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Review Article

Nanocarrier-based Delivery Technologies for Herbal Medicines in Diabetes Management: A Systematic Review

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Abstract

Diabetes mellitus (DM) is a chronic metabolic disease that has substantial global morbidity and mortality rates. Although there are numerous diabetes treatments that can be performed with herbs, a lack of solubility, low bioavailability, and instability are common factors that limit the use of herbs in diabetes treatment. Nanocarrier-based delivery systems have been proven to enhance the delivery and efficacy of herbal bioactive substances, particularly lipid-based and polymeric nanocarriers. In this systematic review, the effectiveness of using nanocarriers to improve the therapeutic outcomes of diabetes treatment with herbal medicine was examined. A search of the literature was performed systematically in the PubMed, Scopus, Cochrane Library, and ProQuest databases to find studies published between 2016 and 2026. The studies were chosen as per PRISMA guidelines. Original studies on herbal formulations in diabetic models using nanotechnology were also included. Thirty-two studies met the inclusion criteria. Lipid-based and polymeric nanocarriers were shown to significantly improve glycaemic indices, lipid profiles, oxidative stress, and inflammatory indicators. Polymeric systems provided a longer release of drugs, whereas lipid-based solutions enhanced bioavailability and absorption. Mechanistically, these systems exhibited protective effects on pancreatic β-cells and other tissues by regulating key signaling pathways that include AMPK, PI3K/Akt, GLUT-4, and NF-κB. Despite the preclinical nature of most data available, nanocarrier-based herbal delivery systems have promising antidiabetic prospects. To realize successful clinical translation, additional clinical research, and standardization of nanoparticle formulations are needed.

Keywords

Diabetes, herbal medicine, nanotechnology, nanoparticles, hyperglycaemia

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Introduction

Diabetes mellitus (DM) is a chronic metabolic disease that is characterized by an excessively high glucose level. Some of the various types of DM include Type 1, Type 2, gestational diabetes, neonatal diabetes, maturity-onset diabetes of the young, and secondary causes due to endocrinopathies, steroid use, and others.[1] There are two prevalent forms of diabetes: Type 1 and Type 2.[2] Chronic hyperglycemia associated with diabetes leads to organ damage, dysfunction, and failure, especially of the eyes, kidneys, nerves, heart, and blood vessels.[3] Type 1 DM, previously called IDDM, or juvenile diabetes, is characterized by an autoimmune mechanism that destroys beta cells, which usually leads to a total deficiency of insulin.[4] The β cells of the pancreatic islets produce insulin according to the blood glucose levels. Insulin regulates the

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consumption and storage of nutrients by stimulating fat and glycogen production and inhibiting their breakdown. Excessive breakdown leads to a catabolic form of the body due to insulin deficiency. Moreover, gluconeogenesis in the liver is involved in the production of glucose, which leads to hyperglycaemia in insulin resistance or insulin deficiency-induced diabetes.[5] Diabetes is associated with microvascular complications including retinopathy, nephropathy, and neuropathy, as well as several other systemic complications, including foot damage, Alzheimer's disease, and hearing impairment.[2] According to the International Diabetes Federation Diabetes Atlas (11th edition, 2025), an estimated 89.8 million adults in India were living with diabetes in 2024, and this number is projected to increase to 156.7 million by 2050. Globally, the number of adults with diabetes is estimated to rise from 589 million in 2024 to 853 million by 2050.[6]

Allopathic (Western) treatments for diabetes are effective but may be associated with adverse effects, particularly during long-term use, and can be prohibitively costly in some settings, especially in developing countries.[7] Inhibitors of α-glucosidase and pancreatic α-amylase, such as acarbose, miglitol, and voglibose, are some of the medications that can be used to treat diabetes to control blood glucose levels; however, their administration is often limited due to gastrointestinal (GI) side effects, including flatulence, vomiting, diarrhea, and stomach pain.[8] These barriers have led to an increasing number of patients resorting to complementary and alternative medicine (particularly herbal medicine), as they are often perceived to be safer and more natural and holistic remedies with multiple target mechanisms. Recent evidence shows that several herbal solutions can improve the glycaemic and metabolic outcomes of T2DM patients.[8,9]

According to the differences in chemical structure, several phytochemicals exhibiting antidiabetic properties in medicinal plants have been identified and divided into several categories. The key categories of phytochemicals include alkaloids, aromatic acids, carotenoids, coumarins, essential oils, flavonoids, glycosides, phenols, and phenolics, phytosterols, protease inhibitors, saponins, steroids, tannins, terpenes, and terpenoids.[10] The antihyperglycaemic effects of therapy are usually due to the potential of plants to improve the function of pancreatic tissues: To increase insulin secretion or reduce the intestinal absorption of glucose.[9]

Numerous bioactive compounds of herbs demonstrate significant antidiabetic activity but are limited by their poor solubility, low bioavailability, instability in vivo, poor absorption, and difficulties in achieving specific delivery. These limitations might reduce the effectiveness of the therapy and prevent the achievement of a constant therapeutic effect. Hence, it is necessary to develop more advanced drug delivery systems to improve the stability, absorption, and delivery of phytochemicals to the intended site. In this context, nanocarrier delivery systems have proven to be a potential approach that could enhance the therapeutic effect of herbal antidiabetic drugs.[11] Modern medicine has seen a revolution with nanotechnology that has allowed customized drug delivery and good control of drug release times, together with enhanced therapeutic effects.[12] Solid colloidal particles with sizes between 1 and 1,000 nm are known as nanoparticles. They can be used to absorb, encapsulate, or trap active agents.[13] A nanotechnology (nanocarrier)-based delivery system is one of the key formulation research initiatives that enhances human health directly through clinical and commercial development. These nanocarriers could lead to better half-lives, precise release over short or extended periods, and site-specific targeted delivery of medicinal substances.[14] Due to the potential of nanostructured systems to enhance the effects of plant extracts, extended release of bioactive compounds, reduced dose, reduced adverse reactions, and increased activity, the combination of plant extracts with nanotechnology has attracted considerable literature interest.[15] Examples of nanocarriers are nanospheres, nanoliposomes, nanoemulsions, and lipid nanoparticles with solid/liquid networks, that is, solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs). One of the above nanocarriers, nanoliposomes, shows promise for encapsulating both hydrophilic and hydrophobic drugs.[16] Self-emulsifying drug delivery systems (SEDDSs), which are lipid-based systems made of oil, surfactant, and cosurfactant that produce fine oil-in-water emulsions with slight agitation in the GI tract, stand out among cutting-edge nanocarriers.[17] Nanotechnology has provided the possibility to treat diabetes and associated complications with multiple therapy drugs at the same time. Nanomedicine has much potential in becoming a revolutionary approach in the treatment of diabetes.[12]

Although there are growing numbers of studies on this topic, there is still a lack of a detailed review on the therapeutic effectiveness and the underlying mechanisms of nanotechnology-assisted delivery systems for herbal medicines to control diabetes. While various nanocarrier platforms have been studied, most systems studied in antidiabetic research are based on lipids and polymers. Therefore, they are considered the focus of this review. Additionally, wherever applicable, emerging nanocarrier systems are also discussed. There is a lack of comparative studies of the different types of nanocarrier systems and their potential for improving metabolic and glycemic health. In this review, valuable data that are currently available are carefully examined, and gaps in research, and clinical translation are emphasized. A schematic overview of the major nanocarrier-based delivery systems and their key therapeutic pathways in diabetes management is presented in Figure 1.

Materials and Methodology

Literature Search

To locate the relevant literature on the benefits of nanotechnology-based systems in the delivery of herbal drugs in the treatment of diabetes, a thorough, and systematic literature search was carried out in a number of electronic databases, such as PubMed, Scopus, Cochrane Library, and ProQuest.

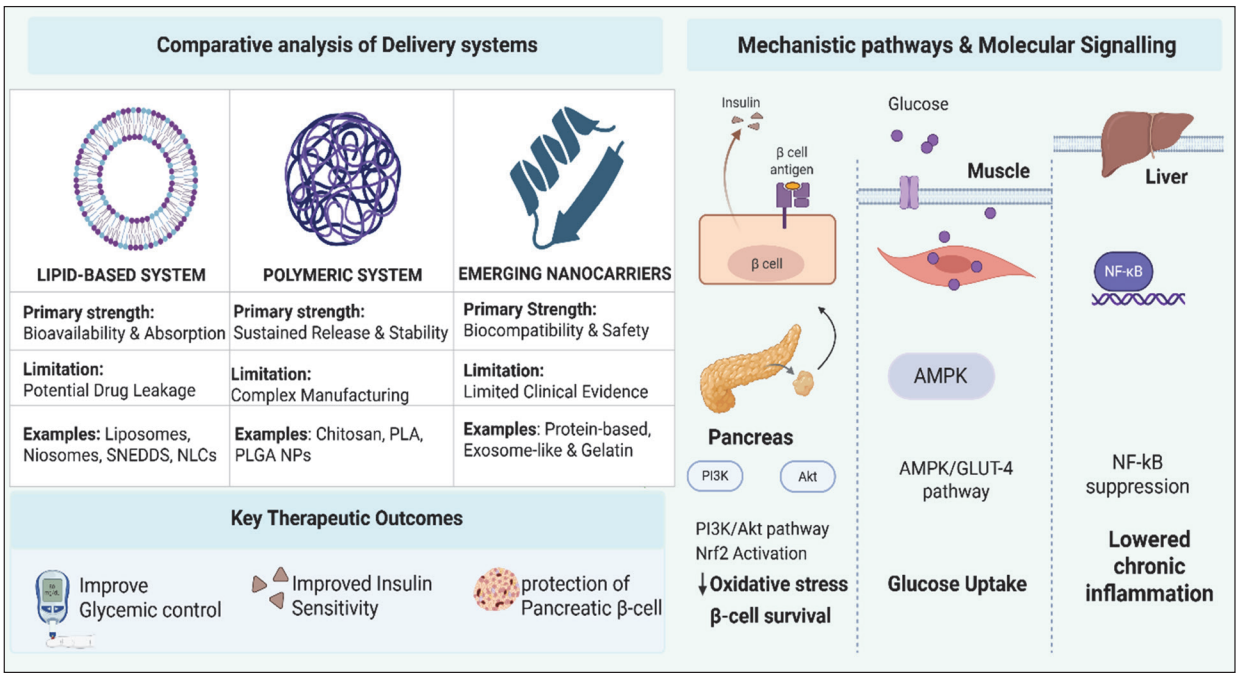

Figure 1. Schematic Representation of Nanocarrier-based Delivery Systems for Herbal Therapies in Diabetes and Key Therapeutic Pathways.

Table 1. Search Strategies.

Databases	Search String	Search Date
PubMed	(((((“Diabetes Mellitus”[Mesh]) OR (“Diabetes Mellitus, Type 2”[Mesh])) OR (“Hyperglycemia”[Mesh])) OR (“Insulin Resistance”[Mesh])) AND (((((“Herbal Medicine”[Mesh]) OR (“Phytotherapy”[Mesh])) OR (“Plants, Medicinal”[Mesh])) OR (“Plant Extracts”[Mesh])) OR (“Phytochemicals”[Mesh]))) AND ((((“Nanoparticles”[Mesh]) OR (“Drug Delivery Systems”[Mesh])) OR (“Liposomes”[Mesh])) OR (“Curcumin”[Mesh]))	03.03.2026
Scopus	TITLE-ABS-KEY ((“Diabetes Mellitus” OR “Diabetes Mellitus, Type 2” OR Hyperglycemia OR “Insulin Resistance”) AND (“Herbal Medicine” OR Phytotherapy OR “Plants, Medicinal” OR “Plant Extracts” OR Phytochemicals) AND (Nanoparticles OR “Drug Delivery Systems” OR Liposomes OR Curcumin))	03.03.2026
Cochrane	((“Diabetes Mellitus” OR “Diabetes Mellitus, Type 2” OR Hyperglycemia OR “Insulin Resistance”) AND (“Herbal Medicine” OR Phytotherapy OR “Plants, Medicinal” OR “Plant Extracts” OR Phytochemicals) AND (Nanoparticles OR “Drug Delivery Systems” OR Liposomes OR Curcumin))	03.03.2026
ProQuest	((“Diabetes Mellitus” OR “Diabetes Mellitus, Type 2” OR Hyperglycemia OR “Insulin Resistance”) AND (“Herbal Medicine” OR Phytotherapy OR “Plants, Medicinal” OR “Plant Extracts” OR Phytochemicals) AND (Nanoparticles OR “Drug Delivery Systems” OR Liposomes OR Curcumin))	07.03.2026

The search strategy for all databases is presented in Table 1. Both free-text and Medical Subject Headings (MeSH) were used as search terms to ensure that every piece of information was addressed. Boolean operators (AND, OR) were used to combine the terms to maximize the search sensitivity and specificity. The search was narrowed down to publications written in English since 2016, as an example was the following keywords: “DM,” “DM, Type 2,” “Hyperglycaemia,” “Insulin Resistance,” AND “Herbal Medicine,” “Phytotherapy,” “Plants, Medicinal,” “Plant Extracts,” “Phytochemicals,” AND “Nanoparticles,” “Drug Delivery Systems,” and “Liposomes.”

PICO Framework

The review question and eligibility criteria are arranged by the population, intervention, comparator, and outcomes (PICO) framework as outlined in Table 2.

Inclusion and Exclusion Criteria

This systematic review is registered with PROSPERO (Registration No. CRD420261373611). A systematic

Table 2. PICO Framework.

PICO Component	Description
Population (P)	Experimental models of diabetes mellitus
Intervention (I)	Herbal medicines, plant extracts, phytochemicals, or herbal bioactive compounds incorporated into nanocarrier systems
Comparator (C)	No predefined comparator
Outcomes (O)	Glycaemic indices, lipid profile, oxidative stress markers, inflammatory mediators, histopathological findings, and molecular signaling pathways

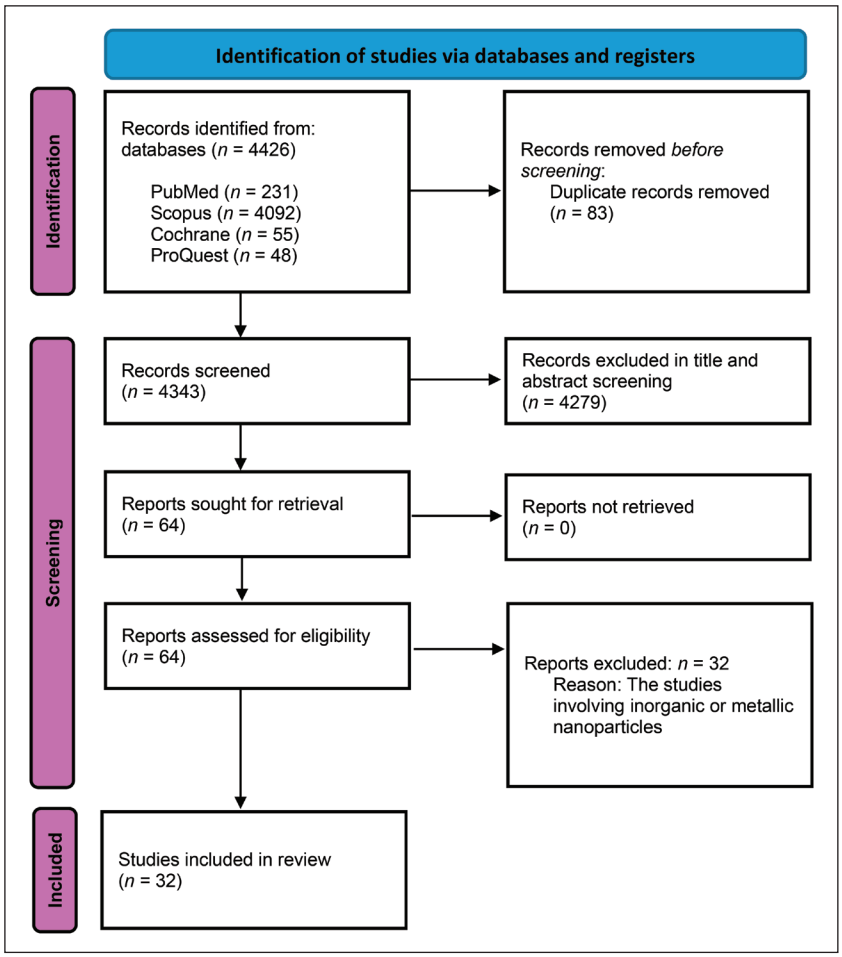

Figure 2. PRISMA Flowchart Showing the Literature Selection Process.

screening procedure was conducted in accordance with the PRISMA 2020 guidelines. The study selection process is shown in Figure 2. To locate relevant articles that explore the nanotechnology delivery of herbal drugs in treating diabetes, predefined inclusion and exclusion criteria were used, as summarized in Table 3.

This review focused on organic nanocarrier systems, as these are the most often used to stabilize and enhance the bioavailability and delivery of herbal bioactive components. Metallic and inorganic nanoparticles were not included because their physicochemical properties, biological activities, and safety profiles differed greatly from those of organic delivery systems and would introduce considerable heterogeneity into the review.

Quality Assessment

Using the SYRCLE risk-of-bias tool, two reviewers independently evaluated the methodological quality of the included in vivo animal studies.[18] The single in vitro study was considered descriptively in the qualitative synthesis but was not included in the formal risk-of-bias assessment because SYRCLE is specifically designed for animal studies. The tool evaluates ten

Table 3. Inclusion and Exclusion Criteria.

Inclusion Criteria	Exclusion Criteria
Original research articles published in peer-reviewed journals	Reviews, editorials, conference articles, and book chapters
Studies evaluating herbal medicines or phytochemicals incorporated into nanocarrier systems for diabetes management	Studies not related to diabetes or herbal medicines
Studies involving organic nanocarriers, including lipid-based, polymeric, protein-based, and biological vesicular systems	Studies involving metallic or inorganic nanoparticles
In vitro and in vivo studies reporting antidiabetic outcomes	Studies without therapeutic efficacy evaluation
Articles published in English (2016–2026)	Non-English publications

domains, including selection, performance, detection, attrition, reporting, and other biases. Any disputes between reviewers were settled through discussion. The ROBVIS tool was used to visualize the risk-of-bias assessment results.

Results and Discussion

Study Selection and Characteristics

The systematic review adhered to PRISMA requirements by employing a systematic screening process.[19] First, databases including PubMed, Scopus, Cochrane Library, and ProQuest were searched, and 4,426 entries were discovered. After eliminating duplicate records (n = 83), title and abstract screening were performed on 4,343 records. These records were excluded (n = 4,279) since they had no information on the applicability of nanotechnology-based herbal medication delivery systems in diabetes. Then, full-text retrieval was requested for 64 reports, and all of them were acquired successfully. After a careful process of eligibility assessment, 32 studies were excluded primarily because they involved metallic or inorganic nanoparticles that were not entirely covered in the predefined inclusion criteria. The qualitative synthesis, which was the basis of this systematic review, eventually included 32 articles.

The articles employed many different experimental designs, including mechanistic biochemical studies and in vivo animal models. Most of the studies employed chemically induced diabetic models, which include alloxan, streptozotocin (STZ) or insulin resistance caused by a high-fat diet. The primary outcomes considered in studies were glycaemic control, lipid metabolism, oxidative stress, inflammatory mediators, and molecular signaling pathways related to glucose homeostasis.

The difference in nanoparticle characterization was an interesting observation across the research included. The most important parameters, such as particle size, zeta potential and encapsulation efficiency (EE), were reported in several studies, but some of them did not provide in depth physicochemical profiling. This gap underscores the need to have uniformity in reporting nanomedicine research to ensure reproducibility and comparability of findings, which may further be useful in clinical applications.

Lipid-based Delivery System

Lipid-based carriers are considered the most suitable technique in the food and nutraceutical sector due to their biocompatibility and biodegradability. Although lipid nanocarriers encompass a wide range of techniques, only selected systems have been successfully commercialized, including nanoemulsions, liposomes, SLNs, NLCs, niosomes, and SEDDSs.[14] Nanoliposomes are promising for encapsulating both hydrophilic and hydrophobic drugs. Niosomes are vesicular systems that have received significant attention due to their increased chemical stability, economic advantage, practicality, and straightforward methods of preparation without the requirement of pharmaceutically unacceptable solvents.[16] SEDDSs are lipid-based formulations of oil, surfactant, and cosurfactant that form fine oil-in-water emulsions in the GI tract, enhancing drug absorption and bioavailability while bypassing first-pass metabolism. Nanoemulsions are stable and transparent lipid-based systems designed to improve the solubility and oral bioavailability of poorly soluble compounds, particularly from herbal extracts.[17]

Lipid-based delivery systems were used in 13 studies, as shown in Table 4, and they showed significant heterogeneity in nanoparticles. The particle sizes ranged from ultrasmall nanoemulsions (12 nm) to larger vesicular systems (494 nm), while the zeta potentials ranged from −42.6 mV to +53.19 mV. These values suggest variable electrostatic stabilization across the formulations; however, zeta potential alone is insufficient to establish formulation stability. The EE varied in the range of 17.4%–98.1% in lipid-based formulations, depending on the type of nanocarriers used and the phytochemical. In particular, a liquid SNEDDS formulation containing curcumin and quercetin encapsulated with the highest efficiency (98.1%) indicates the potential success of some lipid-based formulations for encapsulating hydrophobic bioactive chemicals.

Despite differences in the composition and physicochemical properties of the nanoparticles, most of these lipid-based nanocarriers improved glycaemic control,[16] insulin sensitivity[16,17] and HbA1c, lipid metabolism, such as a reduction in the levels of total cholesterol, triglycerides, and LDL cholesterol, and a subsequent rise in HDL levels.[20]

The use of lipid-based nanocarriers not only resulted in the improvement of glycaemic indices but also led to a controlled reduction in oxidative stress parameters such as

Table 4. Baseline Characteristics of Studies Using Lipid-based Delivery Systems.

Type of System/ Nanocarriers	Encapsulation Efficiency (%)	Zeta Potential (mV)	Particle Size (nm)	Key Features	Ref.
Nanoliposomes	84	−26.6	20–30	↓ FBG, lipid profile and ↑ insulin sensitivity, glucose uptake	16
Niosomes	57	NR	200 ± 0.7	↓ FBG, insulin, total cholesterol, leptin, body weight, visceral fat, liver weight, and pro-inflammatory cytokines; ↑ insulin sensitivity and glucose tolerance	27
SNEDDS	NR	−10.92 ± 0.42	45.93 ± 1.02	↓ Blood glucose levels, insulin resistance, TG, TC, LDL, and MDA levels; ↑ HDL, SOD, and CAT levels; pancreatic islets preserved	17
SNEDDS (nanoemulsion)	NR	NR	12.21	↓ Blood glucose levels; in-silico interaction with α-glucosidase supports a possible α-glucosidase inhibition mechanism.	25
SNEDDS	NR	−32.6	86.48	↓ FBG, insulin resistance, triglycerides, inflammatory cytokines (TNF-α, IL-6) and HOMA-IR; ↑ insulin levels	24
Nanoliposomes	17.4 to 82.94	−22 to −17	179–494	↓ Blood glucose, TAUC; alpha-glucosidase and alpha-amylase were inhibited	28
Phytosomes	NR	NR	NR	↓ blood glucose, TC, TG, lipid profile (LDL), oxidative stress (DPPH scavenging activity ↑); ↑ HDL, body weight	47
Niosomes (vesicular system)	89.12	NR	160	↓ FBG and TC, TG, LDL, ALT, AST, ALP levels; ↑ HDL and body weight; kidney function (creatinine, urea, uric acid); restored pancreas, liver, and kidney	26
Nanoemulsion	91.22	−42.6	36.58	↓ FBG, insulin resistance (HOMA-IR) and serum insulin, TC, TG, AST, ALT, kidney function (creatinine, BUN, uric acid), ↑ glucose tolerance	48
Liquid SNEDDS	98.11 ± 2.72 (curcumin) and 97.25 ± 2.7 (quercetin)	14.8 ± 3.11	63.46 ± 2.12	↓ FBG, TC, TG, LDL, VLDL, MDA levels; ↑ HDL, SOD, CAT, GSH, liver function (SGOT, SGPT, ALP); kidney function (creatinine, BUN); restored pancreas and liver architecture	20
SNEDDS	NR	NR	NR	↓ Insulin resistance (HOMA-IR), inflammatory cytokines (IL-6, TNF-α)	23
Nanoliposomes	88.37 ± 2.28	−20.53 ± 3.57	80	↓ Oxidative stress (ROS, MDA), lipid peroxidation; ↑ mitochondrial function (ATP production, OCR, membrane potential), cell viability, kidney function; restored mitochondrial respiration	22
Solid lipid nanoparticles	75 ± 5	+53.19 ± 3.4	200	↓ FBG, HbA1c, oxidative stress (ROS, MDA, nitrite), apoptotic markers (cytochrome c, caspase-3, caspase-9); ↑ insulin levels, SOD, CAT, GPx, mitochondrial function (complex I, II, IV, V, membrane potential); restored pancreatic, liver, kidney, and muscle histology	21

Note: ↑ = Increase/increased, ↓ = Decrease/decreased, NR = Not reported. All other abbreviations are defined in the list of abbreviations section.

MDA and ROS levels and an increase in the levels of endogenous antioxidants, such as SOD, CAT, and GSH.[20–22] In addition, several studies have shown anti-inflammatory activity, such as the anti-production of pro-inflammatory cytokines (TNF-α and IL-6), which suggests that these formulations not only inhibit chronic inflammation associated with diabetes but also metabolic dysfunction.[23,24]

Significantly, several studies have emphasized the protective outcomes of lipid-based systems on organ structure and functioning. The recovery of pancreatic β-cell health, maintenance of islet structure,[17,25] and liver and kidney compelling indicators were prevalent.[21,26] The therapeutic efficacy was further improved with the help of advanced lipid formulations such as SNEDDS and nanoemulsions, which not only increase the intestinal absorption and bioavailability of phytochemicals but also increase the pharmacological responses at lower doses.

Advanced lipid-based systems, particularly SNEDDSs and nanoemulsions, appear to have higher therapeutic potential than conventional vesicular systems due to their ability to improve the solubility, intestinal absorption, and bioavailability of poorly soluble phytochemicals. However, there are also considerable differences in the formulation characteristics, dosing regimens, animal models used, therapy duration, and outcome measures, so direct comparisons of trials are not easy.

Mechanism of Action of Lipid-based Systems

The action of lipid-based nanocarriers on antidiabetic effects is a complex interaction of molecular and cellular processes, as shown in Table 5. Increased insulin sensitivity and increased glucose uptake are among the primary mechanisms

Table 5. Mechanistic Basis of the Studies Using the Lipid-based System.

Plant Source/Part/Active Component	Experiment Model	Duration/Dose/Route	Mechanism of Action	Ref.
Small cardamom seeds-1,8-cineole	Wistar albino rat	35 days-550 mg/kg-OR	Enhances glucose and lipid metabolism via regulation of G6Pase, G6PD, and HMG-CoA reductase activities	[16]
Vaccinium meridionale (fruit) anthocyanins	High-fat diet-fed C57BL/6J mice	4 weeks-160 µg/mL-OR	Enhances insulin sensitivity and glucose metabolism by activating AMPK/GLUT4 and PPAR-γ signaling, while suppressing inflammatory cytokines and carbohydrate-digesting enzymes	[27]
Passiflora ligularis (leaves)-O-glycosylated flavonoids (isoquercetin, astragalin)	High-fat diet+STZ-induced T2DM CD-1 mice	21 days-250 mg/kg-OR	Enhances GLUT-4 expression and insulin secretion, inhibits carbohydrate-digesting enzymes, and activates MAPK/MEK–ERK signaling with antioxidant effects	[17]
Swietenia mahagoni (seed)-Glycidyl oleate, glycidyl palmitoleate	Alloxan-induced hyperglycaemic male mice (*Mus musculus* L.)	7 days-150 mg/kg-OR	Reduced blood glucose; molecular docking and molecular dynamics support a possible interaction with and inhibition of α-glucosidase	[25]
Moringa oleifera (leaves)-Flavonoids (quercetin, kaempferol, apigenin, luteolin, myricetin)	High-fat diet-induced prediabetic Wistar rat	4 weeks-75, 150, 225 mg/kg-OR	Reduced fasting blood glucose, HOMA-IR, triglycerides, TNF-α, and IL-6, with increased circulating insulin levels	[24]
Murraya koenigii, Coccinia grandis (leaves) and *Senna auriculata* (flower)-Polyphenols, flavonoids	High-fat diet + STZ-induced T2DM male wistar rat	28 days -45-330 mg/kg-OR	Inhibits carbohydrate-digesting enzymes, delaying glucose absorption and reducing postprandial hyperglycaemia	[28]
Crataegus aronia (leaves)-Phenols, flavonoids, alkaloids, tannins	STZ+Nicotinamide-induced diabetic male Wistar albino rats	21 days -150 mg/kg-OR	Enhances insulin secretion and antioxidant activity, inhibiting carbohydrate-digesting enzymes to improve glycaemic and lipid control	[47]
Tradescantia pallida (leaves)-Flavonoids, alkaloids, tannins, terpenoids	Alloxan-induced diabetic Swiss albino mice	28 days -15, 25, 50 mg/kg-OR	Inhibits α-amylase and α-glucosidase, reducing carbohydrate digestion and glucose absorption	[26]
Cinnamomum osmophloeum (leaves)-Cinnamaldehyde, flavonoids, phenolic acids	STZ-nicotinamide-induced T2DM male Wistar rat	4 weeks-20 mg/kg and 60 mg/kg-OR	Reduces oxidative stress and enhances antioxidant activity, improving insulin sensitivity and glucose metabolism	[48]
Curcuma longa (curcumin), quercetin, *Ganoderma lucidum* (whole extract)-curcumin, quercetin, mushroom polysaccharides	High-fat diet + STZ-induced diabetic male Sprague–Dawley rat	28 days-25 mg/kg and 50 mg/kg-OR	Enhances bioavailability and intestinal absorption of curcumin and quercetin, augmenting antioxidant activity and α-glucosidase inhibition to improve glycaemic control	[20]
Petiveria alliacea (leaves)	STZ-induced diabetic male Wistar rats	15 days-50, 100, 200 mg/kg-OR	Reduced insulin resistance and the levels of the pro-inflammatory cytokines IL-6 and TNF-α	[23]
Radix astragali (root)-calycosin	STZ-induced diabetic male Sprague–Dawley rat	4 weeks-60 mg/kg-IP	Restores mitochondrial function and reduces oxidative stress, enhancing cellular energy metabolism, and protecting renal cells	[22]
Ficus religiosa (stem bark)-lupeol	Fructose + STZ-induced diabetic male Wistar rat	28 days-50 mg/kg-OR	Reduces oxidative stress and apoptosis (cytochrome c, caspase-3/9) while enhancing antioxidant activity, improving mitochondrial function, and glycaemic control	[21]

Note: ↑ = Increase/increased, ↓ = Decrease/decreased, NR = Not reported. All other abbreviations are defined in the list of abbreviations section.

that result from the promotion of insulin signaling pathways, such as GLUT-4, AMPK, and PPAR pathways. AMPK is a cellular energy sensor that increases insulin sensitivity, fatty acid oxidation, and glucose uptake to promote metabolic balance. Thus, AMPK activation may contribute to improved glycemic control in diabetes.[27] Lipid-based systems suppress major carbohydrate-digestive enzymes such as α-amylase and α-glucosidase, which lowers intestinal glucose absorption and suppresses postprandial hyperglycaemia. These mechanisms also coordinate hepatic glucose metabolism by adjusting the enzymes glucose-6-phosphatase and glucokinase, leading to reduced gluconeogenesis and increased glycogen synthesis.[20,26,28]

Mitigation of oxidative stress and mitochondrial dysfunction is another important factor. Nanocarriers made of lipids can increase mitochondrial respiration and ATP production and stabilize mitochondrial membrane potential to enhance cellular energy metabolism.[21,22] This is strongly linked with decreased apoptosis, as indicated by the downregulation of the cytochrome c and caspase signaling pathways.

Moreover, these systems have demonstrated anti-inflammatory actions by repressing signaling pathways, including NF-κB and MAPK/ERK, and reducing the production of proinflammatory cytokines.[23] All these processes underscore the potential of lipid-based nanocarriers to concomitantly address numerous pathological pathways underlying diabetes.

Polymeric Delivery System

Polymeric nanoparticles (NPs) have gained significant attention in recent years owing to their nanoscale properties. As drug carriers, they offer controlled release, protect bioactive molecules from degradation, and enhance bioavailability and therapeutic efficiency. Polymer-based nanoparticles effectively carry drugs, proteins, and DNA to target cells and organs. The incorporation of both natural and synthetic polymers, such as chitosan, poly(lactic acid), and hydroxypropyl methylcellulose, contributes to the development of biodegradable systems that support controlled drug release and stability.[29]

There were 15 studies that used polymeric delivery systems (Table 6), and the sizes of the particles used were approximately 10–286 nm. The values of the zeta potential were very different, which was also indicative of the variation in the composition of the polymers and surface modification. The incorporation of phytochemicals into polymeric matrices was generally good, with an EE of up to 96% in some

Table 6. Baseline Characteristics of Studies Using Polymeric Delivery Systems.

Type of System/ Nanocarriers	Encapsulation Efficiency (%)	Zeta Potential (mV)	Particle Size (nm)	Key Features	Ref.
Chitosan nanoparticles	NR	+14.3	200	↓ Blood glucose, lipid profile (TC, TG); ↑ antioxidant activity and cognitive function	30
Chitosan nanoparticles	NR	NR	66–91 nm	↓ Blood glucose, ↑ insulin secretion and restored pancreatic islets	15
Polymeric systems (poly(D, L-lactide) [PLA] nanoparticles)	NR	−28.0	134.4 to 236.8	↓ Hyperglycaemia, lipid peroxidation and dyslipidemia, ↑ insulin secretion, restored antioxidant enzymes (CAT, SOD, GPx), normalized liver enzymes (AST, ALT) and pancreatic β-cell integrity	35
Polymeric systems (chitosan-coated pegagan nanoparticles)	NR	NR	286.2	Suppressed immune-inflammatory responses by ↓ pro-inflammatory cytokines (TNF-α, IFN- γ, and IL-6)	40
Polymeric systems (chitosan and isolated whey protein combination)	96.0	NR	117.4	↓ FBG, HOMA-IR, and ↑ insulin levels and HDL-c and improved pancreatic tissue repair	31
Polymeric systems (polylactic acid [PLA])	NR	NR	NR	↓ Blood glucose, urea, and BUN, urine protein and albumin, body weight, serum protein, albumin, and kidney morphology (better renal function and mitigation of diabetic nephropathy)	36
Polymeric systems (PLGA [poly lactic-co-glycolic acid])	87.52	−8.5 ± 0.53	45 ± 0.15	↓ Blood glucose, HbA1c, oxidative stress levels, DNA damage and genotoxicity, ↑ insulin levels, glucose uptake	32
Polymeric systems (PLGA [poly-lactide-co-glycolide])	NR	NR	58	↓ Blood glucose levels, ROS production, DNA damage and fragmentation, nuclear condensation, cell death, and ↑ p53 and PARP-1 protein expression	39

(Table 6 continued)

(Table 6 continued)

Type of System/ Nanocarriers	Encapsulation Efficiency (%)	Zeta Potential (mV)	Particle Size (nm)	Key Features	Ref.
Polymeric systems (chitosan nanoparticles)	NR	−55	81–83	↓ blood glucose, MDA level, fructosamine, TNF-α, IL-1beta, IL-6, IL-4 and beta-cell damage; ↑ SOD, CAT, GSH, insulin, and C-peptide levels; pancreatic islet size, cellularity, and insulin secretion restored	[34]
Polymeric systems (chitosan nanoparticles)	NR	15.36	50	↑ α-amylase and α-glucosidase inhibition and cell viability; ↑ Bcl-2; ↓ apoptosis, ROS production, Bax, and NF-κB activation	[41]
Polymeric systems (chitosan nanoparticles)	84.00 ± 6.40	NR	10–20	↓ FBG, liver enzymes (AST and ALT), oxidative stress (MDA) and CDKN1A, NF-κB, TP53; ↑ insulin, SOD, and GSH levels, and FGF7; pancreatic regeneration	[38]
Polymeric systems (chitosan nanoparticle)	43.1	NR	39.9	↓ FBG, TC, TG, LDL, HOMA-IR, oxidative stress (MDA), apoptosis (caspase-3); ↑ PDX1, insulin, HDL, SOD, and GSH levels; and beta-cell regeneration	[49]
Polymeric systems (polylactic-co-glycolic acid [PLGA])	92	−38	168 ± 0.01	↓ body weight, FBG, insulin resistance (HOMA-IR), glucose intolerance, and hepatic fat accumulation, lipid profile (TG, LDL)	[37]
Polymeric systems (chitosan nanoparticles)	75.7	+47.2	50	↓ FBG, HbA1c, insulin resistance (HOMA-IR), oxidative stress (MDA), liver enzymes (ALT, AST), inflammation (IL-6, IL-23); ↑ insulin sensitivity (QUICKI, HOMA-β, DI); ↓ lipid profile (TC, TG, LDL, VLDL, FFA), ↑ HDL; ↑ antioxidant capacity (GSH), liver glycogen; restored pancreatic islets	[33]
Polymeric systems (PLGA [poly (lactic-co-glycolic acid)] nanoparticles)	NR	NR	NR	↓ lipid peroxidation (MDA) and fluorescence product; ↑ body weight and pancreatic gland weight	[50]

Note: ↑ = Increase/increased, ↓ = Decrease/decreased, NR = Not reported. All other abbreviations are defined in the list of abbreviations section.

formulations. Polymeric systems demonstrated antidiabetic effects in a variety of experimental models.

There were also consistent improvements in blood glucose levels, insulin resistance, and glycated,[15,30–33] as well as in insulin-secreting islet morphology and cellularity restoration,[34] indicating regenerative properties in pancreatic tissue.

In addition to glycemic control, polymeric nanocarriers were found to have a considerable improvement in lipid metabolism, liver activity, and renal parameters.[35–37] A few studies have attenuated diabetic nephropathy, which is characterized by a reduction in proteinuria, better kidney morphology, and reduced fibrosis-related markers.[32,36]

These results suggest the possibility of polymeric systems to manage not only metabolic dysfunction but also complications associated with diabetes. Additionally, NPs were highly antioxidant and cytoprotective. Decreases in oxidative stress indicators,[34,38] DNA damage, and apoptosis were always observed, as well as increased antioxidant enzyme activity.[39] Such systems also showed immunomodulatory effects by inhibiting pro-inflammatory cytokines[33,40] and modulating immune-signaling pathways.[38,41]

Mechanism of Action of Polymeric Systems

The therapeutic effect of polymeric nanocarriers is, in large part, credited to the capacity to deliver sustained drug release, as well as regulate a variety of intracellular signaling pathways (Table 7). One of the mechanisms is the PI3K/Akt signaling pathway, which enhances insulin sensitivity and promotes β-cell survival by increasing glucose absorption. The PI3K/Akt pathway is a crucial regulator of insulin signaling and regulates processes such as glycogen synthesis, glucose uptake, and cell survival. The activation of this pathway has a positive impact on metabolic regulation and β-cell function in diabetes, while its dysfunction has a detrimental effect on insulin resistance and hyperglycaemia.[30,33] Antioxidant defense pathways are also triggered by polymeric systems, especially via Nrf2 signaling,[33] resulting in the upregulation of antioxidant enzymes and a decrease in cellular damage caused by ROS. This antioxidant effect is essential, as it prevents β-cell dysfunction and maintains cell integrity.

Moreover, the systems suppress the apoptotic pathway by regulating the proteins Bcl-2, Bax, and caspases, which

Table 7. Underlying Mechanism of the Studies Using the Polymeric System.

Plant Source/Part/Active Component	Experiment Model	Duration/Dose/Route	Mechanism of Action	Ref.
Trifolium alexandrinum (leaves)-quercetin and Biochanin-A	High-fat diet-fed STZ-Wistar albino rats	35 days-50 mg/kg-OR	Neuroprotection via PI3K/Akt/GSK-3β pathway modulation, gene expression regulation, and suppression of proinflammatory mediators (TNF-α, NF-κB)	30
Balanites aegyptiaca (fruit)-elaidic acid, linoleic acid, hexadecanoic acid, oleic acid, and stearic acid	STZ-induced Sprague–Dawley rats	8 weeks-50 mg/kg, 100 mg/kg-OR	Antidiabetic effects via antioxidant and anti-inflammatory activity, enhanced insulin secretion and β-cell regeneration	15
Tinospora cordifolia (stem)-alkaloids	STZ-induced T2DM Wistar rat	28 days-5 mg/kg, 10 mg/kg-OR	Reduced hyperglycaemia, lipid peroxidation, and dyslipidaemia; increased circulating insulin and antioxidant enzyme activities (CAT, SOD, and GPx); normalized AST and ALT; and preserved pancreatic β-cell integrity	35
Centella asiatica (whole plant)-madecassoside	STZ-induced chronic diabetic BALB/c mice	28 days-20 mg/kg, 30 mg/kg, 40 mg/kg-OR	↓ Relative numbers of CD4+TNF- α +, CD8+TNF-α+, CD4+IFN-γ+, CD8+IFN-γ+, and IL-6+ cells in splenic cell suspensions	40
Tamarindus indica (seed)-tamarind trypsin inhibitor	Diet-induced insulin-resistant Wistar rat	10 days-12.5 mg/kg-OR	Inhibits trypsin activity, modulating glucose metabolism, improving insulin sensitivity and β-cell function	31
Tinospora cordifolia (stem)	STZ-induced diabetic nephropathy in Wistar albino rat	4 weeks-10 mg/kg-OR	Attenuates oxidative stress and inflammation, downregulating AGE–RAGE pathway genes to reduce renal fibrosis and extracellular matrix accumulation	36
Curcuma longa (rhizome)-curcumin	Alloxan-induced male Swiss albino mice	20 days-12.5–25 mg/kg-OR	Enhances insulin secretion and GLUT-4–mediated glucose uptake, reduces oxidative stress, and modulates apoptosis and DNA repair pathways to restore mitochondrial function and cellular integrity	32
Curcuma longa (rhizome)-curcumin	Alloxan-induced Swiss albino mice	12 days-12.5 and 25 mg/kg-OR	Activates PARP-1/p53-mediated DNA repair, reduces oxidative stress and genotoxicity, and restores cellular integrity and glucose homeostasis	39
Balanites aegyptiaca (seed)-fatty acids (oleic, lauric, myristic), amino acids, minerals	STZ-induced male Sprague–Dawley rat	8 weeks-10 mg/kg, 20 mg/kg-OR	Reduces oxidative stress and inflammation, promoting β-cell regeneration and restoring insulin secretion	34
Nigella sativa (seed)-thymoquinone	STZ-induced diabetes RIN-5F cell line	24 hrs-20, 40, 60, 80, 100 µg/ml	Inhibits carbohydrate-digesting enzymes and NF-κB–mediated apoptosis, protecting pancreatic β-cells	41
Clitoria ternatea (flower)-polyphenols, flavonoids	STZ-induced diabetic male Sprague–Dawley rat	28 days-400 mg/kg-OR	Antioxidant and anti-inflammatory effects, promoting β-cell regeneration and insulin secretion via modulation of FGF7, SOD, GSH, and suppression of NF-κB, CDKN1A, and TP53	38
Curcuma longa (rhizome)-curcumin	STZ-induced diabetic male Sprague–Dawley rat	30 days-100 mg/kg-OR	Reduction of oxidative stress (MDA, SOD, GSH) and inhibition of beta-cell apoptosis (caspase-3, PDX1), leading to improved insulin secretion	49
Eucalyptus tereticornis (leaves)-triterpenes (ursolic acid, oleanolic acid, ursolic acid lactone)	High-fat diet-induced obese male C57BL/6J mice	15 days-214 mg/kg-OR	Regulates gluconeogenesis and lipid metabolism via PEPCK/G6PC1 suppression and AMPK/ACC modulation, improving metabolic homeostasis	37
Nigella sativa (seed)-thymoquinone	STZ+nicotinamide-induced diabetic male Wistar albino rat	6 weeks-50 mg/kg-OR	Activates antioxidant and anti-inflammatory pathways, suppressing NF-κB and enhancing Nrf2 and PI3K/Akt signaling to improve glycaemic and metabolic control	33
Trigonella foenum graecum (seed)	Alloxan-induced diabetic male albino mice	15 days-15 mg/kg-OR	Reduces oxidative stress and lipid peroxidation, protecting pancreatic β-cells and improving pancreatic function	50

Note: ↑ = Increase/increased, ↓ = Decrease/decreased. All other abbreviations are defined in the list of abbreviations section.

suppress cell death and stimulate tissue regeneration.[41] It inhibits the release of pro-inflammatory cytokines and restores metabolic balance by inhibiting NF-κB signaling and JAK/STAT signaling pathways. NF-κB is an important molecule in the inflammatory response that is chronically activated, which causes insulin resistance, malfunction of β-cells, and the development of diabetes-related issues. Hence, NF-κB signaling inhibition might be beneficial for decreasing inflammatory metabolic diseases in diabetes.[33,40]

Furthermore, polymeric nanocarriers regulate hepatic glucose production and lipid metabolism by modulating enzymes such as PEPCK and G6PC1, as well as pathways such as AMPK and ACC.[37] In some cases, inhibition of AGE–RAGE signaling was observed, contributing to reduced fibrosis and protection against diabetic complications such as nephropathy.[36]

Overall, polymeric systems provide a comprehensive therapeutic strategy by integrating glycaemic control with antioxidant,[15,39] anti-inflammatory,[15,40] anti-apoptotic,[32] and regenerative effects.[15]

Emerging Nanocarrier System

New nanocarrier systems are considered a novel method of delivery of herbal drugs, particularly biological vesicular nanocarriers, including protein-based nanoparticles and exosome-like nanovesicles. Limited but encouraging evidence for these systems was found in the current evaluation. A biological vesicular system prepared using tangerine peel contained a high quantity of polyphenols, flavonoids, alkaloids, and essential oils, which exhibited good physicochemical characteristics, including a stable zeta potential (−12.26 mV) and nanoscale solutions (~172 nm), thus making it suitable for use as a drug carrier.[42] Equally, protein-based nanocarriers such as whey protein-based systems and gelatin nanoparticles showed great EE (up to ~89%) and an appropriate range of particle sizes, indicating their potential to enhance the stability and bioavailability of phytoconstituents.[43–45] These systems presented significant therapeutic effects in diabetic animals, including improved glycemic control,[44,45] reduced insulin resistance,[42] altered lipid metabolism, and reduced oxidative stress and inflammatory biomarkers.[43,45] Mechanistically, their effects were linked to the control of important metabolic pathways, such as GLUT2, AMPK, PPAR-γ, and PEPCK signaling.[42,45] Although these are promising outcomes, the number of studies is still low, meaning that a research gap exists and that further research is required to prove their therapeutic value in the management of diabetes.

Emerging nanocarrier systems have demonstrated promising therapeutic applications, such as protein-based and biological systems, which are also biocompatible. However, the evidence that is available is still limited in lipid-based and polymeric systems, and much more work is required to confirm their safety, efficacy, and clinical utility.

Lipid-based, polymeric, and developing nanocarrier technologies all have specific advantages in the delivery of herbal antidiabetic medicines.[14,29,43–45] Polymeric nanocarriers provide enhanced formulation stability and drug release,[29] while lipid-based nanocarriers are particularly beneficial for enhancing the solubility, bioavailability, and intestinal absorption of poorly soluble phytochemicals.[14,16,17] Emerging nanocarriers have been demonstrated to have therapeutic potential and are showing promising biocompatibility.[42–45] Although some promising preclinical results have been found, standardized comparative investigations and further clinical validation are still needed because of the variations in formulation properties, safety evaluation, and clinical translational readiness.[11,14,29,45]

A comparison of the major nanocarrier platforms highlights their respective advantages, limitations, and potential applications in diabetes management. While they may not be very stable and are not as well controlled for the release of drugs over time, lipid-based systems are particularly useful for enhancing the bioavailability, intestinal absorption, and solubility of poorly water-soluble phytochemicals, such as liposomes, niosomes, nanoemulsions, and SNEDDS.[14,16,17] However, polymeric nanocarriers such as chitosan-, PLA-, and PLGA-based nanoparticles have more advantages with respect to formulation stability, protection of encapsulated bioactive compounds, and controlled or sustained drug release for longer-term therapeutic applications.[29,46] The production difficulties and formulation complexity, however, in polymeric systems may be higher. Thus, the desired therapeutic effect and the physical and chemical characteristics of the herbal component need to be considered in selecting the nanocarrier system.[14,34]

Risk-of-bias Assessment

The risk-of-bias assessment of the 31 included in vivo animal studies (Figure 3) showed that the overall methodological quality was moderate, with most domains rated as unclear risk because of insufficient reporting of randomization and blinding procedures. Most of the included animal studies were judged to have a low risk for baseline characteristics, incomplete outcome data, and other biases. Selective outcome reporting was generally judged to be at low risk based on the available information, although this assessment was limited by incomplete methodological reporting in several studies. Methodological reporting, sequence generation, allocation concealment, random housing, blinding of caregivers, and random outcome assessment were mainly assessed as unclear risk because of inadequate reporting. The single in vitro study was not included in the SYRCLE/ROBVIS risk-of-bias assessment because a formal in vitro risk-of-bias assessment was not prespecified for a single included cell line study.

Overall, the certainty of the available evidence was considered low to moderate. Although the included studies

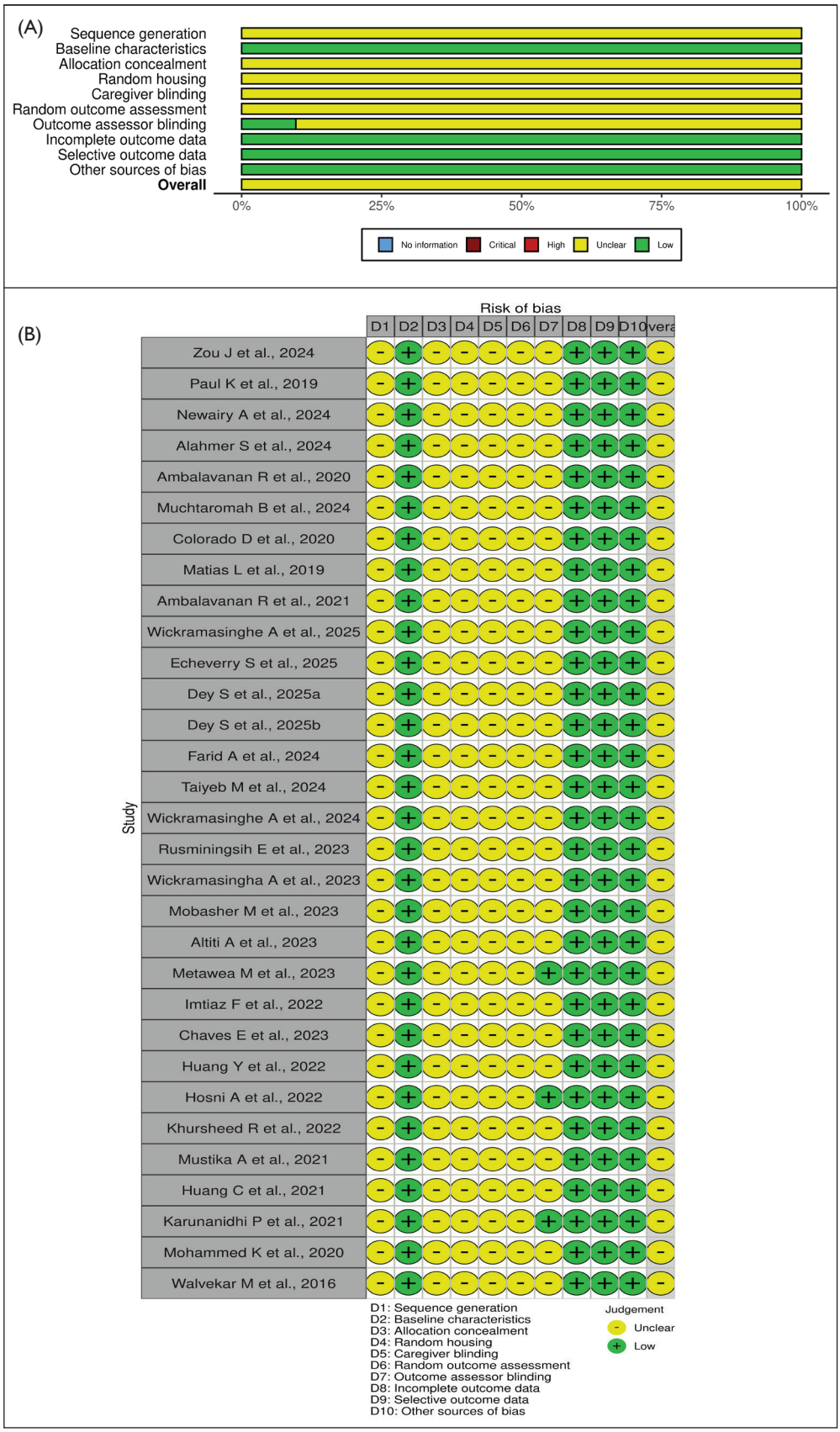

Figure 3. Risk-of-bias Assessment of the Included Animal Studies Using the SYRCLE Risk-of-bias Tool: (A) Risk-of-bias Summary, (B) Risk-of-bias Traffic Light Plot.

consistently demonstrated beneficial effects of nanocarrier-based herbal formulations, confidence in these findings is limited by methodological heterogeneity, variability in animal models, nanocarrier formulations, intervention protocols, outcome measures, and the predominance of preclinical evidence. Therefore, the findings should be interpreted with caution until supported by well-designed clinical studies.

Limitations

This review has several limitations. Only English-language studies were taken into consideration, which led to the introduction of language bias. The evidence base is mostly preclinical with minimal clinical validation. There was considerable heterogeneity in the formulation, characterization, and outcome measures of nanoparticles, which precluded quantitative meta-analysis. Publication bias could not be formally assessed because the included studies were highly heterogeneous with respect to experimental models, nanocarrier formulations, interventions, and outcome measures, precluding quantitative meta-analysis and formal publication bias analyses such as funnel plots or small-study-effects assessment. Therefore, the possibility of publication bias cannot be excluded. In addition, because only one in vitro study met the inclusion criteria, a formal risk-of-bias assessment was not performed for the in vitro evidence. These limitations reduce the overall certainty of the available evidence and should be considered when interpreting the findings.

Future Perspectives

Future studies should address the regulatory and translational issues related to herbal formulations based on nanocarriers in addition to proving their medicinal efficacy. To move these systems forward in clinical development, standardized production procedures, repeatable nanoparticle characterization (particle size, zeta potential, EE, stability, etc.), and quality control of the herbal raw materials are necessary. The intricate makeup of plant extracts and the lack of standardized regulations for nanoherbal products may additionally hinder regulatory approval. Additionally, long-term safety, pharmacokinetic, biodistribution, and regulatory studies will need to be performed in depth for clinical translation for the development of safe and effective nanoherbal therapeutics. Hence, the successful application of nanocarrier-based herbal medicines from laboratory research to the clinic will need to be a collaboration of researchers, industries, and regulatory agencies.

Conclusion

In conclusion, nanotechnology-based delivery systems provide an exciting solution to enhance the therapeutic effect of herbal medicines in the management of diabetes. Although lipid-based systems are able to improve bioavailability and polymeric systems offer sustained release, the current evidence is mostly preclinical. To be effectively integrated into clinical practice in clinics, they will require addressing methodological limitations and moving to a phase of clinical validation.

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Authors' Contribution

All authors contributed significantly to the conception and design of the study, as well as to the acquisition, analysis, and interpretation of data. They were actively involved in drafting the manuscript or revising it for critical intellectual content, approved the final version for publication, and consented to its submission to the journal. In addition, all authors accept responsibility for the integrity and accuracy of the work. Authorship complies with the criteria established by the International Committee of Medical Journal Editors (ICMJE).

Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Data Availability Statement

All the data is available with the authors and shall be provided upon request.

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Informed Consent

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Sustainable Development Goals (SDGs)

This research promotes better methods of treating diabetes as per Sustainable Development Goal (SDG) 3 (Good Health and Well-being) through enhancement of the therapeutic effect of herbal drugs. In addition, it facilitates SDG 9 (Industry, Innovation and Infrastructure) by offering a scientific foundation for

the creation of new drug delivery systems based on nanotechnology to enhance therapeutic approaches and encourage innovation. The research is also informed by evidence-based knowledge about nanocarrier systems and their contribution to enhancing drug effects, which is a part of SDG 4 (Quality Education).

Use of Artificial Intelligence-assisted Tools

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Supplemental Material

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List of Abbreviations

ACC – Acetyl-CoA Carboxylase
AGE–RAGE – Advanced Glycation End Products–Receptor for Advanced Glycation End Products
Akt – Protein Kinase B
ALP – Alkaline Phosphatase
ALT – Alanine Aminotransferase
AMPK – AMP-Activated Protein Kinase
AST – Aspartate Aminotransferase
ATP – Adenosine Triphosphate
Bax – Bcl-2-associated X protein
Bcl-2 – B-cell lymphoma 2
BUN – Blood Urea Nitrogen
CAM – Complementary and Alternative Medicine
CAT – Catalase
DI – Disposition Index
DM – Diabetes Mellitus
DPPH – 2,2-diphenyl-1-picrylhydrazyl
ERK – Extracellular Signal-Regulated Kinase
FBG – Fasting Blood Glucose
G6 Pase – Glucose-6-Phosphatase
G6PD – Glucose-6-Phosphate Dehydrogenase
GLUT-2 – Glucose Transporter Type 2
GLUT-4 – Glucose Transporter Type 4
GPx – Glutathione Peroxidase
GSH – Reduced Glutathione
HbA1c – Glycated Hemoglobin
HDL – High-Density Lipoprotein
HOMA-β – Homeostatic Model Assessment of β-cell Function
HOMA-IR – Homeostatic Model Assessment of Insulin Resistance
IDDM – Insulin-Dependent Diabetes Mellitus
IDF – International Diabetes Federation
IL-1β – Interleukin-1 beta
IL-6 – Interleukin-6
JAK/STAT – Janus Kinase/Signal Transducer and Activator of Transcription
LDL – Low-Density Lipoprotein
MAPK – Mitogen-Activated Protein Kinase
MDA – Malondialdehyde
MeSH – Medical Subject Headings
MODY – Maturity-Onset Diabetes of the Young
NF-κB – Nuclear Factor Kappa B
NLCs – Nanostructured Lipid Carriers
NPs – Nanoparticles
Nrf2 – Nuclear Factor Erythroid 2–Related Factor 2
OCR – Oxygen Consumption Rate
OR – Oral Route
PARP-1 – Poly (ADP-ribose) Polymerase 1
PEPCK – Phosphoenolpyruvate Carboxykinase
PI3K – Phosphoinositide 3-Kinase
PLA – Poly (Lactic Acid)
PLGA – Poly (Lactic-co-Glycolic Acid)
PPAR-α – Peroxisome Proliferator-Activated Receptor Alpha
PPAR-γ – Peroxisome Proliferator-Activated Receptor Gamma
PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QUICKI – Quantitative Insulin Sensitivity Check Index
ROS – Reactive Oxygen Species
SEDDS – Self-Emulsifying Drug Delivery Systems
SLNs – Solid Lipid Nanoparticles
SNEDDS – Self-Nanoemulsifying Drug Delivery Systems
SOD – Superoxide Dismutase
STZ – Streptozotocin
TAUC – Total Area Under Curve
TC – Total Cholesterol
TG – Triglycerides
TNF-α – Tumor Necrosis Factor-alpha