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Review Article

Global Trends and Burden of Diabetes Mellitus (DM): A Comprehensive Review of Epidemiology, Risk Factors, Health Disparities, and Future Projections

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Abstract

Background: Diabetes mellitus (DM) represents one of the most pressing global public health challenges, with rapidly increasing prevalence, substantial morbidity and mortality, and profound socioeconomic consequences. The rising burden of diabetes is driven by demographic transitions, lifestyle changes, urbanization, and persistent health inequities, particularly in low- and middle-income countries.

Objective: The worldwide health problem known as diabetes mellitus (DM) affects people through its growing prevalence which leads to severe health problems and death while creating major economic difficulties for society. The increasing diabetes burden results from demographic shifts and changes in physical activity patterns and the development of cities and the ongoing existence of health disparities which mainly affect people in low- and middle-income nations.

Methodology: The review aims to create a complete summary of existing research which examines diabetes mellitus (DM) global patterns and its impact on different regions and identifies primary risk factors and assesses the disease impact and current clinical trials and patent research and future preventive methods and treatment strategies. The researchers performed a narrative literature review by utilizing major scientific databases which included PubMed and Scopus and Web of Science together with official global health reports from the World Health Organization and International Diabetes Federation and Global Burden of Disease study. The researchers examined and combined peer-reviewed articles together with epidemiological studies and clinical trial data and pertinent patent documents which had been published in the last few years.

Results: Diabetes affects people in all parts of the world but shows different patterns of occurrence and death rates and life years lost to disability. People in low-resource areas experience higher disease burden because they face two main problems: they receive medical treatment too late and they cannot afford healthcare services and they lack economic resources. People who develop this condition face key risk factors which include obesity and lack of physical activity and bad eating habits and their increasing age and their genetic risk factors.

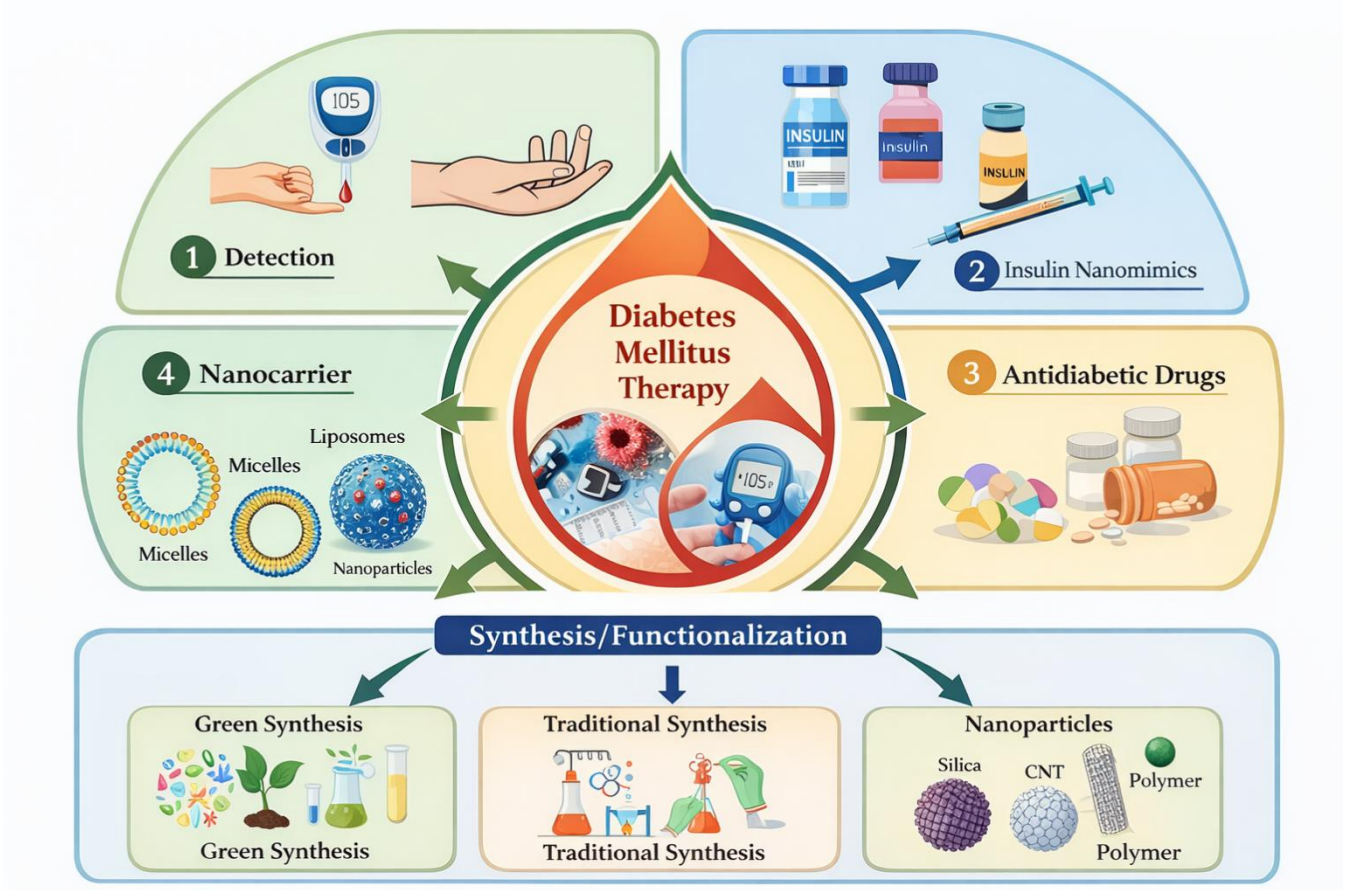
Conclusion: DM poses a substantial and escalating global health burden. Addressing its impact requires coordinated public health policies, equitable healthcare delivery, continued clinical innovation, and sustained research efforts to improve outcomes and reduce disparities worldwide.

Keywords: *Diabetes mellitus; global burden; epidemiology; risk factors; health disparities; clinical trials; patents; future perspectives.*

HIGHLIGHTS OF REVIEW ARTICLE

- The global prevalence of diabetes mellitus is rapidly increasing, driven by urbanization, aging populations, and lifestyle changes, with a disproportionate burden in low- and middle-income countries.
- Type 2 diabetes accounts for the majority of cases, while type 1 and gestational diabetes are also rising, contributing significantly to overall disease burden and long-term complications.
- Major risk factors such as obesity, physical inactivity, unhealthy diet, and genetic susceptibility play a critical role, alongside significant socioeconomic and regional health disparities.
- Nanocarrier-based drug delivery systems offer a promising approach for diabetes treatment by enhancing drug stability, targeted delivery, and therapeutic efficacy, thereby improving glycemic control and patient outcomes.
- Emerging advancements, including clinical trials, patent innovations, and nanocarrier-based drug delivery systems, offer promising future strategies for improved diabetes management and outcomes.

GRAPHICAL ABSTRACT



Graphical Abstract: Schematic overview of global trends and burden of diabetes mellitus (DM), highlighting epidemiology, key risk factors, health disparities, disease burden, and emerging therapeutic strategies including nanocarrier-based drug delivery systems.

1. INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder which results in permanent high blood sugar levels due to defective insulin production or insulin function or both of these factors and it has become one of the most formidable global public health challenges of the twenty-first century[1]. The existing global diabetes situation shows continuous unsafe growth of diabetes cases which affects all age groups and all regions because urbanization progresses and people adopt less active lifestyles and they eat less healthy food and the population ages and obesity rates and metabolic syndrome rates increase[2-3]. Diabetes used to be seen as a condition which affected only high-income nations but now the disease impacts more people in low- and middle-income countries because these countries lack sufficient healthcare systems and proper diagnostic methods and effective treatment programs. Diabetic disease affects hundreds of millions of people worldwide with type 2 diabetes mellitus being the most common form of the disease while type 1 diabetes and gestational diabetes cause significant health issues for children and adolescents and pregnant women[4]. The global diabetes burden is further compounded by high rates of undiagnosed disease, delayed initiation of therapy, and poor glycemic control, which together produce a broad range of acute and chronic complications that include cardiovascular disease, nephropathy, neuropathy, retinopathy, and higher risk of infectious diseases, which together result in increased rates of early death and disability-adjusted life years and rising healthcare expenses. The worldwide distribution of diabetes shows significant differences between regions because Southeast Asia, the Western Pacific, the Middle East, and Africa show fast rising diabetes rates, while high-income regions experience increasing diabetes-related health problems that stem from their aging citizens and extended disease duration, which creates substantial health disparities that result from differences in socioeconomic status and healthcare accessibility and the effects of government policies[5-6].

The historical treatment methods for diabetes required patients to control their eating habits and their daily activities until scientists discovered insulin therapy which changed how doctors treated type 1 diabetes and severe hyperglycemia. The introduction of oral antidiabetic medications which included sulfonylureas and biguanides led to enhanced diabetes treatment methods that established better blood sugar management results for type 2 diabetes patients[7-8]. The introduction of new drug classes to diabetes treatment during the past 30 years has transformed the field because glucagon-like peptide-1 receptor agonists and sodium–glucose cotransporter-2 inhibitors and

dipeptidyl peptidase-4 inhibitors provide better blood sugar control and heart and kidney health advantages[9]. Concurrently, advancements in medical technology, including continuous glucose monitoring systems, insulin pumps, and digital health platforms, have enhanced personalized care and patient self-management; however, access to these innovations remains uneven across regions, reinforcing existing inequities[10].

International organizations including the World Health Organization and International Diabetes Federation and national regulatory bodies establish evidence-based frameworks which guide diabetes prevention and diagnosis and treatment and complication screening while they monitor antidiabetic drug safety and effectiveness through regulatory procedures and post-marketing monitoring[11]. A complete review of existing research stands as an immediate need because persistent health inequalities and changing treatment methods and an expanding worldwide health crisis require it. The present review aims to evaluate global DM trends and its associated burden through the analysis of epidemiological data which includes regional and socioeconomic differences and major risk factors and disease burden metrics while the review examines ongoing clinical trials and patent developments to showcase new medical and technological progress. Furthermore, this review addresses key gaps in detection, treatment, and healthcare delivery, and discusses current challenges, limitations, and future perspectives to inform research priorities, clinical practice, and policy development, ultimately contributing to more effective, equitable, and sustainable strategies for mitigating the global impact of DM[12-13].

The article shows how different countries of the world experience diabetes according to their geographical location and their population growth. The study shows that urbanization and population aging and sedentary lifestyles and unhealthy dietary habits have created a major increase in diabetes cases which affects low- and middle-income countries more than other regions. The review provides a complete understanding of the global diabetes situation because it shows how type 2 diabetes predominates while type 1 diabetes and gestational diabetes show emerging health problems. The article assesses how the world diabetes epidemic spreads through its main risk factors which show different effects on various population groups. The study shows that diabetes mellitus develops through multiple pathways which healthcare profession need to understand because metabolic factors and genetic factors and environmental factors and behavioral factors such as obesity and inactivity and poor diet and socioeconomic status affect its development. Lastly, this review provides insights into emerging advancements in nanocarriers and future perspectives in diabetes management, including ongoing clinical trials, patent developments, and innovative therapeutic strategies such as nanocarrier-based drug delivery systems. It also discusses current challenges and limitations in detection, treatment, and healthcare delivery, while emphasizing the need for integrated, patient-centered approaches.

2. GLOBAL EPIDEMIOLOGY AND TRENDS OF DIABETES MELLITUS

The worldwide prevalence and incidence of diabetes mellitus has become one of the fastest expanding noncommunicable diseases which affects people of all ages and all parts of the world. The rapid growth of current urban areas together with the increasing elderly population and the widespread adoption of inactive living and poor eating patterns constitutes the main reasons behind this rising trend[13-15]. The global distribution of diabetes shows significant differences between regions because low- and middle-income countries lack adequate medical facilities and their populations experience delays in diabetes diagnosis. The increasing age of diabetes onset toward younger people especially with type 2 diabetes will create more extended periods of illness according to research findings[16]. A detailed overview of prevalence, incidence, and temporal trends of DM is summarized in **Table 1**.

2.1. Prevalence, Incidence, and Temporal Trends

Diabetes mellitus has developed into the quickest expanding noncommunicable disease throughout the world because its occurrence and new cases keep increasing without interruption since the past several decades. Global estimates show that diabetes has affected more people than before because population growth and demographic aging and urbanization and changes in eating habits and physical activity have combined to create this situation[17]. The analysis of time-based patterns shows that diabetes has spread faster in developing regions than it has in developed areas because of differences between the two regions in their medical system availability and their ability to identify diabetes and their methods for preventing the disease. The overall diabetes prevalence continues to grow because more people with diabetes now live longer even though some high-income countries have begun to show steady rates of new cases. Notably, the onset of diabetes is occurring at younger ages, particularly for type 2 diabetes, leading to longer disease duration and a higher lifetime risk of complications. These trends collectively underscore the escalating global burden of diabetes and the urgent need for strengthened surveillance and preventive interventions[18-19].

2.2 Type-Specific Epidemiological Patterns

Different types of diabetes mellitus exhibit distinct patterns of epidemiological spread. Type 2 diabetes mellitus represents the most common diabetes form which links to several preventable risk factors that include obesity and physical inactivity and poor dietary practices and socioeconomic disadvantages. The disease shows its highest prevalence within urban populations who experience fast-paced changes to their traditional ways of life. The incidence of Type 1 diabetes mellitus has shown an upward trend in multiple areas especially among children and adolescents which indicates that environmental and immunological and genetic elements

participate in its development. The worldwide occurrence of gestational diabetes mellitus is rising because women are having children at older ages while their obesity rates are increasing and the condition creates long-term health dangers because it raises the risk of future type 2 diabetes development in mothers and their children. Understanding these type-specific patterns is critical for designing targeted prevention, screening, and management strategies that address the diverse and evolving nature of the global diabetes epidemic[21-22].

The global trends of DM highlight an escalating public health concern with wide-ranging implications for healthcare systems and economic stability. The increasing prevalence, coupled with earlier onset and prolonged disease duration, underscores the urgent need for effective prevention and control strategies. Strengthening surveillance systems, promoting lifestyle modifications, and ensuring early diagnosis are essential to curb the rising trend of diabetes[23-24]. The data presented in **Table 1** emphasize the critical need for coordinated global efforts to address this growing epidemic.

3. REGIONAL DISTRIBUTION AND HEALTH DISPARITIES

The global distribution of DM exhibits significant regional variations which show pronounced health disparities because different population groups experience different socioeconomic conditions and healthcare system capabilities and their lifestyles and genetic factors. The diabetes burden is growing in low- and middle-income countries because people in these regions lack access to early diagnosis and preventive methods and effective treatments which increases their risk of developing complications and dying from the disease[25-26]. High-income regions possess superior healthcare systems yet they still encounter difficulties because their populations grow older and people develop health problems through their daily activities. The world shows uneven disease outcomes because urban-rural divides and gender differences and ethnic backgrounds and income brackets create distinct health outcomes for different population groups[27-28]. A comprehensive overview of regional prevalence patterns, contributing factors, and associated health disparities is presented in **Table 1**.

3.1 Continental and Regional Variations

The distribution of diabetes mellitus throughout the world shows distinct regional and continental differences which emerge from varying demographic patterns and economic growth and cultural behaviors and genetic risk factors and medical service availability in different areas. The regions of South-East Asia and the Western Pacific and the Middle East study area face diabetes prevalence rates which increase at the fastest pace because of urban development and changes in their dietary habits and obesity levels[29-30]. The high-income areas of North America and Europe show persistent diabetes rates because their populations have stopped experiencing new cases but their diabetes prevalence remains high. Sub-Saharan Africa currently shows lower diabetes rates but the region experiences a rapid increase in diabetes cases because of two factors: underdiagnosis and limited access to medical services. The countries of Latin America and the Caribbean show different levels of diabetes prevalence which exist between two extreme ends of the spectrum throughout the region. These regional variations underscore the complex interplay between environmental, behavioral, and systemic factors shaping the global diabetes burden and highlight the need for region-specific surveillance and intervention strategies[31-32].

3.2 Socioeconomic and Demographic Inequities

Socioeconomic and demographic inequities work as the primary factors which determine how different populations will experience diabetes risk and disease progression and their final health results. People who belong to lower socioeconomic groups face higher rates of health problems because they cannot reach essential resources such as healthy food and safe places to exercise and medical care and programs that offer preventive health screenings[33]. The difference between urban and rural areas leads to increased health problems because urban residents develop more health conditions through their inactive lifestyles while rural residents deal with medical problems because they do not receive timely diagnosis or proper treatment. The two factors of age and gender create different diabetes pattern variations because older people show higher diabetes rates while women face special diabetes challenges that stem from gestational diabetes and their duties as caregivers. Most regions show higher diabetes risk and worse health results among ethnic and minority groups because they face both systemic discrimination and obstacles to healthcare access. Collectively, these disparities contribute to unequal distribution of diabetes-related morbidity and mortality and emphasize the importance of equity-focused public health policies and culturally tailored interventions to reduce the global impact of DM[34-35].

Table 1: Regional Distribution and Health Disparities in DM[36-38]

Region / Continent	Diabetes Prevalence Trend	Key Contributing Factors	Major Health Disparities
North America	High and steadily increasing	Obesity, sedentary lifestyle, aging population	Socioeconomic and ethnic disparities; unequal access to advanced care
Europe	High but relatively stabilized in some countries	Aging population, dietary patterns, lifestyle factors	East–West and socioeconomic inequities in healthcare access
South-East Asia	Rapidly increasing	Urbanization, dietary transition, genetic susceptibility	High rates of undiagnosed diabetes; limited preventive care
Western Pacific	Very high and rising	Rapid economic growth, lifestyle changes	Urban–rural healthcare gaps; rising youth-onset diabetes
Middle East & North Africa	Among the fastest-growing globally	Obesity, physical inactivity, cultural dietary habits	Gender-related and healthcare access disparities
Latin America & Caribbean	Moderate to high with regional heterogeneity	Urbanization, socioeconomic transition	Inequities linked to income level and healthcare coverage
Sub-Saharan Africa	Currently lower but rapidly increasing	Urbanization, changing diets, limited screening	High underdiagnosis rates; inadequate healthcare infrastructure
Oceania (Pacific Islands)	Extremely high in select populations	Genetic predisposition, obesity, nutrition transition	Geographic isolation; limited access to specialized care

The global diabetes burden gets determined by regional socioeconomic differences that exist across different areas of the world. Targeted public health interventions together with better healthcare access and region-specific prevention and management strategies are necessary to address these inequities. The healthcare system needs strengthening while public awareness needs promotion together with the development of culturally suitable interventions to achieve better health results and reduce health disparities[40]. The data summarized in **Table 1** highlight the need for equitable and sustainable approaches to effectively combat the global diabetes epidemic.

4. NANOCARRIER-BASED THERAPEUTIC STRATEGIES FOR DIABETES MELLITUS

Nanocarrier-based drug delivery systems have developed into a modern treatment method which effectively controls diabetes mellitus because it overcomes the shortcomings found in traditional diabetes medications which include their low bioavailability and quick breakdown and their lack of target distribution and their associated adverse effects from high dosages. The nanoscale systems which contain liposomes and niosomes and polymeric nanoparticles and solid lipid nanoparticles and micelles provide improved drug stability together with controlled sustained drug release and better pharmacokinetic performance and targeted tissue delivery which includes pancreatic β-cells and liver and skeletal muscle[41-42]. The nanocarriers make it possible to transport various medical substances which include insulin and oral hypoglycemic drugs and peptides and phytoconstituents to enhance treatment results while making it easier for patients to follow their medical regimens. Surface modification together with nanocarrier functionalization developments now enables precise target delivery while diminishing overall body toxicity[43-45]. A comprehensive classification and comparative analysis of various nanocarriers, including their drug loading capacity, composition, preparation techniques, and therapeutic outcomes, are summarized in **Table 2**.

Table 2: Classification and Characteristics of Nanocarriers Used in Diabetes Management with Emphasis on Drug Loading, Composition, Preparation Methods, and Therapeutic Efficacy

Type of Nanocarriers	Drug/API	Compositions	Type of Diabetes/ Role in Diabetic	Method of preparation	Research Outcomes	Ref.
Polymeric nanoparticles (Eudragit-based SIT-NPs)	Sitagliptin (SIT)	Eudragit RL100 (polymer)+Tween 80 (surfactant)	Anti-diabetic therapy (prolonged glycemic control; likely Type 2 Diabetes management via DPP-4 inhibition)	Combination of solvent evaporation and nanoprecipitation techniques with statistical optimization	Particle size: 135–193 nm; Drug loading: 6.3–8.8%; Sustained release (24 h); Enhanced release and permeation; Spherical smooth morphology; Prolonged glucose reduction; Stable (~488 days).	[46]
Solid Lipid Nanoparticles (SLNs)	Gliclazide (GLZ)	Glyceryl behenate (Compritol® 888 ATO) + Poloxamer 188 + Trehalose dihydrate	Type 2 Diabetes; enhanced oral bioavailability, prolonged glycemic control, improved anti-diabetic efficacy	Ultrasonication technique followed by freeze-drying; optimized using 2×3 factorial design	Particle size: ~246 nm; PDI: ~0.48; Spherical particles; Biphasic release; ~5× bioavailability; Improved efficacy; Prolonged release; Safe.	[47]
Liposomes (oral liposomal formulation)	Sitagliptin	Soy lecithin + Cholesterol	Type 2 Diabetes; enhanced oral bioavailability and improved antihyperglycemic activity	Thin-film hydration technique	Particle size: ~40 nm; Zeta potential: ~40 mV; Drug release: ~88% (8 h); First-order kinetics; No interaction; Enhanced efficacy; Sustained effect (~4 h).	[48]
Liposomes (HDCA-modified liposomes)	Metformin + Hyodeoxycholic acid (HDCA)	Metformin + Hyodeoxycholic acid + Liposomal components (phospholipids/cholesterol-like structure)	Type 2 Diabetes; enhanced bioavailability, reduced side effects, improved hypoglycemic effect, glucose regulation	Thin-film dispersion method	Improved glucose tolerance; Reduced blood glucose; Controlled oxidative stress; Liver protection; Enhanced efficacy; Optimal (1:1) ratio; High HDCA ↓ drug loading.	[49]
Liposomes in hydrogel	Resveratrol	Resveratrol (RV) + Phospholipids + Cholesterol + Carbopol 940 (1%) + Triethanolamine + Purified water	Diabetic foot wounds (DFUs)	thin-film hydration method	RV-loaded liposomes in hydrogel-based wound dressing significantly accelerate wound healing in diabetic foot ulcers by restoring the altered wound healing process in diabetics.	[50]
Long-circulating liposomes (PEGylated liposomes, PLLs)	Polydatin	Lecithin + DSPE-PEG2000 + Cholesterol	Type 2 Diabetes (obese T2DM); sustained release, enhanced bioavailability, improved antidiabetic efficacy	Membrane dispersion method (orthogonal optimization)	Small uniform particles; High encapsulation; Stable; Sustained release; Enhanced uptake; Prolonged circulation; Reduced glucose & lipids; Lower oxidative stress	[51]
Liposomes (ethanol/propylene glycol-based nasal liposomes, ILEP)	Isoxsuprine	Phospholipid + Cholesterol + Ethanol + Propylene glycol	Diabetes-associated ischemic stroke; improved drug delivery, targeting, and neuroprotection	Optimized liposomal formulation (Design Expert-based optimization) for nasal	Improved permeation & targeting; Sustained drug delivery; Enhanced neurological outcomes; Reduced neuronal damage & vascular congestion; Prevented	[52]

				delivery	stroke severity in diabetic model	
Nanoparticles	Chitosan alginate	Chitosan + Sodium alginate + Glacial acetic acid + Sodium hydroxide + Purified water	diabetic and non-diabetic pressure ulcers	Modified ionic gelation metho.	Chitosan alginate nanoparticles offer a promising platform for diabetic and non-diabetic wound healing applications.	[53]
Metallic nanoparticles (Green-synthesized AgNPs & FeNPs)	Polyherbal formulation (Mehani-derived phytochemicals)	Polyherbal extract (reducing/capping agents) + Silver ions / Iron (zero-valent)	Anti-diabetic (hyperglycemia management via α-amylase inhibition) + Antioxidant activity	Green synthesis (biogenic reduction using polyherbal formulation)	Size: AgNPs (60–80 nm), FeNPs (40–60 nm); Characterized (UV, FTIR, XRD, SEM); Strong antioxidant activity; α-amylase inhibition: ~65% (AgNPs), ~70% (FeNPs); FeNPs superior.	[54]
Polymeric nanoparticles (PLGA-based NPs)	Metformin (MTF)	PLGA polymer	DM (likely Type 2); enhanced oral bioavailability and antidiabetic efficacy	Solvent evaporation method	Particle size: ~178 nm; Zeta potential: ~−22.6 mV; Entrapment: ~84.7%; Biphasic release (~82.5%/24 h); ~2.6× bioavailability; ~62.8% glucose reduction; Improved pancreatic histology	[55]

Nanocarrier-based therapeutic strategies provide a new treatment method for diabetes which solves essential problems that traditional drug delivery systems face. The system demonstrates potential for both diabetes types because it delivers improved BA and targeted drug delivery with controlled release which enhances treatment results. The existing preclinical and clinical data show positive results yet researchers must solve multiple issues related to manufacturing at scale and maintaining safety over time and obtaining regulatory endorsement and proving cost efficiency. The future research will advance their clinical applications while enhancing diabetes treatment results through its focus on developing advanced nanocarrier systems and personalized medical approaches and their use with new medical technologies[57-58].

5. DISEASE BURDEN: MORTALITY, DISABILITY, AND ECONOMIC IMPACT

Diabetes mellitus represents a serious worldwide health problem which increases both death rates and disability rates and generates economic burdens for healthcare systems. The chronic and progressive nature of diabetes has led to increasing diabetes-related deaths because complications of the disease cause both cardiovascular disease and nephropathy and neuropathy and infections[59-60]. Diabetes creates a major disability burden because it results in two different disability measures which include disability-adjusted life years and years lived with disability. The economic consequences of diabetes extend to direct medical expenditures for treatment and hospitalization and to indirect financial losses from decreased work ability and disability and early death[61-62]. These factors collectively highlight the extensive and multifaceted burden of diabetes on individuals, healthcare systems, and global economies.

5.1 Mortality Patterns

Diabetes mellitus serves as a significant worldwide death cause because it directly kills people and serves as a danger that triggers multiple fatal diseases which include heart disease and chronic kidney disease and infectious diseases. The diabetes-related death rate has shown a consistent upward trend during the past several decades because people now develop diabetes at younger ages and live with the disease for extended periods. The global patterns of mortality show major differences between regions, as low- and middle-income countries experience higher diabetes-related death rates due to their common practice of diagnosing diabetes at a later stage and their restricted access to crucial medications and their insufficient capacity to handle the disease[63]. High-income regions report better health outcomes because their residents have access to healthcare services which enables them to receive timely treatment and proper care for their multiple health conditions, but their total death count remains elevated because of their growing elderly demographic. Age- and sex-specific differences in mortality further highlight disparities, with older adults and individuals from socioeconomically disadvantaged groups experiencing disproportionately higher risk of diabetes-related death. These mortality trends emphasize the critical role of early detection, effective treatment, and

integrated management strategies in reducing diabetes-associated deaths[64].

5.2 Disability-Adjusted Life Years, Years Lived with Disability, and Economic Costs Diabetes-related DALYs have increased globally, driven primarily by a rise in YLDs rather than years of life lost, because people now survive longer yet live with chronic health problems. The major disability-causing health problems arise from microvascular and macrovascular complications, which include neuropathy, retinopathy, nephropathy, and cardiovascular disease[65]. The economic impact of diabetes extends beyond direct medical expenses for outpatient treatment and hospital stays and medications and complication management because it also includes indirect costs from lost work time and disability and early death. The economic burden on low- and middle-income countries becomes excessive because healthcare costs take up a substantial portion of household income, which leads to increased poverty and health inequalities. Collectively, the growing disability and economic costs of diabetes highlight the urgent need for cost-effective prevention strategies, early intervention, and sustainable health system investments to mitigate the long-term global impact of the disease[65-66].

Diabetes mellitus creates a substantial burden that extends beyond its clinical effects because it results in high rates of death and permanent disabilities and creates major financial effects. The increasing diabetes burden in low-income and middle-income nations requires immediate development of affordable effective diabetes prevention and treatment programs[67]. The healthcare system requires three essential elements which include better detection methods and expanded medical service access and creation of specific programs that will help reduce health complications. The healthcare system needs both integrated policy solutions and continuous financial support to decrease diabetes-related economic burdens while improving public health outcomes[68].

6. RISK FACTORS DRIVING THE GLOBAL DIABETES BURDEN

The worldwide increase in diabetes mellitus occurs through various metabolic and genetic and behavioral and dietary and environmental and social factors which determine how people develop and advance their illnesses. Obesity especially central body fat distribution represents the primary reversible health hazard which researchers established as a cause of insulin resistance and persistent low-level inflammation and pancreatic β-cell damage[69-70]. Diabetes develops through multiple pathways which share biologic mechanisms that include dyslipidemia and hypertension and metabolic syndrome as risk factors (**Fig. 1**). Genetic predisposition also plays an important role, as evidenced by familial clustering and the identification of multiple susceptibility loci associated with insulin secretion and glucose metabolism[71].

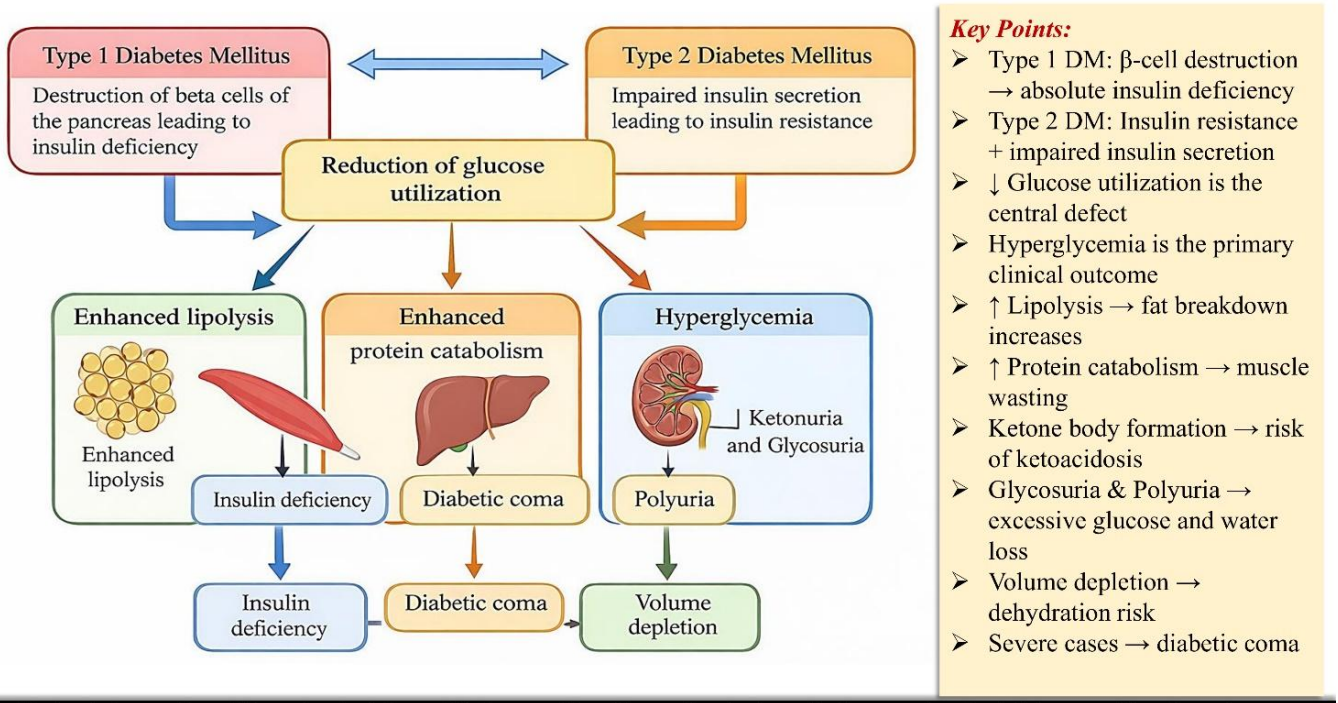


Figure 1: Mechanistic overview of the pathophysiology of DM illustrating the interplay between insulin deficiency and insulin resistance leading to impaired glucose utilization. The figure highlights key metabolic alterations including hyperglycemia, enhanced lipolysis, increased protein catabolism, and associated complications such as diabetic ketoacidosis, glycosuria, polyuria, and systemic metabolic imbalance across major organs.

Genetic risk factors by themselves cannot account for the worldwide rise in diabetes cases since they require environmental elements and human behavioral patterns for their explanation. People who have different lifestyle choices show different levels of risk for developing diabetes according to research studies[72-73]. The combination of physical inactivity and sedentary lifestyles together with urban development and technological progress has resulted in a nationwide surge of insulin resistance (**Fig. 2**). People who use tobacco and drink too much alcohol develop metabolic disorders that lead to problems with their blood sugar control. The two main causes of diabetes risk which people often overlook are psychosocial stress and sleeping problems which occur together with shift work in urban and industrial areas medical work fields[74]. These lifestyle-related factors frequently cluster within disadvantaged socioeconomic groups, amplifying health inequities and accelerating disease burden in vulnerable populations[73-74].

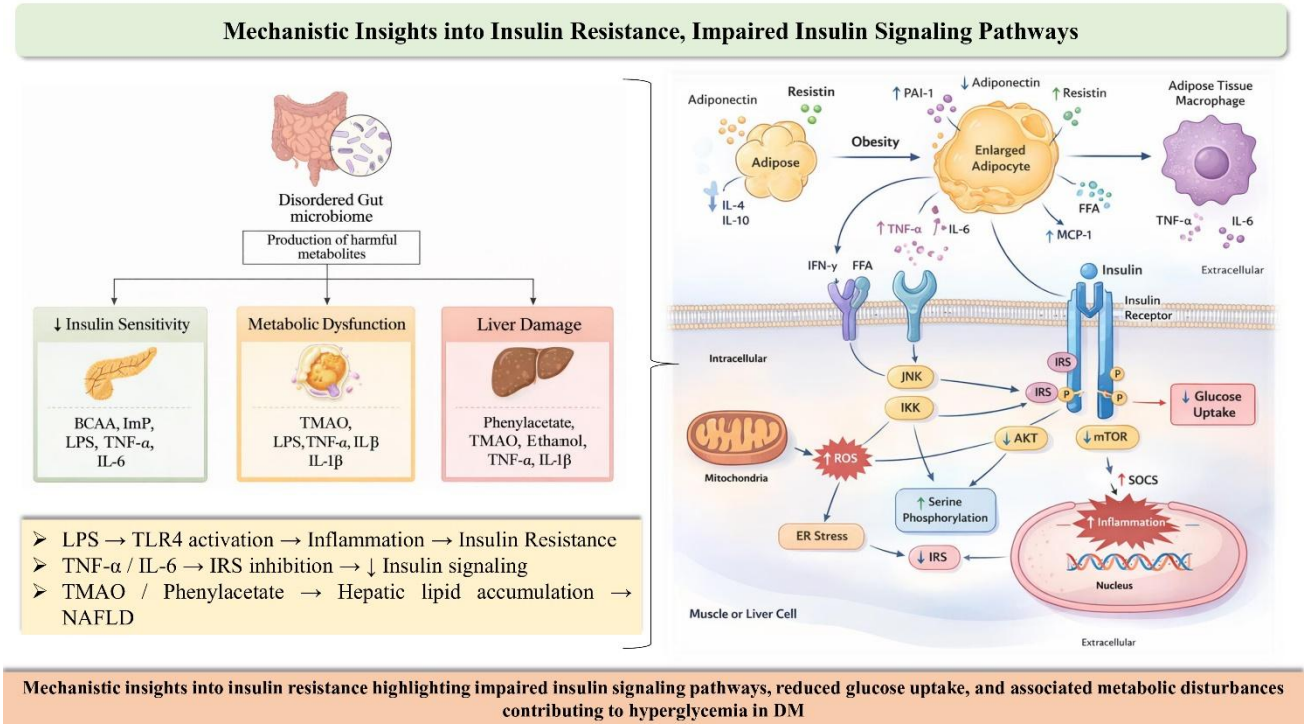


Figure 2: Schematic illustration depicting the mechanistic interplay between insulin resistance and gut microbiota dysbiosis, highlighting how altered intestinal bacterial composition accelerates metabolic dysfunction, promotes inflammation, and contributes to the progression of liver damage, including non-alcoholic fatty liver disease (NAFLD).

The global diabetes epidemic experiences its most significant growth through dietary patterns which result in worldwide health issues. People in various regions have changed their eating habits by choosing energy-dense ultra-processed foods which contain refined carbohydrates and added sugars and saturated fats and sodium instead of their traditional nutrient-rich diets. People who drink high amounts of sugar-sweetened beverages but eat very little dietary fiber and whole grains and fruits and vegetables usually experience higher chances of developing diabetes[75-76]. Globalization of food systems together with food marketing campaigns and restricted access to inexpensive healthy food options especially affects people in low- and middle-income countries which leads to these dietary changes. Worldwide diabetes risk escalates because of environmental changes and demographic shifts. Scientific research increasingly links air pollution exposure together with endocrine-disrupting chemicalsand obesogenic built environments to metabolic health problems. The world population now faces its primary demographic challenge because older people face higher diabetes risk through insulin resistance and reduced β-cell function and long-term exposure to metabolic health problems[77]. The convergence of these metabolic, behavioral, environmental, and aging-related risks highlights the multifactorial nature of DM and underscores the need for comprehensive, multisectoral prevention strategies to effectively curb its growing global burden[77-78].

7. CURRENT STATUS: CLINICAL TRIALS AND PATENT LANDSCAPE

DM research today shows active progression through its ongoing clinical trials and patent developments. Clinical studies currently investigate new drug treatments advanced insulin products and combination treatment methods which include nanocarrier drug delivery systems and digital health solutions[79-80]. The trials seek to enhance glycemic control while they work to treat related health issues which include cardiovascular and renal complications. The patent system currently focuses on creating new drug development methods and delivering technologies which improve treatment

results and make it easier for patients to follow their medical regime[80]. A detailed overview of recent and ongoing clinical trials, including study design, interventions, and status, is presented in **Table 3**, while recent patent developments and technological advancements in diabetes management are summarized in **Table 4**.

Table 3: Summary of Current Clinical Trials in DM Highlighting Study Design, NCT Identification Number, Recruitment Status, Interventions, Initiation Timeline, and Key Descriptive Outcomes

Study Title	Study Type	NCT Number	Status	Interventions	Start Date
A Study of CX11 Tablets in Patients With Type 2 Diabetes Mellitus	Interventional	NCT07340320	Phase-2	Drug: CX11 Other: Placebo	2026-02-05
Short- and Long-Term Effects of Whole-Body Photobiomodulation in Type II Diabetes Patients: A Protocol for a Controlled Clinical Trial (PBM)	Interventional	NCT07047248	Not Applicable	Device: PBM Other: Placebo PBM	2025-08-30
Effects of Core Strengthening Exercises With Diapgragmatic Breathing Versus Core Strengthening Exercises With Pilate Breathing in Diabetes Type II Patients	Interventional	NCT07290231	Not Applicable	Other: Core Strengthening with Diaphragmatic Breathing Other: core strengthening with pilate breathing	2025-08-06
A Participatory Approach to Support Glucose Tolerance Tracking in Real-Life of Patients With Type 2 Diabetes (GluTo Track)	Interventional	NCT06864546	Not Applicable	Behavioral: Physical activity intervention	2025-05
A Clinical Trial to Evaluate the Food Effect of CKD-379 (CKD-379)	Interventional	NCT06652971	Phase-1	Drug: CKD-379	2024-11-05
Efficacy and Safety of Piemonte Association in the Treatment of Type II DM (PIEMONTE)	interventional	NCT05028140	Phase 3	Drug: PIEMONTE Other: PIEMONTE PLACEBO Drug: EMPAGLIFLOZIN	2024-10-08
A Clinical Trial to Evaluate the Food Effect of CKD-378	Interventional	NCT06386328	Phase-1	Drug: CKD-378, QD, PO	2024-05-03
Evaluate HM-002-1005 in Subjects With Type 2 Diabetes Mellitus	Interventional	NCT06498284	Phase-1	Drug: HM-002-1005	2024-04-25
Effects of Eccentric Training on Glycemic Control and Quality of Life in Patients With Type II Diabetes Mellitus	interventional	NCT06387550	Not Applicable	Procedure: Eccentric Training	2024-03-20
Relative Hand Grip Strength and Functional Fitness in Diabetic Patient in Egypt	Interventional	NCT06645418	Not Applicable	Diagnostic Test: relative Hand grip strength Diagnostic Test: senior fitness test	2023-10-15
Study to Evaluate the Safety and Pharmacokinetics of CKD-379	Interventional	NCT05952219	Phase 1	Drug: CKD-379 Drug: D759+D745+D029+D150	2023-06-02
Effect of Coherent Breathing on Elderly Quality of Life	Interventional	NCT05767372	Not Applicable	Other: Coherent Breathing Exercise Device: Inspiratory	2023-03-01

				muscle training	
Pharmacokinetics and Safety/ Tolerability of CKD-379	Interventional	NCT05719155	Phase 1	Drug: CKD-379 Drug: D759+D745+D150	2023-02-27
Development and Exploration of the Effectiveness and Feasbility of a Digital Intervention for Type 2 Diabetes Mellitus (DEsireD)	Interventional	NCT05364476	Not Applicable	Behavioral: 16 weeks digital intervention	2022-04-11
Dual Add-on Therapy in Type 2 Diabetes Poorly Controlled With Metformin Monotherapy	interventional	NCT04667143	Phase 3	Drug: Retagliptin, Henagliflozein, metformin XR	21-01

Table 4: Overview of Current Patents in DM Highlighting Innovative Therapeutic Strategies, Drug Delivery Systems, and Emerging Nanotechnology-Based Approaches

Entitle	Application no./Grant No	Authors	Filling date	Grant/ Publication date
System for Assessing Global Wellness	US19/051,210	Jill Wade	2025-02-12	2025-07-03
Method for inducing weight loss in a type 2 diabetes mellitus patient	US18/987,056	Elisabeth Niemoeller, Louise Silvestre	2024-12-19	25-05-01
Fgf21 variants	US18/932,818	Mark Sommerfeld, Thomas Langer	2024-10-31	2025-05-29
Treatment for diabetes in patients inappropriate for metformin therapy	US18/921,039	Klaus Dugi, Eva Ulrike, Ruth Anne	2024-10-21	2025-10-09
Methods and Compositions for Oral Administration of Proteins	US18/921,419	Miriam Kidron	2024-10-21	2025-09-11
Cardio- and renoprotective antidiabetic therapy	US18/907,618	Odd-Erik, Maximillan Von	2024-10-07	2025-01-23
Fusion proteins	US18/756,062	David Bruce Baldwin, John Michael Beals	2024-06-27	2025-01-30
Treatments for Diabetes Mellitus and Obesity	US18/599,902	Pankaj PasrichaLiansheng Liu	2024-03-08	2024-06-27
Method of treating diabetes type 2 by administering ultrarapid acting insulin	US18/593,204	Peter Richardson, Robert A. Baughman	2024-03-01	2024-06-20
Sdc-2 exosome compositions and methods of isolation and use	US18/425,997	Stephen J. Elliman, Jack Kavanaugh	2024-01-29	24-07-25
Pharmaceutical composition, methods for treating and uses thereof	US18/422,333	Uli Christian, Odd-Erik	2024-01-25	2024-05-16
Methods and systems for determining risk of a pregnancy complication occurring	US18/136,805	Claire Trelford Roberts, Shalem Yiner-Lee	2023-04-19	2024-02-01
Implantable therapeutic delivery system and methods thereof	US18/396,941	Minglin Ma, James A. Flanders	2023-12-27	2024-12-05
Diabetes risk early warning method based on big data analysis	CN202311506972.3A		2023-11-14	2024-01-26
Device for non-invasive detection of skin problems associated with diabetes mellitus	US17/752,755	Mike Van Snellenberg, Anne Weiler	2022-05-24	2022-09-08
Viral vectors for the treatment of diabetes	US17/384,533	Cristina Mallol Dominguez	2021-07-23	2022-06-16
Polymeric bile acid nanocompositions targeting the pancreas and colon	AU2020267191A	Tarek M. Fahmy.Dongin Kim	2020-11-10	2022-08-18

The growing number of clinical trials and patent applications demonstrates that researchers continue their work to develop innovative solutions for diabetes management through their interdisciplinary research efforts. The new developments create potential treatment options but face major challenges which include three main obstacles that prevent widespread implementation and use of the solutions[81-82]. The process of transferring research breakthroughs into practical medical applications needs all parties which include researchers and healthcare professionals and policy makers and business leaders to work together. The information in **Table 3** and **Table 4** shows that new treatment methods continue to develop, which will lead to better health results for patients and improved diabetes management worldwide[83].

8. CURRENT CHALLENEGES, GAPS IN DETECTION, TREATMENT, AND CARE DELIVERY

The diabetes care system still suffers from major treatment gaps which extend from initial patient assessments through to ongoing patient treatment. A significant number of people who have diabetes remain undiagnosed worldwide because they cannot access regular screening tests and the existing methods to identify their risk of diabetes do not work together with their social and cultural background and their type 2 diabetes develops without showing any symptoms during its initial stages. The highest detection gaps exist in regions that experience both low and middle economic development because their healthcare systems lack sufficient resources and their preventive health services do not receive adequate funding[84-85]. After patients receive their diagnosis, treatment gaps develop because people cannot obtain necessary medication and insulin and self-monitoring equipment and new digital health solutions. The existence of multiple insurance plans together with high treatment expenses and supply chain interruptions creates additional challenges which prevent patients from adhering to therapy and maintaining their medical treatment. Healthcare system-level challenges-including shortages of trained endocrinologists and diabetes educators, inconsistent implementation of evidence-based clinical guidelines, limited integration of diabetes care into primary health systems, and poor coordination between levels of care-significantly hinder optimal disease control[86]. The lack of proper patient education and lifestyle counseling and long-term follow-up programs leads to poor glycemic control and increases the risk of developing microvascular and macrovascular diseases. The existing gaps in health systems require immediate action to develop robust health systems and scalable screening methods and affordable treatment options and patient-centered care systems which will help to reduce the rising global diabetes mellitus burden[86-87].

The scientific community has achieved significant progress toward understanding diabetes mellitus epidemiology and treatment yet they still need to solve several persistent critical problems in this field. The primary obstacle exists because researchers worldwide face difficulties accessing high-quality data from developing nations which suffer from both underdiagnosis problems and their inconsistent monitoring systems and their lacking medical facilities. The different diagnostic criteria and reporting standards together with the various study methods used by researchers create difficulties for international researchers who need to make cross-country comparisons and conduct trend analyses[88]. The research field currently shows inadequate representation of vulnerable groups which includes people from rural areas and minority ethnic communities and individuals who come from economically disadvantaged backgrounds, which leads to restricted research applicability and hides actual health disparity between different population groups. The clinical treatment of diabetes problems because its causes include genetic factors and environmental influences and human behavioral patterns. Future perspectives should prioritize the integration of standardized, high-quality global surveillance systems which digital health technologies and real-time data analytics systems will support. The scientific community requires population-based studies which track participant health over time and include genomic data, metabolomic data, and environmental data to investigate disease mechanisms and risk assessment methods[89-90]. The healthcare system requires primary care improvements which combine better screening methods and personalized treatment programs to reduce health disparities. The global health crisis requires artificial intelligence and machine learning to create predictive models while policy interventions need to target both lifestyle changes and the social factors that affect health. The research field requires multidisciplinary teams to create sustainable diabetes prevention and control methods which combine clinical research and public health policy and technological innovation.

CONCLUSION

`The worldwide health issue of diabetes mellitus diabetes now causes severe medical problems and economic damages and social difficulties that continue to grow. The increasing number of cases in different demographic groups shows how demographic changes and urban development and changes in human behavior and genetic factors work together to create this health issue. The research demonstrates that although people now understand diabetes better and there are new treatments available the healthcare system still lacks efficient ways for patients to receive early treatment and proper diabetes management and fair healthcare system benefits particularly in developing countries. The social and environmental health factors need to be tackled because vulnerable groups bear an unequal health burden. The diabetes epidemic requires a complete integrated solution for its resolution. The public health system needs strengthening while preventive programs which focus on helping people change their behavior should be developed and everyone should have access to inexpensive diagnostic

tests and treatments. The health field currently witnesses progress in three key areas which include precision medicine and digital health and data-driven epidemiology. The healthcare systems and policymakers and researchers and communities need to collaborate toward evidence-based practice implementation which will help achieve diabetes mellitus burden reduction goals.

LIST OF ABBREVIAITON

DM: Diabetes Mellitus; **DFUs:** Diabetic Foot Ulcers; **T1DM:** Type 1 Diabetes Mellitus; **T2DM:** Type 2 Diabetes Mellitus; **GDM:** Gestational Diabetes Mellitus; **WHO:** World Health Organization; **IDF:** International Diabetes Federation; **GBD:** Global Burden of Disease; **DALYs:** Disability-Adjusted Life Years; **YLDs:** Years Lived with Disability; **YLLs:** Years of Life Lost; **GLP-1:** Glucagon-Like Peptide-1; **SGLT-2:** Sodium–Glucose Cotransporter-2; **DPP-4:** Dipeptidyl Peptidase-4; **NPs:** Nanoparticles; **SLNs:** Solid Lipid Nanoparticles; **RV:** Resveratrol; **GAGs:** Glycosaminoglycans; **CS:** Chitosan; **ALG:** Alginate; **Mw:** Molecular Weight; **pKa:** Acid Dissociation Constant; **cP:** Centipoise; **BA:** Bioavailability.

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