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Nanotechnology In Central Nervous System Disorders

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Abstract

Drug delivery to central nervous system (CNS) diseases is very challenging because there is presence of the blood–brain barrier (BBB). There are various new strategies to overcome these drawbacks and successfully deliver drugs to the CNS, nanotechnology-based drug delivery platform, offers potential therapeutic approach for the treatment of some common neurological disorders like Alzheimer's disease, frontotemporal dementia, amyotrophic lateral sclerosis, Parkinson's disease, Huntington's disease. This review aimed to highlight advances in research on the development of nano-based therapeutics for their implications in therapy of CNS disorders. The challenges during clinical translation of nanomedicine from bench to bed side is also discussed.

Keywords: CNS ,Nanoparticles, Molecular targets, Oxidative stress, Nanomedicine

1. INTRODUCTION:

1.1 CENTRAL NERVOUS SYSTEM :

The central nervous system (CNS) is a division of the nervous system whose function is to analyze and integrate various intra- and extrapersonal information, as well as to generate a coordinated response to these stimuli. Put simply, the CNS is the supreme command center of the body.CNS plays very much important role in various activities of body.It is an unexchangable part of our body.[1]

Fig 1.1: Central Nervous System

Main parts of CNS are as follows:

1. Grey and white matter
2. Cortex and brain lobes
3. Subcortical structures
4. Brainstem
5. Cerebellum
6. Spinal cord
7. Meninges
8. Brain ventricles and cerebrospinal fluid (CSF)
9. Neural pathways and spinal cord tracts

1.Grey and White matter:

The chief cells of the brain and spinal cord are the neurons, having main function of receive and transmit neural impulses[2]. Each neuron divided into mainly two parts body which is its micro-command center, and it has a gray color when observed microscopically. [3]

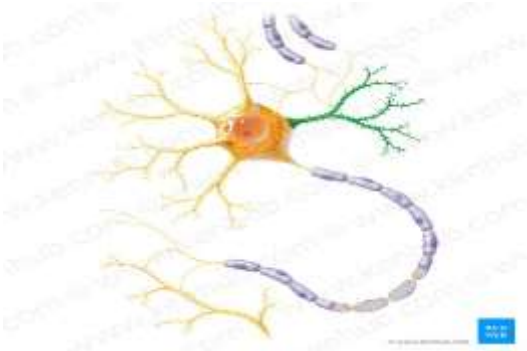


Fig 1.2: Grey and White matter

2. **Cortex and brain lobes**

The cerebrum, or forebrain, is the most prominent part of the brain. It consists of two cerebral hemispheres interconnected by the corpus callosum[5,6]. The surface of the cerebrum is highly irregular, being composed of sulci (ridges) and gyri (folds). The sulci and gyri increase the surface area of the cerebrum, providing it with the highest processing power and cognitive ability in the entire nervous system[8].

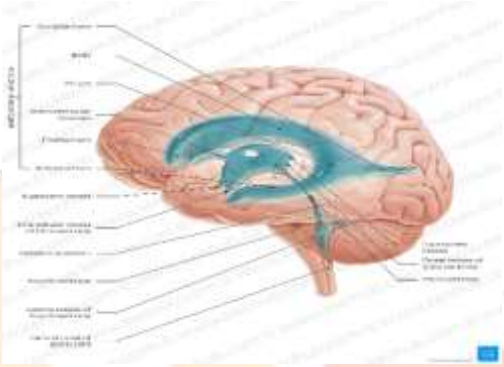


Fig 1.3: Cortex and Brain lobes

3.Brain Stem

The brainstem is the inferior-most part of the brain. It sits in the posterior cranial fossa and consists of three parts**:1. midbrain, pons**

2. **medulla oblongata.**

Internally, it is divided into the basal area, tegmentum and tectum.[9]

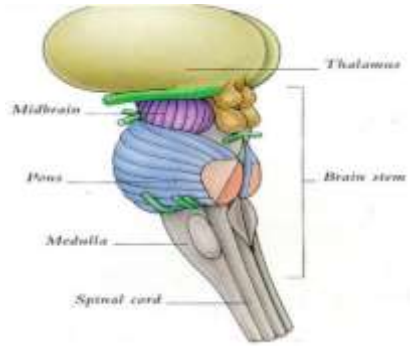


Fig 1.4: Brain Stem

4.Cerebelum:

The functions of the cerebellum include coordination with other motor activities, as well as motor learning. Blood supply to the cerebellum is derived from the posterior inferior cerebellar (PICA), superior (SCA), and anterior inferior (AICA) cerebellar arteries.[10,11]

The cerebellum is mainly divided in three parts:

1.a middle vermis flanked by two hemispheres

3. superior (tentorial) surface points

3.inferior (occipital) surface

Fig 1.5: Cerebelum

2.Various Barriers In Central Nervous Sysytem:

2.1 Blood Brain Barrier:

Blood brain barrier is very difficult barrier to cross the drugs ,only lipophilic drugs can be penetrate through this barriers other drugs cannoth be enter in this tight junction of bloofd brain barrier.[12]

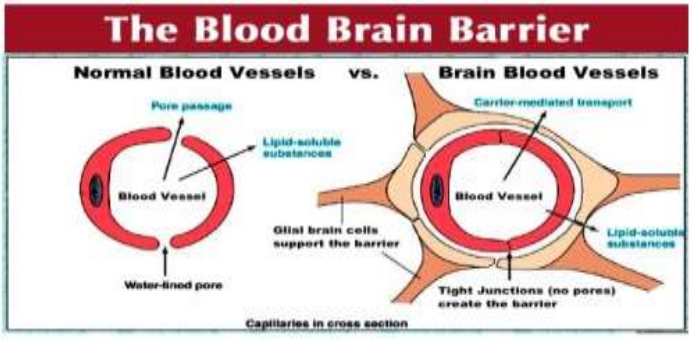


Fig.1.5: Blood brain barrier

Blood CSF barrier:

CSF having main function to provide cushning to the brain.It contains choroid plexus which plays role as barrier to brain.It do not permit any drug to permeat inside brain until its lipophilicity is high.[13,14,15]

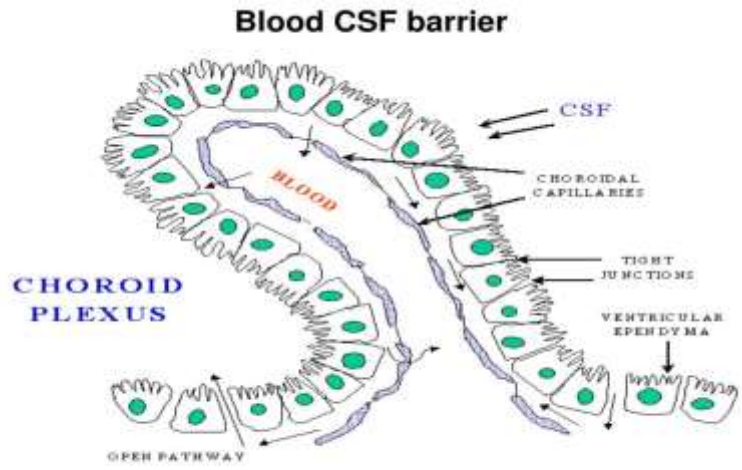


Fig 1.6: Blood CSF barrier

4. Nanoparticles Strategies to overcome CNS Barriers

3.1. Organic Nanopartricles

Main composition of nanoparticles aer proteins, carbohydrates, lipids, polymers, or any other organic compounds.Various examples of this class are dendrimers, liposomes, micelles, and protein complexes such as ferritin .[16] responses and the capacity to deliver drugs across the BBB makes these endogenous nanoparticles potential These NPs are typically non-toxic, bio-degradable hence very much beneficial for drug discovery.[17]

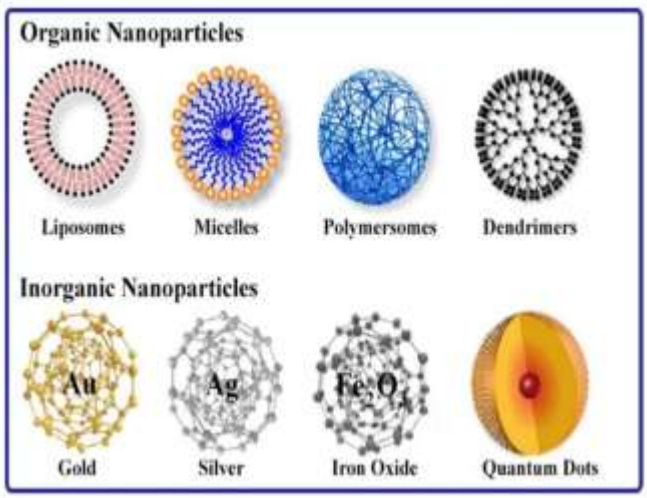


Fig 1.7: Organic and inorganic nanoparticles

3.2 Carbon-based nanoparticles

This class comprises NPs that are made solely from carbon atoms. Famous examples of this class are fullerenes, carbon black NPs, and carbon quantum dots. Fullerenes are carbon molecules that are characterized by a symmetrical closed-cage structure[18,19]

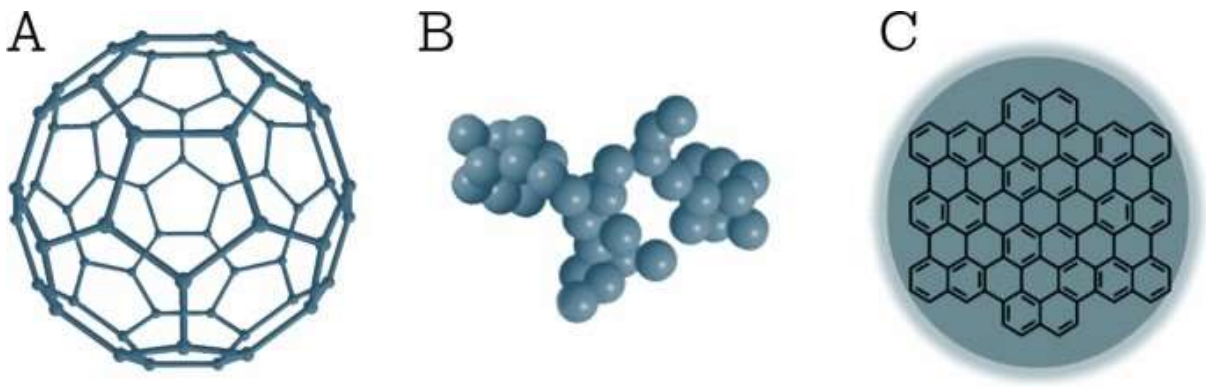


Fig 1.8 Carbon based nanoparticles

4.Brain diseases and nanoparticles

Brain disease involves central nervous system (CNS) and peripheral nervous system (PNS), disorders along with brain cancer like conditions. The blood–brain barrier (BBB) is interrupted in specific pathological states like strokes, Alzheimer's disease (AD), diabetes, Parkinson's disease (PD), seizures, and amyotrophic lateral sclerosis (ALS). As we seen in the elders population CNS problems is growing, worldwide[20].As compared with other drug delievery system CNS drug development is poor because of blood brain barrier.[21]

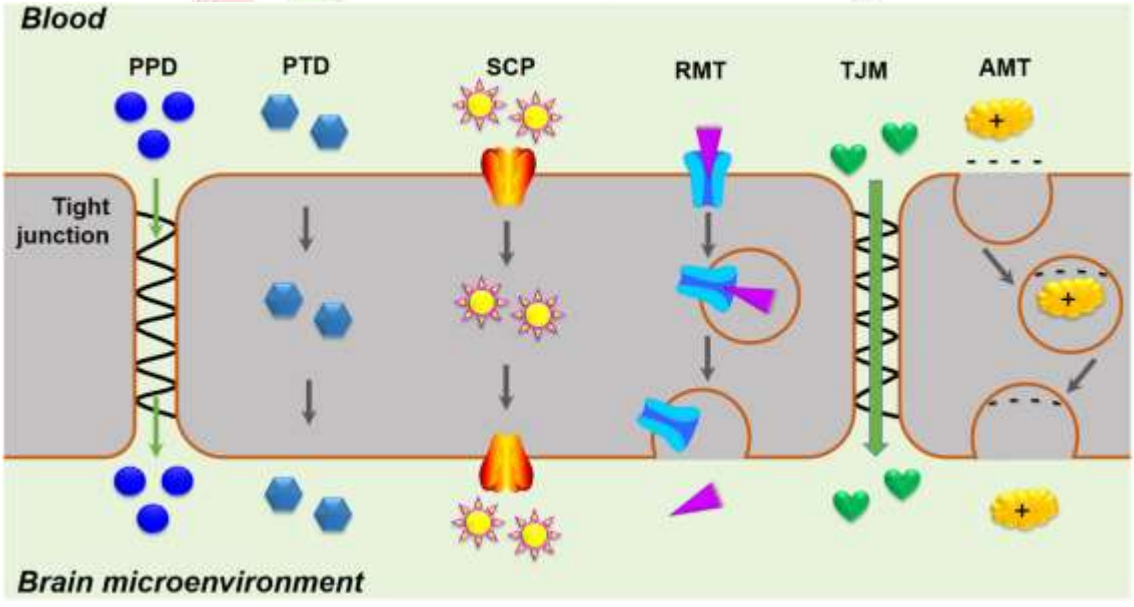


Fig. 1. 9:Transport of solutes from blood to brain across the blood–brain barrier

5. Neurodegenerative diseases and blood–brain barrier

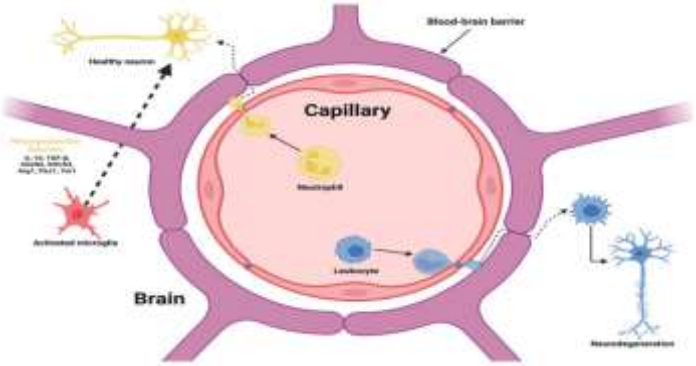
NDs represent a large group of neurological disorders with heterogeneous clinical and pathological expressions affecting specific subsets of neurons in specific functional anatomic systems; they arise for unknown reasons and progress in a relentless manner. The number of Neurodegenerative disease have seen and there treatment is difficult to develope .Many efforts in this research field, patients suffering from debilitating CNS disorders that are gradually increasing.[22] No therapies available to cure neurodegeneration yet but they can only relieves from the symptoms available medications can only alleviate symptoms.Importannt limitation in this medication is only relieve from symptoms but not the disease can be completely get cure.It get devoloped day by day[24].There are a series of barriers in CNS system include the blood-cerebrospinal fluid barrier (CSFB), the blood-brain barrier (BBB), the blood-retinal barrier and the blood-spinal cord barrier to protect itself from invading pathogens, neurotoxic molecules and circulating blood cells, preventing therapeutic available interventions[25,26].

Many available medicinal are rendered ineffective in the treatment of CNS diseases due to inability to effectively deliver and sustain them within the brain[27].

5.1. Nanoparticle Strategies for BBB Penetration

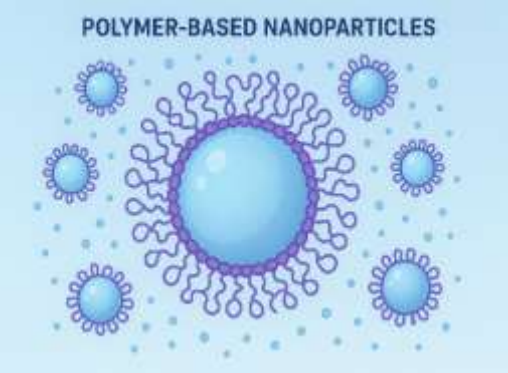
5.1.1. Passive Targeting

Passive targeting exploits the physicochemical properties of NPs to achieve BBB penetration without requiring specific interactions with receptors or transporters. NPs under 100 nm with optimized surface properties, such as lipophilic coatings or PEGylation, can diffuse across the BBB via adsorptive-mediated transcytosis or nonspecific interactions [19]. Lipid NPs, including liposomes and solid lipid NPs (SLNs), excel in this domain due to their stability and ability to encapsulate both hydrophilic and hydrophobic drugs. Recent advances in these systems include modifications for extended circulation and targeted release in diseased CNS regions [highlights the blood–brain barrier's (BBB) intricate interplay with endothelial cells, neurons, and infiltrating immune cells[28]. By depicting how alterations in BBB integrity can facilitate immune cell migration, it underscores the potential progression from localized inflammation to widespread neurodegenerative changes within the central nervous system[29].



5.1.2 Polymer-based Nanoparticles:

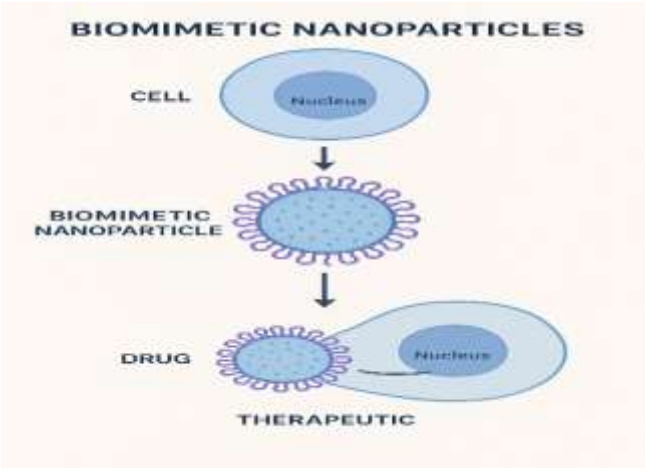
For delievering drugs to blood brain barrier polymer based nanoparticles is best option. For example, they reduce enzymatic and hydrolytic degradation and improve bioavailability[30,31].They increses brain permeation and higher concentrations of drugs. Poly(lactide-co-glycolic-acid) (PLGA), polyethylene glycol (PEG), and poly(lactic acid) (PLA) are basically used they having low toxicity and best shelf life.



5.1.3 Biomimetic nanoparticles (NPs) :

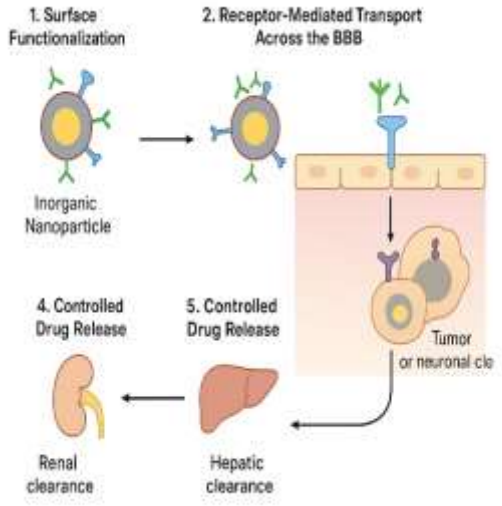
Are gaining significant attention because conventional synthetic NPs used for drug delivery are often quickly detected by the immune system and removed by organs such as the liver and kidneys[32,33]. In contrast, biomimetic NPs can more effectively recognize and bind to target ligands, circulate in the bloodstream for extended periods, and evade immune clearance[34].

Chitosan (CS)—a material derived from the partial deacetylation of chitin—is widely used as a biomimetic drug carrier thanks to its excellent biocompatibility, low immunogenicity, biodegradability, and its capacity to loosen tight junctions between cells. In addition, naturally derived vesicles, including liposomes, exosomes, red blood cell membranes, and “leukocyte-like” coatings, have been extensively investigated as biomimetic NPs for brain-targeted drug delivery. Their high biocompatibility primarily stems from their phospholipid bilayer structures[35].



5.1.4 Inorganic nanoparticles (NPs)

Offer unique advantages for brain drug delivery because of their high stability and their distinct physicochemical properties, which vary with material type and particle size[36,37]. These features often make them superior to polymeric and biomimetic NPs in certain applications. A wide range of inorganic NP structures has now been extensively explored. Importantly, their surfaces can be easily functionalized with polymers or targeting ligands to support the transport of therapeutic agents and macromolecules across the blood–brain barrier (BBB).



5.2 Advantages

1. Drug loading is crucial for maintaining drug activity, as pharmaceuticals can be added to systems without inducing any chemical reactions due to their high drug loading.

2. The effectiveness of a medicine can be improved by regulating or sustaining the release of the substance.[41,42]

3 .Smaller capillaries can be punctured by nanoparticles of small size, which permits medication to accumulate efficiently at specified regions.

4. Because liposomes and polymer nanoparticulate are typically biodegradable and never accumulate in the body, they may not pose a risk.

5. As the bioavailability of a medicine increases, its solubility also increases, allowing for more tailored drug administration.

5.3 Disadvantages

1. It is possible that the solvent system used in the preparation technique may have harmful effects.

2. Prescription leaks and unscheduled releases may be a significant issue.

3. The production expenses are significant and the efficiency of encapsulation is low.[45,46]

4. Manipulating nanoparticles in both their wet and dry states is a significant challen

6.Conclusion:

The advancement in the development of nanotherapeutics for treating and diagnosing neurodegenerative diseases holds excellent potential for clinical translation. Nanotechnology has evolved in the last five years, developing nanocarriers that regulate inflammation and immune-related NDs. Current therapies for NDs and disease states have demanded the development of multifunctional nanocarriers with inherent anti-inflammatory, antibacterial, and antioxidant properties. RNAi has come up with treatments that are in preclinical trials by various companies and research groups. Several pathways can be suppressed using RNAi and it can block specific mRNA. Thus, nanotherapeutics for siRNA-based therapies give rise to new avenues for treating NDs. Nanogels have exclusive potential for noninvasive delivery and can come up with multifunctional smart nanocarriers and may emerge as therapies for NDs. Moreover, CRISPR/Cas9 gene editing utilizing nanocarriers also holds potential for direct treatment. It can target the specific genes in early onset AD and late-onset AD, the apolipoprotein E4 (APOE4) gene.

Natural exosome modulation of immune candidates for nanotherapeutics to treat neurodegenerative diseases (and cancers). Not only are exosomes biocompatible with the ability to easily cross the BBB, but they can be targeted to specific diseased regions of the brain. Natural exosomes from specific cell sources (MSCs, dendritic cells (DCs), and macrophages) represent a novel paradigm of personalized medicine for treatment of degenerative neurological disorders

Nanotechnology has emerged as a transformative force in neuroscience, addressing challenges that have long impeded progress in the diagnosis and treatment of CNS disorders. This review underscores the unparalleled versatility of NPs, which overcome the restrictive BBB and leverage precise targeting to deliver therapeutic and diagnostic interventions for conditions such as neurodegenerative diseases, glioblastoma, stroke, and spinal cord injuries. Through innovations in passive and active targeting, stimuli-responsive systems, and bioactive platforms, NPs are redefining the possibilities in CNS medicine.

Theranostic NPs stand out as a pioneering technology, combining imaging and therapeutic capabilities within a single system. These multifunctional platforms enable dynamic tracking of disease progression and therapeutic efficacy, making personalized medicine a reality. Similarly, regenerative applications of NPs in

neuroprotection and neural repair are breaking new ground by creating permissive microenvironments for axonal regrowth, reducing oxidative damage, and modulating inflammation to preserve neuronal integrity.

While these advances represent monumental progress, challenges related to safety, scalability, and regulatory approval remain substantial. The complexity of nanoparticle interactions with the CNS, coupled with their unique physicochemical properties, demands new frameworks for toxicity evaluation, manufacturing protocols, and approval pathways. Addressing these challenges will require a concerted effort from researchers, clinicians, and policymakers to ensure that these innovations can transition from laboratory breakthroughs to real-world applications

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