Novel Approaches in Drug Designing & Development
ISSN: 2575-8942

Juniper Publishers
key to the Researchers

Mini Review
Volume 1 Issue 1 - May 2017
DOI: 10.19080/NAPDD.2017.01.555554

Nov Appro Drug Des Dev

Should Nano-particles Be Used to Cross Blood Brain Barrier to Deliver Drugs to Neurodegenerative Disease?

Madhuri Sharon*

Department of Nanotechnology, Walchand College of Arts & Science, India

Submission: March 24, 2017; **Published:** May 02, 2017

***Corresponding author:** Madhuri Sharon, Department of Nanotechnology & Bio nanotechnology, Walchand college of Arts & Science, India; Email: sharonmadhuri@gmail.com

Abstract

Treating diseases of central nervous system by delivering therapeutic agents faces a big problem of crossing blood brain barrier. For combating this challenge various types of nano particles such as polymeric nano particles, nano metals, carbon quantum dots are being used with reasonable success in crossing the BBB and enhancing the drug efficacy. However, certain aftermath negative impact of use of nanotechnology for drug delivery to brain has not been considered. In this opinion/short-communication attention has been paid to the need of considering various aspects that may cause damage to brain.

Keywords: Nano particles; Blood brain barrier; Drug-delivery; Neurodegenerative disease; Toxicity

Introduction

A strange leap towards quantum mechanics and properties of materials at nano-scale has altered and enhanced the reactivity and optical properties. This has led to the inputs from all the branches of science into this magnificent field of Nanotechnology. Unfortunately the escalated excitement of scientists involved in therapeutics and diagnostics have started using nanotechnology nano particles as vehicles to deliver drugs, without considering the drawbacks and dark-side of use of nano particles. Even for highly sensitive systems like brain, which otherwise has a protective blood brain barrier (BBB) system, nano particles have been developed that can cross the BBB due to their extremely small size [1]. Development of many technologies in the past have created environmental consequences such as anti mosquito chemical DDT, antibiotics , nuclear waste, plastic waste, present day transport system and the list goes on. Therefore, along with advantages it is imperative to consider the possible draw backs before going ahead with this new technology. Thousands of papers are being published about delivering the drugs using nano particles, but fewer of them have considered examining how engineered nano particles will affect the cellular environment after delivering the drug especially to the brain. At the moment it is too early to assess how different nano materials might harm people and the environment. However I must say that it is heartening that scientists are paying attention to this concern.

The brain is one of the most highly secured organs of the body. Entry of blood circulating agents into the brain is selectively controlled by specific transport machineries at the blood brain barrier (BBB), whose excellent barrier restrictiveness make brain drug delivery and targeting very challenging [2]. As a consequence the passage of drug molecules and drug delivery systems across the BBB is prohibited creating an obstacle in the path to treat the neurodegenerative diseases. Most of the substances gain access to the central nervous system by lipid-mediated free diffusion or potentially by receptor-mediated endocytosis of nano particles.

Nano particles are being considered because many CNS active drugs and even antibiotics fail to cross the BBB. Nano particles are being designed to mimic LDL and interact with the LDL receptor, consequently triggering uptake by brain endothelial cells. Nano particles may effectively mask covalently bound chelators, thus facilitating their delivery past the BBB and minimize toxicity while improving the pharmacokinetics of the chelator itself. To facilitate transport through the BBB via the LDL mechanism, the nano particles may be further functionalized with apolipo proteins [3].

Some of the considerations for delivering drugs to brain for neurodegenerative diseases like Schizophrenia, Brain tumour, Parkinson's and Alzheimer's disease, that needs attention are

a. The nano particles being used biocompatible and bio-inert

b. Resulting toxicity

c. Water soluble

d. Biodegradable to non-toxic material

e. Can they be easily excreted out of the system or get metabolized to safer metabolites

f. At what concentration they are cytotoxic

Biocompatibility

Many polymeric nano particles that are also a part of the cellular metabolism have been envisaged to be biocompatible and safe for use in delivering drugs across BBB such as PLGA. Their first biodegradable product i.e. poly lactic acid and glycolic acid can be easily metabolized and if needed excreted from the system after the drug delivery. However alteration in pH level due to degradation of PLGA cannot be ruled out. Polysorbate 80 was perhaps the first polymer to encapsulate and deliver the anti-nociceptive peptide hexapeptide dalargin that alone does not cross the BBB to brain [4].

Liposome is another suitable polymeric nano particles as it is composed of phospholipid bilayer (sphingomyelin, phosphatidylcholine, cholesterol and glycerophospholipids), which offers many advantages such as it separates the interior from the exterior of the cell; they are biocompatible and biodegradable, protect the drug from degradation, lipids like Cholesterol, increases stability of a liposome. Surface of liposomes can be functionalized with ligands so as to enhance brain-targeted drug delivery Use of natural, biocompatible and biodegradable polymers, which can help in preventing contamination in the CNS should be preferred.

There are reports of use of metal nano particles such as gold nano particle to deliver drug to brain [1,2] of course it has many advantages, but fate of gold nano particle after delivering the therapeutic agents to the brain is an important concern to be looked into. Because it may accumulate causing physical damage to the cells. This holds true for any metal nano particle to be used.

Toxicity

Is another major concern for drug delivery to brain, because high toxicity levels in the body could be detrimental to the biosystem; though some drugs conjugated with nano particles can cross the BBB, and even exhibit lower toxicity and decrease adverse effects. Toxicological assessment of some nano particles have shown induced toxicity [3,4] have shown that nano particles of TiO_2 by producing reactive oxygen species can damage brain cells. Some other biological patho-physiological factors that may get influenced by nanoparticles and may cause alteration in blood flow, edema thus increased intracranial pressure and metabolic perturbations; needs to be taken into account.

Though many research has been conducted with promising results of delivering drugs such asrivastigmine, tacrine, quinoline, piperine, and curcumin; but one aspect has not been looked into or accounted for is accumulation of nanoparticle in the body after drug delivery. Diseases like Alzheimer's disease demands long term treatment; this may cause build up of polymeric nano particles in the body. Research has to be directed in this direction to assess whether there is any undesirable effect of this build up of polymeric compounds or the nano particles.

In conclusion it can be said that growth and development of nanotechnology based drug delivery system to CNS has great potential, however there can be dark side to which should be taken into consideration seriously and systematically.

References

1. Prades R, Guerrero S, Araya E, Molina C, Salas E, et al. (2012) Delivery of gold nanoparticles to the brain by conjugation with a peptide that recognizes the transferrin receptor. Biomaterials 33(29): 7194-7205.
2. Morshed RA, Megan EM, Qing Dai, Michelle LW, Brenda A, et al. (2016) Cell-Penetrating Peptide-Modified Gold Nanoparticles for the delivery of Doxorubicin to Brain Metastatic Breast Cancer Mol Pharm 13 (6): 1843-1854.
3. Dreher KL (2004) Health and environmental impact of nanotechnology: toxicological assessment of manufactured nanoparticles. Toxicol Sci 77(1): 3-5.
4. Lon TC, Saleh N, Tilton RD, Lowry GV, Veronesi B (2006) Titanium Dioxide (P25) produces reactive oxygen species in immortalized brain microglia (BV2): implications for nanoparticle neurotoxicity. Environ Sci Technol 40(14): 4346-4352.

DOI: 10.19080/NAPDD.2017.01.555554

How to cite this article: Madhuri S. Should Nano-particles Be Used to Cross Blood Brain Barrier to Deliver Drugs to Neurodegenerative Disease?. Nov Appro Drug Des Dev. 2017; 1(1) : 555554. DOI: 10.19080/NAPDD.2017.01.555554.