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UTILIZATION OF NANOPARTICLES IN CNS DISORDERS, CURRENT AND FUTURE PERSPECTIVE: A MINI REVIEW

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ABSTRACT

The field of nanomedicine is growing very fast with the development of different- different nanotechnologies day by day. NPs are able to provide potential benefit in the prevention and diagnosis of various CNS diseases, there is more possibility to develop new therapeutic strategies for completely eradicate the CNS diseases (AD, PD %& ALS) and also for the better diagnosis of CNS disease at earlier stage. Alzheimer's and Parkinson' diseases are considered more neurodegenerative diseases worldwide. There is complete understanding of pathology of these disease are unknown, the current therapy is available only for the neuroprotection and symptom management. Understanding of BBB pathophysiology will provide more specific therapy for the management of CNS diseases. Blood brain barrier (BBB) provides protection of brain, Researchers focuses to develop a novel NPs, carry the drug across the BBB and provide good bioavailability in the brain. Here I review the various neurological disorders and different NPs particularly the applications of NPs in diagnosis and treatment of CNS diseases. Collaboration between researchers, and material scientists is possible to develop a novel therapeutic strategy for the diagnosis sand management of CNS diseases.

KEYWORDS: Nanoparticles, liposomes, nanoshells, utilization of nanoparticles/nanomaterials in Alzheimer's, Parkinson's & multiple sclerosis.

1. INTRODUCTION

Nanomedicine are used now a days in various health departments like oncology, cardiology, and in various types of neurological disorders. This field is growing very fast due to development of various nanotechnologies day by day, in this field nanoparticles and devices are develops on nanometer scale.[1&2] There are number of applications of nanotechnology in central nervous system, including new advancement for the diagnosis of CNS disorders, novel drug delivery methods and the most innovative method for regenerating CNS tissues that will helps in the prevention of occurring new neurological disorder. Nanoparticles are known as innovation of nanotechnology which are used in medicine for the treatment/or prevention and diagnosis of human disease, since NPs dimensions are comparable to biomolecules, such as hemoglobin (~5nm), proteins(~1-20nm), viruses(~20nm), cell membranes(~6-10nm), DNA(with a diameter of ~2nm).[2&3]

Nanomaterials may enters in the body via the various route such as Skin, digestive tract, respiratory tract and via the injections, reached into the body's various parts and produce their actions(including oxidative stress, DNA damage, cellular apoptosis, inflammatory response). NPs become an essential part of drug delivery research because researcher can deliver optimum dose of impressive medicine throughout the body organs in the form of NPs where it produce controlled, targeted, and sustainable therapeutic effects.[4] World health organization published a data in December 2018 know as the second chief cause of death is stroke worldwide, while seventh is dementia. Dementia categorizes in broad classes, Alzheimer's and Parkinson disease are the main condition that impairs in human brain. However, form the last decades traumatic brain injury, the autism, schizophrenia, stroke, Alzheimer (apart from depression epilepsy and chronic pain) and Parkinson disease are pathologies are known due to modern neurology research, there is fully functional treatment and cure still unknown.[2& 6]

In the present researcher principally focuses on the characteristics of the Blood Brain Barrier (BBB) and also its permeability for the drugs, the latest strategies for the use of drugs against various CNS disorders conversion of drugs into the nanoparticles to enter the brain so the researchers find out that NPs form of drug is more effective then single drug.

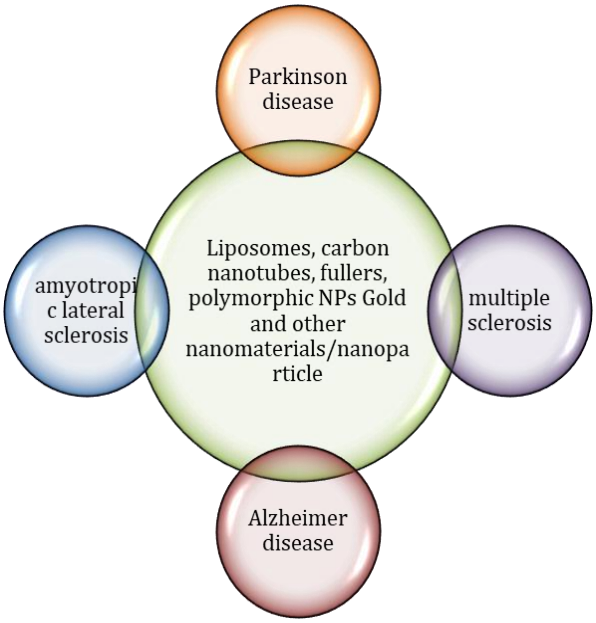

Figure 1.1: Applications of different types of nanoparticles in various neurological disorder treatment and its management.

1.1. Characterization of various nanoscale devices

An explanation of nanoscale device is necessary for the understanding of their benefits, unique properties and their limitation; in this article I focuses only on the nanoparticles rather than their types because the types of nanomaterials are described in more details in another articles.[7& 2]

1.1.1. Liposomes and micelles

It's a nanoparticle form that widely used now a days because of actual medical application these NPs consist of two major components: surrounding phospholipid bilayer membrane and core material. Aqueous core having a cargo so the water soluble drug can be carried, while phospholipid bilayer available for the protective coating.[8] Liposomes containing doxorubicin is in clinical use in humans for the ovarian cancer and multiple myeloma has been approved by the US FDA.[2&10] Moreover, liposomes as chemotherapy formulation are under investigation for the primary and secondary brain tumors (Caraglia M et al 2009). The hydrophilic outer layer help in the crossing of BBB by the micelles, the one of the major obstacle is to cross the BBB for delivery of nanoparticles in CNS disorders.[11]

1.1.2. Nanoshells

It is a another form of nanoparticle known as nanoshells consist of an outer thin metal shell and a spherical dielectric core is also present in surrounding it. Dimension of the core and shell are designed as that nanoshells can either scatter or absorb the light at a specific wavelength.[12]

1.2.3. Carbon Nanotubes

Nanotube is a another type of nanoparticle, it is made up of single element and has cylindrical shape; this NPs structure having broad range of electrical, thermal and elastic properties. Carbon is mostly used element for the formulation of nanatubes also known as carbon nanotubes, commonly used in medical application. Carbon nanotubes are the nanostructure made up of graphene sheets, these sheets are converted in cylindrical shapes.[13] The carbon nanotubes was first discovered by the Iijima in 1991.[14] Currently it has widely used in the treatment of various neurological disorders i.e ischemic stroke, Alzheimer and Parkinson.[15& 16] However, very poor preclinical studies done for the use of CNTs in neurological disorders.

1.2.4. Gold Nanoparticles

Gold nanoparticles are used for the delivery of drugs against various neurological diseases18.they have various important characteristics like better biocompatibility, simplistic surface functionalization and effective delivery to the diseased cell and tissues.[18& 19] Some studies reported by the researcher the the Gold NPs are destruct and dissolved Amyloid Beta fibrils and plaques when they used in AD treatment. Principle cause of Alzheimer is formation of plaques and amyloid beta fibrils in the brain which can be destroyed or prevented by the Gold NPs later. Gold NPs are exposed in weak microwave field and interact with fibrils in the brain, dissolve fibrils by the increasing temperature. It is shown by the in vitro experiment that Gold NPs slow down the progression of AD.[20] Gao et al.[21] Gold NPs reduces cytotoxicity of amyloid beta mediated peroxidase activity and amyloid beta fibrils having size of 22-nm, Triulzi et al.[22] also reported photo chemical ablation of amyloid beta plaques in AD. Nanobubbles based gold NPs deliver the drug in the brain of AD patient, when the bubbles burst by heating they deliver the drug to target site, based on these results it is a better option of AD disease diagnosis, management and treatment.[21& 23]

1.2.5. Microparticles:

Microparticles are in heterogeneous in nature having small size (0.1-1µm), now a days it is mostly used as a vehicle in drug delivery and Alzheimer disease management, these particles are detected in the cerebrospinal fluid in the CNS [24& 25]. It is well known that donepezil drug is approved by the FDA for the cognition and daily life functioning in mild-to-moderate Alzheimer patient, without any changes in the functioning of vital organs, but it has side effect that causes GIT disfuntioning and impaired memory, this problem has been solved by using PLGA donepezil loaded microparticles for long term use.[26]

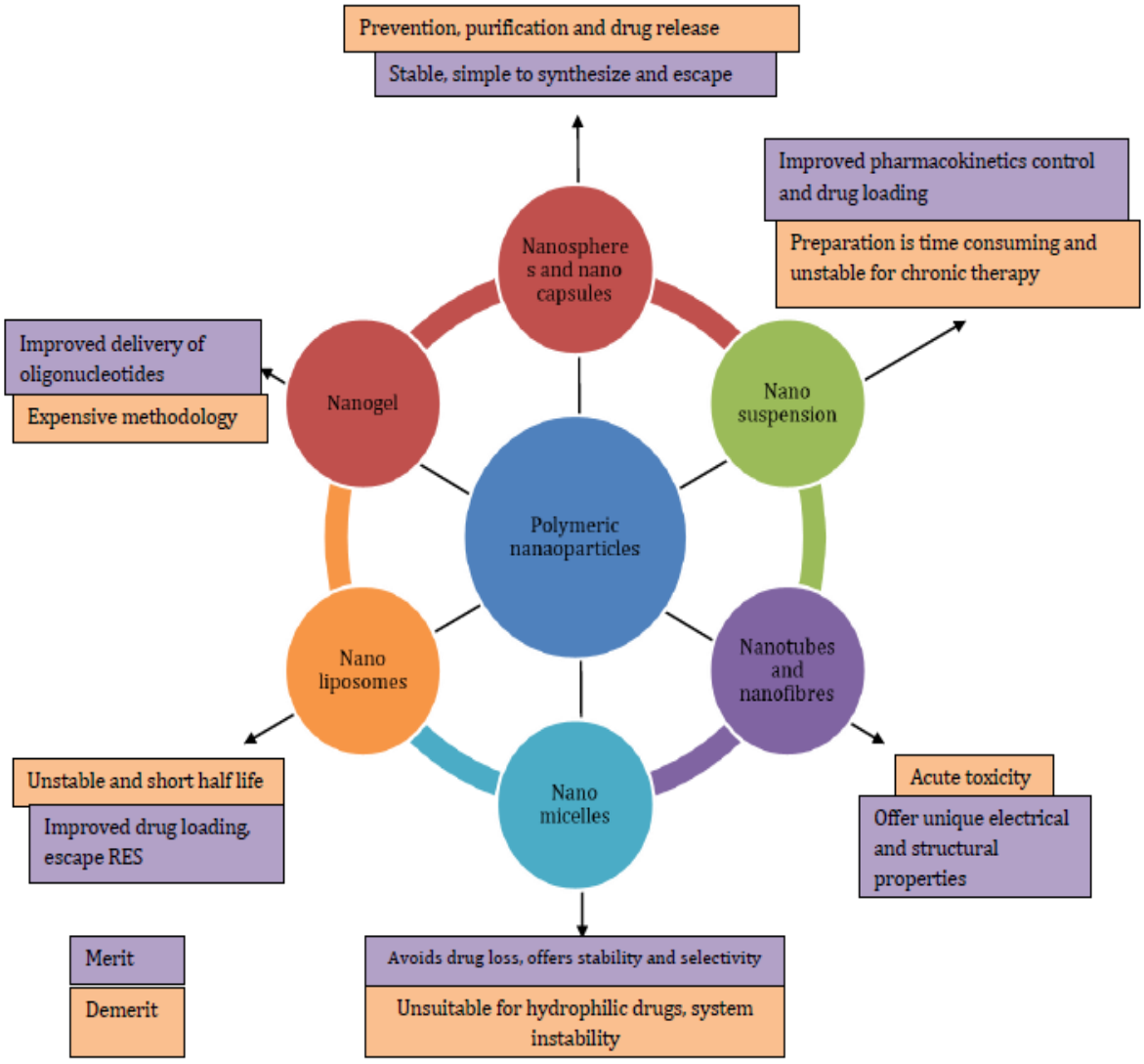

Figure 1.2 Polymeric nanoparticles (NPs) and their merits and demerits. These nanoparticles are more effective for drug delivery by the crossing BBB loaded with essential drug. However, the still having some drawbacks so they need further improvement.

2. Utilization of NPs/NMs in various neurological disorders

2.1. Alzheimer disease

Alzheimer had affected more than 36 million of population worldwide and the cases will be 50million expected by 2050.[27] At present day Alzheimer management is based on symptoms and vascular prevention by the cholinesterase inhibitors and N-methyl-D-aspartate antagonists. Utilization of nanotechnology and nanoparticles has shown shocking results in AD diagnosis and management. There are various methods are used by the researcher for the production of nanoparticles such as ionic gelation emulsion, polymer polymerization, solvent diffusion, solvent evaporation, spray dying and nanoprecipitation.[28] Researcher focuses the Aβ peptide, tau phosphorylation and metabolic dysfunction for the betterment of Alzheimer treatment. The main cause of AD is hyperphosphorylated neurofibrillary tangles and the formation of amyloid plaques in the brain. some other reasons of AD pathology has been suggested that dysregulation of the cholinergic system.[29]

Mainly two classes of medication has been approved for the treatment of Alzheimer, cholinesterase inhibitor (donepezil), galantamine, glutamate antagonist (memantine) and rivastigmine are prescribed by the physician for mild to moderate AD.[30] Improvement of Alzheimer patient's cognition can be alleviated by the using momantine (MEM) drug. Recently reported that physicochemically stable MEM-PEG-PLGA nanoparticles have been developed by the scientist which is having size smaller than 20nm (12.6±0.5), the negative surface charge is-22.4mV. It was reported that the drug is dispersed inside the PLGA matrix and found to be non-cytotoxic in brain cell lines. MEM nanoparticles are tested on transgenic APPsws/PS1dE9 mice and found that they decreased memory impairment as compare to free drug solution, it is also confirmed by the histological studies. Tiwari et al. encapsulated curcumin (the main

pigment of turmeric) into a highly lipophilic biodegredable nanoparticles and found that it stimulate the adult hippocampal neurogenesis and improved the memory of AD patient.[31]

2.2. Parkinson disease

Parkinson is a neurodegenerative disease that affects mainly the person whose age is 65 years or above. This disease causes in alteration is body's natural physiology such as increases body movement, neuronal excitation, body lock. Main cause of PD is degeneration of dopaminergic neurons in area of brain known as substantia nigra (pars compacta). Nanotechnology could be a game changer to alleviate PD. NPs can promote protection and regeneration of affected neurons and enhances the delivery of drug across the BBB. For the betterment of PD treatment an extensive research is being conducted and researchers try to develop some new therapeutic strategies for the PD treatment. Peptides and peptide anoparticles are being used in various CNS disorders not only Parkinson.[28]

A recent study prove that the improvement brain targeting of RSG (Rosagiline, a powerful inhibitor of mono amino oxidase type B MAO-B) by the PLGA-NPs (lactide-co-glicolide) based nanoparticle coated with chitosan. Principally this study conducted for the delivery and an improvement of bioavailability RSG based nano-formulation in the brain tissue and also for diminish the systemic exposure, it was done on the wistar rat brain and the plasma shows high P value (P<.005).[32] In another study it was shown that intracerebroventricular injection of micro RNA-124 loaded nanoparticles in mouse model of Parkinson disease, it initiate the enhancement of motor functions.[33]

2.3. Amyotropic lateral sclerosis

It is another neurodegenerative disease causes the loss of neuromuscular control with fatal outcome. In this disease degeneration of motor neuron occurs in both upper and lower neurons, SODI1 (super-oxide dismutase) and protein inclusion have been found in axons of both neurons.SOD coated gold nanoparticles combined with SODI1 can be used in ALS diagnosis.[34]

2.4. Multiple sclerosis

Multiple sclerosis is also a Central nervous system disease, common symptoms are disruption of information flow to the brain and body. It is reported that therapeutic activity increased in inflamed brain of mice using co-polymer of PEG (PCL-PEG) NPs given by intravenously. However, the combination of poly (ethyleneimine) and therapeutic DNA can reduces the disease severity.[35& 36]

3. CONCLUSION

The well understanding of neurological disorder mechanism has created new opportunity for Nanoparticle technology to eradicate these diseases. Particular NPs have a unique property to cross blood brain barrier, it is difficult to develop a drug that may effectively cross the BBB to reach target site without producing any side effect, and well penetration property Of NPs into the BBB NP-based system enhances the chances of diagnosis/treatment. It is found that various nanoparticles/or nanomaterials had shows significant role in the diagnosis and management of neurological disorders. Stem cell proliferation can be promote by the using NP. Nanoparticle is the better option for drug delivery in various CNS disorders as compare to conventional mode of therapy, therefore the systemic toxicity study is still required for the application of effective formulation in neurological disorders.

4. FUTURE DIRECTION

Development of modern and innovative therapeutic strategies for the treatment of CNS disorders can be possible via the utilization of nanotechnology. Nanoparticles represent an identical molecule for the enhancement of performance of nanopharmaceuticals. Assessment of nanoparticles for the symptom management, disease regression and neuroprotection in case of neurological disorders like Alzheimer and Parkinson had done, as discussed in previous sections. Apart from this certain treatment is not available for chronic CNS diseases, collaboration between material scientists, engineers and health care workers is possible to develop a novel therapeutic strategy for the diagnosis and management of CNS disorders.

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