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Benefit of Turmeric on Human Health -A Review

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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*). Rhizomes are horizontal underground stems that send out shoots as well as roots. The bright yellow color of turmeric comes mainly from fat-soluble, polyphenolic pigments known as curcuminoids. Curcumin, the principal curcuminoid found in turmeric, is generally considered its most active constituent. Other curcuminoids found in turmeric include demethoxycurcumin and bisdemethoxycurcumin. In addition to its use as a spice and pigment, turmeric has been used in India for medicinal purposes for centuries. More recently, evidence that curcumin may have anti-inflammatory and anticancer activities has renewed scientific interest in its potential to prevent and treat the disease.

Key words: *Curcuma longa, Curcuminoids, Curcumin, Anti-Inflammatory, Anti-H. pylori, Anti-cancer, Anti-asthmatic.*

1. INTRODUCTION:

Turmeric is an Indian rhizomatous herbal plant (Curcuma longa) of the ginger family (Zingiberaceae) of well-known medical benefits. [1, 2] The medicinal benefits of turmeric could be attributed to the presence of active principles called curcuminoids. Curcumin, demethoxycurcumin (DMC), and bisdemethoxycurcumin (BDMC) are collectively known as curcuminoids. These yellow colored curcuminoids are isolated from Curcuma longa L. (turmeric) rhizomes. 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 desmethoxycurcumin and bis-desmethoxycurcumin. 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 form is more energetically stable in the solid phase and in solution. Curcumin can be used for boron quantification in the so-called curcumin method. It reacts with boric acid forming a red colored compound, known as rosocyanine. Curcumin is brightly yellow colored and may be used as a food coloring. As a food additive, its E number is E100. One of the most interesting components of curcuminoid is curcumin, which is a small molecular weight polyphenolic compound and lipophillic in nature, hence insoluble in water and also in ether but soluble in ethanol, dimethylsulfoxide, and other organic solvents.

Figure : Turmeric.

Curcumin is stable at the acidic pH of the stomach. The other constituents present are volatile oils including tumerone, atlantone and zingiberone and sugars, proteins and resins. The active constituent of turmeric- curcumin is isolated from curcuma longa and it provides colour to turmeric. Such bioactive component has been thoroughly investigated [8] Curcumin (1, 7-bis (4-hydroxy-3methoxyphenyl)-1, 6-heptadiene-3, 5- dione) is also called diferuloylmethane. [9] It is a tautomeric compound existing in enolic form in organic solvents and as a keto form in water. Turmeric is a plant known by its medicinal use, dating back to 4000 years ago in the Vedic culture in India, where it was used as a culinary spice and had some religious significance. Turmeric is the boiled, dried, cleaned and shine rhizomes of curcuma longa. After harvesting the whole rhizomes are collected. They are usually like fingers 2 to 8 cm long and 1 to 2 cm wide having bulbs and splits. The dried rhizomes are further processed and reprocessed to obtain the turmeric powder. It has different names in different cultures and countries. InSanskrit, turmeric has at least 53 different names. Curcumin has been used in tradition as a medical herb due to its various advantages such as: antioxidant, anti-inflammatory, antimutagenic, antimicrobial and several therapeutic properties Curcumin shows poor absorption, rapid metabolism, and rapid elimination. Several agents have been introduced to improve the bioavailability of curcumin. [10]

2. CHEMISTRY OF CURCUMIN :

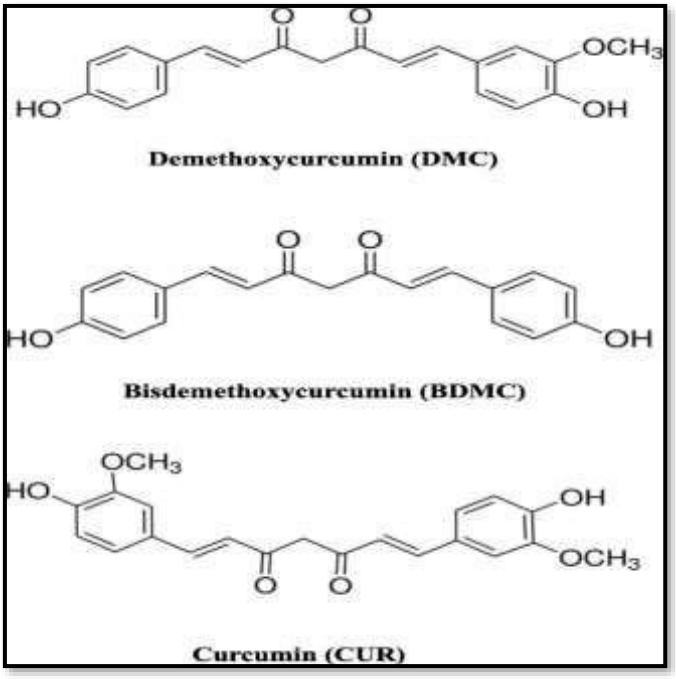

Figure : Structure of Curcumin.

Curcumin is a symmetric molecule, also known as diferuloyl methane. IUPAC name of this compound is (1E-6E)-1, 7-bis (4-hydroxy-3-methoxy phenyl)-1, 6-heptadiene-3, 5-dione. The chemical formula of curcumin is C21H20O6 and the molecular mass is 368.385g/mole. The structure of curcumin contains three chemical entities: two oxy-substituted aryl moieties containing ortho-methoxy phenolic OH– groups, connected through a seven carbon chain consisting of a α, β-unsaturated β-diketone moiety. [11] Curcumin is the most abundantly occurring natural analogue of a crude extract at 60%-70%, followed by demethoxy curcumin(DMC; 20%-30%) in which one methoxy group is absent, then bisdemethoxy curcumin(BDMC; 10%-15%) in which the methoxy group is absent from both the aryl rings, along with numerous and less abundant secondary metabolites. Important chemical reactions associated with the biological activity of curcumin are the hydrogen-atom donation reactions leading to oxidation of curcumin, reversible and irreversible nucleophilic addition reactions, hydrolysis, degradation and enzymatic reactions. All these play important role in different biological activities of curcumin. Curcumin is a hydrophobic molecule with a calculated log P value is 3.43; however it is insoluble in aqueous physiologic media, which displays poor distribution and bioavailability. Curcumin is soluble in polar solvents like DMSO, methanol, acetone and ethanol. [12]

3. ISOLATION OF CURCUMIN :

Curcumin is insoluble in water; an organic solvent has been used for its isolation. developed a technique for isolating CUR from ground turmeric. They magnetically stirred the ground turmeric in dichloromethane and heated at reflux for 1 h. The mixture was suction-filtered, and the filtrate was concentrated in a hot-water bath maintaining at 50o C. The reddish-yellow oil residue was triturated with hexane and the resulting solid was collected by suction filtration. Further TLC analysis (3% methanol and 97% dichloromethane) showed the presence of all three components. Extraction of CUR from turmeric powder with the use of a solvent consisting of a mixture of ethanol and acetone. [14] Chemical analyses have shown that turmeric contains carbohydrates (69.4%), moisture (13.1%), protein (6.3%), fat (5.1%) and minerals (3.5%). The essential oil (5.8%) obtained by steam distillation of the rhizomes contains a-phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%) and sesquiterpines (53%), curcumin (3-6%) is responsible for the yellow color. [13]

4. PHARMACOKINETICS AND PHARMACODYNAMICS :

Prior studies have discussed the difficulty in achieving optimum therapeutic concentrations of the molecule due to low solubility and poor bioavailability of curcumin. Studies suggest that curcumin is first biotransformed to dihydrocurcumin and tetrahydrocurcumin, and subsequently converted to monoglucuronide conjugates. Preliminarily animal studies demonstrate that curcumin is rapidly metabolized and conjugated in the liver, and then excreted in feces with limited systemic bioavailability. A 40 mg/kg intravenous dose of curcumin given to rats resulted in complete plasma clearance at one hour post-dose. An oral dose of 500 mg/kg given to rats resulted in a peak plasma concentration of only1.8 ng/Ml. [15]

5. PHARMACOLOGICAL ACTIVITY WITH MODE OF ACTION :

Anti-Bacterial :

The antibacterial study of curcumin shows the ability to inhibit growth of a variety of periodontopathic bacteria and Porphyromonas gingivitis Arg- and Lys-specific proteinase (RGP and KGP, respectively) activities.

In addition, curcumin suppressed P. gingivitis homotypic and Streptococcus gordonii biofilm formations in a dose-dependent manner. Bacterial growth was suppressed almost completely at very low concentrations of curcumin. A concentration of 20 μg/mL of curcumin inhibited these P. gingivitis biofilm formations by more than 80%. On the other hand, 100 μg/mL of curcumin did not suppress the growth of Aggregatibacter actinomycetemcomitans. Furthermore, at relatively high concentrations, curcumin targets bacterial membranes (Escherichia coli). On another hands, Curcumin - Polymyxin B used clinically for topical therapy to treat or prevent traumatic wound infections of the skin. It would not only increase the spectrum of activity to include Gram-positive bacteria but also combat those isolated resistant. The use of the combination may also reduce the emergence of resistant isolates during treatments, due to the multiple antimicrobial targets of duel drug therapy and ease the selective pressure produced by broad-spectrum antibiotics. Additionally, curcumin loaded in zein (zein-CUR) fibers showed good antibacterial activity towards S.aureus and E. coli and the inhibition efficiency increased with the increase of curcumin contents. Due to the different cell membrane constituent and structure, the antibacterial activity towards S.aureus was better than that towards E. coli. The natural blend films of curcumin and chitosan could be as a promising antimicrobial packaging for food and agriculture products. In addition, Surface charge as well as the small size of curcumin nanoparticles plays a key role in enhancing cell-antimicrobial interaction and antimicrobial efficacy. The fabricated curcumin nano-particles showed the best antimicrobial activity against Listeria monocytogenes. A size reduction to nano-scale is a recently developed strategy used to improve drug/food delivery and matching the public demand for effective and safe antimicrobial formulations for control of food borne pathogen. [16,17,18]

Anti-Viral Activity :

It has been demonstrated that curcumin as a plant derivative has a wide range of antiviral activity against different viruses: papillomavirus virus (HPV), influenza virus, Hepatitis B virus (HBV), Hepatitis C virus (HCV), adenovirus, coxsackie virus, Human norovirus (HuNoV), Respiratory syncytial virus (RSV) and Herpes simplex 1 (HSV-1). Curcumin functionalized graphene oxide shown synergistic antiviral effect against respiratory syncytial virus infection. Respiratory syncytial virus (RSV), which is considered as the major viral pathogen of the lower respiratory tract of infants, has been implicated in severe lung disease. Developing a β-cyclodextrin (CD) functionalized graphene oxide (GO) composite, which displayed excellent antiviral activity and curcumin loading efficiently, showed that the composite could prevent RSV from infecting the host cells by directly inactivating virus and inhibiting the viral attachment, which possessed the prophylactic and therapeutic effects towards virus. The antiviral effect of curcumin was a dose-dependent manner. [19]

Anti-Inflammatory Activity :

Curcumin possesses significant anti-inflammatory activity in acute as well as in chronic models of inflammation. It is as potent as phenylbutazone in the carrageenan oedema test but only half as potent in chronic tests. Curcumin has been demonstrated to be safe in six human trials and has demonstrated antiinflammatory activity. It may exert its antiinflammatory activity by inhibition of a number of different molecules that play a role in inflammation. [20] Curcumin has been shown to regulate numerous transcription factors, cytokines, protein kinases, adhesion molecules, redox status and enzymes that have been linked to inflammation. [21] Tumor necrosis factor α (TNF-α)is a major mediator of inflammation in most diseases, and this effect is regulated by the activation of a transcription factor, nuclear factor(NF)-κB. Whereas TNF-α is said to be the most potent NF-κB activator, the expression of TNF-α is also regulated by NF-κB. In addtion to TNF-α, NF-κB is also activated by most inflammatory cytokines; gram-negative bacteria; various disease-causing viruses; environmental pollutants; chemical, physical, mechanical, and psychological stress; high glucose; fatty acids; ultraviolet radiation; cigarette smoke; and other disease-causing factors.

Anti-Oxidant :

Curcumin has been shown to improve systemic markers of oxidative stress it can modulate the activity of GSH, catalase, and SOD enzymes active in the neutralization of freeradicals. There is evidence that it can increase serum activities of antioxidants such as superoxide dismutase (SOD) A recent systematic review and meta-analysis of randomized control data related to the efficacy of supplementation with purified curcuminoids on oxidative stress parameters—indicated a significant effect of curcuminoids supplementation on all investigated parameters of oxidative stress including plasma activities of SOD and catalase, as well as serum concentrations of glutathione peroxidase (GSH) and lipid peroxides. It is noteworthy to point out that all of the studies included in the meta-analysis utilized some sort of formulation to overcome bioavailability challenges, and four out of the six used piperine [22]. Curcumin's effect on free radicals is carried out by several different mechanisms. It can scavenge different forms of free radicals, such as reactive oxygen and nitrogen species (ROS and RNS, respectively) also, it can inhibit ROS-generating enzymes such as lipoxygenase/cyclooxygenase and xanthine hydrogenase/oxidase. In addition, curcumin is a lipophilic compound, which makes it an efficient scavenger of peroxyl radicals, therefore, like vitamin E, curcumin is also considered as a chain-breaking antioxidant. [23]

Anti-Cancer :

One-fifth of the deaths worldwide annually are caused by various types of cancers. Cancer is a Result of successive genetic and epigenetic alterations resulting in apoptosis, uncontrolled cell Proliferation, metastasis, and angiogenesis. Anti-cancer activity of curcumin has been extensively investigated recently, and significant improvements in gastrointestinal, melanoma, genito-urinary, breast, and lung cancers have been seen Many studies pointed out anticancer activities of curcumin alone or in combination with conventional chemotherapy drugs in treatment of cancer and its cancer-related complications. In-vitro and in-vivo studies have indicated that curcumin prevents carcinogenesis by affecting two primary processes: Angiogenesis and tumor growth Curcumin analogs S1- S3 containing sulfone strongly inhibited the growth of human prostate, colon, lung and pancreatic cancer cells. Scientific studies of plants used in various types of ethnic medicine have led to the discovery of many valuable drugs, including taxol, camptothecin, vincristine and Vinblastine. [24]

Curcumin And Anti-Cancer Drugs Combination (Nanomedicine) :

Almost half a century ago, nanomedicine emerged as a specific niche for drug delivery, within the multidisciplinary field of nanotechnology. A principal focus for the last 20 years has been on the development of nano-formulation driven drug delivery of nanocarriers. Various nanocarriers that have been investigated for drug delivery include polymeric micelles, liposomes, magnetic nanoparticles, conjugates, and peptide carriers. Integration of Nanotechnology within cancer research has proved to be advantageous in several ways, including (a) cancer treatment and detection (diagnostics and imaging agents); (b) biomarker identification for disease prediction and (c) mechanism of cancer progression. A narrow therapeutic window of drugs however is one of the major challenges with anticancer drugs and is the reason for serious side effects due to non-specific drug uptake by healthy cells. The efficacy of cancer drugs is also restrained due to multidrug resistance (MDR), often associated with chemotherapy. To overcome these issues the primary strategy of combination chemotherapy along with drug delivery systems using nanoparticles (NPs) is being actively explored.Curcumin could be a potential elementary candidate to be used for combination chemotherapy as it could overcome the issues associated with anti-cancer therapeutics.[25]

Type Of Nanoparticles In Cancer Therapy :

There are two categories of therapeutic and diagnostic nanoparticles: (a) organic (e.g., polymeric, liposomes, micelles, etc. (b) inorganic (e.g., gold, silica, iron oxide, etc.). Natural or synthetic organic molecules are the template for the formation of organic NPs. Organic and inorganic NPs differ in their technique of fabrication. For organic NPs, the encapsulation techniques of biodegradable materials used are relatively simple and require several self-organizing or chemical binding organic molecules.

Whereas, inorganic NPs involve precipitation of inorganic salts in which atoms are often linked by covalent/metallic/magnetic bonding leading to formation of a three-dimensional array.[26]

Combination Chemotherapy In Cancer :

The interconnected pathways in cancer physiology reduce effectivity of monotherapy strategy. Drug resistance and chances of tumor recurrence due to pathway overlapping cross-talk and neutralizing response, could be various complications hindering full potential of independent drugs. The easiest approach to overcome this issue could involve utilization of combination chemotherapy strategy, which has shown to be successful in preliminary clinical trials. Combination chemotherapy design involves an understanding of several principles likenon-overlapping toxicity, non-cross resistance, and enhanced tumor cell killing efficacy. Nanocarriers like liposomes and polymeric micelles could further help to overcome mono-therapeutic complications. [27] A previous generation of cancer combination chemotherapy comprised of traditional drug combinations including anthracycline, methotrexate, and paclitaxel (PTX)-based combinations. A study on one such combination displayed an effective reversal of chemotherapeutic drug resistance with Dox and rapamycin codelivery. This combination leads to complete tumor remission, as compared to dox and rapamycin alone. In another such study, in vivo effects of curcumin combination with antitumor drug was studied and displayed effectively. Docetaxel (DTX) and Curcumin (CUR) co-encapsulated lipid nanoparticles (LPN's) were evaluated on PC3 tumor xenografts in mice (human prostate cancer-bearing Balb/c nude mice model). These potent nanoparticles inhibited tumor volume growth significantly, when compared to other groups, with no visible side effects. It was concluded that this combination could prove to be an effective prostate cancer treatment. Curcumin has shown to be successful in several types of cancer lines, mainly because of its Ubiquitous action on different modulator of anti-cancer effects. Curcumin inhibits tumor growth by arresting cell cycle progression, inducing apoptosis, inhibiting the expression of antiapoptotic proteins, inhibiting multiple cell survival signaling pathways and their cross-communication, and modulating immune responses.

Anti-Allergy / Anti-Asthma :

Curcumin decreased the nasal airflow resistance by alleviating sneezing, rhinorrhea and nasal congestion. It also suppresses the IL-4, IL-8, and tumor necrosis factor α as well as also enhanced the levels of IL-10 and soluble intercellular adhesion molecule. Curcumin administered through nasal route inhibited allergic airway inflammations and maintaining structural integrity in allergic asthma mices model. The different treatments of curcumin (2.5 and 5.0mg/kg) in ovalbumin (OVA) of Balb/c mice markedly regulates airway inflammation and airway obstruction mainly by modulating cytokine levels (IFN-γ, IL-4, 5, and TNF-α) and sPLA2 activity thereby inhibiting PGD2 release and COX-2 expression. Furthermore, curcumin suppressed the ERK 42/44, p38 MAPK (mitogen-activated protein kinase) and JNK54/56activation in asthma progression rats. [28]

Anti-Fungal :

Due to extensive traditional use of curcumin in food products, various researches have been done in order to study curcumin with the aspect of controlling fungal related spoilage and fungal pathogens. The study of addition the curcumin powder in plant tissue culture showed that curcumin at the 0.8 and 1.0 g/L had appreciable inhibitory activity against fungal contaminations. Reduction in proteinase secretion and alteration of membrane-associated properties of ATPase activity are other possible critical factors for antifungal activity of curcumin. [29] Finding new anti-candida substances seems to be crucial due to development of resistant strain against existing antifungal drug. The investigation of curcumin mediation for photo- dynamic therapy can reduce the biofilm biomass of C. albicans, C. glabrata and C. tropicalis. The results demonstrated that association of four LED influences for light excitation with 40 μM concentration of curcumin at 18 J/cm2 inhibited up to 85% metabolic activity of the tested Candida species.

The use of curcumin with light proved to be an effective method for noteworthy improvement in the antifungal activity against planktonic form of the yeasts. Photodynamic effect considerably decreased C. albicans viability in either planktonic or biofilm cultures probably through increasing the uptake of curcumin by cells. However, to a lesser extent, photodynamic therapy was found to be phototoxic to the macrophages. [30,31]

5.9 Anti-Arthritis :

Rheumatoid arthritis (RA) is a chronic inflammatory disease that is characterized by hyperplasia of the synovial fibroblasts. Curcumin is known to possess potent anti-inflammatory and anti-arthritic properties. Curcumin treatment was carried out on patients with active rheumatoid arthritis and compared with diclofenac sodium reference group. [32,33] Interestingly, the curcumin group showed the highest percentage of improvement in overall rheumatoid arthritis scores and these scores were significantly better than the patients in the diclofenac sodium group. More importantly, curcumin group was found to be safe and did not relate with any adverse events compared to diclofenac sodium group. [34] It is believed that curcumin antioxidant, antiproliferative, anti-inflammatory and immune suppressive activities shared in the improvement of symptoms to patients suffering from rheumatoid arthritis.[35]

5.10. Anti-Venom:

Curcumin was listed as a herbal plant metabolite that can effective against snake venom pla2. researchers studied the structural relationship between medicinally important herbal compounds such as acalyphin, chlorogenic acid, stigmasterol, curcumin and tectoridin and pla2 from russell's viper. The molecular modeling studies revealed favorable interactions with the amino acid residues at the active site of venom pla2 that could result in the inhibition.

6. CONCLUSION:

Curcumin has demonstrated widespread use for its extensive health advantages, which seem to primarily be mediated through its anti-oxidant and anti-inflammatory mechanisms. Curcumin works best when paired with substances like carbs and piperine, which greatly boost its bioavailability. Curcumin may aid in the treatment of oxidative and inflammatory diseases, metabolic syndrome, anti-inflammatory, anxiety, and anti-diabetic disorders, according to research. As a result, recuperation time and subsequent performance in physically active people are facilitated. It may also assist in the management of several pharmacological activities utilised in health and also improve the health for body benefits for human health. Additionally, even those without known medical concerns may benefit from a relatively sufficient dose in terms of their health.

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