Curcuma longa (Theracumin®)

A Bioavailable Form of Curcumin and Its Cognitive Benefits

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As human life expectancy increases, there is a corresponding increase in the incidence of chronic diseases such as dementia. Individuals with cognitive impairment, a known precursor to dementia, experience a decline in previously attained cognitive function. The manifestation of dementia usually occurs in people older than 65 years and is often associated with other age-related health issues.

A bioavailable curcumin (Theracurmin) demonstrates significant memory and attention benefits in nondemented adult patients.

However, cognitive impairment and dementia are not an inevitable consequence of the aging process; implementation of preventable health care strategies that include therapeutic lifestyle considerations, combined with public health initiatives, can greatly reduce the incidence and delay of cognitive decline.[1] Current evidence supports the recognition that neurotransmitter balance, dietary and lifestyle habits, nutritional status, and metabolic mechanisms, which include inflammation, microbiota imbalance, oxidative stress,and impaired mitochondrial function, are important variables that affect brain function.[2] There is an expanding body of clinical research that associates chronic systemic inflammation to a broad spectrum of health problems that include cardiovascular disease, autism, depression, anxiety, and other mental health disorders, as well as cognitive impairment.[3-6] Central to the focus of this article is the accumulating research on the cognitive benefits associated with curcumin, a polyphenolic antioxidant, the major bioactive constituent found in the phytomedicine turmeric (*Curcuma longa*), that has demonstrated neuroprotective and inflammatory properties on brain function.[7,8]

PHYTOMEDICINE PROFILE

Turmeric (*Curcuma longa* L.) is a member of the ginger family (Fam. Zingiberaceae). It is a leafy, acaulescent (stemless) perennial, with large lanceolate leaves and pale yellow tubular flowers that emerge from a fleshy, tuberous rhizome (underground stem). The name turmeric is derived from the Latin word *terra merita*, which refers to its characteristic yellow-orange pigments, known as curcumin, the major bioactive component of this spice herb and the source of its medicinal properties.[9] *Curcuma longa* has a long history of use in traditional medicinal practices of the Ayurvedic and Unani systems of

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herbal medicine, as well as in traditional Chinese medicine, for treating liver and digestive disorders.[10-12] It is a major constituent of *Jiawei-Xiaoyao-san*, a traditional Chinese formula, which has been used to address dyspepsia, stress, depression, and mood-related disorders.[13,14] In Ayurvedic medicine, turmeric has a long history of use as a treatment of inflammatory conditions.

Phytopharmacology

Curcumin, [1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione], or diferuloylmethane is a lipophilic polyphenol molecule that has demonstrated highly pleiotropic activities, including anti-inflammatory, antioxidant, antimicrobial, antitumor, and antiangiogenesis activities. In addition, curcumin's combined pharmacologic bioactivities, specifically its antioxidant, anti-inflammatory, antiamyloid, and possible anti-tau properties, have shown neuroprotective benefits.[15,16]

A cumulative body of research performed over the past 50 years has demonstrated that curcumin can modulate multiple cell signaling pathways, including inflammatory molecules. Curcumin exhibits anti-inflammatory activity through its suppression of proinflammatory transcription factors, such as nuclear factor κB (NF-κB), activator protein-1, and signal transducer and activator of transcription 3 (SAT3) proteins.[17] These transcription factors play a significant role in mediating inflammatory response through the modulation of the production of inflammatory cytokines.[18,19]

Extensive research has shown that curcumin can modulate multiple cell signaling pathways, and clinical studies have indicated curcumin's therapeutic potential in addressing a wide range of human diseases.[20] In a recent double-blinded, placebo-controlled trial study using a bioavailable form of curcumin (Theracurmin), researchers investigated the pharmacologic bioactive protective effects of curcumin on cognitive benefits in nondemented adults.

RESEARCH IN REVIEW[21]

Small GW, Siddarth P, Li Z, et al. Memory and brain amyloid and tau effects of a bioavailable form of curcumin in non-demented adults: a double-blind, placebo controlled 18-month trial. *Am J Geriatr Psychiarty*. 2018;26(3):266-277.

OBJECTIVE

To determine the effects of a highly absorptive curcumin extract dispersed with colloidal nanoparticles (Theracurmin) in the treatment of nondemented adults on memory performance and its potential impact on neurodegeneration by measuring brain deposition of amyloid plaques and tau tangles.

PHYTOMEDICINE TEST AGENT

A bioavailable phytomedicine extract of curcumin (Theracurmin), derived from the dried rhizome of turmeric (*Curcuma longa* L.) (Theracurmin, https://naturalfactors.com/en-us; containing 90 mg of curcumin; Theravalues Corporation, theravalues.com/English, Tokyo, Japan).

STUDY DESIGN

This randomized, double-blinded, placebo-controlled, parallel-group study involved 40 male and female patients, with an age distribution between 51 and 84 years. Subjects were randomized to either a bioavailable form of curcumin ([N = 21], Theracurmin containing 90 mg of curcumin per capsule, taken twice daily) or a placebo group (N = 19) that received 2 capsules daily of identical-appearing placebo treatments for an 18-month duration to determine long-term cognitive effects of curcumin. In addition, this study examined the effects of curcumin on neurodegeneration by using 2-(1-{6-[(2-[F-18]fluoroethyl)(methyl)amino]-2-naphthyl}ethylidene)malononitrile positron emission tomography (FDDNP-PET) binding levels in nondemented older patients.

Test subjects met the inclusion criteria and received a regimen of screening laboratory tests and magnetic resonance imaging to eliminate the possibility of reversible causes of cognitive impairement.[22] Neuropsychological tests were performed to ensure the exclusion of patients with dementia and to verify that patients who met the inclusion criteria had normal aging or experienced mild cognitive impairment.[23] In addition, subjects were administered the Beck

Depression Inventory[24] and the Montreal Cognitive Assessment.[25]

During the baseline appointment, test subjects were assigned to treatment arms using a randomized table. In addition, they received assessments for vital signs, serum electrolytes, electrocardiograms, and complete blood cell counts, as well as a 3-month supply of Theracurmin or placebo. Subjects returned to the medical center every 3 months for curcumin or placebo capsule supplies. Plasma bioavailability and total curcumin analyses were performed to ensure that participants were compliant in taking either curcumin or placebo and that additional curcumin was not ingested. Plasma curcumin levels were taken at baseline and after 18 months of treatment. Safety and compliance were monitored and recorded at 3-month intervals.

Assessment tools

Since previous research demonstrated memory effects of curcumin, researchers selected memory tests as the primary outcome measures after 6, 12, and 18 months of treatment.[26] The Buschke[27] Selective Reminding Test (SRT) was the primary outcome measure for verbal memory and the Brief Visual Memory Test-Revised (BVMT-R)[28] was the primary outcome measure for visual memory. The Trail Making Test Part A was chosen as a secondary outcome measure because a study trial had indicated that curcumin showed a positive effect on sustained attention.[29] The neurodegeneration assessment using FDDNP-PET scans to measure brain deposition of amyloid plaques and tau tangles was performed on subjects at baseline and after 18 months of curcumin supplementation or placebo.

RESULTS

The SRT Long Term Retrieval improved with curcumin (ES [effect size] = 0.63, $P = .002$) but not with placebo (ES = 0.06, $P = .8$; between-group: ES = 0.68, $P = .05$). Curcumin also improved SRT Total (ES = 0.53, $P = .002$), visual memory (BVMT-R Recall: ES = 0.50, $P = .01$; BVMT-R Delay: ES = 0.51, $P = .006$), and attention (ES = 0.96, $P < .0001$) compared with placebo (ES = 0.28, $P = .1$; between-group: ES = 0.67, $P = .04$). The neurodegeneration assessment using FDDNP-PET scans decreased significantly in the amygdala with the curcumin test group (ES = −0.41, $P = .04$) compared with the placebo group (ES = 0.08, $P = .06$; between-group: ES = 0.48, $P = .07$).

SUMMARY OF RESULTS

Subjects taking Theracurmin containing 90 mg of curcumin per capsule, twice daily, demonstrated significant memory and attention benefits in nondemented adult patients after 18 months compared with placebo. In addition, the FDDNP-PET scans suggest that cognitive and behavioral benefits correlate with decreases in plaque and tau tangle accumulation in brain regions that regulate mood and behavior.

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