A Review of α-Glucosidase and α-Amylase Inhibitors for Type 2 Diabetes Isolated From Some Important Indian Medicinal Plants

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Abstract

α-Glucosidase and α-Amylase are the key enzymes involved in the digestion of the carbohydrate. Inhibitors of these enzymes can slow down the liberation of absorbable monosaccharides from dietary complex carbohydrates and is considered a strategy for the treatment of disorders in carbohydrate uptake, such as diabetes and obesity, as well as, dental caries and periodontal diseases. In the Indian context, the traditional system of medicines especially “Ayurveda” describes the use of medicinal plant, for primary health care and treatment of various diseases including diabetes mellitus, in various forms. Several contributions have been made to establish the anti-diabetic potential of plant extracts or isolated constituents from Indian medicinal plants, but so far only a few species have been explored to isolate and identify the constituents with α-glucosidase and α-amylase inhibitory potential. This review found a total of twenty seven species belonging to twenty four genuses of Indian medicinal plants which have been screened so far leading to the identification of fifty eight compounds with potential to inhibit the two enzymes. These constituents belong to flavones, flavone glycosides, triterpenes, alkaloids, tannins and other polyphenolic compounds, as is usually found in such investigations.

Keywords: α-Glucosidase; α-Amylase; Inhibitors; Type 2 diabetes; Indian medicinal plants; Ayurveda

Introduction

Diabetes mellitus, a complex metabolic disorder that results in increased blood glucose level, is considered as one of the major health related problems and is growing rapidly worldwide. The International Diabetes Federation predicts that over 371 million people are struggling with this disease in 2012 with 63 million Indian contributions and 4.2 million deaths occurred. The federation also predicts that half of the cases remain undiagnosed. Type 2 diabetes mellitus contributes to the majority of the cases. Treatment of diabetes includes the drugs which act through different mechanisms to control increased blood glucose level along with changes in diet, following a regimen of exercise and healthy lifestyle. The anti-diabetic drugs are classified into biguinides, sulfonylureas, thiazolidinediones, incretin mimetics and α-glucosidase inhibitors. Usually combinations of different classes of anti-diabetic drugs are used to increase the efficacy of the treatment, and α-glucosidase inhibitors are drugs of choice for the patients suffering from postprandial hyperglycemia [1-3].

α-Glucosidase and α-amylase are the key enzymes involved in the digestion of the carbohydrate. α-Amylase hydrolyses the α-linked polysaccharides in to oligosaccharides, and α-glucosidases, membrane bound enzymes which are located in the brush border of the small intestine, catalyze the final step in the digestive process of carbohydrate to release absorbable monosaccharide’s including glucose. Hence, inhibitors of these enzymes can slow down the liberation of absorbable monosaccharides from dietary complex carbohydrates, delaying the absorption of glucose into blood steam and thus preventing any sudden rise in meal induced blood glucose level [4-6].

Inhibitors of α-glucosidase and α-amylase form Indian Medicinal Plants

Acarbose and miglitol are the clinically used α-glucosidase inhibitors. Of these, acarbose is a natural product isolated from an Actinoplanes strain while miglitol is the N-hydroxyethyl analogue of 1-deoxynojirimycin isolated from Morus species [2]. But these drugs are not free from side effects and produce severe gastrointestinal complaints. The Indian subcontinent has been blessed with
17,000 to 18,000 species of flowering plants of which 6,000 to 7,000 are estimated to have medicinal usage in folk and documented systems of medicine, like Ayurveda, Siddha, Unani and Homoeopathy (http://nmpb.nic.in/). But till date only a few species has been explored so far for their potential to inhibit these enzymes. The present review covers the Indian medicinal plants which have been investigated for the constituents responsible for these enzyme inhibitory activities (Table 1) (Figures 1–4).

**Adhatoda vasica Nees (Family: Acanthaceae)**

Vasaka, indigenous to India, is a well-known plant drug in Ayurvedic and Unani medicine and also popular in Chinese folk
Figure 3: Phytoconstituents with α-glucosidases and/or α-amylases inhibitory potential [26-38].

Figure 4: Phytoconstituents with α-glucosidases and/or α-amylases inhibitory potential [39-58].
Aegle marmelos (L.) Corr.Serr. (Family: Rutaceae)

It is commonly known as ‘bael’ in India and widely used in medicine in Ayurveda for the treatment of diabetes mellitus. A series of phenylethyl cinnamides isolated from the leaves were found to have varying degree of inhibitory effects on the enzyme α-glucosidase and among these anhydroaegeline (3) exerted the greatest inhibition (Table 1) [8].

Alstonia scholaris (Linn.) R.Br. (Family: Apocynaceae)

It is an evergreen tropical small and glabrous tree native to Indian subcontinent and South East Asia with perfumed flowers and commonly known as Devil tree. The plant is reported to exert anti-tussive, anti-asthmatic, expectorant, anti-inflammatory, analgesic, anti-cancer, anti-diarrhoeal, spasmylic, anti-bacterial, anti-plasmodial and anti-oxidant activities [9]. The aqueous methanolic extract of the plant leaves have shown potent inhibition of the enzyme from which two molecules isolated, Quercetin 3-O-β-D-xylopyranosyl (1→2)-β-D-galactopyranoside (4) and (-)-lyoniresinol 3-O-β-D-glucopyranoside (5) as the inhibitors of rat intestinal α-glucosidase using sucrose and maltose as substrate. Among these two isolated molecules compound 5 is potent and exhibited inhibitory activity against both substrate, while compound 4 exhibited only maltase inhibitory activity (Table 1) [10].

Andrographis paniculata Nees (Family: Acanthaceae)

It is herbaceous plant native to India and Sri Lanka and is commonly known as Kalmegh. The plant and/or its major active constituent andrographolide has demonstrated anti-oxidant, cytoprotective, hypolipidemic, immunostimulant, nootropic, antihepilipidemic, anti-diabetic, adose reductase inhibitory effect, antifungal, anti-oxidant, -anti-cancer, anti-inflammatory, hepatoprotective and other health beneficial effects [11-15]. Andrographolide (6), has also shown inhibition of carbohydrate metabolizing enzymes viz yeast α-glucosidase using p-nitrophenyl-α-D-glucopyranoside as substrate and porcine α-amylase using starch as substrate (Table 1). The same have been confirmed by oral glucose and sucrose tolerance tests in-vivo [16].

Azadirachta indica (L.) Adelb. (Family: Meliaceae)

It is commonly known as ‘neem tree’ and its leaves have long been used in the ayurvedic system of medicine for various ailments. Anti-diabetic activity of A. indica seed oil and leaf extracts have been reported in various models of diabetic animals [17-18]. Melicacinolin [24,25,26,27-tetranor-apotirucalla-(apoeupha)-1α-senecioyloxy-3a,7a-dihydroxy-14,20,22-trien-21-23-epoxy] (7) demonstrated significant inhibition of both the enzymes in-vitro (Table 1) [19]. The results of the OGTT study strongly suggest that it reduces postprandial blood glucose levels [19].

Barringtonia racemosa Roxb. (Family: Lecythidaceae)

Barringtonia racemosa is an evergreen mangrove tree that grows in Bangladesh, Sri Lanka and the west coast of India and presents a wide range of therapeutic applications. The plant is reported for its anti-leukemic, anti-oxidant, anti-arthritis, anti-nociceptive, anti-tumour and anti-bacterial potential [20-24]. Methanol extracts of seeds displayed potent yeast and intestinal α-glucosidase inhibitory activities. Bartogenic Acid (8) was isolated as the major constituent responsible for the α-glucosidase inhibitory activity. Although extract accelerated α-amylase activity but the bartogenic acid could inhibit this enzyme (Table 1) [25].

Bergenia ciliate Haw. (Family: Saxifragaceae)

It is a perennial herb having rhizomes. The plant grows at the altitude of 3,000 m in a moist rock land of the Himalayas ranging to Bhutan. (−)-3-O-galloylpepectatein (9) and (−)-3-O-galloylcaffeatin (10) isolated from the plant inhibited rat intestinal glucosidase, using sucrose and maltose as substrate, and porcine pancreatic α-amylase (Table 1) [26].

Bergenia ligulata Wall. (Family: Saxifragaceae)

It is perennial herb which grows in North India especially in between rocks and stones. It is commonly known as Pashanbheda in India. The plant is has been reported for its potential as an insecticidal, antiurolithic, on influenza virus A and kidney stones [27-30]. Ethanolic extract, ethyl acetate fraction, of the rhizome shown inhibition of the enzyme using p-NPG as substrate, from which a compound (+)-azelechelin (11) found to be responsible for the activity (Table 1) [31].

Commiphora wightii (Family: Burseraceae)

It is endemic to the Indian peninsula and grows wild in the arid and semi-arid regions of Rajasthan, as well as Sind in Pakistan. The oleo-gum of the plant is commonly known as Guggul and used traditional for various ailments such as for mitigating metabolic disorders, obesity, inflammation, hypercholesterolemia and atherosclerosis. From the active methanolic extract epi-Mukulins (12), Diasesartemin (13) and (Z)-Guggulsterone (14) were isolated as the active constituents (Table 1) [32].

Corchorus olitorius Linn. (Family: Tiliaceae)

It is a highly fibrous vegetable commonly known as Moroheiya, has long been recognized for its hypoglycemic activity. The plant is reported as anti-diabetic, anti-obesity, protective, anti-bacterial, antiinociceptive, antioxidant and to induce apoptosis [33-38]. Corchorusides A (15) and Corchorusides B (16), isolated from leaf extract of the plant demonstrated significant inhibition of the enzyme (Table 1) [39].

Cuminum longa Linn. (Family: Zingiberaceae)

It is a rhizomatous herbaceous perennial herb, grows to a height of three to five feet and is cultivated extensively in Asia, India, China, and other countries with a tropical climate. Naturally occurring curcumin (17), demethoxycurcumin (18) and bisdemethoxycurcumin (19) isolated from C. longa have shown inhibition of α-glucosidase enzyme. Among these naturally occurring compounds, bisdemethoxycurcumin is most potent and have shown inhibition at a concentration two fold lower than that of acarbose. Further, kinetics studies suggested that the mode of inhibition is non-competitive (Table 1) [40].

Derris scandens Benth. (Family: Fabaceae)

It is commonly known as Gonj and it is an evergreen climbing branched shrub having twining habit. The plant is reported for its potential against inflammation, and as insecticidal. From the hexane and chloroform extract of plant three molecules, Scandinone (20),
<table>
<thead>
<tr>
<th>Plant species and family</th>
<th>Compound Name</th>
<th>Enzyme and source</th>
<th>Substrate</th>
<th>IC50</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Adhatoda vasica</em> Nees (Family: Acanthaceae)</td>
<td>Vasicine (1)</td>
<td>Small intestinal AGLU</td>
<td>Sucrose</td>
<td>125 μM</td>
<td>[7]</td>
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<td></td>
<td>Vasicolin (2)</td>
<td></td>
<td></td>
<td>250 μM</td>
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<tr>
<td><em>Aegle marmelos</em> (L.) Corr. Serr. (Family: Rutaceae)</td>
<td>Anthrahydroageline (3)</td>
<td>AGLU</td>
<td>p-NPG</td>
<td>35.8 μM</td>
<td>[8]</td>
</tr>
<tr>
<td><em>Alstonia scholaris</em> (Linn.) R.Br. (Family: Apocynaceae)</td>
<td>Quercetin 3-O-β-D-xylolpyranosyl(1''''→2'')-β-D-galactopyranoside (4)</td>
<td>Rat intestinal AGLU</td>
<td>Sucrose</td>
<td>1.96 mM</td>
<td>[10]</td>
</tr>
<tr>
<td></td>
<td>(−)-Lyoniresinol 3-O-β-D-glucopyranoside (5)</td>
<td></td>
<td>Sucrose</td>
<td>1.95 mM</td>
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<td></td>
<td></td>
<td></td>
<td>Maltose</td>
<td>1.43 mM</td>
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<tr>
<td><em>Andrographis paniculata</em> Nees (Family: Acanthaceae)</td>
<td>Andrographolide (6)</td>
<td>Yeast AGLU</td>
<td>p-NPG</td>
<td>11.0 mg/mL</td>
<td>[16]</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Starch</td>
<td>11.3 mg/mL</td>
<td></td>
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<tr>
<td><em>Azadirachta indica</em> (L.) Adelb. (Family: Meliaceae)</td>
<td>Meliacininol (7)</td>
<td>AGLU</td>
<td>-</td>
<td>32.18 μg/mL</td>
<td>[19]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Porcine pancreatic AAMY</td>
<td>Starch</td>
<td>46.74 μg/mL</td>
</tr>
<tr>
<td><em>Barringtonia racemosa</em> Roxb. (Family: Lecythidaceae)</td>
<td>Bartogenic Acid (8)</td>
<td>Pancreatic AGLU</td>
<td>p-NPG</td>
<td>168.09 μg/mL</td>
<td>[25]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p-NPG</td>
<td>11.0 μg/mL</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Sucrose</td>
<td>0.13 mM</td>
<td></td>
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<tr>
<td><em>Bergenia ciliate</em> Haw. (Family: Saxifragaceae)</td>
<td>(−)-3-O-Galloylepicatechin (9)</td>
<td>Rat intestinal AGLU</td>
<td>Sucrose</td>
<td>560 μM</td>
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<td></td>
<td></td>
<td></td>
<td>Maltose</td>
<td>334 μM</td>
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<td></td>
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<td>Porcine pancreatic AAMY</td>
<td>Starch</td>
<td>739 μM</td>
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<td></td>
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<td></td>
<td>-</td>
<td>401 μM</td>
<td></td>
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<td></td>
<td></td>
<td>-</td>
<td>168.09 μg/mL</td>
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<tr>
<td><em>Bergenia ligualata</em> Wall. (Family: Saxifragaceae)</td>
<td>(−)-Afzelechin (11)</td>
<td>AGLU</td>
<td>p-NPG</td>
<td>0.13 mM</td>
<td>[31]</td>
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<td></td>
<td></td>
<td></td>
<td>Porcine pancreatic AAMY</td>
<td>Starch</td>
<td>46.74 μg/mL</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>-</td>
<td>401 μM</td>
<td></td>
</tr>
<tr>
<td><em>Commiphora wightii</em> (Family: Burseraceae)</td>
<td>Epi-mukulin (12)</td>
<td>AGLU</td>
<td>p-NPG</td>
<td>159.33 μM</td>
<td>[32]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Deltasartemin (13)</td>
<td></td>
<td>60.55 μM</td>
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<td></td>
<td></td>
<td></td>
<td>(Z )-Guggulsterone (14)</td>
<td></td>
<td>132.14 μM</td>
</tr>
<tr>
<td><em>Corchorus olitorius</em> Linn. (Family: Tiliaceae)</td>
<td>Corchoruside A (15)</td>
<td>AGLU</td>
<td>p-NPG</td>
<td>0.18 mM</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Corchoruside B (16)</td>
<td>-</td>
<td>0.72 mM</td>
</tr>
<tr>
<td><em>Curcuma longa</em> Linn. (Family: Zingiberaceae)</td>
<td>Curcumin (17)</td>
<td>AGLU</td>
<td>p-NPG</td>
<td>37.2 μM</td>
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<td></td>
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<td></td>
<td>Demethoxycurcumin (18)</td>
<td></td>
<td>42.7 μM</td>
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<td></td>
<td></td>
<td></td>
<td>Bisdemethoxycurcumin (19)</td>
<td></td>
<td>23 μM</td>
</tr>
<tr>
<td><em>Derris scandens</em> Benth. (Family: Fabaceae)</td>
<td>Scandanone (20)</td>
<td>Rat intestinal AGLU</td>
<td>p-NPG</td>
<td>34.74 μg/mL</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Scandenone (21)</td>
<td>p-NPG</td>
<td>33.83 μg/mL</td>
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<td></td>
<td></td>
<td></td>
<td>Scandenin A (22)</td>
<td>p-NPG</td>
<td>25.17 μg/mL</td>
</tr>
<tr>
<td><em>Dichrostachys cinerea</em> (L.) Wight et Arn (Family: Mimosaceae)</td>
<td>(−)-Mesquitol (23)</td>
<td>Yeast AGLU</td>
<td>p-NPG</td>
<td>82.32 μM</td>
<td>[46]</td>
</tr>
<tr>
<td><em>Eugenia jambolana</em> Lam. (Family: Myrtaceae)</td>
<td>Iso-oenothein C (24)</td>
<td>Yeast AGLU</td>
<td>p-NPG</td>
<td>8.2 μM</td>
<td>[47]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Oenothein C (25)</td>
<td></td>
<td>7.51 μM</td>
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<td></td>
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<td></td>
<td>Comnussin B (26)</td>
<td></td>
<td>12.2 μM</td>
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<td></td>
<td></td>
<td></td>
<td>Swertisin (27)</td>
<td></td>
<td>146.5 μM</td>
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<tr>
<td><em>Hedychiurn spicatum</em> Smith. (Family: Zingiberaceae)</td>
<td>Spicatol (28)</td>
<td>Intestinal AGLU</td>
<td>p-NPG</td>
<td>-</td>
<td>[48]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Spicatanol methyl ether (29)</td>
<td></td>
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<tr>
<td><em>Hydrcaropus wightiana</em> Blume (Family: Achariaceae)</td>
<td>Luteolin (30)</td>
<td>Yeast AGLU</td>
<td>p-NPG</td>
<td>23.52 μM</td>
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<td></td>
<td></td>
<td></td>
<td>Isohydocrin (31)</td>
<td></td>
<td>23.9 μM</td>
</tr>
<tr>
<td><em>Momordica charantia</em> Linn. (Family: Cucurbetaceae)</td>
<td>D-(+)-Trehalose (32)</td>
<td>Rat acetone powder AGLU</td>
<td>Sucrose</td>
<td>0.002 M</td>
<td>[51]</td>
</tr>
<tr>
<td><em>Nymphae stellata</em> Willd. (Family: Nymphaeaceae)</td>
<td>1,2,3,4,6-penta-O-galloyl-D-glucose (33)</td>
<td>Rat intestinal AGLU</td>
<td>Maltose</td>
<td>0.1 mg/mL</td>
<td>[53]</td>
</tr>
<tr>
<td><em>Piper longum</em> Linn. (Family: Piperaceae)</td>
<td>Pipataline (34)</td>
<td>Yeast AGLU-I</td>
<td>p-NPG</td>
<td>32.10 μg/mL</td>
<td>[56]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pelitorine (35)</td>
<td></td>
<td>34.39 μg/mL</td>
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<td></td>
<td></td>
<td>Sesamine (36)</td>
<td></td>
<td>36.39 μg/mL</td>
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<td></td>
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<td></td>
<td>Brachystamid B (37)</td>
<td></td>
<td>34.09 μg/mL</td>
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<td></td>
<td>Guineensine (38)</td>
<td></td>
<td>19.26 μg/mL</td>
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<tr>
<td><em>Pistacia integerrima</em> (Pistacia chinensis var. Integerrima J. L. Stewart ex Brandis) (Family: Anacardiaceae)</td>
<td>Pistagramic acid (39)</td>
<td>Yeast AGLU</td>
<td>p-NPG</td>
<td>89.12 μM</td>
<td>[60]</td>
</tr>
</tbody>
</table>

Table 1: Compounds isolated from Indian medicinal plants with inhibitory activity against α-glucosidases and/or α-amylases.
Scandenone (21) and Scandenin A (22) isolated as rat intestinal acetone powder α-glucosidase inhibitor using p-NPG as substrate (Table 1) [41].

**Dichrostachys cinerea** (L.) Wight et Arn (Family: Mimosaceae)

It is known as Vurtuli in Hindi. It is a branched thorny shrub sometimes a small tree up to 2 m in height and is distributed throughout the dry and warm parts of India. The plant is reported as anti-asthmatic, hepatoprotective, anti-oxidant and anti-bacterial [42-45]. (-)-Mesquitol (23) isolated from the methanolic extract of the stem bark showed the yeast α-glucosidase inhibition (Table 1) [46].

**Eugenia jambolana** Lam. (Family: Myrtaceae)

It is commonly known as Jambul in India (syn. Syzygium cumini Skeels; Eugenia cumini Druce) and is an evergreen tropical tree. Jambul is native to India and other Asian countries. The seeds of the Jamun fruit are widely regarded in the Indian traditional system of medicine, Ayurveda, for regulating blood glucose levels and treating diabetes. Iso-oenothein C (24), oenothein C (25), cornussin B (26) and swertisin (27) are isolated from the seeds demonstrated better inhibition of yeast α-glucosidase than the positive control acarbose (Table 1) [47].

**Hedychium spicatum** Smith. (Family: Zingiberaceae)

*H. spicatum* Smith, is a perennial smallish hardy ginger that grows to around 1 m, and it possesses green leaves and large orange and white flowers. It is commonly known as ginger lily and Kapoorkachari in India. The plant is reported for its cytotoxic constituents and anti-microbial activity. Labdane type triterpenoids, Spicatanol (28) and Spicatanol methyl ether (29), isolated from the rhizome of the plant have shown inhibition of intestinal α-glucosidase enzyme using p-NPG as substrate. Among the two isolates spicatanol was more potent (Table 1) [48].

**Hydnocarpus wightiana** Blume (Family: Achariaceae)

It is commonly known as chalmoogra in India and has a long history for the treatment of diabetes in India. The plant is reported for anti-diabetic, hypolipidemic, anti-inflammatory, anti-oxidant and anti-neoplastic activity [48]. Luteolin (30) and isohydnocarpin (31) isolated from the acetone extract (IC_{50} 10.55 μg/mL) demonstrated potent inhibition of the enzyme while hydnocarpin showed mild inhibition. The acetone extract inhibits the enzyme in a competitive manner while luteolin and isohydnocarpin demonstrated mixed type inhibition (Table 1) [47].
of inhibition (Table 1) [49].

**Momordica charantia** Linn. (Family: Cucurbetaceae)

*M. charantia* Linn. commonly known as bitter melon or Karela, widely grown in tropical and subtropical regions for fruits which are most bitter among all the fruits. The plant is well known for its anti-diabetic potential with many scientific reports [50]. D-(+)-trehalose (32) isolated from seed inhibited rat aceton powder α-glucosidase at concentration of 0.002 M using sucrose as substrate (Table 1) [51].

**Nymphaea stellata** Wild. (Family: Nymphaeaceae)

It is commonly known as water lily or blue lotus is a common flowering water flower. The plant is reported in ayurvedic system of medicine for liver protective activity and diabetes. The plant is scientifically proved to have antihypertoxic, antihyperglycemic and antihyperlipidaemic activities [52]. 1,2,3,4,6-penta-O-galloyl-β-D-glucose (33) isolated from flower extract shown inhibition of rat intestinal α-glucosidase enzyme using maltose as substrate at an ED50 of 0.1 mg/ml (Table 1) [53].

**Piper longum** Linn. (Family: Piperaceae)

*P. longum* Linn. commonly known as Pippali, is used as a spice and preservative in food stuffs and it is used extensively as a part of Indian traditional medicine system [54]. It is a climber and have perennial woody roots, cultivated for its fruits. It is used for the treatment of gonorrhea, menstrual pain, tuberculosis, sleeping problems, respiratory tract infections, chronic gut related pain, and arthritic conditions, analgesic, diuretic, muscle relaxant, anxiety, immunomodulatory, anti-tumor etc. [55]. Pipatoline (34), pelletorine (35), sesamine (36), brachystamide B (37), guineensine (38) isolated from methanolic extract of the fruits inhibited enzyme (Table 1) [56].

**Pistacia integerrima** (Pistacia chinensis var. integerrima JL Stewart ex Brandis; Family: Anacardiaceae)

It is commonly known as kakar singhi and found in eastern Himalayan range from Indus to Kumaon. The plant is well known for its medicinal purpose in Indian traditional system of medicine. The plant is reported as an analgesic, anti-inflammatory, anti-bacterial and for gout and hyperuricemia [57-59]. A triterpenoid, pistagronic acid (39), isolated from the chloroform fraction of methanolic extract, demonstrated significant inhibition of the yeast and mammalian α-glucosidase (Table 1) [60].

**Psidium guajava** Linn. (Family: Myrtaceae)

It is an evergreen shrub or small tree with wide spreading branches native to tropical America. It is commonly known as guava. The plant is reported to be effective in the treatment of diarrhoea, dysentery and acute gastrointestinal inflammation, spasmylocytic effects, diabetes [61]. Bioactivity guided fractionation of the 75% ethanol extract from guava leaves showed high inhibition of α-glucosidase and α-amylase. Quercetin (40), Kaempferol (41) and Myricetin (42) showed inhibition of α-glucosidase against sucrose and maltose as substrate. These compounds also showed inhibition of α-amylase (Table 1). Among these, myricetin is most potent [62].

**Rheum emodi** Wall (Family: Polygonaceae)

*R. emodi* Wall is a perennial stout herb, distributed in the temperate and subtropical regions of Himalaya at an elevation of 2,800 m and 3,800 m. It is commonly known as Himalayan rhubarb and is reported for its anti-oxidant, anti-cancer, anti-microbial, and anti-fungal properties [63]. Methanolic extract of the rhizome inhibited yeast and mammalian α-glucosidase. Rhapontigenin (43), Desoxyrhapontigenin (44), Chrysohanol-8-O-β-D-glucopyranoside (45), Torachrysone-8-O-β-D-glucopyranoside (46) isolated from the methanolic extract has demonstrated inhibition of yeast α-glucosidase, with 43 being most potent. Desoxyrhaponticin (47), 45 and 46 inhibited mammalian α-glucosidase where 45 exerted greatest inhibition (Table 1). The kinetic analysis of 45 to 47 on mammalian α-glucosidase inhibition showed them to be mixed-noncompetitive inhibitors and presence and position of glycoside moiety in compounds appear important for better inhibition of mammalian α-glucosidase [64-65].

**Salacia reticulate** Wight (Family: Hippocrateaceae)

*S. reticula* is a woody climber grows in Sri Lanka and India. The roots and stems of the plant have been used traditionally as a remedy for prevention of diabetes. Salacinol (48), Kotalanol (49), and De-O-sulfonated kotalanol (50) inhibited N-terminal catalytic domain of maltase-glucoamylase (nMGAM). Among these compounds De-O-sulfonated kotalanol is most potent with Ki=0.03 μM, which is 2,000 times more potent then the clinically used drugs [66].

**Salvia moorcroftiana** Wall (Family: Lamiaceae)

*S. moorcroftiana* Wall. is a tall, perennial, 40 cm to 90 cm tall grows in temperate Himalayas from Kashmir to Kumann. The acetone extract of the aerial parts of the plant led to isolation of 5-hydroxy-7,4'-dimethoxyflavone (51) and oleanolic acid (52), as α-glucosidase inhibitors (Table 1) [67].

**Solanum torvum** Swartz (Family: Solanaceae)

*Solanum torvum* Swartz, is wild, herbaceous perennial plant. This plant is native to India but also distributed to South East Asia and has been reported as an anti-diabetic, anti-hyperglycemic, anti-microbial, anti-viral, analgesic, anti-inflammatory, anti-ucerogenic, and anti-oxidant [68-71]. Methyl caffeate (53) was isolated as rat intestinal sucrose and maltase inhibitor (Table 1) [72].

**Terminalia superba** Engl. & Diels (Family: Combretaceae)

It is a large tree native to tropical western Africa grows in deciduous moist forest and evergreen rain forest. It is reported to prevent glucose induced hypertension, and for its anti-diabetic, vasorelaxant and anti-icribial activities [73-75]. Gallic acid (54) and Methyl gallate (55) isolated from stem bark have shown inhibition of yeast α-glucosidase (Table 1) [76].

**Tinospora cordifolia** (Thunb.) Miers (Family: Menispermaceae)

It is commonly known as Guduchi, grows tropical areas of India, Myanmar and Sri Lanka. The plant is reported for its anti-diabetic activity. Jatrorrhizine (56), palmatine (57) and magnoflorine (58) isolated from stem was found to inhibit the enzyme. Jatrorrhizine and palmatine demonstrated non-competitive inhibition while magnoflorine was found to be reversible, competitive inhibitor of the enzyme when assayed using sucrose and maltose as substrate. *In vivo* studies conducted to determine Oral Glucose Tolerance Test (OGTT) in rats, using different substrates: glucose, sucrose and maltose and increase in plasma glucose level was significantly suppressed (P < 0.01) by all the three alkaloids at 20 mg/kg b.w. Magnoflorine possessed the most potential activity as α-glucosidase inhibitor *in vitro* and *in vivo* [3].

**Discussion**

Medicinal plants are important sources of raw materials for...
traditional systems of medicine (e.g. Ayurvedic, Unani, Homeopathy, and Siddha) and as well as for modern medicine. India has a long history of the traditional uses of medicinal plants for primary health care and treatment or management of various diseases including diabetes mellitus. A majority of the population in India rely on use of plants for their primary health care including diabetes. Several contributions have been made to establish the anti-diabetic potential of plant extracts or isolated constituents from Indian medicinal plants, but so far only a few species have been explored to isolate and identify the constituents with α-glucosidase and α-amylase inhibitory potential. Table 1 is a compilation of such constituents. The review found a total of twenty seven species belonging to twenty four genera which have been screened so far leading to the identification of fifty eight compounds with potential to inhibit the two enzymes. These constituents belong to flavones, flavone glycosides, triterpenes, alkaloids, tannins and other polyphenolic compounds, as is usually found in such investigations.

Conclusion and Future Scope

Diabetes mellitus is a complex metabolic disorder, and treatment of the disease focuses on controlling the blood glucose level and healthy food habits. Based on traditional reports various parts of medicinal plants are used in many formulations and/or are prescribed by traditional practitioners without knowing their active constituents. A wide range of phytochemicals isolated from Indian medicinal plants have been proven to possess significant α-glucosidase and α-amylase inhibitory activities. But still there are several medicinal plants species, used traditionally or reported to possess anti-diabetic activity, which are yet to be explored for their active constituents. Therefore, Indian medicinal plants provide a bright future for further investigation to identify their active constituents, which may serve as a lead for future drug (α-glucosidase and α-amylase inhibitors) development.

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