

TURMERIC

(Curcuma longa)

An Overview of the Research
and Clinical Indications



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PROFESSIONAL RESOURCES

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BACKGROUND AND USES

Turmeric, or *Curcuma longa*, is a spice native to India. Historically, turmeric has been used throughout India, China and Indonesia as a spice and medicinal agent. Turmeric is a mild spice that enhances the flavor of other spices and foods and is the base of most Indian curries. Traditionally, turmeric has been used topically to heal and reduce bleeding associated with bruises, sprains, leech bites and inflamed joints. It has also been used internally for liver and digestive complaints, menstrual insufficiency and cramping, jaundice, and as an anti-inflammatory agent.

In the Ayurvedic tradition, turmeric, or “haldi” as it is known in Hindi, works well with all doshas, with its main action being to reduce mucus from the system¹. Turmeric is considered to be one of the most important herbs in the Ayurvedic tradition. The medical use of turmeric goes back more than 5000 years. Turmeric is ubiquitous in India, and can be found in the turmeric plantations, herbal medicine preparations, spice bazaars, dyes, and in food.

In the United States of America, Turmeric has been granted “Generally Recognized as Safe” (GRAS) status by the FDA.

Turmeric has been used traditionally for almost every human ailment and many of these historic uses have been scientifically validated with application in modern times.

ACTIVE CONSTITUENTS

The rhizome, or root, of Turmeric is the part used medicinally. Numerous constituents have been identified in turmeric. The main constituent group are polyphenolic curcuminoids which include: curcumin (diferuloylmethan), demethoxycurcumin, bisdemethoxycurcumin, and cyclocurcumin.² The yellow-pigmented curcuminoids represent 2% -5% of the root, typically composed of 85% as curcumin, 10% as demthoxycurcumin and 5% as disdemethoxycurcumin. Curcumin is the most well studied constituent. Turmeric also contains: sesquiterpenes (turmerone, atlantone, zingiberone, turmeronol, germacrone, and bisabolene), carbohydrates, protein, resins, and caffeic acid.

MECHANISM OF ACTION

There are over 3000 preclinical studies on turmeric and its constituents. Curcumin is considered to be the most active constituent in *Curcuma longa*. Much of the understanding of the pharmacology of this plant derives from research on curcumin. Curcumin, and turmeric as a whole plant extract, demonstrate **antioxidant** effects. Curcumin can protect DNA against single strand breaks induced by single oxygen.³ Turmeric, and curcumin in particular, suppresses the mutagenicity of several common

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mutagens including cigarette smoke, benzopyrene, DMBA, etc.⁴ Turmeric extracts, and curcumin specifically, have been demonstrated to be potent **anti-inflammatory** agents. When administered orally, curcumin inhibits neutrophil function, inhibits platelet aggregation, inhibits lymphocyte activity, promotes fibrinolysis, and stabilizes lysosomal membranes.⁵ Curcumin also inhibits NF-kB activation, thereby decreasing the activation of multiple downstream inflammatory genes. Curcumin inhibits platelet aggregation by inhibiting the formation of thromboxanes (promoters of aggregation) and increasing prostacyclin (thus inhibiting platelet aggregation).⁶ Curcumin has demonstrated a wide range of **cancer preventive** (chemopreventive) actions.⁷ These actions are the result of a combination of effects including inhibition of phase 1 cytochrome p450 enzymatic activation of pro-carcinogens; enhanced phase 2 detoxification activity, especially glutathione transferase, and inhibition of multiple signal transduction pathways that trigger cell proliferation, angiogenesis, and invasion. Curcumin inhibits NF-kB activation⁸ with resultant down-regulation of multiple inflammatory genes. Down-regulation of these genes result in decreased proliferation signaling, anti-angiogenic effects, and decreased cell invasiveness.

Orally dosed turmeric and curcumin extracts **alter serum lipids**, specifically decreasing total cholesterol, LDL cholesterol and LDL peroxidation, and increasing HDL cholesterol in humans.⁹ Curcumin interferes with intestinal cholesterol-uptake, increases the conversion of cholesterol into bile acids by increasing the activity of hepatic cholesterol-7-alpha-hydroxylase (the rate limiting enzyme in bile acid synthesis), and increasing bile acid secretion.¹⁰ Curcumin possesses **hepatoprotective and choleric properties**. Curcumin has been demonstrated in-vivo to prevent lipid peroxidation from diverse agents such as carbon tetrachloride, and aflatoxin from aspergillus parasiticus.¹¹ In animal models, curcumin is a potent choleric, increasing bile output by almost 100% in one study.¹² Turmeric and curcumin has been historically used as a **carminative and digestive**. Curcumin stimulates digestion of fats and carbohydrates in animal models.¹³

Turmeric has **antimicrobial actions**. The essential oils of turmeric root inhibit the growth of a variety of bacteria, parasites and pathogenic fungi. Several animal studies have shown that animals infected with various pathogens that normally result in topical lesions exhibit a reduction of these lesions with the application of turmeric oil.¹⁴

For the scope of this research review, this paper will focus on the clinical research related to the anti-inflammation actions of turmeric.

CLINICAL RESEARCH SUMMARY

Uveitis

A 12 week pilot study conducted in India enrolled 53 patients with chronic anterior uveitis. The subjects received orally administered curcumin derived from Curcuma

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longa.¹⁵ Thirty-two patients completed the trial. Patients with a strong PPD reaction received anti-tubercular treatment in addition to the curcumin. Both groups demonstrated improvement beginning after 2 weeks of treatment; 86% of the group also receiving anti-tubercular treatment improved and 100% of the curcumin alone group improved. Follow-up for 3 years indicated a recurrence of 55% in the curcumin alone group and 36% in the curcumin and anti-tubercular medication group. These results are comparable to corticosteroid therapy, the standard treatment for this disease.

In 2010, curcumin was studied in a clinical trial of 122 patients with recurrent anterior uveitis.¹⁶ This nonrandomized study utilized a daily dose of 1200 mg of a curcumin-phosphatidylcholine complex in addition to prior conventional steroid and anti-infective therapy for one year. Symptomatic improvement and the frequency of relapse were studied. The study found that after a few weeks of treatment symptoms of eye pain, blurring of vision, and pericorneal hyperemia significantly improved in more than 80% of subjects. Additionally, after one year of treatment with the curcumin-phosphatidylcholine complex, the frequency of relapse decreased significantly ($p < 0.001$). There were 275 relapses 1 year before the treatment and only 36 relapses at the end of the year follow-up period after treatment with the curcumin complex. Overall, of the 128 subjects, 7 worsened and 15 dropped out due to noncompliance and the remainder (88%) demonstrated subjective and objective improvements at one year.

Chemoprevention / Anti-carcinogenesis

As of 2012, curcumin has been the subject of over 20 clinical trials in the context of cancer. This body of data demonstrates significant chemopreventive and anticancer potential for curcumin. Notable studies are summarized below.

Pancreatic Cancer

A phase I/II clinical trial enrolled 21 gemcitabine (Gemzar) resistant patients with advanced pancreatic cancer.¹⁷ All patients received 8g curcumin daily in combination with gemcitabine. The agent used contained curcuminoids with 73% curcumin, 22% demethoxycurcumin, 4% disdemethoxycurcumin. Plasma curcumin levels ranged from 29 – 412 ng/mL. No dose-limiting toxicities were observed and the toxicity profile was comparable with that of gemcitabine, therefore the combination was determined not to increase toxicity. In contrast, several subjects reported an improvement of cancer or chemotherapy-related symptoms after starting curcumin. The median survival after initiation of curcumin was 161 days (95% CI 109-223). The one-year survival rate was 19% (95% CI 4.4% – 41.4%). However, median survival after failure of first-line gemcitabine is 70 days, which makes the results of this study significant. Of note, a prior clinical study failed to demonstrate clinical response in 17 patients with advanced pancreatic cancer with an 8000mg dose of curcumin concurrent with gemcitabine.¹⁸ More clinical study is needed for this indication.

Colorectal Cancer

A placebo-controlled clinical trial randomized 126 patients with colorectal cancer to either receive curcumin or placebo.¹⁹ All patients also received surgery followed by radiotherapy, chemotherapy, chemoradiotherapy, or no additional therapy. The curcumin group received 360mg curcumin three times daily pre-surgery (10 – 30 days). Blood (pre- and post) and tissue samples were analyzed. The body weight of Curcumin patients increased (approx. 4%) vs. weight loss of 6% in placebo group ($p < 0.05$). This was thought to be due to a significant 60% reduction of TNF- α in the curcumin group ($p < 0.5$), as TNF- α causes cancer cachexia. Furthermore, in the resected colon tissue, curcumin increased the prevalence of apoptosis (associated with increased Bax and inhibited Bcl-2) and p53 expression (major tumor suppressor gene) over tissue from placebo group.

Another phase IIa clinical trial assessed the impact of two different doses of curcumin on the prevention of colorectal neoplasia.²⁰ The effects of oral curcumin (2g or 4g per day for 30 days) on the number of aberrant crypt foci was assessed in a nonrandomized, open-label clinical trial in 44 eligible smokers with eight or more aberrant crypt foci on screening colonoscopy. Forty-one subjects completed the study. There was a 40% reduction in aberrant crypt foci number in the 4g group ($P < 0.005$), whereas no significant reduction was observed in the 2g dose group. The reduction in crypts corresponded to increased plasma curcumin/conjugate levels.

Multiple Myeloma

Monoclonal Gammopathy of Undetermined Significance (MGUS) and Smoldering Multiple Myeloma (SMM) are asymptomatic plasma cell disorders which can progress to multiple myeloma (MM) over a long period (up to 20 years). Abnormal serum free light chain ratio increases risk of progression. An abnormal ratio is indicative of an excess of one light chain over the other, indicating clonal (neoplastic) expansion. Curcumin has been shown in-vitro to inhibit proliferation of MM cells by down-regulating IL-6 and NF- κ B, inhibiting osteoclastogenesis and reducing bone turnover by suppressing RANKL signaling. A randomized, double-blinded placebo-controlled cross-over trial with curcumin enrolled 19 patients with MGUS and 17 patients with SMM.²¹ Nineteen patients completed 4g curcumin daily cross-over study and 18 patients completed 8g curcumin daily cross-over study. Both 4 and 8g daily doses reduced the serum-free light chain ratio (35% and 36% respectively) and reduced total serum protein ($P = 0.04$) in the urine in both MGUS and SMM patients. Patients with abnormal serum free light chain ratios at study onset had the greatest response. Curcumin also decreased markers of bone turnover (urinary DPYD) and excretion of crosslinked N-telopeptides by more than 25%.

Cardiovascular disease

Age-related cardiovascular decline in postmenopausal women is characterized, in part, by increased left ventricular afterload, an indication of vascular dysfunction and hypertension. An 8 week pilot study randomized 45 postmenopausal women to one of four interventions: placebo, 150mg curcumin, exercise training plus placebo or exercise training plus curcumin.²² Only in the exercise and curcumin group did the aortic brachial systolic pressure, a measure of left ventricular afterload, decrease significantly ($p < 0.05$). This study suggests that adding curcumin to regular exercise provides enhanced cardiovascular fitness in postmenopausal women.

Arthritis

Based upon earlier studies demonstrating the potential benefit of curcumin in improving joint function, the long-term efficacy and safety of curcuminoid and phosphatidylcholine extract was investigated in an 8 month long pilot study involving 100 osteoarthritis patients.²³ Patients served as controls (standard conventional treatment only) or received additional treatment of 1000mg curcuma extract providing 200mg curcumin daily. The composition of the test material was a natural curcuminoid mixture (20%), phosphatidyl- choline (40%), and microcrystalline cellulose (40%). The clinical end points included the scores on various validated assessment tools, as well as selected inflammatory biomarkers. Five patients in the treatment group and six patients in the control group left the study for non-medical reasons. At the conclusion of the study, all subjective and objective parameters were improved in the treatment group over the control group ($p < 0.05$). The curcumin group had improved scores for joint pain and stiffness, physical function, and social and emotional function.

Diabetes

A randomized, parallel-group, placebo-controlled 8-week study randomized 72 patients with type 2 diabetes to receive either 300mg curcumin twice daily, atorvastatin 10mg daily or placebo.²⁴ Endothelial function was assessed at baseline and post-treatment. Additionally, blood levels of biomarkers IL-6, TNF-alpha, malondialdehyde and endothelin-1 were measured pre- and post-treatment. Sixty-seven patients completed the study. Compared with baseline, there was significant and comparable improvement in endothelial function in both the atorvastatin and the curcumin groups. Additionally all biomarkers decreased in both treatment groups, whereas no improvements were seen in the placebo group.

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Digestive disorders

A pilot demonstrated improved symptoms and reduced medications from oral curcumin in patients with ulcerative colitis and Crohn's disease.²⁵

An open, phase II trial was performed on 25 patients with endoscopically-diagnosed gastric ulcer. Participants were given 600mg powdered turmeric five times daily. After four weeks, ulcers had completely healed in 48 percent of patients. The success rate increased over time, with 76 percent being ulcer free after 12 weeks of treatment. No significant adverse reactions or blood abnormalities were noted.²⁶

A partially blinded, randomized, two-dose pilot study randomized 207 healthy subjects to receive one to two tablets of turmeric extract for 8 weeks.²⁷ The prevalence of IBS decreased by 41% in the one-tablet group and 57% in the two-tablet group. Additional, abdominal pain and discomfort decreased by 22% and 25% in the two groups.

A pilot study of 25 patients positive for H. pylori and functional dyspepsia assessed the efficacy of non-antibiotic therapy.²⁸ Subjects received 20mg of pantoprazole twice daily along with 600mg twice daily of N-acetylcysteine, 100mg twice daily of lactoferrin and 30mg twice daily of curcumin. These three agents were administered orally for 7 days. Assessments included: H.pylori status, assessed by (13)C-urea breath test, a scale of upper gastrointestinal symptoms, and blood levels of pepsinogens, gastrin, and anti-H. pylori IgG antibodies. Twelve percent (3/25) patients were cured of H. pylori infection. There was significant improvement in gastrointestinal symptoms ($p < 0.001$) and in pepsinogen levels ($p < 0.001$) in treated patients. IgG and gastrin levels did not change significantly. The study suggests that this regimen is effective in reducing dyspeptic symptoms associated with H. pylori without eradicating the H. pylori infection.

CLINICAL INDICATIONS, PRACTITIONER DOSING, CONTRAINDICATIONS AND TOXICITY

Clinical Indications

- Generalized chronic inflammation
- Uveitis
- Chemoprevention with specific indication to reduce the risk of colorectal and pancreatic cancers as well as multiple myeloma
- Age-related cardiovascular disease
- Osteoarthritis
- Dyspepsia, irritable bowel syndrome and gastric ulceration

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Dosage range

Doses of 500-8,000mg of powdered turmeric per day have been used in human studies. Standardized extracts are typically used in lower amounts, in the 250-2,000mg range.

Contraindications

Having been granted “Generally Recognized as Safe” (GRAS) status in the United States of America by the Food and Drug Administration (FDA), turmeric is well tolerated by most people. Whole herb curcuma might alter the pharmacokinetics of co-administrated drugs by up-regulating the function and expression levels of intestinal P-gp, a protein involved in drug efflux from the cell. However, curcumin extract does not upregulate P-gp.²⁹ Curcumin inhibits CYP3A4 and CYP2C9 and is itself metabolized by CYP1A1 and CYP2B1.³⁰ Therefore, there is the theoretical possibility of interference with drugs metabolized through 3A4. However, it is possible that curcumin lacks clinically significant (in vivo) CYP3A4 activity.

Toxicity

No significant toxicity has been reported following short or long-term administration of turmeric extracts at standard doses.

CONCLUSIONS

Turmeric is one of the most widely studied herbs in the materia medica and it has been used medicinally for over 5000 years. The main action underlying most of the clinical effects of turmeric is its remarkable anti-inflammatory action. While turmeric is somewhat effective short-term, the long-term use of turmeric potentially carries the greatest benefit. Both as a culinary spice and as a medicinal agent, turmeric may thwart the course of chronic illnesses such as uveitis, cancer, osteoarthritis, diabetes, dyspepsia and cardiovascular disease.

ABOUT THE AUTHOR

Dr. Lise Alschuler is a naturopathic doctor with board certification in naturopathic oncology. She graduated from Brown University with an undergraduate degree in Medical Anthropology and received a doctoral degree in naturopathic medicine from Bastyr University in 1994. Dr. Alschuler has been a practicing naturopathic physician since 1994, and currently practices at Naturopathic Specialists, based in Scottsdale AZ. She is past-President of the American Association of Naturopathic Physicians, a founding board member of the Oncology Association of Naturopathic Physicians, and currently

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serves as a Director on both the American Board of Naturopathic Oncology and the Naturopathic Post-Graduation Association. Dr. Alschuler is the Vice President of Quality and Education at Emerson Ecologics, where she developed and manages the Emerson Quality Program, a rigorous quality assurance program for professional dietary supplement brands. Dr. Alschuler also works as an independent consultant in the area of practitioner and consumer health education. Previously, Dr. Alschuler was the department head of naturopathic medicine at Midwestern Regional Medical Center – Cancer Treatment Centers of America, a JCAHO accredited regional hospital offering comprehensive integrative cancer care. Prior to that, she was the clinic medical director and botanical medicine chair at Bastyr University Natural Health Clinic.

Dr. Alschuler is the co-author of *The Definitive Guide to Cancer: An Integrative Approach to Prevention, Treatment and Healing*, now in its 3rd edition (Random House, 2010) and *Five To Thrive: Your Cutting-Edge Cancer Prevention Plan* (AIM Publishers, 2011). Dr. Alschuler has published numerous articles on herbal medicine and naturopathic medicine in the lay press as well as in the medical literature. She, along with her co-author Karolyn Gazella, have created www.FiveToThrivePlan.com, a multimedia website dedicated to sharing information about integrative cancer prevention and treatment. They also co-host a daily radio show, Five To Thrive Live! on www.w4CS.com which provides listeners with tools for living healthier lives in the face of cancer. She gives presentations internationally and nationally for lay and professional audiences. She makes regular media appearances and has received professional recognition and awards for her work in integrative medicine.

Dr. Alschuler is licensed as a naturopathic doctor in New Hampshire, Arizona and Washington states. Dr. Alschuler's website can be viewed at <http://www.drlise.net>. Dr. Alschuler practices with Naturopathic Specialists, Scottsdale Arizona. Dr. Alschuler resides in Chicago, IL.

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