Use of Turmeric/Curcumin in Inflammation, Arthritis, Osteoarthritis and Colon Cancer

Botanical Name: *Curcuma longa*

Has been used since time immemorial as an important spice in Asian population and also as a traditional medicine.

This narrative review of human trials addresses the scientific evidence for potential health benefits of turmeric and its curcuminoids in the treatment of arthritis, diabetes, and the metabolic syndrome and discusses recommendations for future research.

Reference:

Nutrition Today. 2020; 55(1):45–56

Turmeric is obtained from the rhizome of *Curcuma longa L.* (Zingiberaceae family). Three curcuminoids, curcumin, demethoxycurcumin, and bisdemethoxycurcumin, of which curcumin is the most prevalent, are among many bioactive ingredients in turmeric. The yellow pigment curcumin or diferuloylmethane makes up 60% to 70% of crude turmeric extracts and is the principal curcuminoid evaluated for health-promoting activities.

Reference:

Nelson K, Dahlin J, Bisson J, et al. The essential medicinal chemistry of curcumin. J Med Chem. 2017; 60:1620–1637.

Turmeric contains sugars, proteins, resins, and volatile oils, such as turmerone, atlantone, and zingiberene, some of which may have bioactivity as well.

References:

Eke-Okoro U, Raffa R, Pergolizzi J, et al. Curcumin in turmeric: basic and clinical evidence for a potential role in analgesia. J Clin Pharm Ther. 2018; 43:460–466.

Aggarwal B, Yuan W, Li S, Gupta S. Curcumin-free turmeric exhibits anti-inflammatory and anticancer activities: identification of novel components of turmeric. Mol Nutr Food Res. 2013; 57: 1529–1542.

Kawasaki K, Okuda-Hanafusa C, Aoyagi M, et al. Inhibitory effect of the compounds from the water extract of Curcuma longa pn the production of PGE2 and NO in a macrophage cell line stimulated by LPS. Biosci Biotechnol Biochem. 2018; 82: 2109–2117.

Numerous preclinical investigations identified a variety of potential health benefits, including treatment for heart disease, arthritis, Alzheimer's disease, gastrointestinal disorders, and the metabolic syndrome (MetS).

Reference:

Singletary K. Turmeric: an overview of potential health benefits. Nutr Today. 2010; 45:216–225.

Initial human trials examining the biological actions of oral curcumin given as raw turmeric powder were confronted with its poor water solubility, low intestinal absorption, and rapid metabolic degradation, which limited its systemic distribution and bioavailability.

Reference:

Nelson K, Dahlin J, Bisson J, et al. The essential medicinal chemistry of curcumin. J Med Chem. 2017; 60:1620–1637.

Considerable research led to improvements in curcumin's bioavailability, For example, curcumin can be incorporated into micelles, microemulsions, liposomes, nanoparticles, and in other lipid and biopolymer particles.

Curcuminoids encapsulated with turmeric essential oils, particularly with turmerone, which enhances intestinal permeability, also have been prepared. Noticeable improvements in oral bioavailability in human subjects were reported using these novel formulations.

References:

Sanidad K, Sukamtoh E, Xiao H, McClements DJ, Zhang G. Curcumin: recent advances in the development of strategies to improve oral bioavailability. Ann Rev Food Sci Technol. 2019; 10:597–617.

Douglass B, Clouatre D. Beyond yellow curry: assessing commercial curcumin absorption technologies. J Am Coll Nutr. 2015; 34:347–358.

Prasad S, Tyagi A, Aggarwal B. Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: the golden pigment from golden spice. Cancer Res Treat. 2014; 46: 2–18.

Shoba G, Joy D, Joseph T, et al. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. Planta Med. 1998; 64:353–356.

Briskey D, Sax A, Mallard A, Rao A. Increased bioavailability of curcumin using a novel dispersion technology system (LipiSperse®). Eur J Nutr. 2019; 58:2087–2097. doi.org/10.1007/ s00394-018-1766-2.

Sasaki H, Sunagawa Y, Takahashi K, et al. Innovative preparation of curcumin for improved oral bioavailability. Biol Pharm Bull. 2011; 34:660–665.

Mahale J, Singh R, Howells L, et al. Detection of plasma curcuminoids from dietary intake of turmeric-containing food in human volunteers. Mol Nutr Food Res. 2018; 62. doi:10.1002/mnfr.201800267.

Anti-inflammatory Activities:

We believe that curcumin possesses several advantages over other synthetic NSAIDs such as sulindac, piroxicam, and aspirin that are already in human clinical trials.

Reference:

Chinthalapally V Rao, Anraham Rivenson, Barbara Simi and Bandaru S Reddy. Chemoprevention of Colon Cancer by Dietary Curcumin. Annals New York Academy of Sciences. 1993, Divisions of Nutritional Carcinogenesis, American Health Foundation, Valhalla, New York 10595, p 203.

For centuries, *Curcuma longa* (turmeric) was used as a spice in Asian cuisine and as a medicinal herb for treatment of inflammation, pain, wound healing, and digestive disorders, to name a few.

Reference:

Keith Singletary, Turmeric, Potential Health Benefits; Nutrition Today, Volume 55, Number 1, January/February 2020, p 45

Arthritis and Osteoarthritis:

More than a dozen arthritis trials were performed using a variety of proprietary curcuminoid preparations engineered to improve oral bioavailability. All studies demonstrated some improvement in patients' arthritis symptoms, although changes in specific clinical measures varied among trials. Taken together, the trials that provided statistical comparisons of curcuminoid outcomes with those of placebo controls reported significant improvement in either pain or physical function.

References:

Panahi Y, Rahimnia A, Sharafi M, et al. Curcuminoid treatment for knee osteoarthritis: a randomized double-blind placebocontrolled trial. Phytother Res. 2014; 28:1625–1631.

Belcaro G, Cesarone MR, Dugall M, et al. Efficacy and safety of Meriva®, a curcumin-phosphatidylcholine complex, during extended administration in osteoarthritis patients. Altern Med Rev. 2010; 15:337–344.

Amalraj A, Varma K, Jacob J, et al. A novel highly bioavailable curcumin formulation improves symptoms and diagnostic indicators in rheumatoid arthritis patients: a randomized, doubleblind, placebo-controlled, two-dose, three-arm, and parallel-group study. J Med Food. 2017; 20:1022–1030.

Nakagawa Y, Mukai S, Yamada S, et al. Short-term effects of highly-bioavailable curcumin for treating knee osteoarthritis: a randomized, double-blind, placebo-controlled prospective study. J Orthop Sci. 2014. doi:10.1007/s00776-014-0633-0.

It is noteworthy that a curcuminoid-free polysaccharide fraction isolated from turmeric (Turmacin) significantly decreased arthritis symptom scores, compared with placebo.

Reference:

Madhu K, Chanda K, Saji M. Safety and efficacy of Curcuma longa extract in the treatment of painful knee osteoarthritis: a randomized placebo-controlled trial. Inflammopharmacology. 2013; 21:129–136.

Polysaccharides from C longa have been reported to have antiinflammatory and immunomodulatory activities, as have sesquiterpenoids in water extracts.

References:

Illuri R, Bethapudi B, Anandakumar S, et al. Anti-inflammatory activity of polysaccharide fraction of Curcuma longa extract (NR-INF-02). Antiinflamm Antiallergy Agents Med Chem. 2015; 14:53–62.

Kawasaki K, Okuda-Hanafusa C, Aoyagi M, et al. Inhibitory effect of the compounds from the water extract of Curcuma longa on the production of PGE2 and NO in a macrophage cell line stimulated by LPS. Biosci Biotech Biochem. 2018; 82:2109–2117. doi:10.1080/09168451.2018.1511366.

Systematic reviews of arthritis trials indicate that minor adverse gastrointestinal disturbances were the most common adverse effects of turmeric and curcuminoid administration, although curcuminoids generally exhibited a lower risk of these events compared with prescribed drugs.

References:

Gaffey A, Slater H, Porritt K, Campbell J. The effects of curcuminoids on musculoskeletal pain: a systematic review. JBI Database System Rev Implement Rep. 2017; 15:486–516.

Bannuru R, Osani M, Al-Eid F, Wang C. Efficacy of curcumin and Boswellia for knee osteoarthritis: systematic review and metaanalysis. Semin Arthritis Rheum. 2018; 48:416–429. doi.org/10. 1016/j.semarthrit.2018.03.001.

One study examined knee joint aspirations from patients and found that, when compared with baseline values, the administration of either curcuminoids or diclofenac resulted in similar, not significantly different, suppression of cyclooxygenase-2 secretion by synovial fluid monocytes.

Reference:

Kertia N, Asdie A, Rochmah W. Marsetyawan. Ability of curcuminoid compared to diclofenac sodium in reducing the secretion of cyclooxygenase-2 enzyme by synovial fluid's monocytes of patients with osteoarthritis. Indones J Intern Med. 2012; 44: 105–113.

Systematic reviews and meta-analyses of select arthritis trials provide evidence that supports the efficacy of curcuminoids in treating arthritis with fewer adverse effects than with NSAIDs.

References:

Rahimnia A, Panahi Y, Alishiri G, et al. Impact of supplementation with curcuminoids on systemic inflammation in patients with knee osteoarthritis: findings from a randomized doubleblind placebo-controlled trial. Drug Res (Stuttg). 2015; 65:521–525.

Haroyan A, Mukuchyan V, Mkrtchyan N, et al. Efficacy and safety of curcumin and its combination with boswellic acid in osteoarthritis: a comparative, randomized, double-blind, placebocontrolled study. BMC Complement Altern Med. 2018;18:7–22

Gaffey A, Slater H, Porritt K, Campbell J. The effects of curcuminoids on musculoskeletal pain: a systematic review. JBI Database System Rev Implement Rep. 2017;15:486–516.

Sahebkar A, Henrotin Y. Analgesic efficacy and safety of curcuminoids in clinical practice: a systematic review and metaanalysis of randomized controlled trials. Pain Med. 2016;17: 1192–1202.

Liu X, Machado G, Eyles J, Ravi V, Hunter D. Dietary supplements for treating osteoarthritis: a systematic review and metaanalysis. Br J Sports Med. 2018; 52:167–175.

Daily J, Yang M, Park S. Efficacy of turmeric extracts and curcumin for alleviating the symptoms of joint arthritis: a systematic review and meta-analysis of randomized trials. J Med Food. 2016; 19:717–729.

An alcohol extract of turmeric (1.5 g/d) given to pre-diabetic individuals for 9 months significantly decreased fasting blood glucose (FBG), hemoglobin A1c (HbA1c), and insulin resistance (IR), compared with controls. It also reduced the prevalence of newly diagnosed T2DM patients.

Reference:

Chuengsamarn S, Rattanamongkolgul S, Luchapudiporn R, et al. Curcumin extract for prevention of type 2 diabetes. Diabetes Care. 2012; 35:2121–2127.

In combination with metformin, curcuminoids decreased blood low-density lipoprotein (LDL) levels.

Reference:

Maithili Karpaga Selvi N, Sridhar M, Swaminathan R, Sripradha R. Efficacy of turmeric as adjuvant therapy in type 2 diabetic patients. Ind J Clin Biochem. 2015;30:180–186

Curcuminoid intake was associated with improvements in FBG, TG, and high-density lipoprotein (HDL) levels and diastolic blood pressure.

References:

Saberi-Karimian M, Parizadeh S, Ghayour-Mobarhan M, et al. Evaluation of effects of curcumin in patients with metabolic syndrome. Comp Clin Pathol. 2018; 27:555–563

Avansar S. The effects of eight weeks interval training and curcumin consumption on TNF-α and BDNF levels in men with metabolic syndrome. J Ardabil Univ Med Sci. 2017; 17:299–310.

Another meta-analysis128 of prediabetes and T2DM trials, which were typically of 2- to 3-month duration, found that curcuminoids significantly decreased HbA1c levels in prediabetes and T2DM and decreased FBG levels in T2DM.

References:

Chuengsamarn S, Rattanamongkolgul S, Luchapudiporn R, et al. Curcumin extract for prevention of type 2 diabetes. Diabetes Care. 2012; 35:2121–2127

Usharani P, Mateen A, Naidu A, Raju Y, Chandra N. Effect of NCB-02, atorvastatin and placebo on endothelial function, oxidative stress and inflammatory markers in patients with type-2 diabetes mellitus. Drugs R D. 2008; 9:243–250.

Khajehdehi P, Pakfetrat M, Javidnia K, et al. Oral supplementation of turmeric attenuates proteinuria, transforming growth factor-ß and interleukin-8 levels in patients with overt type 2 diabetic nephropathy: a randomized, double-blind and placebocontrolled study. Scand J Urol Nephrol. 2011; 45:365–370

Chuengsamarn S, Rattanamongkolgul S, Phonrat B, et al. Reduction of atherogenic risk in patients with type 2 diabetes by curcuminoid extract: a randomized trial. J Nutr Biochem. 2014; 25: 144–150.

Jiminez-Osorio A, Garcia-Nino W, Gonzalez-Reyes S, et al. The effect of dietary supplementation with curcumin on redox status and Nrf2 activation in patients with nondiabetic or diabetic proteinuric chronic kidney disease: a pilot study. J Ren Nutr. 2016; 26:237–24

Adab Z, Eghtesadi S, Vafa M, et al. Effect of turmeric on body measurement indices, glycemic condition, and lipid profile in hyperlipidemic patients with type 2 diabetes. Iran J Nutr Sci Food Technol. 2013; 8:217–227.

Colon Cancer:

Colon cancer is the third leading cause of cancer death in the United States. The incidence of colon cancer worldwide can vary up to 20-fold with the highest prevalence in areas such as North America, Europe, Australia, and New Zealand.

Reference:

P. Pisani, F. Bray, D.M. Parkin, Estimates of the world-wide prevalence of cancer for 25 sites in the adult population, Int. J. Cancer 97 (2002) 72–81.

Pre-clinical studies in a variety of cancer cell lines including breast, cervical, colon, gastric, hepatic, leukemia, oral epithelial, ovarian, pancreatic, and prostate have consistently shown that curcumin possesses anti-cancer activity in vitro and in pre-clinical animal models.

Reference:

B.B. Aggarwal, A. Kumar, A.C. Bharti, Anticancer potential of curcumin: preclinical and clinical studies, Anticancer Res. 23 (2003) 363–398.

Overwhelming in vitro evidence and completed clinical trials suggests that curcumin may prove to be useful for the chemoprevention of colon cancer in humans.

Reference:

Jeremy James Johnson and Hasan Mukhtar. Curcumin for chemoprevention of colon cancer. Cancer Letters, 255 (2007): 170–181

Pre-clinical studies in a variety of cancer cell lines have consistently shown that curcumin possesses anti-cancer activity in vitro.
Five human clinical trials have been conducted in colon cancer patients and are attempting to answer basic questions like safety, tolerability, pharmacokinetic, and pharmacodynamic issues. Every clinical trial has concluded that curcumin is safe and poses minimal adverse effects.

Reference:

B.B. Aggarwal, A. Kumar, A.C. Bharti, Anticancer potential of curcumin: preclinical and clinical studies, Anticancer Res. 23 (2003) 363–398.

Doctors are always looking for ways to stop bowel cancer developing, or coming back after surgery and they thought curcumin may help. In this study, researchers gave curcumin capsules to people who had a test to look for bowel polyps or had surgery to remove bowel cancer.

This study looked at the possibility of giving curcumin capsules to people with bowel cancer or bowel polyps to help prevent bowel cancer developing, or coming back after surgery. This study was supported by Cancer Research UK.
Bowel or colon cancer is one of the most common cancers in the UK. Curcumin is a natural substance found in the spice turmeric, a spice used in curries. Cultures that use a lot of turmeric in their cooking seem to have a low amount of bowel cancer in the population. The curcumin in turmeric may be one reason for this. Laboratory studies have also shown that curcumin may help stop bowel cancer cells growing.

The study team found that curcumin was safe to take.

Reference:

A study looking at curcumin to help prevent bowel cancer or stop it coming back; Cancer Research UK (trial number CRUK/07/034).

Long-term feeding of curcumin not only significantly inhibited AOM-induced colon tumorigenesis, but also produced no gross changes in liver, kidney, stomach, intestine, and lungs. It is also noteworthy that when compared to other naturally occurring colon cancer chemopreventive agents such as dithiol thiones and diallyl disulfide, to cite a few, curcumin produced a better or equally potent colon tumor-inhibitory action.

Reference:

M.J. Thun, S.J. Henley, C. Patrono, Nonsteroidal antiinflammatory drugs as anticancer agents: mechanistic, pharmacologic, and clinical issues, J. Natl. Cancer Inst. 94 (2002) 252–266.

Although the precise mechanism by which curcumin inhibits the AOM-induced colon tumorigenesis has not been established, it would appear that one possible action involves anti-inflammatory activity by curcumin.

Reference:

P.M. Calvert, H. Frucht, The genetics of colorectal cancer, Ann. Intern. Med. 137 (2002) 603–612.

An advantage of curcumin over its synthetic counterparts is that curcumin has an established record of safety with an understanding of its mechanism of action. Curcumin is a compound that has been shown to target multiple pathways in vitro and has been shown to be safe in oncology patients. The use of curcumin in oncology patients to assess its efficacy is an exciting and emerging area and warrants further studies in colon cancer as well as other cancers.

Reference:

Jeremy James Johnson and Hasan Mukhtar. Curcumin for chemoprevention of colon cancer. Cancer Letters, 255 (2007): 170–181

Safety:

Turmeric, its essential oils, and oleoresins are generally recognized as safe by the US Food and Drug Administration. A similar designation for curcuminoids has not yet been published by the Food and Drug Administration. Studies in animals indicate that curcuminoids have relatively low potential for toxicity.

References:

Sahebkar A, Henrotin Y. Analgesic efficacy and safety of curcuminoids in clinical practice: a systematic review and metaanalysis of randomized controlled trials. Pain Med. 2016; 17: 1192–1202.

Dadhaniya P, Patel C, Muchhara J, et al. Safety assessment of a solid lipid curcumin particle preparation: acute and subchronic toxicity studies. Food Chem Toxicol. 2011; 49:1834–1842.

Storka A, Vcelar B, Klickovic U, et al. Safety, tolerability and pharmacokinetics of liposomal curcumin in healthy humans. Int J Clin Pharmacol Ther. 2015; 53:54–65.

Soleimani V, Sahebkar A, Hosseinzadeh H. Turmeric (Curcuma longa) and its major constituent (curcumin) as nontoxic and safe substances: review. Phytother Res. 2018; 32:985–995.

In humans, the intake of turmeric powder as high as 8 g/d has apparently been tolerated with only minor adverse consequences, mainly gastrointestinal distress.

Reference:

Cheng A, Hsu C, Lin J, et al. Phase I clinical trial of curcumin, a chemopreventive agent, in patients with high-risk or premalignant lesions. Anticancer Res. 2001; 21:2895–2900.

Research findings on curcuminoids for the treatment of arthritis and possibly of T2DM are promising.

Reference:

Keith Singletary, Turmeric, Potential Health Benefits; Nutrition Today, Volume 55, Number 1, January/February 2020, p 51