Austin Journal of Multiple Sclerosis & Neuroimmunology

Open Access

Austin Publishing Group

Editorial

Nanoencapsulated Polymeric Antioxidants in Combating Neuronal Oxidative Damage

Abhishek Mukherjee*
College of Pharmacy, Seoul National University, South Korea

***Corresponding author:** Abhishek Mukherjee, College of Pharmacy, Seoul National University, 1 Gwanak-Ro, GwanakGu, Seoul 151-742, South Korea, Tel: +82 2135 5034; Email: abhi_biochem81@yahoo.in

Received: April 30, 2015; **Accepted:** May 11, 2015; **Published:** May 13, 2015

Editorial

Toxic reactive oxidative species (ROS) evoked by the induction of oxidative stress in the episodes of neurodegenerative disorders play the key role in neuronal cell death. As mitochondria are the prime source of reactive oxygen species (ROS), neurodegeneration misleads mitochondria for excessive production of ROS. In aging, neurodegeneration accelerates the process of mitochondrial dysfunction. Antioxidant therapy has been shown to exert beneficial effects in protecting brain cells against oxidative damage. However the application of free antioxidants is only effective at high doses as the blood-brain barrier (BBB) limits the passage of molecules from the circulation into the cerebral region and bioavailability becomes a major problem. Hence a suitable system is needed for effective delivery of molecules to the cerebral region.

The brain is vulnerable to oxidative injury because of its high rate of oxidative metabolic activity, intense production of reactive oxygen metabolites, high content of polyunsaturated fatty acids and low antioxidant capacity [1]. Oxidative damage of the brain has complex interactions with excitotoxicity, apoptosis and inflammation [2]. The imbalance between ROS generation and the levels of cellular antioxidants during oxidative stress deregulates the cellular functions and thus leads to various pathological conditions including metabolic dysfunction, neuro-degenerative diseases and premature aging. Oxidation of biomolecules like DNA, proteins and lipids plays a significant role in several age-related disorders. Peroxidation of membrane lipids due to the overproduction of ROS results in the loss of cell membrane integrity, impairment of the functions of membrane transport protein and ion channels, disruption of cellular ion homeostasis and concomitantly increases neuronal vulnerability to excitotoxicity [3]. In cerebral degenerative diseases, the rapid loss of ATP results in uncontrolled leakage of ions across the cell membrane, membrane depolarization and release of neurotransmitters like glutamate and dopamine. The excessive release of glutamate causes stimulation of its receptors and thus resulting in phospholipase activation, phospholipid hydrolysis and arachidonic acid release which ultimately lead to neuronal death. Reduction in reduced glutathione (GSH) level and consequent oxidative damage have been suggested as a major cause of apoptotic neuronal cell death [4]. Loss of GSH triggers the activation of neuronal 12-lipooxygenases, which leads to the production of peroxides, an influx of calcium and ultimately causes cell death [5]. The disturbances in mitochondrial structure and function play major role for the pathophysiological phenomenon in neurodegenerative diseases and in the mechanism of neurodegeneration among aged individuals [6-8]. The rate of ROS generation in mitochondria increases gradually with ageing [8,9]. Peroxidation of mitochondrial membrane lipids by ROS destabilizes the membrane structure that results in the release of apoptotic factors into the cytosol.

During pathogenic conditions, neuronal cells cannot counterbalance the hazardous effects of elevated ROS level and succumb to irreversible damage. Hence attempts with the application of exogenous antioxidants have made to protect neurons from oxygen free radical attack [10,11]. However most of the exogenous antioxidants are effective *in vitro* while they fail to show promising effects *in vivo* due to their poor bioavailability as a result of their inability to cross the BBB.Hence a delivery system is necessary especially for the brain to enhance the bioavailability and consequently the efficacy of exogenously applied antioxidants.

Nanoparticles (NP) are accepted as unique commercial delivery device because of its tendency to accumulate in the inflamed area of the body. Nanoparticles are efficient vehicles for drug delivery due to their small size, nontoxic nature, biodegradability, non-immunogenicity and sustained drug releasing ability in biological systems. A polymeric nanoparticle when targeted to brain provide better penetration and effective release of therapeutic agents of interest and offers a reduced risk in comparison to existing therapies [12]. Nanoencapsulation technology has proven benefits for their ability to cross the BBB as well as their nature to increase cellular drug concentration. The size of nanoparticles is important in determining their stability for drug release and cellular uptake efficiency [13]. Nanoparticles less than 100 nm in size have a higher potential to circulate in the blood for longer periods of time and experience reduced hepatic filtration [14]. Poly(lactic-co-glycolic acid) (PLGA) is known to be one of the most successfully developed biodegradable polymers [15]. PLGA-based nanoencapsulation of antioxidants can improve their therapeutic potential with proper intracellular delivery and prolonged circular retention time [16]. PLGA is non-toxic, biodegradable and biocompatible and has the ability to control the release of drugs from PLGA nanospheres.

The brain is one of the most challenging sites for drug delivery. Hence, the use of antioxidants in polymeric nanocapsules may prove to be the appropriate delivery vehicle for the brain and to serve as suitable drugs to combat ROS mediated neuronal damage. NPs are advantageous for drug delivery as their application decreases drug dose; reduce side effects and increases drug retention time. The enhancement of brain delivery obtained with drug-loaded NPs is very promising. However, further research is needed for assessing

Citation: Mukherjee A. Nanoencapsulated Polymeric Antioxidants in Combating Neuronal Oxidative Damage. Austin J Mult Scler & Neuroimmunol. 2015;2(3): 1015.

the suitability and efficacy of such delivery systems keeping in mind their harmful effects, if any. If successful, the approach may change the course of treatment for neurodegenerative disorders.

References

1. Evans PH. Free radicals in brain metabolism and pathology. Br Med Bull. 1993; 49: 577-587.
2. Warner DS, Sheng H, Batinić-Haberle I. Oxidants, antioxidants and the ischemic brain. J Exp Biol. 2004; 207: 3221-3231.
3. Mattson MP, Pedersen WA. Effects of amyloid precursor protein derivatives and oxidative stress on basal forebrain cholinergic systems in Alzheimer's disease. Int J Dev Neurosci. 1998; 16: 737-753.
4. Rodriguez RJ, Miranda CL, Stevens JF, Deinzer ML, Buhler DR. Influence of prenylated and non-prenylated flavonoids on liver microsomal lipid peroxidation and oxidative injury in rat hepatocytes. Food Chem Toxicol. 2001; 39: 437-445.
5. Schulz JB, Lindenau J, Seyfried J, Dichgans J. Glutathione, oxidative stress and neurodegeneration. Eur J Biochem. 2000; 267: 4904-4911.
6. Navarro A, Boveris A, Bandez MJ, Sanchez-Pino MJ, Gomez C, Muntane G, et al. Human brain cortex: mitochondrial oxidative damage and adaptive response in Parkinson disease and in dementia with Lewy bodies. Free RadicBiol Med. 2009; 46: 1574–1580.
7. Vosler PS, Graham SH, Wechsler LR, Chen J. Mitochondrial targets for stroke: focusing basic science research toward development of clinically translatable therapeutics. Stroke. 2009; 40: 3149-3155.
8. Lin MT, Beal MF. Mitochondrial dysfunction and oxidative stress in neurodegenerative diseases. Nature. 2006; 443: 787-795.
9. Toescu EC, Verkhratsky A. Neuronal ageing from an intraneuronal perspective: roles of endoplasmic reticulum and mitochondria. Cell Calcium. 2003; 34: 311-323.
10. Tasdemiroglu E, Chistenberry PD, Ardell JL, Chronister RB, Taylor AE. Effect of superoxide dismutase on acute reperfusion injury of the rabbit brain. Acta Neurochir (Wien). 1993; 120: 180-186.
11. Truelove D, Shuaib A, Ijaz S, Richardson S, Kalra J. Superoxide dismutase, catalase, and U78517F attenuate neuronal damage in gerbils with repeated brief ischemic insults. Neurochem Res. 1994; 19: 665-671.
12. Dikpati A, Madgulkar AR, Kshirsagar SJ, Bhalekar MR, Singh Chahal A. Targeted Drug Delivery to CNS using Nanoparticles. Journal of Advanced Pharmaceutical Sciences. 2012; 2: 179–191.
13. Kong LD, Zhang Y, Pan X, Tan RX, Cheng CH. Inhibition of xanthine oxidase by liquiritigenin and isoliquiritigenin isolated from Sinofranchetia chinensis. Cell Mol Life Sci. 2000; 57: 500-505.
14. Ghosh S, Dungdung SR, Choudhury ST, Chakraborty S, Das N. Mitochondria protection with ginkgolide B-loaded polymeric nanocapsules prevents diethylnitrosamine-induced hepatocarcinoma in rats. Nanomedicine (Lond). 2014; 9: 441-456.
15. Ghosh A, Sarkar S, Mandal AK, Das N. Neuroprotective role of nanoencapsulated quercetin in combating ischemia-reperfusion induced neuronal damage in young and aged rats. PLoS One. 2013; 8: e57735.
16. Lockman P1, Mumper RJ, Khan MA, Allen DD. Nanoparticle technology for drug delivery across the blood-brain barrier. Drug Dev Ind Pharm. 2002; 28: 1-13.

Austin J Mult Scler & Neuroimmunol - Volume 2 Issue 3 - 2015
Submit your Manuscript | www.austinpublishinggroup.com

Citation: Mukherjee A. Nanoencapsulated Polymeric Antioxidants in Combating Neuronal Oxidative Damage. Austin J Mult Scler & Neuroimmunol. 2015;2(3): 1015.