Clinical Insights: The Role of Turmeric as a Nutritional Adjunct in Surgical Recovery

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No actual or potential conflict of interest in relation to this program/presentation.

Learning Objectives

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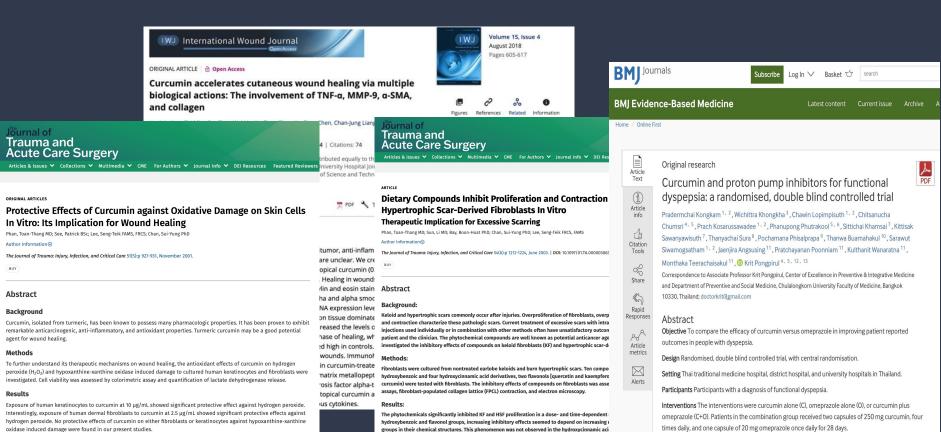
- Investigate pioneering clinical studies on curcumin's impact on longevity biomarkers including sirtuins, cell senescence, inflammaging processes and healthspan extensions.
- Construct evidence-based practical strategies integrating curcumin with lifestyle changes in diet, stress-management and monitoring models to actualize tangible wellness benefits.
- Leave with specific applications of curcumin and Ayurveda for patients with various health issues based on inflammation and/or metabolic disease.

We will dive into curcumin's impact on:

- Chronic Inflammation
- Metabolic Disease
- OA & RA
- Neurodegenerative Diseases



The Science Behind Turmeric

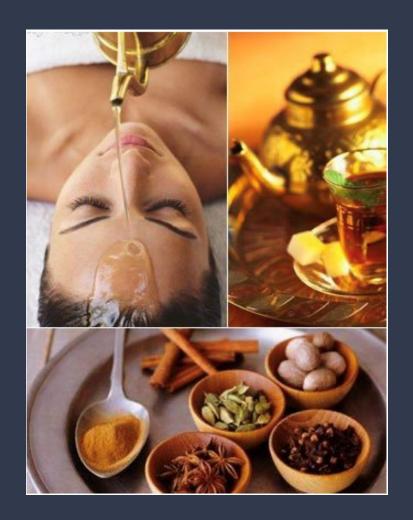


phytochemicals inhibited fibroblast proliferation by inducing cell growth arrest but not apoptosis. T...

Ayurveda: The Science of Life

Ayurveda is Excellent for Patient Optimization: A Daily Preventive Lifestyle

- Reduce Systemic Inflammation
- Gut Health optimization
- Sleep optimization
- Detoxification protocols
- Anti-Inflammatory Diet
- Circadian Rhythm
- Balance the Doshas or Elements





Super Spices

- Turmeric
- Ginger
- Boswellia
- Ashwagandha
- Amla
- Triphala
- Brahmi
- Tulsi
- Cardamom
- Guduchi
- Cinnamon

The Problem: Inflammation

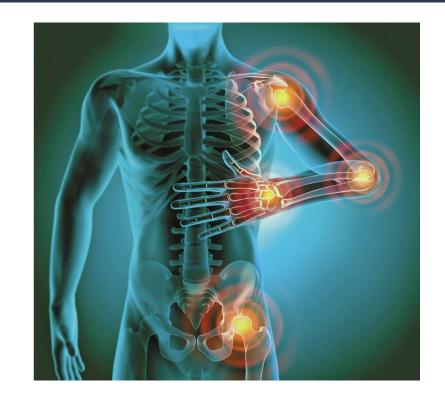
Curcumin helps prevent processes that drive aging and chronic disorders:

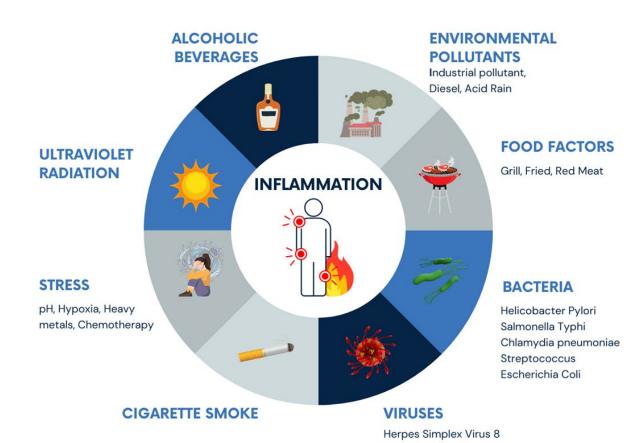
Immunosenescence and Infection Susceptibility:

- Inflammation is linked to immunosenescence, the aging of the immune system.
- An impaired immune response increases susceptibility to infections, posing a threat to the overall health and longevity of an individual.

Impact on Tissue Repair and Regeneration

- Association with frailty
- Chronic inflammation can lead to DNA damage and genomic instability.





Hepatitis Viruses HPVs, HIV, EBV

Chronic Inflammation

Cells naturally age, losing function over time.

- Curcumin intervenes by halting the accumulation of aged cells, disrupting aging-related signaling pathways in the process.
- Research shows that curcumin helps *prevent* processes that drive aging and chronic disorders, including cell senescence and chronic inflammation.

The overall effect may be to improve healthy longevity:

- Healthy longevity involves a complex interplay of genes, environment, and lifestyle. Curcumin contributes with antioxidant properties, influencing various cellular processes.
- Chronic inflammation, a culprit in age-related diseases, faces effective reduction with curcumin. The overall impact extends to potential disease prevention, enhancing overall well-being.



Bielak-Zmijewska A, Grabowska W, Ciolko A, Bojko A, Mosieniak G, Bijoch Ł, Sikora E. The Role of Curcumin in the Modulation of Ageing. Int J Mol Sci. 2019 Mar 12;20(5):1239. doi: 10.3390/ijms 20051239. PMID: 30871021; PMCID: PMC6429134.

Gupta SC, Patchva S, Koh W, Aggarwal BB. Discovery of curcumin, a component of golden spice, and its miraculous biological activities. Clin Exp Pharmacol Physiol. 2012 Mar;39(3):283-99. doi: 10.1111/j.1440-1681.2011.05648.x. PMID: 22118895; PMCID: PMC3288651.

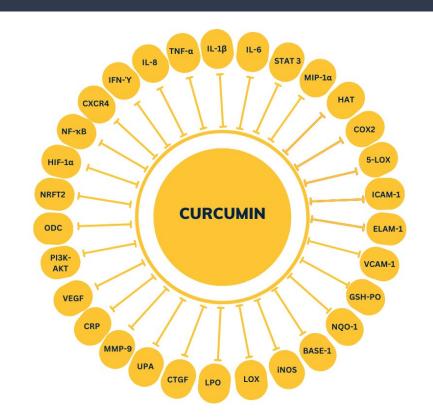
Curcumin: From Farm to Pharmacy

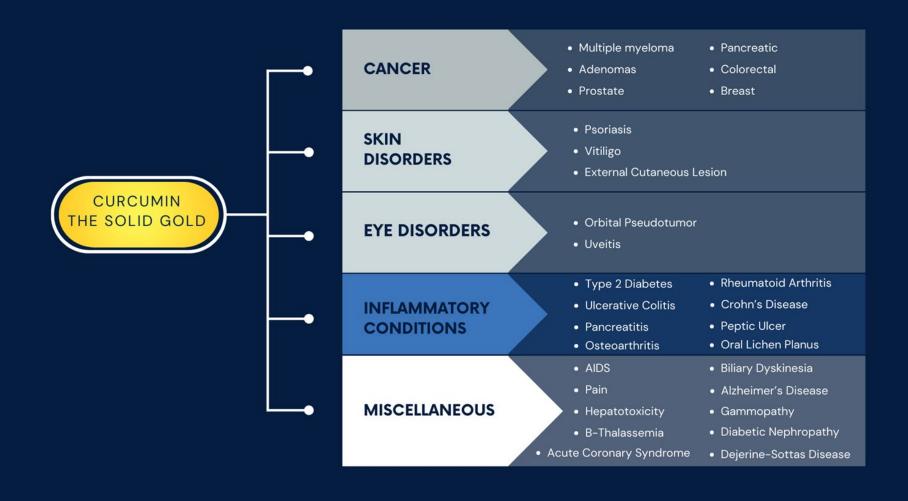
- Curcumin, also known as diferuloylmethane, is a natural polyphenolic compound originally derived from the rhizome of turmeric (*Curcuma longe* L.)
- The three curcuminoids: curcumin [1,7-bis(4-hydroxy-3-methoxy phenyl)-1,6-heptadien-3,5-dione], demethoxycurcumin (DEMC) and bis demethoxycurcumin (BDEMC)
- Anti-inflammatory
- Antioxidant
- Anti-microbial
- Anti-viral
- Anti-fungal
- Anti-obesity
- Anti-coagulant
- Over 10,000 published articles in the last 5 years



Curcumin: Proposed Mechanisms of Action

- Powerful anti-inflammatory
 - O Blocks NF-kb activation and TNF-α
- Powerful antioxidant
 - Increases enzymes that break down Reactive Oxygen Species (ROS)/ Suppresses enzymes that increase ROS, increases Sirtuin (SIRT)
- Curcumin targets other molecules
 - Neuroprotective effects
 - o Energy metabolism cell survival
- Shah, F. A.; Gim, S. A.; Sung, J. H.; Jeon, S. J.; Kim, M. O.; Koh, P. O. Identification of Proteins Regulated b Cerebral Ischemia. J. Surg. Res 2016, 201(1), 141–148. DOI: 10.1016/j.jss.2015.10.025.
- Lutgendorf, S. K.; Aggarwal, B. B.; Sood, A. K., Curcumin Inhibits Tumor Growth and Angiogenesis in Ovari Carcinoma by Targeting the Nuclear Factor-KB Pathway. [Google Scholar]
- Sahebkar, A.; Serban, M. -C.; Ursoniu, S.; Banach, M. Effect of Curcuminoids on Oxidative Stress: A Syster and Meta-Analysis of Randomized Controlled Trials. J. Funct. Foods 2015, 18, 898–909. DOI: 10.1016/j.iff.2015.01.005.
- Sara Fbank, S.; Ahmadi, A.; Paknahad, Z.; Maracy, M.; Nourian, M. Effects of Curcumin Supplementation o Inflammation and Oxidative Stress Among Healthy Overweight and Obese Girl Adolescents: A Randomiz Placebo-controlled Clinical Trial. Phytotherapy Res2019, 33(8), 2015–2022. DOI: 10.1002/ptr.6370.
- Miao, Y.; Zhao, S.; Gao, Y.; Wang, R.; Wu, Q.; Wu, H.; Luo, T. Curcum in Pretreatment Attenuates Inflammat Mitochondrial Dysfunction in Experimental Stroke: The Possible Role of Sirt1 Signaling. Brain Res. Bull'2 15. DOI: 10.1016/j.brainresbull.2015.11.019.













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Original research



Curcumin and proton pump inhibitors for functional dyspepsia: a randomised, double blind controlled trial

Abstract

Objective To compare the efficacy of curcumin versus omeprazole in improving patient reported outcomes in people with dyspepsia.

Design Randomised, double blind controlled trial, with central randomisation.

Setting Thai traditional medicine hospital, district hospital, and university hospitals in Thailand.

Participants Participants with a diagnosis of functional dyspepsia.

Interventions The interventions were curcumin alone (C), omeprazole alone (O), or curcumin plus omeprazole (C+O). Patients in the combination group received two capsules of 250 mg curcumin, four times daily, and one capsule of 20 mg omeprazole once daily for 28 days.

Main outcome measures Functional dyspepsia symptoms on days 28 and 56 were assessed using the Severity of Dyspepsia Assessment (SODA) score. Secondary outcomes were the occurrence of adverse events and serious adverse events.

Results 206 patients were enrolled in the study and randomly assigned to one of the three groups; 151 patients completed the study. Demographic data (age 49.7±11.9 years; women 73.4%), clinical characteristics and baseline dyspepsia scores were comparable between the three groups. Significant improvements were observed in SODA scores on day 28 in the pain (-4.83, -5.46 and -6.22), non-pain (-2.22, -2.32 and -2.31) and satisfaction (0.39, 0.79 and 0.60) categories for the C+O, C, and O groups, respectively. These improvements were enhanced on day 56 in the pain (-7.19, -8.07 and -8.85), non-pain (-4.09, -4.12 and -3.71) and satisfaction (0.78, 1.07, and 0.81) categories in the C+O, C, and O groups, respectively. No significant differences were observed among the three groups and no serious adverse events occurred.

Conclusion Curcumin and omeprazole had comparable efficacy for functional dyspepsia with no obvious synergistic effect.

Trial registration number TCTR20221208003.

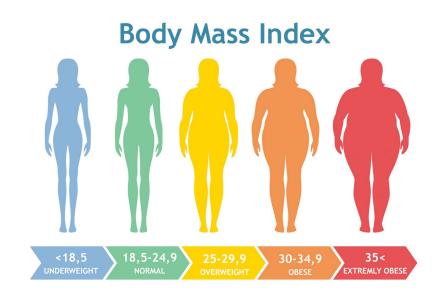
BMJ Journal

- Curcumin and omeprazole had comparable efficacy for functional dyspepsia
- Turmeric may be as good for treating indigestion as a drug to curb excess stomach acid
- This multicentre randomised controlled trial provides highly reliable evidence for the treatment of functional dyspepsia

Kongkam P, Khongkha W, Lopimpisuth C, et alCurcumin and proton pump inhibitors for functional dyspepsia: a randomised, double blind controlled trial BMJ Evidence-Based Medicine 2023: 28:399-

Curcumin: The Anti-Obesity Molecule

- Able to reduce the differentiation of preadipocytes, thus acting as an anti-obesity molecule.
- Curcumin suppresses angiogenesis in adipose tissue together with its effect on lipid metabolism in adipocytes may contribute to lower body fat and body weight gain.
- Increases the catabolism of lipids in adipocytes (by increasing the carnitine palmitoyltransferase 1 (CPT-1) expression involved in β-oxidation).
- Reduces the NF-κB activity and its nuclear translocation, and so it inhibits the recruitmaent of macrophages into the enlarged adipose tissue and reduces the release of IL-6, TNF-α, MCP-1 from adipocytes.



Rheumatoid Arthritis & Osteoarthritis

- Transcription factors and genes involved in inflammation and anti-oxidation are suspected to play a crucial role in RA, suggesting that the antiinflammatory effects and antioxidant properties of curcumin can play a significant role in the treatment and prevention of RA.
- A randomized pilot study found that curcumin treatment in patients with active RA leads to the highest percentage of symptom improvement as compared to patients who were given either NSAIDs alone or a combination of NSAIDs and curcumin.
- Curcumin has similar efficacy to diclofenac but demonstrated better tolerance among patients with knee OA. Curcumin can be an alternative treatment option in the patients with knee OA who are intolerant to the side effects of nonsteroidal anti-inflammatory drugs.



He Y, Yue Y, Zheng X, Zhang K, Chen S, Du Z. Curcumin, inflammation, and chronic diseases: how are thev linked? Molecules. 2015 May 20:20(5):918:-213. doi: 10.3390/molecules.20059183. PMID: 26007179; PMCID: PMC6272784

Shep D. Khanwelkar C. Gade P. Karad S. Safetv and efficacy of curcumin versus diclofenac in knee osteoarthritis: a randomized open label parallelarm study. Trials. 2019 Apr 11:20(1):214. doi: 10.1186/s13063-019-3327-2. PMID: 30975196; PMCID: PMC6460672

Studies: Osteoarthritis

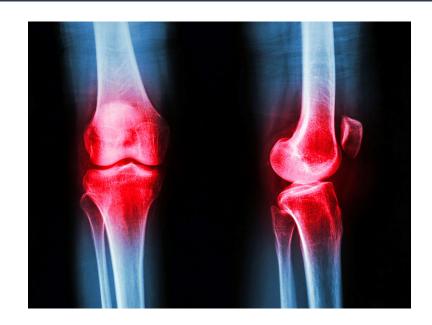
Panahi et al. (2014) study was a randomized, double blind, placebo-controlled trial in 40 knee OA patients:

- Curcumin dramatically improved joint stiffness (measured by WOMAC stiffness subscale) by 507% compared to placebo
- It also significantly improved overall symptoms (WOMAC global score) and pain levels

Randomized controlled trial by Srivastava et al. (2016) with 160 knee OA participants:

 Curcumin provided large improvements in pain (VAS), stiffness, and physical function (measured by WOMAC subscales) at both 60 and 120 days

Another study with 50 OA patients showed curcumin significantly reduced knee pain and celecoxib dependence over eight weeks.



Panahi Y. Rahimnia AR. Sharafi M. Alishiri G. Saburi A. Sahebkar A. Curcuminoid treatment for knee osteoarthritis: a randomized double-blind placebo-controlled trial. Phytother Res. 2014 Nov.28(11):1625-31. doi: 10.1002/ptr.5174. Epub 2014 May 22. PMID: 24853120.

Srivastava, S., Saksena, A.K., Khattri, S. *et al. Curcuma longe* extract reduces inflammatory and oxidative stress biomarkers in osteoarthritis of knee: a four-month, double-blind, randomized, placebo-controlled trial. *Inflammopharmacoi* 24, 377–388 (2016).

Studies: Osteoarthritis

The benefits of curcumin were equivalent or superior to standard NSAID therapy:

- In head-to-head trials comparing curcumin to NSAIDs like diclofenac and ibuprofen, it showed similar efficacy in improving joint pain and function
- Study Design: Randomized, openlabel, parallel, activecontrolled clinical study
- Participants: 139 patients with knee osteoarthritis
- Interventions:
 - Curcumin group: Curcumin 500-mg (BCM-95®) capsule three times daily
 - Diclofenac group: Diclofenac 50-mg tablet two times daily
- Duration: 28 days
- Assessment Time Points: Baseline, days 7, 14, and 28
- Results:
 - Similar improvement in severity of pain and KOOS scale observed in both curcumin and diclofenac groups at days 14 and 28.
 - Significantly greater reduction in episodes of flatulence observed in the curcumin group compared to the diclofenac group at day 7.
 - Weight-lowering effect and anti-ulcer effect observed in the curcumin group at day 28.
 - None of the patients in the curcumin group required H2 blockers, while 19 patients in the diclofenac group did.
 - Adverse effects significantly less in the curcumin group compared to the diclofenac group (13% versus 38%).



Shep D. Khanwelkar C. Gade P. Karad S. Safety and efficacy of curcumin versus diclofenac in knee osteoarthritis: a randomized open-label parallel-arm study. Trials. 2019 Apr 11:20(1):214. doi: 10.1186/s13063-019-3327-2. PMID: 30975196; PMCID: PMC6460672.

Studies: Rheumatoid Arthritis

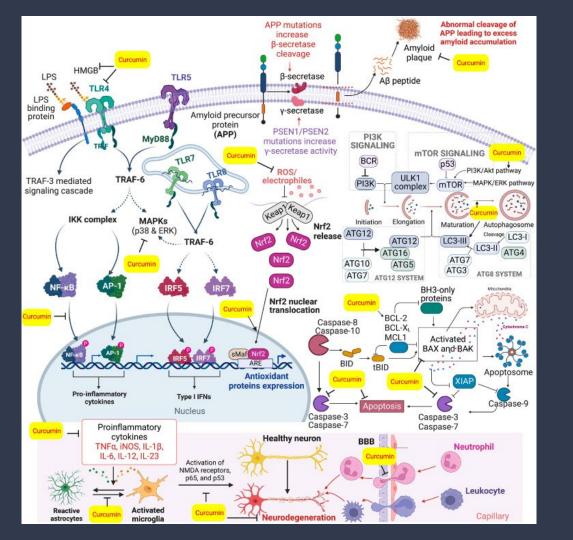
A Novel Highly Bioavailable Curcumin Formulation
Improves Symptoms and Diagnostic Indicators in
Rheumatoid Arthritis Patients: A Randomized,
Double - Blind, Placebo - Controlled, Two - Dose, Three Arm, and Parallel - Group Study

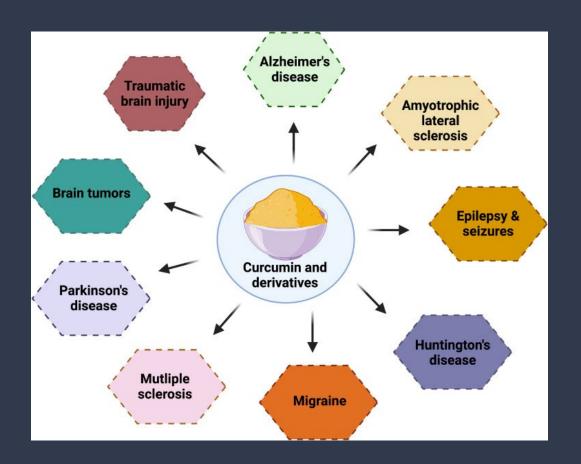
- Randomized, double-blind, placebo-controlled, three-arm, parallel-group study
- Duration: 90 days
- Participants: Patients with active rheumatoid arthritis (RA)
- Treatment groups: Placebo, 250 mg, or 500 mg of curcumin daily
- Significant improvements observed in clinical symptoms compared to placebo
- Measures: American College of Rheumatology (ACR) response, visual analogue scale (VAS), Disease Activity Score 28 (DAS28)
- Both doses of curcumin well-tolerated with no significant adverse effects reported



Amalrai A. Varma K. Jacob J. Divva C. Kunnumakkara AB, Stohs SJ. Gopi S. A Novel Highly Bioavailable Curcumin Formulation Improves Symptoms and Diagnostic Indicators in Rheumatoid Arthritis Patients: A Randomized. Double-Blind. Placebo-Controlled. Two-Dose. Three-Arm. and Paralle-Group Study. J Med Food. 2017 Oct:20(10):1022-1030. doi: 10.1089/jmf.2017.3930. Epub 2017 Aug 29. PMID: 28850308.







Curcumin, inflammation, and neurological disorders: How are they linked?

In particular, *in vitro*, *in vivo*, and clinical studies focusing at the effects of curcumin on NDs revealed that curcumin modulates important signalling pathways and molecules that regulate neuroinflammation. For example, curcumin and its derivatives have been found to regulate Akt/mTOR pathway, NF- κ B pathway, β -catenin pathway, NLRP3 inflammasome pathway, BDNF/TrkB pathway, Nrf2, IL-6/STAT3 inflammatory pathways and DNA repair pathways.

Curcumin's Numerous Benefits on Alzheimer's

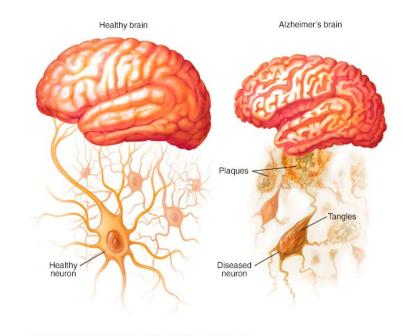
- Reduced Aβ plaques and tau tangles, two key pathological hallmarks of Alzheimer's disease (Frautschy et al., 2001; Ma et al., 2013; Sundaram et al., 2017; Yanagisawa et al., 2015)
- Exerted neuroprotective effects by reducing neuroinflammation and oxidative stress (Agrawal et al., 2010; Bassani et al., 2017; Hoppe et al., 2013)
- Enhanced neurogenes is and synaptic plasticity (Wang et al., 2013a; Wang et al., 2013b; Nam et al., 2014)
- Curcumin has anti-inflammatory and antioxidant properties that may help treat Alzheimer's disease pathology. "As oxidative stress [3] and inflammation [4] are potentially involved in propagating AD pathology, the utility of curcumin in treating and preventing AD is being pursued [5]." (Ringman et al.)
- Curcumin can bind to beta-amyloid plaques in the brain. "Curcumin has a biphenolic structure similar to Congo Red and binds to amyloid plaques in vivo [6]."

 (Ringman et al.)

Curcumin in Alzheimer's Disease

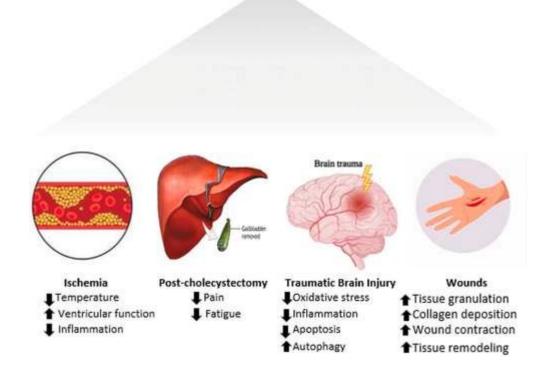
A study by UCLA researchers examined the effects of a bioavailable curcumin supplement on memory and mood in people with mild age -related memory complaints:

- 40 adults between 50-90 years old with mild memory complaints were given either 90 mg of curcumin or placebo twice daily for 18 months (double-blind, placebo-controlled trial)
- Those taking curcumin showed significant improvements in memory and attention compared to placebo after 18 months (28% improvement on memory tests)
 - Curcumin group also had mild improvements in mood
- PET scans revealed those taking curcumin had less amyloid and
- tau accumulation in brain regions related to memory and emotion (amygdala, hypothalamus) compared to placebo
- Curcumin was well-tolerated with only mild side effects (abdominal pain, nausea) reported in a few subjects
 - Researchers concluded curcumin may provide meaningful cognitive benefits over time and reduces Alzheimer's disease pathology based on PET scan results



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The Therapeutic
Role of Curcum in
in Inflam mation
and Post-Surgical
Outcomes

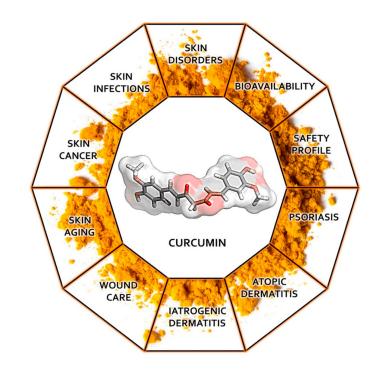


Curcumin

https://www.tandfonline.com/doi/full/10.1080/87559129.2023.2166525

Curcumin: Significant wound healing properties

- Activates/hastens various stages of wound healing
- Discourages bacterial infection of wound tissue
- Decreases body's response to inflammation and oxidation
- Stimulates cell proliferation in damaged tissue in cutaneous wounds
- Huang, Y.; Dan, N.; Dan, W.; Zhao, W. Reinforcement of Polycaprolactone/Chitosan with Nanoclay and Controlled Release of Curcumin for Wound Dressing. ACS Omega2019, 4(27), 22292-22301. DOI: 10.1021/acsomega.9b02217
- Mohanty, C.; Sahoo, S. K. Curcumin and Its Topical Formulations for Wound Healing Applications. *Drug Discovery Today*2017, <u>22(10)</u>, 1582–1592. DOI: 10.1016/j.drudis.2017.07.001.
- Fereydouni, N.; Darroudi, M.; Movaffagh, J.; Shahroodi, A.; Butler, A. E.; Ganjali, S.; Sahebkar, A. Curcumin Nanofibers for the Purpose of Wound Healing. J. Cell. Physiol 2019, 234(5), 5537–5554. DOI: 10.1002/jcp.27362.



Curcumin Contraindications

- Surgery: Turmeric might slow blood clotting. It might cause extra bleeding during and after surgery. Stop using turmeric at least 2 weeks before a scheduled surgery.
- Gallbladder problems: Turmeric can worsen gallbladder problems because of its ability to increase bile secretion.
 People should avoid using turmeric supplements if they have gallstones or bile duct obstruction.
- Iron deficiency: High amounts of turmeric may interfere with iron absorption in the body. Therefore, people with iron deficiency should use turmeric cautiously.
- Gastroesophageal reflux disorder: Turmeric can worsen stomach problems such as GERD. People with GERD should monitor for exacerbation of symptoms while having turmeric.
- Diabetes: Curcumin, a chemical present in turmeric, might reduce blood sugar levels in people with diabetes.



In Conclusion ...

Curcumin can be a viable support for multiple inflammatory conditions as well as disease prevention due to its properties.

For questions or comments please reach out to me:

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