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A CUMULATIVE REVIEW ON THERAPEUTICFLORAE USED TOTREAT DIABETES MELLITUS

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ABSTRACT: Diabetes Mellitus is a chronic ailment characterized by clinical manifestations like hyperglycaemia. The development of novel drugs is based on the understand ding of insulin resistance and oxidative damage leading to secondary complications of diabetes such as Retinopathy, Nephropathy etc. In the modern era, there are numerous allopathic drugs available for the treatment of the ailment. Herbs include a variety of chemical components that are responsible for their therapeutic effects, including polyphenols, saponins, terpenoids, alkaloids, sesquiterpenes, and flavonoids. Herbal remedies, which include traditional medicines, have the ability to treat a wide range of disorders. The use of herbs to treat a condition provides extra benefits by targeting the root cause of the disease. They are less expensive, more effective at lower dose frequencies and have less side effects when compared to allopathic medicines. This review includes a wide range of various phytoconstituents derived from different medicinal plants for the treatment of diabetes mellitus.

INTRODUCTION: Diabetes Mellitus is a chronic metabolic condition known as hyperglycaemia that is brought on by a rise in blood glucose levels. Blood sugar levels will be higher than they would be under normal circumstances. It is mostly caused by a drop in insulin production or activity in the body. When we ingest foods (carbohydrates, lipids, fats, and proteins), glucose enters our cells and gives us the energy we need for daily activities [1]. To provide energy, the blood transports glucose to every single cell. The hormone Insulin is created by pancreatic beta cells and is the final step in the glucose cycle.

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Higher blood glucose levels result from inadequate insulin production or improper body utilisation by the pancreas. Medical consequences brought on by the condition include damage to the eyes and nerves, neurological problems, heart problems, and impairments in metabolic function.

Diabetes causes an imbalance between insulin resistance and pancreatic insulin production [2]. 9.3% of people in the world today have diabetes. In the years after 2045, it will increase by up to 10.2%. Natural herbs are now crucial in the treatment of many diseases following the pandemic of COVID-19. When compared to allopathic medications, herbal remedies are more cost-effective, have fewer adverse effects, and require less frequent administration. In order to control diabetes, numerous herbs have been mentioned in various literature sources [3]. According to ADA, there are three forms of DM [4, 5, 6].

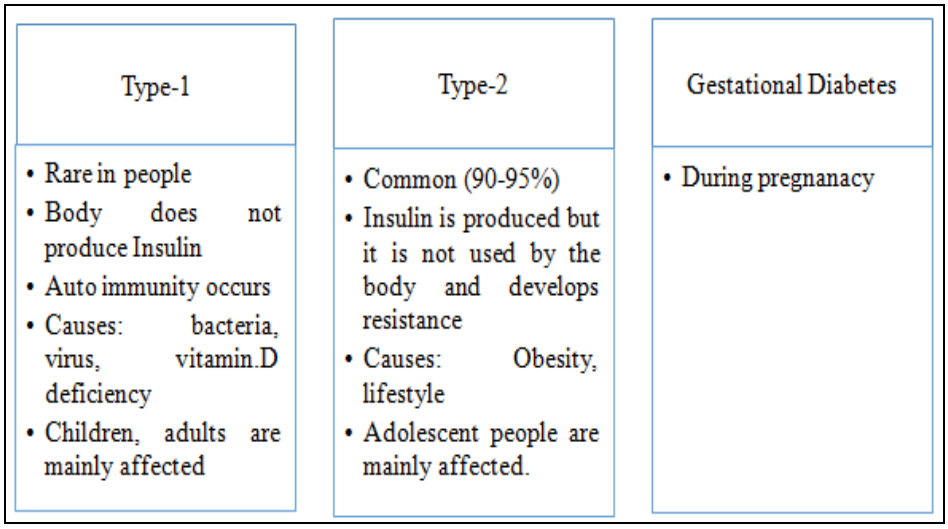

FIG 1: TYPES OF DM

Risk factors involved in Diabetes Mellitus:

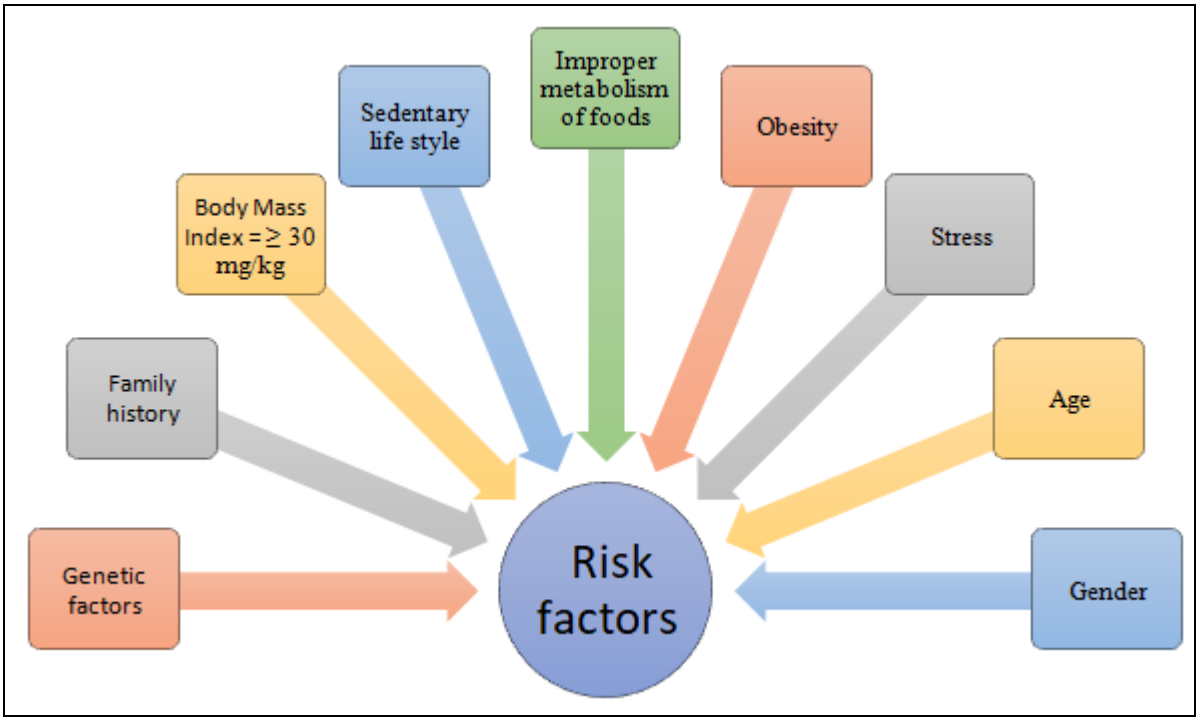

FIG 2: RISK FACTORS INVOLVED IN DM

DM is caused by various genetic, metabolic and environmental factors. White individuals living in the USA, the United Kingdom, and Japan are all significantly impacted. Imbalance in genes like GLUT2 (transportation of glucose into pancreas), GCGR (glucagon hormone), ABCC8 (releases insulin), and TCF7L2 (controls glucose release and synthesis) [7]. Familial history is another important element because it hereditarily transmits the disease to the healthy individuals. Age, gender, stress, high cholesterol levels, an unhealthy lifestyle, and obesity are other risks [8].

TABLE 1: MEDICINAL FLORAE USED INMANAGING DM

S. no.	Vernacular name	Botanical name	Plant part used	Active phytoconstituent	Major Findings	Reference
1	Custard apple	*Annona squamosa*	leaves	Proantho-cyanidin Rutin Squafosacin	Enhances homeostasis and glucose secretion. Additionally, the plant raises GLP-1 levels in the blood.	[9]

2	Bitter apple Fox melon Bitter - Water melon	*Citrullus colocynthis*	fruit seed	Cucurbitacin Elate ricin B	Potent novel insulin promoter to reduce hyperglycaemia by GLUT 4 translocation Reduces hyperglycaemia through glycogenolysis and lowering G-6-P levels	10 11
3	Alanda	*Ephedra foeminea*	Aerial parts	Limonene Kaempferol	The plant's aqueous extract possesses anti-radical properties.	12
4	Loquat	*Eriobotrya japonica*	leaf seed	Naringenin Procyanidin Rutin	Loquat leaf extract in aqueous form is rich in minerals and vitamins and is used to reduce insulin resistance and oxidative stress. The seed's ethanol extract exhibits glucose tolerance properties.	13 14
5	Jamun	*Eugenia jambolana*	seed	Peonidin Malvidin Petunidin Delphinidin	demonstrates HHK-1 gene-mediated hypoglycaemic inhibition and enhances liver, kidneyfunctioning. Utilised to treat both short-term and long-term conditions.	15,16
6	Danshen Gegen	*Salivia miltiorrhiza +Radix* *Pueraria lobata*	Whole plant	Puerarin Tanshinone II A	By lowering oxidative stress, inflammation, and promoting metabolism, the combination of these two herbs is used to treat DM	17
7	Behund Thohar	*Euphorbia nerifolia*	stem	Neriifolin Euphol Cycloartenol Neriifoliene	By enhancing the GLUT 4 transporter, a hydroalcoholic extract of the stem possesses insulin secreting action. Free radical scavenging activity by inhibiting α-amylase	18
8	Alfalfa	*Medicago sativa*	flower leaf	Stachydrine Myristic acid Arginine	The plant's aqueous extract may be able to stimulate the production of insulin from mesenchymal stem cells, which are similar to pancreatic beta cells.	19
9	Baikal skull cap	*Scutellaria coptis*	Whole plant	Baicalin Wogonoside Coptisine Berberine	Regulates intestinal flora and anti-inflammatory activity by interacting with TLR4	20
10	Purple heart	*Tradescantia pallida*	leaves	Spathulenol Caryophyllene oxide α-copaene β-caryophyllene	When compared to pure drug extract, Niosomal leaf extract has a stronger anti-diabetic impact, according to an *in-vitro* glycosylation experiment.	21
11	Stinging needle	*Urtica diocia*	leaves Whole plant	Vitamin B1 Vitamin K Xanthophylls Sistosterin	Reduced insulin resistance and improved lipid metabolism are the effects of leaf extract. Along with treating diabetes, the UD extract also lessens neurological side effects including memory loss	22 23
12	Fenu Greek	*Trigonella foenum-graecum*	seed	Diosgenin Coumarin	The functions of many organs, including the pancreas, liver, and kidneys, are demonstrated by seed extract. Both oral and iv administration lower blood glucose levels	24
13	safflower	*Carthamus tinctorius*	Seed oil	Carthamin Guanosine Cynaroside Dauccossterol	In individuals with metabolic disorders, seed oil extract was utilised to reduce insulin resistance	25

14	Hing	*Ferula assafoetida*	Oleo gum resin	(Z)-β-ocimene β-pinene	Encouraging the development of β-cells in the pancreas, lowering oxidative stress and insulin resistance. Also used to treat chronic DM	26
15	Bael Indian quince	*Aegle marmelos correa*	Stem bark	Aegeline Imperatorin Citral Lupeol	The plant's stem, bark contains UFG and lowers blood sugar and oxidative stress. In the long run, UBD is a powerful chemical to treat diabetes	27
16	Coriander	*Coriandrum sativum*	seed	Linalool Limonene Γ-terpinene α-pinene	Hyperglycaemia can be treated using seed extract, which also functions as an insulin secretor	28
17	Mulberry	*Morus alba*	fruit	Caffeic acid Gallic acid Vanillic acid	In an RCT, mulberry demonstrates its capacity to regulate blood sugar and insulin levels before dawn	29
18	Okra	*Abelmoschus esculentus*	Edible pod	Myricetin 3-O-gentiobioside	Fibres present in okra are responsible for slow absorption of glucose in GIT. It is not advised to use this vegetable and allopathic drugs at the same time	30
19	Gum Arabic tree	*Acacia nilotica*	Pods Leaf Bark	Ellagic acid Kaempferol Quercetin	The effects of diabetes are lessened by the leaf extract	31
20	Giloy	*Tinospora sinensis*	Stem	Berberine Caffeic acid Myricetin Ferulic acid	The stem extract is protective against diabetes by reducing chemical mediators and free radicals	32
21	Red onion	*Allium cepa*	Whole plant	Allicin Fisetin Quercetin Alliinase	It is utilised as a food supplement to lower blood sugar levels	33
22	Barberry	*Berberies vulgaris*	Root Bark	Berberine Oxyacanthine Berbamine Palmatine	Reduced triglyceride and cholesterol levels, controls body weight	34
23	Red silk cotton tree	*Bombax ceiba*	flower	Rutin Resveratrol Baicalein Hesperetin	Flower extract aids in removing free radicals from the body. For the treatment, receptors and DNA are targeted	35
24	Pirampu	*Calamus rotang*	leaves	α-asarone β-asarone Acoradin Galangin Eugenol	HbA1C, LDL, VLDL, and blood sugar levels are all reduced by ethanol leaf extract	36
25	Peri winkle	*Catharanthus roseus*	Leaves	Vinblastine Vincristine Ajmalicine Catharanthine Vindoline	Through the GLUT 2 and 4 genes, the leaf juice extract has an effect on insulin secretion similar to that of the pancreas.	37
26	Sweet lemon	*Citrus limetta*	Fruit peel	Hesperidin Naringin Limonene Γ-terpinene	Reduces oxidative stress, demonstrating anti-diabetic effects	38
27	Yam	*Dioscorea alata*	Tuber	Rosmarinic acid	Low GI. It functions by a number of mechanisms, including reducing hyperglycaemia, inflammation, and mitochondrial dysfunction	39
28	Amla	*Emblica*	Fruit	Rutin	Amla chelates arsenic and reduces	40

		officinalis		Quercetin Catechol Gallic acid Ellagic acid	ROS and cytokines	
29	Fig tree	*Ficus glomerata*	leaf	Glauanol Sitosterol Tiglic acid	Restores uric acid, creatinine, cholesterol levels and also hyperalgesia	[41]
30	Coffee plum	*Flacourtia jangomas*	Leaves stem	Limolin Jangomolide	Enhances a number of chemical characteristics	[42]
31	Garuga	*Garuga pinnata*	bark	Garuganin	Haemoglobin, blood glucose, cholesterol, and triglycerides are all reduced by extract	[43]
32	Bruhati	*Solanum indicum*	fruit	Solasodine Solasonine Solamargine	Demonstrates glucose tolerance and acts as an antioxidant, anti-inflammatory, and anti-hyperglycaemic	[44]
33	Soya bean	*Glycine max*	Leaf	Genistein Glycitin	Unsaturated fatty acids present in soya promotes blood glucose levels and also regulates Insulin resistance	[45]
34	Indian turnsole	*Heliotropium indicum*	Whole plant	Indicine Echinitine Supinene	Improves blood glucose levels in the circulation	[46]
35	Shoe flower/ Chinese hibiscus	*Hibiscus rosasinensis*	flower	Orientin Quercetin β-sitosterol	Used to treat acute and subacute phases of hyperglycemia	[47]
36	Cogon grass	*Imperata cylindrical*	rhizome	Arundoin Cylindrin Simiarenol	Reduces the amount of LDL, cholesterol, and related adverse effects	[48]
37	Sweet potato	*Ipomoea batatas*	peel	Citrusinine Chlorogenic acid	The sweet potato's peel includes a number of active constituents that are thought to have anti-diabetic properties	[49]
38	Physic nut	*Jatropha curcas*	root	Γ-cadinene α-epicadinol Pulegone	Improves parameters such as RBC, WBC, PCV, lymphocytes, neutrophils	[50]
39	Miracle leaf	*Kalanchoe pinnata*	leaves	Bryophillin A	In the early stages of the condition, it is used as an anti-diabetic	[51]
40	Henna	*Lawsonia inermis*	leaf	Lawsone	The plant contains beneficial components that can be used to treat diabetes, such as polyphenols	[52]
41	Mango	*Mangifera indica*	leaves	Mangiferin β-carotene Campesterol	The leaf's phenolic chemicals have an anti-hyperglycaemic action	[53]
42	Banana	*Musa paradisiaca*	Leaves Fruit peel	Phytol Vitamin.E B-sitosterol Stigmasterol Hexa-decenoic acid	lowers IL-6 and TNF-α levels. Increases PPAR-ϒ and GLUT-4 levels	[54]
43	Black cumin	*Nigella sativa*	Seed oil	Nigellicimine Allo-oceminol	Shows hypoglycaemic effect with a daily intake of 1.5–3 ml of seed oil	[55]
44	Creeping wood sorell	*Oxalis corniculata*	leaves	Isovitexine	The disease is treated by increasing the extract's dose and exposure	[56]
45	Piyasal	*Pterocarpus marsupium*	Heart wood	Pterostilbene Epicatechin Pterosupin	lowers the levels of the inflammatory mediators- TNF-α and IL-6	[57]
46	Tulsi	*Ocimum sanctum*	leaves	Eugenol β-bisabolen Elemene Estragole Borneol	It reduces blood glucose levels when given at a dose of 2gm/kg. Additionally, leaves have the ability to scavenge radicals (superoxide, hydroxyl)	[58]

47	Cardamom	*Elettaria cardamomum*	Whole spice	1,8-cineole α-terpinyl acetate Sabinene β-linalool	Cardamom supplementation in T2DM patients reduces oxidative stress and hyperglycemia.	59
48	Gurmar/ Podaparthi	*Gymnema sylvestre*	leaves	Gymnemic acids α, β - chlorophylls	Stimulates the secretion of insulin from the pancreas. preventing the stomach from absorbing glucose	60
49	Ginseng	*Panax ginseng*	roots	Ginsenoside Dammarane	According to research conducted in vitro and in vivo, the ginsenosides found in plant roots have anti-diabetic properties	61
50	Bhuinamla	*Phyllanthus simplex*	Whole plant	Vanillin β-dauccossterol Rutin	Since it lowers oxidative stress, it has potential for reducing secondary complications of DM	62
51	Mountain knot grass	*Aerva lanata*	leaves	Ervine Aervoside Kaempferol Quercetin	As an anti-diabetic drug, the phenolic component of leaves inhibits the actions of α-glucosidase and α-amylase.	63
52	Garden sage	*Salvia officinalis*	leaves	Thujone Eucalyptol Caryophyllene	Used as a dietary additive to safeguard pancreatic β-cells	64
53	Common Chick weed	*Stellaria media*	Whole herb	β-carotene Genistein Coumarin	The herbal tea derived from the plant is thought to function as an anti-diabetic drug via the STAT-3 pathway	65
54	Tamarind	*Tamarindus indica*	Fruit pulp	β-amyrin Compesterol β-sitosterol	It has good inhibitory activity against α-amylase & α-glucosidase and also regulates the negative consequences of diabetes.	66
55	Arjun tree	*Terminalia arjuna*	Stem bark	Arjunic acid Arjungenin Luteolin Pellargonidin	lowers the amounts of the enzymes needed to absorb glucose, such as hexokinase, G-6-P, and F-6-P	67
56	Black gram	*Vinga mungo*	seeds	Carbohydrate Proteins Minerals Vitamins	Regulates the activity of the antioxidant enzymes SOD, CAT, and GPx	68
57	Aswagnadha	*Withania somnifera*	Root leaf	Withanolide Withaferin A Viscosalactone B	Maintains the levels of substances including lipids, ASP, ALT, G-6-P	69
58	Ginger	*Zingiber officinale*	rhizome	Gingerol Zingerone Shogaol Citral	Ginger juice improves metabolism and lowers triglyceride and cholesterol levels	70
59	Indian Sundarban mangrove	*Rhizospora mucronata*	leaves	Rhizophorin – A Phomo-xanthone Lupeol Coumarin B-sitosterol	Improves the body's metabolism to treat diabetic individuals	71
60	Devil's cotton	*Abroma augusta*	leaves	A bromine Abromasterol Digitonide	The extract is employed as a preventive diabetic medication	72

Based on the condition, the following are some of the ways it works as an anti-diabetic agent:

- Insulin secretors and releasers.
- Insulin mimetic substances.
- Enhances metabolism.
- Blocks the action of the enzymessuch as α-glucosidase and α-amylase.

- Lowers the levels of chemical indicators including cholesterol, triglycerides, AST, ALT, ACP.
- Pancreatic stimulators for the release of insulin.
- Supplementation of kitchen spices in case of emergency purpose.
- Radical scavenging activity.
- Lowers the levels of TNF-α, IL-6 (anti-inflammatory).
- Decreases the absorption of glucose from pancreas.
- Enhances serum parameters such as RBC, WBC, lymphocytes, neutrophils.
- Low glucose index to act as an anti-hyperglycaemic.

Future Prospects for Diabetes Mellitus Treatment: Traditional medical practices including Ayurveda, Homoeopathy, Siddha, and Unani offer a wide range of florae for treating various ailments around the world. Plants have gained significant relevance since Covid-19 and people are increasingly turning to natural remedies for positive effects. The therapeutic efficacy of plants is attributed to the presence of a variety of active phytoconstituents, including alkaloids, saponins, flavonoids, polyphenols, triterpenes, and sesquiterpenes. We discovered the future targets for the therapy of diabetes, which is to improve insulin resistance, by studying all the mechanisms, applications, and pathophysiology of the illness. As a result, drugs derived from either chemicals or plants ought to be able to lessen the resistance to insulin. Insilco studies on various anti-diabetic phytoconstituents are in progress.

CONCLUSION: In inference, diabetes is the most prevalent illness in the modern world. Various applications of medicinal plants for the treatment of diabetes are explained in this cumulative review.

CONFLICT OF INTEREST: No Conflict of interest

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