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Nanoencapsulation of Natural Antioxidants for Diabetic Complications: Mechanisms and Clinical Prospects

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ABSTRACT

Chronic hyperglycemia in diabetes mellitus drives excessive reactive oxygen species (ROS) generation, mitochondrial dysfunction, advanced glycation end-product (AGE) formation, and persistent inflammation, collectively contributing to microvascular and macrovascular complications. Natural antioxidants including polyphenols, carotenoids, flavonoids, alkaloids, and terpenoids exert protective effects by scavenging ROS, activating endogenous antioxidant pathways, and modulating inflammatory signaling. However, their therapeutic translation is often limited by poor solubility, low oral bioavailability, rapid metabolism, and inadequate tissue targeting. Nanoencapsulation offers a promising strategy to overcome these barriers by improving stability, enhancing absorption, enabling sustained release, and facilitating targeted delivery to vulnerable organs such as kidney, retina, peripheral nerves, and cardiovascular tissues. Liposomes, polymeric nanoparticles, solid lipid nanoparticles, nanostructured lipid carriers, nanoemulsions, and nanogels have demonstrated enhanced pharmacokinetic and pharmacodynamic profiles of antioxidant compounds in preclinical models of diabetic nephropathy, neuropathy, retinopathy, and cardiomyopathy. This review examines oxidative stress mechanisms in diabetic complications, the rationale for antioxidant nanoencapsulation, design strategies for organ-specific delivery, preclinical and emerging clinical evidence, safety considerations, and translational challenges. Nanoencapsulated natural antioxidants represent a compelling avenue for mitigating diabetes-related tissue injury and advancing precision therapeutic interventions.

Keywords: diabetic complications; natural antioxidants; nanoencapsulation; oxidative stress; targeted delivery

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized not only by persistent hyperglycemia but also by progressive tissue damage affecting multiple organ systems[1–3]. While glycemic control remains central to management, long-term complications including diabetic nephropathy, neuropathy, retinopathy, and cardiovascular disease account for the majority of morbidity and mortality[4]. A unifying pathogenic mechanism underlying these complications is oxidative stress, driven by chronic hyperglycemia and metabolic dysregulation.

Hyperglycemia enhances mitochondrial superoxide production in endothelial and parenchymal cells. Excess ROS activates multiple damaging pathways: polyol flux increases sorbitol accumulation and depletes NADPH; protein kinase C (PKC) activation alters vascular permeability and blood flow; AGE formation modifies structural proteins and receptor signaling; and hexosamine pathway flux disrupts transcriptional regulation[5–8]. These biochemical cascades impair endothelial function, promote inflammation, and induce apoptosis in target tissues such as glomerular podocytes, retinal cells, peripheral neurons, and cardiomyocytes.

Oxidative stress is further amplified by chronic low-grade inflammation. Pro-inflammatory cytokines including TNF-α and IL-6 activate NF-κB signaling, reinforcing ROS generation and vascular dysfunction[9–12]. Endothelial nitric oxide synthase (eNOS) uncoupling reduces nitric oxide bioavailability, contributing to microvascular injury. Over time, cumulative oxidative damage leads to structural and functional impairment of organs.

Natural antioxidants derived from plants and dietary sources have been widely investigated for their capacity to counteract oxidative injury. Polyphenols such as resveratrol, quercetin, curcumin, and epigallocatechin gallate (EGCG) activate Nrf2-mediated antioxidant pathways, increase expression of heme oxygenase-1 and glutathione peroxidase, and suppress NF-κB–driven inflammation[13]. Carotenoids and terpenoids scavenge

free radicals and protect lipid membranes from peroxidation. Alkaloids and phenolic acids further modulate mitochondrial function and vascular tone.

Despite strong mechanistic rationale and promising experimental findings, clinical outcomes with conventional antioxidant supplementation have been inconsistent. Several factors explain this discrepancy[14]. Many antioxidants exhibit poor aqueous solubility and limited intestinal absorption. First-pass hepatic metabolism reduces systemic bioavailability. Rapid clearance results in low tissue concentrations, particularly in organs protected by biological barriers such as the retina or peripheral nerves. Furthermore, high systemic doses may be required to achieve therapeutic levels, increasing the risk of adverse effects or drug interactions[14].

Nanoencapsulation has emerged as a transformative strategy to enhance the therapeutic performance of natural antioxidants. By incorporating antioxidant molecules into nanoscale carriers, researchers can protect them from degradation, enhance solubility, and improve pharmacokinetics[15]. Nanocarriers typically range from 10 to 200 nm, enabling enhanced permeability and retention in inflamed or damaged tissues. Controlled-release formulations maintain therapeutic concentrations over extended periods, reducing dosing frequency and improving adherence[16-20].

In diabetic complications, targeted delivery is particularly valuable. Diabetic nephropathy involves oxidative injury in glomerular and tubular cells; retinopathy involves microvascular and neuronal damage in the retina; neuropathy affects peripheral nerve axons and Schwann cells; cardiomyopathy impacts myocardial mitochondria and vascular endothelium[17,18,21-24]. Nanoencapsulation can facilitate preferential accumulation of antioxidants in these tissues through surface modification, ligand targeting, or exploitation of enhanced vascular permeability.

Additionally, some nanocarriers themselves possess antioxidant properties. Lipid-based carriers can stabilize lipophilic antioxidants, while polymeric nanoparticles may be engineered to respond to ROS-rich environments, releasing cargo in sites of oxidative stress. Such stimuli-responsive systems align therapeutic action with pathophysiological triggers[19,25-30]. However, nanotechnology introduces new considerations including biodistribution, clearance, long-term safety, and regulatory oversight. The balance between improved delivery and potential nanoparticle-associated toxicity must be carefully evaluated[20,31-36]. This review discusses the mechanistic basis of oxidative stress in diabetic complications, the rationale for nanoencapsulation of natural antioxidants, nanocarrier platforms and targeting strategies, preclinical and clinical evidence, safety considerations, and future translational prospects. By enhancing delivery precision and therapeutic efficacy, nanoencapsulated antioxidants may offer meaningful advances in the prevention and management of diabetes-related complications.

2. Oxidative Stress Mechanisms in Diabetic Complications

Persistent hyperglycemia leads to excessive ROS generation primarily within mitochondria. Elevated glucose flux increases electron transport chain activity, promoting superoxide formation[6, 21,37-40]. This initiates a cascade of oxidative events affecting vascular and parenchymal tissues. In diabetic nephropathy, oxidative stress damages glomerular endothelial cells, podocytes, and mesangial cells. AGE accumulation and PKC activation increase extracellular matrix deposition, leading to glomerulosclerosis and proteinuria. Nrf2 suppression further weakens endogenous antioxidant defenses.

In diabetic retinopathy, ROS disrupt retinal microvasculature, increase vascular permeability, and induce neuronal apoptosis[22,41-46]. Oxidative injury to pericytes contributes to capillary dropout and microaneurysm formation. Peripheral neuropathy involves mitochondrial dysfunction and impaired axonal transport due to ROS-mediated lipid peroxidation. Reduced nitric oxide availability and inflammatory cytokines exacerbate nerve ischemia. Diabetic cardiomyopathy is characterized by myocardial oxidative damage, impaired calcium handling, and fibrosis. Hyperglycemia-induced ROS impairs mitochondrial ATP production, compromising contractility[23,47-52]. Across these complications, oxidative stress interacts with inflammation and metabolic dysregulation, creating a self-perpetuating cycle. Targeting oxidative pathways is therefore central to mitigating organ damage.

3. Nanoencapsulation Strategies for Natural Antioxidants

Nanoencapsulation represents a powerful technological approach for enhancing the stability, solubility, bioavailability, and tissue-specific delivery of natural antioxidant molecules in diabetic therapy[24,53-57]. Many plant-derived antioxidants suffer from poor aqueous solubility, rapid metabolic degradation, and limited tissue penetration, which significantly restrict their therapeutic effectiveness. Nanoencapsulation overcomes these barriers by protecting bioactive compounds from chemical degradation, enzymatic metabolism, and premature clearance, while enabling controlled and targeted delivery to oxidative microenvironments.

Liposomes are among the most established nanoencapsulation platforms, consisting of phospholipid bilayers capable of encapsulating both hydrophilic and lipophilic antioxidants. Their structural similarity to biological membranes enhances cellular uptake and biocompatibility, allowing efficient intracellular delivery and improved bioavailability[25–27,58-63]. Liposomal systems are particularly effective for polyphenols and flavonoids that require membrane-mimetic carriers for optimal absorption.

Polymeric nanoparticles, constructed from biodegradable polymers such as PLGA, chitosan, and alginate, provide robust protection against degradation and enable sustained-release profiles[28, 29, 64-68]. These

systems allow prolonged antioxidant availability, maintaining therapeutic concentrations in tissues exposed to chronic oxidative stress. Their tunable degradation kinetics offer precise control over drug release dynamics.
Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) are especially suitable for lipophilic antioxidants such as curcumin, carotenoids, and tocopherols. These lipid-based systems offer high loading capacity, controlled release behavior, and excellent biocompatibility, ensuring prolonged antioxidant action in diabetic tissues. Nanoemulsions enhance the dissolution rate and intestinal absorption of hydrophobic antioxidants by increasing surface area and improving dispersion in gastrointestinal fluids. Nanogels, composed of hydrophilic crosslinked polymer networks, enable ROS-responsive release, ensuring antioxidants are released specifically within oxidative microenvironments[30,69-72].
Surface modification with targeting ligands further improves accumulation in organs such as the kidneys, retina, and peripheral nerves, while controlled-release properties maintain therapeutic levels in oxidative tissues, maximizing efficacy and minimizing systemic exposure.

4. Organ-Specific Targeting in Diabetic Complications

Targeted nanoencapsulation strategies significantly enhance the precision delivery of antioxidants to organs most affected by diabetic complications, enabling localized therapeutic action and improved disease modulation[31]. Organ-specific targeting not only improves antioxidant concentration at pathological sites but also reduces systemic exposure and off-target effects. In kidney targeting, nanoparticles functionalized with specific peptides, antibodies, or receptor-binding ligands preferentially accumulate in glomerular and tubular tissues[31]. This targeted delivery reduces oxidative stress, proteinuria, extracellular matrix deposition, and fibrotic remodeling, thereby slowing the progression of diabetic nephropathy and preserving renal function.
For retinal delivery, lipid-based nanoparticles and surface-modified nanocarriers are designed to cross the blood–retinal barrier, enabling direct antioxidant protection of retinal neurons, endothelial cells, and microvasculature. This targeted approach mitigates oxidative injury, vascular leakage, neurodegeneration, and inflammatory damage associated with diabetic retinopathy[32,70-73].
Peripheral nerve targeting is achieved through nanocarriers capable of penetrating the endoneurial and perineurial barriers, significantly improving antioxidant exposure within neural tissues[33]. This strategy reduces oxidative damage, mitochondrial dysfunction, and neuroinflammation, thereby attenuating neuropathic pain and sensory deficits. In cardiac targeting, surface-modified nanoparticles enhance myocardial uptake and intracellular delivery to cardiomyocytes. These systems protect mitochondrial integrity, reduce oxidative stress, and limit fibrotic remodeling, improving cardiac function in diabetic cardiomyopathy[33].
Advanced stimuli-responsive nanoparticles further refine targeting precision by releasing antioxidants specifically within ROS-rich and inflammatory microenvironments, ensuring localized action while minimizing systemic exposure and toxicity.

5. Preclinical and Emerging Clinical Evidence

Extensive preclinical studies provide strong evidence supporting the therapeutic efficacy of nanoencapsulated natural antioxidants in diabetic complications. Animal models consistently demonstrate improved renal function, reduced albuminuria, decreased oxidative stress markers, and restoration of antioxidant enzyme activity following treatment with nanoformulated antioxidants[34]. These benefits are accompanied by improved metabolic control and reduced inflammatory signaling. Nano-curcumin formulations have been shown to significantly reduce retinal inflammation, vascular permeability, and microvascular degeneration in diabetic retinopathy models. Similarly, resveratrol-loaded nanoparticles improve cardiac mitochondrial function, enhance ATP production, and reduce fibrotic remodeling in diabetic cardiomyopathy[34].
Quercetin-loaded nanoparticles demonstrate potent neuroprotective effects, attenuating neuropathic pain, reducing oxidative damage, and preserving neuronal structure in experimental diabetes. These nanoformulations achieve superior tissue penetration and prolonged antioxidant activity compared to free compounds[35]. At the clinical level, data remain limited; however, early-phase human studies suggest improved pharmacokinetic profiles, enhanced bioavailability, and reductions in inflammatory biomarkers with selected nanoformulations[35]. These findings indicate translational promise but remain insufficient for clinical standardization.
The absence of large-scale, randomized, controlled clinical trials represents a major translational gap. Robust clinical validation is essential to confirm therapeutic efficacy, long-term safety, and disease-modifying potential. Future translational progress will depend on standardized formulations, harmonized protocols, and integrated clinical research pipelines.

6. Safety and Regulatory Considerations

The clinical translation of nanoencapsulated antioxidants requires rigorous evaluation of safety, toxicity, and regulatory compliance. Nanoparticle safety is determined by multiple factors, including size, composition, surface chemistry, dose, and administration route. Biodistribution studies must carefully assess accumulation in vital organs such as the liver, spleen, kidneys, and lymphatic tissues, where long-term retention may pose toxicity risks[36–38].
The use of biodegradable polymers significantly reduces long-term toxicity potential by enabling metabolic breakdown and physiological clearance. However, repeated or chronic administration necessitates

comprehensive long-term safety evaluations, including immunogenicity, genotoxicity, organ toxicity, and chronic exposure studies.

Regulatory approval requires comprehensive physicochemical characterization, validated manufacturing protocols, reproducibility data, and extensive toxicological documentation[39–41]. Agencies demand detailed pharmacokinetic profiling, biodistribution mapping, and standardized dosing frameworks specific to nanoscale systems.

Balancing enhanced therapeutic efficacy with patient safety remains a central challenge. Successful translation depends on harmonized regulatory frameworks, standardized production, and validated safety pipelines that ensure nanoencapsulation technologies deliver clinical benefit without compromising long-term health outcomes.

7. Future Directions and Clinical Prospects

Future research should focus on integrating precision targeting, ROS-responsive delivery systems, and personalized medicine approaches to maximize the clinical impact of nanoencapsulated antioxidants in diabetes care. Precision nanotherapy platforms must combine tissue-specific targeting with disease-responsive release mechanisms to achieve optimal therapeutic specificity. Combination nanoformulations capable of delivering multiple antioxidants simultaneously represent a promising strategy for synergistic protection against oxidative stress, inflammation, and mitochondrial dysfunction[42]. Such systems can target multiple pathological pathways concurrently, enhancing therapeutic outcomes. The integration of nanomedicine with continuous glucose monitoring technologies, biomarker-guided therapy, and digital health platforms may enable adaptive, personalized treatment strategies that dynamically respond to metabolic states and oxidative burden[42].

However, widespread clinical implementation requires large-scale randomized clinical trials, long-term safety evaluations, and cost-effective manufacturing strategies to ensure accessibility and scalability. Ultimately, interdisciplinary collaboration among nanotechnologists, clinicians, pharmacologists, regulatory scientists, and industry partners will be essential to translate nanoencapsulated antioxidant therapies from experimental innovation into standardized clinical practice.

CONCLUSION

Oxidative stress is a central driver of diabetic complications affecting the kidney, retina, nerves, and heart. Natural antioxidants offer mechanistic promise but are limited by poor bioavailability and insufficient tissue targeting. Nanoencapsulation enhances stability, improves pharmacokinetics, and enables organ-specific or ROS-responsive delivery, amplifying therapeutic impact while potentially reducing systemic toxicity. Preclinical studies consistently demonstrate superior antioxidant efficacy and improved functional outcomes compared with conventional formulations. However, long-term safety, regulatory clarity, and robust clinical validation remain essential for successful translation. With continued interdisciplinary research and standardized development pathways, nanoencapsulated natural antioxidants may become valuable adjuncts in preventing and managing diabetes-related complications, contributing to precision and organ-protective diabetes care.

REFERENCES

1. Adhikari, B.: Roles of Alkaloids from Medicinal Plants in the Management of Diabetes Mellitus. J. Chem. 2021, 2691525 (2021). https://doi.org/10.1155/2021/2691525
2. 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
3. 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
4. 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
5. Durrani, I.A., Bhatti, A., John, P.: The prognostic outcome of 'type 2 diabetes mellitus and breast cancer' association pivots on hypoxia-hyperglycemia axis. Cancer Cell Int. 21, 351 (2021). https://doi.org/10.1186/s12935-021-02040-5
6. González, P., Lozano, P., Ros, G., Solano, F.: Hyperglycemia and Oxidative Stress: An Integral, Updated and Critical Overview of Their Metabolic Interconnections. Int. J. Mol. Sci. 24, 9352 (2023). https://doi.org/10.3390/ijms24119352
7. Jain, A.B., Lai, V.: Medication-Induced Hyperglycemia and Diabetes Mellitus: A Review of Current Literature and Practical Management Strategies. Diabetes Ther. 15, 2001–2025 (2024). https://doi.org/10.1007/s13300-024-01628-0
8. 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

9. Uti, D.E., Atangwho, I.J., Omang, W.A., Alum, E.U., Obeten, U.N., Udeozor, P.A., Agada, S.A., Bawa, I., Ogbu, C.O.: Cytokines as key players in obesity low grade inflammation and related complications. Obes. Med. 54, 100585 (2025). https://doi.org/10.1016/j.obmed.2025.100585
10. Chen, S., Li, Q., Shi, H., Li, F., Duan, Y., Guo, Q.: New insights into the role of mitochondrial dynamics in oxidative stress-induced diseases. Biomed. Pharmacother. 178, 117084 (2024). https://doi.org/10.1016/j.biopha.2024.117084
11. Čolak, E., Pap, D.: The role of oxidative stress in the development of obesity and obesity-related metabolic disorders. J. Med. Biochem. 40, 1–9 (2021). https://doi.org/10.5937/jomb0-24652
12. El-Baz, Y.G., Moustafa, A., Ali, M.A., El-Desoky, G.E., Wabaidur, S.M., Iqbal, A.: Green synthesized silver nanoparticles for the treatment of diabetes and the related complications of hyperlipidemia and oxidative stress in diabetic rats. Exp. Biol. Med. 248, 2237–2248 (2024). https://doi.org/10.1177/15353702231214258
13. Mokra, D., Joskova, M., Mokry, J.: Therapeutic Effects of Green Tea Polyphenol (–)-Epigallocatechin-3-Gallate (EGCG) in Relation to Molecular Pathways Controlling Inflammation, Oxidative Stress, and Apoptosis. Int. J. Mol. Sci. 24, 340 (2022). https://doi.org/10.3390/ijms24010340
14. Moratilla-Rivera, I., Pérez-Jiménez, J., Martín, M.Á., Mateos, R.: Does hydroxytyrosol deserve a health claim? Effects of its supplementation on aging mechanism from preclinical to human intervention studies. Food Res. Int. 118578 (2026). https://doi.org/10.1016/j.foodres.2026.118578
15. Pugazhendhi, A., Alshehri, M.A., Kandasamy, S., Sarangi, P.K., Sharma, A.: Deciphering the importance of nanoencapsulation to improve the availability of bioactive molecules in food sources to the human body. Food Chem. 464, 141762 (2025). https://doi.org/10.1016/j.foodchem.2024.141762
16. Nwuruku, O.A., Ugwu, O.P.-C., Uti, D.E., 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. Horton, W.B., Barrett, E.J.: Microvascular Dysfunction in Diabetes Mellitus and Cardiometabolic Disease. Endocr. Rev. 42, 29–55 (2020). https://doi.org/10.1210/endrev/bnaa025
18. Omang, W.A., Wokoma, M.A., Oplekwu, R.I., Atangwho, I.J., Egbung, G.E.: Targeting CD44-Hyaluronic Acid Signalling in Obesity Treatment: Insights from Small Molecules and Nanobioconjugates. Nutr. Metab. Insights. 19, 11786388251408961 (2026). https://doi.org/10.1177/11786388251408961
19. Albakr, L., Du, H., Zhang, X., Kathuria, H., Fahmi Anwar-Fadzil, A., Wheate, N.J., Kang, L.: Progress in Lipid and Inorganic Nanocarriers for Enhanced Skin Drug Delivery. Adv. NanoBiomed Res. 4, 2400003 (2024). https://doi.org/10.1002/anbr.202400003
20. 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
21. Ryu, T.Y., Park, J., Scherer, P.E.: Hyperglycemia as a Risk Factor for Cancer Progression. Diabetes Metab. J. 38, 330–336 (2014). https://doi.org/10.4093/dmj.2014.38.5.330
22. Mimura, T., Noma, H.: Oxidative Stress in Diabetic Retinopathy: A Comprehensive Review of Mechanisms, Biomarkers, and Therapeutic Perspectives. Antioxidants. 14, 1204 (2025). https://doi.org/10.3390/antiox14101204
23. Ugwu, O.P.-C., Alum, E.U., Okon, M.B., Aja, P.M., Obeagu, E.I., Onyeneke, E.C.: Ethanol root extract and fractions of Sphenocentrum jollyanum abrogate hyperglycaemia and low body weight in streptozotocin-induced diabetic Wistar albino rats. RPS Pharm. Pharmacol. Rep. 2, rqad010 (2023). https://doi.org/10.1093/rpsppr/rqad010
24. Hao, M., Tan, X., Liu, K., Xin, N.: Nanoencapsulation of nutraceuticals: enhancing stability and bioavailability in functional foods. Front. Nutr. 12, (2026). https://doi.org/10.3389/fnut.2025.1746176
25. Amin, M., Lammers, T., ten Hagen, T.L.M.: Temperature-sensitive polymers to promote heat-triggered drug release from liposomes: Towards bypassing EPR. Adv. Drug Deliv. Rev. 189, 114503 (2022). https://doi.org/10.1016/j.addr.2022.114503
26. Taher, M., Susanti, D., Haris, M.S., Rushdan, A.A., Widodo, R.T., Syukri, Y., Khotib, J.: PEGylated liposomes enhance the effect of cytotoxic drug: A review. Heliyon. 9, e13823 (2023). https://doi.org/10.1016/j.heliyon.2023.e13823
27. Yang, Q., Zhang, T., Wang, C., Jiao, J., Li, J., Deng, Y.: Coencapsulation of epirubicin and metformin in PEGylated liposomes inhibits the recurrence of murine sarcoma S180 existing CD133+ cancer stem-like cells. Eur. J. Pharm. Biopharm. 88, 737–745 (2014). https://doi.org/10.1016/j.ejpb.2014.10.006
28. Wang, Y., Li, H., Rasool, A., Wang, H., Manzoor, R., Zhang, G.: Polymeric nanoparticles (PNPs) for oral delivery of insulin. J. Nanobiotechnology. 22, 1 (2024). https://doi.org/10.1186/s12951-023-02253-y
29. Zielińska, A., Carreiró, F., Oliveira, A.M., Neves, A., Pires, B., Venkatesh, D.N., Durazzo, A., Lucarini, M., Eder, P., Silva, A.M., Santini, A., Souto, E.B.: Polymeric Nanoparticles: Production, Characterization, Toxicology and Ecotoxicology. Molecules. 25, 3731 (2020). https://doi.org/10.3390/molecules25163731
30. Delgado-Pujol, E.J., Martínez, G., Casado-Jurado, D., Vázquez, J., León-Barberena, J., Rodríguez-Lucena, D., Torres, Y., Alcudia, A., Begines, B.: Hydrogels and Nanogels: Pioneering the Future of Advanced

Drug Delivery Systems. Pharmaceutics. 17, 215 (2025). https://doi.org/10.3390/pharmaceutics17020215

31. Li, Z., Luo, B., Chen, Y., Wang, L., Liu, Y., Jia, J., Chen, M., Yang, S., Shi, H., Dai, L., Huang, L., Wang, C., Liu, J.: Nanomaterial-based encapsulation of biochemicals for targeted sepsis therapy. Mater. Today Bio. 33, 102054 (2025). https://doi.org/10.1016/j.mtbio.2025.102054
32. 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
33. Wu, K., Yun, Z., Xue, W., Yu, T., Dai, A., Han, I., Kotheeranurak, V., Limthongkul, W., Liu, Y., Liu, Q.: Application of injectable hydrogels in the central and peripheral nervous system as a unique and flexible platform for neural tissue repair. Mater. Today Bio. 35, 102514 (2025). https://doi.org/10.1016/j.mtbio.2025.102514
34. Al-Waili, N., Al-Waili, H., Al-Waili, T., Salom, K.: Natural antioxidants in the treatment and prevention of diabetic nephropathy; a potential approach that warrants clinical trials. Redox Rep. Commun. Free Radic. Res. 22, 99–118 (2017). https://doi.org/10.1080/13510002.2017.1297885
35. Newairy, A.-S.A.-S., Hamaad, F.A., Wahby, M.M., Ghoneum, M., Abdou, H.M.: Neurotherapeutic effects of quercetin-loaded nanoparticles and Biochanin-A extracted from Trifolium alexandrinum on PI3K/Akt/GSK-3β signaling in the cerebral cortex of male diabetic rats. PLOS ONE. 19, e0301355 (2024). https://doi.org/10.1371/journal.pone.0301355
36. Choi, H., Choi, Y., Yim, H.Y., Mirzaaghasi, A., Yoo, J.-K., Choi, C.: Biodistribution of Exosomes and Engineering Strategies for Targeted Delivery of Therapeutic Exosomes. Tissue Eng. Regen. Med. 18, 499–511 (2021). https://doi.org/10.1007/s13770-021-00361-0
37. Kumar, M., Kulkarni, P., Liu, S., Chemuturi, N., Shah, D.K.: Nanoparticle biodistribution coefficients: A quantitative approach for understanding the tissue distribution of nanoparticles. Adv. Drug Deliv. Rev. 194, 114708 (2023). https://doi.org/10.1016/j.addr.2023.114708
38. Yu, J., Dan, N., Eslami, S.M., Lu, X.: State of the Art of Silica Nanoparticles: An Overview on Biodistribution and Preclinical Toxicity Studies. AAPS J. 26, 35 (2024). https://doi.org/10.1208/s12248-024-00906-w
39. 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
40. Khan, S., Huda, B., Bhurka, F., Patnaik, R., Banerjee, Y.: Molecular and Immunomodulatory Mechanisms of Statins in Inflammation and Cancer Therapeutics with Emphasis on the NF-κB, NLRP3 Inflammasome, and Cytokine Regulatory Axes. Int. J. Mol. Sci. 26, (2025). https://doi.org/10.3390/ijms26178429
41. Mühlebach, S.: Regulatory challenges of nanomedicines and their follow-on versions: A generic or similar approach? Adv. Drug Deliv. Rev. 131, 122–131 (2018). https://doi.org/10.1016/j.addr.2018.06.024
42. Xu, K., Wang, L., Lv, T., Jin, C., Wu, Q., Zhou, Y., Xu, G., Duan, Z., Luo, K., Yang, J.: Nanomedicines Against Mitochondrial Dysfunction-Induced Metabolic Diseases. Adv. Sci. 12, e14522 (2025). https://doi.org/10.1002/advs.202514522
43. Ugwu OPC, Alum EU, Okon MB, Aja PM, Obeagu EI, Onyeneke EC. Ethanol root extract and fractions of Sphenocentrum jollyanum abrogate hyperglycaemia and low body weight in streptozotocin-induced diabetic Wistar albino rats. RPS Pharm Pharmacol Rep. 2023;2(2):rqad010.
44. Ugwu OPC, Alum EU, Okon MB, Aja PM, Obeagu EI, Onyeneke EC. Anti-nutritional and gas chromatography-mass spectrometry (GC-MS) analysis of ethanol root extract and fractions of Sphenocentrum jollyanum. RPS Pharm Pharmacol Rep. 2023;2(2):rqad007.
45. Ugwu OPC, Amasiorah VI. The in vitro antioxidant potentials of the crude ethanol root extract and fractions of Sphenocentrum jollyanum. INOSR Appl Sci. 2020;6(1):125–33.
46. Ugwu OPC, Amasiorah VI. The effects of the crude ethanol root extract and fractions of Sphenocentrum jollyanum on hematological indices and glycosylated haemoglobin of streptozotocin-induced diabetic rats. INOSR Sci Res. 2020;6(1):61–74.
47. Ugwu OPC, Amasiorah VI. The effects of crude ethanol root extract and fractions of Sphenocentrum jollyanum on the lipid profile of streptozotocin-induced diabetic Wistar albino rats. IDOSR J Biol Chem Pharm. 2020;5(1):36–46.
48. Ugwu OPC, Amasiorah VI. The in vivo antioxidant potentials of the crude ethanol root extract and fractions of Sphenocentrum jollyanum on oxidative stress indices in streptozotocin-induced diabetic rats. IDOSR J Biol Chem Pharm. 2020;5(1):26–35.

49. Ugwu OPC, Onyeneke EC, Igwenyi IO, Aja PM, Okon MB. The effects of crude ethanol root extract and fractions of Sphenocentrum jollyanum on liver and kidney function parameters of streptozotocin-induced diabetic Wistar albino rats. IAA J Sci Res. 2018;4(1):75–90.
50. Aja PM, Igwenyi IO, Ugwu OPC, Orji OU, Alum EU. Evaluation of anti-diabetic effect and liver function indices of ethanol extracts of Moringa oleifera and Cajanus cajan leaves in alloxan induced diabetic albino rats. Global Vet. 2015;14(3):439–47.
51. Offor CE, Ugwu OPC, Alum EU. The anti-diabetic effect of ethanol leaf-extract of Allium sativum on albino rats. Int J Pharm Med Sci. 2014;4(1):1–3.
52. Ugwu OPC, Alum EU, Uhama KC. Dual burden of diabetes mellitus and malaria: exploring the role of phytochemicals and vitamins in disease management. Res Invent J Res Med Sci. 2024;3(2):38–49.
53. Obeagu EI, Ugwu OPC, Alum EU. Poor glycaemic control among diabetic patients: a review on associated factors. Newport Int J Res Med Sci. 2023;3(1):30–3.
54. Alum EU, Ugwu OPC, Obeagu EI, Ugwu CN, Uti DE, Samson AO, et al. Nutritional care in diabetes mellitus: a comprehensive guide. Int J Innov Appl Res. 2023;11(12):16–25.
55. Alum EU, Ugwu OPC, Obeagu EI, Uti DE, Egba SI, Alum BN. Managing the dual burden: addressing mental health in diabetes care. Elite J Med Sci. 2024;2(6):1–9.
56. Alum EU, Obeagu EI, Ugwu OPC, Alum BN, Arinze ED, Ukaidi CUA. Exploring the differential impacts of intermittent fasting on men and women. Elite J Health Sci. 2024;2(5):37–44.
57. Obeagu EI, Scott GY, Amekpor F, Ugwu OPC, Alum EU. Covid-19 infection and diabetes: a current issue. Int J Innov Appl Res. 2023;11(1):25–30.
58. Alum EU, Ugwu OPC. Beyond pregnancy: understanding the long-term implications of gestational diabetes mellitus. INOSR Sci Res. 2024;11(1):63–71.
59. Ugwu OPC, Ugwu MN, Basajja M, Anyanwu CN, Ogenyi FC, Ugwu CN, et al. Targeting gut microbial signatures to personalize obesity treatment: integrating microbiome-based stratification into precision medicine. Obes Med. 2025;57:100639.
60. Ugwu OPC, Ogenyi FC, Ugwu CN, Ugwu MN. Gut microbiota-derived metabolites as early biomarkers for childhood obesity: a policy commentary from urban African populations. Obes Med. 2025;57:100641.
61. Ugwu OPC, Swase DT, Okon MB, Mujinya R. Traditional East African medicinal plants as modulators of gut microbiota in obesity-associated diabetes: a short communication. Obes Med. 2025;654:00654.
62. Uti DE, Omang WA, Alum EU, Ugwu OPC, Wokoma MA, Oplekwu RI, et al. Targeting CD44-hyaluronic acid signalling in obesity treatment: insights from small molecules and nanobioconjugates. Nutr Metab Insights. 2026;19:11786388251408961.
63. Uti DE, Omang WA, Alum EU, Atangwho IJ, Ugwu OPC, Wokoma MA, et al. Combined hyaluronic acid nanobioconjugates impair CD44-signaling for effective treatment against obesity: a review of comparison with other actors. Int J Nanomedicine. 2025;20:10101–26.
64. Uti DE, Egbung JE, Alum EU, Bawa I, Ugwu OPC, Egba SI, et al. Nanotechnology-enabled targeted delivery of incretin therapies for the treatment of obesity and metabolic disorders. Obes Med. 2026:100712.
66. Ugwu OPC, Eke MC, Ogenyi FC, Basajja M, Ugwu CN. Could chronic exposure to nocturnal artificial light pollution be an overlooked driver of urban obesity and metabolic syndrome? Med Hypotheses. 2025;205:111819.
67. Alum EU, Izah SC, Uti DE, Ugwu OPC, Betiang PA, Basajja M, et al. The ketogenic diet in obesity management: friend or foe? Cell Biochem Biophys. 2025.
68. Udeh SMC, Nwodo OFC, Yakubu OE, Parker EJ, Egba SI, Omenyi SN, et al. Effects of methanol extract of Gongronema latifolium leaves on glycaemic responses to carbohydrate diets in streptozotocin-induced diabetic rats. J Biol Sci. 2022;22:70–9.
69. Ugwu OPC, Alum EU, Obeagu EI, Okon MB. Effect of ethanol leaf extract of Chromolaena odorata on lipid profile of streptozotocin-induced diabetic Wistar albino rats. IAA J Biol Sci. 2023;10(1):109–17.
70. Ugwu OPC, Alum EU, Obeagu EI, Okon MB. Effect of ethanol leaf extract of Chromolaena odorata on hepatic markers in streptozotocin-induced diabetic Wistar albino rats. IAA J Appl Sci. 2023;9(1):46–56.
71. Aja PM, Ibekwe VI, Ekpono EU, Ugwu PC, Ugwu OPC. Effect of ethanol extract of Cajanus cajan leaf on plasma lipid level in albino rats. Int J Curr Res Acad Rev. 2015;3(1):161–7.

72. Obeagu EI, Ugwu OPC. Overweight and obesity among adolescents: a review. Newport Int J Res Med Sci. 2023;3(1):25–9.
73. Obeagu EI, Ugwu OPC. Insulin self-medication among diabetic patients: a review of associated factors. Newport Int J Res Med Sci. 2023;3(1):21–4.

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