

SELENIUM ENRICHED MUSHROOMS AS A FOOD SUPPLEMENT FOR PREVENTION OF NEURODEGENERATIVE DISEASES

REX D. A. B.

Centre for Molecular Medicine and Therapeutics, PSG Institute of Medical Science and Research, Coimbatore, India.
Email: rexpem@gmail.com

Received: 20 Aug 2014 Revised and Accepted: 22 Sep 2014

A common feature of current biological science is inter-disciplinary research and collaboration. Herbal formulations, the base for traditional medicine, integrate both basic sciences and clinical medicine with the aim of developing natural drugs for preventive measure and care. Notably, in the area of neurodegenerative disorders, many basic and clinical researchers worldwide have joined forces to explore the interface between basic neurosciences and herbal research. This renowned International Journal of Pharmacy and Pharmaceutical science will provide a perfect platform at the global level to share knowledge and experience of the latest research and medicinal herbs on the epidemiology, etiology, pathogenesis, diagnosis, management and prevention of neurodegenerative diseases.

The term neuro degeneration (NDG) is a combination of two words - "neuro," referring to nerve cells and "degeneration," referring to progressive damage. Neurodegenerative diseases affect the central nervous system (brain, spinal cord) and peripheral nervous system [1]. They can cause progressive cognitive, sensory and/or motor dysfunction [2]. NDG can be applied to several conditions that result in progressive loss of neuronal structure, function and neuronal death which include diseases such as Alzheimer's disease and other dementias, Brain Malformations, Degenerative Nerve Diseases, Encephalitis, Epilepsy, Genetic Brain Disorders, Hydrocephalus, Stroke, Parkinson's Disease, Multiple Sclerosis, Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig's Disease), Huntington's Disease, Prion Diseases, and others [3].

Currently, over 25 million people worldwide suffer from neurodegenerative diseases. The World Health Organization (WHO) projects on neurodegenerative diseases will overtake one of a large number of diseases, 'cancer' as the world's second leading cause of death by the year 2040. WHO fears that by the year 2040 neurodegenerative diseases will become the world's second leading cause of death in the world. Data monitor estimates that the market for neurodegenerative disease treatments will be more than \$20 billion by 2014.

Indeed, several observations have emphasized the oxidative stress hypothesis for early onset and sporadic NGDs. A number of clinical trials in recent years have provided convincing evidence of the central role of selenium, either alone or in combination with other micronutrients or antioxidants, in the prevention and treatment of multiple diseases. Concrete reports on the role of trace elements in the pathology of NDGs in Indian population are lacking.

Selenium (Se) is an essential trace element, taken up by humans with their diet, where it occurs mainly as selenomethionine and selenocysteine. A complex cellular reaction cascade converts inorganic Se compounds to organic forms and vice-versa [4]. Se is incorporated into proteins as selenocysteine (Sec), Selenium is often called "the guardian of the genome" [5]. Se is a potent antioxidant and functions by being a component of various selenoproteins like Selenoprotein P, Glutathione Peroxidase, Selenoprotein H, Thioredoxin reductase etc. The form of se and selenoproteins was found in selenocysteine. Now we call this the 21st amino acid which is coded by UGA codon, originally serving as stop codon [6]. Se is an essential trace element that enters the food chain through

incorporation into plants from the soil. Se is mainly present in the form of selenite in acid soils, which is poorly assimilated by crops, whereas for alkaline soils, it is in the form of selenate, which is more soluble and assimilated by crops. When taken in supplement form, animal and human trials demonstrate that bioavailability of organic forms of selenium (Se-methionine and Se-cysteine) is higher than that obtained for inorganic forms (selenite and selenate). Selenium deficiency has been shown to increase protein oxidation in mice [7]. It act against toxic metals such as mercury and arsenic [8,9]. Though conflicting reports exists on the role of selenium in NDGs, selenium deficiency can lead to Parkinson's disease, epileptic seizures, osteoarthritis, cardiovascular disease, and infertility [10-12].

The brain is observed to retain selenium for its proper functioning. Selenoprotein P (SeP) is a highly glycosylated, selenium rich plasma protein. Aside from its role as selenium carrier protein, an antioxidative function of SeP has also been suggested. Astrocytes, which detoxify ROS in the brain were described as potential target cells of SeP [13]. Genetic inactivation of selenoprotein P in animal models leads to altered synaptic dysfunction in the hippocampus [14] and general neurological dysfunction [15]. Analysis of spatial distribution in postmortem brain tissues showed a significant association between amyloid- β plaques and selenoprotein P. Analysis of differentially expressed genes in transgenic AD mice carrying human mutant presenilin -2 showed that the selenoprotein M (SeM) had significantly suppressed in transgenic mice indicating a neuro protective role for this selenoprotein [16]. Selenoprotein H was found to protect neurons from UV induced damage by preventing superoxide formation [17]. Selenium is also reported to play a role in prevention of seizures [18].

Thus, selenium has a role in prevention of many NDG. Selenium is present in many traditional herbs and mushrooms. The traditional use of medicine is widespread and the plants used as a large constituted source of natural antioxidants that might lead for the novelty of development of new drugs. The use of traditional herbs and medicinal plants has been traced to the occurrence of natural products and their health. However, other phyto constituents could act as antioxidant defences against ROS.

Ascorbic acid (Vitamin C), Vitamin E, glutathione and carotenoids are examples of non enzymatic antioxidant defences [19]. Cu, Fe, Mn and Zn, and Se are most important beneficial elements which mostly bound to proteins and form metalloenzymes that also possess important antioxidant activities. In humans, these essential trace elements accomplish decisive functions to maintain human health. Deficiency originates by low levels of metalloproteins and/or low enzyme activities, which leads to undesirable pathological conditions that may be readily prevented or reversed by adequate supplementation with the missing element [20]. Medicinal herbs, especially mushrooms represent a major source of pharmaceutically active products. Most abundant Mushrooms genus *Albatrellus*, are abundant in selenium. *Bolete (Boletus edulis)* is considered rich in selenium. On average, it contains ~ 20 μ g Se/g dw (maximum up to 70 μ g/g dw). Some other relatively selenium rich mushrooms include the European Pine Cone *Lepidella (Amanita strobiliformis)*, which contains, on average, ~ 20 μ g Se/g dw (up to 37 μ g/g dw);

the *Macrolepiota* spp., with an average range of ~ 5 to < 10 µg/g dw (an exception is *M. rhacodes* with < 10 µg/g dw); and the *Lycoperdon* spp., with an average of ~ 5 µg Se/g dw. For several wild-grown species of the genus *Agaricus*, the selenium content (~ 5 µg/g dw) is much greater than that from cultivated Champignon Mushroom. A particularly rich source of selenium could be obtained from selenium-enriched mushrooms that are cultivated on a substrate fortified with selenium (as inorganic salt or selenized-yeast). The Se-enriched Champignon Mushroom could contain up to 30 or 110 µg Se/g dw, while the Varnished Polypore (*Ganoderma lucidum*) could contain up to 72 µg Se/g dw. Especially *Ganoderma lucidum* (*G. lucidum*) occur throughout the world and is being used as an effective supplement for many years to prevent and treat many diseases. Polysaccharides and triterpenes isolated from *G. lucidum* are reported to have antioxidant and anti-inflammatory function. The water extract and also the polysaccharides isolated from this mushroom shown to exhibit anti-tumor and immune modulatory effect. It also can act as a good source of essential micronutrients like selenium. An increasingly growing database on chemical forms of selenium of mushrooms indicates that the seleno-compounds identified in carpophore include selenocysteine, selenomethionine, Se-methylselenocysteine, selenite, and several unidentified seleno-compounds; their proportions vary widely [21].

Selenium is easily assimilated in the form of organo-selenium. It is reported that dietary factors influence the effective intake of selenium and when provided in the form of selenocystein and selenomethionine, it gets easily incorporated into the proteins. Under normal circumstances, dietary intake of selenium rarely exceeds the need for selenoenzyme synthesis. Hence, when given in the form of a food supplement, Se gets easily incorporated and assimilated. Mushrooms enriched with selenium could act as an effective source of the micronutrient and immunomodulant. It also contains many pharmacologically active compounds which not only provide an anti-inflammatory role but also act as an effective anti-oxidant. Being an edible medicinal herb, it can also be effectively used as a food supplement under the Dietary Supplement Health and Education (DSHEA) act (1994). Though many reports and supplements exist on Se-enriched mushrooms, information on its clinical validity is lacking. Evaluation of Se-enriched mushrooms as effective food supplement in prevention of NDGs could be taken as a topic for research, which would validate the role of these mushrooms as the potent source of antioxidant and anti-inflammatory compounds to prevent neurodegeneration.

REFERENCES

- Jellinger KA. Recent advances in our understanding of neurodegeneration. *J Neural Transmission* 2009;116 Suppl 9:1111-62.
- Swerdlow R, Wright D. Neurodegenerative disorders division overview-institute for neurological disorders. The University of Kansas; 2010.
- Brain and Neurological diseases-Health-EU Newsletter. European Commission Belgium; 2014.
- Ip C. Lessons from basic research in selenium and cancer prevention. *J Nutr* 1998;128:1845-54.
- Julius G Goepf. Selenium. All About Supplements Life Extension Magazine; 2006.
- Tujebajeva RM, Copeland PR, Xu XM, Carlson BA, Harney JW, Driscoll DM, *et al.* Decoding apparatus for eukaryotic selenocysteine insertion. *EMBO Rep* 2000;1:158-63.
- Moskovitz J, Stadtman ER. Selenium-deficient diet enhances protein oxidation and affects methionine sulfoxide reductase (MsrB) protein level in certain mouse tissues. *Proceedings National Academy of Sci USA* 2003;100 Suppl 13:7486-90.
- Yoneda S, Suzuki KT. Equimolar Hg-Se complex binds to selenoprotein P. *Biochem Biophys Res Communications* 1997;231 Suppl 1:7-11.
- Zeng H, Uthus EO, Combs GF Jr. Mechanistic aspects of the interaction between selenium and arsenic. *J Inorganic Biochem* 2005;99 Suppl 6:1269-74.
- Kurz B, Jost B, Schunke M. Dietary vitamins and selenium diminish the development of mechanically induced osteoarthritis and increase the expression of antioxidative enzymes in the knee joint of STR/1N mice. *Osteoarthritis Cartilage* 2002;10 Suppl 2:119-26.
- Ursini F, Heim S, Kiess M, Maiorino M, Roveri A, Wissing J, *et al.* Dual function of the selenoprotein PHGPx during sperm maturation. *Sci* 1999;285 Suppl 5432:1393-6.
- Krishnan S, Rani P. Evaluation of Selenium, Redox Status and Their Association with Plasma Amyloid/Tau in Alzheimer's Disease. *Biological Trace Elements Research* 2014;158:158-65.
- Bellinger FP, He QP, Bellinger MT, Lin Y, Raman AV, White LR, *et al.* Association of Selenoprotein P with Alzheimer's Pathology in Human Cortex. *J Alzheimers Disease* 2008;15 Suppl 3:465-72.
- Brenneisen P. Selenoproteins, ROS, and health aspects. *Research Monographs: UVB, oxidative stress, gene expression*; 2012.
- Hill KE, Zhou J, McMahan WJ, Motley AK, Burk RF. Neurological dysfunction occurs in mice with targeted deletion of the selenoprotein P gene. *J Nutr* 2004;134:157-61.
- Hwang DY, Cho JS, Oh JH, Shim SB, Jee SW, Lee SH, *et al.* Differentially expressed genes in transgenic mice carrying human mutant presenilin-2 (N141I): Correlation of selenoprotein M with Alzheimer's disease. *Neurochemical Res* 2005;30:1009-19.
- Jilani KEB, Panee J, He Q, Berry MJ, Li PA. Overexpression of selenoprotein H reduces Ht22 neuronal cell death after UVB irradiation by preventing superoxide formation. *Int J Biol Sci* 2007;3:198-204.
- Naziroglu M. Role of selenium on calcium signaling and oxidative stress-induced molecular pathways in epilepsy. *Neurochemical Res* 2009;34 Suppl 12:2181-91.
- Valko M, Leibfritz D, Moncol J, Cronin MT, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. *Int J Biochem Cell Biol* 2007;39:44-84.
- Fraga CG. Relevance, essentiality and toxicity of trace elements in human health. *Molecular Aspects of Medicine* 2005;26:235-44.
- Falandysz J. Selenium in Edible Mushrooms. *Journal of Environmental Science and Health, Part C: Environmental Carcinogenesis and Ecotoxicology Reviews* 2008;26 Suppl 3:256-99.