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Antidiabetic Potency of Bangladeshi Medicinal Plants

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ABSTRACT

Diabetes mellitus is a degenerative disease being responsible for about 1.5 million deaths globally. In Bangladesh, the stress of diabetes is on rising and resulting in serious health implications along with significant economic crisis. Due to undesirable and inherent side effects, researchers are now shifting from the conventional therapy and trying to prevent and manage diabetes through traditional medicine. World Health Organization (WHO) also recommends the practice of customary herbal medicine for diabetes management, and support and encourage the augmentation of research to evaluate the hypoglycemic properties of the diverse medicinal plant species. Consequently, in the current review, the antihyperglycemic potency of some Bangladeshi medicinal plants has been evaluated and verified utilizing human as well as experimental animals. The results elucidate the glucose-lowering effects of the plants via different cellular mechanisms, including restoration of pancreatic β-cell, controlling the action of carbohydrate metabolizing enzymes, enhancing peripheral glucose utilization, increase in muscle glycogen store as well as activation of the insulin signaling cascade. In summary, this work may invigorate the researchers for more specific and focused research to provide a better and broad understanding of the antihyperglycemic mechanism and can act as an effective tool for choosing the plants with robust potential for unbolting of novel antidiabetic agents.

Keywords: Diabetes mellitus; antidiabetic medicinal plants; bioactive compounds; hypoglycemic potency; Bangladesh.

INTRODUCTION

Diabetes mellitus (DM) is a chronic, degenerative disease expressed by hyperglycemia (exalted blood glucose levels) arising from inherited and/or attained scarcity in insulin production from β islet cells of the pancreas, or by the incompetence of the insulin made [1]. Over 400 million people in the world are living with DM while an accounted 1.5 million deaths are attributed to it. In the past 35 years, the outbreak of DM has almost increased by twofold globally, rising from 4.7% to 8.5%. Epidemiologic studies have indicated that low- and middle-income countries have experienced a greater percentage of morbidity and mortality due to DM than high-income generating countries [2]. The World Health Organization (WHO) projected that, by 2030, DM is going to be one of the seven leading causes of death if the ongoing trend continues [3].

Diabetes may be classified based on the etiology and clinical symptoms as type 1 (also called insulin dependent diabetes mellitus), type 2 (also called non-insulin dependent diabetes mellitus), and gestational diabetes (a temporary condition during pregnancy). Being responsible for 90-95% of all cases, type 2 DM is the most prevalent one among diabetes. Diabetes of all types, if not controlled, has miserable upshot for health and well-being, and can lead to complications in many parts of the body causing serious damage to different organs, especially the eyes, kidneys, nerves, heart, and blood vessels, and can increase the overall risk of premature death [1]. Bangladesh, a lower-middle income country of South Asia, is stressed with the dual load of malnutrition. Non-communicable diseases like diabetes are on rising and resulting in serious health implications along with significant financial burden. Based on the recent findings, there has been a substantial increase in diabetes among Bangladeshi adults, from 4% in 2000 to 9.7% in 2014. More than half of the population with DM, 56%, are not aware that they have diabetes and don't receive any treatment [4].

Still now, diabetes management is a matter of concern worldwide, and effectual remedy has not been unfolded yet. There are copious therapeutic measurements attainable nowadays for diabetes comprising insulin and a number of oral antidiabetic medicines such as amylin analogs, α-glycosidase prohibitors include acarbose, miglitol and voglibose, sulfonylureas, biguanides, but it is a fact that full recuperation from diabetes, even of a single person, has never been proclaimed. The treatment of diabetes with synthetic drugs (oral hypoglycemic agents) are generally not promoted because of its high charge, and

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undesirable and inherent side effects such as hypoglycemia at higher doses, weight gain, liver problems, disturbances in the gastrointestinal tract (GIT), nausea, and diarrhea [5, 6]. Thus, the exploration of more efficient and safer therapy has continued to be a vital ground for investigation. Except for the prevailing therapeutic choices, abundant traditional herbal medicines have been advised for the amendment of diabetes and other non-communicable diseases. The traditional medicines have demonstrated their potentiality and showed an effulgent future in the therapy of diabetes and therefore, WHO recommends medicinal plants to be used for the rectification of DM [7, 8]. Herbal drugs are often prescribed owing to their efficacy, relatively low cost, and possession of little or no adverse effects [9].

Bangladesh, owing to its location and propitious climate, has been graced with an unbounded diversity of flora, together with medicinal plants. Among 5700 angiosperms growing in the country, above 500 are assumed to have medicinal properties [10, 11]. Being easily accessible and inexpensive, these natural herbal medicines have become an indispensable segment of public health services in Bangladesh. Hence, in this review, an effort was made to focus some experimentally ascertained antidiabetic medicinal plants of Bangladesh, and the bioactive compounds present and the probable mode of action through which they exert hypoglycemic potency.

METHODS

In the existing review, some ethnobotanical and ethnomedicinal surveys conducted in different districts and among different communities of Bangladesh were utilized as a basis for the preparation of a list of medicinal plants commonly practiced to prevent and manage diabetes [12-15]. Afterward, electronic databases including Google Scholar, PubMed, and Cochrane library etc. were explored (till December 2017) for each and every medicinal plant, and all collected papers were reconnoitered to ensure any *in vivo*, *in vitro*, or clinical indication for their competence and pharmacological mechanisms of action. For the present study, published articles were considered solely eligible.

Medicinal plants with antidiabetic potency

In Bangladesh, traditional practices in diabetes treatment using medicinal plants in an unexplored horizon. Though, investigations of medicinal plants with various species were studied in this review (Table 1). Multiple segments of the plants (i.e. leaf, fruit, root, bark, bulb etc.) were used to carry out the studies. The initial phytochemical analysis illustrated the existence of flavonoids, terpenoids, saponins, alkaloids etc. Streptozotocin or alloxan-induced diabetic modules were employed to conduct the efficacy evaluation of the plants. The research results illuminated the glucose-lowering effects while proposing numerous mechanisms of action for the plant extracts which include the resurrection of pancreatic β-cell, regulation of the activity of carbohydrate metabolizing enzymes, increase in peripheral glucose utilization, increase in muscle glycogen store as well as activation of the insulin signaling cascade.

Table 1: Medicinal plants of Bangladesh with antidiabetic activity

Botanical name (Common Name)	Part(s) used	Bioactive constituent(s)	Probable mechanisms of action
Acacia catechu (L.f.) Willd. (Khair) [16]	▪ Bark	▪ Flavonoids	▪ Stimulate insulin secretion ▪ Promote β-cell regeneration
Adhatoda vasica Nees (Basak) [17]	▪ Leaf	▪ Alkaloids	▪ Inhibit activities of α-glucosidase
Aegle marmelos (L.) Corr. (Bel) [18, 19]	▪ Fruit ▪ Bark	▪ Tannins	▪ Increase insulin secretion from pancreatic β-cell ▪ Regulate the activity of carbohydrate metabolizing enzymes
Allium cepa L. (Piaj) [20, 21]	▪ Bulb	▪ Sulphur containing amino acids ▪ Flavonoids	▪ Control glucose metabolizing enzymes activities ▪ Upregulate expressions of insulin receptor and glucose transporter
Allium sativum L. (Rasun) [22, 23]	▪ Bulb	▪ Sulphur containing amino acids	▪ Regulate the activities of glucose metabolizing enzymes ▪ Increase insulin secretion of from pancreatic β-cell
Alocasia macrorrhizos (L.) G. Don [24]	▪ Rhizome	▪ Flavonoids	▪ Stimulate insulin secretion by pancreatic β-cells
Aloe vera (L.) Burm. f. (Ghritakumari) [25, 26]	▪ Leaf	▪ Phytosterols	▪ Control the activity of the carbohydrate metabolizing enzymes ▪ Stimulate synthesis and/or release of insulin
Amaranthus spinosus L. (Katanotey) [27, 28]	▪ Leaf	▪ Alkaloids ▪ Flavonoids	▪ Inhibit α-amylase activity ▪ Enhance insulin from pancreatic β-cells
Amaranthus viridis L. (Notey) [29, 30]	▪ Leaf	▪ Flavonoids ▪ Terpenoids ▪ Saponins ▪ Alkaloids	▪ Inhibit the activity of α-amylase ▪ Increase glucose uptake by diaphragm ▪ Enhance glycogenesis by liver
Amorphophallus paeoniifolius (Dennst.) Nicolson [31]	▪ Corm	▪ Polyphenols ▪ Flavonoids	▪ Alleviate intestinal and renal disaccharides
Ananas comosus (L.) Merr. (Anaras) [32, 33]	▪ Leaf	▪ Alkaloids ▪ Flavonoids ▪ Tannins	▪ Enhance insulin sensitivity ▪ Regulate the activities of glycogen metabolizing enzymes
Andrographis paniculata (Burm.f.) Nees (Kalomegh) [34, 35]	▪ Leaf	▪ Flavonoids	▪ Inhibit activities of α-amylase and α-glucosidase ▪ Reduce the activities of glucose-6-phosphatase
Areca catechu L. (Supari) [36]	▪ Areca nut	▪ Flavonoids	▪ Inhibit activities of α-glucosidase
Asparagus racemosus Willd. (Satamuli) [37]	▪ Root	▪ Flavonoids	▪ Inhibition carbohydrate digestion and absorption ▪ Enhance insulin secretion and action
Azadirachta indica A. Juss. (Neem) [38-40]	▪ Leaf	▪ Flavonoids ▪ Alkaloids ▪ Tannins ▪ Saponins	▪ Improve the insulin signaling molecules ▪ Increase glucose utilization in the skeletal muscle ▪ Increase release of insulin from β-cells

Barringtonia acutangula (L.) Gaertn. (Hijal) [41, 42]	▪ Fruit	▪ Flavonoids ▪ Terpenoids ▪ Tannins ▪ Saponins ▪ Alkaloids	▪ Regenerate β-cells of the pancreas
Basella rubra L. (Puishak) [43]	▪ Leaf	▪ Flavonoids ▪ Terpenoids ▪ Tannins ▪ Saponins	▪ Inhibit activities of α-amylase and α-glucosidase
Boerhaavia diffusa L. (Punarnava) [44]	▪ Leaf	▪ Alkaloids	▪ Reduce the activities of gluconeogenic enzymes
Bombax ceiba L. (Shimul) [45]	▪ Thalamus ▪ Flower	▪ Tannins ▪ Flavonoids	▪ Inhibit activities of α-amylase and α-glucosidase
Butea Monosperma (Lam.) Taub. (Palas) [46, 47]	▪ Flower	▪ Flavonoids ▪ Saponins ▪ Phytosterols	▪ Increase peripheral glucose utilization ▪ Stimulate insulin secretion
Camellia sinensis (L.) Kuntze (Cha) [48]	▪ Leaf ▪ Flower	▪ Alkaloids ▪ Flavonoids ▪ Tannins	▪ Inhibit activities of α-amylase and α-glucosidase
Cardiospermum halicacabum L. (Phutka) [49]	▪ Leaf	▪ Flavonoids ▪ Saponins	▪ Reduce the activity of glucokinase ▪ Elevate the activities of gluconeogenic enzymes
Carica papaya L. (Pepe) [50]	▪ Leaf	▪ Alkaloids ▪ Flavonoid ▪ Saponins ▪ Tannins	▪ Stimulate insulin secretion from pancreatic β-cells
Catharanthus roseus (L.) G. Don (Nayantara) [51-53]	▪ Leaf ▪ Twig	▪ Alkaloids ▪ Flavonoids ▪ Tannins ▪ Saponins	▪ Increase utilization of glucose by liver ▪ Alter the activities of glucose metabolizing enzymes
Centella asiatica (L.) Urb. (Thankuni) [54, 55]	▪ Whole plant	▪ Phenolics ▪ Triterpenoids ▪ Flavonoids	▪ Inhibit the activity of α-amylase ▪ Inhibit intestinal disaccharidase activity
Cinnamomum tamala (Buch.-Ham.) T. Nees & Eberm. (Tejpata) [56, 57]	▪ Bark ▪ Leaf	▪ Essential oils	▪ Inhibit α-amylase activity ▪ Promote peripheral glucose utilization ▪ Increase muscle glycogen store
Cinnamomum zeylanicum Blume (Daruchini) [58]	▪ Bark	▪ Essential oils	▪ Regulate the activity of carbohydrate metabolizing enzymes
Clitoria ternatea L. (Aparajita) [59, 60]	▪ Leaf	▪ Flavonoids	▪ Reduce the activities of glucose-6-phosphatase, and increase the activity of glucokinase ▪ Regenerate β-cells
Coccinia grandis (L.) Voigt (Telakucha) [61, 62]	▪ Leaf	▪ Alkaloids ▪ Flavonoids ▪ Tannins	▪ Regenerate β-cells ▪ Inhibit α-amylase activity
Curcuma longa L. (Halud) [63]	▪ Rhizome	▪ Volatile oils	▪ Inhibit activities of α-amylase and α-glucosidase
Datura metel L. (Dhutura) [64]	▪ Seed	▪ Alkaloids	▪ Enhance secretion of insulin
Dillenia indica L. (Chalta) [65]	▪ Leaf	▪ Phytosterols ▪ Polyphenols ▪ Triterpenoids	▪ Inhibit α-amylase and α-glucosidase activities
Ficus benghalensis L. (Bot) [66]	▪ Bark	▪ Leucopelargonin	▪ Stimulate insulin secretion
Foeniculum vulgare Mill. (Mouri) [67]	▪ Seed	▪ Alkaloids ▪ Flavonoid ▪ Saponins ▪ Tannins	▪ Enhance insulin secretion ▪ Increase liver and kidney hexokinase level
Hibiscus rosa-sinensis L. (Jaba) [68]	▪ Flower	▪ Alkaloids ▪ Tannins ▪ Flavonoids	▪ Regenerate β-cells
Ipomoea aquatica Forssk. (Misti Alu) [69]	▪ Plant	▪ Phenolics ▪ Flavonoid ▪ Alkaloids ▪ Saponins	▪ Preserve islets area and cell population
Jatropha curcas L. (Jamalgota) [70]	▪ Leaf	▪ Flavonoids	▪ Regenerate and protect β-cells ▪ Inhibit α-amylase activity
Kalanchoe pinnata (Lam.) Pers. (Patharkuchi) [71-73]	▪ Leaf	▪ Flavonoids ▪ Triterpenoids	▪ Stimulate insulin secretion ▪ Increase the number of pancreatic β-cells ▪ Inhibit α-amylase activity
Lagenaria siceraria (Molina) Standl. (Lau/Kadu) [74]	▪ Pulp ▪ Seed	▪ Flavonoids ▪ Alkaloids ▪ Saponins	▪ Increase insulin production and secretion
Lagerstroemia speciosa (L.) Pers. (Jarul) [75]	▪ Leaf	▪ Tannins	▪ Suppress gluconeogenesis ▪ Stimulate glucose oxidation

Lawsonia inermis L. (Mehedi/Mendi) [76]	▪ Leaf	▪ Flavonoids ▪ Saponins ▪ Tannins	▪ Inhibit α-amylase activity
Linum usitatissimum L. (Tisi) [77]	▪ Seed	▪ Fixed oil	▪ Prevent damage in pancreatic β-cells
Luffa acutangula (L.) Roxb. (Jhinga) [78]	▪ Fruit	▪ Saponins ▪ Phenols ▪ Flavonoids	▪ Inhibit the activities α-glucosidase
Luffa aegyptiaca Mill. (Dhundal/Dhundul) [79]	▪ Leaf	▪ Steroids ▪ Alkaloids ▪ Saponins	▪ Increase secretion of insulin form pancreatic β-cells
Madhuca indica J. F. Gmel. (Mahua) [80]	▪ Bark	▪ Tannins ▪ Saponins ▪ Sterols	▪ Inhibit α-amylase and α-glucosidase activities
Mangifera indica L. (Aam) [81]	▪ Leaf	▪ Mangiferin	▪ Inhibit the activities of α-amylase and α-glucosidase
Nicotiana tabacum L. (Tamak) [82]	▪ Leaf	▪ Flavonoids ▪ Tannins ▪ Terpenoid	▪ Inhibit activities of α-amylase and α-glucosidase
Nigella sativa L. (Kalojira/Kalijira) [83-85]	▪ Seed	▪ Polyphenols	▪ Increase insulin secretion ▪ Induce proliferation of pancreatic β-cells ▪ Stimulate glucose uptake in muscle and fat cells
Nymphaea stellata Willd. (Sapla) [86, 87]	▪ Flower	▪ Phenolics	▪ Inhibit activities of α-glucosidase ▪ Regulate the activity of glucose metabolizing enzymes
Ocimum sanctum L. (Tulsi) [40, 88, 89]	▪ Leaf	▪ Flavonoids ▪ Phenolics	▪ Stimulate insulin secretion ▪ Regulate the activity of carbohydrate metabolizing enzymes
Oryza sativa L. (Dhan) [90]	▪ Bran	▪ Phenolics ▪ Flavonoids	▪ Inhibit activities of α-amylase and α-glucosidase ▪ Stimulate glucose uptake
Pandanus fascicularis Lam. (Keora) [91]	▪ Root	▪ Flavonoids ▪ Phenolics	▪ Increase secretion of insulin
Phyllanthus emblica L. (Amla/Amloki) [92]	▪ Fruit	▪ Flavonoids ▪ Tannins ▪ Terpenoid ▪ Alkaloids	▪ Inhibit the activities of disaccharidase ▪ Reduce intestinal glucose absorption
Piper betle L. (Pan) [93]	▪ Leaf	▪ Alkaloids ▪ Saponins ▪ Tannins	▪ Control glucose metabolizing enzyme activities
Polyalthia longifolia (Sonn.) Thwaites (Debdaru) [94]	▪ Leaf	▪ Alkaloids	▪ Inhibit α-amylase and α-glucosidase enzymes activity
Punica granatum L. (Dalim/Bedana) [95]	▪ Fruit	▪ Tannins ▪ Flavonoids ▪ Pectins	▪ Regenerate β-cells of pancreas
Saraca asoca (Roxb.) Willd. (Ashok) [96, 97]	▪ Leaf ▪ Flower	▪ Phytosterols ▪ Flavonoids	▪ Increase pancreatic secretion of insulin from the β-cells
Solanum melongena L. (Begun) [98]	▪ Fruit	▪ Phenolics	▪ Inhibit activities of α-amylase and α-glucosidase
Spinacia oleracea L. *(*Palong shak) [99]	▪ Leaf	▪ Flavonoids	▪ Regenerate β-cells of pancreas
Spondias pinnata (L. f.) Kurz (Amra) [100]	▪ Bark	▪ Flavonoids	▪ Increase the biosynthesis of insulin in the pancreas ▪ Regenerate β-cells
Syzygium cumini (L.) Skeels (Jam) [101]	▪ Seed	▪ Tannins ▪ Flavonoids ▪ Phenolics	▪ Inhibit activities of α-glucosidase
Tagetes erecta L. (Genda) [102]	▪ Inflorescence	▪ Flavonoids	▪ Inhibit activities of α-glucosidase and α-amylase
Tamarindus indica L. (Tetul) [103-105]	▪ Seed	▪ Flavonoids	▪ Suppress glucose-6-phosphatase activity ▪ Restore pancreatic β-cells ▪ Inhibit intestinal glucose absorption
Tectona grandis L. f. (Segun) [106]	▪ Bark	▪ Tannins	▪ Regenerate β-cells
Terminalia arjuna (Roxb. ex DC.) Wight & Arn. (Arjun) [107]	▪ Bark	▪ Tannin ▪ Saponin ▪ Flavonoids	▪ Control glucose metabolizing enzyme activities
Terminalia bellirica (Gaertn.) Roxb. (Bahera) [108, 109]	▪ Fruit ▪ Leaf	▪ Gallic acid	▪ Stimulate insulin secretion ▪ Inhibit activities of α-amylase and α-glucosidase
Terminalia chebula Retz. (Haritaki) [110, 111]	▪ Fruit	▪ Tannins ▪ Triterpenoids ▪ Flavonoids	▪ Regulate the activities of glucose metabolizing enzymes ▪ Regenerate pancreatic β-cells ▪ Inhibit activities of α-glucosidase
Vigna radiata (L.) R. Wilczek (Mug) [112]	▪ Seed	▪ Flavonoids	▪ Inhibit α-glucosidase activities
Vigna unguiculata (L.) Walp. (Barbati) [113]	▪ Seed	▪ Fibers	▪ Activate the insulin signaling cascade
Vitex negundo L. (Nishinda) [114, 115]	▪ Leaf	▪ Idopyranose ▪ Iridoid glucoside	▪ Regenerate β-cells of the pancreas ▪ Enhance pancreatic insulin secretion

			▪ Regulate carbohydrate metabolizing enzyme activity
Withania somnifera (L.) Dunal (Aswagandha) [116, 117]	▪ Root ▪ Leaf	▪ Flavonoids	▪ Improve insulin sensitivity ▪ Reduce the activity of glucose-6-phosphatase
Xylocarpus moluccensis (Lam.) M. Roem. (Passur) [118]	▪ Fruit	▪ Limonoids	▪ Alter the activities of glucose metabolizing enzymes ▪ Increase glucose uptake by muscle cells ▪ Inhibit α-glucosidase activities
Zea mays L. (Bhootta) [119, 120]	▪ Kernel	▪ Phenolics ▪ Flavonoids	▪ Inhibit α-glucosidase activities ▪ Protect pancreatic β-cells ▪ Increase insulin secretion
Zingiber officinale Roscoe (Ada) [121, 122]	▪ Rhizome	▪ Gingerol	▪ Increase the activities of glycolytic enzymes ▪ Enhance Glucose uptake

CONCLUSION

Since the advent of human beings, plants continue to be a vital component not only for fostering human health and well-being but also for flourishing the quality of human life via alleviating ailments. Several studies have reported the utility of a number of plants for the cessation and mitigation of many chronic diseases, including DM. So, researchers are pursuing among the native traditional medicinal plants in search of a substitute to antidiabetic drugs owing to the unwanted side-effects, availability, and accessibility of conventional antihyperglycemic drugs. Bangladesh, being a fertile and alluvial land exaggerated with tropical forests and boggy jungles, is an affluent source of a wide variety of medicinal plants applied in the traditional medicinal system for curing disease.

The current review has presented a comprehensive detail of the antidiabetic plants being offered in the historical platform of Bangladeshi medication for management and treatment of DM. The results demonstrated a few pharmacological mechanisms of actions of the medicinal plants to accomplish their therapeutic actions. *In vivo* experiments displayed that inhibition of absorption of glucose in intestinal, an increment in the biosynthesis of liver glycogen or decrement in glycogenolysis, improvement in peripheral glucose absorption etc. are among some antidiabetic mechanistic actions of Bangladeshi natural remedies. Rejuvenation of pancreatic β-cells, inhibiting the decay of islet tissue of pancreas, increase in the restrictive action against α-amylase and α-glucosidase enzyme, a rise of insulin sensitivity or the insulin-like performance of the plant essence is the *in vitro* findings supporting the dexterity of the plants used for DM. It is suggested that the glycemic control properties of the plants are attributed to the bioactive principles like alkaloids, flavonoids terpenoids, glycosides etc. These secondary plant metabolites have already proven their role in preventing and treating many chronic diseases like diabetes. Although, among the clinical experiments, no serious hostile effects were investigated and thus, the natural herbal preparations in gross assumed harmless for the human. However, every plant material is not safe, and so, more investigation of the noxious effect of these herbal plants is needed prior to recommending for human use.

In conclusion, the current review contributes to an insight of the prevailing perception of the efficiency of plant extracts commonly adopted in Bangladesh as a dietary supplement or ancillary therapy for the preclusion and remedy of diabetes. Nonetheless, the evidence found so far is mainly suggestive, and thus, it is crucial to recognize the bioactive component accountable for the antihyperglycemic action with the actual mode of action. More specific and focused research, therefore, will provide a better and broad understanding in this regard. Lastly, this extensive literature review can serve as an efficient mean for the nomination of plants having an intense potential for the unbolting of novel antidiabetic agents.

Conflict of interest

The authors' have no conflict of interest to declare.

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