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CURCUMA LONGA: BOON FOR HEALTH CARE SYSTEM WITH ITS BIOMEDICAL APPLICATION

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ABSTRACT: Turmeric is a spice derived from the rhizomes of *Curcuma longa*, which is a member of the ginger family (*Zingiberaceae*). Turmeric constituents include the three curcuminoids: Curcumin (diferuloylmethane; the primary constituent and responsible for its vibrant yellow color), demethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins. In the Ayurvedic tradition, turmeric, or "haldi" as it is known in Hindi. Turmeric is considered to be one of the most important herbs in the ayurvedictradition and used historically as a component of Indian Ayurvedic medicine since 1900 BCE to treat a wide variety of ailments including those of the skin, pulmonary, and gastrointestinal systems, aches, pains, wounds, sprains, and liver disorders. Extensive research in the latter half of the 20th century has identified curcumin as responsible for most of the biological activity of turmeric. Curcumin has been shown to exhibit anti-oxidant, anti-inflammatory, anti-viral, anti-bacterial, anti-fungal, anti-cancer hyperlipidemic, woundhealing and hepato- protective activities and thus has a potential against various malignant diseases, diabetes, allergies, arthritis, Alzheimer's disease, and other chronic illnesses. Curcumin has been the subject of hundreds of published articles over the past three decades, studying its antioxidant, anti-inflammatory, cancer chemopreventive, and potentially chemotherapeutic properties. Safety evaluation studies indicate that curcumin is well tolerated at a very high dose without producing any toxic effect.

INTRODUCTION: Curcumin is the principal curcuminoid of the popular Indian spice turmeric, which is a member of the ginger family (Zingiberaceae). The other two curcuminoids are desmethoxy curcumin and bis-desmethoxy curcumin. The curcuminoids are polyphenols and are responsible for the yellow color of turmeric. Curcumin can exist in at least two tautomeric forms, keto and enol. The enol formis more energetically stable in the solid phase and in solution[1].

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Curcumin is brightly yellow colored and may be used as a food colouring. Curcuminhas 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. Moreover, Curcumin has been shown in various animal models and human studies to be extremely safe even at very high doses [2-12]. Curcumin exerts anti-inflammatory activity by inhibition of a number of different molecules that play an important role in inflammation.

Turmeric is effective in reducing post-surgical inflammation. Turmeric helps to prevent atherosclerosis by reducing the formation of bloods clumps[1].

Properties of Curcumin:

Curcumin is an orange–yellow crystalline powder practically insoluble in water at acidic or neutral pH and ether but soluble in ethanol, dimethylsulfoxide, and acetone. Its oral bioavailability about 60% [13]. This effect is probably due the poor solubility and slow dissolution. Solid dispersions are one of the successful methods in improving drug dissolution[14], and to obtain better bioavailability. Curcumin has a melting point of 183°C; its molecular formula is C21H20O6 and molecular weight 368.37.

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, antifibrotic, antivenom, antiulcer, hypotensive and hypocholesteremic activities. Its anticancer effect is mainly mediated through induction of apoptosis. It's anti-inflammatory, anticancer and antioxidant roles may be clinically exploited to control rheumatism, carcinogenesis and oxidative stress-related pathogenesis[15]. Curcumin has ability to cross the blood brain barrier may afford protection against neurodegenerative diseases[16, 17].

Active Constituents:

The rhizome, or root, of Turmeric is the part used medicinally. Numerous constituents have been identified in turmeric. The main constituent group are polyphenoliccurcuminoids which include: curcumin (diferuloylmethan), demethoxycurcumin, bisdemethoxycurcumin, and cyclocurcumin. The yellow-pigmented curcuminoids represent 2% -5% of the root, typically composed of 85% as curcumin, 10% as demthoxycurcumin and 5% as disdemethoxycurcumin. Curcumin is the most well studied constituent. Turmeric also contains: sesquiterpenes (turmerone, atlantone, zingiberone, turmeronol, germacrone, and bisabolene), carbohydrates, protein, resins, and caffeic acid[18].

Applications:

The pharmacological properties and applications of Curcumin are rapidly progressing including anti-diabetic activity, anti-inflammatory activity, anticancer activity, anti-aging, anti-fertility, hepactoprotective activity, anti- HIV, opthamalic activity, antioxidant activity, antibacterial activity, antidepressant activity, cardiovascular and neurodegenerative disease [19].

Anti-inflammatory activity:

Curcumin has the ability to suppress both acute and chronic inflammation as it blocks the formation of cyclooxygenases (COX-2) and other enzymes involved in inflammation[2]. Curcumin suppresses the activation of transcription factor NF-kB (responsible to regulate the expression of pro-inflammatory gene products and is responsible for decreasing the expression of various inflammatory cytokines, including TNF, IL-1, IL- 6, IL-8 and chemokines[18]. Curcumin is one of the most promising candidates of natural origin having anti-inflammatory activity with no side effects [2]. In rats with Freund's adjuvant-induced arthritis, oral administration of Curcuma longa significantly reduced inflammatory swelling compared to controls. *C. longa's* anti-inflammatory properties may be attributed to its ability to inhibit both biosynthesis of inflammatory prostaglandins from arachidonic acid, and neutrophil function during inflammatory states.

Anticancer activity:

Curcumin act as a potent cancer preventing agent by blocking the nuclear factor-kappaB and also interferes in the production of dangerous glycation end products that trigger inflammation and thus lead to cancerous mutation in the body [20]. In addition, Curcumin mediates anticancer activities by controlling the increasing levels of vitamins C and E, preventing lipid peroxidation and DNA damage [21]. Curcumin selectivity targeted transformed cells without altering primary astrocytes. Besides its apoptotic effect, curcumin also showed synergistic effect with the chemotherapeutic cisplatin and doxorubicin drugs to enhance cells death [22].

Results based on solid-state NMR and differential scanning calorimetry showed that curcumin has potent action on cell membrane of the tumour cell at very low concentrations [23]. Researcher showed that curcumin effectively inhibited human lens epithelial B3 cell proliferation induced by rhbFGF

[24]. Curcumin was found to reduce the spread of breast cancer in mice and prevented numerous forms of cancers, childhood leukaemia and in pancreatic cancer [25]. Curcumin has been approved to conduct Phase I/ II trial for the treatment of bowel cancer [26]. Curcumin was found to be effective in oral cancer, hepatic cancer and in colon cancer [27]. Curcumin-loaded nanospheres were able to exert a more pronounced effect on the cancer cells as compared to conventional curcumin thus indicating the potential of nanoparticle-based formulation as an adjuvant therapy for clinical application in prostate cancer.

Hepatoprotective activity:

Plant-derived polyphenols such as curcumin act as a potent therapeutic agent in the treatment of chronic liver diseases. However, the major drawback of curcumin is its poor aqueous solubility resulting in poor bioavailability. To overcome this problem, a polymeric nanoparticle formulation of curcumin (NanoCurc™) was synthesized that inhibits the carbon tetrachloride-induced liver injury, inhibits the production of pro-inflammatory cytokines and fibrosis. NanoCurc™ might be an effective therapy for patients suffering with chronic liver disease [28]. Curcumin significantly repair and regenerated liver tissues of diabetic rats. These finding demonstrated the potential role of curcumin as a novel therapeutic agent in liver pathology of diabetic rats [29]. Moreover, it also reduces the ironinduced hepatic damage by lowering lipid peroxidation in rats [30].

Cardiovascular activity:

Turmeric's protective effects on the cardiovascular system include lowering cholesterol and triglyceride levels, decreasing susceptibility of low density lipoprotein (LDL) to lipid peroxidation, and inhibiting platelet aggregation. These effects have been noted even with low doses of turmeric. A study of 18 atherosclerotic rabbits given low-dose (1.6–3.2 mg/kg body weight daily) turmeric extract demonstrated decreased susceptibility of LDL to lipid peroxidation, in addition to lower plasma cholesterol and triglyceride levels. The higher dose did not decrease lipid peroxidation of LDL, but cholesterol and triglyceride level decreases were noted, although to a lesser degree than with the lower dose. Turmeric extract's effect on cholesterol levels may be due to decreased cholesterol uptake in the intestines and increased conversion of cholesterol to bile acids in the liver. Inhibition of platelet aggregation by *C. longa* constituents is thought to be *via* potentiation of prostacyclin synthesis and inhibition of thromboxane synthesis[1].

Gastrointestinal activity:

Constituents of *Curcuma longa* exert several protective effects on the gastrointestinal tract. Sodium curcuminate inhibited intestinal spasm and p-tolymethylcarbinol, a turmeric component, increased gastrin, secretin, bicarbonate, and pancreatic enzyme secretion. Turmeric has also been shown to inhibit ulcer formation caused by stress, alcohol, indomethacin, pyloric ligation, and reserpine, significantly increasing gastric wall mucus in rats subjected to these gastrointestinal insults[1].

Anti-diabetic activity:

Curcumin shows potential as a treatment for Type-2 diabetes. Curucmin ability to ward off the alarming diabetes and obesity occurs by suppressing the cytokines in the body. The diabetes patients pre-treated with Curcumin capsules were less likely to develop symptoms of Type- 2 diabetes, compared with patients not pre-treated with curcumin capsules. In addition, the curcumin treatment improved overall function of β-cells, with very minor adverse effects [31]. Meriva®, a lecithinized formulation of curcumin was well tolerated, and preliminary findings suggest its usefulness in the management of diabetic microangiopathy [32].

Anti-aging activity:

Curcumin as an ingredient of Vicco Turmeric Vanishing Cream helps in preventing the damage of the skin from UV rays of the sun, and thus maintains the original colour of the skin with enhancing the appearance of the skin[1].

Antioxidant activity:

Curcumin is a free radical scavenger as well as hydrogen donor; it binds with metals particularly iron and copper [33]. Curcumin effectively inhibits intracellular amyloid toxicity at low dosages in rats due to its free radical scavenging activity [34]. However, it is also effective in various models of

antioxidant such as DPPH scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, ferric ions reducing power and ferrous ions chelating [35].

Antibacterial activity:
Curcumin act as an antibacterial agent as it effectively targets *Staphylococcus aureus*, *Salmonella paratyphi*, *Trichophytongypseum*, and *Mycobacterium tuberculosis* [36]. It exhibits a wide range of activities in eukaryotic cells including its antiviral effect against herpes simplex virus by a mechanism independent of p300/CBP histone acetyltransferase activity [37].

Opthamalic activity:
Curcumin may suppress cataract onset and progressionin animals when administrated orally [38].

Anti-Fertility:
Curcumin has been found useful for the prevention of CdCl2-induced reproductive damage [39].

Antidepressant activity:
The curcumin loaded solid lipid nanoparticles at a dose of (1, 2.5, 5 and 10 mg/kg, p.o.) exhibited 47.42%, 67.39%, 31.67% and 36.2% reduction in immobility time after administration of the dose in mice using swim model respectively. However, conventional curcumin did not result in a significant reduction, except at 2.5 mg/kg, which could produce a reduction of only 21.7% [40].

Anti- HIV activity:
Preliminary investigation indicated that Curcumin suppress the HIV virus and thus may be exploited in the treatment of Human Immunodeficiency Virus (HIV) [41].

Curcumin in neurodegenerative diseases:
Neurodegenerative diseases involve the abnormality of protein folding which lead to abnormal deposition of insoluble fibrils that disrupt tissue structure and cause disease.curcumin binds with aluminium and inhibit the fibrillation of neurodegenerative proteins [42]. The neuroprotective activity of curcumin has been demonstrated in various models of neurodegenerative diseases [43]. Curcumin possesses therapeutic potential in the amelioration of neurodegenerative ailments due to its antioxidant, anti-inflammatory and antiprotein aggregation effects. Curcumin is able to prevent the destructive formation of alpha-synuclein proteins, binds strongly to alpha-synuclein and rescues the protein from aggregation by increasing the reconfiguration of the cells which proves the potential use of curcumin in treatment of neurodegenerative disease [44]. NanoCurc™ acts as apotent formulation for treatment in Alzheimers disease [45].

Anti microbial activity:
Turmeric extract and the essential oil of Curcuma longa inhibit the growth of a v ariety of bacteria, parasites, and pathogenic fungi[1].Tuberculosis (TB) is a major public health concern worldwide with over 2 billion people currently infected. The rise of strains of *Mycobacterium tuberculosis* (Mtb) that are resistant to some or all first and second line antibiotics, including multidrug-resistant (MDR), extensively drug resistant (XDR) and totally drug resistant (TDR) strains, is of particular concern and new anti-TB drugs are urgently needed. Curcumin, a natural product used in traditional medicine in India, exhibits anti-microbial activity that includes Mtb, however it is relatively unstable and suffers from poor bioavailability.

To improve activity and bioavailability, mono-carbonyl analogs of curcumin were synthesized and screened for their capacity to inhibit the growth of Mtb and the related *Mycobacterium marinum* (Mm). Using disk diffusion and liquid culture assays, we found several analogs that inhibit *in vitro* growth of Mm and Mtb, including rifampicin-resistant strains [46].

Curcumin is a naturally derived substance with innate antimicrobial and wound healing properties. Acting by multiple mechanisms, curcumin is less likely than current antibiotics to select for resistant bacteria. Curcumin's poor aqueous solubility and rapid degradation profile hinder usage; nanoparticle encapsulation overcomes this pitfall and enables extended topical delivery of curcumin. curcumin nanoparticles (curc-np), which inhibited *in vitro* growth of methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* in dose-dependent fashion, and inhibited MRSA

growth and enhanced wound healing in an *in vivo* murine wound model. Curc-np may represent a novel topical antimicrobial and wound healing adjuvant for infected burn wounds and other cutaneous injuries [47]. Curcuma longa dye was most effective and showed maximum zone of inhibition thereby indicating best antimicrobial activity against all the microbes tested. These textiles dyed with these natural dyes can be very useful in developing clothing for infants, elderly and infirm people to protect them against common infections[48].

CONCLUSION: Curcumin is used to produces in different properties like antioxidant, anti-inflammatory, anti-cancer, anti-fertility, antibacterial, antimicrobial, antidepressant activities etc, are believed to account in large measure for its demonstrated ability to help prevent the neurodegenerative changes seen in Alzheimer's as well as Parkinson's disease. As an anti-inflammatory agent, curcumin inhibits damaging COX-2 enzymes but not beneficial COX-1 enzymesand thus beneficial for inflammatory conditions. The review is focus on application of curcuminin different therapeutic efficacy in treatment of various disorders.

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