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REVIEW

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Plant bioactive compounds and their mechanistic approaches in the treatment of diabetes: a review

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Abstract

Background: Diabetes mellitus (DM) is a growing disease across the world; diabetes is a complex metabolic disorder in which blood glucose concentration level increases and continue for a prolonged period due to a decrease secretion of insulin or action, resulting in the disorder of carbohydrate, lipid, and protein metabolism. The plant-related bioactive compounds have proven their efficacy with least toxicities and can be utilized for the disease treatment. Our objective is to elucidate the mechanism of action of plant bioactive compounds which can give future direction in diabetes treatment.

Main body: In this review paper, we briefly study more than 200 research papers related to disease and bioactive compounds that have therapeutic applicability in treatment. The plant contains many bio-active compounds which possess in vitro and in vivo anti-diabetic effect which may be responsible for the hypoglycaemic property by inhibiting the digestive enzyme i.e. alpha-amylase and alpha-glucosidase, by producing mimetic action of insulin, by reducing the oxidative stress, by showing antihyperglycemic activity and hypolipidemic activity, by inhibition of aldose reductase, and by increasing or enhancing glucose uptake and insulin secretion.

Conclusion: Our study revealed that terpenes, tannin, flavonoids, saponin, and alkaloids are important bioactive constituents for anti-diabetic activity. The mechanistic approach on alpha-glucosidase and alpha-amylase, hypolipidemic activity, and AR inhibitory action clear-cut explain the therapeutic applicability of these bioactive compounds in disease. Plants that contain these bioactive compounds can be good drug candidates for future research on diabetes treatment.

Keywords: Diabetes mellitus, Medicinal plant, Phytochemicals, Hyperglycaemia, Insulin, STZ, Alloxan

Background

Diabetes is the collection of metabolic illnesses in which increased blood sugar levels persist for a prolonged period due to a malfunction in insulin production that affects the metabolism of various nutrients such as proteins, lipids, and carbohydrates [1]. Metabolism is normally altered through congenital and environmental variables [2]. The disease pathophysiology suggests that patients may experience frequent urination, thirst, and hunger with other symptoms. Serious complications such as kidney, eye, foot, and another organ failure may be aggravated if properly not managed. In adults, the disease affects 4–5% of people, with the number anticipated to rise to 5.4% by 2025 [3]. Research is now being done on medications that can continually control blood sugar levels. Diabetes is primarily managed with oral hypoglycaemic medications and insulin injections [4]. Injections of hypoglycaemic agents are used in Western medical

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treatment for diabetes (insulin, insulin analogs, etc.), the pharmacotherapy suggests that the biguanides, glinides, sulfonylureas and glycosidase inhibitors, thiazolidinedione used as hypoglycaemic medications in oral formulations [5, 6]. These medications have some adverse effects such as severe hypoglycaemia, weight gain, gastrointestinal discomfort, and nausea [7]. Various new medications, including DPP-4 (Dipeptidyl Peptidase) inhibitors, GLP-1 (glucagon-like peptide) analogues, and SGLT-2 (sodium glucose co transporter) inhibitors, have been developed and are available on the market [1]. With the long-term use of oral anti-diabetic agents in patients, the efficacy of all of these inevitably diminishes. As a result, there is an ongoing need to identify and develop novel anti-diabetic medications, particularly given the fact that diabetes has become a global epidemic [2].

Main text

Types of diabetes

The disease has two major types: Type 1 diabetes (T1DM) is an autoimmune disease characterized by insulin insufficiency, whereas Type 2 diabetes (T2D) is characterized by ineffective insulin action [8].

Type 1 diabetes is defined as insulin-dependent diabetes and have characterized by low insulin secretion in the body due to the degeneration of beta cells in the pancreas [9]. Type 1 diabetes patients are always at risk for developing ketoacidosis, the insulin injections required for the maintenance of blood glucose levels under control. The disease is more common in children and teenagers [10].

Causes

1. Genetic factors
2. Environmental factors

Type 2 Diabetes is noninsulin-dependent diabetes due to ineffective insulin action with hyperglycaemia [11–13]. Many of diabetic patients have NIDDM (Non-insulin dependent diabetes mellitus), also known as Type 2 diabetes mellitus (T2DM), which is a lethal disease with severe disability rates.

Causes

1. Obesity
2. Over weight
3. Insulin resistance

Medicinal plants

Medicinal plants and herbs are excellent sources of alternative and complementary medicine and they have a significant function in disease treatment [14]. The entire medicinal plants specific portions can be used for research purposes in this way.

The plant-derived chemicals are preferred because they were created in a biotic environment and are assumed to have been subjected to evolutionary selection as a result; they communicate better with proteins and are to be prominent medications. Long-term human use of plant extracts provides reliable evidence for diabetes treatment in traditional medicine system. The plant extract contains a variety of phytochemicals that contain many primary and secondary metabolites that can enhance the efficacy of plant-related drugs in treating disease [6].

According to WHO (World Health Organization), to satisfy the primary healthcare needs more the 80% of the world population used natural herbs as a medication furthermore, more than half of all new medications researched and licensed for sale are derived directly from modified medicinal plant products or their active ingredients [15].

Herbal medicine is low in cost, easily available, high effectiveness, and has low side effects due to this feature it is used and prescribed all over the world. As a result, it has been utilized in traditional Indian medicine to treat a variety of ailments and disorders.

Our aim in this review work is to establish the knowledge of plants' bioactive compounds that have the potential to manage diabetes with a full mechanistic approach that can help in future research with regard to efficacy in disease and minimization of toxicities with current allopathic-based medication.

Material and methods

In this review, we systematically reviewed more than two hundred research papers from the Cochrane database. The key words for the search were diabetes, bioactive compounds, plants, and animal models. The exhaustive review was done using the latest information from 2021 and past year data (i.e., 1991), which is relevant to the review work.

Approximately 93 papers were excluded from the review work, of which 57 papers did not have sufficient data related to our work and others did not illustrate significant work.

In the brief review work shown in Table 1, these plants were selected on the basis of their use in the treatment of diabetes in the Indian traditional system of medicine.

Discussion

The various primary and secondary metabolites of the plant are responsible for their activity in diabetes. We conceptualized the available data through a brief literature review. The findings of this work are as follows.

Table 1 Plants potential for anti-diabetic activity

S. no	Plant name	Common name	Part used	Bioactive compound	Animal model	References
1	*Berleria cristata* L.	Kala Bansa	Seeds	a-Tocopherol, pCoumaric acid, Barlerin and Luteolin etc	Alloxan induced diabetic rat	[16]
2	*Melia azadirachta*	Chinaberry	Leaf	Terpenoids, flavonoids, steroids, acids, anthraquinones, saponins, alkaloids, tannins and limonoids	Alloxan induced diabetic rat	[17, 18]
4	*Emblica officinalis* Gaertn.	Indian gooseberry	Leaves	Tannins, amlaic acid, astragalin, ellagic acid, gallo-tannin, kaempferol, kaempferol-3-*O*-glucoside, phyllantidine, phyllantine and rutin	Streptozotocin-induced type-2 diabetes mellitus (T2DM) rats	[19]
5	*Padina boergesenii*	Water primose	Whole algae	Pigments, fucoidans, phycocolloids and phlorotannins	STZ induced rat model	[20]
6	*Pterocarpus marsupium* Roxb.	Indian kino or Bijasar	Bark	(—)-epicatechin, phenolic constituents such as marsupin, protosupin and pterostilbene	Alloxan monohydrate induced male albino wistar rat	[21, 22]
7	*Momordica charantia* L.	Bitter melons	Fresh or dried fruits	Cucurbitane, charantin, Momordicine II	In STZ-induced T2DM mice	[23]
8	*Trigonella foenum-graecum* L.	Fenugreek	Fruits	Polyphenols, steroids, lipids, alkaloids, saponins, flavonoids, hydrocarbons, carbohydrates, galactomannanfiber, and amino acids (4-hydroxyisoleucine)	Streptozocin-induced diabetic rats	[24]
9	*Hibiscus rosasinensis*	China rose	Flower	Tannins, anthraquinones, quinines, phenols, flavanoides, alkaloids, terpenoids, saponins, cardiac glycosides, protein, free amino acids, carbohydrates, reducing sugars, mucilage, essential oils and steroids	Non-obesediabetic (NOD) mouse	[25]
10	*Withania somnifera* (L.)	Ashwagandha	Root and leaves	Withanolides: withaferin A, withanone, withanolide A, withanolide B, and withanoside IV terpenoids, alkaloids and phenylpropanoids	Streptozotocin induced DM	[26, 27]
11	*Ocimum tenufolium*	Tulsi	Fresh or dried leaves	Eugenol, methyleugenol, and _- and _-caryophyllene	Alloxaninduced diabetic rats	[28]
12	*Tinospora cordifolia*	Guduchi	Stem, whole plant	Polyphenol, alkaloid and terpenes	Ehrlich ascites tumor cell model system, alloxan treated albino rats	[29, 30]
13	*Gymnema sylvestre*	Gurmar	Leaves	Tannin, quinones,flavonoids, and phenols, saponins (Oleanane and dammarane)	STZ induced male rat model	[31, 32]
14	*Enicostemma littorale*	Chota-kirayata	Whole plant	Alkaloids like enicoflavin and gentiocrucine, catechins, saponins, two sterols, triterpinoids, phenolic acid, flavonoids, xanthones and volatile oil	Alloxan-Induced Diabetic Rats	[33, 34]
15	*Cinnamomum tamala*	Indian Cassia	Whole plant	Saponins, phytosterols, fatty acids, carbohydrates, monoterpene, sesquiterpene, geraniolandlinolol, cinnamicaldehyde, eugenol	STZ induced male wistar rat model	[34]
16	*Allium cepa* L.	Onion	Freshor dried bulb	Quercetin, Rutin, L-Cysteinesulfoxide, Allyl propyl disulphide	Alloxan induced diabetic rats	[35]

Table 1 (continued)

S. no	Plant name	Common name	Part used	Bioactive compound	Animal model	References
17	*Azadirachta indica* A. Juss	Neem	Dried leaves	Azadirachtins (e.g., azadirachtolide, azadiradione, gedunin and meliacinolin)	STZ induced Mice model	[36]
18	*Anacardium occidentale* Linn.	Cashew	Leaves	Phenolic, triterpenoids, carbohydrate, xanthoprotein and flavonoids	STZ induced rat model	[37, 38]
19	*Brassica oleracea*	Broccoli	Sprouts	Antioxidant, vitamins terpenoids, flavonoids, phenolic compound(kaempferol, quercetin), tannins, saponins	Streptozotocin induced diabetic rats	[39]
20	*Eugenia jambolana*	Indian blackberry or Jamun	Seed	Gallic acid and polyphenolic compounds	Streptozotocin-induced diabetic male albino rat	[40]
21	*Cassia auriculata* Linn.	Tanner's Cassia	Flowers	Flavonoids, proanthocyanidins and β-sitosterol8-9	Alloxan Diabetic Rats	[41]
22	*Curcuma longa*	Turmeric	Rhizomes	Curcumin, diferuloylmethane, curcuminoids, alkaloids, cardiac glycoside and resins, Carbohydrate, terpenes and steroid, Flavonoids, tannins, saponins, balsams and phenols	Alloxan monohydrate induced diabetic rats	[42, 43]
23	*Thunbergia laurifolia* Linn.	Blue trumpet vine	Flower, leaves	Grandifloric acid, benzyl β-glucopyranoside, benzyl β-(2′-*O*-β-glucopyranosyl)- glucopyranoside, 6-C-glucopyranosyl apigenin, 6,8-di-Cglucopyranosyl apigenin, (E)-2-hexenyl-β-glucopyranoside, and hexanol-β-glucopyranoside	Alloxan-induced diabetic rats	[44]
24	*Acacia arabica*	Babul	Bark	Polyphenols, tannins and flavonoids (for example, quercetin)	streptozotocin-induced diabetic albino rat	[45]
25	*Aegle marmelos* (L.)	Bael	Leaves	Carotenoids, phenolic, alkaloids, pectins, tannins, coumarins, flavonoids and terpenoids	Streptozotocin-induced diabetic Rats (Long Evan)	[46, 47]
26	*Agrimony eupatoria*	Common Agrimony	Leaves	TANNINS, volatile oil and coumarin, gum, phytosterol, polysaccharides,	STZ-diabetic mice	[48]
27	*Alliumsativum* L.	Garlic	Bulb	Flavonoid(quercetin), di (2-propenyl) disulphide and 2-propenyl propyl disulphide	Streptozotocin-induced diabetic wistar rats	[49]
28	*Aloe barbadensis*	Ghritkumari	Leaves	Aloe emodin, Aloin/Barbaloin	Streptozotocin (STZ)-induced diabetic rats	[50, 51]
29	*Benincasa hispida*	Ash gourd	Fruits	Volatile oils, flavonoids, glycosides, saccharides, proteins, carotenes, vitamins, minerals, ß-sitosterin and uronic acid	Streptozotocin-induced diabetic albino rat	[52, 53]
30	*Beta vulgaris* L.	Beet root	Root juice	Flavonoids, saponins, sterols and triterpenes	Alloxan monohydrate induced diabetes in albino rats	[54, 55]
31	*Caesalpinia bonducella* Roxb	Fever nut	Seeds	Furanoditerpenes, phytosterinin, β-sitosterol, flavonoids, bonducellin, aspartic acid, arginine, citrulline, β-carotene	Alloxan monohydrate induced diabetes in wistar rats	[56]

Table 1 (continued)

S. no	Plant name	Common name	Part used	Bioactive compound	Animal model	References
32	*Citrullus colocynthis*	Bitter apple or a bitter cucumber	Fruits	Flavonoids alkaloids, saponins, tannins and phenols	Streptozotocin (STZ)-induced diabetic rats	[57]
33	*Coccinia indica*	Ivy gourd	Leaves	Triterpenoids, alkaloids, steroids, carbohydrates, tannins, flavonoids, coumarins, phenols, resins and quinones	Glucocorticoid Induced Insulin Resistance in Wistar Albino rats	[58]
34	*Eucalyptus globulus*	Dried eucalyptus leaves	Leaves	Eucalyptol (cineol), rutin, terpineol, sesquiterpene, alcohols, aliphatic aldehydes, isoamyl alcohol, ethanol, terpenes and tannins	Streptozotocin (STZ)-induced diabetic mice	[59]
35	*Ficus bengalensi*	Bargad or Banyan tree	Fresh aerial roots	f leucocyanidin 3-O-beta-dgalactosyl cellobioside and a dimethoxy ether of leucopelargonidin-3-O-alpha-L-rhamnoside	Streptozotocin (STZ)-induced diabetic Female albino Wistar rat	[60]
34	*Hibiscus rosasinensis*	China-rose, Gurhal	Fresh flowers	Tannins, anthraquinones, quinines, phenols, flavanoides, alkaloids, terpenoids, saponins, cardiac glycosides, protein, free amino acids, carbohydrates, reducing sugars, mucilage, essential oils and steroids	Alloxan monohydrate induced diabetes in wistar rats	[61, 62]
35	*Ipomoea batatas*	Sweet potatoes	Leaves	Polyphenol, vitamins, Anthocyanins, saponin	Alloxan induced diabetic rats	[63, 64]
36	*Jatropha curcas*	Purging nut	Leaves	Alkaloids, tannin, flavonoids, saponins, and triterpenoids	Alloxan-induced diabetic rats	[65]
37	*Mangifera indica* L.	Mango	Leaves	Rhamnetin, catechin, epicatechin, gallic acid derivatives, mangiferin and iriflophenone 3-C-β-D-glucoside, flavonoids and polyphenols	Swiss albino mice	[66]
39	*Morus alba* L.	Mulberry	Branch	Terpenoids, alkaloids, flavonoids (including chalcones and anthocyanins), phenolic acids, stilbenoids	Streptozotocin (STZ)-induced diabetic mice	[67, 68]
40	*Mucuna pruriens* L.	Velvet beans or Cowitch	Seeds	Glutathione, gallic acid, and beta-sitosterol, palmitic, stearic, oleic, and linoleic acids., alkaloids(3-methoxy-1,1-dimethyl-6,7-dihydroxy-1,2,3.4-tetrahydroquinoline and 3-methoxy-1, 1-dimethyl-7,8-dihydroxy-1,2,3.4-tetrahydroquinoline)	Alloxan-induced diabetic rats	[69, 70]
41	*Punica granatum* L.	Pomegranate	Fruits	Punicalagin anthocyanin, phenolic acids, non-phenolic acids, tannins, and glutenins (4)	Alloxan induced diabetic rats	[71]
42	*Vincarosea*	Madagascar periwinkle,	Whole plant	Alkaloids (vinacristine and vinblastine) and tannins	Alloxan induced diabetic rats	[72]
43	*Actinidia deliciosa*	Kiwi	Fruit	Triterpenoids, saponins, and phenolic compounds (flavonoids, polyphenols, anthraquinones, and coumarins	Alloxan induced diabetic rats	[73]

Table 1 (continued)

S. no	Plant name	Common name	Part used	Bioactive compound	Animal model	References
44	*Annona squamosa* L.	Custard apple	Leaves	Steroids, alkaloids, saponins, terpenes, tannins, phenolic substances, carbohydrates, volatile oil and mucilage	Streptozotocin (STZ)-induced diabetic Wistar rats	[74]
45	*Camellia sinensis*	Green tea	Leaves	Alkaloid, flavonoids, tannin	Alloxan induced diabetic rats	[75]
46	*Boerhavia erecta* L.	Tar vine	Whole plant	Flavonoids, tannins and glycosides	Streptozotocin-induced diabetic Wistar rats	[76]
47	*Agaricus bisporus*	Button mushroom	Fruit	Proteins, amino acids, polyphenols, polysaccharides, ergothionins and vitamins	Alloxan-Induced Diabetic Rats	[77]
48	*Semecarpus anacardium* (L.)	Marking nut tree	Tem bark	Phenolic compounds as carbolic acid derivatives, bhilawanols, sterols, glycosides, bhilawanols, anacardic acid, anacardoside and flavonoids	Alloxan induced diabetic Long Evans rats	[78]
49	*Spondias mombin*	Hog plum	Leaves	Phenolics, sterols, triterpenes, saponins, essential oils, amino acids, and polysaccharides	Alloxan induced diabetic Wistar albino rats	[79, 80]
50	*Ruellia tuberosa* Linn	Fever root,	Whole plant	Triterpenoids and flavonoids (apigenin, luteolin, 3, 5-diglucoside, apigenin 7-*O*-glucuronoide,)	Alloxan-Induced Diabetic Rabbits	[81]
51	*Sida rhombifolia*	Bala, Mahabala	Aerial part	Flavonoids, Alkaloid, flavonoids, tannin, glycosides, Phenols		[82]

Saponin

According to some researchers, the root and bark of *Berberis vulgaris* Linn. show a hypoglycaemic effect due to the presence of saponin which has a stimulating effect on remnant beta cells, along this it improves the lipid profile, so it is used in the diabetes treatment [83]. Fenugreeks also contain saponin which inhibits cholesterol absorption and reduce sugar level [84].

Tannin

Many studies indicate that black tea contains many active compounds out of which many are tannins which are 90% catechins that show anti-diabetic action by inhibiting intestinal glucose absorption [85, 86].

Grapes contain epicatechin as a major active compound, which prevents hyperglycaemia by inducing β cell regeneration [87].

Terpenes

Inhibition of α-glucosidase and α-amylase It is reported that a triterpenoid that is heptadienic acid withdrawn from the root of *Potentilla fulgens* inhibits the α-glucosidase enzyme and aids in the treatment of diabetes [88]. A research work reported on stem bark of *Fagara tessmannii* contain Pentacyclic triterpene acetates illustrates inhibition against α-glucosidase [89].

Insulin stimulated action of terpenes The rhizomes of *Costusspeciosus* contain costunolide and help in the management of diabetes by stimulating the restoration of beta cells and producing the insulin resemble action on the peripheral tissue [90].

Action on oxidative stress by terpene compounds Some authors reported that a triterpene known as lupeol found in mango has a significant action in the treatment of diabetes through ROS (Reactive oxygen Species) level and reduced oxidative stress which implicates the antioxidant potential in the liver of Swiss albino mice [91]. A few research works suggests that saffron contain an essential oil known as safranal, a monoterpene that protects diabetic rat against oxidative damage [92]. The reduced blood glucose level and improved antioxidant activity reported by some authors through administration of safranal intraperitoneally in the diabetic rat in a dose-dependent manner [93].

Anti-hyperglycaemic activity of terpene compounds An unsaturated triterpene presents in the root and bark of *Bumelia sartorum* isolated from its ethanolic extraction shows hypoglycaemic action by increased insulin production from β-cells [94]. A clinical trial on *Momordica charantia* reported anti-hyperglycemic activity [95].

Hypolipidemic activity of terpenes A triterpene called momordicoside, which is extracted from the bitter melon *Momordica charantia*, improved the fatty acid oxidation and glucose excretion in both types of mice i.e., insulin sensitive and insulin resistant mice during the OGTT [96]. Some authors reported hypo-lipidemic activity through Momordicoside which stimulates the GLUT4 translocation with increased activity of AMP-activated protein [97].

Terpenes as AR inhibitor Research work reported on rat lens implicated the inhibitory effect on AR (Aldose reductase) through friedelane type triterpene salasones A, B, and C and norfriedelane type triterpene, salaquinone A and acylated eudesmane type sesquiterpene, salasol A, which is extracted from *Salacia chinensis* and *Salviamiltiorrhiza* [98, 99].

Alkaloids

Inhibition of digestive enzymes Some researchers revealed that two digestive enzymes hydrolyse the dietary polysaccharides and increase the levels of blood glucose which is α-Amylase present in the pancreatic juice and saliva catalyzes the hydrolysis of α-1,4-glycosidic linkages of starch, glycogen, and various oligosaccharides and increase the blood glucose level and the second one is α-Glucosidase secreted by cells lining in the epithelial cells of the small intestine catalyzes the hydrolytic breakdown of oligosaccharides into absorbable monosaccharides and causes postprandial hyperglycaemia. Alkaloids inhibit these digestive enzymes and decrease the postprandial blood glucose level [100].

Inhibition of aldose reductase and protein tyrosine phosphatase-1B The compound which has both antioxidant and AR inhibitory activities piqued the interest of the scientific community for research to manage diabetes [101]. In hyperglycaemic conditions, AR increases the sorbitol and its metabolite accumulation in a cell leading to osmotic swelling, overproduction of reactive oxygen species, and cell dysfunction [102].

Effect on insulin secretion Various researchers have concluded that for the rise of insulin release and decrement of blood sugar concentration, inhibition of DPP-IV is required because diminishing DPP-IV enhances glucose tolerance because of latencies in the action of GLP-1 and GIP [103]. GLP-1 and GIP are two hormones that stimulate insulin release [104], decrease glucagon release, improve glucose digestion increased lipoprotein lipase activity and regulate fatty acid production and enhance β-cell proliferation and cell survival [105].

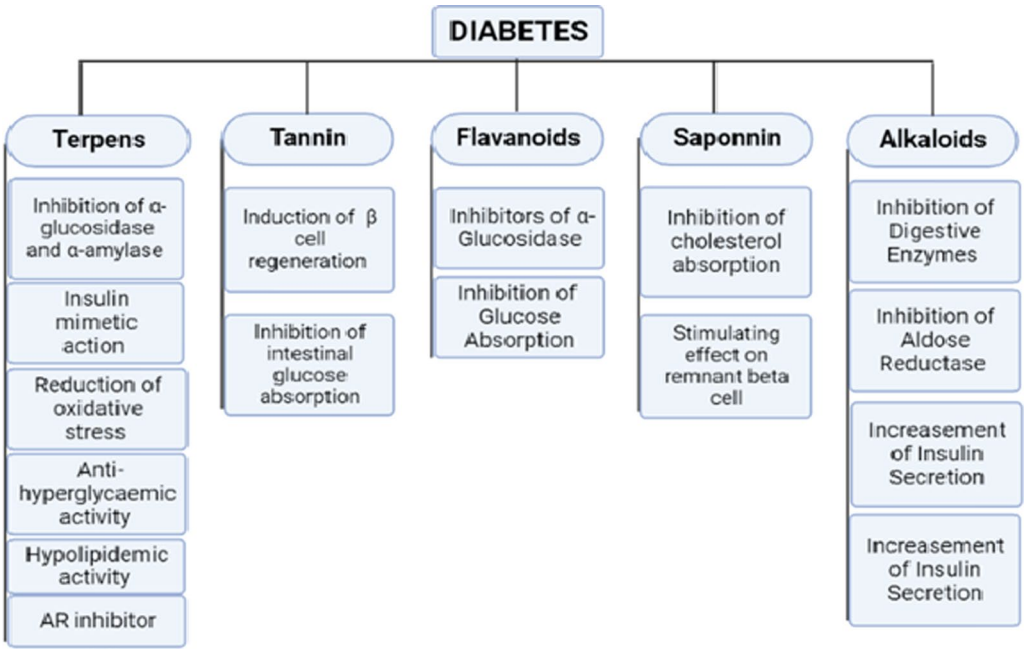

Fig. 1 Bioactive compounds potential for anti-diabetic activity with their mode of action

Enhancement of glucose uptake Vindolicine III an alkaloid isolated from the *Catharanthus roseus* (L.) is beneficial in the treatment of hyperglycaemia because it increases glucose absorption through translocation of glucose transporter 4 (GLUT-4) [106].

Flavonoids

Inhibition of α-glucosidase Flavonoid reduces the postprandial blood sugar concentration by inhibiting the α-Glucosidase enzyme, an enzyme present in the small intestine epithelium and involved in carbohydrate digestion, by delaying the conversion of complex carbohydrates to glucose by -glucosidase inhibition, glucose absorption in the small intestine is also delayed, ultimately lowering postprandial blood sugar levels [107].

Inhibiting glucose absorption Type II diabetes GLUT4 plays an important role in homeostasis through glucose uptake mechanism. Diabetes is managed by inhibiting glucose absorption and this can be achieved by inhibiting the GLUT4 translocation [108].

The mechanism of action can be seen in Fig. 1.

Conclusion

Our review work strongly suggests that plant which contains metabolites such as flavonoids, terpenes and alkaloids is having therapeutic value in the treatment of diabetes. The mechanism of action on alpha-glucosidase and alpha-amylase, hypolipidemic activity, and AR inhibitory action explains that these phyto-constituents can be utilized for future research on diabetes treatment. In our future research work, we will try to emphasize on these bioactive compounds for drug discovery process for diabetes treatment.

Abbreviations

DM: Diabetes mellitus; α-amylase: Alpha amylase; β-amylase: Beta amylase; STZ: Streptozotocin; DPP4: Dipeptidyl peptidase-4; GLP-1: Glucagon-like peptide 1; SGLT-2: Sodium glucose cotransporter-2; T1DM: Type 1 diabetes mellitus; T2DM: Type 2 diabetes mellitus; NIDDM: Non-insulin dependent diabetes mellitus; ROS: Reactive oxygen species; OGTT: Oral glucose tolerance test; GLUT4: Glucose transporter type 4; AMP: Adenosine monophosphate; AR: Aldose reductase; GIP: Gastric inhibitory polypeptide.

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Author contributions

In the present review, A analyzed the data related to disease and treatment approaches with Bioactive compounds and was the most important contribution in making the manuscript. RKP and LS performed the systematic evaluation of points related to results. SK elaborated on the conclusion. PS, MP and SJ contributed in terpene and alkaloids moa. All authors read and approved the final manuscript.

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Availability of data and materials

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Not applicable.

Consent for publication
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Competing interests
The authors declare that they have no competing interests.

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