Review

Assessment of traditional knowledge of the antidiabetic plants of Darjeeling and Sikkim Himalayas in the context of recent phytochemical and pharmacological advances

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ABSTRACT
Darjeeling and Sikkim Himalayas, a part of Eastern Himalayan Hotspot, is characterized by its richness of plant diversity. Herbal medicine has been one of the most popular and reliable healing practices among the different ethnic groups of this region for ages. However, the lack of documentation practice by the traditional healers has led to obscurity regarding the efficacy of herbal medicine among the present generation, though they have to depend on the same quite often. Meanwhile, several reviews have attempted to document the plants used for the treatment of diabetes from this region, but interestingly, very few research works can be obtained regarding the characterization of antidiabetic properties of the plants of this region. Therefore, it demands a better understanding of the potentiality of these plants in the purview of scientific evidence. This review article reports 55 such plant species which have been reported to be frequently used in the treatment of hyperglycemia and our objective was to validate the potentiality of the plants in the light of recent phytochemical and pharmacological researches being carried out locally or elsewhere.

Keywords: hyperglycemia; antidiabetics; antihyperglycemics; phytochemicals; pharmacological processes; herbal medicine


1 Introduction

Diabetes mellitus, a major endocrine disorder resulting from inefficient insulin secretion or impaired insulin function, is one of the most life-threatening diseases[1,2]. Both the developed and developing countries are suffering from a huge burden on medical and productivity issues due to this chronic metabolic syndrome. India is defined as the diabetic capital of the world with highest number of patients[3]. All the three major types of diabetes: type 1, type 2 and gestational diabetes are considered responsible for morbidity and premature mortality of majority of patients[4]. More than 8% of the world population is now suffering from diabetes with about an expected increase of
above 50% prevalence worldwide by 2035\cite{5}.

The primary treatment of diabetes is targeted towards obtaining a good glycemic control by reducing demand for insulin, enhancing endogenous insulin secretion, repairing insulin action, or lowering the rate of carbohydrate degradation\cite{6}. Presently, the treatment of diabetes mainly relies on the synthetic antidiabetic medicines like acarbose, metformin, sulfonylurea, glibenclamide, meglitinides, etc., but all of these drugs exert some deleterious side effects when administered orally or by subcutaneous injection\cite{7}. Exogenous insulin therapy is also used to achieve proper metabolic stability, especially in type 1 diabetes\cite{8}. At the same time, alternative treatment procedures still exist in many ethnic communities that have been practiced for hundreds of years. Though unpopular to the urban population due to the dearth of proper scientific validation, great scope lies in unravelling the basis of traditional knowledge in the treatment of diabetes\cite{9,10}. Various preclinical studies have confirmed that the active constituents isolated from different plants enable lowering of blood glucose\cite{11}. Wide array of secondary metabolites have been isolated and characterized for antidiabetic property. Many of these active principles are also used to prepare antidiabetic herbal formulations\cite{12}. Therefore, thorough investigations on the actual mechanism of action and proper dosage of these marketed mono- and polyherbal formulations could lead us towards an alternative approach to combat the adversities of diabetes.

Darjeeling and Sikkim Himalaya, a part of Eastern Himalayan Hotspot, is situated between 87°59’ and 88°62’E and 26°31’ and 28°10’N (Figure 1). This region contains more than 4 000 species of flowering plants, which include over 600 species of orchids and more than 100 species of medicinal plants\cite{13}. This region aided by rich plant diversity accounts for indigenous knowledge of herbal medicine among the various ethnic communities viz. Lepcha, Bhutia, Tamang, Rai, Sherpa, Limbu, Kami, Damai, etc. to treat several diseases from ages\cite{13}. Several plants of this region are frequently used by the local people for the treatment of diabetes\cite{11,14–16}. On the other hand, very few works have been done to characterize the antidiabetic properties of the plants from this region. However, there is a great scope of the recent

![Figure 1](image_url)
research works in the validation of indigenous traditional knowledge, as these may be either not properly recorded or the information has been modified when passed on from generation to generation. This review article therefore conglomerates 55 plants from Darjeeling and Sikkim Himalayas from different papers and review articles, which have been reported to possess antihyperglycemic properties. In addition, an attempt has been undertaken for the validation of the traditional knowledge in the light of recent phytochemical and pharmacological advances taking into purview. All the research works demonstrating the potential antidiabetic role of the plants are irrespective of the origin of published articles.

2 Methodology

Information was collected regarding the antidiabetic plants from authentic sources viz. literature review and research articles originating from this region and interactions were conducted with various ethnic communities viz. Lepcha, Bhutia, Tamang, Rai, Sherpa, Limbu, Kami, Damai etc. of Darjeeling and Sikkim Himalaya regions of West Bengal to document the last traces of their natural healers of diabetes. The keywords like “antidiabetic plants of Darjeeling and Sikkim”, “hypoglycemic plants of Darjeeling and Sikkim” and “medicinal plants of Darjeeling and Sikkim” were used to generate the preferable records of data for compilation. Subsequently, “The Plant List” (http://www.theplantlist.org/) database was used for verification of correct and accepted name of recorded plants to avoid repetitive enlistment of the same plant with synonyms. Interactions were conducted with the people of this region mainly in the age group of 40–70 years, who were familiar with the herbal treatment of diabetes. The main purpose of the interaction was to confirm the record of enlisted plants with reported antidiabetic properties. This was solely based on an open-ended and flexible questionnaire that included the collection of information by using the local name of the plants as a key. The questionnaire briefly included the following points: occurrence of the plant in their locality, cultivated/wild, availability season, plant parts used, method of treatment, etc. Further appraisal of the antidiabetic potential of the enlisted plants was carried out with the help of recent studies documenting the phytochemical and pharmacological attributes of the plants from across the world.

3 Traditional antidiabetic plants from Darjeeling and Sikkim Himalayas

Darjeeling is a hill district in the state of West Bengal and occupies an area of 3 149 km² with an altitude up to 2 700 m comprising of 4 subdivisions viz. Darjeeling Sadar, Kalimpong, Kurseong and Siliguri with 12 blocks of which majority are earmarked as rural and backward. About 80% of the Darjeeling District is covered by the hilly terrains with a population of about 7.5 lakhs[17]. Eighty percent of the population of Darjeeling Hills is living in the rural areas with a major share of people still devoid of comprehensive healthcare services. Sikkim on the other hand is a state of North-east India adjacent to Darjeeling which historically, culturally and geographically shares an unseparable bond with the Darjeeling Hills. The state of Sikkim is divided into 4 districts and occupies an area of 7 096 km² with an altitude up to 7 000 m. The present population of Sikkim is about 6.1 lakhs and about 75% of the population live in villages[18]. Darjeeling and Sikkim Himalayas harbours a rich floristic diversity and the people of this region are still dependent on the traditional herbal medicine for their primary healthcare needs. The floristic wealth of this region has been reported to account for approximately 40% of the country’s total flora[13]. Many plants have been used by the local people of this region to cure the abnormalities associated with increased blood glucose level. Several workers have reported the usage of different plant parts in the treatment of diabetes. We have enlisted 55 plants of this region which possess hypoglycemic properties, the parts used and method of use from the different scientific documentations (Table 1).

The table enlisting the hypoglycemic plants reveals the diversity of the plants of this region that are used by the local people. The 55 plants enlisted belong to 37 families out of which one member of gymnosperm: Taxus baccata of the family Taxaceae is also present. Majority of the angiosperms belong to the dicots and only 4 monocot families of the Order Liliales, Arecales and Zingiberales are featured (Figure 2). The dicot plants belong to 17 Orders viz. Malvales, Ranunculales, Sapindales, Saxifragales, Rosales, Fabales, Gentianales, Laurales, Cucurbitales, Boraginaceae, Malpighiales, Solanales, Lamiales, Apiales, Dipsacales, Fagales and Myrtales (Figure 2). The Orders Ranunculales, Rosales, Lamiales and Gentianales account for the major share of the antidiabetic plants with 7, 6, 6 and 5 plants, respectively.

It is quite evident that many plants of this region are believed to be helpful in lowering the increased glucose level and are faithfully used by the local people in their daily practices. Several researchers have documented the plant parts used for the treatment of diabetes and also the mode of usage is popular among the people of this region. Some plants have been reported that all the parts are important and some have been reported that only some specific parts are used. For instance, the use of whole plant parts of Boehninghausenia albiflora and Swertia angustifolia, specific plant parts such as roots
<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Name of plant</th>
<th>Local name</th>
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<th>Mode of traditional use</th>
<th>Pharmacological evidence supporting traditional use</th>
<th>Major antidiabetic compounds identified</th>
<th>Probable mode of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Abroma augusta (L.) L. f.</td>
<td>Ulatkambal</td>
<td>Stem, leaf</td>
<td>Stem bark and leaf decoction (10–20 mL) taken one time each alternate day in empty stomach for 4–6 weeks(^{[14]})</td>
<td>Aqueous extract of leaves showed hypoglycemic effect on alloxan-induced diabetic rats(^{[19,20]})</td>
<td>Abromine(^{[21]})</td>
<td>–</td>
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<tr>
<td>2.</td>
<td>Abutilon indicum (L.) Sw.</td>
<td>Ghan-tiphol</td>
<td>Stem</td>
<td>Stem bark decoction (25–50 mL) taken two times daily (after lunch and dinner) for 3–4 weeks(^{[14]})</td>
<td>Aqueous extracts of whole plants exhibited hypoglycemic activity(^{[22]})</td>
<td>Oleanolic acid (OA)(^{[22]}), quercetin-3-rutinoside(^{[23]})</td>
<td>OA improves insulin response, preserves functionality and survival of β-cells, and promotes insulin secretion from pancreatic β-cells</td>
</tr>
<tr>
<td>3.</td>
<td>Aconitum palmatum D. Don.</td>
<td>Setoh-bhumma, Nyini, Bhongn-anukpo</td>
<td>Root</td>
<td>Root decoction (10–15 mL) along with a cup of milk consumed after lunch for 7–10 days(^{[14,24]})</td>
<td>No record found</td>
<td>No record found</td>
<td>–</td>
</tr>
<tr>
<td>4.</td>
<td>Aegle marmelos (L.) Correa</td>
<td>Bael</td>
<td>Leaf, fruit</td>
<td>Aqueous and alcoholic extract as well as powder of leaves and fruits are used(^{[11,25]})</td>
<td>Leaf extract showed antidiabetic activity in rabbit(^{[26]}) anoside(^{[27]}) The fruit extract showed improved functional state of the pancreatic cells and partially reversed the damage caused by streptozotocin (STZ)(^{[28]})</td>
<td>Umbelliferone β-D-alactopyranoside(^{[27]})</td>
<td>Acts by increasing the level of pancreatic insulin secretion</td>
</tr>
<tr>
<td>5.</td>
<td>Aloe vera (L.) Burm. f.</td>
<td>Ghewkumara</td>
<td>Leaf</td>
<td>40–50 g of fresh leaf pulp taken once a day for 10–12 weeks in empty stomach(^{[11,14]})</td>
<td>Antidiabetic effect of leaf extracts on STZ-induced rats was observed(^{[29]})</td>
<td>Aloresin A(^{[30]}), Aloe emodin-8-O-glycoside(^{[31]})</td>
<td>Inhibits α-glucosidase and suppress insulin resistance; stimulates glucose transport and glycogen storage</td>
</tr>
<tr>
<td>6.</td>
<td>Asparagus racemosus Willd.</td>
<td>Kurilo, Neusiri</td>
<td>Tender shoot, root</td>
<td>25 mL of shoot decoction consumed once a day for 6–8 weeks Crushed root extract is given orally(^{[11,14,32]})</td>
<td>Ethanolic extracts of shoots and roots showed hypoglycemic activity in diabetic rats(^{[33,34]})</td>
<td>No record found</td>
<td>–</td>
</tr>
<tr>
<td>7.</td>
<td>Azadirachta indica A. Juss.</td>
<td>Neempate</td>
<td>Leaf</td>
<td>Juice of leaves administered orally(^{[11,16]})</td>
<td>Chloroform extracts of leaves exhibited antihyperglycemic activity on STZ-induced diabetic rats(^{[15]})</td>
<td>Nimbidiol(^{[36]})</td>
<td>Inhibits mammalian and fungal α-glucosidase</td>
</tr>
</tbody>
</table>

Table 1 (to be continued) Plants with reported antidiabetic potential, their mode of usage and concurrent appraisal of the traditional knowledge on the basis of advances in phytochemical and pharmacological research
Table 1 (continuation 1) Plants with reported antidiabetic potential, their mode of usage and concurrent appraisal of the traditional knowledge on the basis of advances in phytochemical and pharmacological research

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Name of plant</th>
<th>Local name</th>
<th>Plant parts used</th>
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<tbody>
<tr>
<td>8.</td>
<td><em>Berberis aristata</em> DC.</td>
<td>Sano Chutro, Sutang-kung, Skyerba</td>
<td>Root, bark, stem</td>
<td>5–10 mL of root, bark and stem extracts taken twice daily for 1–2 weeks(^{11,14})</td>
<td>Root extracts regulate glucose homeostasis in diabetic rats(^{37}) Methanolic extract of stem bark exhibits significant antidiabetic activity in a dose-dependent manner(^{38})</td>
<td>Berberine, berbamine, palmatine(^{37})</td>
<td>Berberine and berbamine activates AMP protein kinase and stimulates glycolysis; palmatine activity is mediated through insulin pathway</td>
</tr>
<tr>
<td>9.</td>
<td><em>Boenninghausenia albiflora</em> (Hook.) Rech. Ex Mein.</td>
<td>Chiribir-patay</td>
<td>Whole plant</td>
<td>Raw plant juice (5–10 mL) taken 1–2 times daily for 3–4 weeks(^{14})</td>
<td>No record found</td>
<td>No record found</td>
<td>–</td>
</tr>
<tr>
<td>10.</td>
<td><em>Bryophyllum pinnatum</em> (Lam.) Oken.</td>
<td>Paashaanabhed</td>
<td>Leaf</td>
<td>Not documented(^{23})</td>
<td>Crude extract of leaves exhibited hypoglycemic activity in alloxan-induced rats(^{39})</td>
<td>No record found</td>
<td>–</td>
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<tr>
<td>11.</td>
<td><em>Calamus rotang</em> L.</td>
<td>Bet</td>
<td>Fruit</td>
<td>Raw fruit (1–2) taken as masticatory two times daily for 6–8 weeks(^{14})</td>
<td>No record found</td>
<td>No record found</td>
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<tr>
<td>12.</td>
<td><em>Cannabis sativa</em> L.</td>
<td>Bhang</td>
<td>Leaf</td>
<td>Leaf extract (5–10 mL) consumed two times a day for 3–4 weeks(^{14})</td>
<td>Hypoglycemic effect of leaf extracts was observed(^{40})</td>
<td>Cannabidiol(^{41})</td>
<td>Attenuates diabetes-induced oxidative stress, inflammation and cell death</td>
</tr>
<tr>
<td>13.</td>
<td><em>Cassia fistula</em> L.</td>
<td>Raj briksha</td>
<td>Fruit</td>
<td>Not documented(^{16})</td>
<td>Leaf and bark showed to have antihyperglycemic activity(^{42,43}) No record of work on fruit extract was found</td>
<td>Vindoline, vindolidine, vindolicine, vindolamine(^{46})</td>
<td>Acts by inducing relatively high glucose uptake in pancreatic β-cells or myoblast cells</td>
</tr>
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<td>14.</td>
<td><em>Catharanthus roseus</em> (L.) G. Don.</td>
<td>Sadabahar</td>
<td>Leaf, root</td>
<td>Raw leaf (1–2) chewed daily for 1–2 weeks Leaf decoction and root decoction taken in empty stomach(^{14,44})</td>
<td>Fresh leaf juice exhibited antidiabetic activity(^{45}) No record of root extract was found</td>
<td>Vindoline, vindolidine, vindolicine, vindolamine(^{46})</td>
<td>Acts by inducing relatively high glucose uptake in pancreatic β-cells or myoblast cells</td>
</tr>
<tr>
<td>15.</td>
<td><em>Cinnamomum tamala</em> (Buch.-Ham.) T. Nees &amp; Eberm</td>
<td>Sinkuli, Napor, Mensing</td>
<td>Decocion of stem bark taken three times daily for 3–4 weeks(^{14,44})</td>
<td>Leaf extracts showed antidiabetic properties(^{47}) No record of work on stem extract</td>
<td>Cinnamonaldehydes(^{48}), procyanidin oligomers(^{49})</td>
<td>Cinnamonaldehydes(^{48}), procyanidin oligomers(^{49})</td>
<td>Induces the secretion of insulin from existing β-cells from the islets of langerhans; acts by immune-suppressive mechanisms</td>
</tr>
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<td>16.</td>
<td><em>Cissampelos pareira</em> (L.)</td>
<td>Batulpatay</td>
<td>Root-bark decoction (5–10 mL) taken 1–2 times for 2–3 weeks [14]</td>
<td>Methanolic root extract showed dose-dependent activity in STZ-induced rats [46]</td>
<td>No record found</td>
<td>–</td>
<td>Promote insulin release from β-cells and improve insulin sensitivity</td>
</tr>
<tr>
<td></td>
<td>Family: Menispermaceae Climer</td>
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<td></td>
<td></td>
<td></td>
<td>Acts by inducing insulin secretion and restoring the altered plasma enzymes like aspartate aminotransferase, alkaline phosphatase and acid phosphatase</td>
</tr>
<tr>
<td>17.</td>
<td><em>Coccinia grandis</em> (L.)</td>
<td>Tilkor</td>
<td>Root</td>
<td>Extract of fresh root (5–10 mL) taken 2 times [14,15]</td>
<td>Alcoholic extract of leaf and fruit exhibited hypoglycemic activity [51,52]</td>
<td>No record found</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Family: Cucurbitaceae Climer</td>
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<td></td>
<td></td>
<td>Methanolic extract of roots produced significant decrease in glucose level [53]</td>
<td></td>
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</tr>
<tr>
<td>18.</td>
<td><em>Cordia myxa</em> L.</td>
<td>Bohori</td>
<td>Fruit</td>
<td>Not documented [22]</td>
<td>No record found</td>
<td>No record found</td>
<td>–</td>
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<tr>
<td></td>
<td>Family: Boraginaceae Tree</td>
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<tr>
<td>19.</td>
<td><em>Ficus racemosa</em> L.</td>
<td>Dumri</td>
<td>Fruit, stem</td>
<td>10–15 mL of fruit juice taken before meals two times a day for 4–8 weeks [14,23]</td>
<td>Fruit extract showed antidiabetic activity [54]</td>
<td>α-amyrin [56]</td>
<td>–</td>
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<tr>
<td></td>
<td>Family: Moraceae Tree</td>
<td></td>
<td></td>
<td></td>
<td>Stem extract show α-amylase and α-glucosidase activity [55]</td>
<td>β-sitosterol [57]</td>
<td></td>
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<td>20.</td>
<td><em>Girardinia diversifolia</em> (Link) Friis</td>
<td>Bhangre- sisnu</td>
<td>Root</td>
<td>Decoction of root (25–50 mL) consumed two times a day for 4–8 weeks [14]</td>
<td>Ethanol extract of leaves exhibited activity in alloxan-induced diabetic rats [58]</td>
<td>No record of work on root extract</td>
<td>Promote insulin release from β-cells and improve insulin sensitivity</td>
</tr>
<tr>
<td></td>
<td>Family: Urticaceae Shrub</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Acts by inducing insulin secretion and restoring the altered plasma enzymes like aspartate aminotransferase, alkaline phosphatase and acid phosphatase</td>
</tr>
<tr>
<td>21.</td>
<td><em>Gynocardia odorata</em> R. Br.</td>
<td>Gantay</td>
<td>Fruit</td>
<td>Fruit juice (10–15 mL) taken one time a day for two weeks [14]</td>
<td>Mehanolic leaf extracts showed activity in STZ-induced rats [59]</td>
<td>No record of work on fruit extract</td>
<td>–</td>
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<tr>
<td></td>
<td>Family: Flacourtiaceae Tree</td>
<td>Tukkung</td>
<td></td>
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<tr>
<td>22.</td>
<td><em>Hellenia speciosa</em> (J. Koening) S.R.Dutta</td>
<td>Betlouri, Ruyang</td>
<td>Rhizome</td>
<td>10–20 mL of rhizome decoction taken orally for 2–4 weeks daily [11,14,42]</td>
<td>Ethanolic extracts of rhizome helped regulate blood glucose [40]</td>
<td>Costunolide [61]</td>
<td>Promote insulin release from β-cells and improve insulin sensitivity</td>
</tr>
<tr>
<td></td>
<td>Family: Costaceae Herb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Eremanthin [61]</td>
<td>Acts by inducing insulin secretion and restoring the altered plasma enzymes like aspartate aminotransferase, alkaline phosphatase and acid phosphatase</td>
</tr>
</tbody>
</table>
Table 1 (continuation 3) Plants with reported antidiabetic potential, their mode of usage and concurrent appraisal of the traditional knowledge on the basis of advances in phytochemical and pharmacological research

<table>
<thead>
<tr>
<th>Sl. No.</th>
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<th>Probable mode of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>25.</td>
<td>Litsea cubeba (Lour.) Pers.</td>
<td>Siltimmur</td>
<td>Fruit</td>
<td>Raw fruit (one) chewed as masticatory two times daily for 4–6 weeks[14]</td>
<td>No record found</td>
<td>No record found</td>
<td>–</td>
</tr>
<tr>
<td>26.</td>
<td>Macropanax undulatus (Wall. ex G.Don) Seem.</td>
<td>Chinday</td>
<td>Bark</td>
<td>Not documented[62]</td>
<td>No record found</td>
<td>No record found</td>
<td>–</td>
</tr>
<tr>
<td>27.</td>
<td>Momordica charantia L.</td>
<td>Karela</td>
<td>Fruit</td>
<td>25 mL of fruit extract taken two times daily for 12–14 weeks[11,14]</td>
<td>Boiling water extract of fruits exhibits pancreatic cell reparining and insulin secreting action[66]</td>
<td>Moromordicicosides[67]</td>
<td>Stimulates glucose transporter 4 translocation and AMP kinase; regulates glucose homeostasis; antigluconeogenic activity</td>
</tr>
<tr>
<td>29.</td>
<td>Nardostachys jatamansi (D. Don.) DC.</td>
<td>Jatamansi, RhiSpanzon</td>
<td>Decoction of rhizome (30–50 mL) taken once a day for 2–3 weeks[11,4,34]</td>
<td>Ethanolic extract of rhizome lowered blood glucose in alloxan-induced diabetic rats[73]</td>
<td>No record found</td>
<td>No record found</td>
<td>–</td>
</tr>
<tr>
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<tr>
<td>31.</td>
<td><em>Oroxylum indicum</em> (L.) Kurz.</td>
<td>Totola, Phagorip, Sonaka</td>
<td>Bark, seed</td>
<td>Juice of stem bark (5–10 mL) or decoction (15–20 mL) used 2–3 times daily</td>
<td>Stem bark extract exhibits antihyperglycemic activity (&lt;sup&gt;74&lt;/sup&gt;)</td>
<td>No record found</td>
<td>-</td>
</tr>
<tr>
<td>32.</td>
<td><em>Paedaria foetida</em> L.</td>
<td>Birilahara, Takpoedrik</td>
<td>Leaf</td>
<td>Leaf infusion (50–60 mL) taken one time daily morning for 2–3 weeks</td>
<td>Leaf extract showed remarkable antihyperglycemic activity associated with antihyperlipidemic and antioxidant activities (&lt;sup&gt;79&lt;/sup&gt;)</td>
<td>No record found</td>
<td>-</td>
</tr>
<tr>
<td>33.</td>
<td><em>Panax pseudoginseng</em> Wall.</td>
<td>Panchpatey</td>
<td>Rhizome, root, fruit</td>
<td>Dried rhizome powder (0.57 g) taken with warm milk one time daily</td>
<td>Plant extract regulates glucose and fat metabolism in mice (&lt;sup&gt;80&lt;/sup&gt;)</td>
<td>No record found</td>
<td>-</td>
</tr>
<tr>
<td>34.</td>
<td><em>Phyllanthus emblica</em> L.</td>
<td>Awla</td>
<td>Bark, fruit, leaf, root</td>
<td>Not documented</td>
<td>Methanolic extracts of fruits were screened by inhibitory action of α-amylase, α-glucosidase and antiglycation assays (&lt;sup&gt;81&lt;/sup&gt;)</td>
<td>No record found</td>
<td>-</td>
</tr>
<tr>
<td>35.</td>
<td><em>Picrorhiza kurroa</em> Royle.</td>
<td>Kutki, Putsesel</td>
<td>Rhizome</td>
<td>0.5 g of dried rhizome powder along with curd and pepper powder taken one time daily for 1–2 weeks</td>
<td>Whole plant extracts show antidiabetic activity (&lt;sup&gt;82&lt;/sup&gt;)</td>
<td>No record found</td>
<td>-</td>
</tr>
<tr>
<td>36.</td>
<td><em>Potentilla lineata</em> Trevir.</td>
<td>Banmula</td>
<td>Root</td>
<td>Root decoction (20–25 mL) taken two times daily for 4–8 weeks</td>
<td>No record found</td>
<td>No record found</td>
<td>-</td>
</tr>
<tr>
<td>37.</td>
<td><em>Quercus lanata</em> Sm.</td>
<td>Banj</td>
<td>Stem</td>
<td>Decoction of stem bark (20–25 mL) taken 1–2 times daily for 2–3 weeks</td>
<td>No record found</td>
<td>No record found</td>
<td>-</td>
</tr>
<tr>
<td>38.</td>
<td><em>Salvia moorcroftiana</em> Wall. ex Benth.</td>
<td>Kalijadi</td>
<td>Whole plant</td>
<td>Not documented</td>
<td>No record found</td>
<td>No record found</td>
<td>-</td>
</tr>
<tr>
<td>Sl. No.</td>
<td>Name of plant</td>
<td>Local name</td>
<td>Plant parts used</td>
<td>Mode of traditional use</td>
<td>Pharmacological evidence supporting traditional use</td>
<td>Major antidiabetic compounds identified</td>
<td>Probable mode of action</td>
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<tr>
<td>39.</td>
<td><em>Saraca asoca</em> (Roxb.) Willd.</td>
<td>Asok</td>
<td>Flower</td>
<td>Dry flower infusion (50–100 mL two times daily (before meals) for 4–5 weeks)</td>
<td>Flower powder and bark decoction reported in treatment of diabetes</td>
<td>No record found</td>
<td>–</td>
</tr>
<tr>
<td>40.</td>
<td><em>Scoparia dulcis</em> L.</td>
<td>Kharatey jhar</td>
<td>Whole plant</td>
<td>Not documented</td>
<td>Aqueous and ethanolic extract of this plant possessed blood glucose lowering activity</td>
<td>Scoparic acid D</td>
<td>Inhibitor of human α-glucosidase enzyme and delays digestion of starch and sucrose</td>
</tr>
<tr>
<td>41.</td>
<td><em>Stephania glabra</em> (Roxb.) Miers.</td>
<td>Tamarkey, Kanthey</td>
<td>Root</td>
<td>Root decoction (20–25 mL taken with milk 2–3 times daily for 1–2 weeks)</td>
<td>Ethanolic extract of tuber helped reduce blood glucose level in alloxan-induced diabetic rats</td>
<td>11-Hydroxy-palmatine</td>
<td>Acts by reducing blood glucose levels</td>
</tr>
<tr>
<td>42.</td>
<td><em>Stephania hernandifolia</em> (Willd.) Walp.</td>
<td>Panhelo-tamarke</td>
<td>Tuber</td>
<td>25% inch of tuber chewed twice a day for at least 4–5 weeks</td>
<td>Ethanolic and aqueous extract of tuber exhibited significant antidiabetic activities in STZ-induced diabetic rats</td>
<td>No record found</td>
<td>–</td>
</tr>
<tr>
<td>43.</td>
<td><em>Stephania rotunda</em> Lour.</td>
<td>Seto-tamarke</td>
<td>Root</td>
<td>Root decoction (1 teaspoon) taken in empty stomach for 10 weeks</td>
<td>No record found</td>
<td>No record found</td>
<td>–</td>
</tr>
<tr>
<td>44.</td>
<td><em>Swertia angustifolia</em> Buch-Ham ex D. Don</td>
<td>Patlay-chireto</td>
<td>Whole plant</td>
<td>Whole plant infusion taken two times daily (before meals) for 3–4 weeks</td>
<td>Extracts exhibit antidiabetic activities</td>
<td>No record found</td>
<td>–</td>
</tr>
<tr>
<td>45.</td>
<td><em>Swertia chirayita</em> (Roxb. Ex Flem.) Karst.</td>
<td>Chireto, Rungkyon, Tagota</td>
<td>Whole plant</td>
<td>Whole plant infusion (50–60 mL taken one time daily in empty stomach for two weeks)</td>
<td>Aqueous extract of leaves has significant antidiabetic activity similar to glibenclamide in STZ-induced diabetic rats</td>
<td>Swerchirin, swertiamarin, sweroside</td>
<td>Lowers blood glucose level by stimulating insulin release from islets of langerhans; antidiabetic activity is due to up-regulation of peroxisome-proliferator activated receptor gene expression</td>
</tr>
<tr>
<td>Sl. No.</td>
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<td>Local name</td>
<td>Plant parts used</td>
<td>Mode of traditional use</td>
<td>Pharmacological evidence supporting traditional use</td>
<td>Major antidiabetic compounds identified</td>
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</tr>
<tr>
<td>46.</td>
<td><em>Swertia pedicellata</em> Banerji</td>
<td>Chireto</td>
<td>Shoot</td>
<td>Decoction of shoot (20–25 mL) taken two times daily (before principal meals) for 4–6 weeks(^{[14]})</td>
<td>No record found</td>
<td>No record found</td>
<td>_</td>
</tr>
<tr>
<td>47.</td>
<td><em>Syzygium cumini</em> (L.) Skeels</td>
<td>Jyamuna, Dzambu</td>
<td>Stem bark decoction (25–30 mL) taken 3 times daily for 2–3 times(^{[14]})</td>
<td>Fruits, seeds, and stem bark show promising activity against diabetes(^{[95]})</td>
<td>Mycaminose(^{[94]}), maslinic acid, valoneic acid, rubuphenol, ellagic acid(^{[95]})</td>
<td>Acts by stimulating insulin secretion from pancreatic β-cells; acts by inhibiting aldose reductase and protein tyrosine phosphatase</td>
<td></td>
</tr>
<tr>
<td>48.</td>
<td><em>Taxus baccata</em> L.</td>
<td>Dhengre, Salla, Heongboo</td>
<td>Bark, Leaf</td>
<td>Not documented(^{[4]})</td>
<td>No record found</td>
<td>No record found</td>
<td>_</td>
</tr>
<tr>
<td>49.</td>
<td><em>Terminalia bellirica</em> (Gaertn.) Roxb.</td>
<td>Borra</td>
<td>Fruit</td>
<td>Not documented(^{[4]})</td>
<td>Hexane, ethyl acetate and methanolic extracts of fruits significantly increased the plasma insulin(^{[96]})</td>
<td>No record found</td>
<td>_</td>
</tr>
<tr>
<td>50.</td>
<td><em>Terminalia chebula</em> Retz.</td>
<td>Harra</td>
<td>Fruit</td>
<td>Not documented(^{[4]})</td>
<td>Fruit extract acts in a dose-dependent manner and helps in lowering blood sugar level and improves insulin sensitivity(^{[97]})</td>
<td>Chebulic acid(^{[98]}), corilagin(^{[99]})</td>
<td>Exert preventive effects against the formation of advanced glycation end products and endothelial cell dysfunction; possess α-glucosidase inhibitory activity</td>
</tr>
<tr>
<td>51.</td>
<td><em>Tinospora cordifolia</em> (Willd.) Hook f. &amp; Thoms.</td>
<td>Gujro, Lahara</td>
<td>Whole plant</td>
<td>Not documented(^{[4]})</td>
<td>Administration of methanolic extract restored the alterations of impaired blood glucose level and antioxidant status in alloxan-induced diabetic rat model(^{[100]})</td>
<td>Saponarin(^{[101]}), palmatin(^{[102]})</td>
<td>Inhibits the activities of α-glucosidase and sucrase; exerts antidiabetic effect by effective expression of glucose transporter 4</td>
</tr>
<tr>
<td>52.</td>
<td><em>Trichosanthes lepiniana</em> (Naudin) Cogn.</td>
<td>Indraynee</td>
<td>Fruit</td>
<td>Dried powder of mature fruit taken after lunch for 3 weeks(^{[15]})</td>
<td>No record found</td>
<td>No record found</td>
<td>_</td>
</tr>
</tbody>
</table>
Table 1 (continuation 7) Plants with reported antidiabetic potential, their mode of usage and concurrent appraisal of the traditional knowledge on the basis of advances in phytochemical and pharmacological research

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Name of plant</th>
<th>Local name</th>
<th>Plant parts used</th>
<th>Mode of traditional use</th>
<th>Pharmacological evidence supporting traditional use</th>
<th>Major antidiabetic compounds identified</th>
<th>Probable mode of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>53.</td>
<td><em>Trigonella foenum-graecum</em> L.</td>
<td>Methi</td>
<td>Seed</td>
<td>Sprouted seeds along with chilly, salt, garlic</td>
<td>Seed powder exhibits hypoglycemic and hyperinsulinemic action as well as neuroprotective action in diabetic rat brain</td>
<td>4-Hydroxyisoleucine&lt;sup&gt;[105]&lt;/sup&gt;</td>
<td>Acts by increasing insulin sensitivity and demonstrated to reduce the high levels of lipids and uric acid</td>
</tr>
<tr>
<td>54.</td>
<td><em>Urtica dioica</em> L.</td>
<td>Sisnu, Sarong</td>
<td>Shoot, leaf</td>
<td>Decoction of young leaves and shoots (50–100 mL) taken with meals 1–2 times daily for 4–8 weeks&lt;sup&gt;[11,14]&lt;/sup&gt;</td>
<td>Aqueous and ethanolic extract of leaves controls the hyperglycemic state of type-2 diabetes&lt;sup&gt;[106]&lt;/sup&gt;</td>
<td>Rutin&lt;sup&gt;[107]&lt;/sup&gt;</td>
<td>Play important role in carbohydrate metabolism and promote insulin secretion from pancreatic β-cells</td>
</tr>
<tr>
<td>55.</td>
<td><em>Zingiber officinale</em> Roscoe</td>
<td>Adua, Heng, Beasga</td>
<td>Rhizome</td>
<td>25–30 mL of rhizome decoction taken as herbal tea</td>
<td>Ethyl acetate extracts exhibited antidiabetic potential via modulating glucose uptake and inhibiting adipocyte differentiation&lt;sup&gt;[108]&lt;/sup&gt;</td>
<td>2-(4-Hydroxy-3-methoxyphenyl) ethanol, 2-(4-Hydroxy-3-methoxyphenyl) ethanoic acid&lt;sup&gt;[106]&lt;/sup&gt;, gingerol&lt;sup&gt;[109]&lt;/sup&gt;</td>
<td>Potent inhibitor of aldose reductase; acts by improving the impaired insulin signalling</td>
</tr>
</tbody>
</table>

Figure 2 Order wise distribution of the traditionally used hypoglycemic plants of Darjeeling and Sikkim Himalayas
of Cissampelos pareira and Coccinia grandis, fruits of Cordia myxa, Litsea cubeba and Gynocardia odorata, etc. have been reported.

4 Phytochemical and pharmacological evidence of antidiabetic potential

The discovery of active compounds and lead molecules for the development of safe and effective treatment approaches relies mainly on the validation of traditional knowledge, which demands a serious challenge in terms of time, labour and money for the pharmacologists. It is not possible to characterize and evaluate the properties of all the reported medicinal plants in one go. Therefore, the further analyses of the medicinal properties mostly depend on the qualitative and acceptable interpretation of the data reported by the local people and traditional healers. In this context, we have focused additionally on the cross-geographical assessment of the phytochemical and pharmacological evaluation of the antidiabetic properties of the plants that have been reported from Darjeeling and Sikkim Himalayas. This would elude the immediate urgency of the assessment of the reported plants as majority of the regional ecotypes have not been characterized till now, and at the same time, first-hand information should also be provided on the efficacy of traditional knowledge of this region.

Different phytochemical and pharmacological research works have been carried out all over the world in relation to many of these species and their ecotypes. Wide range of active secondary metabolites isolated from these plants have been successfully demonstrated to regulate hyperglycemia. Many compounds isolated from these plants have been shown to be effective in lowering the high blood sugar by enhancing insulin secretion, repairing and restoring damaged pancreatic cells or mimicking insulin function. The active principles belong to different types of natural compounds like glycosides (quercetin-3-rutinoside, momordicoside, swertiamarin), coumarin derivatives (umbelliferone β-D-galactopyranoside), alkaloids (berberine), dimeric alkaloids (vindoline), diterpenes (nimbidiol), triterpenes (maslinic acid, α-amyrin), aldehydes (cinnamaldehyde), flavones (morusin), lactones (costunolide), xanthones (swerchirin), phytosterols (β-sitosterol), tannins (corilagin, orocyanidin), amino sugars (mucaminose) and phenols (gingerol), which have been shown to directly or indirectly lower the blood glucose levels. Some of the compounds have been illustrated in Figures 3 and 4. Moreover, these plant-derived active compounds are very much specific and exert their activities without interfering with other cellular processes. Therefore, they offer an alternative approach of treatment where the undesirable side effects of synthetic medicine would be minimal.

A brief outline of the important works describing the antidiabetic potential of the reported plants is as follows:

**Abroma augusta:** Water extracts exhibited hypoglycemic effect on alloxan-induced diabetic rats. Also the efficacy of the aqueous extract of the leaves on biochemical and histological abnormalities of alloxan-induced diabetic rabbits was reported. Abromine was the major antidiabetic compound extracted from leaves of this plant.

**Abutillon indicum:** Phenolic and flavonoid compound extract plays a role in the control of hyperglycemia. The role of oleanolic acid, berberine and caffeic acid to increase glucose uptake in rat myocytes was reported. Oleanolic acid and quercetin-3-rutinoside were the two important antidiabetic compounds isolated.

**Aegle marmelos:** Leaf and callus extracts have shown antidiabetic activity in rabbits. Enhanced glycemic control, protective role in pancreatic function, antioxidant and hepatoprotective properties of umbelliferone β-D-galactopyranoside were shown in streptozotocin-induced diabetic rats. Protective role of this plant in diabetic cataract by inhibition of aldose reductase was also reported.

**Aloe vera:** Hyperglycemic activity of *A. vera* was experimentally proved and compared with conventional antidiabetic drugs. Antidiabetic and antihyperlipidemic effects of *Aloe* extracts in streptozotocin-induced diabetic rats were reported. A, a chromosome standardized *Aloe*-based composition was also reported to facilitate the maintenance of healthy blood glucose levels in diabetic individuals. Aloresin A was found to be a potent inhibitor of α-glucosidase. Another compound *Aloe* emodin-8-O-glycoside extracted from the leaves helped stimulate glucose transport and glycogen formation.

**Asparagus racemosus:** Oral administration of ethanolic extract showed hypoglycemic, antioxidant as well as hypolipidemic activities in diabetic rats. Insulin secreting action of root extracts in perfused pancreas, isolated islets and clonal pancreatic β-cells was also experimentally demonstrated in rats.

**Azadirachta indica:** Antihyperglycemic effect of chloroform extracts of neem leaves on streptozotocin-induced diabetic rats was observed. Inhibitory action of leaf extracts on α-amylase and α-glucosidase was also reported. Nimbidiol isolated from the leaves was reported to have inhibitory activity on α-glucosidase, thus delaying carbohydrate absorption.

**Berberis aristata:** Root extracts have been shown to regulate glucose homeostasis in diabetic rats. Root extract was also effective and safe in improving lipid profile and insulin secretion in euglycemic dyslipidemic patients. Berberine and berbamine were the major
isolated compounds that lowered blood glucose level\[37\].

**Bryophyllum pinnatum**: Crude extract of leaves exhibited hypoglycemic and hypolipidemic effect on alloxan-induced diabetic rats\[39\]. Hydroalcoholic extract reduced both postprandial and streptozotocin-induced blood glucose, triglyceride and low-density lipoprotein levels\[121\]. Aqueous extract of leaves also has significant antidiabetic properties, and the performance of the existing drugs (glibenclamide) could be enhanced with the use of the aqueous extract\[122\].

**Cannabis sativa**: Seeds have been reported to have potent inhibitory effect on α-glucosidase\[123\]. Cannabinoid-1 receptor inhibition exhibited by the extracts has been reported to impart significant benefit in the treatment of diabetic cardiovascular complications and possibly other complications\[41\]. Cannabidiol isolated from this plant was found to indirectly manage the diabetic condition by controlling induced oxidative stress, inflammation and cell death\[41\].

**Cassia fistula**: Oral administration of total alcoholic extract and its ethyl acetate fraction of bark exhibited significant restoring action on elevated levels of blood sugar and lipid in diabetic rats\[124\]. Water soluble fraction of ethanolic extract was reported to decrease serum

![Figure 3](image-url)
Figure 4 Structural representation of some antidiabetic compounds reported from the enlisted plants (Part 2)
The structures have been redrawn with ACD/Chemsketch software. The figure numbers indicate the name and structure of the active principles, viz. 1. Cucurbitacin A (from Momordica charantia L.); 2. Morusin (from Morus alba L.); 3. Cyclomorusin (from Morus alba L.); 4. Neocyclomorusin (from Morus alba L.); 5. 1-Deoxynojirimycin (from Ocimum sanctum L.); 6. Tetracyclic triterpenoid (from Ocimum sanctum L.); 7. Scoparin acid D (from Scoparia dulcis L.); 8. 11-Hydroxyxypalmetine (from Stephania glabra (Roxb.) Miers.); 9. Swerchin (from Swertia chirayita (Roxb. Ex Flem.) Karst.); 10. Swertiamarin (from Swertia chirayita (Roxb. Ex Flem.) Karst.); 11. Sweetside (from Swertia chirayita (Roxb. Ex Flem.) Karst.); 12. Mymccaminose (from Syzygium cumini (L.) Skeels); 13. Maslinic acid (from Syzygium cumini (L.) Skeels); 14. Valoneic acid (from Syzygium cumini (L.) Skeels); 15. Rubuphenol (from Syzygium cumini (L.) Skeels); 16. Ellagic acid (from Syzygium cumini (L.) Skeels); 17. Chebulic acid (from Terminalia chebula Retz.); 18. Corilagin (from Terminalia chebula Retz.); 19. Saponarin (from Tinospora cordifolia (Wildd.) Hook f. & Thoms.); 20. 4-Hydroxyisoleucine (from Tinospora cordifolia (Wildd.) Hook f. & Thoms.); 21. Rutin (from Urtica dioica L.); 22. 2-(4-Hydroxy-3-methoxyphenyl) ethanol (from Zingiber officinale Roscoe); 23. 2-(4-Hydroxy-3-methoxyphenyl) ethanoic acid (from Zingiber officinale Roscoe); 24. Gingerol (from Zingiber officinale Roscoe).

Catharanthus roseus: Improved enzymic action was reported in diabetic rats followed by treatment with leaf and twig extracts.[125] Fresh leaf juice also exhibited antidiabetic activity in diabetic rats.[43]

Cinnamomum tamala: Antidiabetic activities of leaf extract were evaluated by different researchers and were found to lower the blood glucose levels in diabetic rats.[47,49] Cinnamaldehyde and procyanidin oligomers isolated from this plant were reported to promote insulin secretion from β-cells.[48,50]

Cissampelos pareira: Aqueous extract of leaves significantly decreased both the fasting and postprandial blood glucose of type 2 diabetic rats and enhanced insulin levels.[126] The methanolic extract of root showed dose-dependent significant antihyperglycemic activity in streptozotocin-induced diabetic rat model.[120] Aqueous extract of leaves significantly regulated glucose metabolism by stimulation of glycogenesis or inhibition of glycogenolysis in the liver of diabetic mice.[127]

Coccinia grandis: Aqueous extract of leaves lowered the levels of blood glucose, urea, protein and cholesterol
and increased liver glycogen possibly by stimulating glycolysis or by inhibiting glycogenolysis. Alcoholic extract of fruit also exhibited hypoglycemic action by reducing blood glucose content.

**Ficus racemosa**: Leaves of this plant possess blood glucose-lowering effect in normoglycemic and in alloxan-induced hyperglycemic rats. The hypoglycemic potential of ethanolic extracts of fruit along with its antioxidant activity in vivo were reported. Petroleum ether extract of leaves showed significant antidiabetic, antioxidant as well as hypolipidemic action in streptozotocin-induced diabetic rats. α-Amlyn and β-sitosterol were identified as antidiabetic active compounds but exact mechanism of their action is still unknown.

**Girardiana diversifolia**: Ethanolic extract of leaves exhibited significant antihyperglycemic activities by lowering blood sugar level in alloxan-induced diabetic rats.

**Gynocardia odorata**: Hypoglycemic efficiency of methanol extract of leaves in streptozotocin-induced diabetic rats was reported.

**Hellenia speciosa**: Both aqueous and methanolic extract of rhizome helps regulate blood glucose and serum lipid profiles. Ethanolic extract of rhizome exerted antidiabetic activity possibly by restoring normal pancreatic β-cells, increasing insulin secretion and enhancing peripheral glucose utilization. Nanoparticles of *H. speciosa* have been reported to display antidiabetic activity by inhibiting hepatic glucose production and promoting glucose utilization. Costunolide and eremanthin from this plant increased pancreatic insulin secretion effectively associated with other cellular restoration.

**Ipomoea batatas**: Ethanolic and water extract exhibited anti-atherosclerotic activity and inhibited protein glycation, thus can be used to treat hyperlipidemic and hyperglycaemic disorders. Acylated sophorose isolated from aerial parts was found to inhibit maltase and thus delayed carbohydrate breakdown.

**Justicia adhatoda**: Hypoglycemic activity of unani drug Arusa (leaves of *J. adhatoda*) was experimentally demonstrated in alloxan-induced diabetic rabbits. Ethanolic extracts of root and leaf significantly reduced blood sugar level and also have beneficial effect on serum insulin in alloxan-induced diabetic rats. Ethanolic extract and fractions showed dose-dependent inhibition of α-glucosidase and α-amylase enzyme and exhibited lower inhibitory activity than acarbose. Experimental data revealed that the silver nanoparticle synthesized from leaves significantly decreased the blood glucose levels.

**Momordica charantia**: Intensive work has been done for the characterization of antidiabetic properties in this plant. It was suggested that the hypoglycemic activity of leaf extract is due to suppression of hepatic gluconeogenetic enzymes, glucose-6-phosphatase and fructose-6-phosphatase and activation of glucose-6-phosphate dehydrogenase. Cucurbitane-type triterpenoid glycosides from fruits (karavilloside III, momordicoside A, momordicoside C, momordicoside F1, momordicoside F2, momordicoside G, momordicoside I, momordicoside M, and gogalygoside-B) possess promising inhibitory effect on α-glucosidase enzyme. Polypeptide P, a 166 amino acid (AA) polypeptide isolated from seeds has been reported to show hypoglycemic effects on patients with type 1 or type 2 diabetes.

**Morus alba**: Leaf extract potentially reduced blood sugar level in diabetic patients by inhibiting α-amylase and thus can be used in treatment of diabetes without any side effects. Polyphenol extracts of mulberry fruits possess *in vitro* antidiabetic and antioxidant activities.

**Morusin, cyclomorusin and neocyclomorusin** were the major antidiabetic compounds that were reported to exert protective function on pancreatic β-cells.

**Nardostachys jatamansi**: The plant extract protects pancreatic β-cell damage possibly by the suppression of nuclear factor-kappa B activation. Ethanolic extract of rhizome was found to lower blood glucose level in rats diabetically induced by alloxan.

**Ocimum sanctum**: Ethanolic extract of leaves partially attenuates streptozotocin-induced alterations in glycogen content and carbohydrate metabolism in rats. It also helps in lowering blood glucose level along with inhibition of lipid peroxidation, reactivation of the antioxidant enzymes, and restoring levels of trace elements contents in diabetic rats.

**Oroxyllum indicum**: Antihyperglycemic activity of standardized extract of stem bark *via* inhibition of α-glucosidase and BSA glycation as well as stimulation of insulin sensitization was reported.

**Paederia foetida**: Methanolic extract of stem showed significant antihyperglycemic activity in glucose-loaded mice in a dose-dependent manner. Leaf extract also showed remarkable antihyperglycemic activity associated with antihyperlipidemic and antioxidant activities.

**Panax pseudoginseng**: Ethanolic extract of wild ginseng exerts a preventive effect on high-fat diet-induced obesity and hyperglycemic condition. Also ginseng extract regulated glucose and fat metabolism during exercise in mice.

**Phyllanthus emblica**: Evidence suggests that emblica tannoids are effective in delaying the development of diabetic cataract in streptozotocin-induced rats. Antidiabetic activities mediated by antioxidant and anti-apoptotic action were also studied experimentally.

**Picrorhiza kurrooa**: Extract of *Picrorhiza kurrooa*
helps to increase glucose tolerance in type 2 diabetes\[146\]. The antidiabetic action may be mediated through efficient translocation of glucose transporter 4 and increased glucose uptake\[147\].

**Saraca asoca:** Hypoglycemic activity of methanol extract of bark powder has been reported for glucose-loaded mice in oral glucose tolerance tests\[148\]. Ethanolic extract reduced the blood sugar level, normalized the hyperlipidemic condition and reduced renal oxidative stress in streptozotocin-induced diabetic rats\[149\].

**Scoparia dulcis:** Oral administration of aqueous extract of shoots significantly reduced blood sugar level and also improved glucose tolerance in alloxan-induced diabetic rats\[150\]. Presence of tannins and alkaloids may contribute to the hypoglycemic activity of S. dulcis\[151\]. Methanol extracts also exhibited potent antidiabetic and antioxidant activities in streptozotocin-induced diabetic rats\[152\]. Scoparic acid D was isolated and identified as a potent inhibitor of human α-glucosidase\[88\].

**Stephania glabra:** Ethanolic extract of tuber helps to produce significant fall in blood glucose level in alloxan-induced diabetic rats\[87\]. 11-Hydroxypalmatine isolated from the roots helped to regulate blood sugar level\[89\].

**Stephania hernandifolia:** The bulb of the plant exhibited hypoglycemic activities in type 1 diabetes possibly by preventing islet damage or by regenerating β-cells\[153\]. Ethanolic and aqueous extract of corm exhibited significant antidiabetic and antioxidant activities in streptozotocin-induced diabetic rats\[88\].

**Swertia chirayita:** Ethanolic extracts of this plant significantly reduced the levels of serum glucose, cholesterol and triglycerides in streptozotocin-nicotinamide-induced diabetic rats\[154\]. Aqueous extract of leaves has significant antidiabetic activity as compared to standard drug glibenclamide in streptozotocin-induced diabetic rats\[90\]. The antihyperglycemic activity of ethanolic extracts of this plant is partly due to the restoration of pancreatic β-cells and increasing insulin secretion, very similar to sulfonylureas\[155\]. Swertiamarin and sweroside were discovered as highly potent antidiabetic compounds that upregulated peroxisome proliferator activated receptor-γ gene expression which in turn activates the glucose transporter 2 and liver type glucokinase thereby assisting in the amelioration of blood glucose levels\[91\].

**Syzygium cumini:** Chloroform extract of seeds was reported to induce islet regeneration and also inhibit glucosidase to some extent\[156\]. Different parts of the plant especially fruits, seeds, and stem bark showed promising activity against diabetes\[93\]. Many antidiabetic compounds were identified; among these, mycaminose was proved to have insulin-secretagogue activity, and others viz. maslinic acid, valoneic acid, rubuphenol and ellagic acid were found to function by inhibiting aldose reductase and protein tyrosine phosphatase\[94,95\]

**Terminalia bellerica:** Ethanolic and methanolic extracts of fruits significantly increased the plasma insulin, C-peptide and glucose tolerance levels, body weight, and serum total protein. In addition, the plant extracts significantly decreased the serum levels of total cholesterol, triglycerides, low-density lipoprotein cholesterol, urea, uric acid and creatinine in diabetic rats\[96\].

**Terminalia chebula:** Aqueous extract of leaves exerted a long term effect on hyperglycemia and associated hyperlipidemia and also stimulated insulin release from β-cells\[157\]. Fruit extracts acted in a dose-dependent manner and helped in lowering blood sugar level and improving insulin sensitivity\[97\]. Fruits contained chebulic acid that exerted preventive effects against the formation of advanced glycation end products and endothelial cell dysfunction\[98\].

**Tinospora cordifolia:** Administration of methanolic stem extract was reported to restore the alterations of impaired blood glucose level and antioxidant status in alloxan-induced diabetic rat model\[100\]. The aqueous root extract exhibited hypoglycemic action comparable to that of standard oral hypoglycemic drug metformin\[158\]. Aqueous extracts of stem have shown hypoglycemic activity. Its aqueous extracts reversed hyperglycemia, hyperinsulinemia, hypertriglyceridemia, insulin resistance, and elevated levels of hepatic total lipids, cholesterol, triglycerides and free-fatty acids in fructose fed rats\[109\].

**Trigonella foenum-graecum:** The role of seed powder in reversing the histopathological anomalies in diabetic rats besides the metabolic normalization was reported\[106\]. Soluble dietary fibre fraction of seeds exerted antidiabetic effects through inhibition of carbohydrate digestion and absorption, and enhancement of peripheral insulin action\[161\]. Seed extract in moderate concentration along with a hypoglycemic drug was proved to inhibit lipid peroxidation and can be used as antidiabetic agent\[162\]. 4-Hydroxyisoleucine isolated from the plant was demonstrated to improve insulin sensitivity as well as to reduce hyperlipidemia\[105\].

**Urtica dioica:** Aqueous extract of leaves significantly controlled the hyperglycemic state of type 2 diabetes\[106\]. A herbosome formulation of U. dioica has been shown to possess better antidiabetic activity than the conventional powdered market formulations of this plant\[163\]. Rutin is the major compound that was found to play an important role in carbohydrate metabolism by promoting insulin secretion from pancreatic β-cells\[107\].

**Zingiber officinale:** Efficacy of ginger in reducing
the development of diabetic cataract in rats through its antglycating potential has been reported\cite{164}. Ethyl acetate extract of ginger exhibited antidiabetic potential via modulating glucose uptake, glycating protein and inhibiting adipocyte differentiation in in vitro studies\cite{108}.

Although the detailed discussion of the phytochemical and pharmacological advances of all the enlisted plants is beyond the scope of this article, we have attempted to present an overall picture of the efficacy of the enlisted plants. In many cases, the detailed elucidation of the structure and exact functional attributes of the active principles is yet to be reported, however, a few have been characterized at molecular level, the probable mechanisms of which are also recorded in Table 1.

5 Epilogue

Acceptance and requirement of herbal medicine in treatment of diabetes mellitus are increasing worldwide due to the adverse effects of synthetic medicine\cite{165,166}. It has already been proved that plants can successfully ameliorate both type 1 and type 2 diabetes. Some are also used in preparation of mono and polyherbal formulations in ayurvedic and herbal treatments\cite{167,168}. However, determination of proper dosage is tricky, often associated with allergic reactions and treatment is time-consuming. But anyway, the proper analyses of the active principles with proper dose determination could overcome the shortcomings of herbal treatment. In this study, appraisal of the enlisted plants from different sources has revealed a remarkable number of active constituents that have shown promising results in the control of blood sugar level in several in vitro and in vivo experiments. Some of the antidiabetic active principles from the enlisted plants have already been identified and characterised. However, the characterization of the plants from this region could offer some new active compounds or enhanced synthesis of the desired compounds as secondary metabolite accumulation depending on the ecological climate\cite{169}. We found quite a few number of plants (22% of the enlisted plants) often used by the local people that are not supported by pharmacological evidence. These include Boennninghausenia albiflora, Calamus rotang, Cordia myxa, Litsea cubeba, Macropanax undulatus, Potentilla lineata, Quercus lanata, Salvia moorcroftiana, Stephania rotunda, Swertia pedicellata, Taxus baccata and Trichosanthes lepiniana. Also, in certain plants, the usage of plant parts traditionally in the treatment of diabetes differed from the pharmacological evidence. These include about 1% of the plants, viz. Cassia fistula, Cataranthus roseus, Cinnamomum tamala, Girardinia diversifolia and Gynocardia odorata. However, the unavailability of pharmacological evidence is certainly not enough to question the traditional knowledge. Instead the endemicity of the plants and improper documentation may be responsible for the lack of interest for characterization of these plants. Therefore, this presents a challenge to take up the characterization of the antidiabetic properties of the above mentioned plants immediately ahead of the rest. Moreover, till date no plant-based drug has attained an expected level of development to completely replace or substitute the need for the conventional synthetic drugs, though many compounds have been discovered in the last two decades\cite{170}. Therefore, the use of advanced investigation in the plants from this region can thus increase the prospect of finding new active constituents and would lead to the discovery of more effective and safer hypoglycemic compound with all the desired parameters of a drug. In conclusion, the thrust of this article is to emphasize to direct more research works in evaluating more potent active principles at molecular details from the enlisted plants of this region that would contribute in human endeavor significantly, and thus to combat such globally challenging diseases like diabetes.

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7 Competing interests

The authors declare that they have no competing interests.

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