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REVIEW ARTICLE

A Review on Different Types of Therapy for Diabetes Mellitus

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Abstract: Diabetes Mellitus, the second most prevalent global health concern, is characterized by inappropriate insulin production in the body, leading to a metabolic disorder. In the contemporary landscape, numerous medications with distinct therapeutic attributes, targets, and formulations are continually being unearthed to benefit patients. A contemporary trend involves symptom-focused medication use rather than addressing the root cause of illnesses, potentially leading to the onset of additional serious medical conditions. Historically, plant-based remedies were employed, but the subsequent evolution of chemical compound drugs with undesirable reactions became prevalent. Post the COVID-19 era, there is a resurgence of interest in plant-based medications. These remedies offer potential solutions for a range of conditions. Alongside pharmaceuticals and herbal remedies, modern science is progressing, introducing new technologies for the detection and treatment of various illnesses. This includes advancements in homoeopathy, Ayurvedic medicine, Nanotechnology, Artificial Intelligence (AI), Deep and Machine Learning, and Robotics. This review elucidates the innovative technologies and traditional therapies employed in the treatment of diabetes, providing a comprehensive overview of the evolving landscape in diabetes management.

Keywords: Phytomedicine; Nano medicine; Diabetes mellitus; Ayurveda; Insulin, Robotics.

1. Introduction

Diabetes mellitus is a prevalent chronic endocrine disorder, marked by hyperglycemia resulting from absolute or relative insulin deficiency. Its complex etiology encompasses various causes, with the primary classifications being type 1 and type 2 diabetes [1]. The pathophysiology of type 1 diabetes stems from autoimmune destruction targeting insulin-secreting pancreatic β-cells, resulting in a deficiency of insulin and subsequent hyperglycemia. Type 1 diabetes represents approximately 10-15% of the diabetic population. Conversely, type 2 diabetes is characterized by abnormal insulin secretion and peripheral resistance, constituting the predominant form that accounts for 85-90% of all diabetes cases [2]. This research paper aims to elucidate the intricate mechanisms and distinct characteristics of these major diabetes types, contributing valuable insights for the comprehension, diagnosis, and management of this widespread and consequential endocrine disorder.

The management of diabetes has evolved significantly over the years, witnessing the discovery of numerous medications and therapeutic strategies. A contemporary trend in medical practice involves addressing symptoms rather than targeting the root cause of illnesses, potentially leading to the onset of additional serious medical conditions. Historically, plant-based remedies were employed, but the subsequent evolution of chemical compound drugs with undesirable reactions became prevalent. In the wake of the COVID-19 era, there is a resurgence of interest in plant-based medications, which offer potential solutions for a range of conditions. Alongside pharmaceuticals and herbal remedies, modern science is progressing, introducing new technologies for the detection and treatment of various illnesses. This includes advancements in Ayurvedic medicine, Nanotechnology, Artificial Intelligence (AI), Deep and Machine Learning, and Robotics [3]. This paper comprehensively reviews both the traditional and innovative approaches in the treatment of diabetes, exploring the evolving landscape of diabetes management in the context of diverse therapeutic modalities and technologies

2. Traditional methods in the management of diabetes

Ayurveda, an ancient and traditional system of Indian medicine, holds significant relevance in the context of diabetes management. Rooted in the profound wisdom of Ayur, meaning "life," and Veda, signifying "knowledge," Ayurveda was initially conceptualized to promote overall health. Over time, it evolved to become a comprehensive therapeutic approach for addressing various ailments, including diabetes. Ayurvedic treatments harness a wealth of knowledge about herbs with active constituents possessing therapeutic efficacy, providing a holistic perspective on healing. [4]

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The Ayurvedic treatment regimen operates on two fundamental principles: firstly, the patient must comprehend the etiology of the ailment, and secondly, they must maintain awareness of the same. This therapeutic approach aims not only to address the specific disease but also to heal and balance the entire body. Embracing an integrated approach, Ayurveda considers the physical, spiritual, and mental aspects of the body in its treatment methodology. The phytoconstituents derived from diverse herbs contribute significantly to the medicinal activities essential in managing various ailments, including diabetes [5]. In Ayurvedic traditions, delineations are made within two distinct classes: Atreya (Physicians) and Dhanvantari (Surgeons). Clinical medicine is further categorized into eight branches, encompassing Kayachikitsa (Internal medicine), Vajikarana, Shalyatantra, Rejuvenation (Rasayana), Pediatrics, Toxicology, Psychiatry, Ophthalmology, and Otorhinolaryngology [6]. Noteworthy Ayurvedic texts, such as Charaka Samhitha, Sushrutha Samhitha, Ashtanga Hridaya, Vagbhata, Madhav Nidan, Sharangdera Samhitha, and Bhava Prakash, serve as essential reference works in guiding Ayurvedic practices [7]. In the field of diabetes research, Ayurveda contributes valuable insights, offering a holistic and multidimensional approach to managing this metabolic disorder. Various transdisciplinary approaches in the management of diabetes are shown in Figure 1. The ayurvedic drugs used in the management of diabetes are listed out in Table 1.

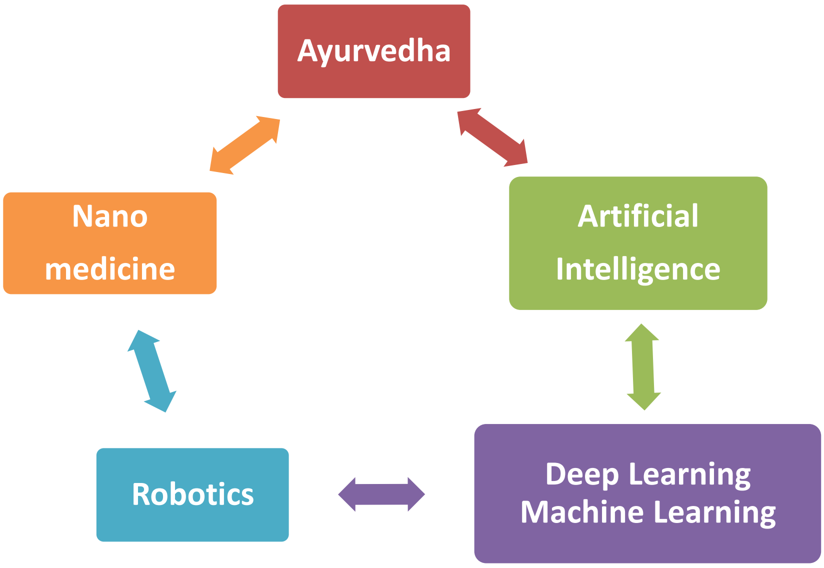

Figure 1. Transdisciplinary approaches involved in the treatment of diabetes

Table 1 Herbal remedies for the management of Diabetes.

S. No	Plant	Plant parts	Active constituents	Mechanism of action
1.	Ficus religiosa [peepal]	leaves	Tannins, Saponins, 3-o-α-l-rhamnoside, polyphenolic compounds	Lowers blood glucose levels and elevates insulin stimulation [8]
2.	Eugenia jambolana [black plum]	seeds, leaves, fruits, bark	Ellagic acid, Myricetin	Increases insulin secretion, reduces blood cholesterol, TGA, fatty acids [9]
3.	Momordica charantia [bitter gourd]	stem, roots	Triterpenes, glycosides	Inhibits α-glucosidase activity, depresses blood glucose levels [10]
4.	Ocimum sanctum [Tulsi]	leaves	Carvacol, Linacol, Limatrol, Eugenol	Decreases elevated serum glucose, reverses LDL values [11]
5.	Pterocarpus marsupium [Indian kino tree]	leaves, flower heartwood	Marsudin, Pterosupin, liquiritigenin	Protects β-cells, corrects glucose levels, reduces glucose [12]
6.	Trigonella foenum graecum [fenugreek]	seeds, leaves	Somatostatin, Trigonelline	Reduces maltase activity, controls insulin [13]
7.	Gymnema sylvestre [Gurmar]	roots	Gymnema saponins, g. sylvestre	Effective against pancreatic β-cell dysfunction, decreases fat [14]

8.	Allium sativum [Garlic]	bulb, leaves	Allicin, Allixin, Ajoene	Increases pancreatic insulin secretion, enhances serum insulin [15]
9.	Acacia arabica [Babul]	bark, root, gum, leaves, seeds, pod	Di catechin, Quercetin, β-amyrin, Gallic acid	Induces hypoglycemic effect, releases insulin, decreases lipid production [16]
10.	Aegle marmelos [Wood apple]	root, leaves, branches	Aegeline, Eucalyptol, Eugenol	Exhibits antioxidant activity, influences hyperlipidemic profile [17]
11.	Aegle marmelos [Wood apple]	roots	Alkaloids, Coumarins	Regulates glycaemic metabolism, decreases cholesterol levels [18]
12.	Coriandrum sativum [Coriander]	leaves and seeds	Aromatic acid, Decenoic acid	Lowers blood sugar levels, removes sugar from blood [19]
13.	Phyllanthus emblica [Amla]	fruits	Ascorbic acid, Emblicanin a, Emblicanin b	Inhibits DPP-IV, possesses anti-diabetic properties [20]
14.	Zingiber officinalis [Ginger]	root extracts	Gingerols, Shogaols, polyphenols	Controls hyperinsulinemia in patients with type-II diabetes mellitus [21]
15.	Cinnamomum verum [Cinnamon]	bark	Cinnamaldehyde, Cinnamyl acetate, Coumarin	Increases insulin sensitivity, improves hyperglycemia [22]
16.	Coccinia indica [Bimba, Kanduri]	leaves	Tyrosine, Histidine, Aspartic acid, Glutamic acid, β-carotene	Enhances glucose oxidation, activates G-6-P, F-6-P enzymes [23]

3. Novel trends in the management of diabetes

3.1. Nanomedicine

Nanomedicine involves the application of nanotechnology in medicine with the aim of treating illnesses and facilitating the restoration of damaged tissues, such as muscles, nerves, and bone. This field encompasses the utilization of nanoparticles, nanoelectronics, biosensors, and potential applications of molecular nanotechnology in the future. Oral insulin delivery represents a promising approach for managing diabetes. However, challenges arise due to the low pH of the gastric medium in the stomach, the presence of digesting enzymes, and the characteristics of the intestinal epithelium, particularly for the oral delivery of protein medications like insulin [24]. Strategies employed include the use of prodrugs, involving insulin-polymer conjugation, liposomes, micelles, and solid lipid nanoparticles (NPs) with a Pegylation formulation. Notably, insulin-PEG prodrugs have demonstrated significant advantages when administered orally.

The development of a system involving mixed micelles of bile salt and fatty acid, facilitated by modern technology, has revealed the inclusion of 30 mm sodium glycolate. Consequently, current efforts are concentrated on enhancing the paracellular transport of hydrophilic medications. Modern approaches, such as the application of intestinal permeation enhancers, have contributed to the improved absorption of hydrophilic macromolecules [25]. These advancements show the potential of nanomedicine, particularly in the context of oral insulin delivery, offering innovative solutions for diabetes management.

3.2. Nanorobots

Nanotechnology, particularly through the application of nanorobot surgeries, holds significant promise in revolutionizing the management of diabetes. Nanorobot surgeries involve the use of miniature robotic devices at the nanoscale to perform precise and targeted interventions at the cellular or molecular level. Nanorobots can be engineered to deliver anti-diabetic medications with unprecedented precision. These miniature devices can navigate through the bloodstream, target specific cells or tissues, and release therapeutic agents at the desired location. This targeted drug delivery approach minimizes side effects and enhances the efficacy of diabetes medications. [26]

Nanoscale sensors integrated into nanorobots can provide real-time monitoring of glucose levels in the bloodstream. These sensors can offer continuous feedback, enabling personalized and adaptive insulin delivery based on individual variations in glucose levels. This responsive approach contributes to better glycemic control for individuals with diabetes. Nanorobot surgeries have the potential to facilitate the repair and regeneration of damaged pancreatic tissues. By precisely delivering therapeutic agents or supporting the natural regenerative processes, nanorobots can contribute to restoring pancreatic function and insulin production.

Nanotechnology may play a role in developing innovative approaches to enhance insulin production within the body. Nanorobots could be designed to stimulate beta-cell regeneration or deliver bioengineered insulin-producing cells to the pancreas, addressing the root cause of insulin deficiency in diabetes. Nanorobots equipped with advanced sensing capabilities can be deployed for the early detection of diabetes-related complications. By identifying subtle changes at the molecular level, these nanorobots can contribute to the timely diagnosis and intervention to prevent or mitigate complications such as neuropathy, nephropathy, or retinopathy. The use of nanorobot surgeries allows for highly individualized and precise interventions, taking into account the unique genetic and physiological characteristics of each patient. This personalized approach enhances the effectiveness of diabetes management strategies and minimizes the risk of adverse effects. [27]

3.3. Artificial intelligence (AI)

Artificial Intelligence (AI) refers to the engineering and scientific discipline dedicated to creating intelligent devices, particularly computer programs. In the context of diabetes management, AI is employed to predict the risk of type-II diabetes using Electronic Medical Record (EMR) data from a cohort of 2000 patients. For type I diabetes, a condition characterized by a lifelong dependency on insulin, the D-NAV insulin guidance system has been developed. This system tracks and predicts blood glucose levels, automatically providing patients with tailored advice for their next insulin dosage [28]. An artificial pancreas comprises three interconnected components designed to replicate the functions of a healthy pancreas: Continuous Glucose Monitor (CGM), Insulin and Infusion Pump This sophisticated system integrates real-time glucose monitoring (CGM) with insulin delivery through an infusion pump, controlled by a computer algorithm. The CGM continuously tracks glucose levels, and the algorithm determines the precise insulin dosage needed to maintain glycemic balance. The insulin infusion pump then administers the required insulin, creating a closed-loop system that mimics the dynamic regulation of blood glucose observed in a healthy pancreas. This technology represents a significant advancement in diabetes care, offering automated and precise glycemic control for individuals with diabetes.

3.4. Deep learning and Machine Learning (ML)

Despite rapid advancements in medical science and technology, diabetes remains a chronic and incurable disease. Diabetes education constitutes a pivotal component of comprehensive diabetes care and prevention, both of which are paramount. Physicians are compelled to rely on the most advanced information available to inform their clinical decision-making processes. In contemporary medical research, data mining techniques are extensively employed for the analysis of vast datasets in the pursuit of enhanced understanding and improved outcomes in diabetes management [29, 30].

The methodology employed in diabetes research encompasses the following key steps: Dataset Collection, Dataset Visualization, Results Evaluation and Application of Machine Learning, Deep Learning, and Algorithmic Techniques [31] The utilization of machine learning and deep learning in diabetes research offers notable advantages: The application is interactive, allowing users to input a single variable for predictive outcomes, Enhanced accuracy is achieved through the implementation of deep learning techniques. This scientific approach involves rigorous dataset collection, visualization, and meticulous evaluation of results, followed by the application of advanced machine learning and deep learning algorithms.

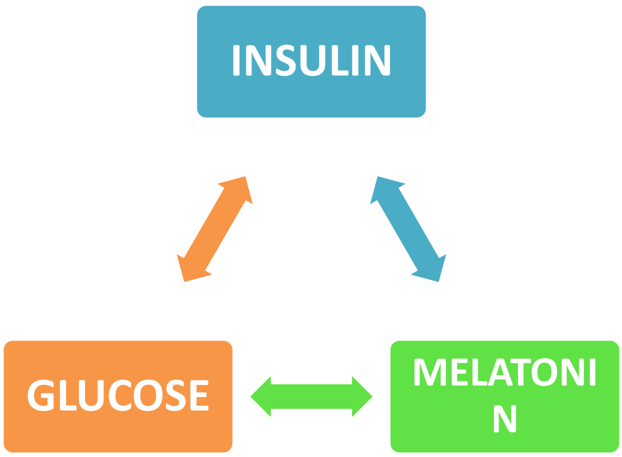

Figure 2. Correlation between Insulin, Glucose and Melatonin

3.5. Chronopharmacological interventions

Chronopharmacology refers to the strategic administration of drugs based on the biological clock, regulated by the hypothalamus in the brain. This biological clock governs various physiological and behavioral aspects of the body, including the daily rhythms of major organ systems such as cardiovascular and metabolic activities, which operate on a 24-hour cycle. The application of chronopharmacology involves aligning drug administration with specific times of the day (morning, evening, midnight) to optimize efficacy in managing respective diseases, as elucidated in the context of Diabetes Mellitus (DM) [32]. The circadian rhythm, orchestrating activities such as sleep, anxiety, blood pressure, glucose levels, hormonal regulation, and immune cell function, plays a pivotal role in our body. In the case of Diabetes Mellitus, a metabolic disorder characterized by elevated blood glucose levels, insulin—secreted by pancreatic beta cells—regulates these levels. The breakdown of consumed food into glucose molecules and the subsequent interplay between melatonin and insulin release are crucial. Proper sleep promotes normal melatonin secretion, contributing to the regulation of insulin secretion, which occurs irregularly throughout the day. Elevated blood glucose levels are associated with factors such as obesity and poor sleep. Diabetes Mellitus manifests in three types: Type-1 DM, Type-2 DM, and Gestational DM. Glucose tolerance is reduced in the evening compared to the morning, and individuals engaged in nighttime activities may be predisposed to Type-2 DM. Medications for DM management need to be administered at specific times during both the day and night to effectively control blood glucose levels [33].

4. Conclusion

In conclusion, Diabetes Mellitus (DM) stands as a significant global health concern characterized by inadequate insulin production, resulting in a metabolic disorder. The contemporary medical landscape witnesses an ongoing exploration of diverse medications, each with unique therapeutic attributes and formulations, aimed at improving patient outcomes. However, a prevailing trend of symptom-focused medication usage, rather than addressing underlying causes, raises concerns about potential complications.

Historically, plant-based remedies were prevalent, but the dominance of chemical compound drugs with adverse reactions became prominent. The aftermath of the COVID-19 era has sparked a renewed interest in plant-based medications, offering potential solutions for various conditions. Beyond conventional pharmaceuticals and herbal remedies, modern science is pushing boundaries, introducing cutting-edge technologies for disease detection and treatment. This includes advancements in homoeopathy, Ayurvedic medicine, Nanotechnology, Artificial Intelligence (AI), Deep and Machine Learning, and Robotics. The evolving landscape in diabetes treatment encompasses a multidimensional approach, integrating both historical wisdom and contemporary advancements. The synthesis of these diverse elements contributes to a holistic understanding of the current state and potential future directions in the field of diabetes care.

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Author's short biography

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Area of Research interest include Insilco Research (Auto dock Vina, PYRX, QSAR tool box). Also interested in Invitro and In vivo works. Completed my M.Pharm in the Dept. of Pharmacology, Sri Padmavathi Mahila Viswavidyalayam, Tirupathi. Completed my internship at Pharma Deep Remedies, Hyderabad. Right now, serving as Assistant Professor in the Department of Pharmacology, Narayana Pharmacy College, Nellore, Andhra Pradesh, India. Myself certified in Clinical SAS. She had also completed a diploma course in "Food & Nutrition" in IGNOU, Vishakhapatnam. Given oral presentation on "Therapeutic Drug Monitoring" in the seminar – "Current Achievements, Challenges and Future Prospects of Drug Delivery" held at Gokula Krishna College of Pharmacy, Sullurpet