     | Day 15               | 250 mg/kg = 104.8 ± 33.16 | 250 mg/kg = − 131.8 ± 20.58 |
|       |       |             |                               |                      | 500 mg/kg = 109 ± 33.46 | 500 mg/kg = − 127.6 ± 21.06 |
|       |       |             | Methanol E                    | Day 15               | 250 mg/kg = 80.2 ± 17.6 | 250 mg/kg = − 31.8 ± 11.75 |
|       |       |             |                               |                      | 500 mg/kg = 61.2 ± 16.74 | 500 mg/kg = − 51.4 ± 7.67 |
|       |       |             |                               |                      | 750 mg/kg = 54.4 ± 14.54 | 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 | 300 mg/kg = 23.27 ± 4.18 |
|       |       |             |                               |                      | 500 mg/kg = − 29.88 ± 1.64 | 500 mg/kg = 12.12 ± 3.03 |
|       |       |             | Ethanol E                     | 14 days              | 300 mg/kg = − 18.84 ± 2.44 | 300 mg/kg = 23.16 ± 3.52 |
|       |       |             |                               |                      | 500 mg/kg = − 19.16 ± 2.36 | 500 mg/kg = 22.84 ± 3.45 |
| Tamiru et al., 2012 [28] | Caylusea abyssinica | Normal mice | Methanolic E | 4 h | 100 mg/kg = 9 ± 5.33 | 100 mg/kg = 11 ± 7.62 |
|       |       |             |                               |                      | 200 mg/kg = 8 ± 4.25 | 200 mg/kg = 10 ± 6.91 |
|       |       |             | streptozotocin induced mice    | 534.4               | 100 mg/kg = 111.67 ± 53.44 | 100 mg/kg = − 33.7 ± 43.6 |
|       |       |             |                               |                      | 200 mg/kg = 149 ± 41.58 | 200 mg/kg = − 39.66 ± 41.89 |
|       |       |             |                               |                      | 300 mg/kg = 105.78 ± 51.61 | 300 mg/kg = − 51.61 ± 51.61 |
| Oral glucose loaded rat | 200 mg/kg = 3.83 ± 6.14 | 100 mg/kg = − 14 ± 10.54 |
|       |       |             |                               |                      | 200 mg/kg = 8.17 ± 4.86 | 200 mg/kg = − 9.66 ± 9.85 |
|       |       |             |                               |                      | 300 mg/kg = − 9.5 ± 12.18 | 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 | 250 mg/kg = 76.4 ± 65.45 |
|       |       |             |                               |                      | 500 mg/kg = − 155 ± 35.71 | 500 mg/kg = 49.8 ± 42.4 |
|       |       |             | Methanol E                    |                      | 250 mg/kg = − 145.6 ± 56.11 | 250 mg/kg = 59.2 ± 60.59 |
|       |       |             |                               |                      | 500 mg/kg = − 171.2 ± 28.91 | 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 | 100 mg/kg = 49.66 ± 2.17 |
|       |       |             |                               |                      | 200 mg/kg = − 71.34 ± 4.79 | 200 mg/kg = 39.66 ± 3.11 |
|       |       |             |                               |                      | 400 mg/kg = − 82.25 ± 4.17 | 400 mg/kg = 28.75 ± 2.03 |
| Tesfaye et al., 2016 [13] | Justicia Schimperi | Normal mice | Aqueous extract | 4 h | 200 mg/kg = − 1 ± 3.81 | 200 mg/kg = − 13.3 ± 4.19 |
|       |       |             |                               |                      | 400 mg/kg = 10.17 ± 2.74 | 400 mg/kg = − 2.16 ± 3.26 |
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.

**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.

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

| Study          | Plant                  | Animal type            | Extraction method/component | Duration of treatment | From diabetic Control | From standard control |
|----------------|------------------------|------------------------|-----------------------------|-----------------------|-----------------------|-----------------------|
| Toma et al, 2012 | Moringa Stenopetala    | Normal                 | Butanol f. of Ethanol extract| 28 days               | 200 mg/kg = −46.66 ± 9.33 | 200 mg/kg = −10.16 ± 8.60 |
|                |                        |                        |                            |                       | 400 mg/kg = 39 ± 11.13 | 400 mg/kg = −2 ± 18.9  |
| Toma et al, 2015 | Moringa Stenopetala    | streptozocin-induced rats | Ethanol fraction            | 14 days               | 500 mg/kg = −2 ± 18.9 |
|                |                        |                        |                            |                       | 500 mg/kg = −2 ± 18.9  |
| Tsegaye et al, 2008 | Urtica simensis Hochst. ex. A. Rich | STZ-induced diabetic mice | Methanol E                | 4 h                   | 152 ± 8.36               | −131 ± 19.5            |
|                |                        |                        |                            |                       | −147.9 ± 33.94           | −273 ± 20.05            |
|                |                        |                        | Petroleum ether F.          |                       | 105 ± 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           |
| Yibru et al, 2015 | Coriandrum Sativum     | STZ induced T2DM Mice  | Ethanol                     | 21 days              | Increased at 300, 400 and 500 mg/kg |
|                |                        |                        |                            |                       | 201.7 ± 40.03            | Decreased at 300, 400 and 500 mg/kg |
| Test                      | Alema et al, 2020 [10] | Belayneh et al, 2019 [12] | Biru et al, 2015 [21] | Hammesso et al, 2015 | Shewamene et al, 2015 [16] | Tafesse et al, 2017 [20] | Taminu 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 | Indigofera spicata Forssk | Aloe megalacantha Baker | Ajuga remota Benth | Caylusea abyssinica | Aloe megalacantha and Aloe monticola | Moringa stenopetala | Aloe pulcherima | Datura stramonium Linn |
| Flavonoids               | +                       | +                         | +                     | +                    | +                         | +                         | +                      | +                         | +               | +                    | +                           |
| Phenols                  | +                       | +                         | –                     | +                    | +                         | +                         | +                      | +                         | +               | +                    | +                           |
| Tannins                  | +                       | +                         | +                     | –                    | +                         | +                         | +                      | +                         | +               | +                    | +                           |
| Saponins                 | +                       | +                         | +                     | +                    | +                         | +                         | +                      | +                         | +               | +                    | +                           |
| Alkaloids                | a                       | +                         | +                     | +                    | +                         | +                         | +                      | +                         | +               | +                    | +                           |
| Terpenoids               | +                       | –                         | +                     | +                    | a                         | +                         | +                      | +                         | +               | +                    | +                           |
| Glycosides               | a                       | +                         | +                     | +                    | a                         | +                         | +                      | +                         | +               | +                    | +                           |
| Steroids                 | a                       | +                         | +                     | –                    | –                         | +                         | +                      | +                         | +               | +                    | +                           |
| Anthraquinones           | 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* *Forsk*, *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 LD$_{50}$ of *Moringa stenopetala* 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 AG1 were 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 Rf 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 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 scantily 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 BSI 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 glyceroldehydes; 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; LD50: Median lethal dose

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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.

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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-graceum L.) on Hyperlipidemia in
Diabetic Patients. J Diabetes Res. 2019. https://doi.org/10.1155/2019/
8507453.
7. Sileshi T, Makonnen E, Debeba 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, Melkonnen Y, Debeba A, Adissawattana S. Intestinal
α-glucosidase and some pancreatic enzymes inhibitory effect of
hydroalcoholic 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, Melkonnen Y, Debeba A, Adissawattana 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 Justicia Schimperiana in cattle. J Ethnobiol Ethnomed.
2013;9:1–7.
11. Belayneh YM, Birhanu Z, Biru EM, Getenet G. Evaluation of in vivo
antidiabetic, antidiyslipidemic, and in vitro antioxidant activities of
hydromethanolic root extract of Datura stramonium L. (Solanaceae). J Exp
Pharmacol. 2019;11:29–38.
12. Tesfaye A, Makonnen E, Gedamu S. Hypoglycemic and antihyperglycemic
activity of aqueous extract of Justicia Schimperiana leaves in normal and
diabetic mice. Pharmacologyonline. 2008;3:1049–55.
13. Mussa A, Makonnen E, Urgu K. Effects of the crude aqueous extract and
isolated fraction of Moringa stenopetala leaves in normal and diabetic mice. J
Ethnopharmacol. 2015;161:61–71.
14. Hammes OW, Emeru YK, Getahun KA, Kahlaiw A. Antidiabetic and
antihyperlipidemic activities of the leaf latex extract of Aloe megalacantha
baker (Asclepiadaceae) in Streptozotocin-induced diabetic model. Evidence-based
Complement Altern Med. 2019. https://doi.org/10.1155/2019/8363796.
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 extract of Oostegia 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/s12906-015-0535-3.

17. Makonnen E, Hunde A, Darnecha G. Hypoglycaemic effect of Moringa stenopetala aqueous extract in rabbits. Phyther Res. 1997;11:147–8.

18. Tsegaye U, Urga K, Shewamene Z. Antidiabetic activity of Senna (Senna unisius Hochst. Ex. A. Rich.) in streptozotocin-induced diabetic mice. Ethiop Pharm J. 2008;27:75–82.

19. 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.

20. Birru EM, Abdelwuhab M, Shewamene Z. Effect of hydroalcoholic leaves extract of Indigofera spicata Forsk. On blood glucose level of normal, glucose loaded and diabetic rodents. BMC Complement Altern Med. 2015;15:1–8. https://doi.org/10.1186/s12906-015-0952-9.

21. Belayneh YM, Birru EM. Antidiabetic activities of hydromethanolic leaf extract of Calypnium ulat. (Ait.) benth. Subsp. aurea (Fabaceae) in mice. Evidence-based Complement Altern Med. 2018. https://doi.org/10.1155/2018/3509073.

22. Nardos A, Makonnen E, Debbela A. Effects of crude extracts and fractions of Moringa stenopetala (baker f.) cufodontis leaves in normoglycemic and alloxan-induced diabetic African. J Pharm Pharmacol. 2011;5:2220–5.

23. 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.

24. Teklu GH, Ayaa 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.

25. Shewasianad A, Bhoumik D, Hishe HZ, Maresha B. Anti-diabetic activity of methanol extract and fractions of Thymus schimperi Ronnier leaves in Normal and Streptozotocin induce diabetic mice. Iran J Pharm Pharmacol. 2019;16:1.

26. Seifu D, Gustafsson LE, Chawla R, Genet S, Debbela A, Holst M, et al. Antidiabetic and gastric emptying inhibitory effect of herbal Mela azedarach leaf extract in rodent models of diabetes type 2 mellitus. J Exp Pharm. 2017:293.

27. Tamiru W, Engidawork E, Asres K. Evaluation of the effects of 80% solvent fractions of Bersama 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.

28. Taye GM, Bule M, Gadisa DA, Tekla F, Abeba 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.

29. Tefeana MM, Masresha Alaye B, Yimer EM, Abebe DF, Bekele ST. Antidiabetic effect of germinated lens culinaris medik seed extract in streptozotocin induced diabetic mice. J Exp Pharm. 2020. https://doi.org/10.2147/JEP.S228834.

30. Melaku BC, Amare GG. Evaluation of antidiabetic and antioxidant potential of hydromethanolic seed extract of Datura stramonium Linn (Solanaceae). J Exp Pharm. 2020. https://doi.org/10.2147/JEP.S258522.

31. Kifle ZD, Atanefait DA, Atanafie SA. Hypoglycemic, anti-hyperglycemic and anti-hyperlipidemic effects of Bersama abyssinica Fresen (Meliaceae) leaves’ solvent fractions in normoglycemic and streptozotocin-induced diabetic mice. J Exp Pharm. 2020. https://doi.org/10.2147/JEP.S272959.

32. Mahadeva RUS, Adinew B. Hypolipidemic effect of dichloromethane as well as methanolic fruit and leaf extract of Ethiothaxia alligator pear (pesna americana mill) on tyloxapol-induced hyperlipidemic experimental rat. J. Asian J Res Chem. 2011;4(4):574–8.

33. 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 (Meliaceae). J Evidence-Based Integr Med. 2020. https://doi.org/10.11177/2515690X20958287.

34. Amare GG, Mehari BG, Belayneh YM. Evaluation of antidiabetic activity of the leaf latex of Aloe polyphylla Gilbert and Sebsebe (Aloaceae). Evidence-Based Complement Altern Med. 2020. https://doi.org/10.1155/2020/8897943.

35. Tekulu GH, Araya EM, Mengesha HG. In vitro α-amylase inhibitory effect of Moringa stenopetala aqueous extract in rabbits. Phyther Res. 1997;11:147–8.

36. Melaku BC, Amare GG, Belayneh YM. Evaluation of antidiabetic activity of the leaf latex of Aloe polyphylla Gilbert and Sebsebe (Aloaceae). Evidence-Based Complement Altern Med. 2020. https://doi.org/10.1155/2020/8897943.