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Nanotheranostics in Obesity: Dual-Function Platforms for Simultaneous Imaging and Treatment of Metabolic Disorders

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ABSTRACT

Obesity and its associated metabolic disorders arise from complex, tissue-specific disturbances in adipose biology, liver and vascular function, pancreatic islet health and systemic inflammation. Conventional diagnostics and pharmacotherapy treat these facets separately, relying on late-stage clinical markers and non-targeted drugs. Nanotheranostics like nanoscale platforms integrating imaging and therapy in a single construct offer an opportunity to visualize and modulate obesity-related pathologies simultaneously, with spatial and temporal precision. In obesity, this includes tracking adipose tissue remodeling, inflammatory adipose tissue macrophages, brown/beige thermogenic activity, and lipid accumulation in liver and vasculature while delivering drugs, energy-converting agents or gene cargos. This review outlines the rationale for nanotheranostics in metabolic disease, the design principles of dual-function platforms, and emerging examples that couple imaging with photothermal, photodynamic, sonodynamic, catalytic or pharmacologic therapies in adipose tissue and other metabolic organs. We highlight adipose-targeted theranostic nanoparticles that promote white adipose tissue browning, locally ablate adipocytes or silence inflammatory pathways, alongside systems for monitoring and treating non-alcoholic fatty liver disease and vascular complications. Translational challenges in safety, regulatory evaluation and personalization are discussed, and future directions are proposed for integrating nanotheranostics into precision obesity management.

Keywords: Obesity; Nanotheranostics; Adipose tissue; Imaging-guided therapy; Metabolic syndrome

INTRODUCTION

Obesity is a chronic, relapsing disease characterized by excessive adipose tissue expansion, ectopic lipid deposition and whole-body metabolic dysregulation[1–3]. It underpins a spectrum of disorders, including insulin resistance, type 2 diabetes, non-alcoholic fatty liver disease (NAFLD), dyslipidemia and cardiovascular disease, collectively captured as metabolic syndrome. Although lifestyle modification and pharmacotherapy can induce significant weight loss and improve metabolic parameters, treatment responses are heterogeneous and relapse is common [4]. Clinicians often lack tools to monitor, in real time, how specific tissues such as visceral white adipose tissue (WAT), brown adipose tissue (BAT), liver or vascular beds are responding to therapy[5–8].

Current diagnostics for obesity-related complications rely on indirect or late-stage markers: body mass index and waist circumference for adiposity; fasting glucose, HbA1c and lipid panels for metabolic risk; liver enzymes and ultrasound for steatosis; and structural imaging for advanced organ damage[9–11]. These measures provide little information about early biological changes such as adipose tissue inflammation, adipose tissue macrophage (ATM) activation, WAT browning, microvascular dysfunction or subtle hepatocellular lipid accumulation. As a result, interventions are often initiated late and adjusted slowly, based on infrequent clinic visits and laboratory tests[12–14].

Nanomedicine has emerged as a promising approach to overcome limitations of traditional anti-obesity drugs by enabling targeted delivery to metabolically relevant tissues[12, 15–17]. Adipose tissue–targeting nanomedicines exploit unique vascular, receptor and extracellular matrix features of WAT and BAT to concentrate drugs and constructs in these depots, thereby enhancing efficacy and reducing off-target toxicity.

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Strategies include vascular-homing peptides, biomimetic lipoprotein-like carriers, photothermal nanoparticles, magnetic nanoparticles and microneedle-based local depots. Nanotheranostics extend this paradigm by incorporating imaging capabilities into therapeutic nanoparticles. In classical oncology, theranostic platforms combine contrast agents for MRI, CT, PET, optical or ultrasound imaging with chemotherapeutics or photothermal/photodynamic agents, enabling real-time tracking of drug delivery, accumulation and therapeutic response[18–20]. The same concept can be applied to obesity and metabolic disorders, where the ability to visualize adipose depots, inflammatory foci, BAT activation or hepatic fat while simultaneously delivering treatment could support more precise, adaptive interventions.

In obesity, nanotheranostic approaches are beginning to appear across several modalities. Photothermal and photodynamic nanoplatforms, often based on gold, iron oxide or porphyrin-like photosensitizers, localize in WAT and convert near-infrared (NIR) light into heat or reactive oxygen species[21]. These systems both image adipose depots via fluorescence, photoacoustic or MR contrast and induce local adipocyte death or WAT browning upon illumination. Ultrasound-based and magnetically responsive nanoparticles extend these concepts to deeper tissues via sonodynamic therapy (SDT) and magnetic hyperthermia [21].

Theranostic nano-systems are also being developed to track and modulate ATMs. A recent review on nanomaterials for the treatment and monitoring of obesity emphasizes multimodal platforms that target ATMs for anti-inflammatory therapy while incorporating imaging agents to monitor depot-specific inflammation and remodeling[20, 22]. These constructs can carry anti-inflammatory small molecules or gases (for example, nanosilicon generating hydrogen in situ), while integrating fluorescent or MR contrast to visualize trafficking and therapeutic impact in visceral adipose tissue[23, 24].

Beyond adipose tissue, theranostic nanoparticles have been proposed for NAFLD, a central manifestation of metabolic syndrome. Nanoplatforms carrying hepatotropic ligands can deliver antioxidants, PPAR agonists or NLRP3 inflammasome inhibitors to the liver while providing MR or optical contrast for non-invasive tracking of hepatic uptake and fat content, paralleling similar systems developed in oncology and fibrotic liver disease.[25, 26] Vascular-targeted nanotheranostics, meanwhile, may address obesity-driven atherosclerosis by imaging inflamed plaques and delivering anti-inflammatory or lipid-lowering therapy directly to the arterial wall.

The rationale for nanotheranostics in obesity therefore rests on three pillars. First, obesity is a multi-organ, spatially heterogeneous disease; dual-function platforms can help disentangle which depots and organs are driving risk in individual patients and monitor how they respond to therapy[22, 26]. Second, many promising agents (for example, thermogenic inducers, gene cargos or nutraceuticals) require targeted delivery and spatiotemporal control that nanocarriers can provide. Third, combining imaging and therapy may accelerate translation by enabling robust pharmacokinetic–pharmacodynamic studies, dose optimization and patient selection based on demonstrated target engagement[27, 28].

However, the metabolic context also raises distinct challenges compared with oncology, including the need for long-term safety in ambulatory patients, the involvement of multiple tissues and the importance of avoiding exacerbation of systemic inflammation. Understanding how dual-function nanoparticles behave in obese organisms, how they interact with ATMs and the liver and how imaging signals correlate with metabolic outcomes will be crucial for responsible development of nanotheranostics in this space. The following sections examine design principles, representative platforms and translational issues in more detail.

2. Design Principles of Nanotheranostic Platforms for Metabolic Disease

Nanotheranostic platforms integrate three functional components: a carrier, an imaging moiety and a therapeutic payload. The carrier can be inorganic (such as gold, iron oxide, silica), organic (liposomes, polymeric micelles, lipid nanoparticles) or hybrid, with properties tailored for metabolic organs[27]. The imaging element may provide MRI (iron oxide, gadolinium), CT (high-Z metals), PET/SPECT (radiotracers), NIR fluorescence, photoacoustic signal or ultrasound contrast, while therapeutics range from small molecules and peptides to RNA therapeutics and photothermal/photodynamic agents[23].

In obesity, design must account for the distinctive microenvironment of adipose tissue and metabolic organs. Adipose depots are highly vascularized, but in obesity they become inflamed, fibrotic and hypoxic, with altered receptor expression on endothelium, adipocytes and ATMs. Active targeting strategies exploit vascular-homing peptides that bind markers such as prohibitin or integrins on adipose endothelium, or ligands that recognize receptors on adipocytes or macrophages[29–31]. Passive targeting relies on depot-specific vascular permeability and prolonged circulation.

Imaging readouts should be selected to match therapeutic mechanisms. Photothermal and photodynamic adipose nanotheranostics typically incorporate NIR-absorbing chromophores (for example, porphyrins, BODIPY derivatives, gold nanostructures) that provide both fluorescence or photoacoustic contrast and heat or reactive oxygen generation under NIR irradiation[21]. Iron oxide cores support MRI and magnetic hyperthermia; gas-generating systems may be visualized by ultrasound. In all cases, imaging is used to confirm depot localization, guide energy delivery and potentially serve as a surrogate for dose and response.

Therapeutic payloads may aim to reduce adipocyte number (for example, local ablation), enhance energy expenditure (via WAT browning or BAT activation), silence inflammatory signaling in ATMs or correct

systemic dyslipidemia[32]. Recent adipose-targeted nanomedicines incorporate PPARγ agonists, β3-adrenergic agonists, thyroid hormone analogues, anti-inflammatory drugs such as simvastatin or H_2-generating nanosilicon to modulate inflammatory stress. Nanotheranostic versions co-load these agents with imaging moieties to monitor distribution and effects[32].
Crucially, dual-function constructs must balance imaging and therapy without compromising either. High loading of metals or chromophores may improve signal but risk toxicity or altered pharmacokinetics; conversely, prioritizing biocompatibility may limit imaging sensitivity. Biodegradable or excretable components and clinically acceptable imaging agents are preferred for chronic metabolic indications[33]. Lessons from nanotheranostics in oncology and gene therapy, including spatiotemporal tracking of nanoparticles for safety and efficacy evaluation, are directly relevant to the metabolic field.

3. Adipose-Targeted Nanotheranostics: Imaging-Guided Browning, Ablation and Inflammation Resolution

Adipose tissue is the most obvious and intensively explored target for nanotheranostics in obesity. White adipose depots not only store triglycerides but also orchestrate endocrine and inflammatory signals that shape whole-body metabolism. Their remodeling during obesity hypertrophy, inflammation, altered vascularization and fibrosis creates opportunities for targeted imaging and intervention[29, 30, 34].
Photothermal and photodynamic theranostic platforms directly exploit adipose accessibility to light, especially in subcutaneous depots. A recent adipocyte-targeted nanocomplex (pTSL@(P+I)), based on peptide-modified thermosensitive liposomes co-loaded with a photothermal agent and an immune modulator, was designed to accumulate in WAT[35]. Upon NIR irradiation, it produced mild hyperthermia and local immunomodulation, promoting WAT browning and significantly improving metabolic parameters in obese mice, with simultaneous fluorescence tracking of distribution. Another system, adipose-targeting hybrid nanoparticles (Pep-PPIX-Baic NPs) integrating an Fe^{3+}–porphyrin photosensitizer and a browning phytochemical, combined photodynamic adipocyte destruction with inducible browning, using optical imaging to guide and evaluate treatment [35].
Mild-photothermal and nanocatalytic theranostic platforms have been developed to convert WAT into a metabolically active tissue without wholesale ablation. One transdermal nanoformulation uses NIR-absorbing nanoparticles to generate sub-lethal heat, activating thermogenic programs and improving glucose and lipid metabolism, while catalytically decomposing reactive oxygen species that contribute to adipose inflammation. Imaging components confirm targeted heating and depots engaged[36]. Cationic albumin nanoparticles co-loaded with rosiglitazone and photothermal agents exemplify another approach. These adipocyte-targeted constructs localize to WAT, where NIR-triggered heating enhances drug penetration and browning while imaging signals provide feedback on depot exposure. In diet-induced obese mice, this localized photothermal plus pharmacologic strategy reduced WAT mass, improved thermogenesis and mitigated systemic metabolic dysfunction more effectively than systemic rosiglitazone, with lower off-target effects[36].
Inflammation-focused theranostics target ATMs and stromal cells. Simvastatin-loaded polymeric nanoparticles directed to ATMs not only reduce local NF-κB–driven cytokine production and promote an M2-like profile but also couple these effects to browning and thermogenesis. Imaging moieties, such as fluorescent or MR labels, allow tracking of ATM targeting and depot remodeling[37–39]. Hydrogen-generating nanosilicon platforms designed for visceral adipose tissue immunomodulation incorporate imaging-compatible cores, enabling spatiotemporal correlation between hydrogen release, inflammation resolution and metabolic outcomes.
Together, these adipose-targeted nanotheranostic systems illustrate several key themes: imaging-guided energy-based therapies (photothermal, photodynamic, potentially sonodynamic and magnetic), coupling of local thermal or oxidative stress with browning or drug action, and concurrent tracking of depot localization and remodeling[40, 41]. As designs mature, integrating multiplex imaging (for example, combining NIR fluorescence with MRI) and multi-payload therapy may further refine spatiotemporal control over adipose reprogramming in obesity.

4. Nanotheranostics Beyond Fat: Liver, Vasculature and Multi-Organ Metabolic Syndrome

While adipose tissue is central to obesity, metabolic syndrome involves coordinated pathology across the liver, vasculature, skeletal muscle, and pancreas. Nanotheranostic strategies are being adapted to these organs, often leveraging concepts initially developed in oncology and cardiovascular disease[22, 26].
In NAFLD and non-alcoholic steatohepatitis, hepatocytes accumulate triglycerides and lipotoxic species, while Kupffer cells and stellate cells drive inflammation and fibrosis [42]. Liver-targeted nanomedicines using galactose derivatives, asialoglycoprotein receptor ligands or high-density lipoprotein (HDL) mimics have been developed to deliver antioxidants, PPAR agonists and antifibrotic agents[43]. Theranostic versions can incorporate MRI contrast (for example, iron oxide cores) or NIR fluorophores to visualize hepatic uptake and distribution. Imaging enables quantification of hepatic fat and fibrosis burden and monitoring of treatment response, complementing or potentially enhancing traditional MR-PDFF and elastography[43].
One recent oral nanoplatform, based on reconstituted HDL (rHDL@RM/MS), was designed to treat systemic obesity and comorbidities by sequentially targeting the intestine, liver, and adipose tissue. It ameliorated NAFLD, gut dysbiosis, systemic lipid abnormalities and chronic inflammation in obese mice[44]. While not yet

fully theranostic, similar rHDL-based constructs could be modified with imaging labels to track transport and tissue engagement, transforming them into multi-organ nanotheranostics for metabolic syndrome[44].
Atherosclerotic cardiovascular disease, a major complication of obesity, is another target. Inflammatory vascular nanotheranostics designed for cancer and plaque imaging use iron oxide, gold or BODIPY-type agents to provide MRI, CT or NIR signals while delivering anti-inflammatory or anti-proliferative drugs to plaques[45]. Translating these platforms to obese populations could enable the identification of "vulnerable" plaques in patients with metabolic syndrome and simultaneous local therapy to stabilize lesions. Skeletal muscle insulin resistance and pancreatic β-cell stress are more challenging for direct theranostic targeting due to diffuse distribution and limited imaging contrast, but nanoparticles that home to inflamed islets or myeloid cells in muscle could, in principle, deliver anti-inflammatory or antioxidant therapy while providing imaging for disease staging[45]. At present, such approaches remain largely conceptual, informed by experiences in autoimmune diabetes and myositis. Ultimately, obesity and metabolic syndrome are systemic disorders. Nanotheranostic strategies that integrate adipose, liver and vascular imaging with local therapy may be best suited to capture the multi-organ nature of disease, for example, by combining adipose photothermal browning with hepatic lipotoxicity monitoring or by coupling ATM-targeted anti-inflammatory therapy with vascular plaque imaging[35, 46]. The challenge is to design platforms that remain safe and manageable in complexity while yielding actionable clinical information.

5. Imaging Readouts, Biomarkers and Response Assessment in Metabolic Nanotheranostics

A defining feature of nanotheranostics is the ability to quantitatively image nanoparticle distribution and therapeutic response. In obesity and metabolic disorders, relevant imaging readouts extend beyond the simple presence or absence of particles to include functional and molecular biomarkers[26, 47].
At the level of adipose tissue, optical and photoacoustic imaging of NIR-absorbing theranostic particles can provide high-resolution maps of depot localization and thermal profiles during photothermal or photodynamic interventions[48]. Changes in signal over time can reflect clearance, browning or fibrosis. MRI with iron oxide–containing nanoparticles can quantify adipose depot volume and, potentially, ATMs, exploiting their phagocytic uptake of contrast agents as in emerging ATM-targeted nanomaterials[48]. In the liver, MR-based nanotheranostics allow assessment of hepatic fat fraction, inflammation and fibrosis. Contrast-enhanced sequences can differentiate steatosis from inflammatory or fibrotic changes, while diffusion and elastography provide complementary structural information. PET tracers linked to nanoparticles might in future track hepatic inflammation or specific metabolic pathways, such as fatty acid oxidation or de novo lipogenesis[48].
Systemic biomarkers, including circulating triglycerides, HDL, glucose, insulin and inflammatory markers such as CRP and cytokines, remain important proxies for metabolic status. However, nanotheranostics can refine interpretation by linking biomarker changes to observed nanoparticle accumulation and depot-specific remodeling[49]. For instance, a photothermal browning theranostic platform that visibly remodels subcutaneous WAT but leaves visceral depots untouched might improve glycemic control modestly but have limited effect on cardiovascular risk, prompting combination with visceral-targeted therapy[49]. Gene-expression and histological analyses in preclinical models provide deeper insight into the mechanism, showing changes in UCP1 and thermogenic genes, macrophage polarization markers and fibrotic signatures after nanotheranostic interventions[49]. Translating these insights to humans will depend on minimally invasive biopsies and circulating cell-free RNA or exosome-based biomarkers that report on tissue-level changes. Importantly, response assessment in metabolic nanotheranostics must consider both benefits and potential harms. Imaging can also detect unintended accumulation in off-target organs, such as the spleen or the kidney, and monitor for structural changes suggestive of toxicity[50–52]. Integrated imaging–biomarker frameworks can help determine whether observed weight loss or metabolic improvements are primarily due to adipose remodeling, hepatic changes, altered food intake or off-target mechanisms, informing dose adjustments and patient selection.
As experience grows, standardized imaging and biomarker endpoints for nanotheranostic trials in obesity will be needed, analogous to RECIST-type criteria in oncology but adapted to multi-organ metabolic outcomes.

6. Translational and Regulatory Challenges for Nanotheranostics in Obesity

Moving nanotheranostics from bench to bedside in obesity involves intersecting translational challenges in materials science, imaging, endocrinology and regulation[53]. Unlike many cancers, obesity is common, chronic and often managed in outpatient settings, requiring particularly stringent safety standards for long-term or repeated nanomedicine exposure[53].
Biocompatibility and biodegradability of carriers are crucial. Platforms based on clinically familiar lipids, polymers and metals (such as iron oxide) have a translational advantage, while complex hybrids and novel materials may face higher regulatory hurdles[54]. Chronic administration raises questions about cumulative organ deposition, immunogenicity and interference with normal immune surveillance, especially when inflammatory pathways are being intentionally modulated. Obesity-associated alterations in pharmacokinetics and immune function further complicate dose extrapolation from lean animal models. Targeting specificity and control over energy-based therapies are additional concerns. Overzealous photothermal or photodynamic ablation risks necrosis, scarring or damage to adjacent structures, particularly in visceral depots near vital

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organs[55]. Sonodynamic and magnetic hyperthermia approaches must ensure precise spatial control to avoid off-target heating. Imaging guidance helps, but standardized protocols for safe energy delivery in obese individuals are still lacking[56].

Regulatory frameworks for nanotheranostics remain evolving. Agencies such as the FDA and EMA typically require full characterization of nanoparticle size distributions, surface properties, drug and imaging-agent loading, release kinetics and in vivo behavior, along with evidence of manufacturing robustness and batch consistency. When imaging and therapy are combined, devices may fall under combination product regulations, requiring coordination across drug and device branches[56]. Clinical trial design must demonstrate not only safety and imaging feasibility but also meaningful metabolic benefit beyond the standard of care. For example, a theranostic browning platform would need to show durable improvements in weight, insulin sensitivity or NAFLD compared with lifestyle intervention plus conventional pharmacotherapy, and ideally reductions in hard outcomes such as incident diabetes or cardiovascular events[57].

Economic and equity aspects are particularly salient. Nanotheranostics often require specialized imaging infrastructure (MRI, PET, NIR systems) and sophisticated manufacturing, which may limit availability to large tertiary centers and high-income settings[58]. Since obesity disproportionately affects disadvantaged populations, ensuring that advanced nanotheranostic interventions do not exacerbate health disparities is an ethical imperative. Strategies to simplify designs, reduce cost, leverage widely available imaging modalities (such as ultrasound) and integrate with public health approaches will be essential for broad impact.

Finally, there are communication and perception challenges. Patients and clinicians may be unfamiliar with nanotheranostics, and the concept of "burning fat with nanoparticles and lasers" may elicit both enthusiasm and concern. Transparent, evidence-based explanations of benefits, risks and alternatives will be needed to support informed decision making and trust.

7. Future Directions: Precision, Multi-Modal and Personalized Nanotheranostics in Obesity

Looking forward, nanotheranostics in obesity are likely to evolve along three intersecting axes: precision targeting of key cell populations and depots, multi-modal integration of imaging and therapy and personalization based on individual metabolic and inflammatory profiles[26].

Advances in single-cell and spatial omics are revealing previously unrecognized adipocyte subsets, ATM phenotypes and stromal niches that differentially contribute to metabolic dysfunction. Ligands that selectively bind pro-inflammatory ATMs, fibrotic stromal cells or beige adipocyte precursors could make adipose nanotheranostics more precise, reducing collateral effects and enabling depot-specific modulation (for example, visceral versus subcutaneous WAT)[12, 13].

Multi-modal platforms will likely combine several imaging and therapeutic capabilities. For instance, a single nanoparticle might integrate MRI contrast, NIR fluorescence, photothermal functionality and drug or RNA cargos, allowing both high-resolution structural imaging and functional monitoring of thermogenesis or inflammation[59]. In metabolic contexts, pairing imaging of BAT activation and WAT browning with simultaneous delivery of thermogenic inducers could support closed-loop adjustments in dosing and energy delivery to reach desired thermogenic responses without overshooting[59].

Personalized nanotheranostics will draw on clinical, genetic and microbiome data. Individuals differ markedly in fat distribution, BAT activity, inflammatory tone and gut microbiota, all of which influence obesity risk and treatment response. Combining baseline imaging of adipose depots (for example, PET–CT for BAT, MRI for visceral fat) with nanotheranostic readouts of depot accessibility and inflammatory state could help tailor therapeutic strategies, prioritizing adipose-targeted browning in some patients and liver- or vascular-focused approaches in others[59].

Integration with digital health ecosystems offers additional leverage. Continuous or frequent data streams from wearable devices, glucose monitors and emerging metabolic biosensors can be merged with nanotheranostic imaging to understand how interventions interact with real-world behaviors. Over time, machine learning models might predict which patients are most likely to benefit from specific theranostic platforms, optimizing patient selection and cost-effectiveness.

Emerging technologies such as exosome–liposome hybrid carriers, cell membrane–camouflaged nanoparticles and gene-editing nanotheranostics add further possibilities. For example, biomimetic theranostic particles derived from adipose or immune cell membranes could exploit natural homing properties to selectively target diseased depots, while CRISPR-based cargos might offer durable correction of obesity-related gene networks. These powerful tools will require particularly careful ethical and safety scrutiny, given the long-term consequences of altering metabolic circuits[50, 60].

Ultimately, nanotheranostics should be viewed as adjuncts rather than replacements for lifestyle, pharmacologic and policy interventions. Their greatest value may lie in treating severe or refractory obesity, high-risk metabolic phenotypes and monogenic or hypothalamic forms of disease, where targeted imaging-guided therapy can meaningfully alter trajectories. If developed thoughtfully, with attention to safety, equity and integration into broader care pathways, nanotheranostics could become a key component of precision metabolic medicine.

CONCLUSION

Nanotheranostics bring together nanoscale imaging and therapy in a single platform, offering a powerful toolkit to tackle the spatially complex, multi-organ nature of obesity and metabolic disorders. By enabling depot- and cell-specific delivery to adipose tissue, liver and vasculature while simultaneously visualizing nanoparticle distribution and biological response, these dual-function systems can support more precise and adaptive interventions than conventional systemic therapies. Early preclinical work demonstrates that adipose-targeted photothermal, photodynamic and anti-inflammatory nanotheranostics can induce WAT browning, resolve inflammation and improve metabolic outcomes, and that multi-organ platforms can address NAFLD and vascular complications. Significant hurdles remain in terms of long-term safety, targeting specificity, regulatory approval, cost and equitable access. As nanotechnology, imaging science and metabolic biology continue to converge, carefully designed and validated nanotheranostic platforms may play an important future role in personalized, imaging-guided obesity treatment and metabolic risk reduction.

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