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Phytochemical evaluation of *curcuma longa* and its beneficial effects

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Abstract

Curcuma (C.) longa L. (Zingiberaceae) has been reported for a range of pharmacological activities including anti-inflammatory, anti-bacterial, anti-human immunodeficiency virus, antioxidant and nematocidal activities. This review summarizes the beneficial pharmacological effects of *Curcuma longa*. As, curcumin is a key component of *C. longa* L., and it is responsible for the plant's biological effects. Other extracts of this plant have been shown to be effective. Curcumin has antispasmodic, anti-parasitic, anti-arthritic and anti-inflammatory properties *in vitro*, as well as antidiabetic, hypolipidaemic, anti-venom, and anti-arthritic properties, and suppresses carcinogenesis and cancer growth. Curcumin and extracts of *C. longa* L. have been shown to have anti-parasitic and anti-inflammatory properties *in vivo* in animal models using parenteral and oral administration. In this current effort we formulate an intuition of the pharmacological potential of *C. longa* L., screening its significance.

Keywords

Curcuma longa L.
Curcumin
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Introduction

Curcuma longa is a perennial herb belongs to Zingiberaceae family grows up to 1 meter tall, has a short stem, and is found in topical and sub-topical environments. (Ammon & Wahl, 1991). There is great variety isolated compounds that can be extracted for their pharmacological action (Iwu et al., 1994). The idea of this article is urge scientist to evaluate the new curcuminoid derivatives for the treatment of many diseases. Derivatives isolated with chemical modification and biological activity relationship in order to treat the diseases with less toxic effect to humans (Araujo & Leon, 2001). In the 19th century turmeric coloring principle was isolated, which was named as Curcumin. Curcumin extracted from the rhizome of *Curcuma longa L.* which is responsible for the yellow color and for the anti-inflammatory activity and other two related compounds bisdemrthoxycurcumin (BDMC) and demethoxyxurcumin (DMC)(Ammon & Wahl, 1991).

Active constituents: The active constituents of turmeric (*Curcuma longa*) were susquiterpenes and curcuminoids isolated from the fresh turmeric extract by using electrospray mass spectroscopy, high performance liquid chromatography and UV-diode array. Five other major components such as ar-turmerone, curcumin, curlone, bidemethoxycurcumin and demethoxyxurxumin were also isolated mass spectra and UV spectra and retention time in compared with standard compound (He *et al*., 1998).

By using mass spectrometry 19 diarylheptanoids constituents were isolated by both positive and negative mode such as Liquid chromatography-electrospray ionization- mass spectrometry/ mass spectrometry (LS-ESI-MS/MS) analysis and this technique supported by the Diode-Array Detection (DAD) spectra. Among these 19 diarylheptanoids bisdemethoxycurcumin,

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Curcumin and demethoxycurcumin were isolated by comparing with standard compound their spectral and chromatographic data (Jiang et al., 2006).

Curcuma longa contains active constituent's essential oils 2-4%, fixed oils 2-3% and various other volatile oils and also contain curcuminoids 4-6%, including atlantone, turmerone and zingiberone (Revathy et al., 2011).

Chemistry: Different constituents of turmeric on chemical study have yielded moistures (10-12.0%), fatty oil (4.4-12.7%) and essential oil (4.2-14%). Srinivasan has isolated the presence of three important constituents such as p, p'–dihydroxy dicinnamoylmethane Curcumin (p hydroxycinnamoyl (feruloyl) methane and third one the most important constituent Curcumin (diferuloylmethane)(Ammon & Wahl, 1991). The chemical structure of Curcumin is given in Figure 1.

Pharmacokinetic study: Curcumin pharmacokinetic studies have demonstrated that the dose of Curcumin powder 40-85% passes unchanged through gastrointestinal tract and liver and intestinal mucosa metabolized most absorbed flavonoids. Curcumin is formulated with bromelain to increase the absorption of Curcumin and anti-inflammatory activity but in simple form Curcumin has low absorption (Akram et al., 2010).

Pharmacological studies

Anti-inflammatory activity: This study was conducted to evaluate the anti-inflammatory activity and human toxicity trails of turmeric powder against the different molecules (cyclooxygenase 2 collagenase, interferon inducible protein, hyaluronidase, elastase, lipooxygenase, leukotrienes, thromboxane A_2, phospholipase, prostaglandin, nitric oxide and tumor necrosis factors involves in inflammation and different doses of powder respectively. Curcumin powder at dose 8000 mg/kg for the time period of three month show no toxic effect on humans and at dose 1125-2500 mg/kg show anti-inflammatory activity by reducing the activity of molecules that cause inflammation (Chainani-Wu, 2003).

*Curcuma longa*powder contains active constituents including three curcuminoids: bidemethoxycurcumin and demethoxycurcumin, Curcumin, as well as volatile oils (atlantone, tumerone and zingiberone) resins, protein and sugars which are responsible for the anti-inflammatory activity. Curcumin effect as anti-inflammatory and on cancer (through anti-inflammatory perspective) by interacting the action of mediators that cause inflammation (Jurenka, 2009).

Curcumin I, (monodemethoxycurccumin) Curcumin II and (bisdemethoxycrcumin) Curcumin III at dose 125µg/ml active against the COX I and COX II inhibition and showed inhibition 32%, 38.5% and 39.2% respectively (Ramsewak et al., 2000).

Anti-oxidant activity: To evaluate the anti-oxidant activity of methanol and n-hexane extract of *Curcuma longa* rhizome by using air oxidation method of linoleic acid, both extracts treated with linoleic acid at different concentration. By using silica gel column chromatography methanolic extract with chloroform-methanol mixture at ration 19: 1 v/v was fractionated repeatedly as an eluent. The inhibitory ratio was measured by using thin layer chromatography (TLC) on the air oxidation when 0.1% concentration of linoleic acid was added. The active components were isolated as bis(4-hydrocycinnomoyl) methane, Curcumin and 4-hydroxycinnamoyl methane on the base of spectral comparison and elemental analysis show anti-oxidant activity. Methanolic extract show maximum inhibitory ratio when added to linoleic acid at 0.1% concentration but n-hexane extract show low inhibitory ratio (ToDA et al., 1985).

Anti-hepatotoxic activity: Hepatoprotective activity of *Curcuma longa* rhizome extract was evaluated against the carbon-tetrachloride and galactosamine induced cytotoxic effect in primary cultured rat hepatocytes. Rhizome of *Curcuma longa* contains active constituent curcuminoids which show significant hepatoprotective activity. Metabolite of curcuminoids and some analogues of p-coumaric acid and ferulic also possess significant hepatoprotective activity (Kiso et al., 1983).

Hypo-lipidemic action: Hypolipidemic activity of *Curcuma longa* powder was evaluated in streptozotocin induced diabetic rats. When Streptozotocin-induced diabetic rats were fed a high-cholesterol diet, the extents of phospholipidemia and hypercholesterolemia were still greater than when they were fed a normal diet. A 0.5 % Curcumin-containing meal was given to diabetic rats for an 8-week period, and the phospholipid and cholesterol levels were dramatically reduced. The liver levels of triglycerol, cholesterol, and phospholipid were higher in diabetes patients, however the Curcumin diet showed a potential to reverse these alterations in the lipid component of the liver.

The activities of hepatic HMG-CoA reductase and cholesterol-7a-hydrocylase were assessed to assess the mechanism of action of dietary Curcumin in combating the effects of a diet rich in phospholipidemia and hypercholesterolemia. Hepatic cholesterol-7a-hydroxylase show significantly high level of activity as compared to HMG-CoA reductase by higher rate of metabolism of cholesterol (Babu & Srinivasan, 1997).

Anti-fungal activity: Curcumin and turmeric oil isolated from rhizome of curcuma longa were evaluated for their anti-fungal activity against the 6 isolates of yeasts, 4 isolates of pathogenic molds and 15 isolated of dermatophytes. Turmeric oil inhibits the growth of four isolates of pathogenic fungi at dilution 1:40-1:80 but none of these were inhibited by Curcumin. Both Curcumin and turmeric oil were insensitive to six

isolates of yeast. Turmeric oil at dilution 1:40-1:320 inhibit fifteen isolates of dermatophytes but Curcumin has no effect on inhibition of dermatophytes. By application of turmeric oil lesions improved observed within 2-5 days and lesions disappeared within 6-7 days (Apisariyakul et al., 1995).

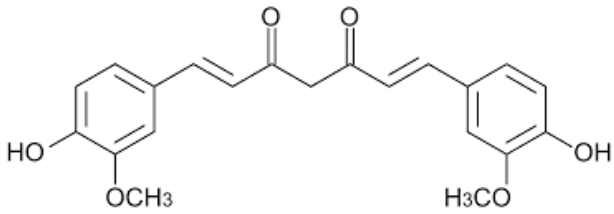

Fig. 1: Chemical structure of Curcumin.

To evaluate the fungicidal activity of *Curcuma longa* against the fungi species such as *Rhizoctonia solani, Puccinia recondite, Pyricularia oryzae, Erysiphe gramins* and *Botrytis cineria* and result was compared with synthetic fungicides. n-hexane and ethyl acetate extracts of turmeric at dose 1000 mg/L showed fungicidal response against the *R. solani, P. recondite* and *E. gramins* and *R. solani, Pu. recondite, P. infestans* and *B.cineria respectively*. Curcumin isolated form turmeric rhizome by using chromatographic fraction techniques administered to control animals at doses 250 and 500 mg/kg and show fungicidal activity against the *R. solani, Pu. recondite* and *P. infestans* with 45-,, 76-, 85% and 63-, 100-, 100% respectively (Kim et al., 2003).

Anti-oxidant and cytotoxic activity: Curcumin I, (monodemethoxycurccumin) Curcumin II and (bisdemethoxycrcumin) Curcumin III isolated from *Curcuma longa* rhizome were evaluated for their cytotoxic and anti-oxidant activity. Curcumin I-III at dose 100 µg/ml showed activity against the breast cancer, CNS, colon, leukemia, melanoma and renal by inhibition of liposome peroxidation at 58, 40 and 22% respectively. Curcumin I-III at dose 125µg/ml active against the COX I and COX II inhibition and showed inhibition 32%, 38.5% and 39.2% respectively. But Curcumin I-III showed best inhibition effect on COX-II enzyme at dose 125 µg/ml with percentage 89.7, 82.5 and 58.9 respectively (Ramsewak et al., 2000).

Anti-bacterial activity: Anti-bacterial activity of turmeric (*Curcuma longa*) was investigated against the pathogenic strains such as gram negative bacteria (*Salmonella typhimurium, Pseudomonas aeruginosa* and *Escherichia coli*) and gram positive bacteria (*Staphylococcus epidermidis* and *staphylococcus aureus*). Essential oil showed significant activity against gram negative and gram positive and compared with erythromycin, doxycycline and ampicillin (Singh et al., 2002).

Poly phenolic constituent (Curcumin) isolated from rhizome of *Curcuma longa*was evaluated for their anti-cancer activity by inhibiting type 1 carcinogen in rodents. Curcumin and methanolic extract of turmeric rhizome were evaluated against the nineteen strains of H-pylori, including 5 cag A + strains and both extracts inhibit the growth of all strains in-vitro at concentration range of 6.25-50 µg/ml with a minimum inhibition. Curcumin exert its chemopreventive response by inhibiting the growth of in-vitro H-pylori cagA+ strains (Mahady et al., 2002).

Toxicity study: Alcoholic extract and turmeric (*Curcuma longa*) were evaluated to check the toxicity on adult rats, monkeys and guineapigs. Alcoholic extract and turmeric administered at doses 300 mg/kg and 2.5g/kg respectively to evaluate their adverse effect on health, histological changes in heart, kidney and liver of adult rats, monkeys and guineapigs, but there was no histological effect and adverse effect (Shankar et al., 1980).

Anti-depressant effect: In order to evaluate the anti-depressant activity of aqueous extract of *Curcuma longa*forced swimming test and tail suspension test were performed in mice. Mice were treated with aqueous extract of *Curcuma longa* at dose 140-560 mg/kg for 14 days and tests were performed. At a dose of 560 mg/kg, the aqueous extract was more effective than the standard anti-depressant drug fluoxetine. The dose 140 mg/kg for 14 days considerably inhibited the monoamine oxidase A enzyme in the entire brain of mice in a concentration-dependent manner, whereas the dose 560 mg/kg considerably inhibited the monoamine oxidase B enzyme in the brain of animals. Fluoxetine also have tendency to inhibit the monoamine oxidase A and B enzyme but both extract and neither fluoxetine nor have tendency to effect significantly locomotors activity. The result showed that *Curcuma longa* had significant anti-depressant activity in animal (Yu et al., 2002).

Anti-diabetic activity: Three extracts of turmeric (*Curcuma longa*) were evaluated for their anti-diabetic activity in type 2 diabetic KK-A^y mice. Theses extracts are prepared by ethanol extraction to yield sesquiterpenes and curcuminoids, n-hexane extract to yield sesquiterpenes and extraction of ethanol extract from n-hexane extract (HE-ext) residue to isolate curcuminoids. To investigate the ant-diabetic activity of theses extracts mice were treated with n-hexane extract at dose 0.1-0.5g/kg, HE-ext at dose 0.5 g/kg and ethanol extract at dose 0.5 g/kg for the time period of four weeks and four weeks blood glucose level of normal control group significantly ($p<0.001$) elevate but blood glucose level significantly controlled with the treatment of extracts at different doses respectively. Turmeric extract and constituents such as ar-turmerone, bisdemethoxycurcumin, Curcumin and demethoxyxur-

cumin have tendency to bind PPAR-γ ligand and also stimulate the human adipose tissue differentiation. Result showed that susquiterpenes and curcuminoids exhibit anti-diabetic effect via activation of PPAR-γ receptors (Kuroda et al., 2005; Nishiyama et al., 2005).

Streptozotocin (STZ) induced hyperglycemia in diabetic rat's leads to excess production of free radicals and this lead to development of diabetic nephropathy. After induction of diabetes by single intraperitoneal dose STZ 65 mg/kg, the treated control rats were administered Curcumin at dose 15mg/kg and 30mg/kg orally for two weeks. Renal function tests were measured by blood urea nitrogen, creatinine, urea albumin excretion and urea clearance. Oxidative stress was measured by anti-oxidant enzymes superoxide catalase and dismutase and reduced glutathione. Rats treated with Curcumin chronic doses significantly attenuated by oxidative stress and renal dysfunction (Sharma et al., 2006).

Anti-Ulcerative colitis activity: Ulcerative colitis is a non-specific inflammatory disease defined by nitrisative and oxidative stress, up-regulation of pro-inflammatory cytokines and leucocyte infiltration. Mitogen activated protein kinases (MAPKs) like c-Jan N-terminal kinase (JNK) and p38 regulate inflammatory process by genes' transcription. This study was done to evaluate the mechanism of Curcumin, which is a polyphenol obtained from *Curcuma longa* for their anti-inflammatory activity. Rats were treated with the dose 50-100 mg/kg/day orally after trinitrobenzensulfonicacid instillation for two weeks. Curcumin significantly attenuated the disease and substantially lower the level tumor necrosis factor-α (TNF-α) rise in MPO activity. Curcumin also cause the down regulation of inducible nitric oxide synthase (INOS) and COX-2 expression and also significantly reduce the level of nitrites colonic(Camacho-Barquero et al., 2007).

Anti-ulcer activity: This study was conducted to evaluate the anti-ulcer activity of an ethanol extract of turmeric (*Curcuma longa*) against injuries caused by the cysteamine administration, hypothermic restraint stress, indomethacin, reserpine administration, pyloric ligation and cyto-destructive agent's ethanol 80%, 25% NaCl and 0.2 M NaoH. Rats treated with turmeric extract at dose 500 mg/kg produce significant anti-ulcer activity in cysteamine administration, hypothermic restraint stress, indomethacin, reserpine administration, pyloric ligation induce ulcer models. The extract also had significant cytoprotective activity in cyto-destructive ulcer models by inhibiting acid secretion and by significantly increasing the gastric mucus secretion (Rafatullah et al., 1990).

Inhibit platelet aggregation: This study was conducted to evaluate the anti-platelet activity of *Curcuma longa* extract by acting on eisosanoid modulating properties. Curcumin is active constituent of turmeric; inhibit the platelet aggregation induced by adrenaline, collagen and arachidonate. This compound from exogenous inhibits the production of thromboxane B_2 (TXB_2) and in washed platelets inhibits the arachidonate production with simultaneous increase the production of 12-lipoxygenase products. Curcumin anti-inflammatory activity, in part, be represent by its effect on eicosanoids biosynthesis (Srivastava et al., 1995).

Turmeric rhizome anti-platelet activity was also tested using a platelet aggregometer and compared to the standard medication aspirin.

Insecticidal activity: The fumigant and contact toxicity of essential oil produced from turmeric leaves (*Curcuma longa* L.) were tested, as well as their influence on progeny production in three distinct storage beetles such as *Tribolium castaneum* Herbest, *Sitophilus oryzae* L. and *Rhyzopertha dominica* F. Oil of turmeric leaves was also investigated for the ovicidal action and oviposition action against the *T. castaneum*. The oil show insecticidal activity in both fumigant and contact toxicity and adults of *R. dominica* were highly susceptible to contact action essential oil of turmeric leaves with LD_{50} value insects weight of 36.71 µg/mg whereas *S.oryzae*were also highly susceptible to essential oil with LD_{50}value of air 11.36mg/litter. Further in essential oil at concentration 5.2mg/cm^2reduced the egg hatching and ovi-position of *T. castaneum* with 72 and 80% respectively. All three test insects' offspring production was completely reduced by oil diet at a dosage of 40.5 mg/g (Tripathi et al., 2002).

Anti-venom activity: The ar-turmerone fraction isolated form turmeric (*Curcuma longa*) was evaluated for its anti-venom activity against the snakebite. Ar-turmerone constituent of turmeric neutralizing the lethal effect of *Crotalus durissus terrificus* venom and hemorrhagic effect present in *Bothrops jararaca* venom in mice. This study demonstrated that the immunological effect of this fraction also inhibit the natural killer and proliferation activity of human lymphocytes (Ferreira et al., 1992).

Anti-arthritis and anti-inflammatory activity: Curcuminoid isolated from turmeric rhizome was evaluated to investigate the anti-arthritis and anti-inflammatory activity in adjuvant-induced arthritis (AIA) in rats. Curcuminoid at dose 200 mg/kg significantly reduce the severity and incidence of arthritis by increasing and decreasing the production pro-inflammatory and anti-inflammatory cytokine and improve the defense system by anti-oxidant effect. Turmeric show percentage of recovery of was 4.6-8.3% and 10.2% which is greater when compared with standard drug indomethacin ($p<0.05$). Due to anti-oxidant and anti-inflammatory activity of turmeric, this

may have proven beneficial effect against the progression and onset of rheumatoid arthritis (Ramadan et al., 2011).

Teratogenic activity: Turmeric powder showed no significant change in chromosomal aberration and bone marrow cells on in-vivo genotoxic testing in mice. But the extract of fresh *Curcuma longa* rhizome showed chromosomal aberration and chromosome breakage on in-vitro study (Ammon & Wahl, 1991).

Conclusion: It can be concluded that curcumin is a key component of *C. longa* L., and it is responsible for antispasmodic, anti-parasitic, anti-arthritic and anti-inflammatory properties *in vitro* and anti-parasitic and anti-inflammatory properties *in vivo.*

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