Therapeutic Potential of Ayurvedic Medicine in Diabetes: Efficacy Mechanisms and Molecular Insights

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Abstract

Diabetes mellitus is a global health challenge and chronic metabolic disorder that possess aserious health issue. Ayurvedic medicine with its longstanding tradition of holistic healing presents a promising complementary strategy for the management of diabetes. Ayurvedic herbs like *Gymnema sylvestre*, *Momordica charantia*, and *Pterocarpus* marsupium have the ability to manage diabetes. They execute this by upregulating the ability of body to produce insulin and help to control sugar levels in blood. Integration of Ayurvedic medicine with contemporary diabetes research to enhance the understanding and application of traditional therapies with modern therapeutic advancements. Even with the optimistic evidences, the necessity of well-designed randomized controlled trials remains to increase the evidence foundation and establish a comprehensive clinical protocol for incorporating ayurvedic methods in diabetes care. This chapter focuses on the efficiency of ayurvedic medicine and its mechanism of action with molecular target in treating diabetes. The aim of this chapter is to provide comprehensive analysis about patient focused and holistic approach to increase glycemic stability and enhance general health outcomes.

Keywords: Diabetes; Ayurvedic medicines; Therapuetic potential; Integration

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Introduction

Diabetes mellitus is referred as a metabolic disorder that is characterized by elevated blood glucose level. This ailment may develop either due to the deficiency in secretion of insulin hormone along with the damage in pancreatic β-cells. Meanwhile, when this blood containing high glucose content flows through different body organs it can cause micro and macrovascular complications that lead to significant damage to target organs and reduce life expectancy (Khursheed et al., 2019). The global prevalence of diabetes in 2021 was reported by International Diabetes Federation (IDF) that was about 536.6 million affected people between age of 20-79 years that will increase to 783.2 million people by the end of 2045 (Sun et al., 2022). On the basis of pathogenesis, etiology as well as clinical evaluation, diabetes can be classified into four distinct categories comprising: type-1 diabetes (deficiency of insulin), type-2 diabetes (insulin resistance), gestational diabetes (glucose intolerance) and diabetes associated with other certain disorders and pathogenesis e.g., neonatal diabetes (Banday et al., 2020).

However, management of this disease is a multifaceted procedure. Today, there are different measures that govern normal blood glucose level such as to acquire better quality of life, appropriate food intake and daily exercise that could decrease 58% disease risk within 3 years (Khursheed et al., 2019). Likewise, pharmacological handlings include intake of certain anti-glycemic drugs namely thiazolidinediones and sulphonylureas to treat type-2 diabetes as well as insulin therapy in which synthetic insulin is injected in type-1 diabetes patients. Although, various adverse effects are linked with pharmacological management, as oral drugs can cause migraine, vomiting, dysentery and many more side effects, similarly procurement through synthetic insulin always remains a global issue to manage at affordable cost. Thus, ayurvedic (herbal) medicines provide a better option rather than synthetic medicines with minimized side effects for the control of diabetes (Verma et al., 2018).

Some historical perspectives demonstrate that several medicinal plants were described in Vedic literature. Ayurveda is considered as a holistic science which involves natural healing processes through herbal medicines and meditation. The anti-diabetic properties of ayurvedic medicines have been proved effective in regulating the blood glucose level and to upgrade the life quality (Gill et al., 2022). However, acceptability and perceive response of ayurvedic medicines is most common among rural, older and poor people due to their health benefits and their association with culture. Thus, the majority of type-2 diabetes patients prefer these medicines instead of western medicines because of number of side effects allied with them. Furthermore, it is postulated that a variety of these medicines act via pancreatic as well as extra-pancreatic outcomes (Chattopadhyay et al., 2022). Although, some anti-diabetic herbal medicines may pose adverse effects such as ketosis and hypoglycemia, therefore, their protection assessments are most important during ayurvedic intervention trial and it is necessary to make sure their wise use for sustainability of health (Suvarna et al., 2021).

However, various approaches still investigating adverse effects of diabetes and its secondary complications with the help of technological advancement and discovery of novel anti-diabetic plant-based drugs to develop target medicines. This trans- disciplinary framework between synthetic and ayurvedic medicines could be a reversal policy for global healthcare against diabetes (Thottapillil et al., 2021). This chapter aims to explore the therapeutic potential of Ayurvedic medicine in diabetes management, emphasizing its efficacy, underlying mechanisms, and molecular sites of action, and to integrate traditional practices with modern medical advancements.

2. Herbal Constituents of Ayurvedic Medicine and their Mechanism of Action in Diabetes Management

2.1 Key Herbs and their Phytochemical Constituents

The World Health Organization (WHO) has enlisted 21,000 medicinal plants globally and among them, more than 400 plants are used for the procurement of diabetes. Despite a great variety of medicinal plants are available for diabetic purpose, inadequate numbers of these plants are subjected to medical and scientific assessment to evaluate their efficacy (Kumar et al., 2021). However, plants have variety of anti-diabetic phytochemical constituents; these compounds are extracted from different parts of plants (fruit, flower, stem, root, leaf) and include flavonoids, alkaloids, glycosides, peptidoglycans, anthranoids, saponins, carboxylic derivatives and so on (Bharti et al., 2018). Here some medicinal plants with their phytochemical constituents and anti-diabetic properties are following in table:

Plant	Phytochemical compounds	Anti-diabetic properties	Reference
Bitter melon *Momordica charantia*	Steroids, momorcosoids, alkaloids, phenolic compounds	Protect β-cells Inhibit glucose absorption in intestine Act as antioxidant	Tran et al., 2020
Onion *Allium cepa*	Thiosulfinates, flavonoids, allicin, quercetin, diallyl disulfide, methyl sulfinyl alanine	Stimulate insulin production and pancreatic secretion Regulate glucose absorption Effective use of insulin	Tran et al., 2020
Neem *Azadirachta indica*	Qurecetin, myricetin, kaemferol, rutin	Anti-inflammatory and antioxidant properties Protect β-cells Improve sensitivity of insulin	Patil et al., 2022
Jamun *Eugenia jambolana*	Tannis, terpenoids, alkoloids, Jamboline, elolagic acid, Glucoside	Control excessive production of glucose Antioxidant and anti-inflammatory properties	Azeem et al., 2023
Ginseng *Panax ginseng*	Polysaccharides, ginsenosides, peptides and polyacetylenic alcohols	Increase insulin sensitivity by decreasing insulin resistance	Guo et al., 2021
Tumeric *Curcuma longa*	Berberine	Block α-glucosidase and reduce the glucose transport via intestinal epithelium	Behl et al., 2022

2.2 Mechanism of Action of Phytochemical Compounds in Regulating Hyperglycemia

Phytochemical constituents of various medicinal plants exert their ameliorative effect in modulating blood glucose level by various mechanisms and pathways such as by increasing insulin sensitivity and secretion, by regulating uptake and metabolism of glucose as well as with their anti-oxidative properties (Prabhakar & Doble, 2011). The elevated level of ROS and oxidative stress (OS) has been noticed in diabetes that can cause various other complications. Therefore, in diabetes management it's also important to averse the level of ROS and OS. So, plant-based compounds are considered potentially useful in diabetes (Samarakoon et al., 2020). Different organs play a role in glucose metabolism to prevent hyperglycemic conditions. The role of pancreas, muscles, liver and intestine in glucose metabolism is shown in figure 1.

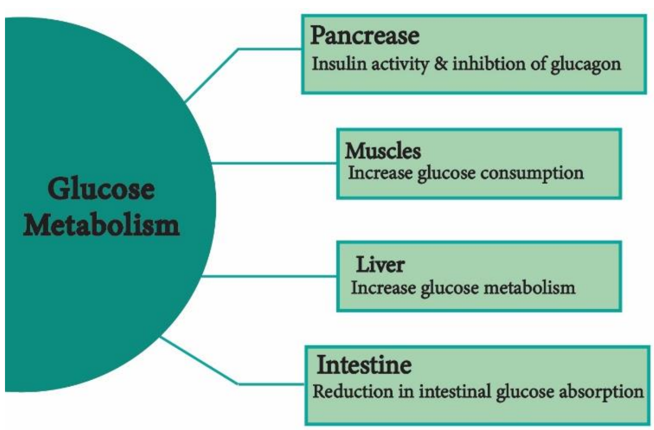

Fig. 1: The mechanism of glucose metabolism

Li et al. (2020) describe that functional irregularities in skeletal muscle have been linked with insulin resistance in diabetes. Adipose tissue and skeletal muscles have high level of Glucose transporter isoform 4 (GLUT-4). Insulin encourages translocation of intracellular GLUT-4 through AMPK pathway to the cytoplasmic membrane which increases glucose absorption in skeletal muscle. Primarily, phytochemical components of Ayurvedic medicine bind with GLUT-4 and increase their expression and translocation to plasma membrane and proved an effective therapy for medication of hyperglycemia.

Feedback inhibition of hyperglycemia can be executed by lowering the glucose absorption via inhibiting the carbohydrate-hydrolyzing enzymes including α-glucosidase and α-amylase. The α-glucosidase is observed at brush border of enterocytes while α-amylase is present in pancreatic juice and saliva (Khadayat et al., 2020). Both these enzymes quickly hydrolyze glucose and starch in diet that enter into blood and blood glucose level rise. Phytochemical constituent of ayurvedic medicines such as *charantia* methanolic has ability to slow down digestion process through inhibition of these enzymes and significantly improve hyperglycemia and insulin (Dirir et al., 2022). Likewise, elevated level of gluconeogenesis in liver leads to high blood glucose level in both type-1 and type-2 diabetes which need a normal gluconeogenic rate to prevent from diabetic pathophysiology. Therefore, to preserve liver glycogen and to decrease gluconeogenesis various phytochemical compounds have been proved beneficial by inhibiting the enzymes that involve in production of glucose from pyruvate. Although, along with decreasing gluconeogenesis these compounds also increase insulin sensitivity in type-2 diabetic patients by activating insulin receptors in hepatocytes which act as anti-glycemic effect in diabetes patients (Mobasheri et al., 2023).

3. Molecular Targets of Ayurvedic Medicine in Diabetes

Numerous genomic, proteomic, and metabolomic methods are available to estimate or elucidate the mode of action of bioactive compounds (Cheng et al., 2010). The molecular docking method is effective for representing the interaction between a small molecule and target proteins at the atomic level, which helps to clarify the behavior of small molecules at target protein binding sites and essential biochemical processes (Bitencourt-Ferreira et al., 2019). A significant step in this process is identification and target validation. Conversely, these kinds of experimental methods have been expensive and time consuming. Numerous plants have been found to be beneficial, and many people utilize complementary and alternative medicine for therapeutic intervention against diabetes (Baliga et al., 2011). Nevertheless, a number of these bioactive components have discovered new uses in medicine as a result of expanded understanding of their target interactions, mechanism of action, and clinical applications (Poovathinal et al., 2017).

Network pharmacology is a research plan that delivers a distinct and revolutionary way to understanding the mechanism of action of both single and multiple components (Banerjee et al., 2019). It has been discovered that terpenoids, flavonoids, phenolics, coumarins, and numerous other bioactive components manifest significant potential in lowering blood glucose levels. These plants have anti-inflammatory, anti-oxidant, anti-obesity, anti-hyperglycemic, and anti-hyperlipidemia characteristics (Parveen et al., 2018). Terpenoids may have multitarget effects on blood glucose level by influencing insulin receptor function and glucose uptake, both of these two processes pivotal to diabetes. It is indicated that pyridine alkaloid, trigonelline, demonstrate anti-diabetic activity by acting directly on β cells, stimulating insulin secretion along with downregulating the activity of intestinal α-amylase (Subramanian & Prasath, 2014)and it also enhances insulin signaling pathway.

3.1 Interaction with Insulin Receptors and Modulation of Glucose Transporters

Among the insulin target tissue, skeleton muscle is accountable of about 75% of glucose disposal in result to insulin in the postprandial state. A significant contributing factor to the development of type 2 diabetes mellitus is the alteration of glucose metabolism caused by elevated free fatty acids, which results in IR (Ischemia reperfusion) in myocytes (Bergman & Ader, 2000). Insulin promotes glucose absorption by binding to its receptor and triggering a divergent signaling cascade that requires several enzymes, with the proteins phosphoinositide 3-kinase (PI3K) and Akt (sometimes identified as "protein kinase B," or PKB) serving as important nodes (Świderska et al., 2018). When the insulin receptor is activated, the insulin signaling pathway provokes the translocation of the Glut4 receptor from the inside to the cell surface, which modulates glucose absorption. Any anomaly in this pathway stimulates the degeneration of hyperglycemia in type II diabetes (Khalilov & Abdullayeva, 2023). Furthermore, chronic ROS production has recently been recognized as a key mediator in the formation of IR linked to type 2 diabetes (Giacco & Brownlee, 2010). ROS alter stress-sensitive kinases and metabolic sensors by inducing redox changes of cysteine residues, which both facilitate and inhibit the insulin signaling pathways. However, by averting cellular oxidative damage and consequently restoring glucose metabolism and insulin sensitivity, these bioactive plants display their ability to combat insulin resistance (Schieber & Chandel, 2014).

Evidence of Efficacy: Preclinical and Clinical Studies

Predicting and preventing diabetes using clinical, biological, genetic, and machine learning methods seems quite feasible given the sharp rise in the prevalence of diabetes each year and the prompt transition of pre-diabetics into clinical diabetics (Balkau et al., 2008). In the past, preclinical experimental models have been pivotal for investigating and characterizing the pathophysiology of disease. Moreover, these *in-vivo* and *in-vitro* preclinical experiments assist in target identification, estimation of novel therapeutic agents and validation of treatments (Shakya et al., 2020). Furthermore, Modern medicine and traditional medicine have a wide gap, with the latter naturally requiring extensive and scientific proof of speculative evidence before accepting the former. Clinical study of medicinal plants with prospective anti-diabetic effects has significant challenges due to the intricacy of plant material constituents and limited understanding of the genesis of diabetes (Campbell-Tofte et al., 2012).

Alloxan and streptozotocin (STZ) are the most popular diabetogenic agents that is utilized for estimating the antidiabetic or hypoglycemic capability of test compounds. Alloxan has been utilized more frequently than STZ given its relative accessibility and cost-efficiency. Alloxan is a urea derivative that selectively kills the pancreatic islets' β-cells (Etuk, 2010). Various doses of alloxan have been used to trigger experimental diabetes in animals with varying degrees of disease severity, including dogs, rats, mice, and rabbits (Iranloye et al., 2011). Figure 2 demonstrates the mode of action of alloxan in diabetes induction.

Alloxan exposure occur through multiple routes (intraperitoneal, intravenous and subcutaneous), administrated in single and multiple doses with the most frequently used method appearing to be single intraperitoneal administration (Ighodaro et al., 2017). Even when large quantities of glucose are executed, alloxan administration triggers a brief increase in insulin production triggered by glucose, which is followed by a total suppression of the islet response to glucose (Lachin & Reza et al., 2012). Furthermore, reducing substances such as reduced glutathione (GSH), cysteine, ascorbate, and protein-bound sulfhydryl (-SH) groups are present when the reduction process occurs in pancreatic beta cells (Zhang et al., 1992). Alloxan inactivate the enzymes by interacting with two SH group in the sugar binding site of glucokinase. This triggers the formation of dialuric acid, which is thereafter re-oxidized to alloxan, generating a redox cycle and producing superoxide radicals and ROS (Das et al., 2012). The superoxide radicals release ferric ions from ferritin and reduce them to ferrous and ferric ions and also endure dismutation to generate hydrogen peroxide (H_2O_2). In the presence of ferrous and H_2O_2, highly reactive hydroxyl radicals are formed. This highlighted why co-administration of thiols such as GSH or cysteine with alloxan tends to alleviate the toxic and diabetogenic impacts of alloxan as reported by a number of other studies (Ighodaro et al., 2017).

5. Integration of Ayurvedic Medicine with Modern Medicines in Management of Diabetes

Modern medicines are frequently considered a preferable healthcare choice because of its substantial research-base, comprehensive approach and elucidated significance of treatments. Although, this medication system has various limitations, including lack of medication for all disorders and considerable expense of healthcare. Alternatively, Ayurveda is a traditional method of medication that originated in India, takes a holistic strategy that focuses on protection and health improvements, provides cost-effective approach and promotes patient self-management (Gupta, 2024). Incorporation of Ayurvedic and Modern diabetic treatments handles not only regulation of blood glucose but further improves the way of living of a person via use of natural products, personalized nutritional suggestions and also through changes in lifestyle (Murugaiyan et al., 2024).

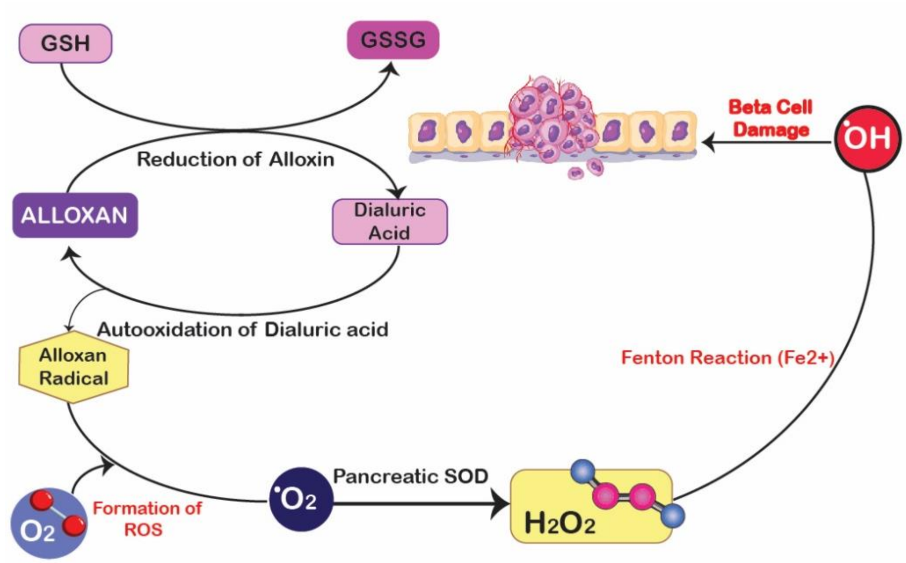

Fig 2: Mode of action of Alloxan

Regardless of the increasing acceptance of collaboration between Ayurvedic and modern medicines, there is still a lack of solid research to support its effectiveness and protection among different diabetic kinds, including T1, T2, prediabetes and secondary diabetes. Despite certain medical research indicate positive results, but integrative-analyses and thorough assessments are required to validate the significance of this holistic approach (Murugaiyan et al., 2024). For instance, Irbesartan is a hypotensive medicine that has antidiabetic characteristics as well. While Curcumin, a phytochemical commonly found in turmeric, used for various disorders but it also has antidiabetic activities. Integration between Irbesartan and Curcumin shows more pronounced anti-diabetic properties (Leve et al., 2013). Furthermore, Glimepiride (an allopathic drug) also shows more considerable hypoglycemic potential when used along with *Aloe vera* (an ayurvedic herb). Thus, *Aloe vera* boost the ability of glimepiride to control and lower the blood glucose level (Mondal et al., 2020)

5.1 Addressing Gap in Conventional Diabetes Therapy using Ayurvedic Approaches

Through the integration of Ayurveda with modern medicines, we can address the gaps between these two systems and can exploit the positive aspects of these methodologies to enhance the satisfactions of patients, minimize the healthcare cost and can tackle the increasing prevalence of diabetes all over the world. Sustained investigations and research are important to encourage the combination of Allopathy with traditional medicines in order to manage the diabetic disease and opens the pathways for an increased holistic and accessible health-care system (Reddy, 2024).

6. Challenges and Future Directions

Despite their admiration, herbal drugs have some irregular effect and lack of cooperation with allopathic medicine. The medication quality or ingredients impose a strong impact on safety and efficacy of Ayurvedic medicines due to their mixed herbal components. So there should be research projects and detailed studies to design their manufacturing, quality, usage, efficacy and progress for future direction (Pore et al., 2023). Disorganized collection, inefficient farming and breeding methods, inefficient harvesting techniques, and a lack of processing technology all contribute to low-quality medications (Shriwastav & Gupta, 2017). Standardization methods should be employed in all facets of Ayurveda with consistency like proper recognition of samples, organoleptic examination, quantitative analysis, pharmacological analysis, volatile substance, microbial load, xenobiotics and toxicity assessments, biochemical and activity evaluation of phytochemicals (Pant el al., 2021).

Adulteration and substitution due to the soil composition, regional factors, deforestation and climate change led to safety and efficacy issues of ayurvedic drugs (Balekundri & Mannur, 2020). Due to geographical origin, authentication, administration route, proper documentation and interaction with other medicines it is difficult to assess the safety of ayurvedic medicines (Saggar et al., 2022). Ayurvedic medicines often fail to meet the rigorous regulatory requirements due to their complexity and difficulty in isolation and testing of individual components (Gupta, 2024). Due to lack of scientific validations, Ayurveda is trailing behind as it has failed to meet the current trends in scientific research. For worldwide acceptance and acknowledgment of Ayurveda, there is a need of evidence based-collaborative medical research. In ayurveda, initiatives should be employed to generate more valuable scientific outcomes from talented and emerging researchers and scholars via startup conclaves and summits (Krishna et al., 2020, Ranade, 2024). Additionally, it is essential for traditional ayurvedic practitioners to make collaborations with modern sciences in order to translate laboratory results into clinical applications (Sebastian, 2024).

Conclusion

To conclude, the therapeutic efficacy of ayurvedic medicine offers a promising avenue for diabetes treatment, with a focus on herbal therapies. Empirical evidence supports that turmeric, fenugreek, and gymnema show powerful glucose-lowering effects alongside improvements in insulin dynamics. Clinical trials further confirm the antidiabetic effects of ayurvedic drugs, supporting its role in glycemic control and metabolic regulation. Combining allopathic and Ayurvedic therapies can help in managing diabetes in a synergistic way, possibly increasing effectiveness and reducing side effects. To create standardized procedures and maximize the advantages of this integrative approach, more study is necessary.

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