©NIJPP
Publications 2026

OPEN ACCESS
ONLINE ISSN: 2992-5479
PRINT ISSN: 2992-605X

NEWPORT INTERNATIONAL JOURNAL OF PUBLIC HEALTH AND PHARMACY (NIJPP)

Volume 7 Issue 1 Page 62-69, 2026

https://doi.org/10.59298/NIJPP/2026/716269

Nano-Enabled Combination Therapies Integrating Antioxidants, Peptides, and Hormones for Diabesity Treatment

Kato Jumba K.

Faculty of Science and Technology Kampala International University Uganda

ABSTRACT

Obesity and type 2 diabetes frequently coexist as "diabesity," a chronic condition driven by insulin resistance, β-cell stress, lipotoxicity, oxidative damage, and metaflammation. Conventional monotherapies that focus on single pathways often produce incomplete or transient benefits, especially in individuals with severe obesity, fatty liver disease and complex cardiovascular risk. Combination regimens that integrate antioxidants, bioactive peptides and metabolic hormones are conceptually attractive because they can simultaneously target redox stress, appetite and energy homeostasis, glucose control and organ protection. However, co-administration of multiple agents in free form is hampered by mismatched pharmacokinetics, off-target toxicity and adherence challenges. Nanotechnology offers a means to co-encapsulate and coordinate these agents within a single platform, enabling synchronized delivery, tissue targeting and controlled release. Nano-enabled combination systems can, in principle, protect labile antioxidants, stabilize peptides and hormones, tune their exposure profiles and direct them toward key metabolic organs such as adipose tissue, liver, skeletal muscle and pancreatic islets. This review discusses the rationale for combining antioxidants, peptides and hormones in diabesity; describes nanocarrier platforms suitable for their co-delivery; and examines how redox modulation, peptide signaling and endocrine control can be integrated at the nanoscale. Preclinical examples are highlighted alongside safety, manufacturing and regulatory considerations. Finally, the article outlines future directions, including stimulus-responsive and patient-tailored nanoformulations that complement lifestyle change and emerging incretin therapies in the personalized management of diabesity.

Keywords: Nanomedicine; diabesity; combination therapy; antioxidants; peptide–hormone co-delivery

INTRODUCTION

Obesity-associated type 2 diabetes is best understood as a systems-level disorder, in which multiple organs and pathways interact to sustain hyperglycemia, dyslipidemia, inflammation and oxidative stress[1–4]. Adipose tissue expansion and remodeling drive insulin resistance through excess free fatty acid release, adipokine imbalance and recruitment of inflammatory immune cells. Hepatic steatosis and hepatocellular stress impair glucose and lipid handling, while skeletal muscle insulin resistance, endothelial dysfunction and subtle defects in pancreatic β-cell function compound metabolic dysregulation[5–7]. Oxidative stress runs through these processes, arising from mitochondrial overload, NADPH oxidase activity, advanced glycation end products and chronic hyperglycemia.

Therapeutically, this complexity has traditionally been addressed by sequentially adding single agents: metformin for hepatic gluconeogenesis, sulfonylureas or insulin for β-cell failure, statins for dyslipidemia, anti-hypertensives for blood pressure, and more recently GLP-1 receptor agonists and SGLT2 inhibitors for weight loss, glucose control and cardiorenal protection[8–11]. While such regimens have transformed outcomes relative to historical standards, they often leave residual risk and can be burdensome in terms of side effects, injections and adherence. Importantly, most do not directly confront oxidative injury and tissue-level remodeling that underlie the progression of complications.

The logic for combination therapy is therefore compelling. Antioxidants can reduce oxidative damage to β-cells, endothelium and mitochondrial networks, potentially slowing functional decline and improving insulin sensitivity[12–14]. Peptides such as GLP-1, GIP, amylin analogues, melanocortin ligands or gut-derived

OPEN ACCESS
ONLINE ISSN: 2992-5479
PRINT ISSN: 2992-605X
satiety signals modulate appetite, gastric emptying, insulin secretion and energy expenditure. Endogenous hormones and hormone analogues—including insulin, glucagon receptor modulators, thyroid hormone analogues and fibroblast growth factor–based agents directly regulate glucose, lipid metabolism and thermogenesis. Combining such agents allows simultaneous targeting of complementary nodes: reducing oxidative and inflammatory stress, correcting endocrine and neuroendocrine signals that govern energy balance, and restoring glycemic control[15, 16].

However, combining free antioxidants, peptides and hormones in conventional formulations presents practical problems. Many small-molecule antioxidants are poorly water-soluble, chemically unstable or extensively metabolized, resulting in low and variable bioavailability[17]. Peptides and protein hormones are prone to enzymatic degradation in the gastrointestinal tract, require parenteral administration, and may have short plasma half-lives. Moreover, their pharmacokinetics differ substantially: an oral antioxidant may exhibit a brief spike in plasma concentration, while a long-acting peptide or hormone shows a slow, sustained profile. Synchronizing their actions becomes difficult, and mismatched distribution may lead to off-target effects, such as stimulation of receptors in tissues where they exacerbate rather than relieve pathology[17].

Nanotechnology offers a route to address these issues by acting as a "platform equalizer" across modalities. Nanocarriers can protect antioxidants from degradation, increase apparent solubility and promote controlled release. The same carriers can encapsulate peptides and hormones, shielding them from proteases and modulating absorption[18–20]. When designed as co-delivery systems, nanocarriers can ensure that all three classes of agents, like antioxidants, peptides and hormones, are presented to target tissues within a coordinated temporal window and at defined ratios. Encapsulation reduces direct exposure of sensitive tissues to high peaks, potentially improving tolerability.

Targeting is a second advantage. Nanoformulations can be engineered to accumulate in specific organs based on size, surface charge and ligand decoration. For diabesity, adipose tissue, liver and the gut–liver axis are particularly attractive targets, as are pancreatic islets and, in some contexts, the central nervous system[21–23]. Adipose-targeted nanoparticles bearing browning inducers, anti-inflammatory antioxidants and appetite-regulating peptide fragments could, in theory, reshape adipose biology toward increased energy expenditure and improved insulin sensitivity. Liver-targeted systems that combine antioxidant payloads with FGF-based hormones and GLP-1 mimetics may tackle steatosis, inflammation and hyperglycemia in an integrated fashion[24–26].

Beyond spatial targeting, nanocarriers enable more nuanced temporal control. By varying polymer composition, lipid matrix properties or shell–core architecture, release kinetics of different cargos can be staggered or synchronized. For example, a burst release of an antioxidant might precede a slower release of a hormone that increases metabolic flux, minimizing oxidative overshoot[27, 28]. Alternatively, a peptide that primes insulin secretion and satiety could be released early, followed by a hormone that sustains fasting-state benefits. Stimuli-responsive designs that alter release in response to pH, glucose, reactive oxygen species or enzymatic patterns add a layer of adaptability, potentially aligning therapy with the dynamic metabolic environment of each patient.

Nanotechnology also offers structural advantages for combination regimens. By co-delivering multiple agents in a single carrier, total injection volume and dosing frequency may be reduced, which is particularly relevant in patients already receiving several injections per week. Co-formulation may also reduce the complexity of adherence and supply chains, as one product replaces multiple separate ones[29, 30]. Furthermore, co-encapsulation can, in some cases, improve chemical stability by sequestering incompatible agents in separate compartments within the same particle.

Importantly, nano-enabled combination therapies for diabesity should not be viewed in isolation from existing pharmacologic and lifestyle interventions. Instead, they are best conceptualized as add-ons or integrators[31]. A nanoformulation containing an antioxidant cocktail and a gut peptide could augment weight loss and tissue protection in patients already on GLP-1 receptor agonists or insulin, extending the durability of response[31]. In individuals undergoing bariatric surgery, perioperative nano-combinations might reduce oxidative and inflammatory stress in vulnerable organs, smoothing the transition to improved metabolic status. In all cases, careful balancing of benefits, risks and costs is required, but the underlying rationale for integrating antioxidants, peptides and hormones within nano-enabled platforms is strong: it embraces the multi-dimensional nature of diabesity while exploiting the tunability of nanomedicine to orchestrate multi-target therapy in space and time[31].

2. Pathophysiologic Basis for Combining Antioxidants, Peptides and Hormones

The pathogenesis of diabesity involves chronic caloric excess, genetic susceptibility and environmental stress converging on a set of interlinked mechanisms. Persistent nutrient overload leads to ectopic lipid accumulation in the liver, muscle and pancreas, promoting lipotoxicity and mitochondrial dysfunction[32]. Excess reactive oxygen species arise not only from overworked mitochondria but also from activation of NADPH oxidases, uncoupled endothelial nitric oxide synthase and auto-oxidation of glucose and lipoproteins. Oxidative stress damages DNA, proteins and lipids, impairs insulin signaling, diminishes nitric oxide bioavailability and accelerates β-cell exhaustion[32]. Antioxidants, especially those that can localize to mitochondria or vascular

OPEN ACCESS
ONLINE ISSN: 2992-5479
PRINT ISSN: 2992-605X

endothelium, therefore represent a logical component of a multi-pronged therapy aimed at slowing structural damage and preserving cellular function.

In parallel, peptides derived from the gut, adipose tissue and the brain regulate appetite, satiety, reward and energy expenditure. GLP-1 and GIP modulate insulin secretion and glucagon suppression, slow gastric emptying and influence food intake. Peptides such as PYY, CCK, amylin and melanocortin agonists signal satiety and alter macronutrient preference, while others influence thermogenesis and sympathetic activity[33]. Dysregulation of these peptide signals in obesity contributes to increased appetite, reduced satiety and impaired nutrient partitioning[34]. Restoring or amplifying beneficial peptide signaling is now a successful therapeutic strategy, as shown by GLP-1 and GLP-1/GIP co-agonists, but further refinement is possible by co-administering additional peptide components or fragments that modulate complementary pathways[33].

Hormones form the third pillar. Insulin remains essential for many individuals with advanced β-cell failure, while glucagon, amylin, leptin, thyroid hormones and fibroblast growth factors modulate glucose and lipid metabolism, thermogenesis and vascular tone[35]. In obesity, leptin resistance, altered glucagon dynamics and subclinical thyroid dysfunction can limit metabolic flexibility. Hormone analogues and receptor agonists or antagonists can recalibrate these axes, but systemic administration often affects multiple tissues indiscriminately.

Combining antioxidants, peptides and hormones offers a way to address both the structural damage inflicted by oxidative and inflammatory stress and the distorted regulatory signaling that drives overeating and metabolic inflexibility[35]. Antioxidants may protect β-cells exposed to oscillating glucose and lipids while peptides ensure that such oscillations are dampened by reduced food intake and improved glucose handling. Hormones such as FGF21 analogues can promote fatty acid oxidation and thermogenesis, aligning with antioxidant support to reduce lipotoxic stress. Without a delivery platform, however, the distinct pharmacology of each class risks leading to temporal and spatial mismatches. Nanotechnology therefore, becomes the enabling layer that can orchestrate these components into a coherent therapeutic whole.

3. Nanocarrier Platforms for Co-Delivery and Spatiotemporal Control

Several nanocarrier classes are suitable for co-encapsulating antioxidants, peptides and hormones. Lipid-based nanoparticles, including liposomes and nanostructured lipid carriers, can accommodate hydrophobic antioxidants within their lipid bilayers or cores while carrying hydrophilic peptides and proteins in aqueous compartments[36, 37]. By adjusting lipid composition, cholesterol content and surface PEGylation, stability, circulation time and tissue distribution can be tuned. Polymer–lipid hybrid nanoparticles add degree of control through degradable polymer cores that govern release kinetics.

Polymeric nanoparticles made from biodegradable materials such as PLGA, polylactic acid, polycaprolactone or natural polymers like chitosan can encapsulate small molecules and, with appropriate formulation techniques, peptides and proteins. Layer-by-layer assembly allows stratification of cargo, for example placing antioxidants in an outer layer for early release and hormones in an inner core for sustained delivery[38–40]. Conjugation of targeting ligands such as peptides or antibodies against adipose vasculature, hepatocyte receptors or islet markers can bias distribution toward desired organs.

Micelles and polymeric micelle systems are particularly useful for enhancing the solubility of hydrophobic antioxidants and small-molecule hormones[41]. When combined with conjugation strategies for peptides, micelles can function as modular platforms for mixed cargo. Inorganic nanoparticles such as mesoporous silica or metal–organic frameworks provide high surface area and pore structures suitable for loading diverse molecules, though their long-term safety profile must be carefully assessed[42].

Temporal control is achieved by manipulating carrier composition and architecture. Faster-degrading polymers or loosely bound cargos provide early-phase release, while more stable matrices or covalent conjugation yield prolonged profiles. Stimuli-responsive designs employ linkers cleaved by acidic pH, elevated ROS levels, specific enzymes or glucose concentrations, aligning release with local pathology[43–45]. For instance, ROS-responsive linkers can release antioxidants preferentially in highly oxidized microenvironments, while pH-sensitive components may activate within endosomes of target cells.

A key design challenge is maintaining the structural integrity and bioactivity of sensitive peptides and hormones within nanocarriers while achieving sufficient loading and stable encapsulation of antioxidants[46]. Process parameters such as solvent choice, shear forces and temperature during formulation must be optimized to avoid denaturation. In some designs, peptides or hormones are not encapsulated but surface-conjugated, providing improved receptor accessibility at the expense of increased exposure to proteases[46]. Balancing these trade-offs is central to effective nano-enabled combination design.

4. Antioxidant Components: Redox Modulation and Organelle Targeting

Antioxidant therapy in diabesity aims to mitigate damage from chronic oxidative stress without abolishing physiological redox signaling. Classic antioxidants include vitamins C and E, polyphenols like resveratrol, quercetin and curcumin, and synthetic molecules targeting specific redox systems[47]. Many of these agents, especially polyphenols, suffer from poor bioavailability and rapid metabolism when administered orally.

OPEN ACCESS
ONLINE ISSN: 2992-5479
PRINT ISSN: 2992-605X
Nanocarriers can enhance their solubility, protect them from degradation and direct them to tissues where oxidative damage is greatest, such as fatty liver, inflamed adipose tissue and vascular endothelium[47].
Mitochondria-focused antioxidants have particular relevance because mitochondrial dysfunction is central to diabetic complications and obesity-associated insulin resistance. Molecules linked to lipophilic cations such as triphenylphosphonium accumulate in mitochondria driven by membrane potential[48]. Incorporating such mitochondria-targeted derivatives into nanoparticles can concentrate antioxidant activity at sites of ROS production, potentially improving efficacy at lower systemic doses. Similarly, nanoparticles themselves can be decorated with mitochondrial-targeting peptides, enabling co-delivery of generic antioxidants and peptides directly to the organelle[48].

Within nano-enabled combinations, antioxidants serve several roles. They protect β-cells from glucolipotoxic stress, thereby preserving endogenous insulin secretion and reducing escalating insulin requirements[49]. They stabilize endothelial nitric oxide signaling, improving vascular function and potentially reducing cardiovascular risk. They may also modulate redox-sensitive signaling pathways in adipocytes and macrophages, attenuating metaflammation and promoting more favorable adipokine and cytokine profiles[49]. Nanocarrier design must carefully consider the pro-oxidant potential of some antioxidants at high concentrations or in certain redox environments. Controlled release and organelle targeting can help maintain concentrations within beneficial windows, avoiding suppression of adaptive ROS signaling necessary for insulin action and host defense[50]. Co-delivery with peptides and hormones that shift metabolism toward greater fatty acid oxidation or thermogenesis may, paradoxically, increase ROS generation; thus, aligning antioxidant release with these metabolic shifts is an important design objective to prevent unintended oxidative injury.

5. **Peptide Components: Appetite, Incretins and Tissue-Specific Signaling**

Peptides bring specificity to nano-enabled combinations, engaging receptors that orchestrate appetite, glucose control and tissue remodeling. GLP-1 analogues are paradigmatic, improving insulin secretion in a glucose-dependent manner, reducing glucagon, slowing gastric emptying and promoting weight loss through central satiety pathways[51]. Dual and triple agonists combining GLP-1 with GIP and glucagon receptors further amplify metabolic benefits. Other peptides of interest include amylin analogues, melanocortin receptor agonists, PYY fragments and peptides derived from fibroblast growth factors, adiponectin or irisin mimetics[51].
Encapsulating peptides in nanocarriers can reduce injection frequency, minimize local site reactions and protect against proteolysis. Oral or inhaled nanoformulations are being explored to bypass injections entirely, although achieving sufficient bioavailability remains challenging. In nano-enabled combinations, peptides may be selected to complement the actions of co-delivered hormones and antioxidants[51]. For instance, a GLP-1 analogue or amylin mimetic can reduce caloric intake and postprandial glycemic excursions, lowering metabolic load on tissues, while antioxidants buffer oxidative stress and hormones like FGF21 analogues promote lipid oxidation.
Targeting peptides to specific tissues via nanocarriers adds dimension. Hypothalamus-directed delivery is conceptually appealing for appetite-modulating peptides but difficult to achieve safely[52]. More immediate are strategies targeting the gut, liver and adipose tissue. Gut-restricted peptides with minimal systemic absorption can engage local receptors and enteric neural circuits, while liver-targeted peptide–nanoparticle conjugates can modulate hepatic glucose output and lipid metabolism. Adipose-directed peptides could influence browning, adipogenesis or local immune cell behavior[52].
Maintaining correct folding and receptor-binding conformation of peptides within nanocarriers is essential. This may necessitate mild formulation conditions and judicious selection of matrix materials[53]. Some systems use self-assembling peptide amphiphiles that form nanofibers or micelles, inherently integrating peptide and nanostructure; others physically entrap pre-formed peptides. Co-encapsulation with antioxidants can protect peptides from oxidative modification, and conversely, peptides that modulate cellular antioxidant defenses, such as those activating Nrf2 pathways, can synergize with direct antioxidant payloads[53].

6. **Hormonal Components: Endocrine Axes and Energy Partitioning**

Hormones within nano-enabled combinations extend therapeutic reach to systemic regulators of energy and substrate partitioning. Insulin is foundational for many patients with advanced diabetes, and nanoformulations may modulate its absorption or tissue targeting, though standard insulin delivery technologies are already highly optimized[54]. More innovative are nanoformulations involving glucagon receptor modulators, long-acting FGF21 and FGF19 analogues, thyroid hormone derivatives selective for hepatic receptors, and leptin or leptin-sensitizing agents[54].
FGF21 analogues enhance fatty acid oxidation, ketogenesis, and energy expenditure while improving insulin sensitivity in the liver and adipose tissue. When delivered via nanocarriers, these agents might be more effectively directed to fatty liver and inflamed adipose depots, where they can reprogram metabolism and reduce steatosis[55]. Thyroid hormone analogues selective for liver receptors can lower LDL cholesterol and hepatic fat; nanoformulations may sharpen hepatic targeting and reduce off-target cardiac effects. Leptin and leptin-sensitizing strategies have historically struggled in common obesity due to leptin resistance, but localized delivery to hypothalamic regions or peripheral tissues involved in leptin signaling, enabled by nanotechnology, may revive therapeutic possibilities, albeit with significant safety considerations[55].

OPEN ACCESS
ONLINE ISSN: 2992-5479
PRINT ISSN: 2992-605X

In combination systems, hormones may be the primary drivers of large-scale metabolic shifts, while peptides fine-tune appetite and nutrient flux and antioxidants protect against collateral oxidative stress. For example, a nanoformulation co-delivering an FGF21 analogue, a GLP-1 fragment and a mitochondrial antioxidant could, in principle, promote weight loss, improve glycemia and shield hepatocytes and β-cells from redox injury[24, 25]. The challenge lies in achieving doses and exposure patterns that replicate or improve upon existing systemic hormone regimens without introducing unpredictable interactions.

7. Preclinical Evidence, Safety and Translational Outlook

Preclinical studies have begun to test nano-enabled combinations conceptually similar to the antioxidant–peptide–hormone triad, though many still focus on dual combinations or simpler payload sets[56]. Animal models of diet-induced obesity and type 2 diabetes have shown that nanoparticles co-encapsulating a polyphenolic antioxidant with a GLP-1 analogue improve weight loss, glycemic control and hepatic steatosis more than either agent alone at equivalent doses. Other studies demonstrate that adipose-targeted nanoparticles carrying browning inducers along with anti-inflammatory and antioxidant agents reduce visceral fat mass and improve insulin sensitivity more robustly than monotherapies[56]. Work with hormone–polyphenol nanoformulations suggests synergistic effects on lipid profile, oxidative stress markers and vascular function.

Safety remains a central concern. Combining multiple bioactive agents increases the potential for adverse effects, including hypoglycemia, excessive weight loss, gastrointestinal intolerance or cardiovascular events[57]. Nanocarriers themselves can trigger immune reactions or accumulate in off-target organs. Rigorous evaluation of biodistribution, immunogenicity, organ function and long-term outcomes is necessary, particularly because diabesity therapies are typically administered chronically. Scaling from murine models to humans introduces further complexity in nanoparticle pharmacokinetics and organ targeting, especially given inter-individual differences in adipose distribution, hepatic fat, renal function and immune status[57].

Manufacturing and regulatory pathways for multi-component nanoformulations are also more demanding than for single-agent products[21, 44]. Consistency in cargo ratios, particle size, surface characteristics and release profiles must be demonstrated and maintained at scale. Regulatory agencies may require evidence that each component contributes to benefit and that the combination does not create new safety liabilities. Cost considerations are non-trivial; sophisticated nano-combinations may be expensive, raising questions about access in populations heavily burdened by diabesity.

Despite these challenges, the translational trajectory is promising. The success of injectable incretin therapies shows that patients and healthcare systems are willing to adopt complex biologic regimens when benefits are substantial[58, 59]. Nano-enabled combinations that demonstrably improve weight loss durability, organ protection and quality of life, especially in patients who respond suboptimally to current drugs, could find a niche as second-line or adjunctive modalities. Integration with digital tools, such as continuous glucose monitoring and behavioral coaching, may further enhance their impact by aligning dosing with individual lifestyle patterns and early detection of side effects.

CONCLUSION

Nano-enabled combination therapies that integrate antioxidants, peptides and hormones offer a conceptually powerful approach to diabesity, reflecting the disorder's multi-organ, multi-pathway nature. By co-encapsulating redox modulators, appetite and incretin peptides, and endocrine regulators within nanocarriers, it becomes possible to coordinate their delivery in space and time, enhance bioavailability, sharpen tissue targeting and potentially widen therapeutic windows. Preclinical data, though still emerging, suggest that such combinations can surpass monotherapies in improving weight, glycemic control and organ health. However, realizing their clinical potential will require careful attention to safety, manufacturability, regulatory requirements and cost, as well as thoughtful integration with existing pharmacologic and lifestyle interventions. As nanomedicine, peptide engineering and metabolic endocrinology continue to advance, rationally designed nano-combinations could become an important component of personalized, mechanism-based strategies to prevent and treat obesity-driven diabetes.

REFERENCES

1. Aamodt, K.I., Powers, A.C.: The pathophysiology, presentation and classification of Type 1 diabetes. Diabetes Obes. Metab. 27, 15–27 (2025). https://doi.org/10.1111/dom.16628
2. Abbasi, M., Boka, D.A., DeLoit, H.: Nanomaterial-Enhanced Microneedles: Emerging Therapies for Diabetes and Obesity. Pharmaceutics. 16, 1344 (2024). https://doi.org/10.3390/pharmaceutics16101344
3. Acevedo-Román, A., Pagán-Zayas, N., Velázquez-Rivera, L.I., Torres-Ventura, A.C., Godoy-Vitorino, F.: Insights into Gut Dysbiosis: Inflammatory Diseases, Obesity, and Restoration Approaches. Int. J. Mol. Sci. 25, 9715 (2024). https://doi.org/10.3390/ijms25179715
4. Ahluwalia, M.K.: Chrononutrition—When We Eat Is of the Essence in Tackling Obesity. Nutrients. 14, 5080 (2022). https://doi.org/10.3390/nu14235080
5. Alum, E.U.: Circadian nutrition and obesity: timing as a nutritional strategy. J. Health Popul. Nutr. 44, 367 (2025). https://doi.org/10.1186/s41043-025-01102-y

OPEN ACCESS
ONLINE ISSN: 2992-5479
PRINT ISSN: 2992-605X

6. 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
7. Umoru, G.U., Atangwho, I.J., David-Oku, E., Uti, D.E., De Campos, O.C., Udeozor, P.A., Nfona, S.O., Lawal, B., Alum, E.U.: Modulation of Lipogenesis by Tetracarpidium conophorum Nuts via SREBP-1/ACCA-1/FASN Inhibition in Monosodium-Glutamate-Induced Obesity in Rats. Nat. Prod. Commun. 20, 1934578X251344035 (2025). https://doi.org/10.1177/1934578X251344035
8. Chen, D., Wang, Y., Wu, K., Wang, X.: Dual Effects of Metformin on Adipogenic Differentiation of 3T3-L1 Preadipocyte in AMPK-Dependent and Independent Manners. Int. J. Mol. Sci. 19, 1547 (2018). https://doi.org/10.3390/ijms19061547
9. Dutta, S., Shah, R.B., Singhal, S., Dutta, S.B., Bansal, S., Sinha, S., Haque, M.: Metformin: A Review of Potential Mechanism and Therapeutic Utility Beyond Diabetes. Drug Des. Devel. Ther. 17, 1907–1932 (2023). https://doi.org/10.2147/DDDT.S409373
10. Gu, C., Loube, J., Lee, R., Bevans-Fonti, S., Wu, T.D., Barmine, J.H., Jun, J.C., McCormack, M.C., Hansel, N.N., Mitzner, W., Polotsky, V.Y.: Metformin Alleviates Airway Hyperresponsiveness in a Mouse Model of Diet-Induced Obesity. Front. Physiol. 13, (2022). https://doi.org/10.3389/fphys.2022.883275
11. La Sala, L., Carlini, V., Macas-Granizo, M.B., Trabucchi, E., Pontiroli, A.E., Berra, C., Naselli, A., D'Anzeo, M., Porta, A., Martin Delgado, J., Vianello, E., Dozio, E., Corsi Romanelli, M., Drago, L.: The eternal struggle between titans: Fecal microbiota transplant (FMT) versus metformin in type 2 diabetes (T2D) gut dysmotility. J. Adv. Res. (2025). https://doi.org/10.1016/j.jare.2025.09.021
12. Abu Shelbayeh, O., Arroum, T., Morris, S., Busch, K.B.: PGC-1α Is a Master Regulator of Mitochondrial Lifecycle and ROS Stress Response. Antioxidants. 12, 1075 (2023). https://doi.org/10.3390/antiox12051075
13. Bešlo, D., Golubić, N., Rastija, V., Agić, D., Karnaš, M., Šubarić, D., Lučić, B.: Antioxidant Activity, Metabolism, and Bioavailability of Polyphenols in the Diet of Animals. Antioxidants. 12, 1141 (2023). https://doi.org/10.3390/antiox12061141
14. Uti, D.E., Atangwho, I.J., Alum, E.U., Ntaobeten, E., Obeten, U.N., Bawa, I., Agada, S.A., Ukam, C.I.-O., Egbung, G.E.: Antioxidants in cancer therapy mitigating lipid peroxidation without compromising treatment through nanotechnology. Discov. Nano. 20, 70 (2025). https://doi.org/10.1186/s11671-025-04248-0
15. Liu, J., Li, K., Yi, Z., Saqirile, Wang, C., Yang, R.: Oxidative–Inflammatory Crosstalk and Multi-Target Natural Agents: Decoding Diabetic Vascular Complications. Curr. Issues Mol. Biol. 47, 614 (2025). https://doi.org/10.3390/cimb47080614
16. Hu, C., Chen, Y., Yin, X., Xu, R., Yin, C., Wang, C., Zhao, Y.: Pancreatic endocrine and exocrine signaling and crosstalk in physiological and pathological status. Signal Transduct. Target. Ther. 10, 39 (2025). https://doi.org/10.1038/s41392-024-02098-3
17. Gulcin, İ.: Antioxidants: a comprehensive review. Arch. Toxicol. 99, 1893–1997 (2025). https://doi.org/10.1007/s00204-025-03997-2
18. 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
19. Bhange, M., Telange, D.: Convergence of nanotechnology and artificial intelligence in the fight against liver cancer: a comprehensive review. Discov. Oncol. 16, 77 (2025). https://doi.org/10.1007/s12672-025-01821-y
20. Chang, W., Meng, Z., Zhao, Y., Qi, Y., Li, Z., Lian, H.: Emerging Nanotechnology Strategies for Obesity Therapy. Adv. Sci. 12, e01813 (2025). https://doi.org/10.1002/advs.202501813
21. Cepero, A., Luque, C., Cabeza, L., Perazzoli, G., Quiñonero, F., Mesas, C., Melguizo, C., Prados, J.: Antibody-Functionalized Nanoformulations for Targeted Therapy of Colorectal Cancer: A Systematic Review. Int. J. Nanomedicine. 17, 5065–5080 (2022). https://doi.org/10.2147/IJN.S368814
22. Kevadiya, B.D., Woldstad, C., Ottemann, B.M., Dash, P., Sajja, B.R., Lamberty, B., Morsey, B., Kocher, T., Dutta, R., Bade, A.N., Liu, Y., Callen, S.E., Fox, H.S., Byrareddy, S.N., McMillan, J.M., Bronich, T.K., Edagwa, B.J., Boska, M.D., Gendelman, H.E.: Multimodal Theranostic Nanoformulations Permit Magnetic Resonance Bioimaging of Antiretroviral Drug Particle Tissue-Cell Biodistribution. Theranostics. 8, 256–276 (2018). https://doi.org/10.7150/thno.22764
23. Patel, J., Roy, H., Khobragade, D.S., Agrawal, S., Das, N.R., Patel, R., Patel, V., Lal, P.: Natural lipid-based nanoformulations for enhancing hepatoprotective activity: mechanisms, efficacy, and clinical translation. Health Nanotechnol. 1, 11 (2025). https://doi.org/10.1186/s44301-025-00010-8
24. Abdallah, H., Klink, W.H., Derienne, J., Voican, C., Perlemuter, G., Courie, R., Dagher, I., Tranchart, H.: Interest in Treatment with GLP-1 Receptor Agonists for the Management of Insufficient Weight Loss

OPEN ACCESS
ONLINE ISSN: 2992-5479
PRINT ISSN: 2992-605X

or Weight Regain After Bariatric Surgery. Obes. Surg. 35, 4286 (2025). https://doi.org/10.1007/s11695-025-08210-y
25. Chai, S., Niu, Y., Liu, F., Wu, S., Yang, Z., Sun, F.: Comparison of GLP-1 Receptor Agonists, SGLT-2 Inhibitors, and DPP-4 Inhibitors as an Add-On Drug to Insulin Combined With Oral Hypoglycemic Drugs: Umbrella Review. J. Diabetes Res. 2024, 8145388 (2024). https://doi.org/10.1155/2024/8145388
26. Liu, Q.K.: Mechanisms of action and therapeutic applications of GLP-1 and dual GIP/GLP-1 receptor agonists. Front. Endocrinol. 15, 1431292 (2024). https://doi.org/10.3389/fendo.2024.1431292
27. Abbasi, H., Kouchak, M., Mirveis, Z., Hajipour, F., Khodarahmi, M., Rahbar, N., Handali, S.: What We Need to Know about Liposomes as Drug Nanocarriers: An Updated Review. Adv. Pharm. Bull. 13, 7–23 (2023). https://doi.org/10.34172/apb.2023.009
28. Dash, P., Piras, A.M., Dash, M.: Cell membrane coated nanocarriers - an efficient biomimetic platform for targeted therapy. J. Controlled Release. 327, 546–570 (2020). https://doi.org/10.1016/j.jconrel.2020.09.012
29. Prosperi, D., Colombo, M., Zanoni, I., Granucci, F.: Drug nanocarriers to treat autoimmunity and chronic inflammatory diseases. Semin. Immunol. 34, 61–67 (2017). https://doi.org/10.1016/j.smim.2017.08.010
30. 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
31. Sarkhel, S., Shuvo, S.M., Ansari, M.A., Mondal, S., Kapat, P., Ghosh, A., Sarkar, T., Biswas, R., Atanase, L.I., Carauleanu, A.: Nanotechnology-Based Approaches for the Management of Diabetes Mellitus: An Innovative Solution to Long-Lasting Challenges in Antidiabetic Drug Delivery. Pharmaceutics. 16, 1572 (2024). https://doi.org/10.3390/pharmaceutics16121572
32. Abel, E.D., Gloyn, A.L., Evans-Molina, C., Joseph, J.J., Misra, S., Pajvani, U.B., Simcox, J., Susztak, K., Drucker, D.J.: Diabetes mellitus—Progress and opportunities in the evolving epidemic. Cell. 187, 3789–3820 (2024). https://doi.org/10.1016/j.cell.2024.06.029
33. Diz-Chaves, Y., Herrera-Pérez, S., González-Matías, L.C., Lamas, J.A., Mallo, F.: Glucagon-Like Peptide-1 (GLP-1) in the Integration of Neural and Endocrine Responses to Stress. Nutrients. 12, 3304 (2020). https://doi.org/10.3390/nu12113304
34. 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
35. Vargas, E., Joy, N.V., Carrillo Sepulveda, M.A.: Biochemistry, Insulin Metabolic Effects. In: StatPearls. StatPearls Publishing, Treasure Island (FL) (2025)
36. Gabel, M., Knauss, A., Fischer, D., Neurath, M.F., Weigmann, B.: Surface Design Options in Polymer- and Lipid-Based siRNA Nanoparticles Using Antibodies. Int. J. Mol. Sci. 23, 13929 (2022). https://doi.org/10.3390/ijms232213929
37. 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
38. Long, Q., Liu, Z., Shao, Q., Shi, H., Huang, S., Jiang, C., Qian, B., Zhong, Y., He, X., Xiang, X., Yang, Y., Li, B., Yan, X., Zhao, Q., Wei, X., Santos, H.A., Ye, X.: Autologous Skin Fibroblast-Based PLGA Nanoparticles for Treating Multiorgan Fibrosis. Adv. Sci. 9, 2200856 (2022). https://doi.org/10.1002/advs.202200856
39. Pereira, A. de S.B.F., Brito, G.A. de C., Lima, M.L. de S., Silva Júnior, A.A. da, Silva, E. dos S., De Rezende, A.A., Bortolin, R.H., Galvan, M., Pirih, F.Q., Araújo Júnior, R.F. de, Medeiros, C.A.C.X. de, Guerra, G.C.B., Araújo, A.A. de: Metformin Hydrochloride-Loaded PLGA Nanoparticle in Periodontal Disease Experimental Model Using Diabetic Rats. Int. J. Mol. Sci. 19, 3488 (2018). https://doi.org/10.3390/ijms19113488
40. Wu, J.-Z., Williams, G.R., Li, H.-Y., Wang, D.-X., Li, S.-D., Zhu, L.-M.: Insulin-loaded PLGA microspheres for glucose-responsive release. Drug Deliv. 24, 1513–1525 (2017). https://doi.org/10.1080/10717544.2017.1381200
41. Ma, Z.-G., Ma, R., Xiao, X.-L., Zhang, Y.-H., Zhang, X.-Z., Hu, N., Gao, J.-L., Zheng, Y.-F., Dong, D.-L., Sun, Z.-J.: Azo polymeric micelles designed for colon-targeted dimethyl fumarate delivery for colon cancer therapy. Acta Biomater. 44, 323–331 (2016). https://doi.org/10.1016/j.actbio.2016.08.021
42. Li, L., Zeng, Y., Chen, M., Liu, G.: Application of Nanomicelles in Enhancing Bioavailability and Biological Efficacy of Bioactive Nutrients. Polymers. 14, 3278 (2022). https://doi.org/10.3390/polym14163278
43. Du, J., Lane, L.A., Nie, S.: Stimuli-Responsive Nanoparticles for Targeting the Tumor Microenvironment. J. Control. Release Off. J. Control. Release Soc. 219, 205–214 (2015). https://doi.org/10.1016/j.jconrel.2015.08.050

OPEN ACCESS
ONLINE ISSN: 2992-5479
PRINT ISSN: 2992-605X

44. 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
45. Salehi, S., Naghib, S.M., Garshasbi, H.R., Ghorbanzadeh, S., Zhang, W.: Smart stimuli-responsive injectable gels and hydrogels for drug delivery and tissue engineering applications: A review. Front. Bioeng. Biotechnol. 11, 1104126 (2023). https://doi.org/10.3389/fbioe.2023.1104126
46. Zhang, X., Li, X., Zhao, Y., Zheng, Q., Wu, Q., Yu, Y.: Nanocarrier system: An emerging strategy for bioactive peptide delivery. Front. Nutr. 9, 1050647 (2022). https://doi.org/10.3389/fnut.2022.1050647
47. Akpoveso, O.-O.P., Ubah, E.E., Obasanmi, G.: Antioxidant Phytochemicals as Potential Therapy for Diabetic Complications. Antioxidants. 12, 123 (2023). https://doi.org/10.3390/antiox12010123
48. Pant, T., Uche, N., Juric, M., Bosnjak, Z.J.: Clinical Relevance of lncRNA and Mitochondrial Targeted Antioxidants as Therapeutic Options in Regulating Oxidative Stress and Mitochondrial Function in Vascular Complications of Diabetes. Antioxidants. 12, 898 (2023). https://doi.org/10.3390/antiox12040898
49. Stoleru, O.A., Burlec, A.F., Mircea, C., Felea, M.G., Macovei, I., Hăncianu, M., Corciovă, A.: Multiple nanotechnological approaches using natural compounds for diabetes management. J. Diabetes Metab. Disord. 23, 267–287 (2024). https://doi.org/10.1007/s40200-023-01376-1
50. Wang, Z., Xu, H., Li, M., Lei, S., Cai, Y., Wu, Y., Lin, J., Huang, P.: Nanotechnology for tumor ferroptosis. Cell Biomater. 100222 (2025). https://doi.org/10.1016/j.celbio.2025.100222
51. Alzahrani, A.M., Alshobragi, G.A., Alshehri, A.M., Alzahrani, M.S., Alshehri, H.A., Alzhrani, R.M., Basudan, S., Alkatheeri, A.A., Almutairi, S.A., Alzahrani, Y.A.: Molecular Pharmacology of Glucagon-Like Peptide 1-Based Therapies in the Management of Type Two Diabetes Mellitus and Obesity. Integr. Pharm. Res. Pract. 14, 59–72 (2025). https://doi.org/10.2147/IPRP.S503501
52. Wang, Y., Zhang, L., Liu, C., Luo, Y., Chen, D.: Peptide-Mediated Nanocarriers for Targeted Drug Delivery: Developments and Strategies. Pharmaceutics. 16, 240 (2024). https://doi.org/10.3390/pharmaceutics16020240
53. Priya, S., Desai, V.M., Singhvi, G.: Surface Modification of Lipid-Based Nanocarriers: A Potential Approach to Enhance Targeted Drug Delivery. ACS Omega. 8, 74–86 (2023). https://doi.org/10.1021/acsomega.2c05976
54. Romero-Carmona, C.E., Chávez-Corona, J.I., Lima, E., Cortés, H., Quintanar-Guerrero, D., Bernad-Bernad, M.J., Ramos-Martínez, I., Peña-Corona, S.I., Sharifi-Rad, J., Leyva-Gómez, G.: Nanoparticle and microparticle-based systems for enhanced oral insulin delivery: A systematic review and meta-analysis. J. Nanobiotechnology. 22, 802 (2024). https://doi.org/10.1186/s12951-024-03045-8
55. Zhang, J., Li, Y.: Fibroblast Growth Factor 21 Analogs for Treating Metabolic Disorders. Front. Endocrinol. 6, 168 (2015). https://doi.org/10.3389/fendo.2015.00168
56. Kevadiya, B.D., Ottemann, B.M., Thomas, M.B., Mukadam, I., Nigam, S., McMillan, J., Gorantla, S., Bronich, T.K., Edagwa, B., Gendelman, H.E.: Neurotheranostics as personalized medicines. Adv. Drug Deliv. Rev. 148, 252–289 (2019). https://doi.org/10.1016/j.addr.2018.10.011
57. Tran, N., Pham, B., Le, L.: Bioactive Compounds in Anti-Diabetic Plants: From Herbal Medicine to Modern Drug Discovery. Biology. 9, 252 (2020). https://doi.org/10.3390/biology9090252
58. Reddy, T.K., Villavaso, C.D., Pulapaka, A.V., Ferdinand, K.C.: Achieving equitable access to incretin-based therapies in cardiovascular care. Am. Heart J. Plus Cardiol. Res. Pract. 46, 100455 (2024). https://doi.org/10.1016/j.ahjo.2024.100455
59. Xu, Y., De Keersmaecker, H., Braeckmans, K., De Smedt, S., Cani, P.D., Préat, V., Beloqui, A.: Targeted nanoparticles towards increased L cell stimulation as a strategy to improve oral peptide delivery in incretin-based diabetes treatment. Biomaterials. 255, 120209 (2020). https://doi.org/10.1016/j.biomaterials.2020.120209

CITE AS: Kato Jumba K. (2026). Nano-Enabled Combination Therapies Integrating Antioxidants, Peptides, and Hormones for Diabesity Treatment. NEWPORT INTERNATIONAL JOURNAL OF PUBLIC HEALTH AND PHARMACY,7(1):62-69. https://doi.org/10.59298/NIJPP/2026/716269