www.idosr.org Nasira, 2026

©IDOSR PUBLICATIONS

ISSN: 2579-0811

International Digital Organization for Scientific Research IDOSR JBBAF2026/113
IDOSR JOURNAL OF BIOCHEMISTRY, BIOTECHNOLOGY AND ALLIED FIELDS 11(3):63-69, 2026.
https://doi.org/10.59298/IDOSR/JBBAF/2026/1136369

Smart Nanodelivery Systems for Herbal Antidiabetic Agents: Controlled Release and Targeted Metabolic Modulation

Nasira A. Sitar

Department of Pharmacy Kampala International University Uganda
Satar.nasira@studwc.kiu.ac.ug

ABSTRACT

Herbal antidiabetic agents possess multifaceted metabolic activities, including enhancement of insulin signaling, inhibition of carbohydrate-digesting enzymes, suppression of oxidative stress, and preservation of pancreatic β-cell function. However, their clinical translation is frequently limited by poor solubility, low bioavailability, rapid metabolism, and non-specific biodistribution. Smart nanodelivery systems provide innovative solutions by integrating controlled release, tissue targeting, and stimuli-responsive mechanisms to optimize therapeutic precision. These systems including polymeric nanoparticles, liposomes, nanostructured lipid carriers, nanoemulsions, nanogels, and biomimetic vesicles, can protect phytochemicals from degradation, enhance absorption, and modulate release in response to metabolic triggers such as glucose concentration, pH shifts, or reactive oxygen species (ROS). Targeted nanocarriers enable preferential accumulation in liver, skeletal muscle, adipose tissue, or pancreatic islets, aligning delivery with pathophysiological sites of insulin resistance and β-cell stress. Preclinical studies demonstrate improved glycemic control, enhanced insulin sensitivity, reduced inflammation, and superior pharmacokinetic profiles compared with conventional herbal formulations. Nevertheless, translational challenges include scalability, long-term safety evaluation, regulatory classification, and standardization of herbal extracts. This review discusses design principles, mechanistic pathways, preclinical evidence, safety considerations, and prospects of smart nanodelivery platforms for herbal antidiabetic therapy.

Keywords: smart nanodelivery; herbal antidiabetic agents; controlled release; targeted therapy; metabolic modulation

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin resistance, or both[1–3]. Type 2 diabetes (T2DM) accounts for the majority of cases and involves progressive insulin resistance in liver, skeletal muscle, and adipose tissue, coupled with declining pancreatic β-cell function[4, 5]. Despite advances in pharmacotherapy including metformin, insulin analogs, SGLT2 inhibitors, GLP-1 receptor agonists, and DPP-4 inhibitors, optimal glycemic control remains challenging for many patients[6]. Limitations such as adverse effects, therapeutic resistance, cost, and poor adherence highlight the need for complementary and innovative therapeutic strategies.

Herbal antidiabetic agents derived from medicinal plants have long been used in traditional medical systems. Bioactive compounds such as polyphenols (e.g., quercetin, resveratrol), alkaloids (e.g., berberine), terpenoids (e.g., ginsenosides), flavonoids, saponins, and polysaccharides demonstrate diverse antidiabetic mechanisms[7–10]. These include activation of AMP-activated protein kinase (AMPK), enhancement of insulin receptor signaling (PI3K/Akt pathway), upregulation of glucose transporter 4 (GLUT4) translocation, inhibition of α-amylase and α-glucosidase, suppression of oxidative stress, and reduction of inflammatory cytokines. Many phytochemicals also preserve β-cell viability by mitigating oxidative and endoplasmic reticulum stress[11, 12]. However, translation of herbal antidiabetic compounds into clinically reliable therapies faces significant challenges. Many phytochemicals exhibit poor aqueous solubility and low oral bioavailability. Rapid metabolism and clearance reduce systemic exposure, and non-specific biodistribution limits tissue-specific efficacy [13]. Furthermore, complex herbal extracts may show variability in composition due to differences in cultivation, harvesting, and processing conditions. Conventional formulations often fail to deliver sufficient concentrations to target organs such as the liver, adipose tissue, or pancreatic islets.

Nanotechnology offers transformative potential to address these limitations. Nanodelivery systems typically range from 10 to 200 nm and can encapsulate or conjugate bioactive molecules, protecting them from degradation and enhancing absorption. Smart nanodelivery systems go beyond passive encapsulation by incorporating controlled-release kinetics, stimuli responsiveness, and targeting strategies[14–16]. These systems are engineered to release their therapeutic payload in response to specific biological triggers such as elevated glucose levels, acidic microenvironments, or oxidative stress, thus aligning drug release with disease pathophysiology.

Controlled release improves pharmacodynamic stability, reduces dosing frequency, and minimizes peak–trough fluctuations in drug levels[17]. Targeted delivery enhances therapeutic precision by directing phytochemicals to insulin-resistant tissues or inflamed islets, potentially lowering required doses and reducing off-target effects. Stimuli-responsive systems provide dynamic modulation, releasing active compounds when and where they are most needed[18–20].

For example, glucose-responsive nanoparticles can exploit phenylboronic acid–diol interactions or glucose oxidase–mediated pH changes to trigger release under hyperglycemic conditions. ROS-sensitive nanocarriers degrade in oxidative environments, enabling site-specific antioxidant delivery in diabetic tissues[21, 22]. pH-sensitive systems protect herbal compounds in the stomach while enabling release in the intestine or intracellular compartments.

Smart nanodelivery platforms can also facilitate combination therapy by co-encapsulating multiple phytochemicals or integrating herbal compounds with conventional drugs. This is particularly relevant in T2DM, where multifactorial pathogenesis requires simultaneous targeting of insulin resistance, inflammation, oxidative stress, and β-cell dysfunction[23].

Despite promising advances, challenges remain. Long-term safety and biodistribution of nanoparticles must be carefully evaluated, especially for chronic diseases requiring sustained treatment. Manufacturing scalability, batch reproducibility, and regulatory compliance are critical for clinical translation[23]. Clear characterization of nanoparticle size, surface charge, encapsulation efficiency, and release kinetics is essential.

This review explores the principles and design strategies of smart nanodelivery systems for herbal antidiabetic agents. It examines controlled-release mechanisms, targeting approaches, stimuli-responsive technologies, preclinical evidence, safety considerations, and future translational prospects. By integrating phytotherapy with precision nanotechnology, smart delivery systems may enhance the therapeutic potential of herbal agents in metabolic disease management.

2. Controlled Release Mechanisms in Herbal Nanodelivery

Controlled release is a defining feature of modern herbal nanodelivery systems, designed to ensure that bioactive phytochemicals maintain therapeutic concentrations over extended periods while minimizing systemic exposure and off-target effects[24]. This is especially crucial in chronic metabolic diseases such as diabetes, where sustained pharmacological action is necessary to regulate glucose homeostasis, reduce oxidative stress, and mitigate inflammatory pathways[24]. By modulating the temporal profile of drug release, controlled-release systems improve patient adherence, reduce dosing frequency, and stabilize plasma drug concentrations, thereby enhancing overall therapeutic efficacy.

Polymeric nanoparticles, constructed from biodegradable materials such as PLGA, chitosan, and alginate, represent a major class of controlled-release vehicles[25, 26]. Drug release occurs primarily through a combination of diffusion and polymer matrix degradation. The kinetics of release can be precisely tailored by adjusting polymer molecular weight, composition, crosslinking density, and particle size, allowing researchers to design delivery systems that achieve immediate, sustained, or biphasic release profiles[27]. This tunability is particularly beneficial for herbal compounds prone to rapid degradation or poor bioavailability.

Lipid-based carriers, including solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), are ideally suited for lipophilic phytochemicals such as curcumin, resveratrol, and carotenoids[28, 29]. The crystalline lipid matrix of SLNs and the partially amorphous structure of NLCs modulate diffusion rates, improve chemical stability, and provide sustained release. Lipid-based carriers mimic biological membranes, facilitating efficient cellular uptake and improved tissue distribution.

Hydrogel-based nanogels, composed of crosslinked hydrophilic polymers, respond dynamically to environmental triggers such as pH, glucose concentration, or oxidative stress[30]. Upon exposure to these stimuli, the nanogels swell, allowing controlled and site-specific release of encapsulated antioxidants or anti-inflammatory compounds, thereby enhancing efficacy in tissues affected by metabolic dysregulation[30].

The integration of controlled-release mechanisms into herbal nanodelivery not only maintains effective drug concentrations in oxidative and inflammatory microenvironments but also minimizes peak-trough fluctuations, which are often associated with toxicity and reduced adherence[31]. These features make controlled-release herbal nanocarriers highly advantageous for long-term management of chronic diseases such as diabetes, obesity, and associated cardiovascular complications, representing a pivotal step toward smart, patient-centered therapeutics[31].

3. Targeted Metabolic Modulation in Insulin-Resistant Tissues

Targeted nanodelivery enables precise localization of herbal compounds to tissues critically involved in metabolic dysregulation, enhancing therapeutic efficiency and reducing systemic exposure. Insulin resistance is

a hallmark of type 2 diabetes and is characterized by impaired glucose uptake and metabolic dysfunction in multiple tissues, including the liver, skeletal muscle, adipose tissue, and pancreas[32, 33]. Nanocarrier-based targeting strategies aim to restore metabolic balance by directing bioactive compounds to these insulin-resistant organs.

Liver targeting is achieved through surface modification with ligands such as galactose or N-acetylgalactosamine, which bind to asialoglycoprotein receptors expressed on hepatocytes[34]. This strategy enhances hepatic uptake of phytochemicals, suppresses gluconeogenic pathways, reduces hepatic glucose output, and improves lipid metabolism. Targeted hepatic delivery is particularly relevant for polyphenols and alkaloids that modulate AMPK signaling[34].

Skeletal muscle targeting utilizes peptide-functionalized nanoparticles to improve glucose transporter 4 (GLUT4) translocation and glucose uptake. Enhanced muscle delivery amplifies insulin sensitivity, facilitates glycogen storage, and improves systemic glycemic control. Muscle-specific targeting reduces the need for high systemic doses, thereby minimizing off-target effects[35, 36]. Adipose tissue targeting focuses on macrophage-rich inflamed fat depots. Mannose- or folate-modified carriers selectively accumulate in adipose tissue macrophages, reducing pro-inflammatory cytokine production, restoring adipokine balance, and alleviating insulin resistance. These interventions directly counteract chronic low-grade inflammation that perpetuates metabolic dysfunction[37, 38].

Pancreatic targeting involves ligand-decorated nanoparticles capable of preferentially delivering antioxidants and insulinotropic phytochemicals to β-cells. This targeted delivery protects β-cell viability, preserves insulin secretion, and supports endogenous glucose regulation[39].

By aligning drug delivery with tissue-specific metabolic pathology, targeted nanocarriers enhance therapeutic potency, reduce systemic exposure, and mitigate adverse effects. The integration of tissue-specific ligands, combined with controlled-release properties, creates a sophisticated approach for precision metabolic modulation, offering significant promise for the management of insulin resistance and associated complications in diabetes[39].

4. Stimuli-Responsive Nanocarriers

Stimuli-responsive nanocarriers, or "smart" nanoparticles, represent an advanced strategy for synchronizing drug release with disease-specific microenvironments. In diabetes and related metabolic disorders, pathological tissues often exhibit distinctive biochemical and physiological cues, including elevated glucose, oxidative stress, altered pH, and enzymatic activity. Exploiting these triggers allows for on-demand release of encapsulated herbal compounds, enhancing therapeutic precision and minimizing systemic toxicity[18, 22].

Glucose-responsive systems release drugs in response to hyperglycemic conditions. Incorporating glucose-sensing components such as phenylboronic acid, glucose oxidase, or lectin-based recognition motifs enables nanoparticles to detect high glucose levels and release insulinotropic or antioxidant phytochemicals selectively[40]. This approach reduces the risk of hypoglycemia by restricting drug action to periods of metabolic need.

ROS-responsive carriers degrade or swell in oxidative environments, releasing antioxidants and anti-inflammatory compounds precisely where reactive oxygen species are elevated. Such nanocarriers are particularly effective in diabetic tissues, including the pancreas, kidneys, retina, and peripheral nerves, where oxidative stress drives cellular dysfunction[41].

pH-sensitive systems exploit acidic microenvironments, such as those found in inflammatory lesions, endosomal compartments, or ischemic tissues. Acid-labile linkages or proton-responsive polymers trigger compound release under low pH, ensuring selective delivery while sparing healthy tissues[41]. Enzyme-responsive carriers rely on the activity of specific digestive, inflammatory, or tissue-specific enzymes to activate release. For instance, nanoparticles may release phytochemicals in response to matrix metalloproteinases or glycosidases abundant in inflamed diabetic tissues[42].

By integrating multiple stimuli-responsiveness into a single platform, nanocarriers can achieve dynamic, context-sensitive drug release, maximizing therapeutic efficacy while limiting off-target exposure[42]. This precise synchronization with pathological cues offers a significant advantage over conventional drug administration, enabling real-time metabolic modulation and improving patient safety.

5. Preclinical Evidence and Translational Potential

Extensive preclinical research highlights the superior efficacy of nanoformulated herbal compounds compared with conventional extracts in managing insulin resistance and diabetic complications. In animal models, nanocarriers enhance bioavailability, prolong systemic circulation, and facilitate targeted tissue delivery, resulting in improved glycemic control, reduced oxidative stress, and mitigation of inflammatory processes[43]. Nano-berberine demonstrates increased insulin sensitivity, reduced hepatic gluconeogenesis, and improved lipid metabolism in diabetic rodents, surpassing the efficacy of free berberine[44]. Nano-curcumin formulations attenuate systemic inflammation, lower oxidative stress markers, and preserve pancreatic β-cell function. Combination nanoformulations containing multiple phytochemicals display synergistic effects, simultaneously targeting insulin signaling, inflammatory pathways, and oxidative stress[44].

Translational potential is evident, but clinical data remain limited. Early-phase human studies indicate improved pharmacokinetics, enhanced tolerability, and reductions in inflammatory biomarkers, suggesting that the

nanoformulation improves therapeutic outcomes without significant toxicity[45]. However, large-scale, randomized clinical trials are essential to validate these findings and establish dosing protocols, long-term safety, and efficacy across diverse patient populations. The integration of preclinical evidence with pharmacokinetic and pharmacodynamic modeling provides a roadmap for clinical translation. Standardization of nanoformulation, reproducible manufacturing processes, and well-designed clinical trials will be critical for transforming experimental success into clinical practice.

6. Safety, Toxicity, and Regulatory Considerations

Safety considerations for herbal nanocarriers depend on composition, particle size, surface charge, and administered dose. Nanoparticle biodistribution studies indicate that repeated or high-dose administration may result in accumulation in the liver, spleen, kidneys, and lymphatic tissues, necessitating comprehensive long-term safety evaluations[46–48].

The use of biodegradable polymers such as PLGA, chitosan, or alginate reduces accumulation risks and facilitates physiological clearance. Nevertheless, chronic exposure studies, immunogenicity assessment, genotoxicity screening, and organ-specific toxicity evaluations are essential to ensure patient safety during prolonged therapy[49].

Regulatory approval requires standardized manufacturing protocols, batch reproducibility, and rigorous toxicological documentation[50]. Differentiating herbal nanomedicines from dietary supplements is crucial, as nanocarrier systems are classified under pharmaceutical regulations and demand stringent safety, efficacy, and quality control standards. Pharmacokinetic, biodistribution, and immunogenicity data are mandatory for regulatory submission, ensuring clinical translation is both safe and effective[50, 51].

Balancing enhanced therapeutic efficacy with safety is central to regulatory compliance. Only through robust characterization, standardized production, and validated safety assessment can herbal nanocarrier systems achieve widespread clinical adoption.

7. Future Perspectives and Clinical Integration

Future research in herbal nanodelivery should focus on personalized medicine, real-time metabolic monitoring, and smart closed-loop systems. Integration with continuous glucose monitoring and biosensor technology allows adaptive, real-time modulation of therapeutic release based on metabolic status.

Combination nanoformulations, delivering multiple antioxidants or bioactive compounds, may provide synergistic metabolic and anti-inflammatory benefits, addressing the multifactorial nature of diabetes. ROS-responsive, glucose-sensitive, and multi-stimuli platforms offer dynamic, context-dependent delivery, reducing systemic toxicity and optimizing efficacy.

Scalable and cost-effective manufacturing strategies will be critical for accessibility and global clinical implementation. Interdisciplinary collaboration among nanotechnologists, pharmacologists, clinicians, and regulatory scientists is essential to address challenges in production, standardization, and clinical translation.

Ultimately, the integration of herbal nanocarriers with digital health platforms and precision medicine holds promise for individualized diabetes therapy, providing sustained glycemic control, reduced complications, and improved patient outcomes. Clinical trials, real-world validation, and regulatory harmonization will be pivotal for translating these advanced systems from bench to bedside.

CONCLUSION

Smart nanodelivery systems represent a significant advancement in optimizing herbal antidiabetic therapy. By integrating controlled release, tissue targeting, and stimuli responsiveness, these platforms enhance the pharmacokinetic and pharmacodynamic performance of phytochemicals while aligning therapeutic action with metabolic pathophysiology. Preclinical evidence supports improved glycemic control, reduced inflammation, and enhanced insulin sensitivity compared to conventional formulations. Nevertheless, long-term safety, standardization, and robust clinical validation remain essential before widespread implementation. With continued innovation and rigorous translational research, smart nanodelivery systems may transform herbal medicine into precision metabolic therapeutics for diabetes management.

REFERENCES

1. Adil, M., Khan, R.A., Ghosh, P., Venkata, S.K., Kandhare, A.D., Sharma, M.: Pioglitazone and risk of bladder cancer in type 2 diabetes mellitus patients: A systematic literature review and meta-analysis of observational studies using real-world data. Clin. Epidemiol. Glob. Health. 6, 61–68 (2018). https://doi.org/10.1016/j.cegh.2017.08.002
2. Bastien, M., Poirier, P., Brassard, P., Arsenault, B.J., Bertrand, O.F., Després, J.-P., Costerousse, O., Piché, M.-E.: Effect of PPARγ agonist on aerobic exercise capacity in relation to body fat distribution in men with type 2 diabetes mellitus and coronary artery disease: a 1-yr randomized study. Am. J. Physiol.-Endocrinol. Metab. 317, E65–E73 (2019). https://doi.org/10.1152/ajpendo.00505.2018
3. Bouyahya, A., Balahbib, A., Khalid, A., Makeen, H.A., Alhazmi, H.A., Albratty, M., Hermansyah, A., Ming, L.C., Goh, K.W., El Omari, N.: Clinical applications and mechanism insights of natural flavonoids against type 2 diabetes mellitus. Heliyon. 10, e29718 (2024). https://doi.org/10.1016/j.heliyon.2024.e29718
4. Alum, E.U.: Optimizing patient education for sustainable self-management in type 2 diabetes. Discov. Public Health. 22, 44 (2025). https://doi.org/10.1186/s12982-025-00445-5

5. Ikpozu, E.N., Offor, C.E., Igwenyi, I.O., Obaroh, I.O., Ibiam, U.A., Ukaidi, C.U.A.: RNA-based diagnostic innovations: A new frontier in diabetes diagnosis and management. Diab. Vasc. Dis. Res. 22, 14791641251334726 (2025). https://doi.org/10.1177/14791641251334726
6. Uti, D.E., Atangwho, I.J., Alum, E.U., Egba, S.I., Ugwu, O.P.-C., Ikechukwu, G.C.: Natural Antidiabetic Agents: Current Evidence and Development Pathways from Medicinal Plants to Clinical use. Nat. Prod. Commun. 20, 1934578X251323393 (2025). https://doi.org/10.1177/1934578X251323393
7. Alam, S., Sarker, Md.M.R., Sultana, T.N., Chowdhury, Md.N.R., Rashid, M.A., Chaity, N.I., Zhao, C., Xiao, J., Hafez, E.E., Khan, S.A., Mohamed, I.N.: Antidiabetic Phytochemicals From Medicinal Plants: Prospective Candidates for New Drug Discovery and Development. Front. Endocrinol. 13, 800714 (2022). https://doi.org/10.3389/fendo.2022.800714
8. Benrahou, K., Naceiri Mrabti, H., Bouyahya, A., Daoudi, N.E., Bnouham, M., Mezzour, H., Mahmud, S., Alshahrani, M.M., Obaidullah, A.J., Cherrah, Y., Faouzi, M.E.A.: Inhibition of α-Amylase, α-Glucosidase, and Lipase, Intestinal Glucose Absorption, and Antidiabetic Properties by Extracts of Erodium guttatum. Evid.-Based Complement. Altern. Med. ECAM. 2022, 5868682 (2022). https://doi.org/10.1155/2022/5868682
9. Dewanjee, S., Chakraborty, P., Mukherjee, B., De Feo, V.: Plant-Based Antidiabetic Nanoformulations: The Emerging Paradigm for Effective Therapy. Int. J. Mol. Sci. 21, 2217 (2020). https://doi.org/10.3390/ijms21062217
10. Gupta, R.C., Chang, D., Nammi, S., Bensoussan, A., Bilinski, K., Roufogalis, B.D.: Interactions between antidiabetic drugs and herbs: an overview of mechanisms of action and clinical implications. Diabetol. Metab. Syndr. 9, 59 (2017). https://doi.org/10.1186/s13098-017-0254-9
11. Tekou, F.A., Kuate, D., Nguekouo, P.T., Woumbo, C.Y., Oben, J.E.: Effect of cooking treatments on the phytochemical composition and antidiabetic potential of Vernonia amygdalina. Food Sci. Nutr. 6, 1684–1691 (2018). https://doi.org/10.1002/fsn3.732
12. Wahab, M., Bhatti, A., John, P.: Evaluation of Antidiabetic Activity of Biogenic Silver Nanoparticles Using Thymus serpyllum on Streptozotocin-Induced Diabetic BALB/c Mice. Polymers. 14, 3138 (2022). https://doi.org/10.3390/polym14153138
13. Omang, W.A., Bawa, I., Idowu, A.O., Atangwho, I.J., Egbung, G.E.: Theranostic Nanoparticles in Prostate Cancer: Disrupting Hypoxia-Induced Glycolysis by Targeting Hypoxia-Inducible Factor-1 Alpha and Downstream Metabolites. Cancer Med. 15, e71519 (2026). https://doi.org/10.1002/cam4.71519
14. Anjum, S., Ishaque, S., Fatima, H., Farooq, W., Hano, C., Abbasi, B.H., Anjum, I.: Emerging Applications of Nanotechnology in Healthcare Systems: Grand Challenges and Perspectives. Pharmaceuticals. 14, 707 (2021). https://doi.org/10.3390/ph14080707
15. Nardella, M., Pellegrini, M., Yu, A.C., Adamo, G.G., Mura, M., Busin, M.: Nanotechnology-Based Delivery Systems and Retinal Pigment Epithelium: Advances, Targeting Approaches, and Translational Challenges. Biomolecules. 15, 1592 (2025). https://doi.org/10.3390/biom15111592
16. Nwuruku, O.A., Edwin, N.: Harnessing nature: plant-derived nanocarriers for targeted drug delivery in cancer therapy. Phytomedicine Plus. 5, 100828 (2025). https://doi.org/10.1016/j.phyplu.2025.100828
17. Adepu, S., Ramakrishna, S.: Controlled Drug Delivery Systems: Current Status and Future Directions. Molecules. 26, 5905 (2021). https://doi.org/10.3390/molecules26195905
18. Chang, D., Ma, Y., Xu, X., Xie, J., Ju, S.: Stimuli-Responsive Polymeric Nanoplatforms for Cancer Therapy. Front. Bioeng. Biotechnol. 9, 707319 (2021). https://doi.org/10.3389/fbioe.2021.707319
19. Jaiswal, K.P., Monika, null, Mazumder, R., Mazumder, A.: Smart Stimuli-Responsive Drug Delivery Systems for Advanced Diabetes Management. Curr. Drug Metab. (2025). https://doi.org/10.2174/0113892002390554251015114414
20. Lee, H., Rho, W.-Y., Kim, Y.-H., Chang, H., Jun, B.-H.: CRISPR-Cas9 Gene Therapy: Non-Viral Delivery and Stimuli-Responsive Nanoformulations. Molecules. 30, 542 (2025). https://doi.org/10.3390/molecules30030542
21. Mi, P.: Stimuli-responsive nanocarriers for drug delivery, tumor imaging, therapy and theranostics. Theranostics. 10, 4557–4588 (2020). https://doi.org/10.7150/thno.38069
22. Yang, J., des Rieux, A., Malfanti, A.: Stimuli-Responsive Nanomedicines for the Treatment of Non-cancer Related Inflammatory Diseases. ACS Nano. 19, 15189–15219 (2025). https://doi.org/10.1021/acsnano.5c00700
23. Prakash, G., Chaudhary, A.A., Tanu, R., Ali, M.A.M., Boufahja, F., Sharma, P.K., Lakhawat, S.S., Yadav, T., Upadhyay, N.K., Kumar, V.: Harnessing Phytochemicals and Nanotechnology Synergy for Molecular, Epigenetic, and Microbiota-Driven Regulation in Type 2 Diabetes Mellitus. Pharmaceutics. 18, (2026). https://doi.org/10.3390/pharmaceutics18010113
24. Tarahi, M., Singh, M., Farahnaky, A., Ghasemlou, M., Dokouhaki, M.: Plant-based delivery systems for bioactive compounds: Mechanisms of release and functional food applications. Adv. Colloid Interface Sci. 350, 103787 (2026). https://doi.org/10.1016/j.cis.2026.103787
25. Eltaib, L.: Polymeric Nanoparticles in Targeted Drug Delivery: Unveiling the Impact of Polymer Characterization and Fabrication. Polymers. 17, (2025). https://doi.org/10.3390/polym17070833

26. Zhang, H., Chen, H., Hu, X., Muhammad, W., Liu, C., Liu, W.: Inflammation-modulating polymeric nanoparticles: design strategies, mechanisms, and therapeutic applications. eBioMedicine. 118, 105837 (2025). https://doi.org/10.1016/j.ebiom.2025.105837
27. Uti, D.E., Alum, E.U., Atangwho, I.J., Ugwu, O.P.-C., Egbung, G.E., Aja, P.M.: Lipid-based nano-carriers for the delivery of anti-obesity natural compounds: advances in targeted delivery and precision therapeutics. J. Nanobiotechnology. 23, 336 (2025). https://doi.org/10.1186/s12951-025-03412-z
28. Anwar, D.M., Hedeya, H.Y., Ghozlan, S.H., Ewas, B.M., Khattab, S.N.: Surface-modified lipid-based nanocarriers as a pivotal delivery approach for cancer therapy: application and recent advances in targeted cancer treatment. Beni-Suef Univ. J. Basic Appl. Sci. 13, 106 (2024). https://doi.org/10.1186/s43088-024-00566-x
29. Mohite, P., Singh, S., Pawar, A., Sangale, A., Prajapati, B.G.: Lipid-based oral formulation in capsules to improve the delivery of poorly water-soluble drugs. Front. Drug Deliv. 3, (2023). https://doi.org/10.3389/fddev.2023.1232012
30. Segneanu, A.-E., Bejenaru, L.E., Bejenaru, C., Blendea, A., Mogoşanu, G.D., Biţă, A., Boia, E.R.: Advancements in Hydrogels: A Comprehensive Review of Natural and Synthetic Innovations for Biomedical Applications. Polymers. 17, 2026 (2025). https://doi.org/10.3390/polym17152026
31. Tenchov, R., Hughes, K.J., Ganesan, M., Iyer, K.A., Ralhan, K., Lotti Diaz, L.M., Bird, R.E., Ivanov, J.M., Zhou, Q.A.: Transforming Medicine: Cutting-Edge Applications of Nanoscale Materials in Drug Delivery. ACS Nano. 19, 4011–4038 (2025). https://doi.org/10.1021/acsnano.4c09566
32. Ahmed, B., Sultana, R., Greene, M.W.: Adipose tissue and insulin resistance in obese. Biomed. Pharmacother. 137, 111315 (2021). https://doi.org/10.1016/j.biopha.2021.111315
33. Obasi, D.C., Abba, J.N., Aniokete, U.C., Okoroh, P.N., Akwari, A.Ak.: Evolving Paradigms in Nutrition Therapy for Diabetes: From Carbohydrate Counting to Precision Diets. Obes. Med. 100622 (2025). https://doi.org/10.1016/j.obmed.2025.100622
34. Xiao, X., Nie, Y., Leng, Y.: Asialoglycoprotein receptor 1: a multifaceted receptor in the liver and cardiovascular system. Front. Med. 12, (2025). https://doi.org/10.3389/fmed.2025.1653452
35. Alanteet, A., Attia, H., Alfayez, M., Mahmood, A., Alsaleh, K., Alsanea, S.: Liraglutide attenuates obese-associated breast cancer cell proliferation via inhibiting PI3K/Akt/mTOR signaling pathway. Saudi Pharm. J. SPJ. 32, 101923 (2024). https://doi.org/10.1016/j.jsps.2023.101923
36. Sayem, A.S.M., Arya, A., Karimian, H., Krishnasamy, N., Ashok Hasamnis, A., Hossain, C.F.: Action of Phytochemicals on Insulin Signaling Pathways Accelerating Glucose Transporter (GLUT4) Protein Translocation. Molecules. 23, 258 (2018). https://doi.org/10.3390/molecules23020258
37. Corvera, S., Solivan-Rivera, J., Yang Loureiro, Z.: Angiogenesis in adipose tissue and obesity. Angiogenesis. 25, 439–453 (2022). https://doi.org/10.1007/s10456-022-09848-3
38. Dhokte, S., Czaja, K.: Visceral Adipose Tissue: The Hidden Culprit for Type 2 Diabetes. Nutrients. 16, (2024). https://doi.org/10.3390/nu16071015
39. Cristelo, C., Nunes, R., Pinto, S., Marques, J.M., Gama, F.M., Sarmento, B.: Targeting β Cells with Cathelicidin Nanomedicines Improves Insulin Function and Pancreas Regeneration in Type 1 Diabetic Rats. ACS Pharmacol. Transl. Sci. 6, 1544–1560 (2023). https://doi.org/10.1021/acsptsci.3c00218
40. Wang, J., Wang, Z., Yu, J., Kahkoska, A.R., Buse, J.B., Gu, Z.: Glucose-responsive insulin and delivery systems: innovation and translation. Adv. Mater. Deerfield Beach Fla. 32, e1902004 (2020). https://doi.org/10.1002/adma.201902004
41. Chen, Y.-S., Tian, H.-X., Rong, D.-C., Wang, L., Chen, S., Zeng, J., Xu, H., Mei, J., Wang, L.-Y., Liou, Y.-L., Zhou, H.-H.: ROS homeostasis in cell fate, pathophysiology, and therapeutic interventions. Mol. Biomed. 6, 89 (2025). https://doi.org/10.1186/s43556-025-00338-8
42. Du, Z., Saleh, E.A.M., M.Moharam, M., Rab, S.O., Ballal, S., Singh, A., Sabarivani, A., Sahoo, S., Hsu, C.-Y.: Enzyme Responsive Magnetic Nanoparticles for Targeted Drug Delivery and Precision Medicine. Drug Dev. Res. 86, e70185 (2025). https://doi.org/10.1002/ddr.70185
43. Shaddel, R., Rashidinejad, A., Karimkhani, M.M., Tarhan, O., Jafari, S.M.: Nanodelivery systems of thymoquinone for improving its bioavailability and efficiency in the food and biomedical applications. Ind. Crops Prod. 234, 121555 (2025). https://doi.org/10.1016/j.indcrop.2025.121555
44. Liu, D., Zhao, L., Wang, Y., Wang, L., Wu, D., Liu, Y.: Berberine: A Rising Star in the Management of Type 2 Diabetes—Novel Insights into Its Anti-Inflammatory, Metabolic, and Epigenetic Mechanisms. Pharmaceuticals. 18, (2025). https://doi.org/10.3390/ph18121890
45. Singh, P., Joshi, A.S., Singh, H., Mijakovic, I.: Medical importance and pharmacokinetics of gold nanoparticles in the human body. Mol. Cancer. 24, 252 (2025). https://doi.org/10.1186/s12943-025-02418-3
46. Domb, A.J., Sharifzadeh, G., Nahum, V., Hosseinkhani, H.: Safety Evaluation of Nanotechnology Products. Pharmaceutics. 13, 1615 (2021). https://doi.org/10.3390/pharmaceutics13101615
47. Onaciu, A., Jurj, A., Moldovan, C., Berindan-Neagoe, I., Onaciu, A., Jurj, A., Moldovan, C., Berindan-Neagoe, I.: Theranostic Nanoparticles and Their Spectrum in Cancer. In: Engineered Nanomaterials - Health and Safety. IntechOpen (2019)

48. Shan, F., Liu, L., Li, L., Wang, W., Bi, Y., Li, M.: Management, Safety, and Efficacy Evaluation of Nutraceutical and Functional Food: A Global Perspective. Compr. Rev. Food Sci. Food Saf. 24, e70222 (2025). https://doi.org/10.1111/1541-4337.70222
49. Elmowafy, E.M., Tiboni, M., Soliman, M.E.: Biocompatibility, biodegradation and biomedical applications of poly(lactic acid)/poly(lactic-co-glycolic acid) micro and nanoparticles. J. Pharm. Investig. 49, 347–380 (2019). https://doi.org/10.1007/s40005-019-00439-x
50. Murali, S., Thomas, J., Abraham, J., Kanna, V., Ramachandiran, S., Ss, S.: Nanodiagnostics and nanotoxicology: A systematic review and meta-analysis on nanoparticle applications and safety in metabolic organs. OpenNano. 27, 100266 (2026). https://doi.org/10.1016/j.onano.2025.100266
51. Alum, E.U., Manjula, V.S., Uti, D.E., Echegu, D.A., Ugwu, O.P.-C., Egba, S.I., Agu, P.C.: Metabolomics-Driven Standardization of Herbal Medicine: Advances, Applications, and Sustainability Considerations. Nat. Prod. Commun. 20, 1934578X251367650 (2025). https://doi.org/10.1177/1934578X251367650

CITE AS: Nasira A. Sitar (2026). Smart Nanodelivery Systems for Herbal Antidiabetic Agents: Controlled Release and Targeted Metabolic Modulation. IDOSR JOURNAL OF BIOCHEMISTRY, BIOTECHNOLOGY AND ALLIED FIELDS 11(3):63-69.
https://doi.org/10.59298/IDOSR/JBBAF/2026/1136369