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Nanotechnology-Driven Microencapsulation for Enhancing Bioavailability of Anxiolytics

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ABSTRACT

Anxiety disorders are among the most common mental diseases, affecting everyday functioning and general well-being. Conventional therapies, such as benzodiazepines and selective serotonin reuptake inhibitors (SSRIs), are frequently limited by low bioavailability, significant first-pass metabolism, and negative side effects. This review investigates the use of nanotechnology-mediated microencapsulation methods to enhance the therapeutic effectiveness of anxiolytic medicines. Advanced nanocarrier systems, such as polymeric nanoparticles, liposomes, solid lipid nanoparticles, and nanoemulsions, provide potential approaches to improving medication solubility, stability, and targeted administration across the blood-brain barrier (BBB). These systems also allow for continuous and regulated medication release, lowering dose frequency and decreasing systemic toxicity. Nanotechnology, by addressing critical limitations of current pharmacotherapy, opens the door to more effective and safer therapies for anxiety disorders. This review emphasizes the revolutionary potential of these new medication delivery systems in transforming anxiety therapy while overcoming the key disadvantages of old techniques.

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1. INTRODUCTION:

Among psychiatric disorders, anxiety disorders are the most frequently encountered. Anxiety manifests as a sense of concern, agitation, or discomfort related to uncertain outcomes. Although it serves as a typical response to stress, it can become overwhelming and enduring, negatively impacting

one's daily functioning. Among various anxiety disorders, specific phobias are the most prevalent, affecting 10.3% of individuals. Next in line is panic disorder, with or without agoraphobia, which has a prevalence of 6.0%. Social phobia is observed in 2.7% of the population, while generalized anxiety disorder is noted at a prevalence of 2.2%¹. The management of anxiety is vital due to its commonality and considerable repercussions on mental and physical well-being. Anxiety disorders can hinder daily activities, impacting productivity at work, personal relationships, and overall health. Neurochemically, anxiety is related to imbalances in neurotransmitters, including serotonin, GABA, norepinephrine, and dopamine, which underscores the need for pharmacological interventions to achieve balance. If not addressed, anxiety can lead to severe outcomes, including depression, heart disease, and cognitive dysfunction².

Conventional drug delivery approaches for anxiety management often lead to fluctuations in drug concentrations within the bloodstream, potentially compromising therapeutic efficacy. These variations arise from the failure to account for individual differences in drug metabolism and patient responses³. Medications such as benzodiazepines and selective serotonin reuptake inhibitors (SSRIs)⁴ face significant challenges, including low bioavailability, extensive first-pass metabolism, and a range of adverse effects. Nanotechnology presents a viable solution to address these challenges by improving the solubility, stability, and targeted delivery of drugs. Nanocarrier systems, including liposomes, polymeric nanoparticles, and solid lipid nanoparticles, enhance bioavailability and promote the transport of drugs across the blood-brain barrier (BBB), resulting in more effective and prolonged anxiety treatment⁵.

This review intends to delve into the application of nanotechnology in microencapsulation as a state-of-the-art technique aimed at improving the bioavailability and therapeutic efficacy of anxiolytic agents. It will provide a detailed discussion on a range of nanocarriers, their mechanisms for optimizing drug delivery, and their potential to significantly alter anxiety treatment paradigms, while also highlighting the limitations of conventional anxiolytic drugs.

2. ANXIOLYTIC DRUGS AND THEIR BIOAVAILABILITY CHALLENGES

The management of anxiety disorders frequently involves the use of anxiolytic drugs, which function by altering neurotransmitter activity in the central nervous system (CNS). These drugs can be divided into multiple classifications as shown in **table 1**.

Table 1: Anxiolytic drugs with their mechanism of action and bioavailability challenges.

S.No.	Drug	Example	Mechanism of action	Bioavailability Challenges	Reference
1.	Benzodiazepines	Diazepam, Alprazolam	Enhance GABAergic activity, leading to CNS depression.	Lipophilic nature and limited solubility in water at physiological pH, hydrolytic degradation once it is solubilized.	[6],[7]
2.	Selective Serotonin Reuptake Inhibitors (SSRIs)	Sertraline	Inhibit serotonin reuptake, increasing serotonin levels in the brain.	Poor water solubility, slow onset of action, GI disturbances	[8],[9]
3.	Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)	Venlafaxine	Inhibit reuptake of serotonin and norepinephrine.	Low permeability across the BBB, hepatic metabolism reduces drug levels	[10],[11]
4.	Herbal Anxiolytics	Lavender, Mimosa, Roseroot, Saffron	Modulate neurotransmitter activity through natural compounds.	Poor aqueous solubility, rapid metabolism, low bioavailability	[12][13]

3. Nanotechnology-Driven Microencapsulation: An Overview

Micro-encapsulation refers to a technique where minute particles or droplets are enveloped by a protective coating, resulting in the formation of small capsules. In its most basic definition, a microcapsule can be described as a small sphere encased in a consistent wall. The substance contained within the microcapsule is known as the core, internal phase, or fill, while the outer layer is often referred to as the shell, coating, or membrane as shown in **figure.01**. Most microcapsules have sizes ranging from a few micrometres to millimetres [14].

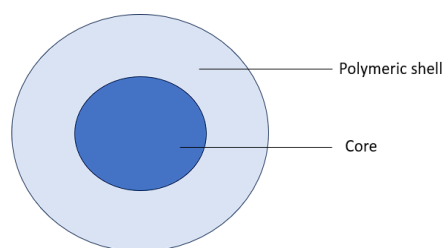


Figure 1. Microcapsule

3.1. TYPES OF MICROCAPSULES

The structure of microcapsules is primarily influenced by the type of core material and the method used to deposit the shell as shown in **figure.2**. Mononuclear (core-shell) microcapsules feature a single core surrounded by a shell. In contrast, polynuclear capsules consist of multiple cores encapsulated within the shell. Additionally, matrix encapsulation involves a uniform distribution of the core material throughout the shell material¹⁵.

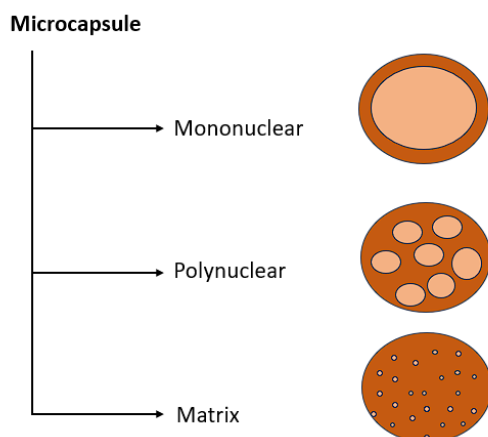


Figure 1. Types of microcapsules

3.2. IMPORTANCE OF MICROENCAPSULATION IN DRUG DELIVERY

- Enhanced shelf life is achieved by inhibiting degradative processes such as dehydration and oxidation.
- The active ingredients are delivered through a regulated and targeted approach.
- To diminish the toxicity, gastrointestinal irritation, and a range of major side effects related to the drugs.
- Protection from First-Pass Metabolism.
- Improved Blood-Brain Barrier (BBB) Penetration
- Improves solubility and absorption of poorly water-soluble drugs like SSRIs and herbal anxiolytics ^{[16][17]}.

3.3. ROLE OF NANOTECHNOLOGY IN MICROENCAPSULATION

In microencapsulation, nanotechnology is pivotal, providing accurate drug delivery systems, enhancing bioavailability, and increasing the overall efficacy of treatments.

Table 2: Role of nanotechnology in microencapsulation.

S.No.	Role	Description	Reference
1.	Enhancing Solubility & Bioavailability	Transforms drugs with low solubility into nano-sized formulations to enhance their absorption.	[18]
2.	Protecting from First-Pass Metabolism	Encapsulation inhibits swift hepatic breakdown, thereby elevating systemic concentrations of the drug.	[19]
3.	Facilitating Targeted Drug Delivery	Nanocarriers, such as liposomes and polymeric nanoparticles, enhance the ability to penetrate the blood-brain barrier, thereby facilitating targeted therapies for the central nervous system.	[20]
4.	Controlled & Sustained Release	Facilitates extended drug release, thereby decreasing the frequency of administration and lessening adverse effects.	[21]
5.	Improving Stability	Preserves vulnerable drugs from breakdown induced by enzymatic action, pH, or oxidation.	[22]

4. ADVANCED NANOTECHNOLOGY-BASED MICROENCAPSULATION STRATEGIES FOR ANXIOLYTIC DRUG DELIVERY

The advent of nanotechnology-based microencapsulation methods has transformed the delivery of anxiolytic medications by enhancing their solubility, bioavailability, and targeting to the brain. These innovative techniques address significant obstacles, including rapid metabolic breakdown, inadequate permeability, and first-pass metabolism, thereby facilitating sustained and controlled release of the drug, which ultimately leads to enhanced therapeutic effectiveness, **figure 3** shows different types of nanotechnology-based microencapsulation.

4.1. Polymeric Nanoparticles (PNPs)

Polymeric nanoparticles, known for their biodegradability and biocompatibility, act as carriers that ensure prolonged drug release and precise delivery to specific sites ^[23].

4.1.1. Polylactic-co-glycolic Acid (PLGA) Nanoparticles:

PLGA, a polymer known for its biocompatible and biodegradable properties, is created through the copolymerization of lactic acid (LA) and glycolic acid (GA). Its advantageous mechanical attributes, along with its non-toxic and biocompatible nature, make it a popular choice in various medical applications, including drug delivery systems for anxiety, gene therapy, and the development of medical fiber materials ^{[24][25]}.

Advantages in anxiety management:

- Improves the prolonged release of medication, thereby minimizing the frequency of administration ^[26].
- Increases drug stability, preventing enzymatic degradation ^[27].
- Suitable for encapsulating anxiolytics ^[28].

4.1.2. Chitosan-Based Nanoparticles:

Chitosan (CS) is a biopolymer characterized by its biodegradable, biocompatible, and non-toxic properties. It consists of β -1 $\rightarrow$ 4 linked residues of 2-amino-2-deoxy-glucopyranose and 2-acetamido-2-deoxy- β -D-glucopyranose. The preparation of CS involves the alkaline N-deacetylation of chitin, a biopolymer derived from the exoskeletons of

crustaceans like crabs and shrimp [29].

Advantages in anxiety management:

- It exhibits bio adhesive characteristics, significant permeation enhancement abilities for hydrophilic substances and a favourable safety profile regarding toxicity [30][31][32].
- Promotes the ability to cross the blood-brain barrier (BBB), thereby improving the delivery of drugs to the central nervous system (CNS) [33].
- Used for encapsulating anxiolytics [34].

4.2. Liposomes and Niosomes:

Lipid-based vesicular systems enhance the solubility, permeability, and targeting of drugs to the brain.

4.2.1. Liposomes:

Liposomes are spherical vesicles of colloidal size that are self-enclosed, characterized by a phospholipid bilayer that encapsulates a portion of the surrounding both hydrophilic and lipophilic drugs within their interior [35].

Advantages in anxiety management:

- Improves the solubility of pharmaceuticals, leading to better absorption within the body.
- Aids in the penetration of the blood-brain barrier, ensuring effective therapy directed at the central nervous system.
- Lowers the risk of drug toxicity by avoiding adverse effects on unintended targets [36][37].
- Used for encapsulating anxiolytics such as eugenol [38].

4.2.2. Niosomes:

Niosomes are tiny lamellar structures that resemble liposomes; however, they are made from non-ionic surfactants instead of phospholipids. Niosomes, similar to other vesicular drug delivery systems with bilayer structures, are capable of encapsulating and transporting both lipophilic and hydrophilic substances within the bilayer membrane and the aqueous layer, respectively [39].

Advantages in anxiety management:

- Being non-toxic and biocompatible, these materials are well-suited for use in both herbal and synthetic anxiolytics.
- Enhances the bioavailability and stability of pharmaceuticals [40].
- Used in encapsulating anxiolytics such as Buspirone Hydrochloride [41].

4.3. Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs)

Lipid-based nanocarriers, including solid lipid nanoparticles (SLNs) and nanostructured lipid

carriers (NLCs), are employed to enhance the stability, bioavailability, and controlled release of pharmaceuticals [42].

4.3.1. Solid Lipid Nanoparticles (SLNs)

Solid lipid nanoparticles (SLN) are colloidal dispersions in an aqueous medium, characterized by a matrix made up of solid biodegradable lipids [43].

Advantages in anxiety management:

- Improve the bioavailability of encapsulated anxiolytics.
- solid lipid nanoparticles (SLNs) demonstrate enhanced stability [44].
- Solid lipid nanoparticles (SLNs) have been utilized to improve the delivery of venlafaxine HCl, a water-soluble antidepressant, by enhancing its stability and enabling a controlled release mechanism [45].

4.3.2. Nanostructured Lipid Carriers (NLCs)

Nanostructured lipid carriers (NLCs) are advanced drug delivery systems that utilize a core matrix made up of a combination of solid and liquid lipids [46].

Advantages in anxiety management:

- Provide enhanced drug-loading capabilities, rendering them suitable for the encapsulation of a range of anxiolytic medications.
- Avoid the expulsion of drugs to maintain the long-term stability of the encapsulated substances [47].
- Nanostructured lipid carriers (NLCs) have been utilized to improve the delivery of curcumin, by enhancing its stability and enabling a controlled release mechanism [48].

4.4. Nanoemulsions:

Nanoemulsions are characterized by droplet sizes approximately 100 nm. Generally, a standard nanoemulsion comprises a combination of oil, water, and an emulsifying agent. They also increase the solubility and bioavailability of lipophilic drugs [49].

Advantages in anxiety management:

- Enhance the bioavailability of anxiolytics.
- Employing nanoemulsion as a drug delivery system for anxiety, increases the effectiveness of medications, which allows for a lower total dosage and helps to mitigate side effects [50].
- Nanoemulsions have been utilized to improve the delivery of Clove volatile oil, by enhancing its bioavailability [51].

4.5. Dendrimers and Nanogels

Dendrimers and Nanogels employed to enhance the stability, bioavailability, and controlled release of

pharmaceuticals.

4.5.1. Dendrimers

Dendrimers are symmetrical, extensively branched polymers characterized by a dense spherical architecture, with diameters varying from 1.1 nm for the 1.0 generation PAMAM dendrimer to 9 nm for the 8.0 generation PAMAM dendrimer [52]

Advantages in anxiety management:

- Facilitates targeted drug delivery.
- Enhances drug solubility and bioavailability [53]
- Used for targeted delivery of synthetic anxiolytics such as risperidone [54].

4.5.2. Nanogels

Nanogels are three-dimensional, sub-micron cross-linked polymer structures. Composed of hydrogel particles that fall within the nanometer size range, nanogels exhibit characteristics inherent to both hydrogels and nanoparticles [55].

Advantages in anxiety management:

- Provides sustained drug release and targeted delivery.
- Highly biocompatible, making them suitable for anxiolytics [56].

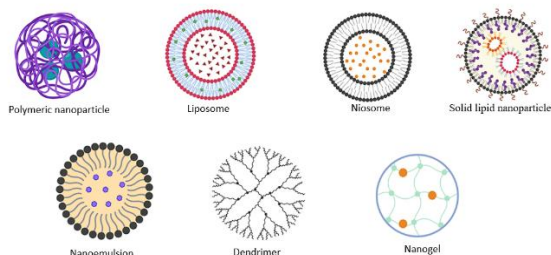


Figure 2. Nanotechnology-Based Microencapsulation

5. MICROENCAPSULATION TECHNIQUES FOR ANXIOLYTICS

There are several techniques for encapsulating core materials, which can be categorized into three main types as shown figure 4.

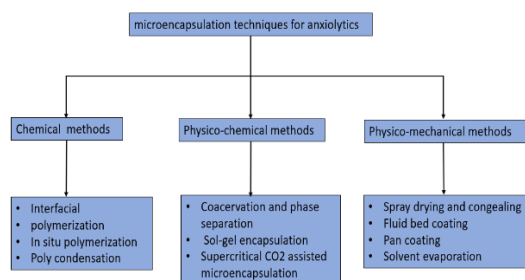


Figure 3. Techniques of microencapsulation for anxiolytics [57]

6. Role of Nanotechnology in Enhancing Anxiolytic Drug Delivery

Nanotechnology presents a revolutionary method for the delivery of anxiolytic medications by enhancing bioavailability, precision targeting, and regulated release. Although obstacles remain, ongoing research and technological progress hold the potential to lead to more effective and safer treatments for anxiety.

6.1. Enhanced Drug bioavailability:

Nanoencapsulation has become a promising approach to improve the effectiveness and bioavailability of anxiolytics. The following case studies illustrate the use of nanoencapsulation methods for enhancing bioavailability:

- A research study examined the impact of nonencapsulated amitriptyline indicated that the nonencapsulated version not only improved the antidepressant effects but also displayed properties similar to anxiolytics. This implies that nanoencapsulation may enhance the therapeutic benefits such as bioavailability of amitriptyline, potentially providing advantages for individuals suffering from both depression and anxiety disorder [58].
- This research highlights the promise of nonencapsulated Withaferin-A as a potent anxiolytic formulation characterized by enhanced solubility and bioavailability. By utilizing nanotechnology, the study seeks to improve the therapeutic effectiveness of natural phytochemicals, providing a safer and more effective option compared to traditional synthetic anxiolytic medications [59].
- The research indicates that the intranasal administration of paroxetine-loaded nanoemulsion markedly improves drug permeation, bioavailability, and the effectiveness of the antidepressant and anxiolytics when compared to oral delivery. This method of delivering medication directly to the brain presents a promising strategy for enhancing the therapeutic results of paroxetine in the treatment of anxiety and depression [60].
- The study explores the development of proteinoid nanoparticles (NPs) for risperidone (RSP) delivery, aiming to enhance its therapeutic efficacy. High-molecular-weight, low-polydispersity proteinoid polymers were synthesized using L-amino acids and poly-L-lactic acid (PLLA) via thermal step-growth polymerization. RSP-loaded proteinoid NPs were then formulated through a self-assembly process, followed by PEGylation to improve stability and bioavailability [61].

6.2. Sustained and Controlled Drug Release:

Nanotechnology-based drug carriers offer significant advantages in achieving sustained and controlled drug release, which contributes to:

- **Ensuring stable drug concentrations in the bloodstream:** Nanocarriers promote a controlled release mechanism that prevents abrupt fluctuations in drug levels, thereby guaranteeing uniform therapeutic outcomes.
- **Reducing dosing frequency:** Nanotechnology-based sustained-release formulations reduce the frequency of dosing, which enhances patient compliance with treatment plans [62].
- **Example:** Nasal nano vesicular gels of buspirone hydrochloride (BH) were developed to enhance bioavailability and sustain drug release. BH nanovesicles (Span 60: cholesterol, 80:20) showed 70.57% encapsulation efficiency and were incorporated into Carbopol 974P (pH-induced) and Poloxamer 407 (thermoreversible) in situ gels [63].

6.3. Targeted Brain Delivery via BBB Penetration

A significant challenge in the administration of anxiolytic medications is the blood-brain barrier (BBB), which limits the passage of drugs into the central nervous system (CNS). The use of nanocarriers enhances the targeting of the brain by:

- **Ligand coated nanoparticles:** Ligand-coated nanoparticles enhance the brain uptake and antianxiety-like activity as compared to uncoated nanoparticles [64].
- **Example:** The research carried out by [65] sought to develop an intranasal nanosystem designed for the controlled release of venlafaxine, ensuring sustained therapeutic levels over an extended duration. The study involved the creation of PLGA polymeric nanoparticles that incorporated two different ligands: transferrin (Tf) and a specific peptide targeting the transferrin receptor. These ligands facilitate surface modification of the nanoparticles, enhancing absorption and increasing permeability through improved interactions between the cells and the nanosystems, thereby enabling targeted delivery.

7. Application Of Nanotechnology-Based Microencapsulation for Anxiolytic Drug Delivery

- Nanoencapsulation enhances the solubility of anxiolytics that are poorly soluble in water [66], such as benzodiazepines [7], selective serotonin reuptake inhibitors (SSRIs) [67], and herbal extracts including CBD and curcumin [68].
- Enhances the absorption and bioavailability within the gastrointestinal tract [69].
- Facilitates extended drug efficacy, thereby decreasing the frequency of administration.
- Reduces side effects by ensuring consistent drug plasma concentrations [70].

- Enhances the bioavailability of herbal anxiolytics such as valerian root, ashwagandha, and curcumin [71].
- Enhances the bioavailability of herbal anxiolytics such as valerian root, ashwagandha, and curcumin [72].
- Protects phytochemicals from degradation, ensuring a prolonged therapeutic effect.

8. CHALLENGES

Although there have been significant advancements in the use of nanotechnology for microencapsulation in the delivery of anxiolytic medications, numerous challenges still persist.

8.1. Manufacturing Complexity

Some microencapsulation methods may incur high costs, especially when implemented on a larger scale. The challenges of large-scale production arise from issues related to achieving consistent particle size, ensuring efficient drug loading, and maintaining stability [73].

8.2. Toxicity and Safety Concerns

The prolonged buildup of nanocarriers within the body could result in possible toxicity and unexpected adverse effects. The following table, **Table 3**, presents the various aspects of nanotoxicity along with their descriptions.

Table 3: Various Aspects of Nanotoxicity with Description [74].

S. No.	Nanotoxicity aspect	Description
1.	Routes of Exposure	Ingestion, inhalation, and skin contact can introduce nanoparticles into the body.
2.	Key Toxic Effects	Cytotoxicity, genotoxicity, neurotoxicity, and oxidative stress.
3.	Influencing Factors	Size, shape, surface area, surface coating, crystallinity, dissolution, and agglomeration.
4.	Mechanisms of Toxicity	Formation of reactive species (ROS), DNA damage, protein denaturation, and inflammatory responses.
5.	Health Implications	Potential risks include organ damage, immune system disruption, and neurodegenerative effects.

8.3. High Production Costs

Formulations utilizing advanced nanotechnology necessitate costly raw materials and complex equipment, which restricts their accessibility. The raw materials utilized in the production of nanotechnology-based microencapsulation are frequently costly, which subsequently raises the overall production expenses. Numerous nanocarriers, including lipid nanoparticles [75], polymeric nanoparticles (such as PLGA and chitosan) [76], dendrimers [77] and liposomes, necessitate expensive, high-purity raw materials to

guarantee both biocompatibility and effectiveness.

8.4. Regulatory Hurdles

Nanotechnology represents a field of product innovation aimed at improving the properties of materials, minimizing material usage, reducing waste, and contributing to lower environmental emissions. The collaboration in sharing research findings and facilities is bolstering the scientific foundation necessary for the regulation of nanomaterials and products derived from nanotechnology [78].

In 2019, the Indian government issued guidelines for the assessment of Nano pharmaceuticals. These guidelines outline the scientific justification for the development of these novel drugs and emphasize the need to compare them with existing medications. The aim is to demonstrate, through in vitro and in vivo studies, enhancements in safety, efficacy, a decrease in toxicity, a reduction in the required dosage or frequency of administration, benefits for patients, cost-effectiveness, and other advantages [79]. Ethical concerns and public skepticism regarding potential health and environmental risks further delay regulatory approvals.

8.5. Drug Stability Issues:

Stability is a fundamental component of any drug delivery system, necessitating a thorough understanding of various factors to successfully develop a commercial drug product. Microencapsulated nanoparticles are prone to instability. While liposomal vesicular systems offer the capability to transport both hydrophilic and hydrophobic substances, they are plagued by physical instability, which undermines the advantageous potential of liposomes [80]. The chemical structure of lipids includes functional groups that are particularly prone to degradation through oxidation and hydrolysis [81].

9. FUTURE PERSPECTIVE:

Future developments in nanotechnology-based microencapsulation present significant opportunities to address different challenges in anxiolytic drug delivery. With continuous research and interdisciplinary collaboration, nanotechnology-based microencapsulation can revolutionize anxiolytic drug delivery, providing more effective, sustained, and targeted therapeutic solutions for anxiety disorders.

9.1. Development of Biodegradable and Biocompatible Nanocarriers

Biodegradable and biocompatible nanocarriers are gaining attention as a promising strategy for drug delivery, especially for anxiolytic medications. These carriers, made from polymers such as polylactic acid (PLA) [82], poly (lactic-co-glycolic

acid) (PLGA), and chitosan [84], facilitate controlled drug release while reducing toxicity and adverse effects. Their biocompatibility allows for extended circulation within the body without triggering immune reactions, and their biodegradability guarantees safe removal through metabolic processes. These nanocarriers improve drug solubility, stability, and bioavailability, thereby enhancing therapeutic effectiveness [85]. Ongoing research aims to refine their design for targeted delivery and to lower production costs, which will broaden their clinical applications.

9.2. Personalized Medicine:

Personalized medicine focuses on customizing treatment plans according to an individual's genetic makeup, health condition, and medication responses. The application of nanotechnology in microencapsulation significantly advances this concept by facilitating accurate drug delivery, regulated release, and targeted therapies. By altering nanocarriers with specific ligands or biomolecules, medications can be directed to specific receptors or tissues, thereby maximizing therapeutic benefits while reducing adverse effects. Furthermore, drugs can be encapsulated in doses tailored to individual patients, enhancing both effectiveness and adherence to treatment. The combination of nanotechnology with genomics and AI-based predictive models presents substantial opportunities to transform personalized medicine, leading to safer and more efficient treatment options [86] [87].

9.3. Stimuli responsive drug release:

Stimuli-responsive drug release utilizes nanocarriers that react to particular physiological or external signals to regulate the release of medication at targeted locations. These advanced drug delivery systems improve therapeutic effectiveness while reducing adverse effects [88]. Oxidative stress is linked to anxiety disorders [89]. Nanocarriers sensitive to redox changes can release anxiolytics in response to increased reactive oxygen species (ROS) in the brain, ensuring site-specific drug action. Magnetic fields or ultrasound waves applied externally can be utilized to guide and regulate the release of anxiolytics in the brain, thereby minimizing systemic side effects [90]. Instances of stress and anxiety frequently correlate with fluctuations in body temperature. Thermosensitive nanocarriers can be engineered to deliver anxiolytic medications when triggered by increased temperatures that occur during acute anxiety episodes.

9.4. Integration with Artificial Intelligence (AI)

AI, along with machine learning, will enhance the design of nanoparticles by forecasting encapsulation efficiency, drug release behaviours, and toxicity

risks, thereby streamlining the development process. The rapid prediction or identification of biological targets through target fishing (TF) could significantly aid in connecting these targets to new compounds. The integration of artificial intelligence and TF techniques, alongside human expertise, has the potential to transform existing theranostic strategies. However, it is essential to implement validation methods to address possible challenges and enhance accuracy [91].

9.5. Advancements in Nasal drug Delivery

Investigation into nanocarrier-based systems for delivering treatments through the nose to the brain will provide non-invasive and effective options for addressing anxiety and neurological conditions. The nasal cavity presents a richly vascularized surface that facilitates swift drug absorption and direct delivery to the brain through the olfactory and trigeminal pathways, effectively circumventing the blood-brain barrier (BBB) and first-pass metabolism. Lipid based nanocarrier such as solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC), liposomes, nanoemulsion and microemulsion, can be used to delivery anxiolytics to the brain [92][94][94]. Ongoing research and technological progress suggest that drug delivery systems utilizing nasal nanotechnology have significant potential to transform anxiolytic treatment.

CONCLUSION:

Microencapsulation using nanotechnology has been a revolutionary strategy for improving the bioavailability and therapeutic potency of anxiolytic drugs by evading the drawbacks inherent in traditional drug delivery systems. Anxiety disorders, which afflict a large majority of world population, typically need pharmacological treatment. Still, old-fashioned drug delivery systems are confronted with issues such as poor solubility, decreased bioavailability, extensive first-pass metabolism, and variable drug plasma levels, which create inconsistent therapeutic efficacy and intensified side effects. Nanotechnology-based microencapsulation provides an answer by applying innovative nanocarriers such as polymeric nanoparticles, liposomes, solid lipid nanoparticles, dendrimers, and nanoemulsions to improve drug stability, enhance solubility, and deliver drugs targeted to the blood-brain barrier (BBB). Through controlled and sustained drug release, this technique reduces peak plasma fluctuations, thereby lessening the chance of adverse effects like sedation, cognitive impairment, and dependence. In addition, ligand-functionalized nanocarriers can enhance BBB penetration further, with the aim of delivering anxiolytic drugs to their desired sites of action more efficiently. In addition, nanotechnology-based microencapsulation can be

customized for personalized therapy, with the possibility of accurate dosage regulation in accordance with the needs of individual patients and metabolic profiles. As technology continues to develop in this area, integrating smart nanocarriers with stimulus-responsive features could revolutionize anxiety disorder therapy by offering demand-based drug release in response to physiological stimuli. By overcoming the limitations of traditional anxiolytic treatment and maximizing drug delivery, nanotechnology has the potential to revolutionize mental health care, providing safer, more effective, and patient-friendly options for the treatment of anxiety disorders.

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CONFLICT OF INTEREST:

The authors declare no conflict of interest. This review was conducted independently, and no financial or personal relationships influenced the content or outcomes discussed in this manuscript.

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