Nanoplatforms for Anxiety Therapy: A Review of Cellular, Animal, and Clinical Studies

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Abstract: Anxiety disorders are among the most prevalent psychiatric conditions, imposing substantial individual and societal burdens. Their pathogenesis involves a complex interplay of neurobiological alterations, including neurotransmitter imbalances, neuroinflammation, hypothalamic–pituitary–adrenal (HPA) axis dysregulation, and oxidative stress. Despite the availability of anxiolytic medications, limitations such as delayed onset of action, suboptimal efficacy, and significant side effects underscore the need for novel therapeutic strategies. Nanoparticles, as advanced drug delivery systems capable of crossing the blood–brain barrier and selectively targeting neural networks, offer promising avenues for the treatment of anxiety disorders. This review aims to examine the therapeutic applications of nanoparticles in anxiety and to elucidate the underlying neurobiological mechanisms. A narrative-analytical review was conducted through a systematic search of PubMed, Scopus, and Web of Science databases from 2010 to 2025. Key terms were selected based on Medical Subject Headings (MeSH) and included "anxiety," "nanoparticles," "targeted drug delivery," "neuroinflammation," and "blood–brain barrier." Eligible studies encompassed preclinical research, animal models, and relevant review articles. Data were extracted qualitatively and thematically analyzed. Evidence indicates that nanocarriers such as chitosan, poly (lactic-co-glycolic acid) (PLGA), zinc oxide nanoparticles, and brain-targeted formulations can enhance blood–brain barrier penetration, improve bioavailability, and attenuate oxidative stress, thereby reducing anxiety-like behaviors and improving cognitive function. Conversely, exposure to certain nanoparticles including silica, polystyrene, silver nanoparticles, and specific inorganic particles has been associated with mitochondrial dysfunction, neuroinflammation, gut–brain axis dysregulation, and hippocampal injury, potentially exacerbating anxiety- and depression-like behaviors. These findings underscore the critical influence of nanoparticle type, dose, size, and surface properties on their biological effects. Nanoparticles and nanocarrier-based drug delivery systems hold significant potential to advance targeted therapy for anxiety disorders through modulation of neuroendocrine pathways, reduction of neuroinflammation, and enhancement of cognitive performance. Nevertheless, concerns regarding potential neurotoxicity and long-term effects highlight the necessity for rigorous preclinical evaluation and standardized clinical trials to ensure safety and therapeutic efficacy.

Keywords: Anxiety, Nanoparticles, Blood–Brain Barrier; Neuroinflammation; Oxidative Stress, Gut–Brain Axis

Nanoplataformas para o Tratamento da Ansiedade: Uma Revisão de Estudos Celulares, em Modelos Animais e Clínicos

Resumo: Os transtornos de ansiedade figuram entre as doenças psiquiátricas mais prevalentes, representando um importante ônus para os indivíduos e para a sociedade. Sua fisiopatologia envolve uma interação complexa de alterações neurobiológicas, incluindo desequilíbrios de neurotransmissores, neuroinflamação, desregulação do eixo hipotálamo–hipófise–adrenal (HHA) e estresse oxidativo. Apesar da disponibilidade de medicamentos ansiolíticos, limitações como o início tardio da ação terapêutica, eficácia limitada e efeitos adversos significativos evidenciam a necessidade de novas estratégias terapêuticas. Nesse contexto, as nanopartículas, como sistemas avançados de liberação de fármacos capazes de atravessar a barreira hematoencefálica e direcionar seletivamente agentes terapêuticos para redes neurais específicas, representam uma abordagem promissora para o tratamento dos transtornos de ansiedade. O presente artigo teve como objetivo revisar as aplicações terapêuticas das nanopartículas no tratamento da ansiedade e esclarecer os mecanismos neurobiológicos envolvidos. Foi realizada uma revisão narrativa de caráter analítico, baseada em uma busca sistemática nas bases de dados PubMed, Scopus e Web of Science, abrangendo publicações de 2010 a 2025. Os descritores foram selecionados de acordo com os Medical Subject Headings (MeSH) e incluíram os termos *"anxiety"*, *"nanoparticles"*, *"targeted drug delivery"*, *"neuroinflammation"* e *"blood–brain barrier"*. Foram incluídos estudos pré-clínicos, pesquisas em modelos animais e artigos de revisão relevantes. Os dados foram extraídos de forma qualitativa e submetidos à análise temática. As evidências disponíveis demonstram que nanocarreadores, como quitosana, poli (ácido lático-co-glicólico) (PLGA), nanopartículas de óxido de zinco e formulações direcionadas ao cérebro, são capazes de aumentar a permeabilidade através da barreira hematoencefálica, melhorar a biodisponibilidade dos fármacos e reduzir o estresse oxidativo, resultando na diminuição de comportamentos do tipo ansioso e na melhora da função cognitiva. Em contrapartida, a exposição a determinadas nanopartículas, incluindo sílica, poliestireno, nanopartículas de prata e algumas partículas inorgânicas específicas, tem sido associada à disfunção mitocondrial, neuroinflamação, desregulação do eixo intestino–cérebro e lesões hipocampais, podendo agravar comportamentos semelhantes à ansiedade e à depressão. Esses achados demonstram que os efeitos biológicos das nanopartículas dependem fortemente de suas características físico-químicas, como tipo, dose, tamanho e propriedades de superfície. Os sistemas de liberação de fármacos baseados em nanopartículas e nanocarreadores apresentam elevado potencial para aprimorar terapias direcionadas aos transtornos de ansiedade por meio da modulação de vias neuroendócrinas, redução da neuroinflamação e melhora do desempenho cognitivo. Entretanto, as preocupações relacionadas à possível neurotoxicidade e aos efeitos em longo prazo ressaltam a necessidade de estudos pré-clínicos rigorosos e de ensaios clínicos padronizados para confirmar sua segurança e eficácia terapêutica.

Palavras-chave: Ansiedade; Nanopartículas; Barreira Hematoencefálica; Neuroinflamação; Estresse Oxidativo; Eixo Intestino–Cérebro

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Introduction

Anxiety is one of the most prevalent psychological challenges in healthcare settings, and supportive as well as non-pharmacological interventions may play an important role in reducing anxiety and improving mental health outcomes among patients and healthcare professionals (TALEBIAZAR ET AL., 2025; ANAMAGH ET AL., 2024; TALEBIAZAR ET AL., 2024; TALEBIAZAR ET AL., 2022; LAGZI ET AL., 2023; ANAMAGH ET AL., 2024).

Anxiety disorders are among the most prevalent psychiatric conditions worldwide and are characterized by persistent feelings of fear, excessive worry, tension, and heightened autonomic arousal (SZUHANY & SIMON, 2022). This group of disorders encompasses a broad spectrum of conditions, including generalized anxiety disorder, panic disorder, specific phobias, social anxiety disorder, and post-traumatic stress disorder, collectively affecting millions of individuals across the globe (SZUHANY & SIMON, 2022). The rising prevalence of anxiety disorders has been attributed to a combination of psychological stressors, lifestyle changes, genetic susceptibility, environmental influences, and dysregulation of central nervous system function (KESSLER ET AL., 2009).

Chronic anxiety can substantially impair cognitive performance, reduce quality of life, disrupt sleep patterns, increase the risk of cardiovascular diseases, and negatively affect overall mental well-being (PINE & KLEIN, 2008). Consequently, the development of safe and effective therapeutic strategies for the management of anxiety disorders remains a major clinical and public health priority (PINE & KLEIN, 2008).

The pathogenesis of anxiety disorders is highly complex and multifactorial, involving intricate neurochemical, neuroendocrine, and inflammatory mechanisms (SCHIELE & DOMSCHKE, 2018). Dysregulation of key neurotransmitter systems, including serotonin, dopamine, gamma-aminobutyric acid (GABA), and norepinephrine, plays a central role in the

development and maintenance of anxiety-related symptoms (BINDER, 2009).

In addition, activation of the hypothalamic–pituitary–adrenal (HPA) axis, excessive cortisol secretion, neuroinflammation, and oxidative stress have been recognized as critical contributors to anxiety pathophysiology (SCHIELE & DOMSCHKE, 2018; BINDER, 2009). Recent evidence suggests that increased production of reactive oxygen species (ROS) and elevated levels of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6), may contribute to neuronal damage, synaptic dysfunction, and behavioral abnormalities associated with anxiety disorders (SCHIELE & DOMSCHKE, 2018; BINDER, 2009).

These observations indicate that anxiety disorders are not solely psychological in origin but are also driven by a wide range of molecular and cellular alterations within the central nervous system. Current pharmacological management of anxiety disorders primarily relies on benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), and other anxiolytic agents (BANDELOW ET AL., 2017). Although these medications can effectively alleviate symptoms in many patients, their clinical utility is often limited by poor bioavailability, inadequate penetration across the blood–brain barrier (BBB), delayed therapeutic onset, long-term treatment requirements, and a variety of adverse effects, including sedation, cognitive impairment, drug dependence, and tolerance development (BANDELOW ET AL., 2015).

Furthermore, the nonspecific systemic distribution of many psychotropic drugs may contribute to unwanted off-target effects. Therefore, the development of advanced drug delivery systems capable of selectively transporting therapeutic agents to the brain has become an important objective in neuropsychiatric research (BANDELOW ET AL., 2015).

In recent years, nanotechnology has emerged as one of the most promising innovations in biomedical science (HEYDARI et al., 2026; SEPORD EH SEYDANI et al., 2026), offering new opportunities for the treatment of neurological and psychiatric disorders (JINTA ET AL., 2026). Owing to their nanoscale dimensions, large surface-area-to-volume ratio, tunable physicochemical properties, and ability to cross biological barriers, nanoparticles have attracted considerable attention as next-generation

therapeutic platforms (TORABI ET AL., 2013).

One of their most significant advantages is the ability to facilitate drug transport across the blood–brain barrier and deliver therapeutic compounds directly to targeted regions of the central nervous system, thereby overcoming a major limitation of conventional therapies. Nanoparticle-based systems can also enhance drug stability, improve solubility, enable controlled release, and reduce premature degradation during systemic circulation (CEÑA & JÁTIVA, 2018).

A diverse range of nanoparticle formulations, including polymeric nanoparticles, lipid-based nanoparticles, metallic nanoparticles, liposomes, nanoemulsions, dendrimers, and polysaccharide-based nanocarriers, has been investigated for the treatment of anxiety disorders (UPADHYAY, 2014). Studies have demonstrated that these platforms can improve the brain delivery of anxiolytic drugs, antioxidant compounds, neuroprotective agents, and plant-derived bioactive molecules (SHARMA ET AL., 2024).

Moreover, certain nanoparticles may exert therapeutic effects by attenuating neuroinflammation, reducing oxidative stress, regulating neurotransmitter activity, and enhancing neuroplasticity. Emerging applications involving small RNA delivery, gene therapy, and molecularly targeted interventions have further expanded the potential of nanotechnology in the management of anxiety disorders (SINGH ET AL., 2025).

Despite these promising advantages, the application of nanoparticles in neuropsychiatric medicine is accompanied by several challenges and safety concerns (YADAV ET AL., 2025). Potential nanoparticle-induced toxicity, accumulation within neural tissues, unintended immune activation, alterations in neuronal function, and uncertainties regarding long-term safety remain important limitations of this technology (YADAV ET AL., 2025). Certain metallic nanoparticles, in particular, have been reported to induce oxidative stress and neuronal injury under specific conditions. Furthermore, the complexity of the blood–brain barrier, pharmacokinetic constraints, and difficulties associated with formulation standardization continue to hinder clinical translation. Therefore, comprehensive assessments of biocompatibility, toxicity, and long-term safety are essential before widespread clinical implementation can be achieved (REHMAN ET AL., 2020).

Given the rapid growth of research at the intersection of nanomedicine and anxiety disorders, a comprehensive evaluation of current evidence is warranted. Although numerous studies have explored the therapeutic applications of nanoparticles in neurological diseases, information specifically addressing their role in anxiety disorders remains fragmented. Therefore, the present review aims to critically examine the therapeutic potential of nanoparticles in anxiety disorders, with particular emphasis on targeted drug delivery strategies, underlying neurobiological mechanisms, therapeutic benefits, safety considerations, and future clinical prospects.

Materials and Methods

Study Design

This study was conducted as a narrative and analytical review aimed at evaluating the therapeutic applications of nanoparticles in anxiety disorders and highlighting recent advances in nanomedicine and innovative neuropharmaceutical drug delivery systems. To identify relevant evidence, a comprehensive literature search was performed across several major scientific databases, including ISC, SID, PubMed, Scopus, and Web of Science. Publications published between January 2010 and March 2025 were screened to capture the most recent developments concerning nanoparticle-based interventions for anxiety disorders.

Search Strategy

The search strategy was developed using a combination of specialized keywords and Boolean operators. The primary search terms included *"Anxiety," "Anxiety Disorders," "Nanoparticles," "Nanomedicine," "Neuroinflammation," "Blood–Brain Barrier," "Nanocarriers,"* and *"Neuroprotective Nanoparticles."* Various combinations of these keywords were employed using the Boolean operators AND and OR to maximize the retrieval of relevant studies.

A representative search query was as follows:

(Anxiety OR Anxiety Disorders) AND (Nanoparticles OR Nanocarriers OR Nanomedicine) AND (Drug Delivery OR Targeted Therapy OR Neuroinflammation).

Eligibility Criteria

Original research articles, review papers, preclinical investigations, animal studies, in vitro experiments, and reports addressing the therapeutic application of nanoparticles in anxiety disorders were considered eligible for inclusion.

Studies were included if they met the following criteria: publication in English, availability of the full-text article, direct relevance to the therapeutic applications of nanoparticles in anxiety disorders, and evaluation of nanoparticle mechanisms of action, central nervous system (CNS) drug delivery strategies, neuroprotective properties, or anti-inflammatory effects.

Studies were excluded if they focused exclusively on nanoparticle toxicity without relevance to anxiety treatment, were unrelated to anxiety disorders or neuropsychiatric applications, consisted solely of conference abstracts, editorials, letters to the editor, or non-peer-reviewed reports, or lacked sufficient scientific evidence or methodological rigor.

Study Selection and Data Extraction

Following the initial search, all retrieved records underwent a structured screening process. Titles and abstracts were first reviewed to assess relevance, and duplicate publications were removed. Subsequently, the full texts of potentially eligible studies were carefully examined.

Data extraction was conducted independently using a standardized data collection form. The extracted information included the first author's name, year of publication, study design, animal or cellular model, nanoparticle type, route of administration, proposed mechanism of action, therapeutic targets, anxiolytic effects, principal findings, and reported limitations.

Quality Assessment and Data Synthesis

To enhance the scientific rigor of the review, all selected studies were critically evaluated with respect to methodological quality, study design, sample size, data reliability, and relevance to the objectives of the review. The extracted evidence was organized using both descriptive and analytical approaches.

Findings were categorized according to nanoparticle type, neuroprotective mechanisms, anti-inflammatory properties, blood–brain barrier penetration capabilities, drug delivery strategies, and therapeutic applications. Particular attention was given to the ability of nanocarriers to improve central nervous system targeting, modulate neuroinflammatory pathways, reduce oxidative stress, and enhance therapeutic efficacy in anxiety-related conditions.

In addition, the advantages, limitations, safety concerns, translational challenges, and future perspectives of nanoparticle-based therapies for anxiety disorders were systematically analyzed to provide a comprehensive overview of the

current state of research and potential directions for clinical development.

Results

Collectively, the reviewed preclinical and animal studies indicate that nanoparticles exert complex and bidirectional effects on the nervous system and anxiety-related behaviors, with outcomes largely dependent on nanoparticle composition, physicochemical properties, administered dose, and route of exposure. Evidence from the included studies suggests that nanoparticle-based interventions can function either as therapeutic agents with anxiolytic and neuroprotective properties or as potential neurotoxic factors capable of exacerbating anxiety-like symptoms.

On the therapeutic side, several nanoparticle formulations including zinc oxide (ZnO) nanoparticles, iron oxide (Fe_2O_3) nanoparticles, chitosan-based nanocarriers, poly(lactic-co-glycolic acid) (PLGA) nanoparticles, and peptide- or phytochemical-loaded nanosystems demonstrated significant beneficial effects in experimental models of anxiety. These nanoplatforms enhanced drug transport across the blood–brain barrier, improved bioavailability, facilitated targeted neural delivery, and promoted sustained release of therapeutic compounds. Furthermore, many of these formulations were associated with reduced oxidative stress, attenuation of neuroinflammatory responses, modulation of neurotransmitter systems, and improvement of cognitive and behavioral outcomes, ultimately resulting in decreased anxiety-like behavior and enhanced neuroprotection.

In contrast, several engineered and environmentally derived nanoparticles including nanoplastics, silicon dioxide (SiO_2) nanoparticles, copper oxide (CuO) nanoparticles, and rare-earth element nanoparticles were reported to induce adverse neurological effects. These nanoparticles have been associated with neuroinflammation, mitochondrial dysfunction, disruption of gut–brain axis homeostasis, increased oxidative stress, and activation of cellular pathways involved in neuronal injury. Such alterations frequently translated into behavioral abnormalities characterized by heightened anxiety-like responses, cognitive impairment, and various manifestations of neurotoxicity.

Taken together, the available evidence highlights the dual role of nanotechnology in anxiety disorders. While nanoparticle-based platforms represent promising tools for targeted drug delivery and neurotherapeutic interventions, certain nanoparticle formulations may also pose

potential neurological risks. Therefore, alongside the continued development of brain-targeted nanocarriers for the treatment of neuropsychiatric disorders, comprehensive evaluation of nanoparticle safety, dose–response relationships, biodistribution, and long-term neurological effects remains essential.

Detailed characteristics, experimental models, molecular mechanisms, therapeutic targets, and principal outcomes of the included studies are summarized in Table 1.

Table 1. Preclinical Studies Investigating the Effects of Nanoparticles on Anxiety-Related Behaviors, Neurobiological Mechanisms, and Therapeutic Outcomes

Study	Animal Model / Design	Nanoparticle Type / Intervention	Target / Route of Administration	Key Findings	Overall Effect	Conclusion
TORABI ET AL., 2013	Wistar rat	ZnO NPs vs. bulk ZnO	Intraperitoneal (i.p.), Elevated Plus Maze (EPM)	↑ OAT%, altered pH, increased serum Zn levels	Anxiolytic (NPs > bulk ZnO)	Dose-dependent anxiolytic effect
VINZANT ET AL., 2017	Rat	Fe_2O_3 NPs + ASV-30	i.p., BBB targeting	Crossed the blood–brain barrier (BBB), bound to CRF2 receptors	Anxiolytic	Enhanced peptide delivery to the brain
LIN ET AL., 2021	Mouse	Rare-earth nanoparticles	Chronic exposure	↓ ATPase activity, behavioral impairments	Neurotoxic	Induced anxiety- and depression-like behaviors
MA ET AL., 2024	Mouse	Polystyrene nanoparticles (PS-NPs)	Oral administration	Neuronal mitochondrial	Neurotoxic	Promoted anxiety- and depression-

				dysfunction		like phenotypes
BARI ET AL., 2015	Rat	Chitosan–buspirone nanoparticles	Intranasal	↑ Brain drug concentration	Strong anxiolytic effect	Effective nose-to-brain delivery system
GONG ET AL., 2024	Mouse	SiO_2 nanoparticles	12-week exposure	Gut–brain axis dysbiosis	Neurotoxic	Anxiety associated with microbiota alterations
HUBBARD ET AL., 2018	Rat	PLGA-loaded dexamethasone (PLGA-Dexa)	Blast injury model	↓ BBB damage, ↓ anxiety-like behavior	Neuroprotective	Reduced brain injury–associated anxiety
LI ET AL., 2017	Zebrafish	SiO_2 nanoparticles	Environmental exposure	↓ Locomotor activity, ↑ depression-like behavior	Neurotoxic	Reserpine-like neurobehavioral effects

HAFEZ & GAD, 2018	Rat	ZnO nanoparticles	Oral administration	↓ Oxidative stress	Neuroprotective	Improved memory and reduced anxiety
CHEN ET AL., 2023	Mouse	Polystyrene micro-/nanoplastics	Oral administration (60 days)	Gut microbiota dysbiosis	Neurotoxic	Gut–brain axis-mediated behavioral impairment
TORABI ET AL., 2013	Female rat	ZnO nanoparticles	i.p., electrocardiographic assessment	Improved ECG parameters and anxiolytic activity	Anxiolytic and cardioprotective	Systemic beneficial effects
SOLAS ET AL., 2018	Mouse	PEGylated nimodipine nanoparticles	Oral administration	↑ Bioavailability	Cognitive enhancement	Limited effect on anxiety outcomes
NAGPAL ET AL., 2013	Mouse	Gallic acid nanoparticles	Brain-targeted delivery	↑ Brain uptake	Anxiolytic	Demonstrated the value of targeted drug delivery

KESMATI ET AL., 2019	Rat	MgO nanoparticles	i.p. combined with exercise	↑ OAT%	Mild anxiolytic effect	Limited synergistic effect with exercise
KESMATI & KHORSHIDI, 2014	Rat	Fe_2O_3 nanoparticles	Intraperitoneal administration	Analgesic and anxiolytic activities	Anxiolytic	Dual therapeutic action
DALFARDI ET AL., 2020	Rat	Silver nanoparticles (AgNPs)	Oral administration	↑ Hippocampal damage	Neurotoxic	Royal jelly exerted protective effects against toxicity
KHODADADI ET AL., 2024	Rat	Crocin-loaded chitosan nanoparticles	Stress model	↑ BBB integrity	Neuroprotective	Anxiolytic and cognitive-enhancing properties
SHARMA ET AL., 2023	Mouse	Polystyrene nanoparticles (PS-NPs)	Oral administration	↓ Expression of neurotransmitter-related genes	Neurotoxic	Oxidative stress-mediated neurotoxicity

MAHMOUD ET AL., 2023	Mouse	Quercetin nanoparticles	Intranasal administration	↑ Anxiolytic efficacy	Anxiolytic	Efficient nose-to-brain delivery
SACHDEVA ET AL., 2021	In vitro	Gold nanoparticles (AuNPs)	Biosensor platform	Detection of clonazepam	Diagnostic application	Potential forensic and analytical utility

The findings of the reviewed studies indicate that the effects of nanoparticles on anxiety-related behaviors are highly dependent on nanoparticle composition, size, dosage, and duration of exposure. While several nanoparticle formulations, including zinc oxide nanoparticles (ZnO NPs), chitosan–buspirone nanocarriers, quercetin-loaded nanoparticles, and crocin-based nanosystems, demonstrated significant anxiolytic and neuroprotective effects, environmental nanoparticles such as polystyrene nanoplastics, silica nanoparticles, and rare-earth nanoparticles were predominantly associated with neurotoxicity and increased anxiety-like behaviors.

A substantial proportion of the beneficial effects observed in therapeutic nanoplatforms can be attributed to their ability to enhance drug transport across the blood–brain barrier (BBB) and improve targeted delivery to the central nervous system. Studies conducted by Bari et al. and Mahmoud et al. demonstrated that intranasal nose-to-brain delivery systems significantly increased drug concentrations within neural tissues, thereby enhancing therapeutic efficacy and producing more pronounced anxiolytic effects. These findings highlight the potential of nanoparticle-mediated drug delivery strategies to overcome one of the major limitations of conventional pharmacotherapy for anxiety disorders.

The adverse effects of certain nanoparticles were primarily associated with oxidative stress, mitochondrial dysfunction, impaired neurotransmitter signaling, neuronal injury, and disruption of gut–brain axis homeostasis. Several studies reported reductions in the expression of neurotransmitter-related genes, increased production of reactive oxygen species, and alterations in intestinal microbial composition following chronic nanoparticle exposure. Collectively, these pathological changes contributed to the development of anxiety-like and depressive-like behaviors in experimental models.

In addition, multiple investigations demonstrated the neuroprotective potential of nanoparticle-based formulations in mitigating neural damage. Nanocarriers loaded with dexamethasone, crocin, and selected metal oxide nanoparticles were shown to reduce neuroinflammation, preserve blood–brain barrier integrity, attenuate oxidative stress, and improve cognitive performance. These protective effects were frequently accompanied by reductions in anxiety-related behavioral abnormalities.

Overall, the available preclinical evidence suggests that nanotechnology represents a promising strategy for improving the treatment of anxiety disorders and enhancing the therapeutic efficacy of neuropsychiatric medications. However, the growing body of evidence documenting the neurotoxic effects of certain nanoparticles underscores the importance of comprehensive safety assessments, careful dose optimization, and long-term toxicological investigations before widespread clinical implementation can be considered.

Discussion

Anxiety disorders are among the most prevalent psychiatric conditions worldwide and continue to pose substantial therapeutic challenges because of their complex and multifactorial pathophysiology (SZUHANY & SIMON, 2022). Growing evidence indicates that, beyond alterations in classical neurotransmitter systems such as serotonin, dopamine, and γ-aminobutyric acid (GABA), additional mechanisms including neuroinflammation, oxidative stress, mitochondrial dysfunction, and dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis play critical roles in the development and persistence of anxiety disorders. The findings of the present review suggest that nanoparticle-based drug delivery platforms may provide a novel multidimensional therapeutic strategy by simultaneously targeting several of these interconnected pathological pathways (SZUHANY & SIMON, 2022).

One of the most significant advantages of nanocarrier systems is their ability to overcome the blood–brain barrier (BBB), which remains one of the principal obstacles limiting the effective delivery of psychotropic agents to the central nervous system (MULVIHILL ET AL., 2020). The studies reviewed herein demonstrated that chitosan-based nanoparticles, poly (lactic-co-glycolic acid) (PLGA) nanoparticles, and other brain-targeted nanosystems can enhance drug transport into neural tissues, thereby improving bioavailability and therapeutic efficacy (LI ET AL., 2017).

Enhanced brain delivery may also permit dose reduction while maintaining clinical effectiveness, potentially minimizing systemic adverse effects and improving long-term treatment tolerability in patients with anxiety disorders.

Preclinical investigations further indicate that several nanomaterials possess intrinsic neuroprotective properties independent of their drug-carrying function (SANAD ET AL., 2023).

Reduction of reactive oxygen species (ROS) generation, attenuation of neuroinflammatory responses, and preservation of mitochondrial function represent key mechanisms through which these nanoplatforms may alleviate anxiety-like behaviors (ESTEVEZ ET AL., 2011). In particular, nanoformulations containing antioxidant or anti-inflammatory compounds have been shown to reduce inflammatory cytokine production and protect vulnerable brain regions, including the hippocampus and amygdala, from neuronal injury in experimental models (ESTEVEZ ET AL., 2011). These findings suggest that nanoplatforms may function not merely as passive drug carriers but also as active modulators of neurobiological processes implicated in anxiety pathogenesis (SHARMA ET AL., 2024).

A major finding of this review is the dual nature of nanoparticle effects on the nervous system. While certain nanoparticles exhibit therapeutic and neuroprotective properties, others may induce adverse neurological outcomes (SIMKÓ & MATTSSON, 2010). Silver nanoparticles, silica nanoparticles, polystyrene nanoplastics, and several inorganic nanomaterials have been associated with increased oxidative stress, neuroinflammation, mitochondrial impairment, and disruption of blood–brain barrier integrity, all of which may contribute to the exacerbation of anxiety-like behaviors (TRIPATHY ET AL., 2025). These observations underscore the importance of rigorous neurotoxicity assessment and highlight the fact that the biological effects of nanoparticles are strongly influenced by their physicochemical characteristics, including size, morphology, surface charge, chemical composition, and administered dose (MOHAMMADIPOUR & ABUDAYYAK, 2022).

Another emerging area of interest involves the interaction between nanoparticles and the gut–brain axis (DIAO ET AL., 2021). Accumulating evidence suggests that certain nanoparticles can alter gut microbial composition and function, thereby influencing neural, immune, and endocrine pathways involved in emotional regulation. Because gut dysbiosis has been linked to systemic inflammation, cognitive dysfunction, and mood disorders, understanding the impact of nanoparticles on gut–brain communication may provide important insights into both their therapeutic potential and toxicological consequences (TORABI ET AL., 2013).

Nanotechnology also aligns closely with the principles of precision medicine and personalized therapeutics. Given the substantial biological and clinical heterogeneity observed among anxiety disorders, the development of nanocarriers capable of selectively targeting patient-specific molecular pathways may significantly enhance treatment outcomes. In the future, integrating nanoplatforms with biomarker-guided approaches, molecular imaging technologies, and smart stimulus-responsive drug delivery systems may facilitate the development of highly individualized therapeutic strategies for anxiety disorders (DAS, 2023).

Despite these promising advances, the translation of anti-anxiety nanoplatforms from experimental research to routine clinical practice remains challenging. Most available evidence is derived from in vitro and animal studies, whereas human data regarding long-term safety, pharmacokinetics, biodistribution, and pharmacodynamics remain limited. Furthermore, concerns persist regarding nanoparticle accumulation within neural tissues, the possibility of chronic neurotoxicity, and unforeseen effects on normal brain function. Addressing these issues will require comprehensive toxicological investigations, standardized characterization protocols, and well-designed clinical trials before widespread clinical implementation can be achieved.

Conclusion

In summary, current evidence indicates that nanoparticle-based drug delivery systems hold considerable promise for improving the treatment of anxiety disorders. By enhancing drug transport across the blood–brain barrier, modulating neuroinflammatory pathways, reducing oxidative stress, and supporting neuronal function, these platforms have the potential to substantially improve therapeutic efficacy while reducing the limitations associated with conventional pharmacotherapy. Nevertheless, successful clinical translation will depend on the development of safer and more biocompatible nanocarriers, standardization of manufacturing processes, and the completion of large-scale clinical studies evaluating long-term efficacy and safety. Continued advances in nanotechnology, neuroscience, and precision medicine are expected to pave the way for more targeted, effective, and personalized interventions for patients with anxiety disorders in the coming years.

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