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Curcumin Promotes Neuronal Health

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Abstract

In this Asian diet comprises of several spices which contain medicinal properties that may be useful for a healthy life and wellness of the individual. Use of natural ingredients such as curcumin, which is an ingredient found in turmeric, shows promises in therapy of different chronic diseases. Curcumin is widely used as a spice, food additive as well as rejuvenator of skin lesions in India and other Asian countries. Curcumin is known to produce therapeutic benefit in cancer, inflammatory diseases etc. The mechanism by which curcumin can reduce microglial inflammation is still not understood completely. Neurodegenerative diseases are caused by different factors including neuroinflammation. The cellular mediators which trigger the inflammation are primarily secreted by the microglial cells (the supporting cells of neuron). Acute inflammation could promote immunologic responses and protect any cellular damage. A prolonged chronic inflammatory response could be damaging to the cells and are characterized by continuous secretion of mediator molecules such as inflammatory interleukins and cytokines by genetic regulation. Different chemical interventions are applied to regulate such scenario to regulate cellular damage, but with limited success in promoting neural health. This review is trying to summarize the novel mechanism of curcumin in promoting neural health in neurodegenerative diseases by diminishing inflammatory reactions.

Introduction

Curcumin, an ingredient found in turmeric is widely used as spice, food additive as well as a rejuvenator of skin lesions in different parts of the world, primarily in India and other south Asian countries. Recent molecular studies have shown that curcumin produces enormous therapeutic benefits in different types of cancer, inflammatory diseases, skin lesions etc. (Somasundaram et.al., 2002; Tiwari et.al., 2016; Vollono et.al., 2019;). Studies have shown positive impact of curcumin in maintaining a healthy brain function as well (Chongtham et.al., 2016). Curcumin has been used as a potent anti-inflammatory agent in ayurvedic medicine (traditional Indian medicine) as well. This is also traditionally applied to cure various skin diseases and joint pain as well. Daily consumption of curcumin

boosts immune power which is critical to fight against different microbial diseases including Covid-19 and other emerging diseases. All this goodness of curcumin was known for ages in certain parts of the world. However, scientists were trying to enhance the bioavailability of curcumin, which is currently highly variable in every individual. Some isoforms of curcumin are now developed by different pharmaceutical companies which exhibit higher potency and increased bioavailability; this is very promising. Various clinical trials around the world are underway to show the potency of curcumin in different ailments. Scientific advancement has established and proposed different mechanisms by which curcumin could be effective in chronic diseases such as arthritis, cancer, and brain diseases.

Different brain disorders including neurodegenerative diseases, dementia, post-traumatic stress disorders (PTSD), amylotropic lateral sclerosis (ALS), autism, various aging related symptoms are rapidly increasing in today's world due to our lifestyle, lack of proper nutrition and consuming unhealthy diet (Gooch et.al., 2017). Neurodegenerative diseases are often characterized by oxidative stress induced damages and genetic mutations and patients often suffer with various cognitive disorders and dementia. This situation is becoming severe, and therefore it is crucial to define some preventive strategies which can overcome such outcomes.

Curcumin and its positive impact on human ailments have long been reported form older scriptures and evidence. But, only recently molecular and clinical studies have been performed to intersect the impact of curcumin in disease models and in human trials.

Neurodegenerative diseases are caused by different factors including neuroinflammation. The cellular mediators which trigger the inflammation are primarily secreted by the microglial cells (the supporting cells of neuron). Acute inflammation could promote immunologic responses and protect any cellular damage. Contrarily, a prolonged chronic inflammatory response could be damaging to the cells and are characterized by continuous secretion of mediator molecules such as inflammatory interleukins and cytokines by genetic regulation (Porro et.al., 2019). Different chemical interventions are applied to regulate such scenario to regulate cellular damage, but with limited success in promoting neural health. Use of natural ingredients such as curcumin, shows promises in therapy of different chronic diseases. Porro (2019) reported that curcumin

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could be a potential therapeutic for preventing individuals from getting neurodegenerative disorders. Scientists also identified a novel mechanism by which curcumin could lower the microglial inflammation in neurodegenerative disorders. It is hypothesized that nutritional intervention by curcumin could be useful to promote neural health by regulating the inflammation in brain diseases. Investigators mimicked neurodegenerative like syndromes in a microglial cell line followed by treating those cells with curcumin. Disease specific clinically relevant hallmarks associated with inflammation were found to be significantly reduced after curcumin treatment. Many of these hallmarks are relevant in a patient suffering from neurodegenerative disease.

Nguyen (2018) genetically engineered the mutations critical to Parkinson's disease in drosophila (house fly), which generates oxidative damage. It is to be noted that Parkinson's and other neurodegenerative diseases produces extreme oxidative damage which has a negative impact on neuronal health. They have shown that curcumin could reduce this oxidative damage by decreasing the level of reactive oxygen species and enhanced the locomotive abilities in the flies, which could be correlated to the cognitive abilities in human being. Cognitive abilities are often found to be reduced drastically with development of neurodegeneration.

Small and group (2018) in their study proven the effectivity of a bioavailable form of curcumin in improving brain condition in some non-demented adults. The purpose of this research is to show whether curcumin could enhance cognitive abilities in normal individuals in the age group of 50-90. This is interesting that the age group 50-90 is also the vulnerable group which may suffer from neurodegenerative diseases. Many neurodegenerative diseases tend to develop dementia in the patients.

Based on several previous studies, the authors have hypothesized that long term cognitive effects could be significantly elevated by consumption of curcumin. individuals were selected for this study (out of 259 volunteers) and out of that 21 individuals received curcumin and 19 individuals were given placebo, as a control group. The selections were made after randomization. The treatment was followed up for 18 months and the subjects were undergone different cognitive analyses, genetic analyses, and PET scan by the end of the study. The baseline data were obtained prior to administration of the drug and placebo. All subjects provided consent in accordance with the regulations set by University of California, Los Angeles (UCLA), human subjects protection committee. Curcumin treated group showed significantly higher verbal memory compared to placebo treated group, whereas visual memory was not significantly up in curcumin treated group. The study outcome also showed that curcumin consumption may lead to less neuropathological accumulation in the amygdala and hypothalamus. Both amygdala and hypothalamus play important role in memorization, decision making and emotional responses (Small et.al., 2018).

Curcumin can enhance the cognitive responses according to the findings by Small (2018), however Ringman (2012) were unable to find a significant change in the Alzheimer's patients (mild to moderate) treated with curcumin for 6 months. These findings were negative and showed reduced bioavailability in these patients as well. To overcome the issues associated with bioavailability different preparations of curcumin are tried by different investigators. Hishikawa (2012) studied the impact of curcumin in Alzheimer's patients and found significant improvement in the patients after one year of treatment. The findings were mostly related to behavioral changes which are an important aspect in Alzheimer's disease.

Tiwari (2016) have successfully proved that curcumin is able to rescue bisphenol impaired neurogenesis in vitro and in vivo model which strongly suggests that curcumin is a potent agent to treat various neurological disorders. Wang (2017) have demonstrated that curcumin activates wnt-beta catenin pathway to protect the brain from oxidative stress induced damage in rat model of Parkinson's disease.

Although low bio availability of curcumin has stalled its progress to be translated as a cure for many neurological diseases, as per Kuunumakkara (2019) the safety range of curcumin can overpower the lower bioavailability of curcumin. Many studies were designed to support this notion as well, Gupta et al (2017) have reported that higher concentration of curcumin can inhibit adipogenesis and dyslipidemia and can significantly increase gastrointestinal stability. Chemists tried to increase the impact of curcumin using nanoparticles fused curcumin molecules which could be potentially make better impact by crossing blood brain barrier and can enhance therapeutic benefits in neurological disorders (Prado-Audelo et.al. 2019).

Neurological diseases are difficult to diagnosis in early stages and only be confirmed in advanced stage when the patient develops non-specific symptoms which relate to brain diseases. According to Gooch (2017) approximately 100 million Americans were suffered by some sort of neurological disorders and almost \$800 billion spent per year for the treatment for such diseases.

From a patient's perspective, a neurological disease is always complicated due to lack of proper diagnosis and is often misdiagnosed due to non-specific symptoms and unavailability of biomarkers. In a recent study conducted by Felgin (2019) it is reported that neurological diseases all together contribute to 9 million deaths worldwide along with an increasing disability-adjusted life years. Changes in lifestyle related factors can make differences in well-being of the individual and contribute towards less severe symptoms.

The impact of regular usage of curcumin to yield prevention against neurodegenerative diseases is well proven and traditionally applied as a seasoning agent in Indian cuisine. This report summarizes the scientific advancement on immunomodulating effects of curcumin and suggests everyone to consider curcumin in daily consumption for a improving neuronal health.

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