A REVIEW ON PHARMACOLOGICAL ACTIVITIES OF TURMERIC

Priyanka Chaudhary*, Pramod Kumar Sharma, Vipin Kumar Garg, Jonish Varshney
Department of Pharmaceutical Technology, Meerut Institute of Engineering & Technology, NH-58, Baghpat By-pass Crossing, Delhi-Haridwar Highway, Meerut-250005, India.
e-mail:- priyankampharm123@gmail.com

Summary

Curcuma longa L. is an herbaceous perennial plant, belonging to the family *Zingiberaceae*. In English it is known as Turmeric and in Hindi as Haldi. Turmeric possesses divergent pharmacological activities. Curcumin, a major constituent of turmeric, a yellow pigment present in the Indian spice turmeric (associated with curry powder), has been linked with suppression of inflammation, antioxidant, anticancer, anti-HIV, hepatoprotective, angiogenesis, tumorigenesis, diabetes, diseases of the cardiovascular, pulmonary, neurological systems of skin, and of liver, loss of bone and muscle, depression, chronic fatigue, and neuropathic pain. The pharmacological properties of turmeric are reviewed in reference to anti-inflammatory, antioxidant, antimicrobial, anticancer and anti-carcinogenic, antivenom, anti-HIV, wound healing, and photo-protector activities.

Key words: *Curcuma longa* L., Turmeric, Curcumin, Anti-inflammatory, Anticancer.

Introduction

Curcuma longa L. is an herbaceous perennial plant, belonging to the family *Zingiberaceae*. It has a large oval rhizome with sessile cylindrical tubers, orange coloured inside. Its leaves start from the rhizome, are elliptical and can reach up to 1.2 m in length. Its flowers are yellow, between 10 to 15 cm in length and they group together in dense spikes, which appear from the end of spring until the middle of summer. No fruits are known for this plant. The Curcuma genus contains around 30 species. The plant originates from India and South-East Asia. In India, it is popularly known as “Haldi”. It has been well studied in Malaysia, Indonesia and India due to its economic importance. The rhizomes of turmeric are commonly used as a flavoring, coloring agent and preservative. Commercially, it is traded as a dye, spice and source of industrial starch **[1]**.

Fig: Turmeric

GEOGRAPHICAL SOURCE: - Turmeric is distributed throughout tropical and subtropical regions of the world, being widely cultivated in Asiatic countries, mainly in India and China and used as household remedy in Nepal **[2]**.

HISTORY

A coloring principle of turmeric was isolated in the 19th century and was named curcumin, which was extracted from the rhizomes of *C. longa L.* with yellow color and is the major component of ant, being responsible for the anti-inflammatory effects. It is commonly used as a dietary spice and colouring agent in cooking and is used as an herb in traditional Indian and Chinese medicine. As a powder called turmeric, it has been in continuous use for its flavoring, as a spice in both vegetarian and non-vegetarian food preparations and it also has digestive properties **[3]**.

Curcumin possesses diverse pharmacological effects including anti-inflammatory, antioxidant, anticancer, antidiabetic, antirheumatic, angiogenic, antifertility, antiviral and anti-infectious activities and wound healing properties. Recently, it has attracted much attention due to its significant medicinal potential **[4]**. The main yellow bioactive substances in the rhizomes are due to curcumin, demethoxycurcumin and bisdemethoxycurcumin. Many studies have reported the biological, physiological and chemical properties of turmeric. Turmeric has been reported to possess anti-inflammatory, hepatoprotective, antitumor, antiviral activities **[5]** and anticancer activity **[6]** and is used in gastrointestinal and respiratory disorders **[7]**. Curcuminoids exhibit free-radical scavenging properties, antioxidant activity **[8-12**] and act as inhibitors of human immune deficiency virus type 1 (HIV-1) integrase **[13]**.

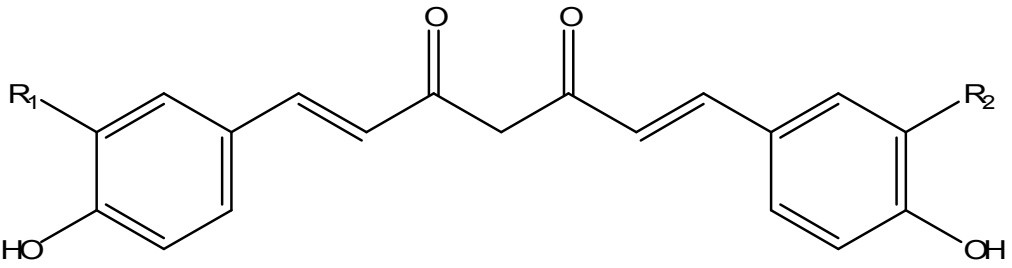
Turmeric oil is composed of several monoterpene and sesquiterpene compounds such as zingiberene; ar-turmerone, alpha-turmerone and beta-turmaerone **[14]**. The main biological activities of the oil are carminative, antiflatulence, antifungal and as an antiplatelet agent **[15]**. Curcumin, commonly called diferuloyl methane, is a hydrophobic polyphenol derived from the rhizome (turmeric) of the herb Curcuma longa. Turmeric has been used traditionally for many ailments because of its wide spectrum of pharmacological activities. Curcumin has been identified as the active principle of turmeric; chemically, it is a bis-a, b-unsaturated b-diketone that exhibits keto-enol tautomerism. Curcumin has been shown to exhibit antioxidant, anti-inflammatory, antimicrobial, and anticarcinogenic activities. It also has hepatoprotective and nephroprotective activities, suppresses thrombosis, protects against myocardial infarction, and has hypoglycemic and antirheumatic properties.

CHEMICAL CONSTITUENTS

The principle constituent of turmeric is Curcumin, which is diferuloyl methane. Other constituents are curcuminoids and an essential oil called zingiberine. Its chemical study shows that it contains proteins, carbohydrates and fibre. Its mineral and vitamin contents are calcium, phosphorus, iron, carotene, thiamine and niacin. It contains 5% of volatile oil, resin, abundant Zingiberaceous starch grains and yellow coloring substances known as curcminoids. The components of curcuminoids are known as curcumin (50-60%).Chemically, curcuma species contain volatile oil, starch and curcumin. Curcumin and other related curcuminoids are reported to be responsible for the yellow colour in some species. Volatile oil content ranges from 1 to 6.5% and composed of mono and sesquiterpenes such as alpha and beta -pinene, alpha- phellandrene, camphene, camphor, zingibereneand alpha, beta curcumenes. Species like C. angustifolia and C. caulina have high starch content and are used as a substituted for arrow root. Chemical constituents are known to vary as per geographical locations and curcumin is reported to vary from 1 to 10% **[16]**.

CHEMISTRY

The major constituent, curcumin (diferuloylmethane) is in the most important fraction of C. longa L. and its chemical structure was determined **[17]**. It melts at 176-177°C and forms red-brown salts with alkalis. Curcumin is soluble in ethanol, alkalis, ketone, acetic acid and chloroform; and is insoluble in water. In the molecule of curcumin, the main chain is aliphatic, unsaturated and the aryl group can be substituted or not. Curcuminoids are between 2 and 9%. Their main components are: curcumin (60%), desmethoxycurcumin, monodemethoxycurcumin, bisdemethoxycurcumin, dihydrocurcumin and cyclocurcumin. Curcumins oxidation yields vanillin.



	R_1	R_2
Curcumnia	OCH_3	OCH_3
Desmetoxicurcumnia	H	OCH_3
Bisdesmetoxicurcumnia	H	H

Fig: Structure of the main curcuminoids of turmeric **[18]**. Curcumina: curcumin; Desmetoxicurcumina: desmethoxycurcumin; Bisdesmetoxicurcumina: bisdesmethoxycurcumin).

USES

Curcumin is the part of turmeric that gives curry food its golden color. This also provides turmeric with curcuminoids, which are believed to have health properties such as antioxidant, antibacterial and anti-inflammatory qualities. Turmeric benefits have been known for centuries and have always been an important part of Chinese herbal medicine and also the Ayurvedic medicine of India. This natural food is believed to support liver health, help prevent bad cholesterol, and it is being studied for its ability to block tumors. A strong antioxidant, turmeric is rich with a substance believed to protect body cells from damage caused by oxidation. Oxygen free radicals may suppress immune function and cause tissue damage. In addition to their anticancer effects, antioxidants in turmeric protect the brain, kidneys, and liver from damage by alcohol, drugs, radiation, heavy metals or chemicals. For skin problems, turmeric ointment, or a paste made from powdered turmeric is applied directly to the skin, as often as needed. It's used to treat cuts, scrapes, and skin conditions such as acne, diaper rash, and psoriasis. Turmeric essential oil is also used in eczema and eliminates spots. Turmeric is used as carminative, which means it is used as a tonic to remove gases from the stomach that causes stomach upset **[19]**.

PROPERTIES OF TURMERIC

ANTIINFLAMMATORY ACTIVITY: - There are a great number of compounds extracted from C. longa L. being potent inhibitors of inflammation.
Anti-inflammatory activity of curcumin and other semi-synthetic analogues (sodium curcuminate, diacetyl curcumin, triethyl curcumin and tetrahydro curcumin) in carrageenan- induced rat paw edema and cotton pellet granuloma models of inflammation in rats was reported **[20]**. Curcumin and its analogues showed similar action in carrageeninin induced paw edema in rats; however the sodium curcuminate was the most potent analogue and was more water-soluble than curcumin. Among the curcumin analogues, triethyl curcumin was the most potent anti-inflammatory in the chronic model of inflammation, when compared with the others and with the drug reference; and tetrahydro curcumin showed no activity.
In the acute inflammation condition, all the substances were more effective. Activity of the compounds used in these experiments, would depend on the model of inflammation.
The anti-inflammatory activity in different fractions of the petroleum ether extract of the rhizomes of turmeric (two constituents) in animals was investigated **[21]**. Inflammation is the starting point in the skin ageing process. An inflamed area is in reality, a micro -wound, which, stimulated by certain environmental factors (ultra-violet rays, contamination, etc.), progresses to a wrinkle or skin imperfection. The inflammation also affects the skin pigmentation.
Mode of action: - Curcumin showed anti-inflammatory properties in animal models by inhibiting the activity of the enzymes cycloxygenase-2 and lipoxygenase as well as the enzyme nitric oxide synthase **[18]**.

ANTIOXIDANT ACTIVITY: - It is known that the damages caused by oxidation in the different cellular components are one of the main causes of many diseases, including ageing **[22]**.
Mode of action: - Curcumin has a free radical scavenger activity, especially on the hydroxyl radical, which explains its capacity to protect DNA from damage in human cell cultures exposed to radiation. In vitro studies have demonstrated its capacity to block the activity of the cyclooxygenase and lipooxygenase enzymes. Topical applications of curcumin on the skin of mice increase the glutathione level and the glutathione Stransferase activity, while at the same time, inhibits lipid peroxidation in the skin tissue. The local application of turmeric extract has a recognised antioxidant and anti-inflammatory activity. It is more efficient than vitamin E as an anti-radical agent and as an inhibitor of lipid peroxidation **[23]**. Local applications of curcumin may noticeably inhibit the ODC (ornithine decarboxylase) activity induced by simultaneous UVA radiation and TPA (tetradecanoylphorbol acetate) application on mouse epidermis. It is accepted that such activity of curcumin may be due to its capacity to scavenge free radicals or to interrupt the activation of protein kinase C **[24]**.In rats with ethanol-induced brain damage, curcumin exerted protective effects, which were mainly due to its antioxidant activity resulting form the increased glutathione levels and decreased lipid peroxidation in neuronal membranes. Additionally, certain curcuminoids are present in the rhizome. Curcumin, demethoxycurcumin and bisdemethoxycurcumin protected in vitro human umbilical cord endothelial cells and rat pheochromocytome cells against the entry of beta-amyloid, a substance that induces oxidative stress and is involved in the neuronal deterioration observed in Alzheimer. It was demonstrated that the water and ethanol extracts of turmeric rhizomes inhibit the oxidation of erythrocyte membranes and hepatic microsomes of rabbits undergoing an atherogenic diet **[18]**.
Tetrahydrocurcumin, a hydrogenated derivative has been isolated from curcumin **[22]**. This molecule has a strong antioxidant action because its structure includes a phenol group and a β-diketone. The relationship between molecular structure and activity of tetrahydrocurcuminoids has also been reported **[23]**. Thus, the antioxidant activity of turmeric extract makes it highly recommendable when formulating cosmetic products destined to protect the skin and hair from oxidative processes. The

antioxidant activities of curcumin and related compounds have been investigated by a variety of assay systems, in both in vitro and in vivo conditions. The disparity in assay conditions makes exact comparisons rather difficult.

ANTIMICROBIAL ACTIVITY: - It has been shown that curcumin in vitro is highly toxic to Salmonella sp. but not to Escherichia coli.
Mode of action: - The water and ethanol extracts of turmeric rhizome have a moderate inhibitory activity on Staphylococcus sp. and Escherichia coli. Other in vitro studies evidenced that the essential oil has a weak inhibitory activity on Staphylococcus aureus, S.epidermidis, Proteus vulgaris and Aspergillus fumigatus. As anti-protozoa agents, curcumin and bisdemethoxycurcumin showed moderate in vitro activity against Plasmodium falciparum and Leshmania major. The water and ether extracts of turmeric showed repellent effects on the insect species Aedes aegypti, Rhizopertha dominica, Sitophilus oryzae, Spodeptera litura and Tribolium castaneum, antifungal effects against Helminthosporium sp., Pyricularia oryzae, Rhizoctonia solani, Sclerotium oryzae and Sclerotium rolfsii, and nematicide effects against Meloidogyne incognita. Turmeric essential oil showed repellent effects on the mosquitoes Aedes aegypti, Anopheles dirus and Culex quinquefasciatus. Such repellent activity is strengthened by the addition of 5% vanillin. The hexane extract of turmeric rhizome inhibited the growth of the fungi Piedraia hortae, Trichophyton mentagrophytes and Microsporum cannis. It also inhibited Aspergillus sp. A preliminary study carried out in India with 814 patients with scabies demonstrated the efficacy of local applications of a turmeric rhizome paste, which did not produce toxic or adverse effects **[18]**. The anti-bacterial in vitro activity of the turmeric alcohol extract, curcumin and its essential oils against Gram-positive bacteria is well known. Significant anti-fungal activity has also been described. Turmeric essential oils have demonstrated anti-fungal activity on being applied topically on guinea pigs and in vitro tests against different isolated pathogens **[25]**. Thus, the antimicrobial action of turmeric extract makes it a very recommendable component when formulating cosmetic products with antiseptic activity as well as cosmetic products with an insect repellent function.

ANTICANCER AND ANTICARCINOGENIC ACTIVITY: - It was recognized that anticarcinogenic properties of classical Michael acceptors **[26]** have been demonstrated in curcumin **[27]** and it has been suggested that the presence of a hydroxyphenyl group in compounds analogous to curcumin, especially in the 2-position, is supportive of the chemoprotective activity through the ability to induce Phase II detoxification enzymes.
Mode of action: - The inhibition of formation of the Fos-Jun-DNA complex, the presence of a 4-hydroxyphenyl, flanked by an adjacent methoxy or nitro group on the phenyl ring in curcumin analogues, conferred better potency than curcumin.
[28] Showed that the monosemicarbazone of curcumin has greater cytotoxic activity than curcumin itself. In one of the more significant findings on the anticancer activity of compounds inspired by curcumin **[29],[30]** announced the superior activity of 2,6-bis(2-fluorobenzylidene) piperidon in antiangiogenesis, cell cycle arrest, and apoptosis of cancer cells. These authors observed that the bis-benzylidenepiperidone, pyrone, and cyclohexanone derivatives, containing α, β-unsaturated ketone unit, exhibit much greater anticancer and antiangiogenesis activities than curcumin, with its 1, 3-diketone unit.

ANTIVENOM ACTIVITY: - The fraction consisting of ar-turmerone, isolated from C. longa L., neutralized both the hemorrhagic activity and lethal effect of venom in mice. In this study ar-turmerone was capable of abolishing the hemorrhagic activity of Bothrops venom and about 70% of the lethal effect of Crotalus venom. Ar-turmerone can act as an enzymatic inhibitor in the case of venom enzymes, with proteolytic and hemorrhagic activities **[31]**

ANTI-HIV ACTIVITY: - [13] demonstrated that curcumin has an antiviral activity, being a HIV-1 integrase inhibitor and suggested that curcumin analogs may be developed as anti-AIDS drugs. Curcumin inhibited the replication of HIV-1 integrase protein. **[2]** Reported that curcumin was claimed for anti-HIV-1 and HIV-2 activities in a recent patent application.

WOUND HEALING ACTIVITY:-
The topical administration of curcumin extracts on skin wounds on the skin of diabetic rats demonstrated an improvement in the wound healing process.
Mode of action: - The reparation action mechanism involved an increase in the levels of beta transforming growth factor plus an increase in the activity of the enzyme nitric oxide synthase **[18]**. The wound-healing activity of turmeric has been widely studied and it has been seen that its local application is effective. In Chinese medicine it has been used for this purpose since ancient times **[25]**. This action makes turmeric extract a good ingredient when formulating cosmetics with regeneration activity.

PHOTO-PROTECTOR ACTIVITY:-
Mode of action: - The action is due to its antioxidant activity, 25% of the lipids of the surface of the skin are unsaturated, and therefore, are easily attacked by free radicals. The ultraviolet rays of the sun penetrate the skin and accelerate the damage caused by these radicals. Prolonged exposure to these radiations means that the collagen and elastin fibres, responsible for the elasticity and integrity of the skin, may be degraded by inherent enzymes, thus causing deterioration in the texture of the skin. In laboratory studies, extract of turmeric was shown to be effective in suppressing inflammation and protecting the epidermal cells from the damages caused by ultraviolet B radiation **[23]**. Curcumin in small doses has been shown to have the capacity to protect against chromosomal damage caused by gamma radiation. Curcumin has also been shown to inhibit the mutagenic induction effect of UV rays **[18]**.

Conclusion

Turmeric is an aromatic spice, traditionally used as a food additive in curries, giving them their distinctive flavour and color. It has been used in traditional medicine for the treatment of various diseases as discussed above. The present investigation was an attempt to explore few of the diverse pharmacological properties of turmeric. The main activities like anti-inflammatory, antioxidant, antimicrobial, anticancer and anti-carcinogenic, antivenom, anti-HIV, wound healing, photo-protector has been described. The fast growing research on turmeric and its metabolites clearly confirms the versatility and flexibility of curcumin for structural modifications. However the actual role of different functionalities in curcumin in influencing its special physico-chemical properties and pleiotropic effects of natural and synthetic curcuminoids is far from understood. This review describes various approaches that have been undertaken to prove the biological importance of turmeric.

References

1. Scartezzini P, Speroni E. Review on some plants of Indian traditional medicine with antioxidant activity. J Ethnoparmacol. 2000; 71: 23-43.
2. Eigner D, Scholz D. Ferula asafetida and Curcuma longa in traditional medical treatment and diet in Nepal. J Ethnopharmacol. 1999; 67: 1-6.
3. Govindarajan VS. Turmeric-chemistry, technology and quality. CRC Cr Rev In Fd Sci Nut 1980; 199-301.
4. Cousins, M, Adelberg J, Chen F, Rieck J. Antioxidant capacity of fresh and dried rhizome
from four clones of turmeric (Curcuma longa L.) grown in vitro. Indust. Crops Prod.2007; 25: 129-135.
5. Ammon HPT, Wahl MA. Pharmacology of Curcuma longa. Planta Med.1991;57;1-7.

6. Polasa K, Raghuram T C, Krishna TP. Turmeric (Curcuma longa L.) induced reduction in urinary mutagens. Food Chem.Toxic. 1991; 29: 699-706.
7. Anwarul HG, Abdul J, Muhammad N, Kashif M. Pharmacological basis for the use of turmeric in gastrointestinal and respiratory disorders. Life Sci.2006; 76: 3089-3105.
8. Toda S, Miyase T H, Arichi H, Tanizawa Takin Y. Natural Antioxidants III: Antioxidative components Isolated from Rhizome of Curcuma longa L. Chem. Phram. Bull. 1985; 33: 1725-1728.
9. Soudamini, KK. Inhibition of chemical carcinogenesis by curcumin. J.Ethnopharmacol. 1989; 27: 227-233.
10. Ammon HTP, Mack T, Sabieraj J. Mechanism of anti inflammatory actions of curcumin and boswellic acids. J. Ethnopharmacol. 1993; 38: 113-119.
11. Selvam R, Subramanian L, Gayahtri R, Angayarkanni N. The anti-oxidant activity of turmeric (Curcuma longa L.). J. Ethnopharmacol. 1995; 47: 59-67.
12. Masuda T, Kidaka K, Shinihara A, Mackawa T, Takeda Y, Yamaguchi, H. Chemical studies on antioxidant mechanism of curcuminoid: Analysis of radical reaction products from curcumin. J. Agric. Food Chem. 1999; 47: 71-77.
13. Mazumder A, Raghavan K, Weinstein J. Inhibition of human immunodeficiency virus type-1 integrase by curcumin. Biochem. Pharmacol. 1995; 49: 1165-1170.
14. Apisariyakul A, Vanittanakorn N, Buddhasuk, D. Antifungal activity of turmeric oil extracted from Curcuma longa L. (Zingiberaceae). J. Ethno-pharmacol. 1995; 49: 163-169.
15. Lee HS. Antiplatelet property of Curcuma longa L. rhizome derived ar-turmerone. Bioresour. Technol. 1996; 97: 1372-1376.
16. Kokate CK, Purohit AP, Gokhale SB. Pharmacognosy. 2006; 36: 401.
17. Roughley PJ, Whiting DA. Experiments in the biosynthesis of curcumin. J Chem Soc. 1973; 20: 2379-2388.
18. Alonso J. Tratado de Fitofármacos y Nutracéuticos. Barcelona: Corpus. 2004;395-403.
19. file:///H:/Turmeric%20(Curcuma%20longa)%20%20Pure%20Herbs.htm
20. Mukhopadhyay A, Basu N, Ghatak N, Gujral PK. Anti inflammatory and irritant activities of curcumin analogues in rats. Agents Actions.1982; 12: 508–15.
21. Arora RB, Basu N, Kapoor V, Jain AP. Anti-inflammatory studies on Curcuma longa (Turmeric). Indian J Med Res.1971; 59: 1289-1295.
22. Osawa T. Plant Antioxidants: Protective Role against Oxygen Radical Species. C&T.1994; 77-81.
23. Prakash L, Majeed S. (2003) Multifunctional Ingredients: The Novel Face of Natural. C&T. 2004; 118: 41-47.
24. Pons L. Fotoprotección vegetal (II). OFFARM. 2003; 22: 163-64.
25. Srimal RC. Turmeric: a brief review of medicinal properties. Fitoterapia. 1997; 68: 483-94 .
26. Talalay P. The importance of using scientific principles in the development of medicinal agents from plants. Acad Med. 2001; 76: 238–47.
27. Dinkova-Kostova AT, Talalay P. Relation of structure of curcumin analogs to their potencies as inducers of Phase 2 detoxification enzymes. Carcinogenesis.1991; 20: 911–4.
28. Dutta S, Padhye S, Priyadarsini KI, Newton C. Antioxidant and antiproliferative activity of curcumin semicarbazone. Bioorg Med Chem Lett . 2005;15: 2738–44.
29. Adams BK, Cai J, Armstrong J, Herold M, Lu YJ, Sun A, et al. A novel synthetic curcumin analog, induces apoptosis in cancer cells via a redox-dependent mechanism. Anticancer Drugs. 2005; 16: 263–75.
30. Adams BK, Ferstl EM, Davis MC, Herold M, Kurtkaya S, Camalier RF, et al. Synthesis and biological evaluation of novel curcumin analogs as anti-cancer and antiangiogenesis agents. Bioorg Med Chem . 2004;12: 3871–83.
31. Ferreira LAF, Henriques OB, Andreoni AAS, Vital GRF, Campos MMC, Habermehl GG, Moraes, VLG. Antivenom and biological effects of ar-turmerone isolated from Curcuma longa (Zingiberaceae). Toxicon. 1992;30: 1211-1218.