

BRIEF REPORT

Clinical Utility of Curcumin Extract

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ABSTRACT

Turmeric root has been used medicinally in China and India for thousands of years. The active components are thought to be the curcuminoids, primarily curcumin, which is commonly available worldwide as a standardized extract. This article reviews the pharmacology of curcuminoids, their use and efficacy, potential adverse effects, and dosage and standardization. Preclinical studies point to mechanisms of action that are predominantly anti-inflammatory and antineoplastic, while early human clinical trials suggest beneficial effects for dyspepsia,

peptic ulcer, inflammatory bowel disease, rheumatoid arthritis, osteoarthritis, uveitis, orbital pseudotumor, and pancreatic cancer. Curcumin is well-tolerated; the most common side effects are nausea and diarrhea. Theoretical interactions exist due to purported effects on metabolic enzymes and transport proteins, but clinical reports do not support any meaningful interactions. Nonetheless, caution, especially with chemotherapy agents, is advised. Late-phase clinical trials are still needed to confirm most beneficial effects. (*Altern Ther Health Med.* 2013;19(2):20-22.)

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Turmeric (*Curcuma longa*) is a perennial shrub native to southern Asia and cultivated extensively throughout Asia and Africa. The yellowish root is dried and powdered to yield a commercially available spice that is used worldwide and gives curry its characteristic yellow color.¹ *C longa* is a member of the ginger family (Zingiberaceae) that has been used in the ancient medicinal traditions of India and China for thousands of years. In 2010, sales of *C longa* in the United States exceeded \$11 million, an increase of over 10% from the previous year, making it the fourth most popularly sold botanical in the United States.²

Curcumin is the fraction of the root that gives turmeric its color and is commonly used as a flavoring, additive, preservative, and coloring agent that is considered nontoxic.³

Capsules containing curcumin extract are widely available commercially around the world.

A number of recent reviews have summarized the extensive literature on the mechanisms of curcumin's purported effects. A wide range of preclinical evidence suggests that curcumin has a diverse range of molecular targets and acts both directly with proteins and indirectly through modulation of gene expression. Curcumin has been reported to be anti-inflammatory, antioxidant, antineoplastic, proapoptotic, antiangiogenic, cytotoxic, immunomodulatory, and antimicrobial, with the ability to modulate numerous targets, including growth factors and growth-factor receptors, transcription factors, cytokines, enzymes, and genes regulating cell proliferation and apoptosis.⁴⁻⁶

PHARMACOLOGY

The major constituents of turmeric roots are the volatile oils and the curcuminoids (ie, curcumin, demethoxycurcumin, and bisdemethoxycurcumin). Typical curcumin extracts available commercially contain about 75% curcumin, 20% demethoxycurcumin, and 5% bisdemethoxycurcumin, all of which are thought to be primarily responsible for the extracts' pharmacologic effects.³

The majority of studies on curcumin extracts are in vitro and animal studies. Anti-inflammatory and tumor-regulatory properties of curcumin are attributed to its effects at multiple targets, including NFκB, AP-1, Nrf2, JNK, COX-2, PPAR-α, cyclin D1, EGFR, p53, procaspases, bcl-2, and VEGF.⁴⁻⁶

Table 1. Key Points About Curcumin

Effectiveness	May be beneficial for inflammatory and malignant disorders, including rheumatoid arthritis, osteoarthritis, uveitis, orbital pseudotumor, a variety of premalignant or preinvasive malignancies, familial adenomatous polyposis, and dyspepsia.
Adverse Effects (AE).	Is “Generally Regarded as Safe” (GRAS) by the FDA; observed AEs include diarrhea, nausea, and increased frequency in bowel movements (resolving spontaneously after 1-3 days).
Interactions.	No interactions with prescription drugs have been observed; has known effects with cytochrome P450 1A1, 1A2, 3A4, 2B6, 2C9, 2D6, glutathione S-transferase, and P-glycoprotein.
Contraindications.	Has potential to trigger biliary colic in individuals with gallstones.
Dosage.	Most effective dosage is currently unknown; recommended dosages range from 1000-8000 mg per day in 1-3 divided doses.
Cost.	Is \$6.50-\$12.00 per month, based on a 1200-1800 mg daily dosage.
Bottom Line.	Curcumin appears to be well-tolerated and safe for general use; may be effective for a wide variety of conditions, including gastrointestinal diseases, such as dyspepsia, and some cancers; evidence from late-phase clinical trials is needed before confident recommendations can be made.

Although in vitro studies show curcumin to be a potential chemotherapeutic agent against a broad range of cancer cells, its advance toward clinical use has been hindered by its short half-life and low bioavailability after oral administration.⁷

POTENTIAL USES AND EFFICACY

A number of early-phase clinical studies provide evidence that curcumin may be beneficial for inflammatory and malignant disorders. Although these early trials often emphasized pharmacokinetics and safety, beneficial effects of curcumin have been demonstrated for dyspepsia,⁸ osteoarthritis,⁹ rheumatoid arthritis,¹⁰ uveitis,¹¹ orbital pseudotumor,¹ a variety of premalignant or preinvasive malignancies,¹³ familial adenomatous polyposis,¹⁴ inflammatory bowel disease,¹⁵ and pancreatic cancer.¹⁶

Other uses may include treatment of chronic neurodegenerative conditions because curcumin has shown protective abilities against neurotoxic and genotoxic agents. For example, in the case of Alzheimer’s disease, curcumin has shown disaggregation of amyloid-β peptide. Other activities include inhibition of NFκB, prevention of fibril and oligomer formation, inhibition of Egr-1, amyloid-β peptide cell death, and activation of transcription factors.¹⁷

CONTRAINDICATIONS, ADVERSE EFFECTS, AND INTERACTIONS

Due to their ability to increase bile secretion, turmeric extracts have the potential to trigger biliary colic in predisposed individuals with gallstones.¹⁸ Therefore, patients with cholelithiasis should avoid turmeric or curcumin extracts.

Turmeric is on the FDA’s “Generally Regarded as Safe” (GRAS) list. Curcumin doses up to 8 g daily have been administered for several months of treatment in clinical trials without serious adverse events. Only a few clinical studies

of oral curcumin and curcuminoids have reported perceptible side effects at doses ranging from 180 mg to 12 g.¹⁹ In the few cases where side effects have been observed, those effects have mainly involved gastrointestinal discomfort, which may have been due to underlying symptoms. Two types of gastrointestinal side effects, diarrhea and nausea, have been most commonly reported, and they are probably related to curcumin consumption. Increased frequency in bowel movements has been observed in clinical trials. The diarrhea, however, does not appear to be dose-related and resolves spontaneously after 1 to 3 days regardless of whether the curcumin is discontinued.²⁰

Based on in vitro and animal models, several potential drug interactions exist. Curcumin has known effects on a variety of metabolic enzymes, such as cytochrome P450 (CYP) 1A1, 1A2, 3A4, 2B6, 2C9, 2D6, and glutathione S-transferase, as well as on the efflux pump, P-glycoprotein.²¹⁻²³ Because curcumin also has effects at a large number of molecular targets associated with tumor initiation and progression, it is possible that curcumin may alter the efficacy of some chemotherapy agents. Until there is better understanding of the effects of curcumin on chemotherapy agents, use of curcumin during cancer chemotherapy is not recommended. However, no interactions with prescription drugs have been observed in individual patients or during human clinical trials.²⁴

TOXICOLOGY

In animal studies, no acute or chronic toxicity has been shown, even at high doses. Likewise, mutagenicity and reproductive toxicity have not been observed in rodents.²⁵⁻²⁷

In humans, several studies have demonstrated minimal toxicity with moderate doses of curcumin. Even at doses as high as 12 g, curcumin is not associated with increases in adverse events over placebo.^{28,29}

USE IN PREGNANCY

Turmeric has been used during pregnancy in a variety of traditional medical systems for thousands of years, and no traditional or Western authority recommends against its use during pregnancy.^{30,31} The isolated curcuminoids, although apparently safe in rodents, are less well understood in humans. Therefore, for use during pregnancy or breastfeeding, consultation with a clinician who has expertise in phytotherapy is advised.³

DOSAGE AND STANDARDIZATION

A common, therapeutic curcumin dose is 400 to 600 mg three times daily, corresponding to 60 g of fresh turmeric root or about 15 g of turmeric powder. In clinical cancer trials, doses of 4 to 8 g per day of curcumin are typical. Because curcumin is poorly absorbed into the blood stream, several proprietary formulations purport to increase its bioavailability via lipid complexes or nanoparticle formulations. Lower doses of these special preparations may be equivalent to higher doses of standard powder, but further study is needed to confirm the effect.³² Other strategies to increase curcumin absorption include coadministration of the naturally occurring volatile oils from turmeric root, or piperine, a product from black pepper.³³

While turmeric and curcumin powders are uncommonly adulterated, some concern exists that lead may contaminate some batches of prepared supplements.³⁴ For that reason, it is recommended to purchase curcumin supplements only from US manufacturers that follow recommended Good Manufacturing Practices (GMP), which require testing for heavy metals.

BOTTOM LINE

Turmeric and curcumin supplements appear to be well-tolerated and safe for general use. Preclinical and early clinical trials provide some evidence of efficacy for a wide variety of conditions including gastrointestinal diseases, such as dyspepsia, and some cancers. Evidence from late-phase clinical trials is needed, however, before a confident recommendation for or against its use can be made.

ACKNOWLEDGEMENTS

This project was supported by award number UL1RR025747 from the National Center for Research Resources (GNA).

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