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USE OF CURCUMIN IN PARKINSON'S DISEASE

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ABSTRACT

Parkinson's disease an age-associated slowly progressive neurodegenerative disease clinically characterized as a movement disorder. The motor symptoms in PD arise due to selective degeneration of dopaminergic neurons in the substantia nigra of the ventral midbrain thereby depleting the dopamine levels in the striatum. In recent years increasing evidence supports the pharmaceutical potential of curcumin against Parkinson disease.[1]

Curcumin is a polyphenol and an active component of turmeric (Curcuma longa), a dietary spice used in Indian cuisine and medicine. Curcumin exhibits anti-oxidant, anti-inflammatory , crosses the blood-brain barrier . Previous studies reported the neuroprotective properties of curcumin in in vitro and in vivo Parkinson's disease models induced by several different environmental factors such as neurotoxins and genetic factors including α-synuclein, PINK1, DJ-1, and LRRK2.[2]

This article reviews the therapeutic potential of curcumin in PARKINSON'S disease.

INTRODUCTION

Now a days with the increasing ageing population of the world, incidence of neurological disorders have increased simultaneously. Which led to increase a major burden in healthcare system. One of the common increasing neurological disorder these days is Parkinson's Disease. It is clinically manifested as movement disorder. Parkinson's disease was first described in 1817 by the scientist named James Parkinson's. This syndrome shows multiple physical signs such as rigidity, imbalance of body posture, bradykinesia and resting tremor. Parkinson's disease is characterized as the successive loss in the dopamine level of brain or neurons of brain in substantia nigra .[3] Substantia nigra is located at ventral mid brain which results in decreased dopamine at the striatum. At present both pharmacological and surgical remedies are available for the treatment. It also includes some non motor symptoms such as depression . The pharmacological drug such as levodopa has distinctive side effects such as delay in motor function and dyskinesia , however Levodopa is required drug for the relief of symptomatic effects but they do not effectively tackle tremor, poustural disbalance and cognitive effects. Most significantly, these therapies are protective against dying of neurons and to prevent further loss of neuron .[4] The Modern medications are very commonly used and are more likely to cause defects such as dysfunction of mitochondria, protein aggression and neuro inflammation which target multiple pathways. Therefore more herbal products are preferred as they cause less / no side effects and help for the treatment of Parkinson's disease. One of such product is curcumin (turmeric). It has properties like antioxidant , anti inflammatory and anti cancer, it easily crosses blood brain barrier and shows neuroprotective properties . Herbal products having photo chemicals are being extensively explored as they possess highly beneficial medicinal properties.[5]

METHODOLOGY

Curcumin exhibits antioxidant, anti-inflammatory and anti-cancer properties, crosses the blood-brain barrier and is neuroprotective in neurological disorders.

In therapeutic medicine, researchers found that turmeric may protect the nervous system from the toxins involved in causing the nervous system degeneration in Parkinson's disease.[6]

Human studies of curcumin's pharmacokinetics yielded results that were similar to those obtained from animal studies. Because of its poor absorption, curcumin has a low bioavailability in plasma and tissues, rapid hepatic metabolism, as well as rapid systemic elimination through the gut with a peak human plasma level of 0.41–1.75 µmol/L after the oral administration of 4–8 g of curcumin. Many studies have shown that curcumin is primarily metabolized in the liver, where it undergoes extensive reduction via alcohol dehydrogenase, followed by glucuronate and sulfate conjugation. Furthermore, Perkins and colleagues reported that humans require a daily dose of 1.6 g curcumin to achieve the desired results.[7]

Various formulations have been developed to improve curcumin bioavailability. Nano curcumin, for example, was developed to improve curcumin solubility in an aqueous solution. Polylactic-co-glycolic acid and liposomal-formulated curcumins improved water solubility of the compound. In regards to curcumin permeability, cyclodextrin encapsulated curcumin improved curcumin permeability compared to unformulated curcumin. Concomitant administration of piperine with curcumin significantly reduced elimination and half-life clearance of curcumin . Alginate–curcumin nanoparticles , glyceryl mono-oleate nanoparticles loaded with piperine and curcumin,curcumin-loaded lactoferrin nanoparticles , and curcumin-loaded polysorbate 80-modified cerasome nanoparticles,are different preparations developed to maximize curcumin bioavailability.[8]

Using midbrain slice cultures – laboratory cellular models that mimic brain activity , the team analysed the effects of a natural form of aromatic turmerone and eight structurally similar

derivatives. They tested the derivatives' anti-inflammatory effects, as well as their ability to protect dopamine-producing neurons.

Those with the strongest anti-inflammatory effects were found to prevent the loss of dopamine-producing neurons. Among these were aromatic turmerone and its derivatives, suggesting their role as a "potential candidate for treating Parkinson's disease".

Their findings support the known properties of aromatic turmerone , a compound found in turmeric essential oil, which helps in reducing inflammatory responses caused by cells associated with Parkinson's-related neurodegeneration.[9]

The study, "Aromatic-turmerone analogs protect dopaminergic neurons in midbrain slice cultures through their neuroprotective activities," was published in the journal Cells by researchers in Japan.

By measuring the amount of curcumin transferred from the blood to nerve cells in the brain following intravenous injection, we can determine optimal dosages for each of the three formulations.

Curcumin is unique in its multiple actions in protecting dopamine neuronal loss through regulating enzymes breaking down dopamine and hitting multiple signals and genes "turned off or off ". Curcumin also reduces inflammation. Curcumin formulations can be the novel frontier in Parkinson's disease therapeutics.

Curcumin has been shown to protect cells from damage caused by oxidative stress. We hypothesized that curcumin, which has potent antioxidant activity, may reduce Reactive Oxygen Species levels induced by Drosophila Ubiquitin carboxyl terminal hydrolase knockdown in brain. As expected, curcumin reduced Reactive Oxygen Species levels induced by Drosophila Ubiquitin carboxyl terminal hydrolase knockdown.[10]

Treatment with curcumin did not affect the ability of the larvae to consume food. Locomotor deficit due to specific Dopaminergic neuronal destruction in Drosophila Ubiquitin carboxyl

terminal hydrolase corrected with curcumin treatment. Curcumin therapy reduces neuro-dopamine degeneration by the knockdown Drosophila Ubiquitin carboxyl terminal hydrolase in Larvae. High doses in excess of the recommended daily dose may cause nausea, headache, or stomach upset.[11]

FUTURE SCOPE

1.A compound naturally found in turmeric essential oil, called aromatic turmerone (ar-turmerone), and its derivatives were seen to protect dopaminergic neurons in a tissue culture model of Parkinson's so it may offer new ways of treating the disease.

• Three of the derivatives were found to have stronger anti-inflammatory effects : (R)-ar-turmerone (R-Tur), ar-atlantone (Atl), and analog 2 (A2).

• Analog 2 was more worth advancing into animal studies as a potential, oral dopaminergic neuroprotective agent for Parkinson's disease, the researchers wrote.

2. Novel approaches to improve the bioavailability followed by pre-clinical and clinical investigations of curcumin application as an adjunctive therapy along with dopamine therapies such as Levodopa are required for successful application of curcuma therapy in Parkinson's disease.

3. Development of pro drugs such as the di-glutamoyl derivative with improved uptake and better radical scavenging properties could combat oxi-dative and nitrosative stress in Parkinson's disease.

4. In one of the researches it indicated that curcumin formulations composed with liposomes, acrylic polymers, and poly D,lactic-co-glycolic acid. A injected intravenously cross the blood brain barrier. The novel observations of curcumin

localization in specific brain sites at concentrations known to induce neurogenesis and neuroplasticity support clinical applications of site-specific diseases.

5. The recent development of highly bioavailable forms of curcumin as BioCurc® now permits its full therapeutic potential to be determined.

6. Nutraceutical application of curcuminoids has high potential to increase in the society.[12]

DISCUSSION

Turmeric is a spice used in traditional Indian cuisine and medicine with antioxidant, anti-inflammatory, and potential neuroprotective properties. To study the neuroprotective properties of turmeric in Parkinson's disease, rats were given a dietary supplement with an aqueous suspension of turmeric simulating continuous ingestion for 3 months and then in vivo induced 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine. Brain samples from the untreated and treated groups were characterized by mitochondrial complex activity, protein nitration, and tyrosine hydroxylase immunoreactivity.

Turmeric extract is a great supplement for overall brain health and can help boost antioxidant activity and reduce inflammation.

Recommended Dosage of over-the-counter medications contain 150-250mg of curcumin per serving, which is usually a safe starting point. Turmeric is a powerful anti-inflammatory and antioxidant agent that can cause significant positive changes in the body. Its ability to reduce inflammation may help people with Parkinson's disease manage some of the symptoms of stress. Previous research has also shown that curcumin is beneficial for promoting brain health, and may also be helpful in treating other neurological disorders such as Alzheimer's and dementia. Because of this, researchers believe that turmeric may have potential benefits in Parkinson's disease.

CONCLUSION

Parkinson disease is a progressive nuerogenerative movement disorder which is characterized by the loss of dopaminergic nuerons and deficiency of dopamine.

Curcumin are the natural compound which has a large variety of therapeutic properties in particular interactions and biological targets which are linked to numerous disease.

Curcuminoids is a nueroprotective agent with iron chelating properties, mitochondrial properties, anti-inflammatory, which enhances the Dopamine levels in the brain and can cross the Blood brain barrier and produce nueroprotective effects, But unfortunately the clinical applications of circumin are restricted by low absorption, high metabolism rate, bioavailability and poor solubility to overcome these limitation the derivatives of curcumin have been modified and attached to nanoparticles, lipids and Michelles.

Curcumin is also a polyphenol, inexpensive and also easily accessible nontoxic bioactive compound, with minimal reported toxicity as demonstrated in both in vitro and in vivo studies in Parkinson's disease, curcumin could have a significant therapeutic implications.

Hence the evidence reviewed supports that curcumin is a powerful molecular and cellular effects in nuerogenerative disorder as a strategy for improving the Parkinson's disease condition, prognosis and management.

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