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Euro Neuropharmacology 2018: Early identification and efficient therapy of neurodegenerative disorders: Nanotechnology as a tool - Jerzy Leszek - Wroclaw Medical University.

Jerzy Leszek[1]

[1]Wroclaw Medical University, Poland

Abstract:

Alzheimer's disease is an intensifying disorder that affects brain cells to degenerate and die. It's a kind of dementia that makes a person abnormally in thinking, behavioral and social skills. Loss of Memory is the first sign of an individual with Alzhemier's disease. It is a neurodegenerative disease characterized by the buildup of toxic amyloid plaque and intracellular neurofibrillary tangles, which results in the progressive loss of cognitive function and memory. Neurodegeneration in AD patients is characterized by changes in neurotransmitter expression, reduced neutrophil numbers, synaptotoxicity, accumulation of Aβ-protein deposits (amyloid/senile plaques), and large scale neuronal death and neural atrophy in the final phase of the disease. The mechanism of disease was explained as the degeneration of the cholinergic system and a reduction in acetylcholine. While much data supports this hypothesis, it fails to explain the accumulation of amyloid plaque, a hallmark of the disease. Biocompatible nanomaterials with increased magnetic and optical properties can act as excellent alternative agents for an early diagnosis of AD. Vitro BBB model capable of copy geometrical, cellular and rheological features of the human cerebrovasculature has been developed. This is useful for cloaking CNS nanoparticles or therapeutics prior to in vivo and clinical investigation. Nanotechnology's discoveries, known as nanoparticles (NPs), have been applied in medicine for the diagnostic, treatment and/or prevention of human diseases, since NPs' dimensions are comparable to those of biomolecules, such as proteins (1–20 nm), DNA (with a diameter of ~2 nm), haemoglobin (~5 nm), viruses (~20 nm), cell membranes (~6–10 nm). In nanomedicine and nanotechnology, it is known to extend the range of nanoscale materials and devices to 1000 nm . The latest market reports anticipate that the use of nanotechnology in medicine could extent the financial implications to $528 billion by 2019 and will continue to grow substantially. Nanotechnology-derived materials and devices proved attractive and efficient platforms for modern biomedicine (including detection, imaging, diagnosis, medication, restoration and regeneration), a particular acceptance for AD and PD management relies on nanoparticle-based therapy. Nanoparticles ranging from 1 – 100 nm diameters can effectively cross blood brain barrier in Targeted Drug Delivery System. Nanoparticles interacts with intracellular and the extracellular environment that triggers the sequence of biological effects. These effects depend on physicochemical characteristics of nanoparticles, which determine the biocompatibility and efficacy of the intended outcomes. The small particle size coupled with their unique chemical and physical properties underline the exploitable biomedical activities. It is in the form of latex body, polymer, ceramic particle, metal particles, and the carbon particles. Nanoparticles emerges as potential pharmacological carriers that can be applied in the regenerative medicine, diagnosis and drug delivery. Various types of nanoparticles posses ability to cross the brain blood barrier (BBB) and accumulate in several brain areas. Then, efforts have been done to develop safer nanocarrier systems to treat disorders of central nervous system (CNS). Many in vitro and in vivo studies demonstrated that nanoparticles of different materials posses a wide range of neurotoxical effects inducing neuroinflammation and cognitive impairment. For this reason, polymeric nanoparticles considers as biocompatible and biodegradable properties.Due to their small size and physical resemblance to physiological molecules such as proteins, NanoParticles exhibit the capacity to revolutionise screening, medical imaging, diagnostics, therapeutics, as well as carry out functional biological processes. But these features may exhibit their toxicity. The size of NanoParticles is not more than 100 nm micro. These are obtained by many ways: wet chemical treatment (chemical reactions in solution), mechanical processing (milling and grinding technology), vacuum deposition, and gas phase synthesis. Its form may be latex body, polymer, ceramic particle, metal particles, and the carbon particles. Any disruption to the Blood Brain Barrier associated with genetic defects triggers with local antigenic invasion (either neurotoxic blood-derived metabolites and residues or microbial pathogens). These further related to systemic inflammatory or immune disorders, which can subsequently initiate several neurodegenerative pathways. Degenerative process relates the CNS results in progressive and incurable impairment of neuronal cells. The particular neurons are mostly scanty or incapable of self-repair and regeneration processes. Alzheimer's and Parkinson's diseases are conditions found around the world, being considered the most rampant degenerative pathologies related to CNS. The development of NPs for biomedical applications including medical imaging, magnetic hyperthermia, and gene or drug delivery is currently ongoing process. For biomedical uses, emerging nano-structures requires stringent evaluations for their biological security. There are a number of different classes of NanoParticles promising for biomedical purposes.

Rivastigmine is the drugs which is used for the alleviation of symptoms related to mild to moderate dementia, making it a target candidate for NP-mediated drug delivery in brain. The occurance of hallucinations appears to be a predictor of especially strong responses to rivastigmine, both in Alzheimer's and Parkinson's patients. The effects reflect the inhibition of butyrylcholinesterase, which is implicated in symptom progression and providebenefits over acetylcholinesterase-selective drugs. Like other cholinesterase inhibitors, it requires doses to be increased gradually over several weeks; this is usually referred to as the titration phase. It works by inhibiting these cholinesterase enzymes, which would otherwise break down the brain neurotransmitter acetylcholine. Fullerenols, the water soluble hydroxyl derivative of fullerene, (fullerenols) are another species with the ability to scavenge free radicals and exert neu-

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roprotective effect on cortical cell cultures. Increasing evidences have provided a strong link between unusual concentration of some metals in brain and the AD associated neurodegeneration which is an antioxidant therapy (Chelation Therapy). The use of probes targeting amyloid fibrils by positron emission tomography might represent a powerful tool to assess early-stage of AD onset. Amyloid βeta self assembles has been reported to be inhibited by PEGylated phospholipid nanomicelles by inducing a conformational change which makes the peptide reluctant to aggregation; a diminished neurotoxicity was observed in cytotoxic studies on human neuroblastoma cells. Selectively and remotely dissolve the fibrillar deposits by utilizing concentrated thermal energy generated by a mixture of gold NPs-Aβ and weak microwave. The gold NPs were preferred and selected because of their high mobility, biocompatibility and high surface:volume ratio. In current review, he focus will be on materials with dimensions < 100 nm, which are the length scales even below the observation capacity of simple, optical or confocal microscopy. The nanosized objects are about 100 to 10000 times smaller than the size of mammalian cells. The primary structural characterization techniques at this scale include confocal/optical/fluorescence microscopy, scanning/transmission electron microscopy, nuclear magnetic resonance (NMR) and X-ray crystallography.

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