

# NOVEL NANOTECHNOLOGY-BASED STRATEGIES FOR SCHIZOPHRENIA TREATMENT: FROM BRAIN-TARGETED DRUG DELIVERY TO CARBON NANOMATERIAL BIOSENSORS<sup>1</sup>

## NOVAS ESTRATÉGIAS BASEADAS EM NANOTECNOLOGIA PARA O TRATAMENTO DA ESQUIZOFRENIA: DE SISTEMAS DE LIBERAÇÃO CEREBRAL A BIOSENSORES DE NANOMATERIAIS DE CARBONO

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### ABSTRACT

This review examines current advances in nanotechnology applied to schizophrenia treatment, focusing on nanosystems such as liposomes, solid lipid nanoparticles, and nanostructured lipid carriers for brain-targeted antipsychotic drug delivery, as well as on carbon-based nanomaterials and biosensors. The results suggest that these approaches can enhance bioavailability, improve drug absorption via alternative routes, such as the intranasal route, and reduce side effects of conventional therapies. Most studies are still preclinical and limited to animal models. In conclusion, nanotechnology is promising for schizophrenia treatment, but further clinical trials in humans are needed, along with discussions on long-term safety, accessibility, and regulatory feasibility.

**Keywords:** Nanoscience; Neuropsychiatric disorders; Schizophrenic syndrome.

### RESUMO

*Esta revisão examina os avanços atuais da nanotecnologia aplicada ao tratamento da esquizofrenia, com foco em nanossistemas - como lipossomas, nanopartículas lipídicas sólidas e carreadores lipídicos nanoestruturados - para a entrega direcionada de antipsicóticos ao cérebro, bem como em nanomateriais à base de carbono e biosensores. Os resultados sugerem que essas abordagens podem aumentar a biodisponibilidade, melhorar a absorção de fármacos por vias alternativas, como a intranasal, e reduzir os efeitos colaterais das terapias convencionais. No entanto, a maioria dos estudos é pré-clínica e limitada a modelos animais. Em conclusão, a nanotecnologia representa uma estratégia promissora para o tratamento da esquizofrenia, embora ainda sejam necessários mais ensaios clínicos em humanos, juntamente com discussões sobre segurança a longo prazo, acessibilidade e viabilidade regulatória.*

**Palavras-chave:** Distúrbios neuropsiquiátricos; Nanociência; Síndrome esquizofrênica.

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## 1 INTRODUCTION

Disorders related to the central nervous system (CNS), particularly schizophrenia, have become a major concern in global public health. According to the World Health Organization (WHO) and recent global studies, over 24 million people are affected by schizophrenia worldwide (WHO, 2023; WHO, 2022). Alongside other mental illnesses like depression and bipolar disorder, schizophrenia presents significant challenges in understanding and treatment, requiring urgent attention in modern healthcare (IHME, 2021).

In addition to these high prevalence rates, current treatments for these diseases frequently induce unwanted side effects. The extrapyramidal motor system is a primary site of these effects during schizophrenia treatment, causing symptoms like muscle stiffness, tremors, reduced facial expression, and slowed movement. This often leads patients to abandon antipsychotic therapy (Gebru *et al.*, 2025).

Schizophrenia, a prevalent mental illness, involves abnormal neuronal discharge in the brain, as well as genetic and epigenetic factors. The syndrome varies in severity and primarily affects cognition, leading to fragmented thoughts, incoherent actions, and auditory hallucinations - its most common manifestation. Additional symptoms include less frequent visual, olfactory, and tactile hallucinations, as well as motor dysfunctions like catatonia (characterized by immobility and environmental indifference) and agitated activity. These symptoms often lead to social isolation due to loss of personal identity (Yang *et al.*, 2025; Bere; Rossell; Toh, 2024; Russell *et al.*, 2024).

The discovery of pharmacological treatment for schizophrenia was a milestone in the 20th century. Until the 1950s, the lack of effective medications for neuropsychiatric disorders led to social exclusion and hospitalization in mental institutions, which often aggravated clinical symptoms. The introduction of antipsychotic drugs revolutionized psychiatric care, allowing patients to be treated at home and reintegrated into society. This shift is now understood in the light of epigenetics (Jašović-Gašić *et al.*, 2012; Pow *et al.*, 2022).

Despite their therapeutic benefits, antipsychotics are also known as neuroleptics due to their significant neurological side effects. While they reduce symptoms such as impulsivity and agitation, these drugs can paradoxically produce adverse effects mirroring the disease, such as loss of initiative and reduced emotional expression (Lungu *et al.*, 2024; Biso *et al.*, 2025).

Extrapyramidal side effects of antipsychotics in schizophrenia are notable, including tardive dyskinesia - repetitive, involuntary mouth and lip movements - and acute dystonia, which involves muscle spasms in the trunk, neck, eyes, and tongue (Govil; Kantrowitz, 2025). Such adverse effects highlight the complexity of treating schizophrenia and the necessity of close monitoring.

Given the serious side effects of treatments for schizophrenia, there is a pressing need for novel therapies. Nanotechnology offers a promising strategy, enabling targeted drug delivery across

the blood-brain barrier, reduced drug doses, and controlled release. This may improve efficacy while decreasing toxicity and adverse effects (Pires *et al.*, 2022; Ferreira *et al.*, 2023).

## 2 MATERIALS AND METHODS

The methodology employed for this work consisted of a literature review using the PubMed database. The search strategy used these keywords in the database: (“nano\*” [Title/Abstract] OR “nanotechnological” [Title/Abstract]) AND “central nervous system” AND “schizophrenia”. The articles were then selected and read. These were organized by author and year of publication, with titles restricted to the last five years on the topic addressed. After this restriction, fifteen articles related to the topic were obtained. With these results, a reflective analysis of the studied topic was conducted, allowing comparisons of its relevance and the existing gaps in knowledge about it.

Articles selected from this search over the last 5 years (2020-2025) and experimental articles that directly reported the use of nanotechnology applied to the alternative or adjunctive treatment of schizophrenia were included. Exclusion criteria included articles published before 2020 and review articles on the same topic addressed in this study.

## 3 REVIEW AND DISCUSSION

This section reviews nanotechnology applications in schizophrenia, outlining the disorder, treatment challenges, and key nanotechnological approaches.

### 3.1 SCHIZOPHRENIA: CLINICAL OVERVIEW AND THERAPEUTIC CHALLENGES

Schizophrenia stands as one of the most severe neuropsychiatric disorders. It is, characterized as a multifactorial condition with significant genetic and epigenetic components. Current pharmacological treatments are foundational but often present limited efficacy for negative. In addition, they carry a considerable burden of adverse effects, leading to high rates of treatment discontinuation (APA, 2013; Gebru *et al.*, 2025).

The global impact of schizophrenia is substantial, affecting about 24 million people worldwide (WHO, 2023). The clinical presentation is heterogeneous. Positive symptoms include hallucinations, particularly auditory ones, which are among the most prevalent features. These are frequently observed in paranoid schizophrenia, the most common subtype. Negative symptoms include social withdrawal, apathy, and affective flattening. Disorganized thinking and speech further contribute to the functional impairment associated with the disorder (Stompe *et al.*, 2005; Lungu *et al.*, 2024).

Standard pharmacotherapy relies on antipsychotic medications. These are classified into first-generation (typical) and second-generation (atypical) agents. Typical antipsychotics primarily antagonize dopamine D2 receptors, but also interact with cholinergic, noradrenergic, and histaminergic systems. These interactions contribute to their high incidence of extrapyramidal side effects (EPS), such as akathisia, dystonia, and tardive dyskinesia (Chokhawala; Stevens, 2023). Atypical antipsychotics combine D2 and serotonin 5-HT<sub>2A</sub> receptor antagonism. They exhibit a reduced risk of EPS, but their use is often constrained by high cost in many healthcare settings. This necessitates the continued use of typical agents (Ayano *et al.*, 2016; Abou-Setta *et al.*, 2012). High doses of second-generation antipsychotics have also been associated with cognitive impairment, which highlights a critical therapeutic dilemma (Éllie *et al.*, 2009; Hori *et al.*, 2012; Moritz *et al.*, 2002).

There is a pressing need for novel therapeutic strategies. New approaches should enhance drug delivery to the brain, reduce the effective dose, and minimize systemic side effects. In this context, nanotechnology emerges as an up-and-coming tool. Nanoformulations offer distinct advantages, including sustained drug release, improved targeting, and the potential to reduce doses. These features may help overcome major limitations of conventional antipsychotic therapies (Pires *et al.*, 2022; Ferreira *et al.*, 2023).

### 3.2 CENTRAL NERVOUS SYSTEM AGONISTS AND THEIR IMPORTANCE IN UNDERSTANDING SCHIZOPHRENIA

Understanding schizophrenia's pathophysiology requires moving beyond molecular genetics. It is important to examine the functional consequences of abnormal gene expression. Investigating why specific genes are overexpressed or under expressed and how this affects protein function is crucial for identifying new therapeutic targets (Bilecki; Maćkowiak, 2023). Receptor agonists - molecules that activate receptors to elicit a biological response - have emerged as valuable tools. They help clarify disease mechanisms and identify possible treatments.

The Trace Amine-Associated Receptor 1 (TAAR1) represents one such promising target. TAAR1 is a type of protein known as a receptor, found widely in mammalian brain regions involved in mood, memory, and attention regulation. TAAR1 has gained significant research interest. Human genetic studies localize this gene to chromosome 6 (specifically, 6q23) and identify variants (altered forms of the gene) that confer susceptibility to schizophrenia and bipolar disorder (Rutigliano *et al.*, 2018). Accumulating evidence indicates that TAAR1 activation serves important neuromodulatory (nerve signal-modulating) functions, while TAAR1 agonists (compounds which activate TAAR1) demonstrate therapeutic potential by inhibiting behavioral sensitization (increased response to a stimulus) and Levodopa-induced dyskinesias (involuntary muscle movements caused by medication).

The G-protein-coupled receptor 52 (GPR52) constitutes another compelling target for CNS drug development. GPR52 is a receptor protein that helps transmit signals within cells. Wang *et al.* (2020) identified compound 12c (pw0787), a potent, orally bioavailable (effective when taken by mouth) GPR52 agonist with a pyrimidine core (a chemical structure). This compound effectively suppressed amphetamine-induced hyperactivity (increased activity due to the drug amphetamine) in a dose-dependent manner in preclinical models (studies conducted before human testing), suggesting its potential applicability for treating neuropsychiatric (related to disorders of both the mind and nervous system) disorders, including schizophrenia.

While receptor agonists aim to modulate neural circuitry directly, epigenetic approaches seek to normalize disease-associated gene expression patterns. The efficient delivery of epigenetic (related to modifications that affect gene expression without changing DNA sequence) modulators (agents that alter biological responses) to CNS targets represents a major pharmacological challenge. Here, nanotechnology offers promising solutions, as nanocarriers can potentially deliver these agents to genomic targets more effectively than free drugs, leveraging their small size, enhanced permeability, and large surface area to improve therapeutic outcomes (Rajendran *et al.*, 2022).

### 3.3 NANOTECHNOLOGY IN SCHIZOPHRENIA TREATMENT: FROM FUNDAMENTAL CONCEPTS TO CLINICAL APPLICATIONS

#### 3.3.1 Fundamental concepts and historical development

The term “nano”, derived from the Greek meaning “dwarf”, defines the scale at which nanotechnology operates - one nanometer (1 nm) representing one billionth of a meter ( $1 \times 10^{-9}$  m). This scale becomes tangible when considering that a human hair measures approximately 100,000 nm in diameter, while a red blood cell spans about 7,000 nm (Merkoçi, 2009). Nanoscience encompasses the study and manipulation of matter at the atomic and molecular levels, where materials exhibit significantly altered physical, chemical, and biological properties compared to their bulk counterparts.

The biological relevance of this scale becomes apparent when recognizing that fundamental biological structures - including DNA, viruses, and cellular organelles - operate at the nanoscale (Whitesides, 2005). The term “nanotechnology” was first introduced by Norio Taniguchi in 1974 to describe manufacturing processes at the nanometer scale. However, practical manipulation at this scale only became feasible with advances in microscopy techniques. The field gained significant momentum following the discovery of fullerenes in the 1980s (Kroto *et al.*, 1985) and the subsequent synthesis of carbon nanotubes (Iijima; Ichihashi, 1993), which transitioned nanotechnology from theoretical concept to tangible reality.

A material or particle on a nanometric scale acquires different properties than when on a micro or macro scale, because when at least one of the three dimensions is reduced to nanometers, changes occur in the optical, electronic, magnetic, and/or biological properties. These changes occur due to increased reactivity resulting from the increased particle or material surface area (Joudeh; Linke, 2022).

Due to these properties, nanotechnology has a wide range of applications, from engineering to healthcare (Hussain; Ladha; Khan, 2025), with nanomedicine gaining prominence in the latter. Nanomedicine benefits greatly from advances in nanotechnology, ranging from the development of nanomaterials and sensors to the potential to improve imaging tests and targeted drug delivery (Kurul *et al.*, 2025).

The drug delivery system provides more effective delivery of the active ingredient to the therapeutic target and may also reduce the effective dose by sustained release from the carrier nanoparticles. This targeted delivery also offers the potential to reduce toxicity, as it decreases the release of the drug or active ingredient into non-target tissues, corroborating the reduction of bioaccumulation in tissues other than the therapeutic target (John, 2025).

Thus, given the promising possibility of delivering drugs using nanotechnology, schizophrenia is one of the diseases whose treatment can be improved and targeted more effectively, because, in addition to the targeted system, the nanometric size allows for better interaction with the BBB, a major challenge for the treatment of neuronal diseases, which can be circumvented with the use of nanoscale active ingredients (Yuan *et al.*, 2025).

### 3.3.2 Nanomedicine applications in central nervous system drug delivery

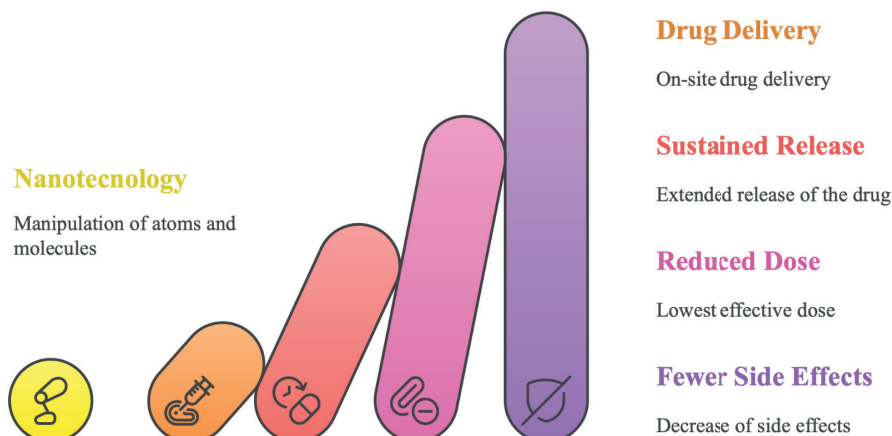
The application of nanotechnology in medicine has opened new frontiers for treating central nervous system disorders. Specifically, nanomedicine leverages nanomaterials to overcome limitations of conventional therapies (Rehan *et al.*, 2024). For instance, biocompatible and biodegradable nanoparticles, typically spherical and ranging in size from 100 to 700 nm, have shown remarkable potential as drug delivery vehicles. These nanoparticles enhance the brain concentration of therapeutic compounds by improving BBB permeability, that is, enabling substances to cross the brain's protective barrier. Furthermore, they facilitate membrane fusion and increase contact area, thus providing a greater surface for drug absorption (Cai *et al.*, 2024; Asimakidou *et al.*, 2024).

Various nanopatforms have been engineered for CNS delivery, including polymer-based nanoparticles, lipid-based systems, gold nanoparticles, peptide-modified nanoparticles, nanoemulsions (NE), and liposomes. Of these, liposomes are recognized for their superior biocompatibility and low toxicity (Liu *et al.*, 2022). These systems facilitate sustained drug release, enhance brain targeting, and enable lower therapeutic doses, thereby minimizing systemic side effects (Asimakidou *et al.*, 2024).

The strategic advantages of nanotechnology for schizophrenia treatment include: (i) targeted drug delivery; (ii) sustained release kinetics; (iii) reduced effective dosage; (iv) decreased side effects and non-target organ bioaccumulation; (v) enhanced BBB permeation; (vi) improved stability against degradation; (vii) increased drug solubility; and (viii) flexibility in administration routes (Zorkina *et al.*, 2020; Rabaan *et al.*, 2022; Jampilek; Kralova, 2022; Usharani; Kanth; Saravanan; 2023; Teixeira *et al.*, 2023). In addition to these benefits, nanostructures can also revitalize pharmaceutical compounds that were previously unsuitable for CNS applications due to bioavailability limitations (Kuskov; Kukovyakina, 2025).

Precise surface characterization of nanoparticles is critical to success. This dictates their biological interactions and targeting efficiency. Understanding nanoparticle behavior in biological systems is essential for optimizing their application parameters - where, when, and how they should be deployed (Teixeira *et al.*, 2023). However, significant challenges remain. These include an incomplete understanding of CNS disease mechanisms, complex biological barriers, and the relative novelty of nanotechnology. These knowledge gaps currently impede the translation of nanotherapies from laboratory research to clinical practice (Toader *et al.*, 2024). Figure 1 schematically illustrates the multifaceted benefits of nanoformulations for schizophrenia treatment.

**Figure 1** - Benefits of using the properties of nanoformulations for the treatment of schizophrenia.



Source: author's construction.

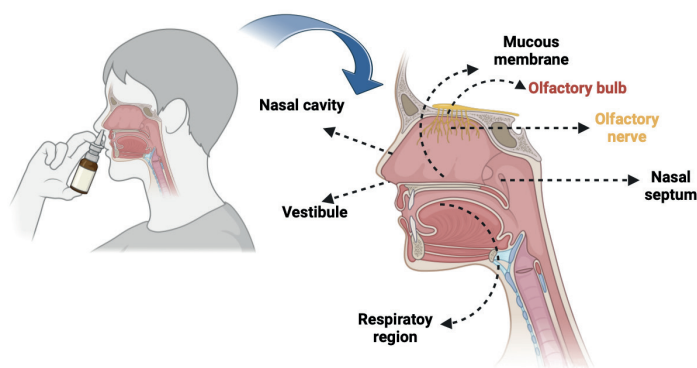
### 3.3.3 Intranasal administration: A direct pathway to the central nervous system

The pursuit of non-invasive CNS access routes has positioned intranasal administration as a particularly promising strategy. It utilizes both direct nose-to-brain pathways and indirect nose-blood-brain routes to bypass the BBB (Formica *et al.*, 2022; Huang *et al.*, 2024). This method holds clear potential to treat various CNS disorders, including Parkinson's, Alzheimer's, and schizophrenia. However, further investigation into the efficiency of BBB crossing remains necessary (Formica *et al.*, 2022).

The brain's structural complexity and metabolic sophistication present substantial challenges for biomolecule delivery. The nasal cavity's mucociliary clearance mechanism also acts as a protective system. It causes enzymatic degradation and limits mucosal permeability (Goel *et al.*, 2022). The olfactory nerve endings in the nasal mucosa provide direct neural connections to the cerebral cortex. Yet, the region's morphophysiology inherently restricts drug absorption (Tan *et al.*, 2020; Formica *et al.*, 2022; Huang *et al.*, 2024).

To address these challenges, nanotechnology offers promising solutions through a range of innovative formulations, including solid lipid nanoparticles (SLNs), NE, nanostructured lipid carriers (NLCs), and liposomes. By enhancing drug availability, solubility, and permeation, these systems also reduce enzymatic degradation and increase therapeutic potential (Bahadur *et al.*, 2020; Formica *et al.*, 2022; Huang *et al.*, 2024). Figure 2 shows how the intranasal pathway connects with the brain's neurons.

Figure 2 - Intranasal pathway and neuronal system contact.



Source: author's construction.

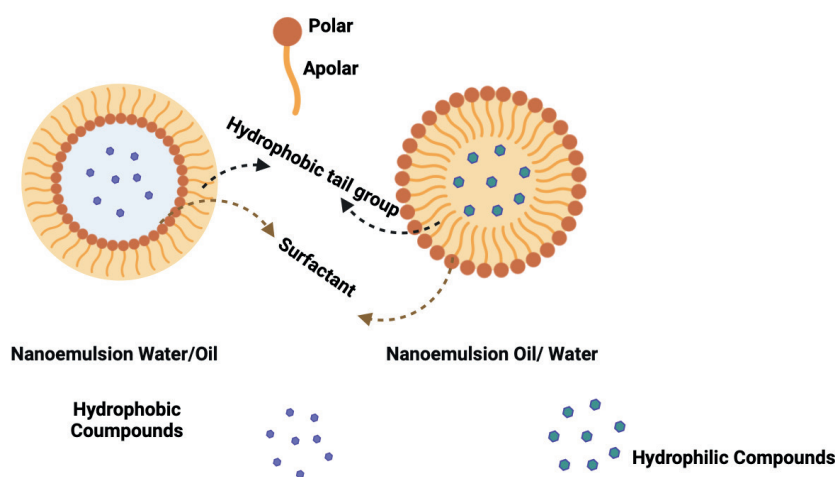
Nguyen and Maeng (2022) quantified SLNs and NLC accumulation in animal brain tissue using technetium-labeled nanoparticles. They used scintigraphic analysis for measurement. Their research showed that these lipid-based formulations reduce enzymatic activity. They also enhance mucosal biocompatibility and improve drug solubility and permeability. The assessments included comparisons of efficacy between nanoformulations and free drugs. The studies examined mucosal toxicity by histopathology and analysis of protein, lactate dehydrogenase, alkaline phosphatase, and immunoglobulin levels.

Rodent models provide valuable preliminary data. However, animal and human nasal systems differ anatomically and physiologically, so interpretation must be cautious. The human nasal cavity has distinct histology and function. These differences prevent direct extrapolation from animal results to humans (Chamanza; Wright, 2015; Tian *et al.*, 2019). Despite promising preclinical results, further validation is essential before clinical use.

### 3.3.4 NE for intranasal delivery

Nanoemulsions are lipophilic nanocarriers with high potential for mucosal absorption. They are particularly suited for intranasal administration (Bahadur *et al.*, 2020; Savale; Mahajan, 2017). These systems are classified as either water-in-oil or oil-in-water emulsions (Figure 3). Oil-in-water emulsions are especially effective for encapsulating lipophilic compounds. They also enhance aqueous solubility and bioavailability (Sessa *et al.*, 2014).

Figure 3 - Nanoemulsions structure.



Source: author's construction.

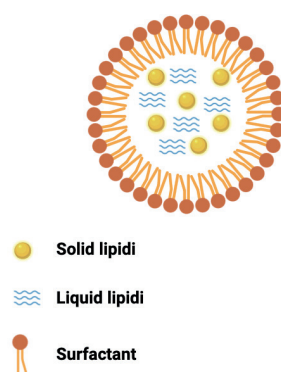
Mucoadhesiveness is a critical factor in the efficacy of intranasal drugs. NE can be engineered to increase the nasal residence time. This overcomes clearance mechanisms and improving drug absorption (Savale; Mahajan, 2017). Bahadur and Pathak (2012) demonstrated that ziprasidone-loaded nanoemulsions had superior mucoadhesive properties and diffusion characteristics compared to the free drug, with no evidence of nasal cytotoxicity.

Other antipsychotics also show improved performance in NE formulations. Quetiapine NE achieved more than double the brain concentration of the pure drug. The cerebral half-life was extended compared to oral or intranasal administration of conventional formulations (Boche; Pokharkar, 2016; Priya *et al.*, 2024). Risperidone which is limited by first-pass hepatic metabolism, also showed enhanced efficacy when delivered a via mucoadhesive NE containing chitosan. This approach led to faster transport and higher CNS drug levels, surpassing even intravenous administration (Kumar; Pathak; Misra, 2009).

### 3.3.5 Nanostructured lipid carriers

NLCs have a core made of both solid and liquid lipids. This structure allows them to encapsulate amphiphilic molecules. Surface modification with polymers or mucoadhesive components can increase intranasal permeation and improve drug release (Khan *et al.*, 2023). Figure 4 shows the typical structure of NLCs.

Figure 4 - Nanostructured lipidic carrier's structure.



Source: author's construction.

Recent investigations have examined NLC-based formulations for intranasal delivery of antipsychotics such as olanzapine (Kaur *et al.*, 2021), lurasidone (Jazuli *et al.*, 2019; Kadam; Agrawal; Shetty, 2025), and sulpiride (Tawfeek *et al.*, 2024). Kaur and colleagues (2021) demonstrated efficient CNS delivery of chitosan-coated olanzapine NLCs *in vivo*, as confirmed by *ex vivo* analyses. These formulations also demonstrated enhanced mucoadhesive properties, further reinforcing their suitability for intranasal use. Comparable gains in mucoadhesion and CNS targeting have been observed in other antipsychotic-loaded NLCs compared with free drug formulations (Jazuli *et al.*, 2019; Kadam; Agrawal; Shetty, 2025), Tawfeek *et al.*, 2024).

Key limitations include the potential sensitivity of the nasal mucosa to lipid, surfactants, and other formulation constituents (Kumari; Jaiswal; Kamboj, 2023). Consequently, thorough tolerability evaluations should accompany efficacy studies to ensure clinical feasibility.

## 3.4 BIOSENSORS AND CARBON NANOMATERIALS IN SCHIZOPHRENIA MANAGEMENT

### 3.4.1 Biosensing platforms

The biological heterogeneity of schizophrenia, along with the absence of clear, objective biomarkers, complicates early diagnosis and effective treatment planning. To address these challenges,

recent advances have centered on identifying accessible biomarkers in peripheral samples, such as blood and saliva. These biomarkers - including neurochemical indicators (dopamine, glutamate), inflammatory markers (cytokines), neurotrophic factors (BDNF), and metabolic markers - are now being actively explored for their potential integration into point-of-care biosensor detection platforms. However, developing specific biomarker panels remains difficult due to the disorder's multifaceted presentation and overlap with symptoms of other psychiatric conditions (Zheng, 2023; Wang *et al.*, 2024).

Several promising biomarker categories have emerged: (i) neurotransmitters, such as dopamine and serotonin; (ii) inflammatory markers, including Interleukin-6 (IL-6), Tumor necrosis factor alpha (TNF- $\alpha$ ), and C-reactive protein (CRP); (iii) neuronal plasticity proteins, such as brain-derived neurotrophic factor (BDNF); and (iv) metabolic indicators. Given the complexity of schizophrenia, research indicates that combining these biomarkers with clinical data - rather than relying on a single marker - could enhance diagnostic accuracy (Wang *et al.*, 2024). This multimodal approach is viewed as crucial for supporting personalized treatment strategies and addressing the disorder's clinical complexities.

Building on this, current biosensor technologies - including electrochemical, optical (e.g., surface plasmon resonance and fluorescence), and field-effect transistor (FET) platforms - have shown significant promise in detecting these biomarkers. Advances in nanomaterials have enabled sensors to achieve exceptional sensitivity, enabling the detection of low-abundance markers, such as cytokines, at extremely low concentrations (sub-pg/mL). Electrochemical biosensors that incorporate materials like graphene or carbon nanotubes (CNTs), as well as CNT-based FET devices, provide real-time, highly sensitive monitoring of neurotransmitters and small proteins (Zheng, 2023). These technological innovations are advancing both the understanding and monitoring of schizophrenia, with particular promise for continuous mental health assessment via wearable technologies (Wang *et al.*, 2024).

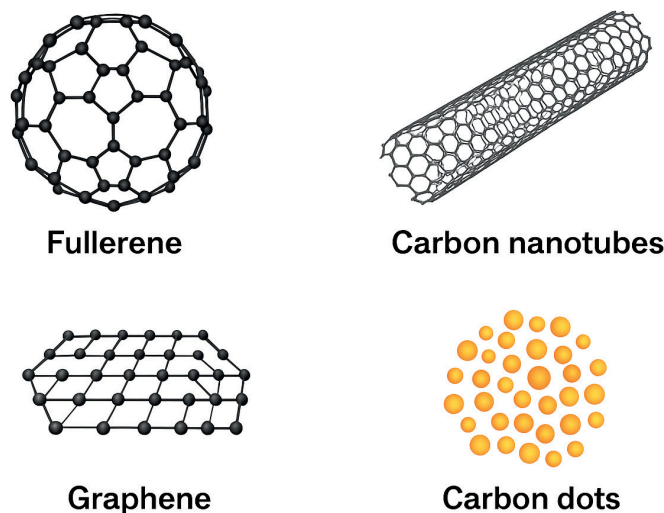
### 3.4.2 Carbon nanomaterials in biosensing

Carbon nanomaterials - including graphene, carbon nanotubes (CNTs), and other carbon allotropes - are central to the development of biosensors for schizophrenia diagnosis and monitoring. They enhance biosensing in three keyways. (1) **Sensitivity:** Graphene and CNTs increase electronic state density and electron transfer efficiency. This lowers the detection threshold for biomarkers such as dopamine. (2) **Miniaturization:** Carbon-based materials, like CNT-FETs and graphene transducers, enable compact and wearable devices. These allow real-time monitoring. (3) **Specific functionalization:** The surfaces of carbon nanomaterials permit selective immobilization of biomarker-detecting agents. These include antibodies, aptamers, and enzymes. This increases the specificity of sensors for target molecules (Sheffield, 2024).

The landscape of nanomaterials has expanded. A growing variety of carbon allotropes is now used in biosensing applications. These include graphene, graphite, fullerenes, nanorods, nanotubes,

nanowires, nanoribbons, and nanoparticles. Each material contributes unique properties to biosensor functionality (Zheng, 2023). This diversity opens new possibilities for developing efficient, portable, and specific diagnostic tools. Such tools can help in diagnosing schizophrenia and other complex neurological disorders.

**Figure 5** - Carbon nanomaterials examples.



Source: author's construction.

Researchers have developed graphene and CNT-FET sensors that detect dopamine and related amines at physiologically relevant concentrations, although most applications remain at the proof-of-concept stage. Neuroscience, engineering, and materials science experts must collaborate to translate these platforms to clinical settings (Ramoso; Rasekh; Balachandran, 2025).

In conclusion, carbon nanomaterials-based biosensors have the potential to transform schizophrenia diagnosis and care. Realizing this promise requires overcoming current challenges in biomarker discovery and panel development through focused research and innovation that leads to tangible clinical advances.

### 3.4.3 Challenges and future directions

Significant obstacles to clinical implementation include: (a) biomarker specificity limitations; (b) inter-patient biological variability; (c) matrix effects from biological samples; (d) requirements for clinical validation through multicenter longitudinal studies; and (e) regulatory approval hurdles. Ethical issues, such as continuous monitoring and data privacy, must also be addressed proactively.

The most promising development pathway involves: (i) creating multiplexed platforms that combine neurotransmitter, cytokine, and metabolic detection; (ii) integrating carbon-based sensors with low-power electronics and machine learning algorithms for pattern recognition; and (iii) conducting standardized clinical studies that correlate biomolecular signatures with clinical subtypes

and treatment response. The convergence of carbon nanomaterials, microelectronics, and translational neuroscience could ultimately yield auxiliary tools for schizophrenia diagnosis and monitoring. However, rigorous validation must remain a prerequisite to clinical adoption (Sheffield, 2024).

## 4 CONCLUSIONS

This analysis shows that while research on nanotechnology applications for schizophrenia treatment is still emerging. A clear trend is developing toward investigating diverse nanosystems, including liposomes, SLNs, and NLCs. These systems have considerable potential to enhance drug bioavailability, facilitate brain permeation, and reduce the toxicity of conventional antipsychotic therapies.

Most current evidence is from animal studies, limiting direct application to humans. The central nervous system's complexity and protective barriers, such as the blood-brain barrier and mucociliary clearance, require more robust translational models and validation before clinical use.

From a clinical perspective, advances in nanotechnology could fundamentally reshape the management of schizophrenia. They may enable dose reduction, minimize adverse effects, and improve treatment adherence. Nevertheless, significant bioethical and regulatory challenges remain. These include concerns about the long-term safety of nanoparticles, the standardization of characterization methods, and the scalability of manufacturing processes.

Nanotechnology is a promising frontier for schizophrenia treatment, but it remains mostly experimental. Future research should focus on controlled human trials to confirm preclinical results, compare administration routes (oral, intranasal, intravenous), and assess chronic toxicity and nanoparticle build-up.

In summary, while nanotechnology is not a cure for schizophrenia, it is an innovative, potentially transformative approach to management, offering new opportunities for science and clinical practice.

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