Antidiabetic Potentials of Bangladeshi Fruits

Subjects: Endocrinology & Metabolism | Food Science & Technology | Integrative & Complementary Medicine
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Diabetes mellitus is a life-threatening disorder affecting people of all ages and adversely disrupts their daily functions. Despite the availability of numerous synthetic-antidiabetic medications and insulin, the demand for the development of novel antidiabetic medications is increasing due to the adverse effects and growth of resistance to commercial drugs in the long-term usage. Antidiabetic phytochemicals isolated from fruit plants can be a very nifty option to develop life-saving novel antidiabetic therapeutics, employing several pathways and MoAs (mechanism of actions). The antidiabetic potential of commonly available Bangladeshi fruits and other plant parts are discussed, such as seeds, fruit peals, leaves, and roots, along with isolated phytochemicals from these phytosources based on lab findings and mechanism of actions.

HbA1c Insulin Hyperglycemia Fruit Diabetes Asia Bangladesh

1. Banana (*Musa sapientum* L.)

Musa sapientum L., a large-sized herbaceous monocot from the Musaceae family, is a well-known tropical Bangladeshi fruit and locally called ‘Kola’ [1]. The Kuk valley of New Guinea is the earliest occurrence of banana cultivation that has been documented. About 300 different types of bananas are cultivated in several regions, including Asia, Indo-Malaysia, and the Australian tropics [2]. It incorporates various bioactive phytochemicals, including anthocyanins, phenolic acids, flavanones, and terpenoids, which reportedly exhibit potential antidiabetic, anti-inflammatory, galactagogue, and antioxidant activities [3].

The lyophilized juice of *M. sapientum* stem (50 mg/kg dose) manifested antihyperglycemic action by enhancing insulin content in streptozotocin-induced diabetic rats [4]. The methanol extract of *M. sapientum* leaves at 250 and 500 mg/kg significantly reduced α-amylase activity by 79.6% in alloxan-induced male albino diabetic rats [5]. According to a report, the chloroform extracts of the flowers of *M. sapientum* displayed a notable antidiabetic effect (0.15, 0.20 and 0.25 g/kg b.w. dose) by lowering the glycosylated hemoglobin and blood glucose levels [2]. According to a research study, the aqueous extract of dried flowers of *M. sapientum* tends to exert antihyperglycemic activity in patients with type 2 diabetes at a dose of 5 mL/day [3].

2. Bengal Quince (*Aegle marmelos* (L.) Corrêa)

Aegle marmelos (L.) Corrêa, a slow-growing moderate-sized tree in the Rutaceae family, is a well-known subtropical Bangladeshi fruit and is locally known as 'Bel', 'Bael' [6]. It is widely found in several Asian countries, including India, China, Nepal, Sri Lanka, Myanmar, Pakistan, Bangladesh, and Vietnam [7]. Numerous bioactive phytoconstituents extracted from this plant are carotenoids, phenolic, alkaloids, pectins, tannins, coumarins, flavonoids, and terpenoids. These phytoconstituents reportedly exert an extensive spectrum of therapeutic actions, including antioxidant, cytotoxic, hypoglycemic, antimicrobial, hepatoprotective, anti-inflammatory, and cardioprotective potentials [8].

The methanol extract of bark of *A. marmelos* decreased the glucose content at 2 and 4 g/kg doses in streptozotocin-induced diabetic rats by 19.14% and 47.32%, respectively, which appears to be accomplished by rejuvenating pancreatic β-cells [9]. In the same rats at 120 mg/kg b.w. ip dose, the methanol extract of the leaves of *A. marmelos* also diminished the blood-sugar content by 54% [7]. Another in-vitro evaluation of the methanol extract of these leaves also showed notable antihyperglycemic action by hindering rat lens aldose reductase (RLAR) at an IC_{50} value of 15.00 ± 0.54 mg/mL [10]. According to a study, aqueous-leaf extracts of *A. marmelos* manifested hypoglycemic action(400 mg/kg b.w. dose) through lowering the blood glucose by 60.77% and improving the insulin content by 30.49% in alloxan-induced Albino Wistar diabetic rats [11].

3. Black Currant (*Carissa carandas* L.)

Carissa carandas L. is a deciduous thorny shrub of the Apocynaceae family [12]. Locally, *C. carandas* is known as "Koromcha" containing prospective bioactive phytochemicals [13]. *C. carandas* displayed notable antidiabetic, antioxidant, anti-inflammatory, antimicrobial, and antifungal properties [12].

Methanol extract of *C. carandas* leaves could sufficiently lower the increased blood- glucose concentration at 400 mg/kg dosage in alloxan induced diabetic rats [14]. Based on another study, methanolic extract of *C. carandas* fruit exhibited strong inhibition against α-amylase and β–glucosidase. The aqueous extract of *C. carandas* fruit has been demonstrated to have significant inhibitory activity against β–glucosidase, suggesting that it might be utilized as a sufficiently efficient treatment for postprandial hyperglycemia with minimum adverse effects [15].

4. Black Plum (*Syzygium cumini* (L.) Skeels)

Syzygium cumini (L.) Skeels from the Myrtaceae family, locally known as "Jaam", "Kalajaam", is a large-sized everlasting tropical tree [16] that is indigenous to the Indian subcontinent [17][18]. It is generally distributed throughout South Asia, including India, Indonesia, Sri Lanka, Bangladesh, Nepal, and a few other countries [18]. The chief bioactive phytochemicals of this plant are flavonoids, phenolic compounds, anthocyanins, carotenoids, essential oils, terpenes, and tannins, which reportedly demonstrate potential antidiabetic, anti-cancer, anti-inflammatory, antioxidant, and antimicrobial actions [19].

Black plum is a potent source of antidiabetic agents which can exert both antihyperglycemic and insulinotropic actions (Ayyanar et al. 2013, Teixeria et al. 2006). The ethanolic leaf extract of *S. cumini* is reported to exert in vitro

antidiabetic action by halting α-glucosidase activity [20]. According to a report, the methanol and ethyl acetate extract of *S. cumini* seeds (400 and 200 mg/kg dose, respectively) tend to lessen the glucose content of blood in streptozotocin-induced diabetic rats [21]. The aqueous extract of the seeds of *S. cumini* manifests noteworthy hypoglycemic action in male albino-wistar rats (2.5 gm per kg body weight) by upraising the insulin secretion of pancreatic cells [22]. The methanol extract from the kernel fraction of *S. cumini* fruit displayed significant antihyperglycemic activity at an IC_{50} dose of 8.3 µg/mL by hindering α-amylase action by 98.2% [23]. Another research revealed that, high-fat diet-fed wistar rats with streptozotocin induced hyperglycemia were treated with the black-plum-aqueous-seed extract for 21 days which resulted in amelioration of insulin resistance and nourishment of the function β-cells [22][23].

5. Coconut (*Cocos nucifera* L.)

Cocos nucifera L. from the Arecaceae family, locally known as “Narkel”, is a long-lived single-stemmed tree and a renowned tropical Bangladeshi fruit. It has its origin in the Mexico, Brazil, Central America, India, Sri Lanka, and Indonesia [24]. Various bioactive phytoconstituents, such as phenols, tannins, leucoanthocyanidins, flavonoids, triterpenes, saponins, steroids, and alkaloids, have been extracted from this plant which exhibited a vast spectrum of pharmacological attributes, including bactericidal, anti-inflammatory, antineoplastic, antioxidant, hypoglycemic, anti-osteoporosis, and anthelmintic activities [25].

The hydro-methanol extract obtained from the spadix of *C. nucifera* tends to display remarkable antihyperglycemic activity in streptozotocin-induced diabetic Albino Wistar rats at 250 and 500 mg/kg body weight by escalating the insulin secreting power of the pancreatic β-cells [26]. According to a study, methanol extract of *C. nucifera* (200 mg/kg b.w. dose) manifested an antidiabetic effect by improving the content of not only sugar but also insulin in the blood stream in diabetic rats [25]. The extract obtained from *C. nucifera* husk using methanol tends to exert antihyperglycemic action in alloxan-induced diabetic rats having an IC_{50} range of 51.70 ± 4.66 µg/mL by significantly hindering the α-amylase activity [27]. The lyophilized coconut water of mature *C. nucifera* (1000 mg/kg b.w. dose) has been used to lower the glucose content from 275.32 ± 4.25 mg/dL to 129.23 ± 1.95 mg/dL in alloxan-induced male Sprague-Dawley rats [28].

6. Elephant Apple (*Dillenia indica* L.)

Dillenia indica L., locally known as “Chalta” in Bangladesh, is an evergreen tree [29] which belongs to the Dilleniaceae family [30] and mostly grows in the moist forests of sub-Himalayan region to Assam; it is a very familiar tree in household of Bangladeshi rural area [29]. *D. indica* has been reported to have phytochemicals, such as flavonoids, tannins and terpenoids, polyphenolic compounds, and saponins [31], which exert significant biological activities, namely antidiabetic, antimicrobial, antioxidant, dysentery, anti-inflammatory, and analgesic properties.

The extract of *D. indica* has shown the possible mode of antidiabetic action by enhancing the insulin impact by raising the insulin secreting potential of the pancreatic β-cells or its bound-state release or cell rejuvenation [29].

The methanol extract of *D. indica* demonstrated a notable antihyperglycemic action in alloxan and streptozotocin induced diabetic rats [30]. Furthermore, the methanol extracts of the leaves of *D. indica* enhanced the serum-insulin level by halting the function of α-amylase and α-glucosidase enzymes [32]. Based on a study, the leaves of *D. indica*, which have concentrations of 250 and 500 mg/kg b.w., were administered via the oral route and showed favorable impacts on the glucose content of blood [30].The alcohol extract of *D. indica* leaves given at doses of 100, 200, and 400 mg/kg for 45 days exerted remarkable depletion in the increased blood sugar content of rats at a fasting state (266.17 ± 7.07, 221.83 ± 5.70, 182.17 ± 3.59 mg/dL respectively). Consequently, the given doses cause a notable elevation in the insulin levels of serum (8.92 ± 0.15, 9.83 ± 0.13, 11.48 ± 0.39 mU/mL) [31]. The glucose content was prominently lessened in the blood by the methanol-leaf extracts of *D. indica* in streptozotocin-induced diabetic rats having the doses of 250 and 500 mg/kg [30].

7. Guava (*Psidium guajava* L.)

Psidium guajava L. is a large-sized everlasting tropical shrub belonging to the Myrtaceae family [33]. It is a popular pan-tropical fruit [34] and locally known as “Peyera” in Bangladesh. Though it is aboriginal to Central America, it is also found in southern Florida, Bermuda, and throughout the West Indies, from the Bahamas and Cuba through Trinidad and all the way south to Brazil [35]. It incorporates various bioactive phytoconstituents, such as saponins, alkaloids, tannins, cardiac glycosides, terpenes, flavonoids, and sterols. These compounds are likely to exert an extensive range of therapeutic attributes, including antidiabetic, antitumor, antimicrobial, antioxidant, and hepatoprotective activities [35].

The ethanol of stem bark of *P. guajava* tends to exhibit antihyperglycemic action (250 mg/kg oral dose) in alloxan-induced hyperglycemic rats [36]. In an in-vitro study, the ethanol and aqueous extracts of *P. guajava* leaf (1 mL concentration) halted the function of the enzyme alpha-amylase by 97.5% and 72.1%, respectively [37]. According to a study, ethanol extract of bark and leaf of *P. guajava* demonstrated hypoglycemic action by hindering α-glucosidase activity at an IC_{50} of 0.5 ± 0.01 and 1.0 ± 0.3 µg/mL, respectively [34]. The fruits also exhibited noteworthy glucose-diminishing activities in streptozotocin-induced diabetic rats. *P. guajava* reportedly safeguarded the pancreatic β-cells resulting from lipid peroxidation and DNA strand breakage mediated by streptozotocin and thus preserved insulin secretion. It also arrested the protein manifestation of pancreatic nuclear factor-kappa B caused by streptozotocin induction and attributed to its antihyperglycemic efficacy [38].

8. Hog Plum (*Spondias mombin* L.)

Spondias mombin L. is a rapid-growing perennial tree from the Anacardiaceae family. This is regarded as one of the renowned tropical fruits in Bangladesh, and is locally known as ‘Amra’. It is indigenous to America and Brazil, especially in the western Atlantic and Amazon forest [39]. The effective bioactive phytochemicals extracted from this plant are alkaloids, flavonoids, saponins, phenolic compounds, and tannins [40]. These phytochemicals reportedly exert a broad spectrum of notable pharmacological attributes, including anti-inflammatory, antioxidant, antidiabetic, antimicrobial, and antipsychotic activities [39].

The ethyl-acetate-soluble fraction obtained from the methanol extract of leaves of *S. mombin* manifested antihyperglycemic action in vitro by halting α-amylase and α-glucosidase with an IC_{50} level of 28.12 ± 0.48 µg/mL and 12.05 ± 0.002 µg/mL, respectively [41]. According to a study, methanol extract of leaves of *S. mombin* at concentrations of 200 and 400 mg/kg b.w. lowered blood sugar content by 20.03% and 33.33%, respectively in alloxan-induced diabetic male Wister rats. Consequently, in the same experimental animals, the applied doses displayed antidiabetic action by declining the glycosylated hemoglobin having concentrations of 7.72 ± 0.21% and 5.16 ± 0.09%, respectively [42].

9. Indian Goose Berry (*Phyllanthus emblica* L.)

Phyllanthus emblica L. (or *Emblica officinalis* Gaertn.), a prominent species from the Euphorbiaceae family is well-known as “Amlaki”, “Amla” in Bangladesh. This species is a medium-sized deciduous tree that has the height of about 8–18 m and is endemic to southeastern Asia, namely central India and Bangladesh [43]. *P. emblica* has been reported to have phenolic compounds, flavonoids, saponins, tannins, [44] alkaloids, proteins, glycosides, and amino acids [45], which exert a bunch of medicinal active properties, such as antidiabetic, hypolipidemic, antiatherogenic, antioxidative, anti-inflammatory, antibacterial, and cytotoxic properties [46].

Ethanol extract of *P. emblica* fruit (200 mg/kg b.w. for 45 days) exhibited substantial decrease in blood glucose and a notable rise in plasma insulin in streptozotocin-induced type 2 diabetic mice. Furthermore, *P. emblica* fruit extract inhibited α-glucosidase and α-amylase (IC_{50} values = 94.3 and 1.0 g m/L, respectively) [46].

10. Indian Olive (*Elaeocarpus floribundus* Blume)

Elaeocarpus floribundus Blume, an evergreen medium-sized tree popularly known as “Jalpai” in Bangladesh, is a member from the Elaeocarpaceae family which is commonly found in Bangladesh, Madagascar, India, Southeast Asia, Malaysia, China, Japan, Australia, Fiji, and Hawaii [47]. *E. floribundus* has been reported to contain glycosides, flavonoids, steroids, terpenoids in fruits [48], phenolic acid, and anthocyanins, according to Zaman [49]. It displayed prospective pharmacological actions, such as antidiabetic, anticancer, antitumor, and antioxidant activities [47].

The methanol extract of *E. floribundus* leaf rendered noteworthy decrement of α-glucosidase enzyme having an IC_{50} value lesser in comparison to acarbose that establishes the antidiabetic activity of *E. floribundus* [47]. Based on another study, the stem bark of *E. floribundus* had also showed notable α-glucosidase inhibitory actions with an IC_{50} of 14.56 ± 1.20 µg/mL [50].

11. Indian Jujube (*Zizyphus mauritiana* Lam.)

Zizyphus mauritiana Lam. is a shrub belonging to the Rhamnaceae familyis, found from western Africa to India in the warm temperate zone [51], and widely cultivated in Bangladesh; it is also locally known as “Boroi”. *Z. mauritiana*

has been shown to contain a variety of phytochemicals, including flavonoids, alkaloids, terpenoids, pectin, saponins, triterpenoic acids, lipids, and jujuboside saponins, which exerted potential sedative and hemolytic properties, sweetness-inhibitory effects and as an anxiolytic [51]. The cyclopeptide alkaloids were reported to have antibacterial, anticonvulsant, hypoglycemic, anti-infectious, diuretic, analgesic, antiplasmodial, and anti-inflammatory properties [52].

A study conducted on a hyperglycemic rat model with petroleum ether, chloroform, acetone, ethanol, aqueous, and crude aqueous extracts of *Z. mauritiana* fruits reveal to have antihyperglycemic action. The non-polysaccharide fraction of the aqueous extract of fruits of *Z. mauritiana* is said to have substantial antihyperglycemic and hypoglycemic effects [52]. Furthermore, aqueous and petroleum ether extracts of *Z. mauritiana* at 200 and 400 mg/kg dosages demonstrated significant antidiabetic effects [53]. The combination of aqueous and ethanol extracts of *Z. mauritiana* seeds (800 mg/kg extract of seeds and 10 mg/kg glyburide) improved glucose tolerance in both diabetic and normal mice. This finding implies the synergistic hypoglycemic action of *Z. mauritiana* extracts. According to the same study, aqueous and ethanolic extracts of *Z. mauritiana* seeds contain strong principles that may exert numerous activities involving several pathways to exert hypoglycemic and antihyperglycemic effects [54].

12. Indian Persimmon (*Diospyros malabarica* (Desr.) Kostel.)

Diospyros malabarica (Desr.) Kostel. is an intermediate evergreen shrub that may reach a height of 15 m, has dark grey or black bark, and exfoliates in rectangular scales [55][56]. Its fruits are locally known as “Gaab” which belongs to the Ebenaceae family. It thrives throughout the humid tropical climates of India and Bangladesh which constitutes phenols, tannins, proteins, flavonoids, alkaloids, and saponins [57]. *D. malabarica* has been reported to exert antioxidant, hypoglycemic, antidiarrheal, antiviral, antiprotozoal, anthelmintic, and cytotoxic activities [58].

Ethanol extract of *D. malabarica* bark restored the cell number and size of islet cells in diabetic rats. It also greatly enhanced the glucose tolerance test and blood glucose lowering action for up to 4 h [55]. Based on another research, methanol extract from *D. malabarica* fruits reduced fasting blood glucose, pancreatic thiobarbituric acid reactive compounds (TBARS), and serum lipid levels of alloxan-induced diabetic mice [56]. Furthermore, methanol extract of *D. malabarica* bark had a strong antihyperglycemic effect, resulting in an increased concentration of plasma protein and adrop in cholesterol and triglyceride levels [59].

13. Jackfruit (*Artocarpus heterophyllus* Lam.)

Artocarpus heterophyllus Lam. from the Moraceae family, is a medium-sized [60] everlasting monoecious tree locally known as “Kathal” [61]. Various studies revealed that A. heterophyllus was first introduced in the rain forests of the Western Ghats of Southwestern India though it also grows largely in Malaysia, Burma, Sri Lanka, Bangladesh, Indonesia, Philippines, and Brazil. [62]. It incorporates several bioactive phytochemicals like carotenoids, flavonoids, volatile acids, sterols, and tannins which exerted a vast array of therapeutic actions including, antioxidant, antidiabetic, antibacterial, and antitumorigenic properties [63].

The aqueous extract of *A. heterophyllus* fruit exerted antidiabetic action by impeding hemoglobin glycation with an IC_{50} value of 56.43% [64]. The hot water extract of leaves of *A. heterophyllus* displayed hypoglycemic action in the usual subjects and the diabetic patients at 20 g/kg equivalent dose by enhancing glucose tolerance [61]. According to a study, *A. heterophyllus* aqueous leaf extract enhances the glucose content of rat plasma in vitro, having concentrations from 125 to 2000 µg/mL by halting the function of α-amylase [62]. The ethyl acetate extract of leaves also showed notable antihyperglycemic action against streptozotocin-induced diabetic animal models (20 mg/kg b.w. dose) by enhancing insulin secretion of β-cells [63].

14. Java Apple (*Syzygium samarangense* (Blume) Merr. & L.M.Perry)

Syzygium samarangense (Blume) Merr. & L.M.Perry, a small-sized [60] evergreen tree which belongs to the Myrtaceae family [60], is a non-climacteric tropical Bangladeshi fruit [65] and locally known as “Jamrul”. Alongside Bangladesh, it is also available across Malaysia and also in the surrounding countries such as Thailand, Indonesia, and Taiwan [65]. It comprises several bioactive phytochemicals like phenols, flavonoids, flavonol glycosides, proanthocyanidins, anthocyanins, ellagitannins, chalcones, carotenoid, and triterpenoids which showed an extensive spectrum of potent therapeutic attributes, including antioxidant, anti-inflammatory, hypoglycemic, and antitumorigenic activities [66].

The methanol extracts of leaves of *S. samarangense* impeded serum glucose content by 59.3% in glucose-induced hyperglycemic mice at a 400 mg/kg b.w. dose [67]. Furthermore, according to a report, *S. samarangense* methanolic leaf extracts displayed antidiabetic action by impeding the alpha-glucosidase activity [68]. *S. samarangense* methanolic fruit extract showed hypoglycemic action in streptozotocin-induced diabetic rats at 100 mg/kg b.w. dose by effectively elevating the insulin-secreting power of the β-cells residing in the pancreas [66]. The aqueous extract of *S. samarangense* fruit tends to exert a remarkable antihyperglycemic action on the insulin-resistant FL83B mouse hepatocytes by effectively increasing glucose utilization and thereby improving the glycogen level [69].

15. Key Lime (*Citrus aurantiifolia* (Christm.) Swingle)

Citrus aurantifolia (Christm.) Swingle is a shrub that belongs to the Rutaceae family [70]. It has emerged from East Asian origins and more specifically, from northern Malaysia or India which is next to North Africa [71]. Locally, it is known as “Kagoji Lebu” and constitutes numerous phytochemicals among which pectins, flavonoids, and vitamins are biologically active. *C. aurantifolia* is likely to display promising antibacterial, antifungal, analgesic, anti-inflammatory, antioxidant, anthelmintic, [72] antidiabetic as well as antihyperglycemic potencies. The phytoconstituents present in *C. auirantifolia* are mainly flavonoids and coumarins which exerted antidiabetic actions [70]. In hyperglycemic rats, intraperitoneal administration of *C. aurantifolia* oil (100 mg/kg for 14 days) exerted a substantial decrease in fasting hepatic and blood glucose though the hepatic glycogen concentration was considerably enhanced [73].

Methanol and ethanol extracts of *C. aurantifolia* dried fruit have been reported to show substantial α-amylase inhibition and also being potent hypoglycemic agents [74]. Methanol extract of *C. aurantifolia* elevated TGF-β expression with an increased number of β-cells whereas LDL concentration and islets of Langerhans got dropped in hyperglycemic rats [75]. A methanol extract of its fruit peel demonstrated a progressive drop in fasting blood glucose volume and reduction in serum triglycerides in diabetic rats, establishing the antidiabetic potential of *C. aurantifolia* [76].

16. Lemon (*Citrus limon* (L.) Osbeck)

Citrus limon (L.) Osbeck from the Rutaceae family is a tiny, thorny, and evergreen tree attaining height of 10–20 feet and a native in Asian regions. In Bangladesh, *C. limon* is known as 'Lebu'. The chief bioactive phytoconstituents that are secluded from both *C. limon* fruit and its juice are flavonoids, volatile oils [77], phenolic acids, coumarins, and amino acids [78]. Recently, notable therapeutic attributes of *C. limon* have been reported that include anti-inflammatory, antimicrobial, cytotoxic, and antiparasitic actions [78].

The extract of *C. limon* peel acquired using hexane remarkably lessened the glucose content in the bloodstream in alloxan-induced diabetic rats [79]. At 400 mg/kg daily dose via oral route for twelve days, the blood sugar range had been depleted notably by the ethanol extract of *C. limon* peels in streptozotocin-induced diabetic rats [78]. It can also inhibit the incidence of gluconeogenesis to prevent diabetic disorders [78].

17. Lotkon (*Baccaurea motleyana* (Müll.Arg.))

Baccaurea motleyana (Müll.Arg.) is an everlasting, deciduous tree that attains an altitude of 30 m. It is widely known as Rambai and as "Lotkon" in Bangladesh which belongs to the Phyllanthaceae family [80]. It is also found in Peninsular Malaysia to Sumatera, Borneo, and Halmahera [80]. *B. motleyana* contains phenols, flavonoids, fats, organic acids, and vitamins. [80][81]. Different parts of the Rambai tree were claimed to exert antibacterial, antihyperglycemic, and skincare properties [82]. Based on a previous study, the fruit of *B. motleyana* is quite beneficial for keeping blood sugar under control [80].

18. Lychee (*Litchi chinensis* Sonn.)

Litchi chinensis Sonn., a medium-sized everlasting subtropical tree from the Sapindaceae family [83], is said to be a non-climacteric type of Bangladeshi fruit [84]. It is locally famous as 'Litchi' [85]. In spite of its wide availability in Bangladesh, it is native to China's Kwangtung and Fukien provinces and northern Vietnam [85]. This plant contains various effective bioactive phytochemicals such as sterols, coumarins, phenolic acids, chromanes, anthocyanins, flavonoids, lignans, sesquiterpenes, fatty acids, proanthocyanidins, and triterpenes [84]. *L. chinensis* is claimed to display potential anti-inflammatory, antioxidant, antidiabetic, and cytotoxic properties [86].

The crude extract of the seed of *L. chinensis* tends to exhibit antihyperglycemic action by hindering α-glucosidase activity at an IC_{50} of 0.691 µg/mL [87]. Again, in another study, *L. chinensis* seed water extract rendered hypoglycemic action in alloxan-induced diabetic rats by obstructing the glucose utilization of blood capillaries [88]. The pulp extract of *L. chinensis* demonstrated antidiabetic action with an IC_{50} of 10.4 mg/mL by halting alpha-glucosidase activity [84]. Based on a research study, an in vitro analysis of methanol and ethyl acetate extracts of *L. chinensis* exhibited noteworthy inhibitory actions on rat lens aldose reductase (RLAR) having IC_{50} values of 3.6 and 0.3 mg/mL, respectively [85].

19. Mango (*Mangifera indica* L.)

Mangifera indica L., a rapid-growing everlasting tree and also a member of the Anacardiaceae family, is said to be a renowned tropical Bangladeshi fruit [89] that is locally known as 'Aam' [90]. Despite having origins in semitropical countries like India, Bangladesh, and Myanmar, this is, however, still extensively farmed in the Philippines, Malaysia, Indonesia, Singapore, and Thailand [91]. Bioactive phytochemicals of this plant include saponins, flavonoids, terpenoids, steroids, tannins, anthraquinones, cardiac glycosides, and alkaloids. Based on previous reports, *M. indica* can render potential antidiabetic, antibacterial, antioxidant, and anti-inflammatory actions [91].

The ethanolic leaf extract of *M. indica* tends to exert notable antidiabetic action against streptozotocin-induced diabetic animal models (250 mg/kg b.w. dose) by elevating insulin secretion from β-cells [89]. According to a report, the extract of *M. indica* leaves obtained with ethanol normalizes blood glucose content at an IC_{50} dose of 2.28 mg/mL by impeding the activity of pancreatic α-amylase [91]. The alcohol extract of *M. indica* leaf can also display antihyperglycemic action in rabbits at dose concentrations of 50, 100, 150, and 200 mg/kg body weight [90]. The ethyl acetate fraction from *M. indica* methanol leaf extract manifested antihyperglycemic action in vitro by halting α-amylase and α-glucosidase enzyme at an IC_{50} of 24.04 ± 0.12 µg/mL and 25.11 ± 0.01 µg/mL, respectively [41]. According to a study, *M. indica* leaf extract rendered antidiabetic action in rats at an IC_{50} value of 1.45 mg/mL by hindering α-glucosidase activity [92]. An in vitro essay of *M. indica* methanol leaf extract exhibited notable hypoglycemic action by blocking the function of dipeptidyl peptidase-4 (DPP-4) with an IC_{50} value of 182.7 µg/mL [91].

20. Muskmelon (*Cucumis melo* L.)

Cucumis melo L. is an ancient herb that belongs to the Cucurbitaceae family [93]. This horticulture crop is found across the globe and widely cultivated in Bangladesh which is locally known as "Bangi". *C. melo* contains enormous phytochemicals for example phenolic compounds, glycolipids, carbohydrates, flavonoids, and terpenoids following apocaretonoids which possess several biological activities including antidiabetic, antibacterial, anti-inflammatory, anti-hypothyroidism, antioxidant, and antiangiogenic activities [93].

The toluene soluble fraction of the ethanol extract of *C. melo* fruit was found to be highly effective in lowering blood glucose levels which are attributed to enhanced insulin secretion, suppression of glucose absorption from the gut,

enhanced glucose absorption by adipose tissues and skeletal muscle, and ultimately reduction of glucose synthesis from hepatic cells [93]. Administration of *C. melo* leaf extract to streptozotocin-induced diabetic rats notably lessened the blood sugar together with glycated hemoglobin content [94]. On the basis of a previous report, seeds roasted at various temperatures of 150 °C, 200 °C, 250 °C, and 300 °C suppressed α-amylase at 2.0 mg/mL by 61.8 percent, 60.9 percent, 50.5 percent, 72.0 percent, and 45.7 percent, respectively. Furthermore, the hexane extract of *C. melo* seeds inhibited α-glucosidase activity significantly [95].

21. Orange (*Citrus reticulata* Blanco)

Citrus reticulata Blanco, a small-sized thorny everlasting tree from the Rutaceae family, is a widely popular fruit in Bangladesh and locally called 'Komola', 'Kamala lebu'. Alongside Bangladesh, this fruit is grown worldwide and is also a horticultural crop in India [96]. It comprises various bioactive phytoconstituents like flavonoids, phenolics, tannins, monoterpenes, and sesquiterpenes and reportedly demonstrates a broad spectrum of remarkable antioxidant, antidiabetic, antifungal, anti-neurodegenerative, and antibacterial activities [96].

Orange peel and/or a combination of other citrus peels can exert potential action against diabetic disorders (Gosslau et al. 2018). The hydroethanolic extracts of *C. reticulata* fruit peel (100 mg/kg b.w./day dose) tend to exhibit hypoglycemic action in nicotinamide (NA)/streptozotocin(STZ)-induced type 2 diabetic rats by rejuvenating the function of β-cells found in the pancreas [97]. On the other hand, ethanol and aqueous peel extract manifested antihyperglycemic action by impeding the α-glucosidase by 70.8% and 14.8%, respectively, and also by hindering α-amylase 90.67% and 15.33%, respectively in rats with type 2 diabetes [98]. According to a report, the essential oil of *C. reticulata* rind and leaves (200 µL/kg b.w. dose) significantly lowered the blood glucose content from 251 ± 0.85 mg/dL to 90 ± 0.70 mg/dL, and 200 ± 0.67 mg/dL to 96.2 ± 0.86 mg/dL respectively in alloxan-induced diabetic rabbits [99].

22. Papaya (*Carica papaya* L.)

Carica papaya L., from the Caricaceae family, an ephemeral perennial [100] herbaceous laticiferous tree, is a popular tropical fruit and is locally known as "Pepe" [101]. It is widely available in Bangladesh, tropical America, southern Mexico, and neighboring Central America [100]. Several bioactive phytoconstituents like tannins, flavonoids, saponins, alkaloids, anthraquinones, cardiac glycosides, steroids, cardenolides, and phenolic compounds [102] have been reported from *C. papaya* which rendered a vast range of therapeutic attributes like antibacterial, anti-inflammatory, antiviral, hypoglycemic, and antitumorigenic activities [103].

The ethyl acetate extract of papaya seeds manifested antidiabetic action in vitro by impeding α-glucosidase and α-amylase enzymes at an IC_{50} of 83.54 and 36.84 mg/mL, respectively [104]. According to a study, the aqueous leaf extract (400 mg/kg b.w. dose) improved the blood sugar concentration in alloxan-induced diabetic albino rats [105]. In the streptozotocin-induced diabetic rats, aqueous extract of the leaves of *C. papaya* displayed antihyperglycemic action at a dose of 0.75 and 1.5 g/100 mL by upgrading the islet cells' regenerative ability [106]. Consequently, the

chloroform extract of *C. papaya* leaves also demonstrated remarkable hypoglycemic action in streptozotocin-induced diabetic rats [107].

23. Pineapple (*Ananas comosus* (L.) Merr.)

Ananas comosus (L.) Merr. is a monocot perennial plant and a member of the Bromeliaceae family. In Bangladesh, it is known as “Anarosh” in Bangladesh [108]. *A. comosus* consists of various effective bioactive phytoconstituents like alkaloids, acids, coumarins, flavonoids, glycoside, phenols, polyphenols, saponin, steroids, sterols, tacorin, tannins, terpenoids, and triterpenes [108]. It is claimed to exhibit an extensive spectrum of therapeutic actions like anti-hyperglycemic, anti-proliferative, anti-rheumatic, anti-inflammatory, antioxidant, antimicrobial, anti-coagulant, anthelminthic, anti-plasmodial, anti-pyretic, and cardioprotective properties [108].

The methanolic leaf extract of *A. comosus* leaves manifested a dose-dependent lowering of glucose content in the blood when given through an oral route to glucose-loaded Swiss albino mice models [109]. On the basis of a study conducted previously, the ethanol extract of *A. comosus* leaf notably halted the increase of glucose levels in the bloodstream having a concentration of 0.40 g/kg in diabetic rats. Also, the ethanolic leaves extract of *A. comosus* improved the sensitivity of insulin levels in rats with type 2 diabetes, which relates to enhancing the action of insulin in the hepatic cells [110]. Moreover, its fruit juice also showed synergistic action with glimepiride in lessening the blood sugar concentration in alloxan-induced diabetic rats [109].

24. Pomelo (*Citrus maxima* (Burm.) Merr.)

Citrus maxima (Burm.) Merr., an everlasting fragrant shrub from the Rutaceae family [111], is a famous pear-shaped Bangladeshi fruit [112] and is locally known as ‘Batabi lebu’, ‘Jambura’ [113]. This fruit is apparently endemic to South East Asia, India, and also many other tropical nations [112]. It incorporates various bioactive phytochemicals like phenolic acids, flavonoids, phytosterols, triterpenoids, saponins, and steroids which exerted potential biological activities like antidiabetic, antitumorigenic, hepatoprotective, anti-bacterial, and anti-hypercholesterolemic properties [111].

The peel extract of *C. maxima* manifested indispensable antihyperglycemic action in Alloxan-induced diabetic Wister rats (400 mg/kg body weight dose) by lowering the sugar content in the bloodstream by 70.17% [114]. Consequently, in the same model, the juice extract of *C. maxima* fruit improved the glucose content at 10 mL/kg b.w. dose [115]. With the help of an in vitro model, fruit juice of red *C. maxima* halted the functionality of both α-amylase and α-glucosidase enzymes by 79.75% and 72.83%, respectively, and thereby demonstrating antidiabetic action [112]. According to a report, the leaf extract obtained with methanol tends to exhibit a hypoglycemic effect in streptozotocin-induced diabetic rats when an amount of 200 and 400 mg/kg body weight is administered via an oral route [113].

25. Pomegranate (*Puncia granatum* L.)

Punica granatum L., often known as pomegranate, is a shrub that grows well in warm valleys and belongs to the Punicaceae family [116]. The fruit of the plant is locally known as “Dalim”. *P. granatum* is reported to have compounds such as alkaloids, tannins, flavonoids, anthocyanidins and hydroxybenzoic acid compounds [116]. It is efficacious as antidiabetic, antibacterial, anthelmintic, antifertility, antioxidant, antifungal, and antiulcer agents [117].

The aqueous extract of *P. granatum* fruit significantly raised the mRNA levels of IRS-1, Akt (Protein kinase B), GLUT-2, and GLUT-4, resulting in improved glucose uptake and storage and contributing to the regulation of both hyperglycemia and hyperlipidemia in alloxan-diabetic Wistar rats [118]. Ethyl acetate extract of its fruit peel halted α-glucosidase having an IC_{50} 285.21 ± 1.9 g/mL [119]. Furthermore, the methanolic flower extract of *P. granatum* increased cardiac PPAR-g mRNA expression and restored the down-regulated cardiac glucose transporter GLUT-4 (the insulin-dependent isoform of GLUTs) mRNA in rat models indicating that *P. granatum* flower extract has anti-diabetic activity due to improved insulin receptor sensitivity [120]. The methanolic extract of pomegranate fruit rinds also showed strong antidiabetic action in aldose reductase, α-amylase, and PTP1B suppression tests in a dose-dependent manner by controlling blood glucose concentrations within normal ranges in an alloxan-induced diabetes model [121].

26. Sapodilla (*Manilkara zapota* (L.) P.Royen)

Manilkara zapota (L.) P.Royen, well known as Sapodilla, is a medium to large tree which has its roots in the Indian subcontinent and is a species from the Sapotaceae family [122] that is locally known as “Sofeda”. Phytochemicals extracted from *M. zapota* are steroids, flavonoids, phenols, alkaloids, tannins, glycosides, and saponins which displayed enormous pharmacological effects like anti-diabetic, anti-arthritis, anti-inflammatory, anti-oxidant, anti-bacterial, anti-fungal, and anti-tumor activities [122].

Different phytochemicals from *M. zapota* seeds, leaves, and root extracts have been reported to exhibit hypoglycemic activity [122]. In addition, *M. zapota* leaf extract has shown improved hypoglycemic action in animal models [123]. Ethanol and aqueous extracts of *M. zapota* seeds displayed significant in vivo hypoglycemic action in experimental mice [124]. Another study found that alcohol and aqueous extracts of its seeds remarkably reduced the model group’s blood glucose levels when compared to metformin [125]. Furthermore, ethanol extract from the seed and methanol extract from the leaf of *M. zapota* decreased blood glucose levels by controlling insulin production from the few remaining β-cells. According to the findings of this research, enhanced peripheral glucose consumption also aided in the lowering of blood glucose levels [126].

27. Star Fruit (*Averrhoa carambola* L.)

Averrhoa carambola L., a slow-growing multi-stemmed tree from the Oxalidaceae family, is a popular nutrient-enriched fruit in Bangladesh and is locally called ‘Kamranga’ [127]. This plant is available in tropical areas such as India, Malaysia, Indonesia, and the Philippines [127]. Numerous bioactive phytochemicals extracted from this plant are saponins, flavonoids, alkaloids, tannins, phenols, anthocyanin and anthocyanidin, chalcones, aurones,

catechins, and triterpenoids which exert a wide range of potential antioxidant, antidiabetic, antihypertensive, anti-hypercholesterolemic, anti-inflammatory, anti-infective, and cytotoxic activities [128].

The methanolic leaf extract of *A. carambola* (400 mg/kg b.w. dose) exhibited antidiabetic action with a blood glucose-reducing potential of 34.1% in glucose-filled Swiss albino mice [67]. According to a study, the hydroalcoholic leaf extract of *A. carambola* exhibited promising antidiabetic action by upgrading the glucose intake of muscles in male Wistar rats [128]. The ethanol extract of its bark manifested noteworthy antihyperglycemic action in vitro by effectively hindering the α-glucosidase enzyme at an IC_{50} value of 7.15 ± 0.06 µg/mL [129]. Besides, the ethanol extract from air-dried roots also demonstrated antidiabetic action by restoring the pancreatic β-cells function in streptozotocin-induced diabetic rats [130]. The juice of *A. carambola* fruits remarkably lowered glucose content at 25, 50, and 100 g/kg b.w. dose for three weeks in streptozotocin-induced diabetic mice [131].

28. Sugar apple (*Annona squamosa* L.)

Annona squamosa L., a small, evergreen, semi-deciduous tree from the Annonaceae family [132], is well-known nutritious tropical Bangladeshi fruit and is locally known as ‘Ata’ [133]. It is also found in India, the West Indies, southern America, and Thailand [133]. It comprises numerous bioactive phytochemicals like volatile Oils, alkaloids, terpenoids, flavonoids, polyphenols, glycosides, saponins, and tannins. Based on previous reports, A. squamosa can exhibit promising antioxidant, cytotoxic, anti-inflammatory, hypoglycemic, antimicrobial, hepatoprotective, and antiplasmodial actions [133].

A. squamosa hydroalcoholic leaf extract (350 mg/kg b.w. oral dose) tends to exert antidiabetic action with glucose reducing activity by 50.11% in streptozotocin-induced diabetic rats [134]. An in vitro analysis of methanol extracts of barks and leaves of *A. squamosa* manifested hypoglycemic action by impeding α-amylase at an IC_{50} value of 123.91 and 153.89 µg/mL, respectively [135]. The hexane extract of the leaf of *A. squamosal* obtained using reportedly exerted antihyperglycemic action in vivo having a concentration of 500 mg/kg p.o by hindering the human PTP1B enzyme with an IC_{50} level of 17.4 µg/mL [136]. Its ethanolic leaf extract at 50 mg/kg dose lessened the blood sugar content in alloxan-induced diabetic rabbits by 52.7% [133]. The ethanol and methanol extracts of *A. squamosa* seeds (200 mg/kg b.w. dose) demonstrated a notable antihyperglycemic effect by reducing the blood sugar levels by 43.96% and 45.99%, respectively, in alloxan-induced diabetic rats [137].

29. Watermelon (*Citrullus lanatus* (Thunb.) Matsum. & Nakai)

Watermelon, scientifically known as *Citrullus lanatus* (Thunb.) Matsum. & Nakai is the most commonly grown species from the Cucurbitaceae family. It is widely farmed throughout the globe, including Bangladesh [138], and is locally known as “Tormuj”. This plant’s bioactive phytochemicals are mostly ascribed to triterpenes, sterols, and alkaloids which can be reportedly used as antidiabetic, anthelmintic, diuretic, antibacterial, antifungal, and antihypertensive agents [139].

Previous research has revealed that the ethanol extract of *C. lanatus* leaf can inhibit pancreatic α-amylase with an IC_{50} value of 36.75 ± 3.47 g/mL [140]. The aqueous ethanol and aqueous extracts of *C. lanatus* leaves profoundly rendered anti-diabetic action via α-glucosidase suppression, with IC_{50} values ranging from 26.26 ± 0.29 to 180.33 ± 1.31 g/mL [138]. In another study, its juice was also discovered to have promising anti-diabetic efficacy in an experimental diabetic animal model via several mechanisms involving the regulation of glucose transporters and domination of α-glucosidase and α-amylase activity [140]. The seed extracts of yellow-skinned *C. lanatus* hindered α-glucosidase with IC_{50} values ranging from 32.50 ± 0.36 to 313 ± 1.36 g/mL for 70 percent aqueous ethanol and aqueous extracts, respectively [138]. A recent study also found that the alcalde and tryptic hydrolysates of *C. lanatus* seeds had a very strong α-amylase inhibitory capacity (IC_{50} values of 0.149 to 0.234 mg/mL) via a non-competitive suppression mechanism [141].

30. Tal Palm (*Borassus flabellifer* L.)

Borassus flabellifer L., a famous species of the Arecaceae family is locally known as “Tal” in Bengali and is a tall palm reaching up to 12–33 m height having a black stem and crown of leaves at the top [142]. It is extensively disseminated and grown in tropical Asian nations like Thailand, India, Myanmar, Sri Lanka, Malaysia, and Bangladesh. It is a promising source of alkaloids, flavonoids, glycosides, tannins and so many phenolic compounds [142]. *B. flabellifer* reportedly exerts an extensive spectrum of therapeutic actions like antihyperglycemic, anti-inflammatory, antipyretic, antibacterial, and anthelmintic activities [142].

Ethanolic extract of tal palm roots at 250 and 500 mg/kg displayed a promising reduction in the glucose content of serum in rats with type 2 diabetes [143]. Numerous portions of *B. flabellifer* like leaves, roots, pulp, and fruit fibers. are claimed to be utilized to treat diabetes [142]. Ethanolic extract of the flower of *B. flabellifer* significantly improved the glucose tolerance up to 4 h and lowered the glucose content of blood significantly in alloxan-induced diabetic rats. Furthermore, ethanol extracts of *B. flabellifer* flowers showed notable regeneration of pancreatic β cells comparable to glibenclamide [144]. Methanol extract of tal palm fruits demonstrated raised content of insulin in the plasma when compared to diabetic controls in diabetic rats. Again, methanol extract from tal palm fruits also impeded PTP1B remarkably with an IC_{50} value of 23.98 mg/mL, and this decreased PTP1B expression which might increase the mass of β-cells in the pancreas which subsequently improved the release of insulin triggered by glucose and ultimately lowered the glucose content in blood [145].

31. Tamarind (*Tamarindus indica* L.)

Tamarindus indica L. from the Fabaceae family, a large-sized everlasting tree, is a nutrient-enriched tropical fruit is locally named “Tetul”. Though this fruit is mostly endemic to tropical regions of Africa, still tamarind is farmed and developed well in all other tropical continents. *T. indica* is reported to have phytoconstituents like flavonoids, tannins, glycosides, organic acids, and phenolic compounds [146]. *T. indica* is reported to be useful as an antidiabetic, antimicrobial, and anti-inflammatory agent [147].

The aqueous extract of *T. indica* fruit pulp showed promising postprandial hypoglycemic effect by impeding the function of α-amylase and α-glucosidase enzymes and raising the glucose uptake [148]. Aqueous extract from *T. indica* seed and seed coat showed improvement in hyperlipidemia, which is foundnotably in rat models and humans [147]. On the basis of a study conducted previously, the aqueous extracts of *T. indica* seeds exerted hypoglycemic activity which was mediated by lowering the diffusion rate of blood glucose, increasing glucose adsorption, and upgrading the transportation of blood glucose at the cellular level throughout the plasma membrane [149]. According to a report, the extract of *T. indica* seed obtained using methanol demonstrated a significant reduction of blood glucose content at the fasting state in mice models [150]. In addition, the alcoholic extract of its stem bark functioned as a potent hyperglycemic agent in the treatment of diabetes mellitus [151]. The ethanolic fruit pulp extract also effectively changed alloxan-induced alterations in serum glucose, enzyme, and lipid profile [152].

32. Wood Apple (*Limonia acidissima* Groff)

Limonia acidissima Groff, a slow-growing, fragrant, large-sized, deciduous tree from the Rutaceae family is a popular nutrient-enriched Bangladeshi fruit and is locally known as “Kod-bael” [153][154]. Bangladesh, India, Pakistan, Sri Lanka, Myanmar, and Vietnam are among the countries where it appears to be growing naturally [154]. It incorporates major bioactive phytochemicals like coumarins, lignans, flavonoids, phenolic acids, quinones, alkaloids, triterpenoids, sterols, and volatile oils which reportedly exert a vast range of therapeutic attributes like antioxidant, cytotoxic, hypoglycemic, antimicrobial, and hepatoprotective activities [155].

The aqueous and ethanol extracts of *L. acidissima* stem bark (200 mg/kg b.w. dose) remarkably lessened the blood glucose content from 250–358 mg/kg to 99.8 and 112.6 mg/kg, respectively in alloxan-induced diabetic rats [153]. According to a report, the methanolic fruit extract of *L. acidissima* tends to exhibit antidiabetic action by lowering the glucose content by 39% and 54.5% at an oral dose of 200 and 400 mg/kg b.w., respectively in streptozotocin-induced male Albino diabetic rats [156]. The methanol and aqueous extract of its fruit manifested antihyperglycemic action in vitro (100 µg/mL concentration) by impeding the α-glucosidase at an IC_{50} of 66.738 and 84.548 µg/mL, respectively and also by hindering α-amylase at an IC_{50} of 119.698 and 167.505 µg/mL, respectively [157].

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