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Review Article

Neuronal Malady in Epileptic Brain – Amendment with Mushroom

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Abstract

Epilepsy is a neurological disorder of the central nervous system usuallay manifested through frequent seizures. Though epileptic symptoms had been recognized since ancient times, it could not be kept under control. Its treatment strategy varies from culture to culture and society to society. Modern medicinal approaches to withstand epileptic signs and symptoms are yet to become fully successful. Thus, alternative, easy to reach, cheap and traditional and complementary medicine-based anti-epileptic therapeutic approaches have reached momentum. Here, we report the distorted neuronal status in epileptic brain, its causes and remedy through culinary and medicinal mushrooms, the macrofungi. Both edible and medicinal mushrooms seem promising in keeping the neuronal normalcy and also in recovering the distorted neuronal health of the epileptic subjects as manifested through anti-oxidative and neuroprotective attributes as manifested by the amelioration of frequency and duration of the seizures of the mushroom fed epileptic subjects.

Keywords: Anti-oxidant; Epilepsy; mushroom; Neuron; Oxidative stress; Reactive oxygen species

Background

According to the world health organization (WHO), "epilepsy" is "a chronic noncommunicable disease of the brain that affects people of all ages and more than 50 million people have been suffering from epilepsy globally [1-2]. Thus, epilepsy stands among the topmost neurological diseases (ND) of the world [1-2]. Traits of epilepsy include recurrent seizures i.e. brief episodes of involuntary movement of the whole body (generalized epilepsy) or a part of the body (partial epilepsy) [3-5]. Recurrent neuronal discharge at different part of the brain provokes epileptic seizures that might accompany muscle jerking, attention deficiency and mild to extreme convulsions [3-5]. Very often, bowel and bladder function of the epileptic patient goes beyond his or her control [3-5]. Though, epilepsy is among the oldest characterized ailments of the world, social and ritual taboos hindered its treatment for the centuries [6]. Epidemilogical studies suggest that over 80% of the epileptic patients live in the under-developed and developing countries of whose more than 70% could live normalcy if properly diagnosed and treated [1-2,6]. Epileptic patients also suffer from associated physical and psychological as well as social complication [7-8]. Thus, combined therapeutic and psycho-social intervention could aid in enjoying normalcy to the epileptics.

Oxidative Stress, Neurodegeneration and Epilepsy

Aetiological information regarding epilepsy include, but not limited to, genetic, metabolic, infectious, immunologic, side effects of other diseases, head injury, trauma, stroke, brain tumor, hypoxia, encephalitis, septicemia and idiopathic mechanisms [8-9]. Among the known reasons behind epileptogenesis, reactive oxygen species

(ROS), deficiency of antioxidants, paucity of brain's own shield against oxidative stress (OS) have received recent momentum [10]. In neuronal and other cells, mitochondria provide energy in the form of ATP through oxidative phosphorylation of the electron transport system (ETS) [10-14]. Leakage of electron from ETS across the inner mitochondrial membrane could react with molecular oxygen (O2) and form super oxide radical (O2-). Superoxide dismutases converts O2- into H2O2 [10-14]. At the outer membrane of mitochondria, monoamine oxidase reduces O2 into H2O2 [10-14]. Antioxidant enzymes Catalase and glutathione peroxidase converts H2O2 into H2O and O2 [10-14]. At compromised neuronal level of the antioxidant enzymes, level of H2O2 skyrockets [10-14]. Divalent cationic (Fe2+, Cu2+) attack on H2O2 releases much potent free radical -OH that further oxidatively attck on cellular and neuronal macromolecules (DNA, protein and lipids) ultimately generating ROS and RNS (reactive nitrogen species) [10-14].

Brain is comparatively much prone to oxidative damage by ROS and RNS as its oxygen demand is high and mitochondria content is profuse to meet galore metabolic demand [15]. Additionally, seizures promote heightened production of ROS/RNS that cause oxidative damage to the brain biomolecules [16]. Curbing mitochondrial generation of excessive ROS has recently been implicated as an epilepsy withstanding mcechanism [11,17]. Even, OS has been reported to be independent of anti-epileptic drugs [11,17-19]. Excessive lipid peroxidation generated malondialdehyde (MDA) and lowered activity of anti-oxidant enzyme superoxide dismuatase (SOD) had been found in a case control study of epileptic patients. Thus, lipid peroxidation has presently been considered as a marker of OS in epilepsy [20]. OS in association with neuroinflammation, provoke epileptogenesis [15,21]. Based on these findings, antioxidant therapy has been considered as a protective measure against epilepsy [15, 22-24].

Mushroom as Anti-Epileptic Agent

Oligosaccharide isolated from the ling zhi or reishi mushroom (Ganoderma lucidum) had been found to be neuroprotective and convulsion thwarting in experimentally induced epileptic rats [25]. Ingestion of G. lucidum spore powder for eight weeks (dosage: 1000 mg daily, 3 times) significantly reduced the frequency of weekly seizure in epileptics [26]. Anti-epileptic effect of G. lucidum polysaccharide had been linked with downregulation of intra-neuronal Ca2+accumulation along with upregulation of the Ca2+/ calmodulin-dependent protein kinase II (CaMK II) expression in the hippocampi of the experimentally induced epileptic rats [27].

Mushroom polysaccharides could be thought of as the future prospective candidate for the treatment of epilepsy [28]. This speculation is based on the observation that polysaccharides isolated from edible and medicinal mushrooms had been found capable of regulating neurotransmission, neuroinflammation, neuronal ion-channel activity, immunomodulation, antioxidative support as well as growth and development of gut microbiota [29-32]. Aqueous extract of G. lucidum had been reported in inhibiting pentylenetetrazole (PTZ) induced and maximal electroshock (MES) induced convulsion in rats along with hippocampal increased level of gamma amino butyric acid (GABA) [33]. This anti-epileptic effect had been attributed to the tri-terpenes and phenolics especially the flavonoids present in the aqueous extract of G. lucidum [33]. Mechanistically, biocomponents of G. lucidum might have blocked the GABAA receptors and/or thalamic T-type Ca2+ channels and thus ameliorated onset and duration of epileptic seizures in the PTZ-induced epileptic rats [33].

Ganoderma curtisii had been found anti-convulsive and neuroprotective in the kainic acid administered epileptic rats [34]. Normally, kainic acid (KA) causes epileptic seizures and hippocampal and cortex neuronal death through apoptosis triggered by the activation of transduction factors caspase-3, Bcl-2, and Bax. Ganoderma curtisii soluble polysaccharide protected the hippocampus and cortex neurons against KA-induced excitotoxicity [34]. In addition, G. curtisii soluble polysaccharide prevented the increase of KA-induced Bcl-2 levels [34]. Similar neuroprotective effect in the pilocarpine-induced status epilepticus (SE) mice had been observed in case of Hereicium erinaceus. Both the level of cyclo-oxygenase 2 (COX 2) in the hippocampi and death of hippocampal neurons were reduced in the H. erinaceus treated SE mice [35]. Pediatric patients treated with Lentinula edodes mycelia had been found improving in refractory epilepsy along with improved immunological condition such as elevated level of serum IgG, CD3, CD4 and CD20 lymphocytes [36]. Aqueous extract of the ear mushroom (Auricularia polytrica) had demonstrated clonic seizure ameliorating effect on the maximal electroshock (MES) and isoniazid (INH)–induced epileptic model mice signinicantly at a dose dependent manner (400 and 600 mg/kg bodey weight) [37].

Conclusion

Epilepsy has been plaguing the humanity since ancient times. Mushroom-based nutritive and prophylactive support to the epileptic patients could be an alternative therapeutic approach in withstanding the global epileptic burden. Thus, efficacy and safety study of the mushroom nutraceuticals and biocomponents on the epileptic patients at large scale seem pertinent.

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Conflict of Interest

Authors declare no conflict of interest.

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