

## Review Article

# The Effects of Turmeric on Alzheimer's Patients

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## Abstract

Turmeric, also known as *Curcuma longa*, is growing in popularity across the globe due to its countless historically recognized benefits to human health. People are incorporating this spice in one way or another into their diets because of the positive impacts it is known for. In many clinical aspects, this spice has proved to heal and show positive results in various types of illnesses amongst patients. Most importantly, turmeric is known for its crucial roles in the ancient Indian practice of Ayurveda medicine, also known as homeopathic medicine in the western world. Alzheimer's disease (AD), an irreversible type of dementia that causes patients to have problems with their memory and behavior, is one of the leading causes of death in the United States of America. When comparing the statistics of AD related deaths in the United States to Asian countries, the numbers are quite high. With

turmeric being one of the key ingredients in Asian foods, a potential correlation between Alzheimer's disease and the consumption of turmeric may be the reasoning behind the low deaths related to AD. Related studies were explored to examine the benefits of turmeric and its role in prevention of Alzheimer's disease.

**Keywords:** Alzheimer's Disease; Turmeric; *Curcuma Longa*

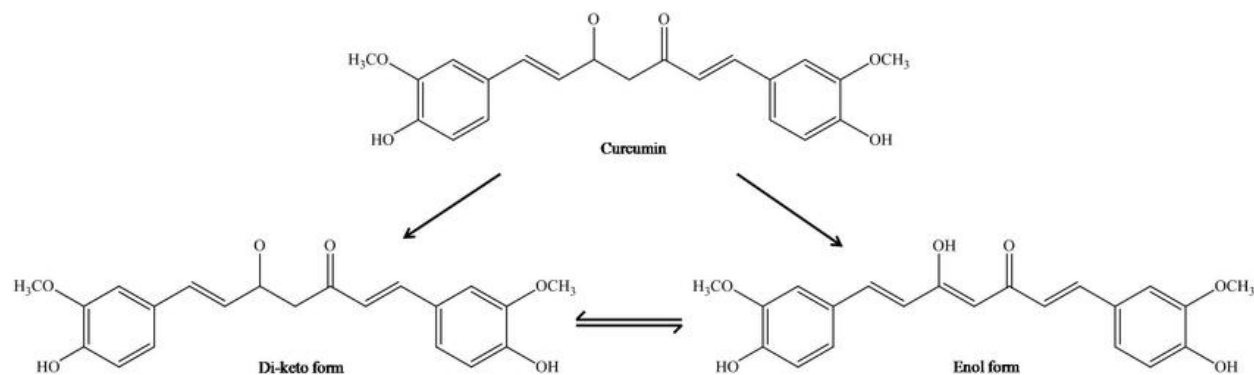
## 1. Introduction

### 1.1 Turmeric

Turmeric is the most common, and yet the oldest spice known for its role in foods of many Asian recipes. This herbal spice is not only used in Asian foods, but also in the form of medicine. Turmeric is derived from the

rhizome of *Curcuma longa*, which contains the beneficial properties like anti-inflammatory and antioxidant. Does *Curcuma longa* in turmeric help prevent Alzheimer's disease? Through the exploration of what the herbal spice is, its history, role in homeopathic medicine, and its potential use in the fight against Alzheimer's, this review paper's intention is to find the crucial role *Curcuma longa* plays in preventing Alzheimer's disease. Turmeric, also called *Curcuma longa*, is a plant that is a member of the Zingiberaceae, or also known as the ginger family [1]. It also comes in a powder form that is derived from the herb root of *Curcuma longa* [2]. Turmeric is better known for its value in the ability to maintain freshness in Asian foods [1]. Turmeric is commonly used in food dye as well as curry powder [1]. Most importantly, turmeric is known for its crucial roles in the ancient Indian practice of

Ayurveda medicine, also known as homeopathic medicine in the western world [1]. Turmeric extracts consist of curcumin, demethoxycurcumin, and bisdemethoxycurcumin, also known as curcuminoids [3]. Curcumin stems are extracted from the dried rootstock of *Curcuma longa* that are beneficial in Chinese and Indian medicine [3]. It is the most active component in turmeric and makes up between two and five percent of the spice [4]. Despite the different variations of the spice, they all play an important role in medicine. Many benefits have been studied behind the commonly used spice in regard to human health. Turmeric is known to have antioxidant, anti-inflammatory, and cholesterol-lowering properties that are significant to the pathogenesis of Alzheimer's disease [2].



**Figure 1:** Chemical structure of curcumin in Enol and Keto Form. Adapted from 'Curcumin and its Derivatives: Their Application in Neuropharmacology and Neuroscience in the 21<sup>st</sup> Century' [5].

In the chemical structure of Curcumin, Enol and Keto forms of the chemical are shown. This displays the tautomer relationship between the two forms, which show the molecules with the same molecular formula, but with different isomers that can interconvert in equilibrium.

## 1.2 Alzheimer's disease

Alzheimer's disease (AD) is a type of dementia that causes patients to have problems with their memory and behavior. It involves a chronic central nervous system inflammatory response that is associated with beta amyloid pathology. Patients affected by AD are unable to perform simple daily life activities, which makes it harder for them to go about their daily lives.

Alzheimer's Disease severely impacts the elderly. The most common and simple tasks to Alzheimer patients may seem difficult and frustrating. The pathophysiology of AD results in the gradual aggregation of amyloid peptides as well as Tau proteins in the brain that form neurofibrillary tangles and are highly toxic to the brain's neuronal pathways [6]. This ultimately leads to the deficiencies in the cholinergic and acetylcholine systems [6]. According to the World Health Organization, both men and women above the age of sixty can be a victim of this deadly disease [7]. Statistics show that women over the age of sixty are six percent likely to develop the disease compared to five percent in men [7]. In the United States of America alone, Alzheimer's affects approximately 4.5 million people and it is projected to reach four times that number by the year 2050 [7].

## **2. Methods**

The data presented here were gathered via Research Gate, National Center for Biotechnology Information, PubMed, and Google Scholar to identify peer reviewed articles regarding turmeric and its effects on Alzheimer's Disease.

## **3. Discussion-Mechanism of Action of Turmeric**

### **3.1 Anti-inflammatory properties**

Neurologically, patient's afflicted with Alzheimer's disease are known to have inflammation in certain regions of the brain due to the presence of highly insoluble amyloid beta deposits as well as neurofibrillary tangles [3]. Studies have shown that peroxisome proliferator-activated receptor gamma (PPAR- $\gamma$ ) has been associated with anti-inflammatory effects in turmeric [8]. Specifically, it has been demonstrated that curcumin inhibits amyloid beta induced expression of Egr-1 DNA binding activity in THP-1 cells. Egr-1 is a key inflammatory transcription factor that when inhibited, would prevent the

characteristic inflammation observed in patients with Alzheimer's disease [9]. Furthermore, researchers have found that curcumin also inhibits cyclooxygenase and transcription factors involved in the metabolism of phospholipids into prostaglandins [10]. Prostaglandins are lipid compounds with a diverse set of functions including the regulation of the inflammatory response. Thus, the inhibition of prostaglandins reduces neutrophil action which, in turn, prevents the release of reactive oxygen species and activation of proinflammatory cytokines [3]. Moreover, curcumin has been shown to play a role in the inactivation of the master regulator in the inflammatory process. This master regulator, NF-kappa B transcription factor, activates expression of TNF-alpha, IL-1 beta, and IL-6 which, much like the proteins discussed previously, invoke the inflammatory response. It is important to note that TNF-alpha participates in a positive feedback loop with NF-kappa B which explains, at least in part, the chronic inflammatory state observed in particular brain regions of Alzheimer's disease patients [3].

### **3.2 Potent immunomodulatory agent**

Turmeric can modulate the activation of T cells, B cells, macrophages, neutrophils, natural killer cells, as well as dendritic cells. Dendritic cells are antigen-presenting cells that are involved in the initiation of the adaptive immune system. Research has illustrated that curcumin treated dendritic cells induce regulatory T cell development as well as the production of IL-10 which inhibits inflammation [10]. Similarly, neutrophils have been observed to express a marked decrease in oxygen radical formation when treated with curcumin [10]. Natural killer cells, lymphocytes which eliminate tumors and infected cells, have been shown to increase antibody responses in rats that have had a curcumin diet. Additionally, curcumin was also found to increase the activation of natural killer cells in the presence of a tumor. As such, curcumin is able to modify natural

killer cells depending on the pathology a given subject is undergoing [10]. As it pertains to macrophages, curcumin was found to inhibit tumor necrosis factor alpha which, by extension, led to the inhibition of intercellular adhesion molecule 1, vascular cell adhesion molecule-1, and endothelial cell leukocyte adhesion molecule-1 [10]. The suppression of these proteins has been implicated as a major factor in the curcumin's inhibitory effect on NF-kappa B. In regards to curcumin's effect on B cells, it was found that IgM secretion, CpG, and B cell proliferation were all reduced in the presence of curcumin. Specifically, the TLR ligand, phosphorylation of ERK, I-kappa B, and p38 kinase, which all perform various roles in the immune response, are all suppressed resulting in a diminished or anti-inflammatory effect [10]. Curcumin is proven to inactivate NF-kappa B transcription factor, which is a protein complex that controls DNA transcription, production of cytokines, and cell survival. Studies have shown nothing but positive effects of curcumin making it an ideal potent immunomodulatory agent.

### **3.3 Antioxidant**

Turmeric exhibits properties of antioxidants. This is to say that, the major component in turmeric, curcumin, protects cells from damage incurred by free radicals within the intracellular environment. This damage occurs through the accumulation of reactive oxygen species which have a harmful effect on polyunsaturated fatty acids [3]. This reaction, commonly referred to as lipid peroxidation, is a self-propagating chain reaction such that the oxidation of a minimal amount of lipid molecules can lead to extensive and long-lasting damage. Multiple studies have demonstrated that curcumin is a particularly potent free radical scavenger [11]. Additionally, curcumin not only protects the cell from reactive oxygen species produced through lipid peroxidation, but has also been shown to remove NO-based radicals [12]. Specifically, it was found that when

transgenic mouse models that exhibited the human Alzheimer's disease gene were given curcumin their initially elevated carbonyl protein formation was considerably suppressed. This decrease in carbonyl protein formation was found to be proportional to the dose of curcumin. That is, a low dose of curcumin decreased carbonyl protein levels by 46%, while a high dose reduced carbonyl proteins by approximately 61.5% [11]. Thus, it was concluded that the antioxidant properties of curcumin prevented oxidative damage caused by lipid peroxidation products, which include carbonyl compounds such as hydroxynonenal [11]. This study strongly supports the notion that the primary component of turmeric, curcumin, not only exemplifies antioxidant characteristics, but that these qualities play a significant role in limiting the amount of reactive oxygen species thereby hindering the pathogenesis of Alzheimer's disease.

### **3.4 Cholesterol lowering effects**

As described previously, cellular oxidative damage has been strongly associated with the pathogenesis of Alzheimer's disease. This damage occurs as a result of the accumulation of beta amyloid fragment of the amyloid precursor protein [13]. That is, the assembly of beta amyloid proteins into clusters causes the formation of plaques. These plaques trigger an immune response that eventually causes the characteristic inflammation observed in the brains of patients with Alzheimer's disease [14]. Studies have shown that beta amyloid molecules can attach to cholesterol containing cells leading to an accelerated path to plaque formation<sup>16</sup>. Turmeric, however, has been shown to prevent these proteins from congregating and creating plaques by increasing the resistance of low-density lipoproteins to oxidation [15]. Specifically, researchers observed that, in the presence of curcumin, copper (II) sulfate was significantly hindered in its oxidation of low-density lipoproteins. It is important to note, however, that the

effectiveness of curcumin on low density lipoproteins seemed to vary based on dosage. As such, scientists have concluded that curcumin acts in a dose-dependent manner such that a moderate dose is beneficial to preventing plaque formation and oxidative damage, but a high dose is ineffective and may even induce lipid peroxidation [15]. Additional studies have led to similar conclusions establishing a link between a curcumin induced reduction of cholesterol levels and incidence of neurodegenerative disease. It has been hypothesized that curcumin causes the efflux of cholesterol from cells, specifically adipocytes, through the PPAR- $\gamma$ -LXR-ABCA1 pathway. In this pathway, LXR acts as a target for PPAR- $\gamma$  and these receptors collaboratively regulate ABCA1 expression [16]. ABCA1 is a major cholesterol regulator whose main function is both cholesterol and phospholipid homeostasis [17]. As such, it is clear that cholesterol lowering effects of turmeric has an important preventative impact on the development and progression of Alzheimer's disease.

### **3.5 Reduction of tau hyperphosphorylation**

Turmeric's neuroprotective effects include its ability to inhibit tau hyperphosphorylation. Tau proteins are involved in regulating microtubule dynamics and axonal transport [18]. As such, interference of certain phosphorylation events leads to tau dysfunction which contributes to the pathogenesis of Alzheimer's disease [18]. Specifically, improper tau phosphorylation may result in decreased microtubule binding as well as increased tau-tau interactions. An increase in such interactions in conjunction with abnormal hyperphosphorylation of the tau protein leads to intracellular aggregates that form the discernible neurofibrillary tangles in Alzheimer's pathology. Once tau proteins begin to detach from microtubules due to a reduction in affinity, axon transport of synaptic vesicles is disturbed and, as a result, the synapses deteriorate [19]. Furthermore, tau hyperphosphorylation has been

demonstrated to be a major component in beta amyloid neurotoxicity [19]. The presence of beta amyloid causes tau kinases including cdk-5, GSK-3 beta, p38/MAPK, JNK- $\frac{1}{2}$ , and ERK to phosphorylate the tau protein [19]. Researchers have shown that rats that have been infused with beta amyloid display a measurable increase in GSK-3 beta activity. The brains of these rats were found to have a pronounced increase in tau phosphorylation in the hippocampal region of the brain. This particular region of the temporal lobe is widely known as the main memory center of the brain. When the aforementioned rats were fed curcumin, however, the GSK-3 beta kinase was inactivated preventing the phosphorylation of tau [19]. This, in turn, impeded the construction of neurofibrillary tangles which are commonly observed in Alzheimer's patients. Thus, curcumin's capacity to act as a neuroprotective agent through inhibition of tau hyperphosphorylation exemplifies another mechanism by which this substance may prove valuable in treating patients with Alzheimer's disease [20-23].

### **4. Conclusion**

Incorporating turmeric into the diet has shown many health benefits as mentioned above. From its Anti-inflammatory properties to its potential in fighting Alzheimer's disease, turmeric has the ability to change the outlook of human health in regard to the holistic approach. Taking small precautional measures, like adding more spices like turmeric into the human diet, can prevent many infectious diseases. The Joint United Nations and World Health Organization Expert Committee on Food Additives advise the daily intake amount of curcumin to be 0-3 mg/kg body weight [8]. With this review, individuals should be aware of the numerous health benefits that turmeric has to offer especially when it comes to Alzheimer's disease. Research suggests that turmeric can help in reduction of tau hyperphosphorylation, lowering cholesterol levels, antioxidative effects, potent immunomodulatory as well

as anti-inflammatory properties. Consuming even the slightest amount of turmeric into the human diet can provide health benefits in those individuals who are considered healthy.

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