

Artificial Intelligence-Guided Nanoformulations for Personalized Management of Obesity and Diabetes

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ABSTRACT

Obesity and type 2 diabetes are heterogeneous, chronic disorders driven by complex genetic, behavioral and environmental factors, leading to widely variable responses to lifestyle and pharmacologic therapies. Conventional treatment paradigms rely on population averages rather than individual biology, contributing to suboptimal control, weight regain and treatment failure. Nanotechnology offers powerful tools to enhance bioavailability, tissue targeting and safety of metabolic therapeutics, while artificial intelligence (AI) provides data-driven methods for pattern discovery, prediction and optimization across high-dimensional clinical, biochemical and behavioral datasets. Integrating AI with nanoformulation design and deployment enables a new paradigm: AI-guided nanotherapies tailored to the molecular, phenotypic and lifestyle profile of individual patients with obesity and diabetes. This review explores how AI can support rational design of nanoformulations (materials selection, composition, size, surface chemistry), predict pharmacokinetics and tissue distribution, and match patients to specific nano-enabled interventions. It discusses emerging examples of machine learning in nanomedicine and metabolic disease management, the role of digital biomarkers and multi-omics in building personalized models, and the architecture of closed-loop systems that couple AI analytics with smart nanocarriers and sensors. Key ethical, regulatory and equity considerations are addressed, and future directions for AI–nano convergence in “precision diabetes” are outlined.

Keywords: Artificial intelligence; nanoformulations; obesity; diabetes; precision medicine

INTRODUCTION

Obesity and type 2 diabetes mellitus (T2DM) are no longer viewed as uniform entities but as syndromes encompassing distinct biological subtypes, shaped by genetics, epigenetics, gut microbiota, early-life exposures, diet, physical inactivity and social determinants of health[1–3]. Clinical classifications such as BMI, fasting glucose and HbA1c capture only part of this diversity. Patients with similar BMI and HbA1c may differ markedly in fat distribution, hepatic and muscular insulin resistance, β -cell reserve, inflammatory tone and response to medications[4]. Large cohort analyses and clustering studies have identified reproducible T2DM subgroups based on age of onset, BMI, autoimmunity, insulin secretion and resistance indices, with differential risks for complications and variable responses to therapies[5, 5, 6].

This heterogeneity helps explain why population-derived guidelines often fail at the individual level. A drug that produces average weight loss and glycemic improvement in randomized trials may yield limited benefit or intolerable side effects in particular patients. Even highly effective new agents such as GLP-1/GIP receptor agonists show wide interindividual variability in weight loss and glycemic outcomes and raise questions about long-term tolerability, cost and access[7]. Meanwhile, lifestyle interventions, although foundational, are notoriously hard to sustain over time. There is a growing consensus that precision strategies—matching therapies to the biology and behavior of each individual—are needed to improve durability and safety of obesity and diabetes management[8–10].

Nanotechnology offers complementary capabilities. Nanoformulations, including lipid nanoparticles, polymeric nanoparticles, liposomes, micelles and hybrid nanosystems, can improve the pharmacokinetic and pharmacodynamic profiles of metabolic drugs and nutraceuticals by enhancing solubility, stability, tissue targeting and controlled release[11–13]. For obesity and diabetes, nanoformulations have been explored to increase bioavailability and reduce gastrointestinal side effects of plant polyphenols and metformin-like agents, to target anti-inflammatory or browning compounds to adipose tissue, and to deliver nucleic acids or peptides to liver or pancreatic islets. In principle, nanoformulation parameters—particle size, surface charge, ligand density, core composition—can be tuned to target specific depots (for example, visceral adipose, fatty liver) or immune and stromal cells implicated in diabetes. However, the design space is huge and highly non-linear:

small changes in composition or process conditions can alter stability, biodistribution and immunogenicity in unpredictable ways[14–16].

Artificial intelligence, particularly machine learning (ML) and deep learning, excels at uncovering complex relationships in high-dimensional data. In drug discovery and formulation science, ML models already predict solubility, permeability, toxicity and nano–bio interactions from molecular and materials descriptors[16, 17]. In diabetes care, AI has been used to forecast glucose excursions from continuous glucose monitoring (CGM) data, support insulin dosing, and predict T2DM onset and complications from electronic health records and wearable data. What is emerging is the convergence of these capabilities: AI-guided nanoformulations that are optimized *in silico* and then matched to patient-level phenotypes and behavior for personalized metabolic therapy[18–20].

Conceptually, AI can contribute at several levels. First, during nanoformulation design, ML models can map relationships between formulation inputs (materials, process parameters), intermediate properties (size, polydispersity, encapsulation efficiency, zeta potential) and outputs (stability, cellular uptake, organ distribution) to accelerate optimization and reduce trial-and-error[21]. Generative AI models can propose novel nanocarrier structures or ligand combinations predicted to achieve specific targeting and release profiles. Second, at the interface with the patient, AI can integrate multi-omics (genomic, transcriptomic, metabolomic, microbiome), imaging (MRI or ultrasound-based adiposity measures), CGM, wearable activity and diet logs to characterize each individual's metabolic state and trajectory. These models can then recommend nano-enabled interventions most likely to succeed, adjust dosing and scheduling, and anticipate side effects[21].

Third, in a more advanced vision, AI may be embedded into closed-loop systems where nanoformulations, sensors and algorithms interact dynamically. Smart nanocarriers might change release rates in response to local cues (pH, enzymes, temperature), while external AI platforms process CGM and wearable data to modulate injection timing or to switch between different nanoformulations over time[22, 23]. For example, a system could intensify adipose-targeted anti-inflammatory nanotherapy during periods of weight regain and high inflammatory markers, while tapering back during sustained lifestyle adherence and GLP-1-induced weight loss.

The promise of AI-guided nanoformulations for diabetes lies in combining mechanistic control at the nanoscale with personalized decision-making at the patient level. Yet there are substantial challenges[24–26]. Data scarcity and bias in nanomedicine, heterogeneity of clinical datasets, explainability, regulatory acceptance and equity concerns all need to be addressed. There is also a risk of over-engineering solutions that are technologically elegant but impractical or unaffordable for those most affected by obesity and diabetes. The following sections examine the technical foundations and early applications of AI in nanoformulation design, the construction of patient-specific models in metabolic disease, and the architecture and governance of AI–nano systems for personalized management of obesity and diabetes[24, 25].

2. AI in Nanoformulation Design and Optimization

Nanoformulation development has traditionally relied on empirical screening: researchers vary materials, surfactants, solvent ratios and process conditions, then measure size, encapsulation, stability and *in vitro* performance[27]. This process is labor- and time-intensive and can miss optimal combinations. ML approaches now offer more systematic routes. Supervised models such as random forests, support vector machines and neural networks have been trained to predict critical quality attributes of nanoparticles from descriptors of polymer composition, lipid structures, drug physicochemical properties and processing parameters. Bayesian optimization and active learning frameworks can iteratively propose new experiments that are maximally informative, converging on optimal formulations with far fewer laboratory trials[27, 28].

In the context of obesity and diabetes, such AI tools could be used to design nanoformulations that maximize oral bioavailability of poorly soluble anti-obesity phytochemicals, minimize burst release of GLP-1 analogues, or tune the circulation half-life of adipose-targeted anti-inflammatory nanoparticles[7, 8, 29]. Deep learning models trained on large nanomaterials databases can also predict protein corona composition and immune cell interactions, which are important for macrophage-targeted therapies in metabolic tissues.

Generative models variational autoencoders and generative adversarial networks have been explored for *de novo* design of molecular structures and could analogously be used for “inverse design” of nanocarriers with desired size, surface patterns or ligand architectures[30]. Multi-objective optimization can balance trade-offs between stability, targeting efficiency, drug loading and manufacturability. As standardized nanomedicine databases grow and reporting practices improve, AI-driven formulation platforms may become integral to early-stage design of nano-based obesity and diabetes therapies, reducing development costs and accelerating translation[30].

3. Patient-Level Data, Digital Biomarkers and AI Phenotyping in Diabetes

Personalized management requires detailed characterization of each patient's metabolic profile and its temporal dynamics. CGM systems generate high-frequency glucose traces, revealing time in range, glycemic variability and responses to meals, exercise and medications[31]. Wearable devices add continuous streams on physical activity, heart rate, sleep and sometimes electrodermal activity or temperature. Electronic health records provide diagnoses, medications, laboratory tests and imaging, while emerging consumer tools capture diet and stress via apps and ecological momentary assessment[31].

Machine learning models applied to these multimodal data can identify latent phenotypes of obesity and diabetes beyond simple BMI or HbA1c categories. For example, unsupervised clustering of CGM features has revealed distinct glycemic patterns associated with different risks of complications and responses to insulin therapy[31]. Integration of body composition imaging with laboratory markers and genomics has identified T2DM subgroups with predominant hepatic steatosis versus visceral adiposity versus β -cell failure. Digital biomarkers such as postprandial glycemic excursions, sleep-activity rhythms and heart rate variability provide proxies for insulin sensitivity, autonomic balance and behavioral adherence.

These AI-derived phenotypes can guide nanoformulation selection. A patient with prominent hepatic insulin resistance and steatosis might be prioritized for liver-targeted nanoformulations delivering AMPK activators or lipid-lowering agents, whereas a patient with pronounced adipose inflammation and minimal steatosis might benefit more from adipose-targeted anti-inflammatory nanoparticles or browning inducers[24, 32]. Those with erratic eating patterns and high glycemic variability could be candidates for nano-enabled long-acting incretin formulations combined with AI-based behavioral coaching. Incorporating genomics and pharmacogenomics further refines stratification, for example highlighting individuals at risk of rare adverse events or differential drug metabolism[33].

Real-world deployment requires robust, interpretable models that clinicians and patients can trust. Techniques such as feature attribution, causal modeling and counterfactual explanations can help clarify how AI systems reach recommendations. Importantly, data sources must be representative of populations disproportionately affected by diabesity, including individuals in low-resource settings, to avoid amplifying existing inequities.

4. Matching Patients to Nanoformulations: AI-Driven Treatment Recommendation

Once both nanoformulation performance characteristics and patient phenotypes are modeled, AI can act as a matching engine, recommending nano-enabled interventions that maximize expected benefit while minimizing risk and cost. This resembles recommendation systems in other domains but with stricter constraints[31]. Supervised learning models can be trained on clinical trial and real-world data linking patient features, treatments (including nanoformulations when available) and outcomes such as weight change, HbA1c reduction, hepatic fat fraction and adverse events[26].

Causal inference methods propensity-score modeling, targeted maximum likelihood estimation and causal forests can estimate individualized treatment effects, supporting decisions about whether a given patient is more likely to benefit from, for example, a GLP-1-loaded depot formulation versus an orally delivered nanoformulation of a polyphenol combination[34]. Reinforcement learning approaches, already applied to insulin dosing, may be extended to longer time scales, learning policies that adapt treatment sequences based on observed responses over months[34].

In practice, AI-guided recommendation engines for nanoformulations would exist within clinical decision-support systems rather than operate autonomously. They would propose options with estimated probabilities of achieving agreed-upon goals (for example, 10% weight loss, HbA1c <7%, resolution of steatosis), accompanied by confidence intervals and explanations[35]. Clinicians and patients could then select from these options, considering preferences, contraindications and access. As more data accumulate on nano-enabled regimens, models could be updated in a federated way across institutions, preserving privacy while improving performance.

5. Toward Closed-Loop Systems: Coupling Nanoformulations, Sensors and AI

A longer-term vision involves closed-loop or semi-closed-loop systems that dynamically adjust nanoformulation dosing and scheduling based on continuous sensing and AI analytics. In diabetes, fully closed-loop glucose control “artificial pancreas” systems coupling CGM, insulin pumps and control algorithms has already demonstrated improved time in range and reduced hypoglycemia[25]. Extending this concept to diabesity management would add new layers: nanoformulations as the therapeutic actuators and multi-analyte sensing as the input.

Wearable or minimally invasive nano-biosensors can track not only glucose but also lactate, ketones and perhaps inflammatory markers or adipokines. AI algorithms could integrate these signals with activity and dietary data to estimate short-term changes in insulin sensitivity, energy expenditure and inflammatory tone[36–38]. Based on these estimates, the system might recommend adjusting the frequency of injections of a long-acting adipose-targeted nanotherapy, altering the timing of oral nanoformulations relative to meals, or temporarily intensifying a hepatic-targeted nanoformulation during periods of increased steatosis risk (for example, holidays).

Smart nanocarriers themselves can incorporate stimuli-responsive elements that modulate drug release in response to local pH, enzymes or temperature, effectively implementing a local control loop at the tissue level[22, 23]. AI would operate at a higher systems level, deciding which formulation to use when and in what dose. Although such architectures remain conceptual, they illustrate how AI and nanotechnology could converge to create multi-scale control systems for diabesity that combine systemic, tissue-level and microenvironment-level feedback.

6. Ethical, Regulatory and Equity Considerations

The integration of AI-guided nanoformulations into obesity and diabetes care raises important non-technical questions[39]. First is safety and accountability. Both AI decision-support systems and nanoformulations can fail in subtle ways: biased data may lead to suboptimal recommendations for underrepresented groups, and nanocarriers may exhibit rare but serious off-target effects. Regulatory agencies are developing frameworks for

“software as a medical device” and for complex biologic–device combinations, but AI–nano hybrids challenge boundaries. Transparent reporting of training data, model performance across subgroups, and rigorous preclinical and clinical evaluation of nanoformulations are essential[39].

Second is explainability and consent. Patients and clinicians must understand, at least qualitatively, why a given AI system recommends a particular nano-enabled therapy. Black-box recommendations risk eroding trust. Interfaces that show key contributing factors such as high visceral adiposity, particular CGM patterns or elevated hepatic enzymes can support shared decision-making. Informed consent must cover both nanoformulation-specific risks (for example, long tissue residence, immunogenicity) and data-driven aspects (for example, use of personal health data for model training)[39].

Third is equity. Obesity and T2DM disproportionately affect socioeconomically disadvantaged and marginalized populations, who may have limited access to advanced therapeutics and digital infrastructure. There is a risk that AI-guided nanoformulations become available only to those in well-resourced settings, widening disparities. Mitigation strategies include inclusive data collection across diverse populations, cost-conscious nanoformulation design, integration with low-cost digital platforms (for example, basic smartphones), and policy measures to ensure coverage for high-impact interventions[40, 41].

Finally, environmental and lifecycle considerations should not be neglected, particularly if large-scale production of nanoformulations is envisaged. Safe manufacturing, disposal and potential ecological impacts of nanomaterials require attention.

7. Future Directions: Roadmap for AI–Nano Precision Diabesity Therapies

Several concrete steps can advance the field. On the nanotechnology side, building standardized, publicly accessible datasets that link formulation parameters, physicochemical properties, *in vitro* behavior and *in vivo* biodistribution and efficacy will provide the substrate for robust AI models. Community-wide efforts to harmonize reporting standards and ontologies in nanomedicine will increase interoperability and enable meta-analyses.[14, 42]

On the AI side, prospective studies in obesity and diabetes that systematically integrate CGM, wearables, imaging and multi-omics with treatment and outcome data are needed[43]. These should oversample populations at highest risk and explicitly evaluate fairness metrics. Hybrid mechanistic–ML models that combine physiological understanding (for example, minimal models of insulin–glucose dynamics) with data-driven components may offer better generalization and interpretability than purely black-box approaches[43]. Clinically, early applications of AI-guided nanoformulations are likely to focus on high-risk subgroups where conventional approaches fail: individuals with severe obesity and insulin resistance who are poor responders or intolerant to current drugs, those with advanced non-alcoholic steatohepatitis, or those with rapid diabetes progression despite standard care[44]. Pilot trials might compare AI-guided nanoformulation strategies versus standard-of-care intensification, assessing not only weight and glycemic outcomes but also liver fat, cardiovascular risk markers and patient-reported outcomes.

Interdisciplinary collaboration will be critical. Materials scientists, computational modelers, endocrinologists, hepatologists, behavioral scientists, ethicists, and patient representatives must co-design systems that are scientifically sound, clinically relevant and acceptable to users. Regulatory science initiatives can help clarify evidentiary requirements and support adaptive approval pathways for AI–nano combination products[44].

Looking further ahead, the convergence of AI-guided nanoformulations with other emerging technologies such as gene editing, microbiome engineering and advanced bariatric endoscopy could yield integrated platforms that address multiple axes of diabesity pathophysiology. For example, a combined regimen might pair a liver-targeted nanoformulation carrying an AMPK activator, an adipose-targeted anti-inflammatory nanotherapy, a microbiome-modulating probiotic and an AI-driven coaching app, with dosages and timing continuously adapted based on sensor data.

CONCLUSION

Artificial intelligence–guided nanoformulations represent a promising frontier for the personalized management of obesity and diabetes. By uniting the tunable, tissue-specific capabilities of nanomedicine with the pattern-recognition and predictive power of AI, it becomes possible to design, select and adapt therapies to the biological and behavioral profile of each individual. Early work in AI-driven formulation design, digital phenotyping and metabolic decision support provides key building blocks, while advances in adipose- and liver-targeted nanotherapies create a growing palette of interventions. Realizing this vision will require high-quality data, rigorous validation, attention to safety and equity, and close collaboration across disciplines. If these conditions are met, AI–nano convergence could help shift diabesity care from reactive, trial-and-error escalation toward proactive, mechanism-based and patient-tailored strategies, improving outcomes while making better use of therapeutic resources.

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