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Theranostic Nanoplatforms in Obesity-Associated Comorbidities

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ABSTRACT

Obesity is strongly linked to metabolic disorders such as type 2 diabetes, cardiovascular disease, non-alcoholic fatty liver disease, and certain cancers. The complex and progressive nature of these comorbidities requires approaches that integrate both diagnosis and treatment. Theranostic nanoplatforms engineered nanosystems capable of combining therapeutic delivery with diagnostic imaging or biomarker sensing offer a promising strategy to address this dual challenge. By enabling real-time monitoring of disease progression and simultaneous targeted therapy, these platforms enhance precision, reduce off-target toxicity, and improve treatment outcomes. Liposomes, polymeric nanoparticles, gold nanoshells, magnetic nanoparticles, and hybrid nanomaterials have been explored for theranostic applications in obesity-associated diseases. This review discusses the principles of theranostic nanoplatforms, their advances in managing obesity-related comorbidities, translational challenges, clinical perspectives, and future opportunities. These systems represent an important step toward precision nanomedicine in obesity care.

Keywords: Theranostics, Nanoplatforms, Obesity, Comorbidities, Precision medicine

INTRODUCTION

Obesity has emerged as a global epidemic, with prevalence rates continuing to rise across age groups and populations[1–3]. Beyond excessive fat accumulation, obesity profoundly disrupts metabolic homeostasis, giving rise to a constellation of comorbidities collectively referred to as obesity-associated disorders. These include type 2 diabetes mellitus, cardiovascular disease, dyslipidemia, non-alcoholic fatty liver disease (NAFLD), chronic kidney disease, and certain cancers such as breast, colorectal, and prostate cancer[4, 5]. Together, these conditions account for significant morbidity, mortality, and healthcare costs.

The pathophysiology of obesity-associated comorbidities involves multiple interconnected mechanisms. Insulin resistance and impaired glucose metabolism underlie diabetes development. Chronic inflammation, endothelial dysfunction, and atherogenic lipid profiles promote cardiovascular complications[6–8]. Excessive hepatic lipid accumulation progresses to steatohepatitis and fibrosis in NAFLD. Moreover, adipose tissue–derived cytokines and hormones create a systemic pro-inflammatory and pro-tumorigenic environment, increasing cancer risk[9–12]. Because these conditions often develop insidiously and progress silently until advanced stages, early diagnosis and precise monitoring are crucial for effective management.

Conventional diagnostic techniques such as imaging, biochemical assays, and tissue biopsies provide valuable information but are limited in sensitivity, invasiveness, or ability to detect early subclinical changes[13, 14]. Similarly, therapeutic approaches ranging from lifestyle interventions and pharmacotherapy to bariatric surgery struggle to address the heterogeneity and complexity of obesity comorbidities. Pharmacological treatments are often hampered by poor bioavailability, systemic side effects, and lack of tissue specificity. Lifestyle interventions, while essential, rarely achieve sustained remission in advanced disease [15].

Nanotechnology offers innovative solutions by improving both diagnostics and therapeutics. Nanoparticles can be engineered to enhance solubility, stability, and bioavailability of drugs, as well as to deliver them selectively to diseased tissues[16–18]. At the same time, their optical, magnetic, or acoustic properties can be harnessed for imaging and sensing applications. This dual functionality theranostics integrates therapy and diagnostics into a single platform, enabling simultaneous treatment and real-time monitoring.

Theranostic nanoplatforms have been investigated in cancer extensively, but their application to obesity-associated comorbidities is gaining traction[19–22]. For example, magnetic nanoparticles can deliver anti-diabetic drugs while providing magnetic resonance imaging (MRI) contrast for monitoring pancreatic or hepatic changes. Gold nanoshells can be functionalized with ligands to target inflamed vasculature, combining

photothermal therapy with optical imaging in cardiovascular disease. Lipid-based theranostic systems encapsulating natural compounds such as curcumin or resveratrol can deliver anti-inflammatory effects while allowing near-infrared imaging[23].

The integration of therapeutic and diagnostic functionalities provides unique advantages. Real-time monitoring enables clinicians to assess drug biodistribution, therapeutic efficacy, and disease progression simultaneously. This feedback loop allows for adaptive therapy tailored to patient responses, advancing the principles of precision medicine. Moreover, by concentrating treatment at disease sites and minimizing systemic exposure, theranostic nanoplatforms reduce side effects and enhance patient compliance[24–26].

Despite these promises, theranostic platforms face challenges, including safety concerns, manufacturing complexity, regulatory hurdles, and cost-effectiveness. Given the chronic nature of obesity comorbidities, long-term safety studies are particularly critical[27–29]. This review focuses on the potential of theranostic nanoplatforms in obesity-associated comorbidities. Section 2 discusses their principles and design. Section 3 highlights advances in diabetes, cardiovascular disease, NAFLD, and cancer. Section 4 examines translational challenges. Section 5 explores clinical perspectives. Section 6 discusses future directions for integrating theranostic systems into obesity management.

2. Principles of Theranostic Nanoplatforms

Theranostic nanoplatforms integrate therapeutic and diagnostic functionalities into a single nanosystem. Their design relies on combining drug delivery with imaging or biosensing capabilities, allowing simultaneous treatment and monitoring of disease. Several core principles underlie their function.

Nanocarrier structure: Lipid-based systems, polymeric nanoparticles, dendrimers, and inorganic nanoparticles form the backbone of theranostic platforms. Their small size and high surface area permit efficient drug encapsulation and functionalization with imaging agents[30, 31].

Diagnostic components: Nanoparticles can be equipped with imaging modalities such as fluorescent dyes, quantum dots, gold nanostructures, or magnetic nanoparticles. These confer optical, magnetic, or acoustic properties, enabling detection through MRI, CT, ultrasound, or near-infrared fluorescence imaging[32–35].

Therapeutic components: Encapsulated drugs, peptides, natural compounds, or nucleic acids form the therapeutic payload. Co-delivery of multiple agents is possible, allowing combination therapies[36].

Targeting and functionalization: Surface ligands such as antibodies, peptides, or aptamers allow specific binding to receptors overexpressed in diseased tissues such as insulin-resistant hepatocytes in NAFLD or inflamed endothelium in atherosclerosis[37].

Stimuli responsiveness: Many theranostic platforms incorporate stimuli-responsive features, releasing drugs in response to pH, enzymes, or redox gradients typical of diseased tissues. External triggers such as light, ultrasound, or magnetic fields can also be employed for controlled release and imaging[10, 25, 33, 38].

Theranostic integration: By combining these components, nanoplatforms enable clinicians to track biodistribution, confirm drug delivery, and evaluate therapeutic outcomes in real time. This feedback loop supports adaptive and personalized treatment strategies[39, 40].

These principles form the foundation of applying theranostic nanoplatforms to obesity-associated comorbidities.

3. Advances in Obesity-Associated Comorbidities

Theranostic nanoplatforms have shown promise in addressing several major comorbidities linked to obesity.

Type 2 diabetes: Polymeric nanoparticles carrying insulin or GLP-1 analogs have been combined with fluorescent probes to monitor delivery and action in pancreatic or hepatic tissues. Magnetic nanoparticles have been used to deliver insulin-sensitizing drugs while providing MRI contrast to track distribution[41, 42].

Cardiovascular disease: Gold nanoshells and nanorods functionalized with peptides targeting inflamed endothelium deliver anti-atherosclerotic drugs while enabling photoacoustic imaging. Iron oxide nanoparticles loaded with statins provide both cholesterol-lowering therapy and MRI-based plaque visualization[43, 44].

Non-alcoholic fatty liver disease (NAFLD): Lipid nanocarriers encapsulating curcumin or resveratrol have been used for anti-inflammatory and anti-fibrotic therapy, combined with near-infrared imaging agents for real-time monitoring of hepatic fat content. Smart nanoparticles responsive to oxidative stress release antioxidants in diseased liver regions[45–47].

Cancer: Theranostic nanoparticles have targeted obesity-related cancers such as breast and colorectal cancer. For example, doxorubicin-loaded liposomes functionalized with tumor-targeting ligands combine chemotherapy with fluorescence imaging. Gold nanoparticles provide photothermal therapy while simultaneously enabling imaging to track tumor regression[27, 48].

Collectively, these advances highlight the versatility of theranostic platforms in addressing the wide spectrum of obesity comorbidities. Although most studies are preclinical, they establish a strong foundation for future clinical applications.

4. Translational Challenges

Despite promising advances, translation of theranostic nanoplatforms to clinical practice is limited by several challenges.

Safety and toxicity: Nanoparticles may accumulate in non-target organs such as the liver and spleen, raising concerns about long-term toxicity. Imaging agents such as quantum dots may release toxic heavy metals. Ensuring biocompatibility and biodegradability is essential for chronic conditions[49].

Manufacturing complexity: Producing theranostic platforms that integrate drugs and imaging agents requires precise control over size, loading efficiency, and release kinetics. Scaling up these processes while maintaining reproducibility is difficult and expensive[50, 51].
Regulatory hurdles: Regulatory agencies face challenges in classifying theranostic nanoplatforms, which function as both drugs and devices. Comprehensive data on pharmacokinetics, safety, and diagnostic performance are required, prolonging approval timelines.[52–54]
Patient variability: Differences in comorbidity profiles, genetic backgrounds, and metabolic states may affect nanoparticle distribution and efficacy. Personalized approaches may be necessary, complicating clinical trial design.
Cost-effectiveness: Theranostic systems are expensive to develop and manufacture. Without demonstrating clear superiority over existing diagnostic and therapeutic modalities, they may face barriers to adoption in routine clinical care.
Overcoming these challenges requires advances in materials science, scalable manufacturing technologies, standardized evaluation protocols, and interdisciplinary collaboration.

5. Clinical Perspectives

From a clinical standpoint, theranostic nanoplatforms offer several advantages. By combining therapy and diagnosis, they reduce the need for multiple interventions, streamline patient care, and enable real-time monitoring. This is particularly valuable in chronic conditions like obesity-associated diabetes or cardiovascular disease, where disease progression is gradual and requires continuous evaluation[26, 29, 39].
Clinical translation is beginning to emerge. Iron oxide nanoparticles are already approved as MRI contrast agents, and similar systems are being adapted for combined diagnostic and therapeutic applications. Lipid-based theranostic formulations encapsulating curcumin have reached early clinical testing for liver diseases. In oncology, several theranostic nanoparticles have entered clinical trials, offering insights into regulatory pathways applicable to obesity comorbidities[44].
In practice, theranostic platforms could provide targeted drug delivery to atherosclerotic plaques while simultaneously allowing clinicians to visualize plaque regression. In diabetes, insulin or GLP-1 delivery could be tracked in real time, optimizing dosage and timing. For NAFLD, anti-inflammatory nanoparticles could provide simultaneous therapeutic benefit and non-invasive monitoring of hepatic fat content, potentially replacing invasive biopsies[55].
However, adoption depends on demonstrating not only efficacy and safety but also practicality and affordability. Patient acceptance will be influenced by the perceived complexity of nanomedicine, requiring clear communication and education. Healthcare systems will require evidence of cost-effectiveness compared to conventional diagnostics and therapies.

6. Future Directions

The future of theranostic nanoplatforms in obesity comorbidities lies in personalization, multifunctionality, and integration with digital health. **Personalized nanomedicine** will tailor theranostic systems to individual metabolic and genetic profiles, enhancing therapeutic efficacy. Advances in genomics, metabolomics, and microbiome analysis will guide the design of patient-specific nanoplatforms.
Multi-functional platforms combining therapy, imaging, and biosensing will become increasingly important. For instance, nanoparticles could deliver anti-diabetic drugs, monitor glucose fluctuations, and provide imaging readouts in a single system. Such integration would allow adaptive, real-time therapy adjustments.
Stimuli-responsive theranostics will enhance specificity. Redox- or enzyme-responsive systems could release drugs only in diseased tissues, while external triggers like magnetic fields or ultrasound could provide spatiotemporal control.
AI integration will accelerate development and deployment. Machine learning models can optimize nanoparticle design, predict patient responses, and analyze imaging data from theranostic platforms, improving precision and efficiency.
Collaboration across disciplines—including nanotechnology, medicine, bioinformatics, and regulatory science—will be essential. Global harmonization of regulatory standards and investment in scalable manufacturing will determine the pace of clinical translation.
If these efforts succeed, theranostic nanoplatforms could transform obesity management by enabling early detection, targeted therapy, and real-time monitoring of comorbidities, moving toward a truly personalized healthcare paradigm.

CONCLUSION

Theranostic nanoplatforms represent a transformative approach to managing obesity-associated comorbidities. By integrating therapeutic and diagnostic functions, they enable targeted delivery, real-time monitoring, and adaptive treatment. Preclinical evidence demonstrates significant potential in diabetes, cardiovascular disease, NAFLD, and cancer. While barriers remain in safety, manufacturing, regulation, and cost, future innovations in personalization, multifunctionality, and AI integration hold the promise of bringing theranostic nanomedicine into clinical practice for obesity and its complications.

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