COPPER NANOPARTICLES USED IN NEURODEGENERATIVE DISEASES

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ABSTRACT:

INTRODUCTION: Neurodegenerative diseases (NDD's) are devastating heterogeneous diseases, in which degeneration of axons, neurons in the central nervous system that causes oxidative stress and abnormalities in cellular functions in the brain results in Alzheimer's diseases, Parkinson's disease and Huntington's diseases, the three major neurodegenerative diseases and Amyotrophic lateral sclerosis, Prion diseases, Friedreich ataxia. Many drugs are available for treatment of these diseases, but the restrictive nature of Blood-Brain Barriers (BBB), the vital boundary between neural tissue and circulating blood creates an obstacle preventing entry of drug into the brain. By overcoming BBB and also due to physicochemical characteristics of nanoparticles, Nanoparticle mediated drug delivery plays a significant role in enhancing the amount and concentration of therapeutic compounds in brain in treating NDD's. Copper, an essential element for human body founded many applications in nanotechnology due to its low cost, high elimination capacity from the body

Objective: This review aims to highlight the recent proposed copper nanoparticles used in neurodegenerative diseases. This review begins with a brief history of nanoparticles, their types, synthesis and gives an insight to understand the applications of copper nanoparticles in Alzheimer's disease, Parkinson's disease and Huntington's disease. This review touches on the current status of nanotechnology in treating NDDs.

Conclusion: Finally, the review gives significance of copper nanoparticles in therapy of NDD's besides the drawbacks and toxic manifestations as neurotoxicity. Novel physicochemical characteristics of copper nanoparticles are producing new engineering applications in treating NDDs. Nanotechnology has emerged as one of the leading fields of science having huge applications and becoming ideal therapy in early diagnosis and treatment of neurodegenerative diseases or cancer.

Keywords: Neurodegenerative diseases, Blood Brain Barriers, Nanoparticles, Nanotechnology, Neurotoxicity.

INTRODUCTION

Neurodegenerative diseases (NDD's) are incurable and debilitating conditions that results in progressive degeneration or death of nerve cells which has been implicated in progression of Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis and other Neurodegenerative diseases NDD's with very different pathophysiology and improper understanding of the mechanisms ,causes of diseases which leaded to lack of treatment. To provide a number of therapeutic targets, different strategies are developing due to Restrictive nature constitutes of Blood-Brain Barriers (BBB), the vital boundary between Neural tissue and circulating blood. Nanotechnology is one the most important drug targeting system employs engineered materials or particles or devices that interacts with biological systems at a molecular level and interacting with target sites to treat NDD's by minimizing side effects.[1],[2]

2. Neurodegenerative Diseases:

Degeneration of axons and neurons causes abnormalities in cellular function and eventual cellular demise in the central nervous system in the brain results in NDDs. NDDs are age dependent disorders which are closely linked to environmental cues , advancing age , disordered immunity, and the genetic makeup of the affected individual.

[3][4]Oxidative stress causes   oxygen regulation mechanisms results in formation of free radicals progresses Alzheimer's disease, Parkinson's disease and other neurodegenerative diseases.[5]

Neurodegeneration is the progressive loss of structure or function of neurons that may lead to death of cells. Neurons are information messenger between different areas of the brain and the nervous system[5] ,[6].Neurons normally don't reproduce or replace themselves ,so when they die or damaged they can't replace by body, so that no NDD is curable , but treatment is to manage the symptoms or halt the progression of the disease.

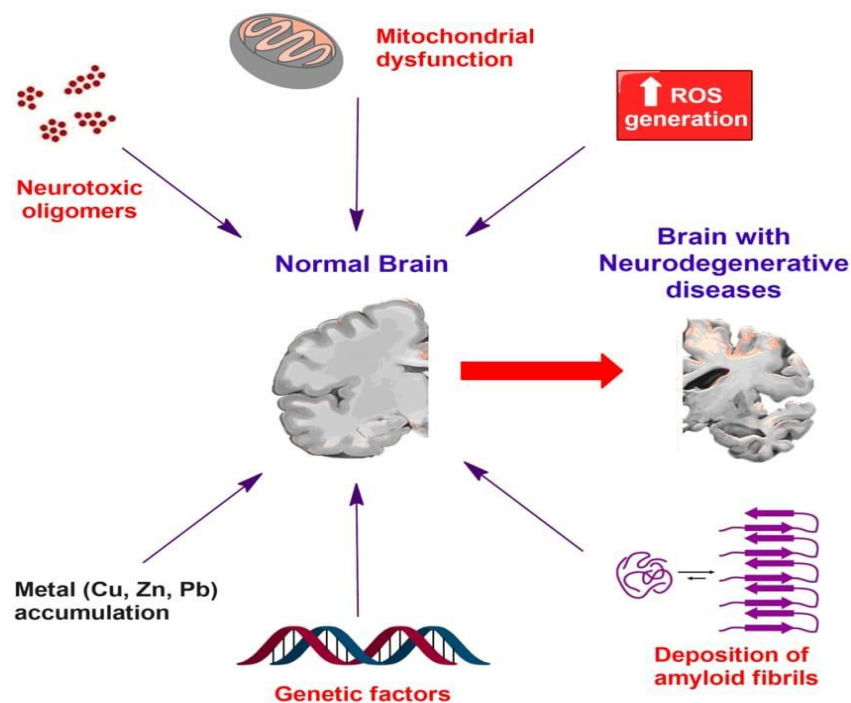**3**. **Major Neurodegenerative disorders**

Alzheimer's disease

Parkinson's disease

Huntington's disease

Amyotrophic lateral sclerosis

Prion disease

Spinal muscular atrophy

3.1 ALZHEIMER'S DISEASE (Senile dementia)

A progressive disease, in which degeneration and death of brain cell connections and the cells leads to destroying memory and mental functions.It is believed that the cause of Alzheimer's is deposition of amyloid plaques in the brain leading to neuronal and synaptic loss. Language impairment, psychological impairment, disorientation and behavioral symptoms are the major symptoms of Alzheimer's[7]. A Multifactorial disease,having several modifiable and non modifiable risk factors associated with its development and progression causes dementia in late adult life.The progression of pathophysiology field in last couple of years,new therapeutic targets are available for

treatment ,as it is believed that lack of understanding of pathogenic process may be the reason for nonavailability of effective treatment[8].

Treatment:Approved medications for the treatment of probable Alzheimer's disease,it helps control the symptoms but do not slow the progression or reverse the cause of disease.Alzheimer's disease therapy are drugs that target neurotransmitter system in the brain.[9],[5]

FDA approved acetylcholinesterase inhibitors:

➤ Rivastigmine
➤ Glutamine
➤ Donepezil

Glutamate receptor antagonist :

➤ Memantine
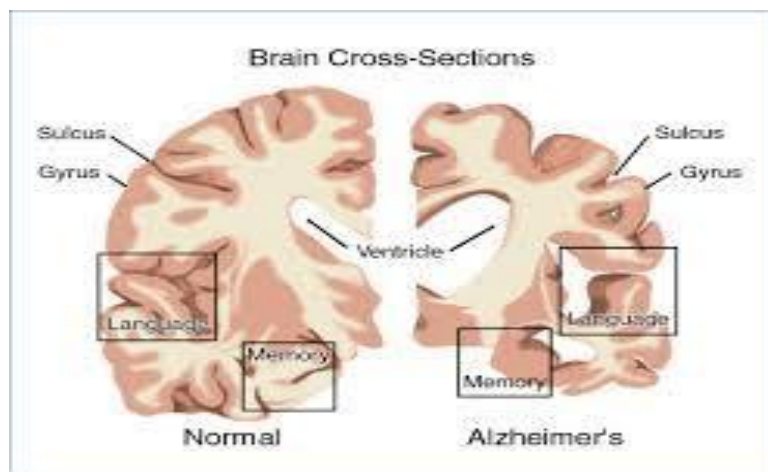
3.2Parkinson's disease:

A disorder of the central nervous system in which nerve cell damage in the brain causes decreased dopamine levels leads to Parkinson's disease,supportive therapies such as physiotherapy medication and nanoparticle drug delivery is used in Parkinson's diseases.[10],[11].Neurological movement disorders – tremors , slowness of movement, stiffmuscle and unsteady balance walk are symptoms of Parkinson's disease[12].
Treatment:
 No definite treatment to cure the disease ,but treatment is only to reduce symptoms

Dopamine   promoter-stimulation   of   dopamine   receptors   in   brain[10]
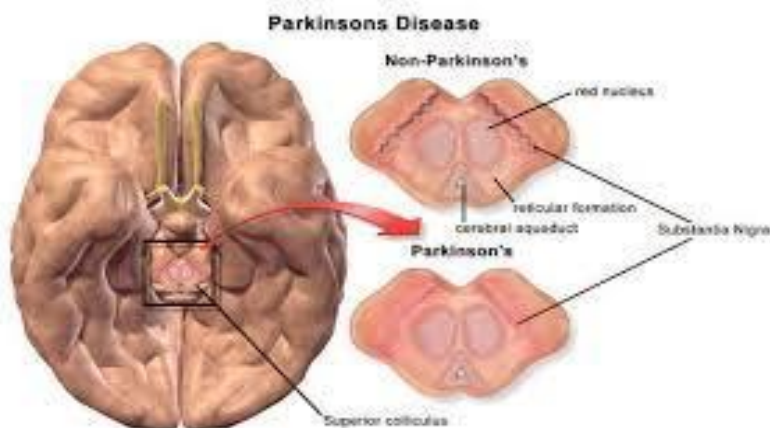
3.3 Huntington's disease:[Huntington's chorea]

An inherited condition in which nerve cells in the brain break down over time. It typically starts at the age of 30 years or 40 years. This disease results in progressive movement, thinking and psychiatric symptoms[13].
Treatment: It depends on the stage no cure exists, but drugsphysiotherapy talk therapy can help to manage symptoms
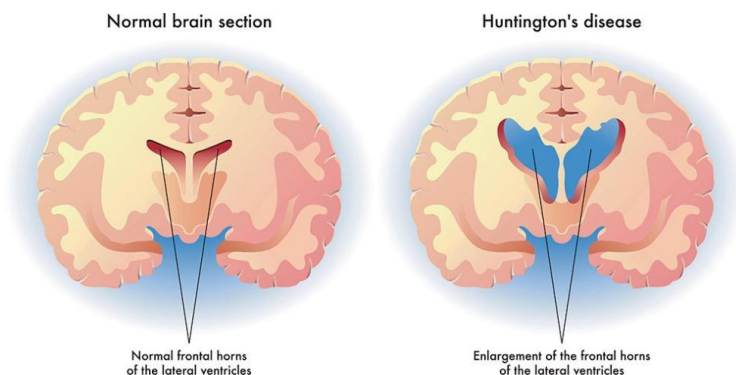
4. Nanotechnology:

Nanotechnology is a drug targeting system for delivery of drugs to specific sites of the brain to treat various brain diseases. Nanotechnology producing   new engineering applications due to novel physicochemical properties and definite characteristics of nanomaterial   provides various strategies for drug delivery[14].Various strategies have been developed to enhance the amount and concentration of therapeutic compounds in the brain,these studies are performed for better nanoparticle therapy[15].
Nanomaterials are different types
1.Nanoparticles
2.Nanoemulsions
3.Solid lipid nanoparticles
4.Liposomes
5. Nanoparticles:

The nanoparticle such as gold copper and copper oxide selenium zirconium oxide and silver nanoparticle are highly used in anti cancer activates against lung liver breast skin and colon cancer e.t.c… and drug delivery system .The

nanoparticle are the major drug carrier for delivering very sensitive and highly valuable drug to complicated diseases .Nanoparticles can be classified into different types according to size,morphology, physical and chemical properties .[16].

Some of them are;

- Carbon based nanoparticle
- Ceramic nanoparticle
- Metal nanoparticle
- Semiconductor nanoparticle
- Polymeric nanoparticle
- Lipid based nanoparticle

5.1 Carbon based nanoparticle:

 Lipid bond nanoparticle It includes two main materials carbon nanotubes and fullerenes, carbon nanotubes are graphene sheets rolled into tubes.They are hundred times stronger than steel and is used for structural reinforcement.Fullerenes are allotropes having a structure hollow cone of six or more carbon atom .The carbon units in these structureshaving a pentagonal and hexagonal arrangement. These have commercial applications due to their electrical conductivity,structure,high strength and electron affinity[17].
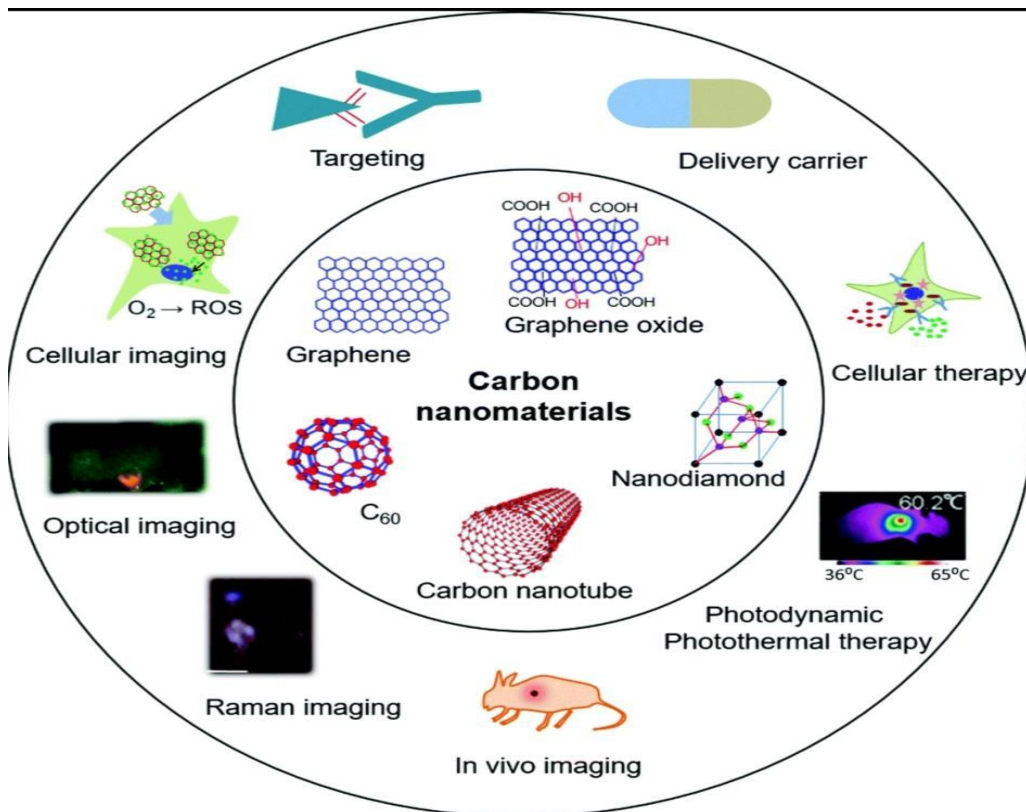
5.2 Ceramic nanoparticles : These inorganic non metallic solids are getting great attention for researchers due to their use in applications such as catalysis photocatalysis photodegradation of dyes and imaging applications[18],[19].

5.3 Metal nanoparticles : Metal nanoparticles are prepared from metal precursors These nanoparticles can be synthesised by chemical electrochemical or photochemical methods.Metal nanoparticle have applications in research areas detection and imaging of bio molecular and in environmental and bio analytical.Physical properties of metal nanoparticles such as size and shape ,controlled synthesis of metal nanoparticles is done[20].

5.4 Semiconductor nanoparticle: Semiconductor material possess properties between metals and non metals. Semiconductor nanoparticles possess wide bond gaps and show significant alteration are their properties with bandgap tuning .They are very important materials in photocatalysis, photo optics and electronic devices,reducing semiconductor materials to nano scale radically changes their physical or chemical properties semiconductor nanoparticle have attracted a lot of attention in past few years because of research promise they hold for applications in many different fields[21].A few examples are information precursor solar cells ,nanoscale electronic devices

5.5 Polymeric nanoparticle: polymers are firmly established in technological advancement in our daily lives due to their excellent chemical and physical properties[22]..A deep understanding of polymers and development of polymers properties in polymeric nanotechnology provides a broad area of application opportunities like pharmaceutics and biotechnology and in literature[23],[24].

 5.6 Lipid bond nanoparticle :These nanoparticles contain lipid moieties and are used in bio medical applications as drug carriers . Lipid nanoparticle are also regarded as highly promising systems for deriving nucleic acid in gene therapy .lipid nanotechnology is a special field,which focus the designing and synthesis of lipid NPs for various applications such as drug carriers and delivery.[25],[26]

6.Chemistry of copper : Copper is an essential element for every living organism[27].

Copper is an important chemical element found in the lithosphere in the environment as copper areas.Copper shows good electrical and thermal conductivity through importance in technology in the environment as nanoparticles .Copper shows good electrical and thermal conductivity through importance in technology[28].The third most abundant trace element copper shows useful properties like high electrical and thermal conductivity , low corrosion ability to form alloy and malleability.Copper is a reddish metal face centered cubic crystalline structure[29]

Atomic number	29
Atomic mass	63.546g.mol
Electronegativity according to Pauling	1.9
Density	8.9g.cm at 20°c
Melting point	1083°c
Boiling point	2595°c
Van Der Waals radius	0.128nm
Ionic radius	0.096nm(+1);0.069nm(+3)
Isotopes	6
Electronic shell	[Ar]3d 4s
Energy of first isolation	743.5kj.mol
Standard potential	+0.522v+0.345v
Discovered by	The ancients

7. Copper nanoparticles:
Copper nanoparticles are relatively stable in terms of both chemical and physical properties, making copper nanoparticles easily mixed with polymers. Copper Nanoparticles due to their cheaper price and abundance compared to the expensive metals like gold ,silver and their competent potential applications as microbial agents.[30]
Synthesis of copper nanoparticles:

Copper nanoparticles are synthesized by various methods

1.Green synthesis of copper : The synthesis of copper nanoparticles from natural sources is called green synthesis of copper.

2.One pot synthesis: One pot synthesis is a chemical method of synthesis of copper nanoparticles .

$$N_2H_4 \cdot H_2O$$

Conclusion :

Neurodegenerative Diseases are the most prevalent cause of death,after cardiovascular diseases. Nanoparticles are major drug carriers for delivering very sensitive and highly valuable drugs to complicated diseases as they are sensitive and nanosized particles for drug delivery.

Copper nanoparticles due to their definite physicochemical characteristics are widely used in neurodegenerative diseases for effective drug delivery to the brain. The application of copper nanoparticles for various neurodegenerative diseases produces new strategies of drug targeting to the brain in spite of their toxicological profile.[31]

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