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Turmeric: Antioxidant Plant

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ABSTRACT

Turmeric, a spice that has long been recognized for its medicinal properties, has received interest from both the medical/scientific world and culinary enthusiasts, as it is the major source of polyphenol curcumin. It aids in the management of oxidative and inflammatory conditions, metabolic syndrome, arthritis, anxiety, and hyperlipidemia. It may also help in the management of exercise-induced inflammation and muscle soreness, thus enhancing the recovery and performance inactive people. Also, a relatively low dose of the complex can provide health benefits for people that do not have diagnosed health conditions. Most of these benefits can be attributed to its antioxidant and anti-inflammatory effects. Ingesting curcumin by itself does not lead to the associated health benefits due to its poor bioavailability, which appears to be primarily due to poor absorption, rapid metabolism, and rapid elimination. Several components can increase bioavailability. For example, piperine is the major active component of black pepper and, when combined in a complex with curcumin, has been shown to increase bioavailability by 2000%. Curcumin combined with enhancing agents provides multiple health benefits. The purpose of this review is to provide a brief overview of the plethora of research regarding the health benefits of curcumin.

INTRODUCTION

Turmeric (*Curcuma longa*L.) is the dried underground rhizome belongs family 'Zingiberaceae'. India and chaina is native of turmeric. The world turmeric is derived from the French word 'Terre-merite'. The genus name curcuma is probably derived from the Persian word 'kurkum' a name also applied to saffron. Turmeric is also called as 'Yellow gold', 'Indian saffron', and 'The golden spice of life'. It is one of the most essential spice used as an important ingredient in culinary all over the world. The plant is an herbaceous perennial, 60-90 cm high with short stem and tufted leaf. It is tropical herb and can grow on the different type of soils. Turmeric cultivation does occurs in India, Maharashtra,China, Indonesia, Iran, Sri Lanka, Peru and Pakistan. India is leading country in the spices scenario and enjoy monopoly in the production of the spice because of suitable climatic condition. India is known as "Home of Spices".

Maharashtra is largest producer, consumer and exporter of turmeric in the India . Turmeric is grown only in 6% of the total area under spices and condiments in India. India is the largest producer and exporter of turmeric in the world and accounts for 80% therefore (50%of cultivated turmeric in Maharashtra) world's total production and 60 % of world export. Turmeric production in India has shown most of the production in last five years. It was 43000 tons in 2011-12, and increased to 65000 tons in 2012-13. Again decreased to 37000 tons in 2013-14 and then increased to 70000 tons in 2014-15. The annual turmeric production was 48500 tons in 2015-16. Hence price of turmeric is not fixed and tend to fluctuate year by year. Maharashtra state in India ranks sixth in area under turmeric cultivation. The area under crop was 11000 hectares with a production of 45000 tons and productivity of 4.09 tonnes/hectare during 2015-16. In Maharashtra Sangali, Satara, Hingoli, Nanded, Parbhani are the major turmeric growing districts. It is one of the major crop in the Sangli district. In Sangli the area under turmeric is 1500 hectares, whereas production and productivity is 13000 tonnes and 8.6 tonnes/hectare, respectively in 2015- 16.

Scientific classification

Kingdom: Plantae

Clade: Tracheophytes

Clade: Angiosperms

Clade: Monocots

Clade: Commelinids

Order: Zingiberales

Family: Zingiberaceae

Genus: Curcuma

Species: C. longa

Binomial name : Curcuma longa

Synonyms : Curcuma domestica Valeton

Organic production : Turmeric production in Maharashtra at least 18 months a crop should be under organic management and second production turmeric can sold as organic. The cultivation of turmeric a land where chemicals are not previously used provides sufficient area is available. A desirable method of cultivation in organic farming production is followed entire farm but this is case large area is available. Turmeric is best component crop in agri-hoti system. Coconut, mango rubber etc recycling in farm waste can be effectively done with growth. Avoid from contamination of organically cultivated plots for neighbouring cultivated non-organic farms. Proper soil and water are followed by good organic farming. Turmeric as a best component crop in agri-horti and silvi-horti systems, recycling of farm waste can be effectively done when grown with coconut, arecanut, mango, Leucaena, rubber etc. As a mixed crop, it can also be grown or rotated with green manure/ legumes crops or trap crops enabling effective nutrient built up and pest or disease control. When grown in a mixed cultivation system, all the crops in the field must be also subjected to organic methods of production.

To avoid contamination of organically cultivated plots from neighbouring non-organic farms, a suitable buffer zone with definite border is to be maintained.

Botanical description

Turmeric is a perennial herbaceous plant that reaches up to 1 m (3 ft 3 in) tall. Highly branched, yellow to orange, cylindrical, aromatic rhizomes are found. The leaves are alternate

and arranged in two rows. They are divided into leaf sheath, and leaf blade. From the leaf sheaths, a false stem is formed. The petiole is 50 to 115 cm long. The simple leaf blades are usually 76 to 115 cm long and rarely up to 230 cm. They have a width of 38 to 45 cm).

Cultivation & Collection

Climate

Turmeric can be grown from sea level to 1500m in the hills, at a temperature range of 20-30^{0}C with a rainfall of 1500-2250mm per year. It is also grown as an irrigated crop. Maharashtra in state of Sangli in the rainy season highly cultivated turmeric to minimum temperature.

Soil

It increases best in a well-drained sandy or clayey loam rich in humus content. It can be grown on different soil viz. light black, ashy loam and red soils to clay loams.

Varieties

CO1, BSR.1, Suguna, Suvarna, Sudharshana, Krishna, Sugundham, Roma, Suroma, Rajendra Sonia, Ranga, Rasmi.

Material And Planting

In the areas where the rainfall is sufficiently early, crop can be planted during April-May with the receipt of pre-monsoon showers. Since turmeric is a shade loving plant, castor or *Sesbania grandiflora* may be raised along the borderlines in the field. Well developed healthy and disease free whole or split mother rhizomes weighing 35-44g are used for planting. Turmeric planting Small pieces of are made with a hand hoe in the beds in rows with a spacing of 25x 30 cm and covered with soil. The optimum spacing in furrows and ridges is about 45-60 cm between the rows and 25 cm between the plants. A seed rate of 2500kg of rhizomes is required for one hectare or two hectare.

Fertilizers

Fertilizers are to be applied in 2-3 split doses. Phosphorus applied in basal of planting time.. The dose of n and k area of one hectare. Whole Phosphorus (P) and Potash (K_2O) is given as basal dose at the time of planting while Nitrogen (N) is applied as 25kg each at basal,

30,60,90 and 120 days after planting. Turmeric also recommended 60 and 90 DAP higher yield.

Intercultural Operations

Mulching and weeding: The crop is to be mulched immediately after planting with green leaves at the rate of 12-15 tons per hectare. It may be repeated for the second time after 40 days with the same quantity of green leaves after weeding of fertilizers. Weeding may be done thrice at 60,110and 150 days after planting depending upon the plant.

Irrigation

Irrigation depending on the soil types, irrigated crops require 15-20 irrigations in heavy soils and 35-40 in light soils. Moisture stress affects the growth and development of the plant, especially during the rhizome bulking stage.

Plant protection

Pest

Shoot borer

The presence of borehole on the big through which the grass is extruded and the withered central shoot are the symptoms of pest infestation.

Control

Spray Malathion 0.1% at a monthly intervals from July to October. They feed on the plant sap and in the field in severe cases plants wither and dry. In storage, the pest infestation results in shriveling of buds and rhizomes and may also affect the sprouting of rhizomes. Dip the rhizomes in quinalphos 0.1% twice prior to storage and sowing.

Diseases

Rhizome rot (*Pythium graminicolum*)

The Collar region of the pseudostems becomes soft and water-soaked, and the plant collapses.

Control

Dry the soil with 0.3% Dithane M-45. Dip rhizomes in the same chemical solution for 30 minutes before storage and at the time of sowing. Leaf blotch (*Taphrina maculans*).

There are small, oval, rectangular or irregular brown spots on either side of the leaves. The leaves turn yellow. Spray 0.2% Dithane M.45.Nematodes.

Apply to soil aldicarb or carbofuran granules at 1kg a.i/ha.

Harvesting

A haveresting depending upon the variety, the crop becomes ready for harvest in seven to nine months. The land is plowed and the most are gathered by handpicking or the clumps are carefully lifted with a spade. Harvested rhizomes are cleaned of mud and other extraneous matter adhering to them. The average yield per hectare is 20-25 tonnes of green turmeric. Rhizomes for seed purposes must be stored in well-ventilated rooms to minimize rot, but covered with the plant dry leaves to prevent dehydration.26 They can also be stored in pits covered with sawdust, sand, or panel (Glycosmis pentaphylla) leaves that may act as an insect repellent.10 The Indian Institute of Spice Research recommends the following fungicides as a pre-storage dip treatment for rhizome seeds: quinalphos at 0.075%, and mancozeb at 0.3%.10 Studies indicate that bulbs (mother rhizomes) are preferred to fingers as a seed stock.

Processing

Curing

The fresh turmeric is cured before marketing. Curing involves boiling fresh rhizomes in water and drying them in the sun. The mother rhizomes and the fingers are generally cured separately. In the traditional method, the cleaned rhizomes are boiled in copper or galvanized iron or earthen vessels, with water just enough to soak them. Boiling is stopped when froth comes out and white fumes appear giving out a typical odor. The boiling lasts for 45-60 minutes when the rhizomes are soft. In the improved scientific method of curing the cleaned fingers (approximately 50kg) are taken in a perforated trough of size 0.9 X 0.55x0.4m, The perforated trough containing the lingers are then immersed in the pan. The alkaline solution (0.1% sodium carbonate or sodium bicarbonate) is poured into the trough to immerse the turmeric fingers. The whole mass is boiled till the fingers become soft. The cooked fingers are taken out of the pan by lifting the trough and draining the solution into the pan. The

cooking of turmeric is to be done within two to three days after harvesting. The cooked fingers are dried in the sun by spreading 5-7 cm thick layers on a bamboo mat or drying floor. During night time, the materials should be heaped or covered. Drying is completed in 10-15 days.

Polishing

The appearance is improved by smoothening and polishing the outer surface by manual or mechanical rubbing. The improved method is by using hand-operated barrel or drum mounted on a central axis, the sides of which are made of expanded metal mesh. When the drum filled with turmeric is rotated at 30 rpm, polishing is effected by abrasion of the surface against the mesh as well as by mutual rubbing against each other as they roll inside the drum. The turmeric is also polished in power-operated drums. The yield of polished turmeric from the raw materials varies from 15-25%.

Colouring

To impart attractive yellow colour, turmeric suspension in water is added to the polishing drum in the last 10 minutes. Composition of emulsion for colour coating of 100kg of half boiled turmeric is Alum powder 2kg, castor seed oil 0.14kg, sodium bisulfate 30g, concentrated hydrochloric acid 30ml. When the rhizomes are uniformly coated with suspension, they may be dried in the sun.

Grading, packing, and storage

Quality specifications are imposed by the importing country, and pertain to cleanliness specifications rather than quality of the spice (see cleanliness specifications in 1.5.1). Proper care must be taken to meet minimum requirements, otherwise, a lot may be rejected and need further cleaning and/or disinfection with ethylene oxide or irradiation. Bulk rhizomes are graded into fingers, bulbs, and splits.13 The Indian Standards for turmeric follow the Agmark specifications.

Storage

Turmeric pigment is highly unstable as compared to the yellow synthetic colorant, tartrazine.15 However, if protected from light and humidity, the curcuminoid pigments in turmeric powder and oleoresin are stable. Therefore, turmeric rhizomes and powder should be stored away from light and in a very dry environment.43 Additionally, all water or ethanol

solvent should be removed from the oleoresin to assure pigment stability (Agricultural Directorate of Marketing), to ensure quality and purity.

Pharmacological actions

Several medical properties have been attributed to Curcuma longa Linn. Rhizome of Haridra is known to possess therapeutic activities and has been used by medical practitioners as an anti-diabetic hypolipidemic, anti-inflammatory, anti-diarrhoeal, hepatoprotective, anti-asthmatic and anti-cancerous drug. Haridra is widely used in cosmetology. The following section discusses its various therapeutic uses in medicine.

Medicinal uses:

Gastrointestinal disorders: The fresh juice of Haridra is considered to be anthelmintic. The Curcumin acts through nuclear factor inhibition and it reduces the production of adhesion molecules and inflammatory cytokines, resulting in the amelioration of gastric injury in NSAIDs-induced gastropathy in rats. It also improves gastric mucosal damage and decreases in leukocyte adhesions, and intercellular adhesion molecule 1 and tumor necrosis factor (TNF)-α production after curcumin administration. Curcuma longa extract tablet decreased IBS prevalence and abdominal pain/discomfort score significantly between baseline and after treatment of eight-week.

Respiratory disorders: The fresh juice of rhizome is given in bronchitis. In rhinitis and cough boil Haridra in milk and mixed with jiggery given internally. In catarrhal cough, sore throat, and throat infection the decoction of rhizome is used for gargle and also the piece of rhizome is slightly burnt and given for chewing. The chemical constituents of *Curcuma longa* like Tumerones, curcuminoids, Curcumin, and tetrahydrocurcumin has an anti-asthamatic action. In asthma and congestion, fumes of Haridradidhumvarti is given.

Inflammatory disorders: Curcumin has been shown to inhibit some different molecules involved in inflammation including phospholipase, lipooxygenase, COX-2, leukotrienes, thromboxane, prostaglandins, nitric oxide, collagenase, elastase, hyaluronidase, MCP-1, interferon-inducible protein, tumor necrosis factor, and interleukin-12 [18]. Studies has proven bisdemethylcurcumin is more potent as an anti-inflammatory agent as indicated by suppression of TNF-induced NF-κB activation, more potent as an anti-proliferative agent, and more potent in inducing reactive oxygen speciesHispolon analogs, which lacks one

aromatic unit in relation to curcumin, also exhibited enhanced anti-inflammatory and anti-proliferative activities..

Diabetes mellitus: Turmeric rhizome powder is very useful with Amla juice and Honey in Madhumeha (diabetes mellitus). The ingestion of 6 g *Curcuma longa* increased postprandial serum insulin levels, but did not seem to affect plasma glucose levels or GI, in healthy subjects. The results indicate that Curcuma longa may have an effect on insulin secretion. The active principles in the rhizome of Turmeric plant viz; curcuminoids lower lipid peroxidation by maintaining the activities of antioxidant enzymes like superoxide dismutase, catalase and glutathione peroxidase at higher levels. Antioxidant properties of curcuma longa is due to curcumin and its three derivatives (demethoxy curcumin, bisdemethoxy curcumin and diacetyl curcumin). A scientific and systemic exploration reveals the antidiabetic, hypolipidemic and hepatoprotective effects of *Curcuma longa* freeze dried rhizome powder dissolved is milk which could be used as an effective and safe antidiabetic dietary potential.

Cardiovascular disorders: The antioxidants in turmeric also prevent damage to cholesterol, thereby helping to protect against **atherosclerosis**. In fact, the ability of the antioxidants in turmeric to decrease free radicals is similar to that in vitamins C and E. Since the antioxidant activities of turmeric are not degraded by heat even using the spice in cooking provides benefits. Animal studies show that curcumin lowers cholesterol and triglycerides, another fat that circulates in the bloodstream and is a risk factor for cardiovascular disease. In a recent study of atherosclerosis, mice were fed a standard American diet, rich in refined carbohydrates and saturated fat, but low in fiber. Some of the mice, however, received this diet plus turmeric mixed in with their food. After four months on these diets, the mice that consumed the turmeric with their food had 20 percent less blockage of the arteries than the mice fed the diet without the turmeric.

Neuroprotective activity: Curcuma oil significantly reduces the ill effect of ischemia by attenuating nitrosative and oxidative stress. Ischemia induces collapse of mitochondrial membrane potential, cytochrome c release, altering the Bax: Bcl-2 ratio and subsequently caspases activation led to induction of apoptosis successively was reverse significantly by Curcuma oil. So there is evidence for the high efficacy of Curcuma oil as a neuroprotective, with an excellent therapeutic window for the prevention of ischemic brain injury.

Alzheimer's disease: Curcumin when fed to aged mice with advanced plaque deposits similar to those of Alzheimer's disease, curcumin reduced the amount of plaque deposition. It

reduced oxidative damage and reversed the amyloid pathology in an Alzheimer's disease transgenic mouse. Alzheimer's disease symptoms characterized by inflammation and oxidation were also eased by curcumin's powerful **antioxidant** and anti-inflammatory properties.

Chemoprotective activity: Curcumin activates the DDR (DNA damage response), providing an opportunity and rationale for the clinical application of these nutraceuticals in the chemoprevention of prostate cancer. **Chemoprotective** effects in esophageal epithelial cells exposed to bile acids; Curcumin reverses bile acid suppression of gene expression of SOD-1 and also able to inhibit bile acid induction of COX-2 gene expression. Curcumin has demonstrated these chemopreventive properties in cell cultures, animal models, and human investigations.

Anticancer activity: Curcumin has been found to possess anticancer activities via its effect on a variety of biological pathways involved in mutagenesis, oncogene expression, cell cycle regulation, apoptosis, tumorigenesis and metastasis. Curcumin has shown an anti-proliferative effect in multiple cancers and is an inhibitor of the transcription factor NF-B and downstream gene products (including c-myc, Bcl-2, COX- 2, NOS, Cyclin D1, TNF-a, interleukins and MMP-9). Besides, curcumin affects a variety of growth factor receptors and cell adhesion molecules involved in tumor growth, **angiogenesis**, and metastasis.

Anti-allergic activity: Curcumin suppressed compound 48/80-induced rat peritoneal mast cell degranulation and **histamine** release from RPMCs. Curcumin inhibited compound 48/80-induced systemic anaphylaxis *in-vitro* and anti-DNP immunoglobulin E mediated passive cutaneous anaphylactoid response *in-vivo*. Curcumin has the ability to inhibit nonspecific and specific mast cell-dependent allergic reactions.

Bacterial Reverse Mutation Test

A bacterial reverse mutation test was conducted to investigate the mutagenic potential of synthetic curcumin according to the procedures described by Ames et al., Green and Muriel, Mortelmans and Zeiger, Maron and Ames, and the test laboratory's standard operating procedures for preparations of frozen stock culture, raw data, and bacterial genotype confirmation. It was conducted in compliance with OECD 471 guidelines for the bacterial reverse mutation test and Good Laboratory Practices (GLP) C(97)186/Final. Bacterial tester strains *Salmonella typhimurium* TA98, TA100, TA102, TA1535, and TA1537 and S9

metabolic activation system (S9) were purchased from Molecular Toxicology, Inc. (NC, USA).

For the preliminary cytotoxicity assay, test solutions were prepared by dissolving curcumin in DMSO to achieve concentrations of 16.0, 5.0, 1.6, 0.5, 0.16, 0.05, and 0.016 mg/mL. For the mutagenicity assay, test solutions were prepared by dissolving the test item in DMSO to achieve concentrations of 5.0, 1.6, 0.5, 0.16, and 0.05 mg/mL. All test item preparations and dilutions were carried out under sterile conditions. S9 mix (cofactors and liver homogenate, 5% v/v) and positive controls were prepared freshly on the day of the experiment. Sodium azide and mitomycin C were diluted in water; all other positive controls were diluted in DMSO.

A preliminary cytotoxicity assay was performed utilizing the plate incorporation method in triplicate by exposing tester strains TA98 and TA100 with and without metabolic activation to the following concentrations of the test article: 1.6, 5.0, 16.0, 50.0, 160.0, 500.0, 1600.0, and 5000.0 μg/plate. Positive controls for the experiments without S9 were 2-nitroflourine (25.0 μg/plate) for TA98, sodium azide (20.0 μg/plate) for TA100 and TA1535, and 9-aminoacridine (50.0 μg/plate) for TA 1537 and mitomycin C/ametycine (0.25 μg/plate) for TA102. The positive control for all of the experiments with S9 was 2-aminoanthracine (20.0 μg/plate).

The mutagenic assay was performed utilizing the plate incorporation method, in triplicate, by exposing tester strains TA98, TA100, TA102, TA1535, and TA1537, with and without S9, to the following test article concentrations: 5.0, 16.0, 50.0, 160.0, 500, and 1600.0 μg/plate. All treated plates were incubated at 37 ± 2°C for 68:25 in the preliminary cytotoxicity test and 66:10 in the mutagenicity assay after which the plates were manually examined for background lawn inhibition, precipitation, and revertant colonies.

A result was considered positive if

(i) There was at least a 2-fold increase (for TA100, TA102, and TA98) or 3-fold increase (for TA1535 and TA1537) in the mean revertants per plate of at least one of the tester strains over the mean revertants per plate of the appropriate vehicle control;

(ii) The increase in the mean number of revertants per plate was accompanied by a dose-response in a minimum of 2–3 concentrations.

In-vitro Mammalian Chromosomal Aberration Test

The *in-vitro* mammalian chromosomal aberration test was conducted to evaluate the ability of curcumin and/or its metabolites to induce structural chromosome aberrations in cultured HPBL. It was performed in compliance with OECD 473 and GLP C(97)186/Final.

Test article formulations were prepared on the day of treatment by diluting the stock solution with DMSO to achieve the test concentrations. HPBLs were obtained by drawing blood from healthy, young, nonsmoking males with no known illness or recent exposure to genotoxic agents and subsequently pooling and culturing blood in Roswell Park Memorial Institute Medium, with 15% Fetal Bovine Serum (FBS). Whole blood cultures were incubated at 37 ± 2°C in a humidified environment.

Positive controls were mitomycin C/ametycine, dissolved in water to a concentration of 0.25 μg/mL for experiments without metabolic activation, and cyclophosphamide, dissolved in water to a concentration of 12.5 μg/mL for experiments with metabolic activation.

A preliminary cytotoxicity assay was performed to determine the test concentrations for the chromosome aberration assay. HPBL cultures were exposed to the test article with and without metabolic activation at concentrations of 1.9, 3.9, 7.8, 15.6, 31.3, 62.5, 125.0, and 250.0 μg/mL for four hours; additional HPBL cultures were continuously exposed to the same concentrations without metabolic activation for 22 hours. Experiments for all test groups including the vehicle control were performed in duplicate. At least one thousand cells in each culture were analyzed for mitotic index (MI; the number of mitotic cells/total number of cells scored, expressed as a percentage). Cytotoxicity was defined as a reduction in MI to 45 ± 5% of the vehicle control.

The chromosome aberration assay consisted of two independent, concurrent experiments, a short-term exposure assay, and a continuous exposure assay. In the short-term exposure assay, cells were exposed to the test article at concentrations of 10.0, 20.0, and 40.0 μg/mL in the absence of metabolic activation, and to concentrations of 6.3, 12.5, and 25.0 μg/mL in the presence of S9 metabolic activation and to corresponding positive and negative controls, and incubated. Following incubation, all cultures were washed with plain media and placed into a fresh culture medium with 15% FBS to continue incubation until harvest.

In the continuous exposure experiment, cells were exposed to the test article at concentrations of 6.3, 12.5, and 25.0 μg/mL, vehicle, and positive controls, and incubated in the absence of

metabolic activation. Culture media was changed at the time of cell harvest. The pH was measured before and after all experiments.

Approximately 20 hours after exposure initiation in all experiments, 0.1 mL of colchicine was added to arrest mitosis. Approximately 2.5 hours after application of colchicine (approximately 1.5 normal cell cycle lengths from initiation of treatment) cells were harvested and chromosome slides were prepared for analysis.

Slides were coded and scored blind and at least 1000 cells from each group were evaluated for MI. Scoring occurred based on good chromosome morphology and only cells with equal numbers of centromeres and modal numbers (46 ± 2) were analyzed. Three hundred metaphases (150 from each duplicate) were evaluated for structural chromosome aberrations. The percent of polyploidy and endoreduplication was calculated by evaluating 250 metaphases per culture. Gaps were recorded separately but were not included in the total aberration frequency as gaps are considered achromatic lesions similar to nucleolar constrictions, which are easily broken by the pressure exerted during slide preparation or most often the result of a single-stranded DNA break, which is a reversible phenomenon as DNA has the innate capability to repair such aberrations.

The test was considered positive if a significant increase in the number of cells with chromosome aberrations was observed at one or more test concentrations and the increase was dose-dependent. The test was considered negative if none of the above criteria were met under all experimental conditions.

Side effects

Curcumin has a long-established safety record. For example, according to JECFA (The Joint United Nations and World Health Organization Expert Committee on Food Additives) and EFSA (European Food Safety Authority) reports, the Allowable Daily Intake (ADI) value of curcumin is 0–3 mg/kg body weight Several trials on healthy subjects have supported the safety and efficacy of curcumin. Despite this well-established safety, some negative side effects have been reported. Seven subjects receiving 500–12,000 mg in a dose-response study and followed for 72 h experienced diarrhea, headache, rash, and yellow stool In another study, some subjects receiving 0.45 to 3.6 g/day curcumin for one to four months reported nausea and diarrhea and an increase in serum alkaline phosphatase and lactate dehydrogenase contents.

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