International Journal of Research in Health and Allied Sciences

Journal home page: www.ijrhas.com

Official Publication of "Society for Scientific Research and Studies" [Regd.]

ISSN: 2455-7803

Review Article

Traditional Functional Spice – Turmeric, Curcumin and Mental Health

[1]Monal Velangi, [2]Yukta Sharma

[1,2]Department of Nutrition and Dietetics, K.J. Somaiya Hospital and Research Centre, Mumbai, India

ABSTRACT:

Background: Mental health disorders are a grave public health concern and rising across the globe. Risk factors - stress, heredity, work life imbalance, environmental stresses, physical inactivity, improper diet can lead to onset and accelerate this disease. Right therapeutic approach and preventive health methods can help in managing mild symptoms of stress and anxiety, improve quality and delay onset of neurological diseases. Functional foods have reported neuroprotective benefits including the widely consumed traditional Indian spice - turmeric and its bioactive curcumin. **Methods:** This review focused on the last 11 years (January 2011 - June 2022) research studies on turmeric, curcumin and mental health. Research articles on turmeric and mental health, neuro-degeneration, stress, anxiety, depression, neuro-protection, brain health and cognition were searched from PubMed database from January 2011 - June 2022. The eligible studies were reviewed and the data was discussed. **Results:** Turmeric was found to be effective in mental health due to its antioxidant and anti-inflammatory properties. It was beneficial in improving neurotransmitter activities, reducing dopamine, a stress neurotransmitter hence providing anti-stress, neuro-protective effects. **Conclusion:** Turmeric and curcumin can be a promising spice and bioactive respectively to be incorporated in the diet and nutraceuticals as a way to promote mental health.

Keywords: Turmeric; curcumin; neuroprotection; mental health; antioxidant; anti-inflammatory

Received: 17 September, 2022 Accepted: 7 October, 2022

Corresponding Author: Monal Velangi, Department of Nutrition and Dietetics, K.J. Somaiya Hospital and Research Centre, Mumbai, India **Email:** drmonalvelangi@gmail.com

This article may be cited as: Velangi M, Sharma Y. Traditional Functional Spice – Turmeric, Curcumin and Mental Health. Int J Res Health Allied Sci 2022; 8(5):11-17.

INTRODUCTION

Mental health plays a significant role in maintaining a good overall well-being. The World Health Organization (WHO) constitution states that "Mental health is a state of well-being in which an individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and is able to make a contribution to his or her community." (WHO, 2022). Globally, 301 million people, 58 million children and adolescents lived with anxiety in 2019 (IHME, 2019). Global Burden of Disease in 2019, pre-pandemic era was one in eight; 970 million people (52.4% female and 47.6% males) (IHME, 2019). WHO also reported a global increase of anxiety by 25% during COVID-19 pandemic in 2022 (WHO, 2022). A study by the Center of Healing, New Delhi reported 88% of Indians suffered from anxiety. COVID-19 has resulted in a persistent anxiety problem extending beyond the pandemic (Kwong et al., 2020).

Mental health disorders were the second leading cause of disease burden in terms of years lived with disability (YLDs) and the sixth leading cause of disability-adjusted life-years (DALYs) across the globe in 2017 therefore posing a grave problem for health systems, particularly in low-income and middle-income countries (IHME, 2019). Mental health is being identified as one of the primary areas in health policies around the world and has also been included in the Sustainable Development Goals (Choksi et al., 2016).

Mental health conditions include stress, anxiety, depression and neurological disorders. Chronic stress alters the overall homeostasis of the human body and disturbs nervous, endocrine and immune systems, thus affecting normal life. If not managed well it may lead to anxiety and depression. Studies with brain imaging revealed altered neurotransmitter levels in patients with depression and mental health issues (Ruda-Kucerova et al., 2015). The etiology of mental health disorders is complex and includes risk factors such as

individual psychological and biological factors, emotional, social, lifestyle as well as genetics. Many of the risk and protective factors are influenced through alterations in the structure and function of the brain and nervous system (WHO, 2022). Different ancient medicine practices have been using medicinal plants and herbs to treat innumerable health conditions. Some of the most common medicinal herbs include tulsi, turmeric, aloe and Neem (National Health Portal of India, 2016). Turmeric, widely used as a spice in India is now gaining global attention due to its medicinal properties such as antibiotic, anti-carcinogenic, anti-inflammatory, antidepressant and anxiolytic. Research has revealed positive effects of turmeric on brain and nervous system and therefore it may be used for preventing or treating mental health conditions such as stress, anxiety, depression and reducing neuro-inflammation or neuro dysfunction.

Human emotions, negative or stressful, activate the autonomic nervous system, that regulates not consciously directed physiological functions, and affect dietary and eating patterns of an individual. This further leads to increase in oxidative stress via NF- KB activation as metabolic responses to food. This unanimously causes inflammation which in turn aggravates anxiety or negative emotions. This marks a notable bidirectional relationship among diet and mental health (Kiecolt-Glaser, 2010). Diet and its bioactive components are considered to be modifiable mental health risk factors due to the beneficial effects of various dietary factors such as micro- and macronutrient intake towards the brain. Excessive intake of simple sugar in the context of glucose metabolism and adiponectin regulation and cause neuro-inflammation. Individual dietary bioactive molecules posing antioxidant anti-inflammatory properties, such as omega-3 fatty acids and polyphenols are found to be beneficial for the central nervous system via modulation of adult neurogenesis, synaptic and neuronal plasticity, and microglia activation (Godos et al., 2020).

With the increasing stressful and unhealthy lifestyle and the added burden of an exponentially rising world population, mental health conditions are also rising. Undeniably, it is the need of the hour to promote, protect and restore mental health through economical, effective and possible strategies. Mental health promotion, protection and restoration requires a combination of medical, dietary and lifestyle interventions such as yoga, meditation, deep-breathing and de-stressing techniques. Eating a correct, well balanced diet consisting of "brain-friendly" food components may help prevent or delay mental health disorders. Recently, there has been an increase in research focusing on the role of food and mental health. Functional foods are those dietary components that impart additional physiological health benefits along with basic nutrition. Turmeric is an ancient medicinal herb widely used in India and China as home remedy to heal cuts and wounds (National Health Portal of India, 2016). It has known antibiotic, antiseptic and anti-inflammatory properties. Turmeric due to its component curcumin has been demonstrated to be effective in the treatment of mental health disorders as well.

The aim of this review article is to focus on the mental health fostering role of a selected traditional food of Indian-origin, turmeric, in order to address the issue of mental health and find integrative functional medicine ways to prevent it.

TURMERIC

Turmeric (*Curcuma longa L.*), famously known as the 'Golden Spice of India' (Rathaur et al., 2012) is an herbal plant belonging to the ginger family of Zingiberaceae. *Haridra is* the Sanskrit name for turmeric (Durga, Prakash and Harini, 2016) and holds great importance in the traditional Indian Medicine – Ayurveda and its use dates back to as early as 4000 years to alleviate numerous health conditions (Chetan et al., 2022). It accommodates a plethora of medicinal properties such as antibacterial, antioxidant, antiviral, antifungal, anti-inflammatory, anti-carcinogenic and neurotrophic. These properties are due to the bioactive component of turmeric, curcumin (diferuloylmethane), a polyphenolic phytochemical present in the rhizome of Curcuma longa. The natural pigment curcumin imparts the characteristic orange-yellow color and its bioavailability in the body can be increased by 2000 per cent on adding piperine (Chetan et al., 2022), the bioactive compound of black pepper. Curcumin may be highly beneficial in the treatment of various brain-related disorders such as Alzheimer's disease, Parkinson's disease, autism, multiple sclerosis, and aging-associated neuro-dysfunction. A diet that involves regular use of turmeric has been observed to prevent and treat numerous diseases such as cancer, diabetes and has been shown to reduce inflammation. Along with curcumin, turmeric contains potent phenolic and flavonoid anti-oxidants and curcuminoids and few functional monosaccharides (Yazdi et al., 2019). The effect of curcumin in neurological diseases, such as anxiety, depression, spinal muscular atrophy; Alzheimer's disease; Parkinson's disease; amyotrophic lateral sclerosis; multiple sclerosis; neuro-dysfunction, neuro-inflammation and has only recently been brought to the attention of scientists and general population (Adami and Bottai, 2022). Curcumin interacts with a number of neurotransmitter systems and intracellular signaling pathways associated with mood regulation. Also, curcumin has anti-inflammatory, antioxidant and neurotrophic effects, suggesting a strong potential to manage conditions associated with neurodegeneration, such as psychiatric disorders (Kaufmann et al., 2016). Majority of literature focused on the role of curcumin in behavioral and neurochemical changes in preclinical models of depression (Kaufmann et al., 2016).

MECHANISM OF ACTION

Turmeric's polyphenol, curcumin, exerts its neurological benefits by modulating different signaling molecules including transcription factors, chemokines, cytokines, tumor suppressor genes, adhesion molecules and microRNAs (Ghosh, Banergee and Sil, 2015). Curcumin crosses the blood brain barrier (BBB), reaches neurons and protects from various toxic insults of aging and prevents amyloid-β aggregation in humans. Recent research has also reported that curcumin improves cognitive decline and synaptic functions in mouse models of Alzheimer's disease (Reddy et al., 2018). Curcumin shows neuroprotective effects on neuro-inflammaging, which is characterized by a down regulation of the vitagene system and Nuclear factor erythroid 2-related factor 2 (Nfr2) activity with the consequent upregulation of nuclear factor κB (NF-κB) activation, also trough Tool Like Receptor 4 (TLR4), it induces TNFα, IL1b, IL6, COX2 and iNOS proinflammatory factors (Concetta et al., 2019). Curcumin has cellular pleiotropic activity through protein interaction, can provoke cellular responses to external stimuli and up- and down-regulates various miRNA causing epigenetic changes in cells. Neuroinflammation, the inflammatory response of the brain or spinal cord, is common in a number of brain diseases, including Alzheimer's disease (AD), Parkinson's disease (PD), Multiple Sclerosis (MS). This process is mediated through the production of cytokines, chemokines, reactive oxygen species (ROS) and secondary messengers, which could destroy the BBB resulting in cell damage and neuronal functions loss (Benameur et al., 2021).

Curcumin reduced the disruption of plasmatic membrane due to Aβ, thus avoiding elevated calcium influx and cell death (Thapa et al., 2013). Its neuroprotective effect is probably membrane-mediated by reducing toxicity induced by monomeric, oligomeric, pre-fibrillary and fibrillary Aβ conformers. It has also been described that curcumin promotes "off-pathway" soluble oligomers formation and non-toxic pre-fibrillar aggregates (Thapa, Jett and Chi, 2016).

In depression conditions, curcumin affects the NMDA receptor/Ca2+ pathway and prevents cell damage induced by Aβ (Thapa et al., 2013). Aβ accumulation activates microglia, which produces inflammatory mediators thus promoting further Aβ accumulation, leading to positive feedback loop. Curcumin reduces neurotoxicity by activating Aβ induced microglia, blocks ERK1/2 and p38 kinase signaling in Aβ activated microglia thus reducing the production of TNF-α, IL-1β and IL-6 (Sundaram et al., 2017) and, in addition, attenuates the release of nitric oxide. Moreover, curcumin suppresses phosphoinositide 2 kinase (PI3K)/Akt phosphorylation and the activation of NF-κB, which drive microglia activation and neuroinflammation pathways (Cianciulli et al., 2016). Curcumin is protective against mitochondrial dysfunction and cell death in a siRNA-mediated PINK1 knock-down model of PD (Van der Merwe et al., 2017). A study reported that curcumin affects mitochondrial dysfunction in a paraquat-induced toxicity model of PD, in fibroblasts derived from LRRK2-mutation positive PD and lead to better health control. In fact, pre-treating with curcumin improved maximal respiration and ATP-associated respiration without affecting the respiratory capacity versus post-treatment thus suggesting the preventive effect of curcumin even before the onset of PD (Abrahams et al., 2021).

IN-VITRO STUDIES

Turmeric extract has been found to function as a prebiotic as it showed excellent resistance to human gastric and intestinal juices as compared to inulin, a standard prebiotic. It was seen to be digested by probiotic bacteria of the gut and promoted their growth beyond 72 hours in simulated laboratory conditions (Yazdi et al., 2019). Curcumin pretreatment shows protective effect on neurotoxic Acrylamide (ACR) induced cytotoxicity via inhibiting pancreatic endoplasmic reticulum kinase (PERK) -dependent eukaryotic initiation factor-2α (eIF2α) phosphorylation, which provides empirical evidence between curcumin and PERK-eIF2α signaling in ACR-induced neurotoxicity (Yan et al., 2022).

IN-VIVO ANIMAL STUDIES

Chronic administration of curcumin (40 mg/g) for a period of 6 weeks in pre-stress exposed rat models of chronic, unpredictable, mild, stress (CUMS) -induced depression significantly suppressed depression symptoms. Furthermore, curcumin exhibits neuroprotection and antidepressant-like effects in the CUMS-induced depression model by modulating synapse-associated proteins within the lateral amygdala part of the brain (Zhang et al, 2014). Oral curcumin administration increases postsynaptic reactivity and cell viability of intact hippocampal circuits and inhibits COX-2 expression in chronically stressed rats. Thus through suppression of inflammation and upregulation of brain derived neurotrophic factor (BDNF), curcumin displays antidepressant- like effects (Choi et al., 2017). Curcumin acts against depression as it improves dopamine, 5-hydroxyindoleacetic acid and noradrenaline levels (Chang et al., 2016) that become deficient in the frontal cortex of the brain in depression. Experimental studies revealed protective effects of curcumin (15, 30 and 60 mg/kg, 10 weeks) in chronic alcohol induced cognitive dysfunction and nuclear factor kappa beta (NF-κβ) mediated inflammatory signaling in the brain, preventing associated behavioral, biochemical and molecular alterations (Tiwari and Chopra, 2013). However, curcumin and γ-aminobutyric acid receptor A (GABAA) receptor interaction has not been observed

(Ceremuga et al,. 2017) demonstrating no changes in behavioral despair and anxiolytic effects .Curcumin is considered to be the most promising therapeutic way to treat depressive behavior due to its positive antidepressant and anti-anxiety effects on specific physiological mechanisms in Wistar rats. Turmeric dissolved in olive oil when administered at a dose of 60 mg/kg showed therapeutic benefits in disturbed rat behavior and degree of anxiety using the open-field test and the light and dark box test as against the deficits caused by formaldehyde (Nouacer et al., 2021). This gives rise to higher levels of formation of docosahexaenoic acid (DHA) from its precursor compound ie alpha linolenic acid (ALA). In addition to this the enzymes playing role in DHA formation-elongase 2 and fatty acid desaturase 2 (FADS2) increased in brain tissues of rats (Wu et al., 2015).

HUMAN CLINICAL TRIALS

Curcumin intervention reduced mental, behavioral and physical symptoms of premenstrual syndrome through enhancing serum brain-derived neurotrophic factor (BDNF) levels (Fanaei et al., 2016). It has been observed that curcumin improves mood, reduces tension, anger, mental confusion and total mood disturbance in non-depressed adults for a short time of supplementation of 4 weeks only (Abdolahi et al., 2018). Curcumin supplementation singly (160 mg/day), for 16 weeks in overweight/obese non-depressed adults (50–80 years) improved mood and reduced subjective memory complaints (SMCs) as compared to control group. Only fish oil supplementation benefits were limited to apolipoprotein E4 (major known Alziemer's Disease risk factor) non-carriers, such as increased vigor and reduced total mood disturbances. Otherwise fish oil did not affect any mood states, SMCs or QoL. No additive effects on mental health seen for curcumin and fish oil combination (Kuszewski, Howe and Wong, 2020). Therefore, either curcumin or fish oil constant supplementation can improve mental well-being and ultimately QoL.

In an experiment, no treatment effect was seen when curcumin was ingested by trained men, fire-fighters and military personnel three days prior and in the morning of dual stress challenge testing, involving 20 min of mental stress challenges during 35 min of cycling at 60% V̇O2 peak (McAllister et al, 2020). In healthy, overweight participants, curcuma longa extract containing 100 μgTurmeronol A and B each, improves serum inflammatory markers and mental health, MOS SF-36 mental health score and POMS anger-hostility score, lowers serum C-reactive protein (Uchio et al., 2021).

DISCUSSION

Mental health conditions are usually managed pharmacologically. A right combination with non-pharmacological preventive strategies can help in mental health promotion. Turmeric is a widely used traditional Indian spice, also a functional food with anti-inflammatory and antioxidant properties (Lopresti, Hood and Drummond, 2012; Abrahams et al., 2019) with neuroprotective benefits, and found to be effective in mental health (Maiti and Dunbar, 2018). US Food and Drug Administration (USFDA), has reported turmeric and curcuminoids as safe, cost effective, readily available; curcumin has better ability to cross the blood brain barrier, and has pleiotropic therapeutic effects on neurological diseases due to its ability (Yavarpour-Bali, Ghasemi-Kasman and Pirzadeh, 2019). WHO has recommended the desirable daily intake of curcumin to be between 0-3 mg/kg bodyweight (Amalraj et al., 2017).

In the Indian diet, on an average approximately 2- 2.5 g of turmeric for a 60 kg individual, corresponding to approximately 60-100 mg of daily curcumin is consumed (Mahmood et al., 2015). Curcuminoids are highly susceptible to heat induced degradation. Total antioxidant capacity of curcumoinoids is slightly lowered by cooking, relatively enhanced by boiling than roasting, weakest after frying. However, cooked curcumin retains its antioxidant and neuro-protective activity (Sun, Ji and Shen, 2019).

In vitro studies reported the potential role of turmeric in enhancing the growth of gut probiotics. Thus, it may play a role in the gut-brain axis and may have an effect on mental health, which could be explored further.

The animal trials of curcumin supplementation in mental health are summarized (Table 1). The animal trials reported curcumin's mechanism of action such as antioxidant, anti-inflammatory. It revealed its role as an anti-depressant, anxiolytic; thus, providing mental benefits such as calmness, improved memory, cognition, neuronal viability. Overall, it reduced neurodegeneration and promoted neuroprotection. Also, the curcumin dosage incorporated for animal trials were as follows, a mean dose of 8024 mg, with the minimum and maximum doses were 0.01 to 40,000 mg respectively.

On the other hand, the human clinical trial of curcumin supplementation for mental health (Table 2) confirmed the animal trial findings. Interestingly, human trials established evidence for curcumin's neuro-promoting role. Curcumin was found to have antioxidant and anti-inflammatory properties in human body. It was also found to improve neurotransmitters – acetylcholine functions, reduce and/or delay neuro-degeneration and improve cognition and also prevented migraine. Its anti-stress, anxiolytic and anti-depressant effects could be a preventive as well as a management strategy in stress, anxiety, depression and related complications.

Table 1: Animal Trials on Curcumin Supplementation and Mental Health.

Name of Authors, Year	Type of study	Mechanism of Action	Intervention period	Curcumin Dosage	Benefits of Curcumin
Tiwari and Chopra, 2013	Experimental	Anti-inflammatory, anti-stress and neuroprotective	10 weeks	15, 30 and 60 mg/kg	Improved cognitive function and memory
Zhang et al., 2014	Experimental	Neuroprotection, antidepressant	6 weeks	40g/kg body weight	Prevented neuronal and biochemical alterations
Wu et al., 2015	Experimental	Anti- anxiety	3.5 weeks	500 ppm curcumin	Increased DHA production in brain
Choi et al., 2017	Experimental	Antioxidant, improves neural response and Neuroprotection	20 days	10 μM curcumin	Enhancement of postsynaptic electrical reactivity and cell viability in intact neural circuits , reduced long term depression, COX2 inhibition, increased BDNF
Nouacer et a.l, 2021	Experimental	Anti-anxiety, anti-depressant	4 weeks	Turmeric 60 mg/kg	Increased anxiolytic behavior in curcumin treated epileptic rats.

Table 2: Human Clinical Trials on Curcumin Supplementation and Mental Health.

Name of Authors, Year	Type of study	Mechanism of Action	Intervention period	Curcumin Dosage	Benefits of Curcumin
Abdolahi et al., 2018	Randomized Controlled Trial	Anti- neuro inflammatory, neuroprotective, migraine prevention	2 months	Nanocurcumin-80 mg	Down regulation of IL-R and CRP levels
Kuszewski et al., 2020	Randomized Controlled Trial	Anti-depressant, improved mood, memory	16 weeks	Curcumin 160 mg/day	Prevented neuronal and biochemical alterations
McAllister et al., 2020	Randomized Controlled Trial	Anti-inflammatory, anti-oxidant	3 days	1.5 g curcumin /day	Increased DHA production in brain
Uchio et al., 2021	Randomized Controlled Trial	Anti-inflammatory	12 weeks	Turmeronol A and B- 100 µg each	Enhancement of postsynaptic electrical reactivity and cell viability in intact neural circuits, reduced long term depression, COX2 inhibition, increased BDNF

Timely and right management of mental health may delay the onset of neurological disorders such as Epilepsy, Alzheimers, Parkinsons, Dementia, Multiple Sclerosis etc. and delay the disease progression. , the curcumin dosage incorporated for animal trials were as follows, a mean dose of 435 mg, with the minimum and maximum doses were 0.1 to 1500 mg respectively.

CONCLUSION

Mental health needs urgent attention as it may impact all other health aspects, activities of daily living and quality of life. Emphasis on incorporation of curcumin in daily diet can be a preventive dietary strategy in mental health. Curcumin intake could reduce neurodegeneration and improve cognitive functions. However, more research could reveal the exact role of curcumin in the gut brain axis and mental health promotion. There is a need for well-designed human trials on the role of dietary turmeric and nutraceutical curcumin in cognition, stress, anxiety and depression.

ACKNOWLEDGMENTS

None.

FUNDING

Not applicable.

CONFLICT OF INTEREST

The authors do not have any conflicts of interest to declare.

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