

Nanotechnology-Based Herbal Therapeutics for Diabetes Mellitus Recent Developments

Shivam K. Bhite¹, Nita S. Shingade², Nikita V. Waghmare³, Aarti S. Desai⁴, Saniya Y. Mahajan⁵
Nikhil D. Ghorpade⁶

¹Assistant. Professor Department of Pharmacy Practice Dr. V. V. P. F'S. College of Pharmacy Ahilyanagar

^{2,4}Lecturer Department of Pharmaceutical Quality Assurance Delonix Society's Baramati College of Pharmacy Barhanpur

³Lecturer Department of Pharmacy Delonix Society's Baramati College of Pharmacy Barhanpur

⁵Lecturer Department of Pharmaceutical Quality Assurance Dr. L. H. Hiranandani College of Pharmacy

⁶Lecturer Department of Pharmacology SGVSS'S Sakeshwar College of Pharmacy Chas Ahilyanagar

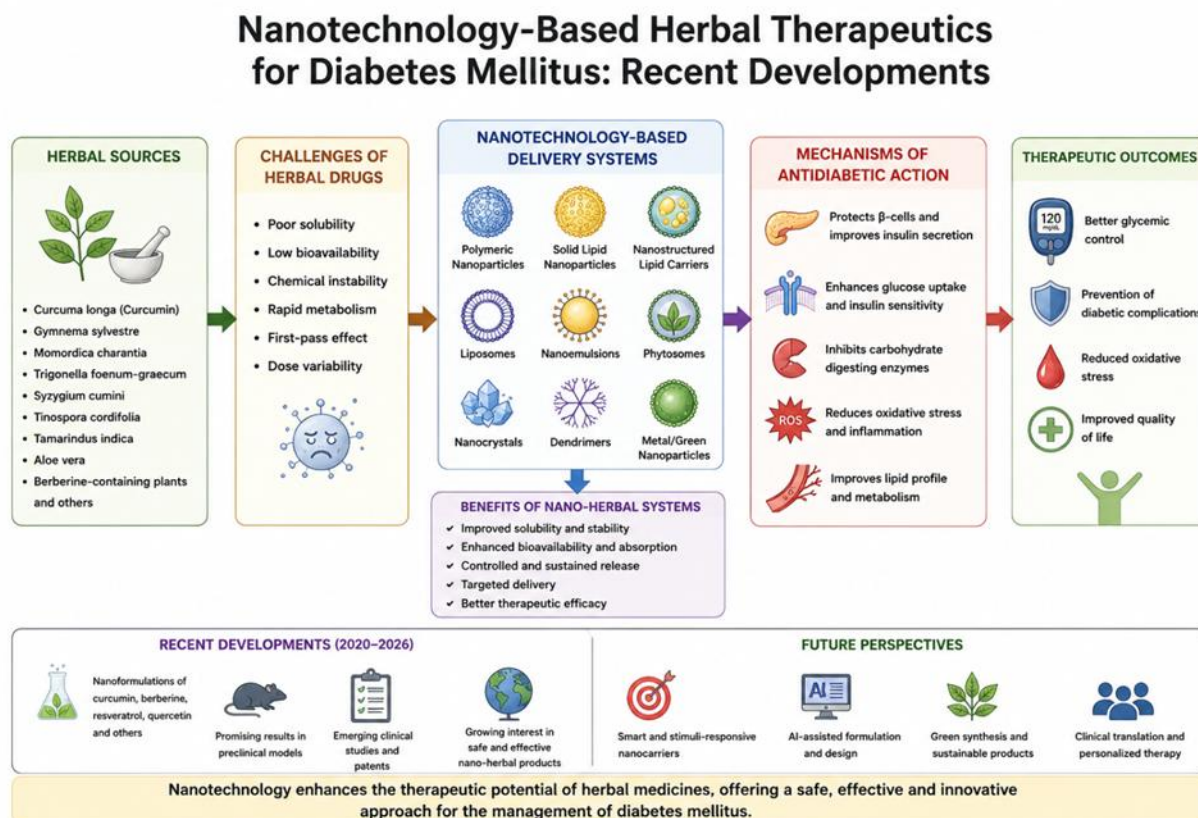


Figure 1. Graphical Abstract

Abstract—Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The global prevalence of diabetes has increased dramatically over recent decades, creating substantial healthcare and economic burdens worldwide. Despite the

availability of several conventional antidiabetic medications, long-term therapy is frequently associated with adverse effects, poor patient compliance, and inadequate prevention of diabetic complications. Consequently, medicinal plants and their bioactive phytoconstituents have attracted considerable attention

as alternative or complementary therapeutic options due to their multitarget mechanisms and favorable safety profiles. However, the clinical application of herbal therapeutics is often limited by poor aqueous solubility, low bioavailability, instability, rapid metabolism, and insufficient target specificity.

Recent advances in nanotechnology have provided innovative strategies to overcome these limitations through the development of nano-enabled herbal drug delivery systems. Nanocarriers such as polymeric nanoparticles, liposomes, solid lipid nanoparticles, nanostructured lipid carriers, nanoemulsions, phytosomes, dendrimers, and metallic nanoparticles have demonstrated the ability to enhance drug solubility, stability, absorption, controlled release, and tissue targeting. These systems facilitate improved pharmacokinetic and pharmacodynamic performance of phytochemicals including curcumin, berberine, quercetin, resveratrol, gymnemic acid, and other plant-derived antidiabetic compounds.

This review comprehensively discusses the pathophysiology of diabetes mellitus, antidiabetic medicinal plants, challenges associated with herbal therapy, nanocarrier systems, nano-herbal formulations, recent developments from 2020–2026, safety considerations, clinical translation, and future perspectives. Special emphasis is placed on *Tamarindus indica*-based nano formulations as an emerging research opportunity. Nano-herbal therapeutics represent a promising approach for improving glycemic control, reducing oxidative stress and inflammation, protecting pancreatic β -cells, and minimizing diabetic complications, thereby offering new possibilities for next-generation diabetes management.

Index Terms—Diabetes Mellitus; Nanotechnology; Herbal Therapeutics; Nanoparticles; Phytochemicals; Bioavailability; Drug Delivery Systems; Antidiabetic Therapy.

I. INTRODUCTION

Diabetes mellitus is one of the most prevalent non-communicable diseases worldwide and constitutes a major public health challenge. The disease is characterized by chronic elevation of blood glucose levels resulting from defects in insulin secretion, insulin action, or both. According to recent estimates from the International Diabetes Federation (IDF), approximately 589 million adults are currently living with diabetes globally, and the prevalence is expected to increase substantially over the coming decades [1,2].

The pathogenesis of diabetes involves multiple metabolic disturbances including impaired glucose utilization, altered lipid metabolism, oxidative stress, inflammation, and progressive pancreatic β -cell dysfunction. Persistent hyperglycemia contributes to severe microvascular and macrovascular complications such as diabetic nephropathy, retinopathy, neuropathy, cardiovascular diseases, and delayed wound healing [3,5,9].

Conventional antidiabetic therapies include insulin preparations, biguanides, sulfonylureas, meglitinides, thiazolidinediones, DPP-4 inhibitors, SGLT2 inhibitors, and GLP-1 receptor agonists. Although these medications effectively reduce blood glucose levels, prolonged administration may be associated with adverse effects such as hypoglycemia, gastrointestinal disturbances, weight gain, edema, and reduced patient adherence [2,4].

Medicinal plants have been used for centuries in traditional systems of medicine for the management of diabetes. Numerous phytochemicals including polyphenols, flavonoids, alkaloids, terpenoids, glycosides, and saponins exhibit antidiabetic activities through multiple mechanisms. These compounds can stimulate insulin secretion, improve insulin sensitivity, suppress carbohydrate digestion enzymes, reduce oxidative stress, and protect pancreatic β -cells [5].

Despite their therapeutic potential, herbal medicines face several limitations including poor aqueous solubility, low permeability, rapid metabolism, instability under physiological conditions, poor absorption, and low oral bioavailability. These limitations often result in inadequate therapeutic concentrations at target sites and inconsistent clinical outcomes [6].

Nanotechnology has emerged as a transformative platform for overcoming these challenges. Nanocarriers can improve drug solubility, stability, permeability, controlled release, and targeted delivery. The integration of nanotechnology with herbal therapeutics has created a new field known as nano-herbal medicine, which offers enhanced efficacy and improved pharmacokinetic profiles compared with conventional herbal formulations [7,8].

The present review aims to critically evaluate recent developments in nanotechnology-based herbal therapeutics for diabetes mellitus, focusing on medicinal plants, nanocarrier systems, nano-herbal

formulations, mechanisms of action, clinical potential, safety concerns, and future research directions.

II. TYPES OF DIABETES MELLITUS

2.1 Type 1 Diabetes Mellitus

Type 1 diabetes mellitus (T1DM) is an autoimmune disorder characterized by immune-mediated destruction of pancreatic β -cells, resulting in absolute insulin deficiency. Genetic susceptibility, environmental factors, viral infections, and autoimmune mechanisms contribute to disease development. Clinical manifestations include polyuria, polydipsia, polyphagia, weight loss, fatigue, and ketoacidosis [8].

2.2 Type 2 Diabetes Mellitus

Type 2 diabetes mellitus (T2DM) accounts for approximately 90–95% of all diabetes cases and is characterized by insulin resistance combined with progressive β -cell dysfunction. Major risk factors include obesity, sedentary lifestyle, aging, genetic predisposition, hypertension, and dyslipidemia. Chronic inflammation and oxidative stress further contribute to disease progression [9,10,11].

2.3 Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) refers to glucose intolerance first recognized during pregnancy. Hormonal changes during pregnancy induce insulin resistance, leading to hyperglycemia. Untreated GDM increases maternal and fetal complications and predisposes both mother and child to future diabetes [10,11].

2.4 Prediabetes

Prediabetes represents an intermediate metabolic state characterized by impaired fasting glucose and impaired glucose tolerance. Individuals with prediabetes are at significantly increased risk of progressing to T2DM and cardiovascular diseases [9,11].

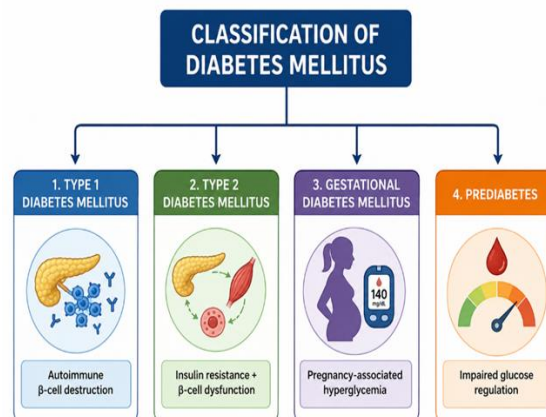


Figure 2. Classification of Diabetes Mellitus

III. PATHOPHYSIOLOGY OF DIABETES MELLITUS

The maintenance of glucose homeostasis depends on the coordinated actions of insulin, glucagon, liver, skeletal muscle, adipose tissue, and pancreas. In healthy individuals, elevated blood glucose stimulates insulin secretion from pancreatic β -cells, facilitating cellular glucose uptake.

In diabetes mellitus, several pathological events disrupt this regulatory mechanism. Insulin resistance reduces cellular responsiveness to insulin, resulting in decreased glucose uptake by peripheral tissues. Simultaneously, pancreatic β -cell dysfunction impairs insulin secretion, leading to chronic hyperglycemia [12,13].

Chronic inflammation further contributes to disease progression through increased production of inflammatory cytokines such as TNF- α , IL-6, and IL-1 β . These mediators interfere with insulin signaling pathways and exacerbate metabolic dysfunction [14,15].

Persistent metabolic abnormalities ultimately result in microvascular complications including nephropathy, neuropathy, and retinopathy, as well as macrovascular complications such as coronary artery disease and stroke [15].

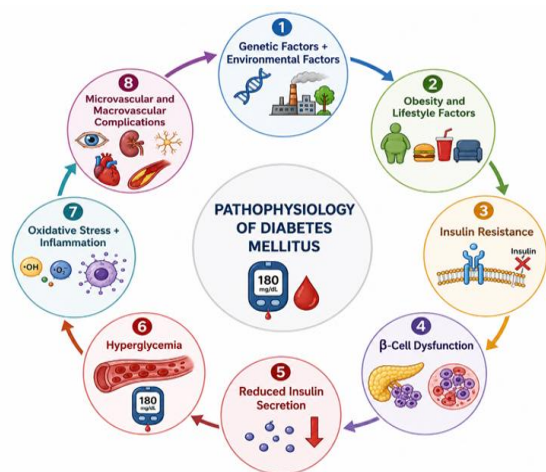


Figure 3. Pathophysiology of Diabetes Mellitus

Table 1. Classification of Diabetes Mellitus

Type	Characteristics	Main Cause
Type 1 DM	Absolute insulin deficiency	Autoimmune β -cell destruction
Type 2 DM	Insulin resistance	Obesity, genetics, lifestyle
Gestational DM	Pregnancy-induced hyperglycemia	Hormonal changes
Prediabetes	Intermediate hyperglycemia	Metabolic dysfunction

IV. MECHANISM OF ACTION OF HERBAL ANTIDIABETIC DRUGS

Medicinal plants contain numerous bioactive constituents including flavonoids, alkaloids, terpenoids, polyphenols, saponins, tannins, and glycosides that exert antidiabetic effects through multiple molecular pathways. Unlike conventional drugs that generally act on a single target, phytochemicals exhibit multitarget therapeutic actions, making them particularly useful in the management of complex metabolic disorders such as diabetes mellitus [16,17].

4.1 Stimulation of Insulin Secretion

Several phytoconstituents stimulate pancreatic β -cells and enhance insulin secretion. Compounds such as 4-hydroxyisoleucine from *Trigonella foenum-graecum* and gymnemic acids from *Gymnema sylvestre* have

demonstrated insulinotropic activity, leading to improved glycemic control [18,19,20].

4.2 Improvement of Insulin Sensitivity

Polyphenolic compounds including curcumin, berberine, quercetin, and resveratrol improve insulin sensitivity through activation of insulin receptor signaling pathways and enhancement of glucose transporter (GLUT-4) translocation [19,20].

4.3 Activation of AMPK Pathway

AMP-activated protein kinase (AMPK) functions as a metabolic master regulator. Berberine, curcumin, and quercetin activate AMPK signaling, resulting in increased glucose uptake, enhanced fatty acid oxidation, and reduced hepatic gluconeogenesis [20,21].

4.4 Inhibition of α -Amylase and α -Glucosidase

Many herbal constituents delay carbohydrate digestion by inhibiting α -amylase and α -glucosidase enzymes. This mechanism reduces postprandial hyperglycemia and improves overall glycemic control [20,21].

4.5 Enhancement of Glucose Uptake

Flavonoids and polyphenols stimulate GLUT-4 translocation in skeletal muscles and adipose tissues, facilitating cellular glucose utilization and reducing blood glucose concentrations [22,23].

4.6 Antioxidant Activity

Oxidative stress plays a central role in diabetes progression and complications. Curcumin, quercetin, anthocyanins, and polyphenols neutralize reactive oxygen species and enhance endogenous antioxidant defenses [23].

4.7 Protection of Pancreatic β -Cells

Phytochemicals reduce β -cell apoptosis and preserve pancreatic architecture through antioxidant and anti-inflammatory mechanisms [24].

4.8 Anti-inflammatory Effects

Many medicinal plants suppress inflammatory mediators including TNF- α , IL-6, and NF- κ B, thereby improving insulin sensitivity and preventing diabetic complications [25,26].

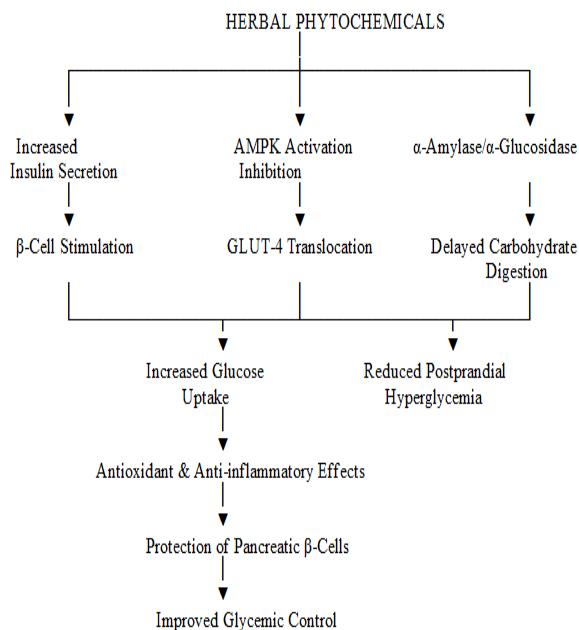


Figure.4 Mechanism of Action of Herbal Antidiabetic Drugs

V. MEDICINAL PLANTS USED IN DIABETES MANAGEMENT

A large number of medicinal plants have demonstrated significant antidiabetic potential. Their therapeutic activities are primarily attributed to phytochemicals capable of modulating glucose metabolism, insulin secretion, insulin sensitivity, oxidative stress, and inflammation [26,27].

5.1 *Curcuma longa* (Turmeric)

Family: Zingiberaceae

Part Used: Rhizome

Active Compound: Curcumin

Curcumin exhibits antidiabetic effects through activation of AMPK, suppression of inflammatory pathways, enhancement of insulin sensitivity, and reduction of oxidative stress. Several studies have shown improved glucose tolerance and reduced diabetic complications following curcumin administration [27,28].

5.2 *Trigonella foenum-graecum* (Fenugreek)

Family: Fabaceae

Part Used: Seeds

Active Compounds: Trigonelline, 4-Hydroxyisoleucine, Galactomannan

Fenugreek improves insulin secretion, delays glucose absorption, and enhances insulin sensitivity.

Galactomannan contributes to delayed gastric emptying and reduced postprandial glucose levels [28].

5.3 *Momordica charantia* (Bitter Melon)

Family: Cucurbitaceae

Part Used: Fruit

Active Compounds: Charantin, Vicine, Polypeptide-p
These compounds possess insulin-mimetic properties and promote glucose utilization while reducing hepatic glucose production [29,30].

5.4 *Gymnema sylvestre*

Family: Apocynaceae

Part Used: Leaves

Active Compound: Gymnemic Acids

Gymnemic acids stimulate insulin secretion, promote β -cell regeneration, and inhibit intestinal glucose absorption [30].

5.5 *Syzygium cumini*

Family: Myrtaceae

Part Used: Seeds

Active Compounds: Jamboline, Anthocyanins

The plant exhibits antioxidant and antihyperglycemic properties while improving insulin sensitivity [31,32].

5.6 *Azadirachta indica* (Neem)

Family: Meliaceae

Part Used: Leaves

Active Compounds: Nimbin, Azadirachtin

Neem reduces blood glucose levels through antioxidant and insulin-sensitizing mechanisms [32].

5.7 *Tinospora cordifolia*

Family: Menispermaceae

Part Used: Stem

Active Compound: Tinosporaside

Enhances insulin secretion and improves glucose metabolism while reducing oxidative stress [33].

5.8 *Aloe vera*

Family: Asphodelaceae

Part Used: Gel

Active Compounds: Acemannan, Aloin

Aloe vera improves insulin sensitivity and reduces fasting blood glucose levels [34].

5.9 Tamarindus indica

Family: Fabaceae

Part Used: Fruit Pulp, Seeds, Leaves

Active Compounds: Polyphenols, Flavonoids, Tartaric Acid

Tamarindus indica exhibits antioxidant, anti-inflammatory, and antihyperglycemic activities. Polyphenols improve insulin sensitivity and reduce oxidative stress. Despite promising findings, nanoformulations of Tamarindus indica remain relatively unexplored, presenting significant opportunities for future research [35].

5.10 Berberis aristata

Family: Berberidaceae

Part Used: Root

Active Compound: Berberine

Berberine activates AMPK signaling, enhances insulin sensitivity, and suppresses hepatic glucose production [36].

5.11 Pterocarpus marsupium

Family: Fabaceae

Part Used: Heartwood

Active Compound: Pterostilbene

Exhibits antioxidant and β -cell protective properties [37].

5.12 Ocimum sanctum (Holy Basil)

Family: Lamiaceae

Part Used: Leaves

Active Compounds: Eugenol, Rosmarinic Acid

Improves glucose metabolism and reduces oxidative stress [38].

5.13 Moringa oleifera

Family: Moringaceae

Part Used: Leaves

Active Compounds: Quercetin, Chlorogenic Acid

Moringa reduces blood glucose levels and improves insulin sensitivity [39].

5.14 Cinnamomum verum (Cinnamon)

Family: Lauraceae

Part Used: Bark

Active Compounds: Cinnamaldehyde, Procyanidins

Cinnamon improves insulin receptor function, glucose uptake, and glycemic control [40].

Table 2. Major Herbal Antidiabetic Plants

Plant Name	Active Compound	Mechanism of Action	Anti-diabetic Activity	Reference
Curcuma longa	Curcumin	AMPK activation	Improves insulin sensitivity	[27,28]
Trigonella foenum-graecum	Trigonelline	Insulin secretion	Lowers glucose	[28]
Momordica charantia	Charantin	Insulin mimetic action	Anti-hyperglycemic	[29,30]
Gymnema sylvestre	Gymnemic acid	β -cell regeneration	Glycemic control	[30]
Syzygium cumini	Anthocyanins	Antioxidant action	Improves glucose metabolism	[31,32]
Azadirachta indica	Nimbin	Insulin sensitization	Anti-diabetic	[32]
Tinospora cordifolia	Tinosporoside	Insulin secretion	Anti-hyperglycemic	[33]
Aloe vera	Acemannan	Improves insulin sensitivity	Blood glucose reduction	[34]
Tamarindus indica	Polyphenols	Antioxidant action	Glycemic control	[35]
Berberis aristata	Berberine	AMPK activation	Anti-diabetic	[36]
Pterocarpus	Pterostilbene	β -cell protection	Anti-hyperglycemic	[37]

marsupium				
Ocimum sanctum	Eugenol	Antioxidant activity	Anti diabetic	[38]
Moringa oleifera	Quercetin	Glucose uptake	Improves insulin sensitivity	[39]
Cinnamomum verum	Cinnamaldehyde	Insulin receptor activation	Glycemic control	[40]

VI. CHALLENGES ASSOCIATED WITH HERBAL ANTIDIABETIC DRUGS

Despite promising pharmacological activities, herbal antidiabetic agents face several limitations that hinder their clinical application.

6.1 Poor Solubility

Many phytochemicals such as curcumin, quercetin, and resveratrol exhibit poor aqueous solubility, resulting in inadequate dissolution and absorption [28,29].

6.2 Poor Permeability

Limited intestinal permeability reduces systemic bioavailability of several herbal constituents.

6.3 Low Bioavailability

Extensive metabolism and poor absorption significantly decrease plasma drug concentrations.

6.4 First-Pass Metabolism

Many phytoconstituents undergo rapid hepatic metabolism before reaching systemic circulation.[22]

6.5 Instability

Polyphenols and flavonoids are susceptible to degradation by light, heat, oxygen, and gastrointestinal conditions.[21]

6.6 Rapid Elimination

Short biological half-lives necessitate frequent dosing and may reduce therapeutic efficacy.[27]

6.7 Standardization Issues

Variations in plant source, cultivation, harvesting, extraction, and processing contribute to inconsistent therapeutic outcomes.

These challenges have driven the development of nanotechnology-based delivery systems designed to improve stability, bioavailability, and therapeutic efficacy of herbal antidiabetic agents [25]

VII. NANOTECHNOLOGY IN DIABETES TREATMENT

Nanotechnology refers to the design, development, and application of materials and systems with dimensions ranging from 1 to 1000 nm. In pharmaceutical sciences, nanotechnology has emerged as a revolutionary approach for improving the delivery and therapeutic performance of drugs, particularly poorly soluble herbal bioactives. In diabetes management, nanotechnology offers significant advantages including enhanced bioavailability, controlled drug release, targeted delivery, improved pharmacokinetics, and reduced systemic toxicity [36,38].

Conventional antidiabetic therapies often suffer from poor patient compliance, rapid drug elimination, frequent dosing requirements, and undesirable adverse effects. Similarly, herbal antidiabetic compounds such as curcumin, berberine, quercetin, resveratrol, and gymnemic acids exhibit poor aqueous solubility and limited oral bioavailability. Nanotechnology-based delivery systems can overcome these challenges by protecting phytochemicals from degradation and facilitating their transport across biological barriers [39, 40].

Advantages of Nanotechnology in Diabetes Treatment

- Improved solubility of phytochemicals
- Enhanced oral bioavailability
- Protection from enzymatic degradation
- Controlled and sustained drug release
- Targeted tissue delivery
- Improved therapeutic efficacy
- Reduced systemic toxicity

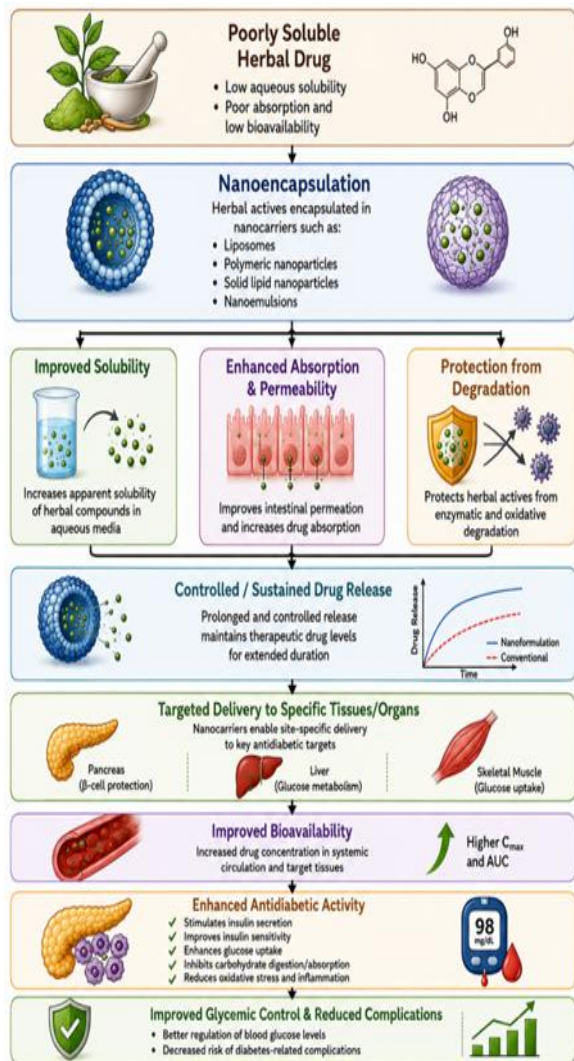


Figure 5. Advantages of Nanotechnology in Diabetes Treatment

VIII. NANOCARRIERS USED FOR HERBAL DRUG DELIVERY

Numerous nanocarrier systems have been investigated for the delivery of herbal antidiabetic agents. Selection of a suitable carrier depends on physicochemical characteristics of the phytoconstituent, desired release profile, route of administration, and therapeutic objectives [31].

8.1 Polymeric Nanoparticles

Polymeric nanoparticles are colloidal systems prepared using biodegradable polymers such as PLGA, chitosan, alginate, and polycaprolactone. These carriers provide controlled release, enhanced

stability, and protection of encapsulated phytochemicals from degradation [31,32].

Advantages

- Biodegradable
- Controlled release
- High encapsulation efficiency
- Improved stability

Limitations

- Complex manufacturing process
- Potential polymer-related toxicity

Applications

Curcumin-loaded PLGA nanoparticles, berberine nanoparticles, and quercetin-loaded chitosan nanoparticles.

8.2 Solid Lipid Nanoparticles (SLN)

Solid lipid nanoparticles consist of biocompatible lipids that remain solid at room and body temperature. SLNs improve oral absorption and enhance stability of lipophilic phytoconstituents [33].

Advantages

- Excellent biocompatibility
- Controlled drug release
- Enhanced oral absorption

Limitations

- Limited drug loading capacity
- Potential drug expulsion during storage

Applications

Curcumin SLNs and resveratrol SLNs.

8.3 Nanostructured Lipid Carriers (NLC)

NLCs represent second-generation lipid nanocarriers prepared using mixtures of solid and liquid lipids. The imperfect lipid matrix allows greater drug loading and improved stability [38,40].

Advantages

- Higher drug loading
- Improved stability
- Better controlled release

Limitations

- Formulation complexity

Applications

Berberine NLCs and quercetin NLCs.

8.4 Liposomes

Liposomes are phospholipid vesicles capable of encapsulating both hydrophilic and lipophilic compounds. Their structural similarity to biological

membranes contributes to superior biocompatibility [35].

Advantages

- Biocompatibility
- Targeted delivery potential
- Improved bioavailability

Limitations

- High production cost
- Physical instability

Applications

Curcumin liposomes, berberine liposomes, and insulin-loaded liposomes.

8.5 Nanoemulsions

Nanoemulsions are thermodynamically stable dispersions of oil and water stabilized by surfactants. They enhance dissolution and absorption of poorly water-soluble phytochemicals [36].

Advantages

- High surface area
- Enhanced absorption
- Easy scale-up

Limitations

- Surfactant-related toxicity

Applications

Curcumin nanoemulsions and cinnamon oil nanoemulsions

8.6 Nanocrystals

Nanocrystals consist of pure drug particles reduced to nanoscale dimensions. Reduction in particle size increases dissolution rate and bioavailability [37].

Advantages

- High drug loading
- Improved dissolution

Limitations

- Physical instability

Applications

Quercetin nanocrystals and berberine nanocrystals.

8.7 Phytosomes

Phytosomes are complexes formed between phytoconstituents and phospholipids. These systems improve membrane permeability and oral bioavailability [38].

Advantages

- Enhanced absorption
- Improved stability

Limitations

- Costly phospholipid materials

Applications

Curcumin phytosomes and quercetin phytosomes.

8.8 Dendrimers

Dendrimers are highly branched nanoscale polymers possessing numerous surface functional groups capable of drug conjugation.

Advantages

- High drug loading
- Surface modification flexibility

Limitations

- Potential cytotoxicity
- Complex synthesis

Applications

Targeted antidiabetic drug delivery.

8.9 Metallic Nanoparticles

Metallic nanoparticles such as silver, gold, zinc oxide, and selenium nanoparticles exhibit intrinsic biological activities including antioxidant and antidiabetic properties [39].

Advantages

- High surface area
- Multifunctionality

Limitations

- Long-term toxicity concerns

Applications

Gold nanoparticles loaded with phytochemicals.

8.10 Green-Synthesized Nanoparticles

Green nanotechnology utilizes plant extracts as reducing and stabilizing agents for nanoparticle synthesis. This environmentally friendly approach minimizes toxic reagents and improves biocompatibility [38,39,40].

Advantages

- Eco-friendly
- Cost-effective
- Biocompatible

Limitations

- Batch-to-batch variability

Applications

Plant-mediated silver, gold, and zinc oxide nanoparticles.

Table 3. Nanocarriers Used for Herbal Drug Delivery

Nanocarrier	Principle	Advantages	Limitations	Application
Polymeric Nanoparticles	Polymer encapsulation	Controlled release	Complex preparation	Curcumin, Berberine
SLN	Solid lipid matrix	High stability	Low drug loading	Curcumin
NLC	Solid-liquid lipid matrix	Higher loading	Complex formulation	Berberine
Liposomes	Phospholipid vesicles	Biocompatible	Expensive	Curcumin, Insulin
Nanoemulsions	Oil-water nanosystems	Enhanced absorption	Surfactant toxicity	Cinnamon oil
Nanocrystals	Nanosized drug particles	High dissolution	Instability	Quercetin
Phytosomes	Phospholipid complex	Better permeability	Costly	Curcumin
Dendrimers	Branching polymers	Targeted delivery	Cytotoxicity	Herbal compounds
Metallic NPs	Metal-based nanosystems	Multifunctional	Toxicity concerns	Gold nanoparticles
Green NPs	Plant-mediated syntheses	Eco-friendly	Variability	Herbal nanoformulations

IX. CONCLUSION

Diabetes mellitus remains one of the most significant global health challenges, necessitating the development of safe, effective, and patient-friendly therapeutic strategies. Herbal medicines have gained considerable attention due to their multitarget pharmacological activities, favorable safety profiles,

and historical use in traditional medicine systems. Numerous medicinal plants including *Curcuma longa*, *Trigonella foenum-graecum*, *Momordica charantia*, *Gymnema sylvestre*, *Syzygium cumini*, *Tinospora cordifolia*, *Berberis aristata*, *Moringa oleifera*, and *Tamarindus indica* have demonstrated substantial antidiabetic potential through mechanisms involving enhancement of insulin secretion, improvement of insulin sensitivity, inhibition of carbohydrate-digesting enzymes, reduction of oxidative stress, and suppression of inflammatory pathways.

Despite these therapeutic benefits, the clinical application of herbal bioactives is frequently limited by poor aqueous solubility, low permeability, instability, rapid metabolism, and inadequate bioavailability. Nanotechnology-based drug delivery systems have emerged as an effective solution to overcome these limitations. Nanocarriers such as polymeric nanoparticles, solid lipid nanoparticles, nanostructured lipid carriers, liposomes, nanoemulsions, phytosomes, dendrimers, and green-synthesized nanoparticles significantly improve the pharmacokinetic and pharmacodynamic properties of phytochemicals.

Recent advances between 2020 and 2026 have highlighted the growing importance of nano-herbal therapeutics, smart nanoparticles, glucose-responsive delivery systems, green nanotechnology, and AI-assisted formulation development. These technologies have demonstrated enhanced antidiabetic efficacy, improved β -cell protection, reduced oxidative stress, and better glycemic control compared with conventional herbal formulations.

However, several challenges remain, including limited clinical evidence, regulatory uncertainties, scale-up difficulties, and standardization issues. Future research should focus on clinical translation, long-term safety evaluation, and personalized nanomedicine approaches. Special attention should be directed toward *Tamarindus indica*-based nanoformulations, which represent a promising yet underexplored area with significant potential for future pharmaceutical development.

Overall, nanotechnology-based herbal therapeutics offer a transformative platform for next-generation diabetes management and may contribute substantially to improving therapeutic outcomes while reducing disease burden worldwide.

REFERENCES

- [1] Sunita, Kaushik R, Verma KK, Parveen R. Herbal nanoformulations for diabetes: mechanisms, formulations, and clinical impact. *Curr Diabetes Rev.* 2025;21(3):68-85.
- [2] Bhadouria N, Alam A, Kaur A. Nanotechnology-based herbal drug formulation in the treatment of diabetes mellitus. *Curr Diabetes Rev.* 2024;21(1).
- [3] Jadhav S, Yadav A. Phytoconstituents based nanomedicines for the management of diabetes: a review. *Pharm Nanotechnol.* 2023;11(3):217-237.
- [4] Wickramasinghe ASD, Kalansuriya P, Attanayake AP. Nanoformulation of plant-based natural products for type 2 diabetes mellitus: from formulation design to therapeutic applications. *Curr Ther Res Clin Exp.* 2022; 96:100672.
- [5] Karthikeyan A, Senthil N, Min T. Nanocurcumin: a promising candidate for therapeutic applications. *Front Pharmacol.* 2020; 11:487.
- [6] Nouri Z, Sayyad N, et al. Nanophytomedicines for the prevention of metabolic syndrome: a pharmacological and biopharmaceutical review. *Front Bioeng Biotechnol.* 2020; 8:425.
- [7] Ruan S, Guo X, Ren Y, Cao G, Xing H, Zhang X. Nanomedicines based on trace elements for intervention of diabetes mellitus. *Biomed Pharmacother.* 2023; 168:115684.
- [8] Bonifácio BV, Silva PB, Ramos MA, Negri KM, Bauab TM, Chorilli M. Nanotechnology-based drug delivery systems and herbal medicines: a review. *Int J Nanomedicine.* 2014; 9:1-15.
- [9] Marella S, Tollamadugu NVKVPP. Nanotechnological approaches for the development of herbal drugs in treatment of diabetes mellitus – a critical review. *IET Nanobiotechnol.* 2018;12(5):549-556.
- [10] Amjad S, Jafri A, Sharma AK, Serajuddin M. A novel strategy of nanotized herbal drugs and their delivery in the treatment of diabetes: present status and future prospects. *J Herb Med.* 2019;17-18:100279.
- [11] DeFronzo RA. Pathogenesis of type 2 diabetes mellitus. *Med Clin North Am.* 2004;88(4):787-835.
- [12] Atkinson MA, Eisenbarth GS. Type 1 diabetes: new perspectives on disease pathogenesis and treatment. *Lancet.* 2001;358(9277):221-229.
- [13] International Diabetes Federation. *IDF Diabetes Atlas.* 10th ed. Brussels: IDF; 2021.
- [14] American Diabetes Association. *Standards of Medical Care in Diabetes.* *Diabetes Care.* 2024;47(Suppl 1).
- [15] Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates. *Diabetes Res Clin Pract.* 2019; 157:107843.
- [16] Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin. *Int J Biochem Cell Biol.* 2009;41(1):40-59.
- [17] Hewlings SJ, Kalman DS. Curcumin: a review of its effects on human health. *Foods.* 2017;6(10):92.
- [18] Cicero AFG, Baggioni A. Berberine and its role in chronic disease management. *Nutrients.* 2016;8(12):1-17.
- [19] Imenshahidi M, Hosseinzadeh H. Berberis vulgaris and berberine. *Phytother Res.* 2019;33(3):504-523.
- [20] Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin. *AAPS J.* 2013;15(1):195-218.
- [21] Kesharwani P, Gorain B, Low SY, et al. Nanotechnology based approaches for anti-diabetic drug delivery. *J Control Release.* 2022; 343:1-21.
- [22] Singh RP, Gangadharappa HV, Mruthunjaya K. Phytosome technology. *Acta Pharm Sin B.* 2017;7(5):557-562.
- [23] Patel VR, Agrawal YK. Nanosuspension: an approach to enhance solubility. *J Adv Pharm Technol Res.* 2011;2(2):81-87.
- [24] Mozafari MR. Liposomes: an overview of manufacturing techniques. *Cell Mol Biol Lett.* 2005;10(4):711-719.
- [25] Pardeike J, Hommoss A, Müller RH. Lipid nanoparticles in drug delivery. *Int J Pharm.* 2009;366(1-2):170-184.
- [26] Sharma G, Sharma AR, Lee SS, et al. Advances in nanocarriers for drug delivery. *Nanoscale Res Lett.* 2016; 11:1-14.
- [27] Ahmad N, Ahmad R, Alam MA, et al. Enhancement of oral bioavailability through nanotechnology. *Drug Deliv.* 2018;25(1):1-14.
- [28] Choudhury H, Gorain B, Pandey M, et al. Recent advances in lipid-based nanocarriers. *Drug Discov Today.* 2019;24(7):1-15.
- [29] Yadav N, Khatak S, Sara UVS. Solid lipid nanoparticles. *Int J Appl Pharm.* 2013;5(2):8-18.

- [30] Singh SK, Lillard JW Jr. Nanoparticle-based targeted drug delivery. *Exp Mol Pathol.* 2009;86(3):215-223.
- [31] Ahmad A, Khan RM, Alkharfy KM. Nanotechnology and diabetes management. *Drug Discov Today.* 2020;25(6):1040-1050.
- [32] Shukla R, Cheryan M. Nanoemulsion-based herbal drug delivery systems. *Pharmaceutics.* 2021;13(8):1221.
- [33] Yallapu MM, Jaggi M, Chauhan SC. Curcumin nanoformulations for biomedical applications. *Drug Discov Today.* 2012;17(1-2):71-80.
- [34] Habtemariam S. Berberine pharmacology and nanotechnology perspectives. *Pharmacol Res.* 2020; 155:104709.
- [35] Naseri R, Farzaei MH, Bahramsoltani R, et al. Medicinal plants and diabetes mellitus. *Front Pharmacol.* 2022; 13:835742.
- [36] Kesharwani P, Jain K, Jain NK. Dendrimers as nanocarriers. *Prog Polym Sci.* 2014;39(2):268-307.
- [37] Patel DK, Prasad SK, Kumar R, Hemalatha S. An overview on antidiabetic medicinal plants. *Asian Pac J Trop Biomed.* 2012;2(4):320-330.
- [38] Singh B, Dahiya D, Kumar A. Green synthesized nanoparticles in biomedical applications. *J Drug Deliv Sci Technol.* 2021; 61:102308.
- [39] Yousaf I. The current and future perspectives of zinc oxide nanoparticles in the treatment of diabetes mellitus. 2024.
- [40] Sharma A, Verma M, Gupta R. Smart antidiabetic nanomedicine: a revolutionized therapeutic approach for treatment of diabetes mellitus. *Bioengineering.* 2025;12(12):1309.