Review Article

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Curcumin: Significance in Treating Diseases

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Abstract

Turmeric (Curcuma longa) is extensively used as a spice, food preservative and coloring material in India, China and South East Asia. It has been used in traditional medicine as a household remedy for various diseases, including biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatism and sinusitis. For the last few decades, extensive work has been done to establish the biological activities and pharmacological actions of turmeric and its extracts. Curcumin (diferuloylmethane), the main yellow bioactive component of turmeric has been shown to have a wide spectrum of biological actions. These include its anti-inflammatory, antioxidant, anticarcinogenic, antimutagenic, anticoagulant, antifertility, antidiabetic, antibacterial, antifungal, antiprotozoal, antiviral,anti-fibrotic, antivenom, antiulcer, hypotensive and hypocholesteremic activities. Its anticancer effect is mainly mediated through induction of apoptosis. Its anti-inflammatory, anticancer and antioxidant roles may be clinically exploited to control rheumatism, carcinogenesis and oxidative stress-related pathogenesis. Clinically, curcumin has already been used to reduce post-operative inflammation.

Introduction

The Indian Solid Gold Turmeric

Curcumin is extracted from turmeric which is derived from rhizome of plant curcuma longa. Curcuminoids give turmeric its characteristics yellow color. Curcumin is an orange-yellow crystalline powder which is the most active component of turmeric, which makes up to 2-5% of the spice [1,2]. It is also referred to as Indian saffron, yellow ginger, yellow root, kacha Haldi, or natural yellow [3]. Kasthuri turmeric (Curcuma aromatica Salisb) belonging to the family Zingiberaceae is a medicinal and aromatic plant with multiple uses. Turmeric is known as the "golden spice" as well as the "spice of life" [3,4]. It has been used in India as a medicinal plant. The wild turmeric is called C.aromatica and domestic species is called C.longa. India is the largest producer, consumer and exporter of turmeric. Several commercially produced cosmetics and ayurvedic preparations contain kasthuri turmeric. Skin care is the major domain of application of this aromatic plant. Rhizome of Curcuma aromatica is also used in medicines as a stomachic, carminative and emmenogogue for skin diseases and recently as a health food in Japan [5,6].

Biological Activity of Turmeric and Its Compounds

1. Turmeric powder, curcumin and its derivatives and many other extracts from the rhizomes were found to be bioactive structures of some of these compounds.
2. Turmeric powder has healing effect on both aseptic and septic wounds in rats and rabbits.
3. It also shows adjuvant chemo protection in experimental forestomach and oral cancer models of Swiss mice and Syrian golden hamsters.
4. Curcumin also increases mucin secretion in rabbits.
5. Curcumin, the ethanol extract of the rhizomes, sodium curcuminate, [feruloyl-(4-hydroxycinnamoyl)-methane] (FHM) and [bis-(4-hydroxycinnamoyl)-methane] (BHM) and their derivatives, have high anti-inflammatory activity against carrageenin-induced rat paw oedema.
6. Curcumin is also effective in formalin induced arthritis.
7. Curcumin reduces intestinal gas formation and carbon tetrachloride and D-galactosamine induced glutamate oxaloacetate transaminase and glutamate pyruvate transaminase levels [7,8].
8. It also increases bile secretion in anaesthetized dogs and rats, and elevates the activity of pancreatic lipase, amylase, trypsin and chymotrypsin.
9. Curcumin protects isoproterenol-induced myocardial infarction in rats. Curcumin, FHM and BHM also have anticoagulant activity. Curcumin and an ether extract of C. longa have hypolipemic action in rats and lower cholesterol, fatty acids and triglycerides in alcohol induced toxicity.
10. Curcumin is also reported to have antibacterial, anti-amoebic and anti-HIV activities.
11. Curcumin also shows antioxidant activity. It also shows anti-tumor and anticarcinogenic activities.
12. The volatile oil of C. longa shows anti-inflammatory, antibacterial and antifungal activities.
13. The petroleum ether extract of C. longa is reported to have anti-inflammatory activity.
14. Petroleum ether and aqueous extracts have 100% antifertility

effects in rats.

15. Fifty per cent ethanolic extract of C. longa shows hypolipemic action in rats. Ethanolic extract also possesses anti-tumour activity [9,10].
16. Alcoholic extract and sodium curcuminate can also offer antibacterial activity.
17. The crude ether and chloroform extracts of C. longa stem are also reported to have antifungal effects. A C. longa fraction containing ar-turmerone has potent antivenom activity [11,12].

Biological Activity of Turmeric and Its Compounds

COMOUNDS/EXTRACTS	BIOLOGICAL ACTIVTY
• Curcumin	Antifungal, Antiinflammatory,
	Antibacterial, Anti-protozoan
• Methyl curcumin	Antiviral, Hypolipemic,
	Hypoglycemic, Anticoagulant
	Antioxidant , Antitumor
• Demethoxycurcumin	Antioxidant
• Bisdemethoxycurcumin	Anti-inflammatory
• Sodium curcuminate	Wound-healing
• Turmeric powder	Anti-inflammatory
• Ethanol extract	Hypolipemic
• Petroleum ether extract	Antitumor
• Alcoholic extract	Anti-protozoan
• Crude ether extract	Antiinflammatory
• Chloroform extract	Antifertility
	Antibacterial
	Antifungal

Clinical Studies and Medicinal Applications of Curcumin

Although various studies have been carried out with turmeric extracts and some of its ingredients in several animal models, only a few clinical studies are reported so far:

Curcumin

1. Powdered rhizome is used to treat wounds, bruises, inflamed joints and sprains in Nepal.
2. In current traditional Indian medicine, it is used for the treatment of biliary disorders, anorexia, cough, diabetic wounds, hepatic -disorders, rheumatism and sinusitis.
3. Data are also available showing that the powder, when applied as capsules to patients with respiratory disease, gives relief from symptoms like dyspnoea, cough and sputum.
4. In patients undergoing surgery, oral application of curcumin reduces post-operative inflammation.
5. Recently, curcumin has been formulated as slow-release biodegradable microspheres for the treatment of inflammation in arthritic rats. It is evident from the study that curcumin biodegradable microspheres could be successfully employed for therapeutic management of inflammation [13,14].

Turmeric

1. A short clinical trial in 18 patients with definite rheumatoid arthritis showed significant improvement in morning stiffness and joint swelling after two weeks of therapy with oral doses of 120 mg/day.
2. Application of the powder in combination other plant products is also reported for purification of blood and for menstrual and abdominal problems [15,16].

Safety Evaluation with Turmeric and Curcumin

Detailed studies have been reported on the safety evaluation of the rhizomes of C. longa and its alcohol extract, curcumin. The major findings are presented below.

Turmeric

1. The average intake of turmeric by Asians varies from 0.5 to 1.5 g/day/person, which produces no toxic symptoms.
2. Male and female Wistar rats, guinea pigs and monkeys were fed with turmeric at much higher doses (2.5 g/kg body wt.) than normally consumed by humans.
3. No changes were observed in the appearance and weight of kidney, liver and heart. Also, no pathological or behavioral abnormalities were noticed and no mortality was observed [17,18].

Curcumin

1. Curcumin was given to Wistar rats, guinea pigs and monkeys of both sexes at a dose of 300 mg/kg body wt. No pathological, behavioral abnormalities or lethality was observed.
2. No adverse effects were observed on both growth and the level of erythrocytes, leucocytes, blood constituents such as haemoglobin, total serum protein, alkaline phosphatase, etc. [19,20].
3. Human clinical trials also indicate that curcumin has no toxicity when administered at doses of 1-8 g/day140 and 10 g/day.

Dosage Formulations of Curcumin Capsules

1. Formula: Contains 200mg curcumin extract, and the remainder is 300mg Turmeric spice.
2. Orally delivered Curcumin 95% extract showed antioxidant, anti-inflammatory, antidiabetic, and anticancer beneficial effect.
3. This study shows that in order to investigate the degradation of a practically water-insoluble compound like curcumin (in the form of the commercially available curcuminoid mixture), an appropriate aqueous organic solvent mixture has to be identified to solubilize the present compounds.
4. It can thus be concluded that the fast “degradation” of curcumin from the curcuminoid mixture under the applied condition (buffer plus 2% (v/v) methanol, concentration of the curcuminoid was 100 μM) is mostly due to precipitation (total recovery is 85%, so 15% degradation).
5. It is therefore concluded that the concentration of organic co-solvents used in previous studies (e.g., in ref 13) was insufficient to fully dissolve the Curcuminoids resulting in precipitation. This study confirms that autoxidation, and not chain scission, is the main pathway for degradation of curcumin.
6. Loading in mPEG-HPMA-Bz and Triton X-100 micelles substantially stabilizes curcumin against oxidative degradation likely because deprotonation of one of the hydroxyl groups, the first step in the degradation process, in the hydrophobic core of the micelles is prevented.
7. Therefore, loading into polymeric micelles is a promising approach for the stabilization of curcumin making such formulations suitable for further pharmaceutical development and ultimately clinical translation [21].

Marketed Curcumin Capsules

Nanocurcumin

1. Nanoparticle-based drug delivery approaches have the potential for rendering hydrophobic agents like curcumin dispersible in aqueous media.
2. Formula: Curcumin, EC, HPC and Ethanol.
3. Method: Nanoparticle-encapsulated formulation of curcumin. Cross-linked polymeric nanoparticles with a hydrophobic core EC and a hydrophilic shell HPC were used for encapsulation of curcumin, generating drug-encapsulated nanoparticles consistently in size less than 100 nm. These studies indicated that nanotechnology can formulate curcumin effectively, and this nano formulated curcumin with a potent ability against various cancer cells, were represented to have better efficacy and bioavailability under in vivo conditions.

Curcumin Gel

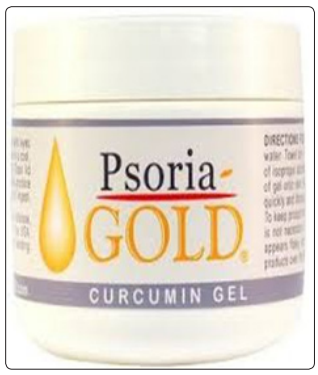
1. A topical gel delivery of curcumin for its anti-inflammatory effects.
2. Formula: Carbapol, HPC and Menthol.
3. Method: Carbapol (CRB) and hydroxypropylcellulose (HPC) were used for the preparation of gels.
4. The penetration enhancing effect of menthol (0-12.5% w/w) on the percutaneous flux of curcumin through the excised rat epidermis from 2% w/w CRB and HPC gel system were studied.

Preparation of Gels by Simple Dispersion Method

1. The composition of different gel formulations is shown. Carbapol was soaked overnight in purified water containing Sodium benzoate 0.2% w/v. HPMC/Sodium Alginate Solution was prepared & homogenized it at 3000rpm in tissue homogenizer.
2. Then drug solution was prepared with ethanol and Propylene Glycol in glass stopper vial. Drug solution was transferred in HPMC /Sodium Alginate/CRB solution and homogenized.
3. Then Polymer drug solution was transferred in Carbapol solution & neutralized it with triethanolamine followed by homogenization. Similarly for other formulation, drug polymer mixture was transferred to CRB solution in ratio of Drug: Polymer 1:1, 1:2, 1:3 [(CRB: HPMC): CUR], [(CRB): CUR], [(CRB: Sodium Alginate): CUR].
4. The percent drug diffused from gel formulations containing only one polymer such as CRB and combination of CRB + Sodium Alginate was low compared to formulation containing combinations of CRB + HPMC.
5. The addition of HPMC to CRB enhanced the gel base properties. Formulations containing [1(CRB: HPMC):1CUR] gave gel of highest viscosity structure and best drug diffusion.
6. It was observed that topical herbal gel prepared from combination of Synthetic & Semi synthetic polymers had maximum firmness, work of shear and stickiness and work of adhesion.
7. Propylene Glycol not only acts as co solvent but also acts as stabilizer.
8. Menthol not only avoids DMSO irritation but also gives cooling effect. Synergistic effect of DMSO & Menthol was showed in drug diffusion.
9. All the prepared formulations were evaluated for various properties such as compatibility, drug content, viscosity, in

vitro skin permeation and anti-inflammatory effect.

10. The drug and polymers compatibility was confirmed by differential scanning calorimetry and infrared spectroscopy.



Other Uses of Turmeric in Traditional System

1. It is an essential substance to purify the gum resin of Commiphora mukul (Guggul) before it is made use of in ayurvedic formulations.
2. Turmeric powder is mixed with the latex of Snuhi (Euphorbia nerifolia) plant and is then coated over the surgical thread repeatedly. This thread is known as Ksharasoothra, which is tied on piles and fistula to cure them effectively.
3. In veterinary medicine, turmeric is used to heal wounds or ulcers of animals.
4. In "leech therapy," turmeric powder is sprinkled over the leech to detach it from the biting site. Again turmeric powder is added to the water, in which the leech is kept, to make it vomit the sucked blood.
5. Turmeric powder is used as an insect and ant repellant.
6. Sprinkled around the vessels to be protected.
7. Turmeric is included in the group of yellow substances (Peethavarga) in Rasa sastra (Alchemy), used in the processing of mercury.

Future Prospects

1. Turmeric has been used in ayurvedic medicine since ancient times, with various biological applications. Although some work has been done on the possible medicinal applications, no studies for drug-development have been carried out as yet.
2. Although the crude extract has numerous medicinal applications, clinical applications can be made only after extensive research on its bioactivity, mechanism of action pharmacotherapeutics and toxicity studies.
3. It would be easier to develop new drugs from this compound after extensive studies on its mechanism of action and pharmacological effects.
4. Recent years have seen an increased enthusiasm in treating various diseases with natural products.
5. Curcumin is a non-toxic, highly promising natural antioxidant compound having a wide spectrum of biological functions.
6. It is expected that curcumin may find application as a novel drug in the near future to control various diseases, including inflammatory disorders, carcinogenesis and oxidative stress-induced pathogenesis.

Biomedical Applications of Turmeric

1. Curcumin (diferuloylmethane), a polyphenol, is a low molecular-weight active principle of the perennial herb Curcuma longa (commonly known as turmeric). Recent evidence suggests that curcumin is a highly pleiotropic molecule that interacts physically with its diverse range of molecular targets including transcription factors, growth factors and their receptors, cytokines, enzymes, and genes regulating cell proliferation and apoptosis.
2. Curcumin possesses antioxidant, anti-inflammatory, anticarcinogenic, and antimicrobial properties, and suppresses proliferation of a wide variety of tumor cells.
3. Several clinical trials dealing with cancer have addressed the pharmacokinetics, safety, and efficacy of curcumin in humans [6]. Despite extensive research and development, poor solubility of curcumin in aqueous solution remains a major barrier in its bioavailability and clinical efficacy.
4. Being hydrophobic in nature, it is insoluble in water but soluble in ethanol, dimethylsulfoxide and acetone.
5. To increase its solubility and bioavailability, attempts have been made through encapsulation in liposomes, polymeric and lipo-NPs, biodegradable microspheres, cyclodextrin, and hydrogels.
6. Recent studies suggested preparation of a novel nanocomposites formulation, i.e. biodegradable chitosan-alginate (CS-ALG) nanocomposites incorporated with medical clay, Cloisite 30B called CS-ALG/ C 30 B nanocomposites, for oral chemotherapy by using curcumin as a prototype drug due to its excellent therapeutic effects against a wide spectrum of cancers and its great commercial success as the best seller among various anticancer agents.

Conclusion

Turmeric is one of the most precious and powerful plant on earth and is being used as a natural wonder by the ancient people of India. Turmeric is proving beneficial in the treatment of many different health conditions from cancer to Alzheimer's disease. Studies at Jawaharlal Nehru Centre for Advanced Scientific Research in Bangalore, India shown that turmeric may play a vital role in fighting HIV/AIDS, particularly HIV, Type 1.

Regardless of all these Curcumin has established as a foodstuff and also a natural medicine because of its low cost, proven chemopreventive and therapeutic potential and potent pharmacological activities of turmeric at in-vivo and in-vitro which made it a nature's precious drug.

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