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THERAPEUTIC USES OF *CURCUMA LONGA* (TURMERIC)

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ABSTRACT

***Curcuma longa* commonly known as turmeric is traditionally used as a spice in Indian food. A wide range of biological activities e.g. anticancer, antimicrobial, anti-inflammatory and free radical scavenging activity of the plant suggests a logical basis for its traditional use in foodstuff. Various phytothreapeutic uses of *Curcuma longa* have been reviewed.**

KEY WORDS : *Curcuma longa*, Antioxidant, Anticancer, Antiinflammatory, Insecticidal, Nematocidal, Antimicrobial

INTRODUCTION

Curcuma longa Linn. Syn. *Curcuma domestica* Val. (Fam: Zingiberaceae) has been used as an ethno-medicine from time immemorial in Ayurvedic system and is also used as a dietary spice and coloring agent. *Curcuma longa is* known as turmeric in English and Ukon in Japanese. In India it is known as haldi in Hindi, pasupu in Telugu, Aarishina in Kannada and nalud in Bengali. Turmeric is used as a coloring agent to dye wool, silk and unmordent cotton. It is used as an antacid, carminative, stomachic, blood purifier wound healing and anti-inflammatory in Indian medicinal system (1). The biological activity of turmeric is attributed to the presence of curcuminoids and sesquiterpenoids (2). The vast number of biological activities of *C.longa* are briefly reviewed here.

Antioxidant

Cell possesses an elaborate defense system to destroy reactive oxygen species (free radicals) and lipid peroxidation products that cause considerable damage to the cell. Antioxidants neutralize free radicals and stop the chain reaction. Natural antioxidants from wheat grain, turmeric, rose merry, sage, rue and fennel added to stored anhydrous butter fat improved the stability of butter and reduced its autooxidation (3). Turmeric was the second most active spice among 23 spices studied for antioxidant activity. The fresh spices ginger and turmeric were more potent than garlic and onion in inhibiting lipid peroxidation in salted cooked ground fish (4). The lipid peroxidation was 29% and 35 % lower in liver homogenates and microsome respectively of turmeric fed rats, as compared to rats fed with control diet (5). Effect of the hydroalcoholic extract of *C.longa* (equivalent to curcumin 20 mg/day) was examined in 18 healthy men for a period of 75 days. Significant decrease in concentration of serum lipid peroxide was observed even after 45 days of treatment (6). The curcuminoids in turmeric protected the normal human keratinocytes from hypoxanthine/xanthine oxidase injury and synergistically inhibited nitroblue tetrazolium reduction indicating a decrease in superoxide radical formation (7). Curcumin (50mmol) with rose bengal inhibited the light induced hemolysis of rabbit and was shown to be potent scavenger of free radicals (8). Lung fibrosis (monitored by increased lung collagen hydroxy proline) produced by gamma irradiation of rats was significantly reduced by oral administration of antioxidant curcumin, ellagic acid, bixin, a- tocopherol at a concentration of 200 fmol/kg body weight (bw) (9). Turmeric and curcumin induced significant increase in hepatic level of glutathione -S-transferase and acid soluble sulfhydryl after 14 to 21 days of

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treatment in lactating dams. Cytochrome b_5 and cytochrome P450 levels were significantly elevated in dams as well as suckling pups of both 14 or 21 days age group (10). The turmeric and its constituents may be showing antioxidant activity due to their competition with peroxidant metals (iron and copper) for cell binding site and may also protect the cell against free radicals damage by defending the oxidation of sulfhydryl groups (1).

Anticancer activity

Turmeric possesses anticancer activity because curcuminoids present in turmeric show tremendous free radical scavenging property. The anticancer activity of turmeric has been reported in oral, skin, colonic and mammary cancer. The development of oral neoplasma, identified histopathologically as sqamous cell carcinomas in animals painted with 4-nitroquinoline-1-oxide (NQO) on their cheek mucosa showed a decrease in lipid peroxidation and tumor burden when administered with turmeric extracts simultaneously (11). Turmeric 2 or 5% in diet significantly inhibited benzopyrene (BP) induced forestomach pappilomas (12,13). Dietary turmeric with catechin was also used as a chemopreventive agent in BP induced forestomach tumors in swiss mice and methyl (acetoxymethyl) nitro amine induced oral mucosal tumors in syrian golden hamsters probably due to increased forestomach and hepatic glutathione -S-transferase (GST) activity when compared to controls (14). The rats fed with 0.5% turmeric in diet showed no decrease in xenobiotic metabolizing phase I enzymes, aryl hydrocarbon hydroxylase (AHH) while phase II enzymes, UDP glucuronyl transferase (UDGPT) and GST level were significantly elevated in rats fed with 5 and 10% turmeric (15,16). The increased activity of phase II enzymes is related to faster metabolism of xenobiotics thus leading to anticancer effects. It is suggested that binding of curcumin to the active site of GST might be involved in the modulation of GST activity in chemoprevention and chemoprotection of cancer.

Chromosomal aberration was examined by micronuclear assay. Turmeric extract did not induce an increased level of chromosomal damage. It was postulated that the clastogenic effect of turmeric might be due to its content of curcumin (17). Turmeric was found to be non mutagenic in Ames assay with *Salmonella typhimurium* strains TA 100, TA98 and TA 97 before or after activation with liver microsomal fraction on cell free extracts of rat cecal microorganisms (18). The study conducted on human beings fed with turmeric in a dose of 1.5 gm/day for 30 days showed significant reduction in the urinary excretion of mutagens in 16 chronic smokers (19).

Turmeric extract and curcumin reduced expression of pappilomas in mouse skin induced by 7,12 dimethylbenzo (a) anthracene (DMBA) (20). Administering 5% turmeric to 2 months old rats showed suppression of DMBA induced mammary neoplasma, virus related reverse transcriptase activity and preneoplastic changes in the mammary glands (21). A dose dependent decrease in binding of [^{3}H] benzo (a) pyrene metabolite to calf thymus DNA was observed in presence of turmeric, curcumins (Cs) and aqueous turmeric extract but not in presence of curcumin free aqueous turmeric extract suggesting Cs to be active principle (22). Curcumin in a dose dependent manner reduced the occurrence of DMBA and 12-O-tetradeconylphorbol-13-acetate (TPA) promoted skin tumor formation in male Swiss albino mice (23). Curcumin mediated effects on the TPA induced formation of oxidized epidermal DNA (62-77%) base 5-hydroxymethyl 1, 2-deoxyuridine (HMdU), and tumor promotion was inhibited at all doses of curcumin (24). Colonic tumors induced by azoxymethane at a dose of 15 mg/Kg bw for 52 weeks to the rats containing curcumin 2000mg/Kg in the standard diet and to the rats fed on standard diet, were evaluated histopatholgically and by analyzing phospholipase A2, phosholipase C gamma 1, ex vivo prostaglandin (PG) E2, cyclooxygenase and lipoxygenase activities. The incidence of colon adenocarcinomas ($P< 0.004$) and multiplicity of invasive ($P<0.015$), non invasive ($P<0.01$) and total (invasive plus non invasive) adenocarcinomas ($P<0.001$) was inhibited in rats fed with curcumin diet (25). Aflatoxin induced liver damage in ducklings causing change in concentration of fatty acid, necrosis and biliary hyperplasia was reversed by turmeric and curcumins (26). Curcumin in a dose dependent

manner, inhibited the formation of covalent adducts between aflatoxin B, and DNA as catalyzed by microsomes or a reconstituted microsomal monooxygenase system. The 50 % inhibition of aflatoxin B_1-DNA adducts formation by curcumin in this system could be reversed by increasing the amount of cytochrome P_{450} (27). A cytotoxic sesquiterpene, (+) arturmerone isolated from *C. domestica* was active against L 1210 cell lines (28).

Antiinflammatory

In Indian system of medicine turmeric is a household remedy for reducing pain, swelling, wound injury and various types of inflammation (1). In the carrageenin induced oedema, the turmeric oil at 1.6 ml/kg bw. has shown as much antiinflammatory activity as phenylbutazone (29). The two new phenolics isolated from rhizome of *C. longa* exhibited strong anti inflammatory action against TPA induced oedema in mice (30). Curcumin 30mg/kg bw/day delayed the onset of arthritis and reduced the extent of inflammation. Curcumin fed to arthritic rats also lowered paw inflammation (31). It is concluded that curcumin can decrease the incidence, delay the onset and reduce the extent of inflammation of adjuvant induced arthritis in the rats (32). Curcumin inhibited 5-lipoxygenese activity in rat peritoneal neutrophils. It also inhibited 12 - lipoxygenese and cycloxygenase in human platelets in cell free peroxidation system (33).

Antifungal

Herbal drug preparation containing turmeric powder cured ringworm infection caused by *Trychophyton verrucosum* in 12 cattles and *T. verrucosum* and *Microsporum canis* in 21 dogs within 12-15 days of treatment (34). Turmeric oil and curcumin were tested against 15 isolates of dermatophytes, 4 isolates of pathogenic moulds and 6 isolates of yeast. Turmeric oil inhibited dermatophytes and pathogenic molds *in vitro*, curcumin showed no antifungal activity (35,36). The *in vitro* mycelial growth of *Rhizoctonia soloni* was inhibited with the essential oil of *Curcuma longa* at MIC of 2000 ppm. The ether and chloroform extract of *C.longa* were found to be fungistatic at MIC of 5mg/ml *in vitro* against *Trichophyton mentagrophytes, T.mentagrophytes, T. rubrum* and *Microsporum gypseum. C.longa* was found to be fungistatic at MIC of 5 mg/ml. The extracts were comparable with chemical agents like theomersal and 1% tincture of iodine contained 2% salicyclic acid (37). The turmeric extracts prepared by extraction with benzene followed by n-butanol and water were inactive against *Candida albicans, Cryptococcus neoformans, T. mentagrophytes, M. canis* and *Aspergillus niger* (38). The aromatic unsaturated carbonyl compound AF 853 isolated from *C. longa* showed remarkable antifungal activity (39).

Antibacterial activity

The *C.longa* rhizome extracts showed no activity against *Bacillus subtilis, Staphylococcus aureus* (gram +ve) *Salmonella typhimurium, Escherechia coli, Agrobacterium tumefaciens* (gram -ve) and one acid fast *Mycobacterium tuberculosis* strain (38). *C. longa* rhizome extracts were evaluated for antibacterial activity against pathogenic strains of gram positive (*S. aureus, Staphylococcus epidermidis*) and gram negative (*E. coli, Pseudomonas aeruginosa, S. typhimurium*) bacteria. Petroleum ether extract showed remarkable activity against gram positive bacteria at the dose of 1000 μg/ml. The petroleum ether component was further fractionated to give pure compounds. A novel antibacterial compound was isolated in our laboratory that showed remarkable activity on clinical isolate of *S.aureus* as compared to known antibiotics. (40). The clinical and bacteriological assessment of Teeberb (capsules containing extract of seven medicinal plants including turmeric) was made against pyoderma dogs. Turmeric showed promising results (34). Various extracts of *C.longa* plant alone or in combination with some other plants were found to be active against *B. subtilis, S.aureus* (gram +ve), *E.coli* and *P.aeruginosa* (gram –ve) bacteria by cup plate method at a dose of 250 mg/ ml. Water extract was however inactive against *S.aureus* (41). *C. longa* oil was active against most of the bacterial strains of *E.coli* (9 strains), *Salmonella* (8 strains), *Proteus moragini* (1 strain), *S.aureus* (1 strain) and *Shigella soniei* (1 strains) (42). The MIC of oil was minimum for *Bacillus subtilis* (0.1ml) and maximum for *Klebsiella aerogenes* (0.2ml) (36). Animal and fish bacterial infection was controlled by

plants containing curcumin (43).

Antiviral activity

Water extract of *C. longa* decreased the number of local necrotic lesions on infected leaves of *Nicotiana glutinosa* by 68% compared with untreated controls. Water and acetone extracts (dilution 1:10) inactivated Tobacco Mosaic virus (TMV) and potato virus filtrate by 74-88% of the control tobacco leaves and mesophyll protoplast. Acetone extract inactivated TMV filtrates at a dilution of 1:50 (81% of the control) (44). Curcumin and its derivative containing boron inhibited the HIV 1 protease (45). Curcumin used at the concentration of 10 to 100 nmol inhibited Tat transcription of HIV I-ltr Lac Z by 70-80% in HeLa cell models (46). Curcumin is also known to inhibit DNA polymerase, HIV and avian myeloblastosis virus reverse transcriptase (1).

Insecticidal and nematocidal activity

Turmeric powder (2%) and *Lantana Camera* powder (2%) were nearly as effective as the chemical insecticide against *Sitophillus oryzae* in stored maize (47). Combination of turmeric powder (TP) and mustard oil enhanced the efficacy of inhibiting the *S. oryzae* which attacks milled rice by completely suppressing progeny (48). Different extracts of *C.longa* were tested against *Pasterulla xylostella* and *Nilaparvata lugens.* Only petroleum ether and water extracts caused 94% and 87-90% mortality to *P.xylostella* (49). *Tribolium castaneum* settled in rice grain treated with 100, 500 or 1000 ppm of turmeric oil in a food preference chamber exhibited increased repellency with increasing concentration of the oil (50). Antimoth paper was produced by adding some plant extracts including *C.longa* extract to the paper (51). The minimum lethal concentration of (+) arturmerone extracted from *C.longa* was shown to be 25mg/ml and was effective most strongly against *Anisakis larvae* (52). Nematocidal activity against *Toxocara canis* was shown by cyclocurcumin isolated from *C.longa* when combined with other curcuminoids like curcumin, demethoxycurcumin and bisdemethoxycurcumin suggesting their synergistic action (53).

Antidiabetic, antiageing and lipid lowering effects

Turmeric showed hypoglycemic activity on glucose metabolism in rat epididymal fat assay for insulin potentiating activity (54). The skin lightening cosmetics contain extracts from many aromatic plants including *C.longa*. The extracts were observed to show tyrosinase inhibiting activity in human beings. Curcumin showed 51.8% inhibition against tyrosinase at 50 mmol (55,56). Rats fed on essential oil and benzene soluble fraction had lower hepatic fatty acid synthetase activity (57). Spices including turmeric stimulate the conversion of cholesterol to bile acids, which is an important pathway of elimination for cholesterol from the body. Addition of essential oil (0.02%) to diet resulted in lower concentration of serum as well as liver triglycerides. Wistar rats fed with 0.5% curcumin for 3 months showed significant increase in the cholesterol 7 a-monooxygenase (EC. 1.14.13.17), the rate limiting enzyme of the bile acid biosynthesis in liver (58,59).

Antiallergic and immunological system activating properties

Ethylacetate extract of *C.longa* inhibited histamine release and type I allergy (60). Turmeric extract showed significant suppression of IgE and IgG antibody response and a marked induction of interferon in serum samples after IP injection (61). A polysaccharide Ukonan A isolated from hot water extract of *C.longa* has shown the reticulo-endothelial system potentiating and alkaline phosphatase inducing activity (62,63).

Miscellaneous

The effect of turmeric on tissue repair (wound healing) in buffalo was studied (64). A preparation containing plant growth promoter inositol hexaphosphate and/or choline derivatives and extracts from medicinal plants including turmeric was shown to promote the growth of vegetable, fruit and trees etc (65). The curcumionoids from *C.longa* rhizome inhibited testosterone 5 α-reductase enzyme activity with IC 50 at 90 ppm (66).

Conclusion

Turmeric holds the promise of providing both

significant clinical benefits and key insights into the patho-physiology of cancer, arthritis, inflammation, respiratory disorders, and gastrointestinal disturbances allergy, microbial (bacterial, fungals viral and insecticide infectiogy. Numerous demonstrations of preclinical efficacy of turmeric in animal models for preventing cancer and cardiovascular disorders due to several kinds of xenobiotics present in the environment necessitates exploration of this natural product further. The individual component, responsible for the specific activity has to be explored.

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