OMICS International
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Hari S Sharma et al., J Nanomed Nanotechnol 2015, 6:6
http://dx.doi.org/10.4172/2157-7439.C1.025

5th International Conference on
Nanotek & Expo
November 16-18, 2015 San Antonio, USA

Superior neuro-protective effects of TiO_2 nano-wired cerebrolysin vs. poly (D, L-lactide-co-glycolide) nano-particles loaded delivery in Alzheimer's disease brain pathology

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Nano-delivery of drugs induces better therapeutic effects in preventing neurological diseases and their effects are also prolonged than the parent compounds. Thus, the need of the hour to examine whether drugs tagged with different kinds of nanoparticles may have different effects following their nano-delivery in treating neurological diseases e.g., Alzheimer's disease (AD). AD is mainly characterized by deposition of amyloid ß-peptide (ABP) in various brain regains leading to cell and tissue destruction. It is widely believed that breakdown of the blood-brain barrier (BBB) to serum constituents activates a series of abnormal reactions leading to immunological, biochemical and pathological changes culminating in AD. Thus, to reduce the BBB breakdown and induce neuro-regeneration or neuro-repair using several neuro-trophic factors in combination could alleviate AD symptoms. Our laboratory is engaged to find out whether cerebrolysin, a multimodal drug (Ever Neuro Pharma, Austria) comprising a well-balanced composition of several neuro-trophic factors and active peptide fragments could induce neuro-protection in animal models of AD. AD like symptoms were induced in rats by chronic infusion of amyloid ß-peptide (ABP 1-40) intra-ventricularly (I.C.V) in the left cerebral ventricle (250ng/10 µl) once daily for 4 weeks. Cerebrolysin was delivered in identical fashion using two different modes of nano-delivery. Thus, TiO_2 nano-wired delivery of cerebrolysin was compared with identical doses of poly (D, L-lactide-co-glycolide) nano-particles (PLG-NPs) loaded delivery. Our observations showed marked deposition of ABP and neuronal, glial and myelin pathology in the cerebral cortex, hippocampus and cerebellum. BBB breakdown was evident by enhanced penetration of serum albumin as seen using immunohistochemistry in the identical brain areas showing neuronal loss, gliosis and myelin damage. Interestingly, TiO_2 nano-wired delivery of cerebrolysin in a dose of 25µl infused daily 2 weeks after ABP infusion for 1 week remarkably reduced ABP deposition, and brain pathology. However, identical doses of PLG-NPs loaded cerebrolysin were much less effective after ABP infusion. Interestingly, 50 µl dose of PLG-NPs-Cerebrolsyin was sufficient enough to reduce AD pathology. These observations strongly suggest that TiO_2 nano-wired delivery of cerebrolysin has superior effects over PLG-NPs loaded delivery in AD. This indicates that mode of nano-drug delivery of the same compounds is crucial in achieving desired results in neurological diseases.

Biography

Hari S Sharma, Director of Int. Expt. CNS Injury & Repair (IECNSIR), Professor of Neurobiology (MRC), Docent in Neuro-anatomy (UU) is currently working in Uppsala University Hospital, Department of Surgical Sciences, Division of Anesthesiology & Intensive Care Medicine, Uppsala University, Sweden. He obtained his PhD in Neuroscience in 1982 from Banaras Hindu University, Varanasi, India and Dr. Med Sci. from Uppsala University in 1999. He has published over 300 peer reviewed research articles (ISI database h-index 36) related to Neuro-protection and Neuro-regeneration in relation to the Blood-brain barrier in stress, trauma, and drugs of abuse in health and disease. His research on brain pathology and neuro-protection in different model is supported by Laerdal Foundation of Acute Medicine, Stavanger, Norway; role of nano-particles in neuro-degeneration and Neuro-protection for treatment strategies from European Aerospace Research & Development (EOARD), London, UK and US Air Force Research Laboratory, Wright Patterson Air Force Base, Dayton, Oh, USA; drug abuse research and neuro-protection from National Institute on Drug Abuse (NIDA); National Institute of Health (NIH).

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