Canterbury District Health Board
Te Poari Hauora ō Waitaha

Clinical Pharmacology Bulletin

Department of Clinical Pharmacology, Christchurch Hospital, Private Bag 4710, Christchurch

Medicines Information Service **Phone:** 80900 **Fax:** 80902
Medicines Utilisation Review **Phone:** 89971 **Fax:** 81003

June 2018 No. 006/18

Complementary and Alternative Medicine: focus on Turmeric

Quick Take

Please note: there is much less information about the safety, potential for drug interactions and effectiveness of complementary and alternative medicines (CAMs) compared to conventional medicines. Also, there is no regulation of their quality and contents in New Zealand.

Medsafe have issued an early warning that products containing turmeric/ curcumin can interact with warfarin. The warning was issued following a case report to the Centre for Adverse Reaction Monitoring (CARM) describing a patient taking warfarin with stable INR, who within a few weeks of starting a turmeric supplement their INR increased to over 10, where turmeric was believed to be the causative agent [1].

Consider reporting all adverse effects believed to be due to Complementary and Alternative Medicine (CAM) or an interaction between CAM and medicine to CARM (https://nzphvc.otago.ac.nz/).

Pregnancy & Lactation: Turmeric is probably safe to take in quantities commonly found in foods (up to 200 mg/ day), but safety in higher doses has not been studied.

What is it?

Turmeric (C*urcuma longa)* is a plant native to South Asia, and is used as a spice in regional cuisines and a colouring agent in food and cosmetics. Traditionally it has been used as a medicine for improving "circulation and digestion" [2]. The main active constituent in turmeric is curcumin [2]. Curcumin has anti-inflammatory activity, with modest inhibition of cyclooxygenase-2 (COX2), and may disrupt synthesis of prostaglandins at other [3, 4]. It may also inhibit platelet activating factor and arachidonic acid platelet aggregation [5].

What do people use it for?

Turmeric has been used in Ayurvedic medicine to treat a wide range of disorders, although there is limited evidence to support its use. Evidence is generally from small short-term studies, comparing turmeric against placebo.

Indications	Supporting Data
Hyperlipidaemia	Two small, short-term studies compared turmeric to placebo both showed turmeric reduced total cholesterol, but had inconsistent results on lipoproteins [6, 7].
Osteoarthritis	Meta-analysis of 8 randomised clinical trials (n=937 patients) showed turmeric reduced pain [8], although the effects were generally modest and comparable to low doses of ibuprofen [9].
Pruritis	In a single trial of 100 patients with end stage renal failure, turmeric was shown to be more effective than placebo at relieving itch [10].
Depression	Meta-analysis of 6 clinical trials, (n=377 patients) in trials of 4 to 8 weeks, turmeric was only marginally more effective than placebo at ameliorating depressive symptoms [11].

Other conditions: Turmeric has been proposed to treat a wide range of other conditions including dyspepsia, rheumatoid arthritis, ulcerative colitis, diabetic nephropathy, and Alzheimer's disease. We found no clinical trial data to support these claims.

Curcumin has been shown to have inhibitory effects on cancer cells, however any beneficial effects at preventing or treating cancers are only seen at serum concentrations much higher than those that can be obtained from currently available formulations of turmeric [12].

Contraindications

Turmeric may increase contractions of the gallbladder [13] and is contraindicated in patients with gallbladder disorders, bile duct obstruction, gallstones, gastrointestinal ulcers, or hyperacidity disorders [2].
Pregnancy & Lactation: Turmeric is probably safe to take in quantities commonly found in foods (up to 200 mg/ day), but safety in higher doses has not been studied [5].

Pharmacokinetics

Curcumin is very unstable and rapidly degrades in the presence of heat, light, oxygen, and humidity [3], therefore manufacturing and storage processes may greatly affect product efficacy. Curcumin undergoes extensive metabolism in intestinal mucosa, liver, blood, and kidneys, resulting in it being rapidly cleared with a half-life of approximately 1 hour [3].

Dose

Doses of turmeric used in clinical trials reviewed were typically in the range 1000 mg to 2000 mg per day, taken in two or three divided doses. We found no information regarding dose adjustment in renal or liver impairment.

Adverse effects
When taken orally the most common adverse effects are dyspepsia, diarrhoea, gastrointestinal reflux, nausea, and vomiting [4], and if applied topically turmeric may cause dermatitis [2, 5].

Interactions with medicines
Concurrent use of any narrow therapeutic index drug with herbal products requires caution and appropriate monitoring. Curcumin has the potential to interact with many medicines, with the principal classes of interaction being:

Interaction Category	Interaction	Details
Pharmacokinetic	Cytochrome P450 enzymes	In vitro and animal testing has demonstrated that curcumin may be a moderately potent inhibitor of CYP1A2, CYP2C19, CYP2D6, and CYP3A [12]. Curcumin may increase serum concentrations and adverse effects of medicines that are extensively metabolised by these enzymes, although there are few reported interactions in humans [14].
Pharmacokinetic	P-Glycoprotein	In vitro and animal research shows curcumin can inhibit p-glycoprotein activity [4, 15]. Theoretically, curcumin may increase absorption of p-glycoprotein substrates with potential for increased concentrations and adverse effects.
Pharmacodynamic	Antiplatelet Drugs	In vitro curcumin has been shown to have antiplatelet effects. Curcumin should be used with caution in patients taking medicines that decrease platelet aggregation [2, 5].
Pharmacodynamic	Antidiabetic Drugs	Animal and case reports suggest curcumin may reduce levels of blood glucose and glycosylated haemoglobin (HbA1C). This may increase risk of hypoglycaemia if taken with antidiabetic drugs [4].

Toxicity
Turmeric has been shown to be safe in doses of up to 6 g/ day when taken for 4 to 7 weeks [16]. We found no data regarding safety of turmeric when taken in overdose.

References

1. Medsafe. Safety Information. Early Warning System – Monitoring Communication. Beware turmeric/ curcumin containing products can interact with warfarin. http://www.medsafe.govt.nz/safety/EWS/2018/Turmeric.asp, 30 April 2018.
2. About herbs. Memorial Sloan Kettering Cancer Center. www.mskcc.org/cancer-care/treatments/symptom-management/integrative-medicine/herbs/search
3. Heger M., van Golen R.F., Broekgaarden M., Michel M.C. The molecular basis for the pharmacokinetics and pharmacodynamics of curcumin and its metabolites in relation to cancers. Pharmacological Reviews. 66 (1) (pp 222-307), 2014.
4. Shen C.-L., Smith B.J., Lo D.-F., Chyu M.-C., Dunn D.M., Chen C.-H., Kwun I.-S. Dietary polyphenols and mechanisms of osteoarthritis. Journal of Nutritional Biochemistry. 23 (11) (pp 1367-1377), 2012.
5. Natural Medicines [Internet]. 2016 [cited 2018 Mar 20]. Available from: https://naturalmedicines.therapeuticresearch.com/
6. Pashine l, Singh JV, Vaish AK, Ojha SK, Mahdi AA. Effect of turmeric (Curcuma longa) on overweight hyperlipidemic subjects: Double blind study. Indian J Comm Health 2012;24(2):113-117.
7. Tappia P.S., Xu Y.-J., Dhalla N.S. Reduction of cholesterol and other cardiovascular disease risk factors by alternative therapies. Clinical Lipidology. 8 (3) (pp 345-359), 2013
8. Daily J.W., 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 Clinical Trials. Journal of Medicinal Food. 19 (8) (pp 717-729), 2016.
9. Kuptniratsaikul V, Thanakhumtorn S, Chinswangwatanakul P, Wattanamongkobnsil L, Thamlikitkul V. Efficacy and safety of Curcuma domestica extracts in patients with knee osteoarthritis. J Altern Complement Med. 2009 Aug;15(8):891-7.
10. Pakfetrat M., Basiri F., Malekmakan L., Roozbeh J. Effects of turmeric on uremic pruritus in end stage renal disease patients: A double-blind randomized clinical trial. Journal of Nephrology. 27 (2) (pp 203-207), 2014.
11. Ng Q.X., Koh S.S.H., Chan H.W., Ho C.Y.X. Clinical Use of Curcumin in Depression: A Meta-Analysis. Journal of the American Medical Directors Association. 18 (6) (pp 503-508), 2017
12. Heger M., van Golen R.F., Broekgaarden M., Michel M.C. The molecular basis for the pharmacokinetics and pharmacodynamics of curcumin and its metabolites in relation to cancers. Pharmacological Reviews. 66 (1) (pp 222-307), 2014.
13. Rasyid A., Rahman A.R., Jaalam K., Lelo A. Effect of different curcumin dosages on human gall bladder. Asia Pacific journal of clinical nutrition. 11 (4) (pp 314-318), 2002.
14. Sasaki T., Sato Y., Kumagai T., Yoshinari K., Nagata K. Effect of health foods on cytochrome P450-mediated drug metabolism. Journal of Pharmaceutical Health Care and Sciences. 3 (1) (no pagination), 2017
15. Li Y., Revalde J., Paxton J.W. The effects of dietary and herbal phytochemicals on drug transporters. Advanced Drug Delivery Reviews. 116 (pp 45-62), 2017.
16. Soleimani V., Sahebkar A., Hosseinzadeh H. Turmeric (Curcuma longa) and its major constituent (curcumin) as nontoxic and safe substances: Review.Phytotherapy Research. (no pagination), 2018.