Editorial:

RECENT ADVANCEMENT OF NANOMATERIAL IN DIAGNOSTIC AND TREATMENT OF NEUROLOGICAL AND PSYCHIATRIC DISORDERS

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ABSTRACT

Nanomaterials are materials that have at least one dimension with less than approximately 100 nanometers. A variety of nanomaterials are used to treat the neurological and psychiatric disorders, for example liposomes, carbon-based nanotubes, Quantum dots and nanoparticles etc. are examples of nanomaterials that showed significantly positive results. Due to high sensitivity, selectivity, surface area and ability to cross blood-brain barrier, scientists are now relying on these materials for diagnostic and therapeutic approach towards the brain disorders because of complex structure and barriers in which the brain is naturally protected. This paper focuses on the recent advancements in the diagnostic and therapeutic application of nanomaterials in the domains of neurology and psychiatry.

KEYWORDS

Brain Diseases, Blood-Brain Barrier, Liposomes, Nanoparticles, Nanostructures, Quantum Dots

INTRODUCTION

Brain disorders can be defined as any disruption in the brain's structure or normal function. It can be either neurological or mental (4). Neurological disorders are defined as any damage either by illness or accident to the nervous system, which includes the brain, nerves and spinal cord, whereas psychiatric disorders are characterised by disturbance in behavior and emotional state of the patient.[1] Alzheimer's, Parkinson, epilepsy, multiple sclerosis and Huntington's disease are the most prevalent examples of neurological disorders, while Schizophrenia (SZ), Autism, Bipolar,

Anxiety Disorders, amnesia are some examples of psychiatric disorders.[1,2] According to the WHO (World health organization) report, 970 million people in the world are suffering from a mental disorder which is about every 1 in 8 people.[3] The major hindrance to the lack of treatment is that the brain is protected inside a physical and biochemical wall called the blood-brain barrier (BBB) that blocks toxins from reaching brain cells. Approximately 95% of drugs are not able to cross the BBB because of their molecular property. Besides this, the Blood–Cerebrospinal Fluid Barrier (BCFB) and P-glycoproteins are also considered as a main barrier in treatment of brain disorders.[5] Previously, solvent like dimethyl sulfoxide, ethanol, and polysorbate 80 (PS-80) were used in drug formulation to disrupt the blood–brain barrier (BBB) increase their penetration and sensitivity.[6] Photothermal and photodynamic therapies are known as great alternatives for the treatment of brain disorders. However, all of these traditional therapies have side effects which ultimately cause damage to tissues and cause photosensitization.[7] Therefore, in order to avoid these side-effects and increase drug distribution, sensitivity and availability, scientists are looking for potential therapeutic agents that have the ability to cross the BBB without any side effects.[8] Due to this reason nowadays nanomaterial is gaining much attention in terms of diagnosis and treatment of brain disorders.[5,8]

Nano materials are substances that have at least one dimension less than 100 nanometers.[9] Nanoparticles (NP), Nanotubes, Quantum dots, dendrimers, liposomes, and micelles are some examples of nanomaterials that are used to treat brain disorders (figure). Nowadays, nano materials are engineered in order to increase specificity and sensitivity of cells, and to cross the blood-brain barrier by acting as a vehicle for drugs in order to provide improved sensitivity, efficacy and safety compared to traditional medicines.[10] Nano materials also play an important role in providing an early diagnosis of brain disorder by detecting biomarkers or play a role as a probe in molecular imaging (MI).[11] Therefore, in this review we are focusing on potential application of nanomaterial and its recent advancement in diagnosis and treatment of brain disorders.

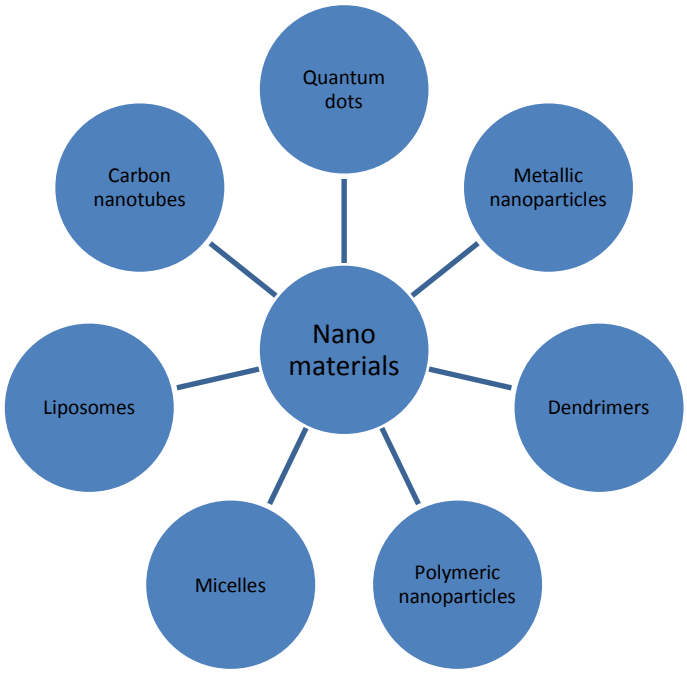

Figure: Types of Nanomaterials used in treatment of brain disorders.[53]

Nanomaterial as Early diagnostic tool

Molecular Imaging

In order to diagnose brain diseases, it is very crucial to obtain 3-D images with high quality and accuracy, and for that traditionally MRI, PET and CT Scan are used. MRI is considered as a more reliable and efficient method for diagnosis but it requires more efficient contrasting probe for its high resolution, and this can only be achieved by successful delivery of contrasting material to brain across the BBB. [12] many magnetic nanoparticles are used for this purpose including monocrystalline iron oxide nanoparticles -Fe2O3,[13] superparamagnetic iron oxide nanoparticles (Fe3O4),[14] cobalt nanoparticles,[15] gadolinium-loaded polymer nanoparticles.[16] The specificity of molecular imaging (MI) can also increase by using either target probe or activatable probe using nanotechnology.[11] Previous study reported that oligopeptides NPs have the ability to produce fluorescence in low pH of tumor microenvironment hence can act as activatable probes (that bind with specific indicator to give signals).[17,18] Another study reports that PS-80–coated PBCA dextran polymeric NPs can be helpful in the visualisation of Amyloid beta (Aβ) plaques in the Alzheimer disease model by transporting targetable probes across the BBB.[19] Another study on rare-earth

doped (RE-doped) NPs showed that nanoparticles when bind with integrin α Vβ3 (alpha V beta 3) give the fluorescence image because of emission of short-wave infrared light.[20]

Biomarker:

A biomarker is a substance that helps to indicate a certain condition or disease. Hence biomarkers play an important role in diagnosis and helping in disease management.[11] Nanomaterials, specifically nanoparticles play an important role in detection of these biomarkers. A study proposed that Nanoparticle-Enabled Protein Biomarker can be used as a diagnostic tool for Saliva-Based Traumatic Brain Injury.[21] Another study showed Gold Nanoparticles (Au NPs) give 100% sensitivity in highly efficient detection of Human ubiquitin C-terminal hydrolase (UCH-L1) biomarker in traumatic brain injury patients. Many studies have proved graphene based nanosensor role in early diagnosis of brain diseases, including MS and AD and Parkinson's disease.[22,23,24] Another study on anticholesterol antibody-bound magnetic NPs has further shown to be effective in detecting elevated cholesterol levels, which is also a key marker for Alzheimer's disease.[25] Dithiobis (succinimidyl propionate) and N-acetyl-L-cysteine (NALC) along with Gold Nanoparticles are used to detect serotonin level in patients with schizophrenia.[29]

Study on Alzheimer disease report that gold nanoparticles (AuNPs) and Graphene and carbon nanotubes (CNTs) are considered as widely used biosensor for the detection of Alzheimer disease.[54]

Nanomaterial in treatment of psychiatric disorders

Schizophrenia

schizophrenia is included in top 25 diseases worldwide that causes emotional and economical effects on society.[26] Schizophrenia is a chronic psychiatric disorder resulting in hallucination and delusions (27). The precise cause of schizophrenia is still unknown, but it is assumed that it is a multifactorial disorder with genetic and environment etiology.[28] Typical antipsychotic drugs, including haloperidol and chlorpromazine, are commonly used for the treatment of schizophrenia by targeting dopamine receptor 2 but they lead to some serious side effects like extrapyramidal side effects (EPSE) which include involuntary muscle movement such as parkinsonism. [30] Atypical drugs available in markets show higher affinity towards serotonin, hence show low extrapyramidal side effects when compared with typical antipsychotic drugs.[30] Nanomaterial based drug delivery is gaining more attention as they decrease the side effects by directly targeting the tissue or site of interest and, thus, less drug is used to reach the target. Nano DD's enhance the pharmacokinetics

and enhance the distribution of their active load (drug) by protecting it from degradation enzymes.[31] A study was conducted on Poly-L-Lysine – PLGA, clozapine loaded nanocapsules successfully cross the blood-brain barrier in in-vitro study. [32] Scientists encapsulate from 92.8% to 99.9% of the drugs (AM 251, URB597 or Rimonabant) in a nanostructured lipid carrier (NLC) and successfully deliver it to the brain.[33] Clozapine solid lipid nanoparticles (SLN) carrying drugs (Clozapine, Haloperidol and Olanzapine) showed significant increase in blood serum as compared to the drug alone.[34] In another study, Risperidone drug with chitosan nanoparticle was used for intranasal bioavailability in the treatment of schizophrenia.[35] Another study on antipsychotic drug (quetiapine fumarate) which has poor bioavailability, was used with nano-liposomes and interestingly, showed improved bioavailability on administration through the nasal route.[36] A study on nanogel using a polymer poloxamer-407 cross-linked with 2-acrylamide-2-methyl propane sulfonic acid showed increased solubility in tissue fluids.[37,38]

Bipolar disorder:

Bipolar disorder is known as manic mental illness that leads to the changes in mood, energy level, behavior, sleep and thinking.[39] Recent studies showed that lithium have ability to prevent new manic and depressive episodes hence have anti-suicidal effects which is ultimately the main concern of bipolar disease.[40] Biopolymeric nanocomposites encapsulating lithium carbonate showed significant results by enhancing the drug delivery, stability and oral absorption.[41] Scientists developed mucoadhesive buccal tablet by using risperidone (atypical neuroleptic) drug, and this systemic delivery system showed 90% release of the drug within approximately 8 hours.[42]

Anxiety disorder:

Anxiety disorders are the most prevalent psychiatric disorders, and are associated with symptoms of pounding heart and sweating.[43] Study showed that the anxiolytic effect of ZnO NPs is much higher than its conventional drug form.[44] Study showed that peptide antisauvagine-30 (ASV-30) Iron oxide NP significantly reduced amphetamine withdrawal-induced anxiety in rats.[45] Study was conducted on Buspirone Hydrochloride with Nano vesicular Gel forming anxiolytic nasal drug delivery System which show an increase of 3.26 times in bioavailability.[46] Diazepam formulated with biodegradable polymers like poly(lactic-co-glycolic acid) (PLGA) showed promising drug delivery.[47]

Amnesia:

Amnesia is a psychiatric disorder characterized by memory loss, which is caused by illness or injury.[48] A study reports that the PS-80–coated rivastigmine with chitosan based nanoparticle in mouse model of amnesia showed a significant increase in memory recovery rate (49). Another study was conducted on galantamine-loaded thiolated CS NPs in treatment of amnesia, showed regain in memory of amnesia induced animal model.[50] Another study on gallic acid–loaded CS NPs showed increased drug delivery to the brain when coated with PS-80 and ZnO nanoparticles.[51]

Nanomaterial in treatment of Neurodegenerative disorder:

Alzheimer's disease:

Alzheimer's disease refers to a complex neurodegenerative disorder that is characterized by progressive and severe dementia (memory loss) with neuropsychiatric symptoms like hallucination, eating disorder etc.[52] Study was conducted showing nanostructures prevent oxidative stress and anti-inflammatory activities in rat model of Alzheimer's disease.[55]

Nanomedicine is offering a promising evidence in the diagnostic-cum-therapeutic application in the field of medicine, particularly in neurosciences and mental health, giving hope to the ailing population and their formal and informal caregivers.

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