

The effect of curcumin (turmeric) on Alzheimer's disease: An overview

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Abstract

This paper discusses the effects of curcumin on patients with Alzheimer's disease (AD). Curcumin (Turmeric), an ancient Indian herb used in curry powder, has been extensively studied in modern medicine and Indian systems of medicine for the treatment of various medical conditions, including cystic fibrosis, haemorrhoids, gastric ulcer, colon cancer, breast cancer, atherosclerosis, liver diseases and arthritis. It has been used in various types of treatments for dementia and traumatic brain injury. Curcumin also has a potential role in the prevention and treatment of AD. Curcumin as an antioxidant, anti-inflammatory and lipophilic action improves the cognitive functions in patients with AD. A growing body of evidence indicates that oxidative stress, free radicals, beta amyloid, cerebral deregulation caused by bio-metal toxicity and abnormal inflammatory reactions contribute to the key event in Alzheimer's disease pathology. Due to various effects of curcumin, such as decreased Beta-amyloid plaques, delayed degradation of neurons, metal-chelation, anti-inflammatory, antioxidant and decreased microglia formation, the overall memory in patients with AD has improved. This paper reviews the various mechanisms of actions of curcumin in AD and pathology.

Keywords: Alternative approach to Alzheimer's, beta amyloid plaques, curcumin, curcumin and dementia, epidemiology, turmeric

Curcumin

Curcumin (*Curcuma longa* - Haldi) is the source of the spice Turmeric [Figure 2] and is used in curries and other spicy dishes from India, Asia and the Middle East. Similar to many other herbal remedies, people first used curcumin as a food and later discovered that it also had impressive medicinal qualities. It has been used extensively in Ayurveda (Indian system of Medicine) for centuries as a pain relieving, anti-inflammatory agent to relieve pain and inflammation in the skin and muscles. It has also proven to have anti-cancer properties.[4,5] Curcumin holds a high place in Ayurvedic medicine as a “cleanser of the body,” and today, science is finding a growing list of diseased conditions that can be healed by the active ingredients of turmeric.[6]

Curcumin and Alzheimer's Disease

Worldwide, there are over 1000 published animal and human studies, both *in vivo* and *in vitro* in which the effects of curcumin on various diseases have been examined. Studies include epidemiological, basic and clinical research on AD.

Effects of Curcumin on Macrophages

A study conducted at UCLA found that curcumin may help the macrophages to clear the amyloid plaques found in Alzheimer's disease. Macrophages play an important role in the

immune system. They help the body to fight against foreign proteins and then effectively clear them. Curcumin was treated with macrophages in blood taken from nine volunteers: six AD patients and three healthy controls. Beta amyloid was then introduced. The AD patients, whose macrophages were treated with curcumin, when compared with patients whose macrophages were not treated with curcumin, showed an improved uptake and ingestion of the plaques. Thus, curcumin may support the immune system to clear the amyloid protein.[11]

Curcumin as an Anti Inflammatory in Alzheimer's

One of the important pathogenesis in Alzheimer's disease is the chronic inflammation of nerve cells. Several studies have demonstrated the associated inflammatory changes such as microgliosis, astrocytosis and the presence of pro-inflammatory substances that accompany the deposition of amyloid- β ($A\beta$) peptide. Patients with the prolonged use of certain nonsteroidal anti-inflammatory (NSAID) drugs such as ibuprofen have been shown to have a reduced risk of developing the symptoms of AD; however, the chronic use of NSAID can cause a toxic effect on the kidneys, liver and GI track. Curcumin has a potent anti-inflammatory effect. Through its various anti-inflammatory effects, it may have a role in the cure of AD. Curcumin inhibits $A\beta$ -induced expression of Egr-1 protein and Egr-1 DNA-binding activity in THP-1 monocytic cells. Studies have shown the role of Egr-1 in amyloid peptide-induced cytochemokine gene expression in monocytes. By inhibition of Egr-1 DNA-binding activity by curcumin, it reduces the inflammation. The chemotaxis of monocytes, which can occur in response to chemokines from activated microglia and astrocytes in the brain, can be decreased by curcumin.[13,14]

Curcumin is found to inhibit cyclooxygenase (COX-2), phospholipases, transcription factor and enzymes involved in metabolizing the membrane phospholipids into prostaglandins. The reduction of the release of ROS by stimulated neutrophils, inhibition of AP-1 and NF-Kappa B inhibit the activation of the pro-inflammatory cytokines TNF (tumor necrosis factor)-alpha and IL (interleukin)-1 beta.[15,16] Overall, curcumin decreases the main chemical for inflammation and the transcription of inflammatory cytokines. Curcumin inhibits intracellular IL-12 p40/p70 and IL-12 p70 expression. The exposure to curcumin also impaired the production of pro-inflammatory cytokines (IL-1, IL-6 and TNF-). These studies indicate a potent inhibitor of pro-inflammatory cytokine production by curcumin and it may differ according to the nature of the target cells

Curcumin as an Anti-oxidant

Curcumin inhibits the activity of AP-1, a transcription factor involved in expression of amyloid, which is linked to AD. Curcuminoids are proven to have strong antioxidant action demonstrated by the inhibition of the formation and propagation of free radicals. It decreases the low-density lipoprotein oxidation and the free radicals that cause the deterioration of neurons, not only in AD but also in other neuron degenerative disorders such as Huntington's and Parkinson's disease.[16] In one study, curcuma oil (500 mg Kg(-1) i.p.) was given 15 min before 2 h middle cerebral artery occlusion, followed by 24 h reflow in rats. This significantly diminished the infarct volume, improved neurological deficit and counteracted oxidative stress.[17]

A study conducted at Nanjing Medical University (China) showed that a single injection of curcumin (1 and 2 mg/kg, i.v.) after focal cerebral ischemia/reperfusion in rats significantly diminished the infarct volume, improved neurological deficit, decreased mortality and reduced the water content in the brain.[18]

Curcumin has powerful antioxidant and anti-inflammatory properties; according to the scientists, these properties believe help ease Alzheimer's symptoms caused by oxidation and inflammation.[19] A study conducted at Jawaharlal Nehru University (India) demonstrated that the administration of curcumin significantly reduced lipid peroxidation and lipofuscin accumulation that is normally increased with aging.[20] It also increased the activity of superoxide dismutase, sodium-potassium ATPase that normally decreased with aging. In another study, curcumin has been shown to protect the cells from betaA (1-42) insult through antioxidant pathway.[21] Curcumin protects brain mitochondria against various oxidative stress. Pre-treatment with curcumin protects brain mitochondria against peroxynitrite (a product of the reaction of nitric oxide with superoxide) a potent and versatile oxidant that can attack a wide range of cells *in vitro* by direct detoxification and *in vivo* by the elevation of total cellular glutathione levels.[22]

Cholesterol Lowering Effect

High-fat diets and increased blood cholesterol are linked to increased amyloid plaques by the intracellular accumulation of cholesteryl esters.[37] Researchers believe that by inhibiting cholesterol formation and decreasing serum peroxides, curcumin might exert beneficial effects on AD.[38]

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