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Review Article

CURCUMIN, A POTENT ANTICARCINOGENIC POLYPHENOL – A REVIEW

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ABSTRACT

Turmeric the common name for *Curcuma longa* is an Indian flavor inferred from the rhizomes of the plant and has a long history of utilization in Ayurvedic medication. Curcumin, the principal curcuminoid found in turmeric, is in general considered its most active constituent. Curcumin, a standout amongst the most widely used natural active constituents with a great variety of beneficial biological and pharmacological activities, is a basically water-insoluble substance with a short biologic half-life. Extensive research has addressed the chemopreventive potential of this non toxic polyphenol. The anticancer potential of curcumin is resolved from its ability to suppress proliferation of a wide variety of tumor cells, down regulate transcription factors NF-κB, AP-1 and Egr-1; down-regulate the expression of COX-2, LOX, NOS, MMP-9, uPA, TNF, chemokines, cell surface adhesion molecules and cyclin D1; down-regulate growth factor receptors (such as EGFR and HER2); and inhibit the activity of c-Jun N-terminal kinase, protein tyrosine kinases and protein serine/threonine kinases. This review will summarize the unique properties of curcumin that may be exploited for successful cancer prevention.

Keywords: Turmeric, *Curcuma longa,* Chemopreventive, Curcumin, Polyphenol, Anticancer activity.

INTRODUCTION

Turmeric the common name for *Curcuma longa* is an Indian flavor inferred from the rhizomes of the plant and has a long history of utilization in Ayurvedic medication [1]. *C. longa* is a perennial member of the Zingiberaceae family and is cultivated in India and different parts of Southeast Asia [2]. The essential dynamic constituent of turmeric and the one answerable for its vibrant yellow shade is curcumin first identified in 1910 by Lampe and Milobedzka (Fig 1) [3].

Scientific classification

Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Subclass	Zingiberidae
Order	Zingiberales
Family	Zingiberaceae
Genus	Curcuma
Species	Longa
Scientific name	Curcuma longa

Figure 1: Turmeric from Koehler's Medicinal

Antiquity of turmeric

Haridra in Sanskrit signifies 'an efficacious drug for jaundice. It is known to be one of the oldest spices that have been utilized within Western and Southern parts of India for thousands of years and is a major part of Ayurvedic medicine [4]. This spice of Indian origin is also referred to as 'Indian saffron' [5]. Originating in India, Turmeric had arrived at China by 700 AD, East Africa by 800 AD and West Africa by 1200 AD, and also had started to get prominent all through the world [6]. It is known that the Arab traders had carried with them turmeric to Europe in the 13th century [7]. Marco Polo, while on his several legendary voyages to India via the Silk Route, was so impressed by turmeric that he had specified it as a vegetable that possesses properties of saffron, but actually is not saffron.

Customary uses of curcumin

Traditionally, turmeric has been put to use as a foodstuff, cosmetic, and medication. As a spice, it is used to furnish curry with its distinctive yellow color and as a coloring agent in cheese, butter, and other foods [8]. In folk medicine, turmeric and natural curcuminoids have been applied as therapeutic preparations over the centuries in diverse parts of the world [9]. In Ayurvedic medicine, curcumin is a generally reported medicine for various respiratory conditions like asthma, bronchial hyperactivity, allergy, liver disorders, anorexia, rheumatism, diabetic wounds, runny nose, cough, and sinusitis [10]. In customary Chinese medicine, it is used to treat diseases associated with abdominal pain and in the treatment of diabetes [11].

In ancient Hindu medicine, it was utilized to treat sprains and swelling. Throughout the East, it has traditionally been used to great remedial impact, particularly as antiinflammatory, antioxidant an, anticarcinogenic, antimicrobial, hepatoprotective, thrombosuppressive, cardiovascular, hypoglycemic and antiarthritic [12,13]. The most compelling and key reason for the continuing traditional therapeutic use of curcumin is its extremely good safety profile [14]. Till date, no studies in either animals or humans have discovered any toxicity associated with the use of curcumin, and it is clear that curcumin is not toxic even at very high doses [15].

Active constituents

Turmeric is comprised of three curcuminoids: curcumin, demethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins (Fig 2) [16,17]. The contents of curcuminoids and essential oils in the rhizome varied with the species and went down with the increment of storage years. [18]. Best-researched dynamic constituent is curcumin, which comprises 0.3–5.4 percent of raw turmeric.

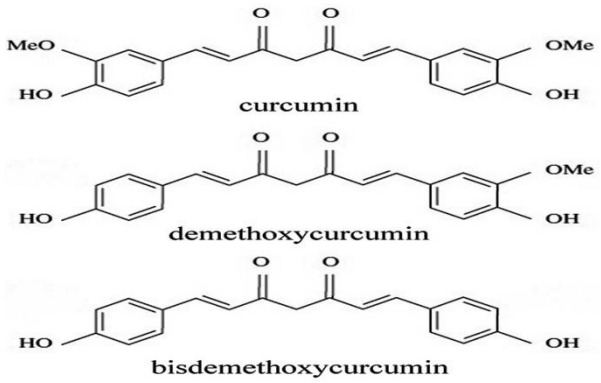

Fig.2: Components of Turmeric

Chemistry of curcumin

Curcumin, a standout amongst the most widely used natural active constituents with a great variety of beneficial biological and pharmacological activities, is a basically water-insoluble substance with a short biologic half-life [19]. Curcumin, a bis-αβ-unsaturated β-diketone. It can exist in solution as a tautomeric mixture of keto and enol forms, and the enol form was found to be responsible for the rapid degradation of the compound [20]. The bis-keto form prevails in acidic and neutral aqueous solutions and in the cell membrane [21]. At pH 3–7, curcumin acts as a potent H-atom donor. This is because, in the keto form of curcumin, the heptadienone linkage between the two methoxy phenol rings contains a highly activated carbon atom, and the C–H carbon bonds on this carbon are exceptionally weak due to delocalization of the unpaired electron on the adjacent oxygen [22]. In contrast, above pH 8, the enolate form of the heptadienone chain predominates, and curcumin acts as an electron donor, a mechanism more typical for the scavenging activity of phenolic antioxidants. Curcumin is poorly insoluble in water, but dissolves in acetone, dimethylsulphoxide, methanol and ethanol [23].

Curcumin is unstable at basic pH, and perhaps degrades within 30 min to trans -6-(40-hydroxy-30-methoxyphenyl)-2, 4-dioxo-5-hexanal, ferulic acid, feruloylmethane and vanillin. The presence of foetal calf serum or human blood, or addition of antioxidants like ascorbic acid, N-acetylcysteine or glutathione, completely blocks this degradation in culture media or phosphate buffer above pH 7. Under acidic conditions, the degradation of curcumin is much slower, with less than 20% of total curcumin decomposed at 1 h. Several investigators have also found that curcumin is more stable in cell culture medium containing 10% foetal calf serum or in human blood, with less that 20% decomposition within 1 h compared to 90% within 30 min in serum-free medium. These investigators went on to examine curcumin's photochemical stability, offering the first suggestions of its potential antimicrobial activity by photosensitization [24]. As a consequence of light sensitivity, samples containing curcumin should be protected from light. Above pH 7, curcumin's hue is less yellow and red.

Curcumin has a melting point of 183°C and a molecular weight of 368.37. Commercial grade curcumin holds the curcuminoids demethoxycurcumin (MW 338; typically 10–20%) and bisdemethoxycurcumin (MW 308; typically less than 5%, for structures see Fig. 2).On ultraviolet–visible spectrophotometric investigation, maximum light absorption of curcumin happens at 420 nm.

Bioavailability and pharmacokinetics

Various studies have indicated the biotransformation of Curcumin. It was initially biotransformed to dihydrocurcumin and tetrahydrocurcumin; these compounds were than subsequently converted to monoglucuronide conjugates. Thus the significant metabolites of Curcumin are Curcumin-glucuronide, dihydrocurcumin glucuronide, tetrahydrocurcumin-glucuronide and tetrahydrocurcumin [25]. Biotransformation of Curcumin occurs basically in the liver, although some metabolism occurs in the kidney and gastrointestinal tract [26]. The systemic bioavailability of Curcumin is quite low; therefore the pharmacological activity of Curcumin may be intervened, in parts, by its metabolites [27]. The major metabolites of Curcumin in the suspension of human hepatocytes are hexahydrocurcumin and hexahydrocurcuminol while the overwhelming metabolites of Curcumin in human plasma *in vivo* are Curcumin glucuronide and Curcumin sulfate.

Pharmacological properties of curcumin

Curcumin has been credited numerous pharmacological activities, including antioxidant, anti-inflammatory and antimicrobial properties, chemopreventive and chemotherapeutic activity [28]. This article keeps tabs on one of the best-explored actions, the anti-cancer effects of curcumin.

Turmeric is compelling in reducing post-surgical inflammation. Turmeric helps to avert atherosclerosis by reducing the formation of bloods clumps [29]. Curcumin inhibits the growth of *Helicobacter pylori*, which causes gastric ulcers and has been interfaced with gastric cancers [30]. Curcumin can bind with heavy metals such as cadmium and lead, subsequently reducing the toxicity of these heavy metals. This property of curcumin demonstrates its protective action to the brain [31]. Curcumin acts as an inhibitor for cyclooxygenase, 5-lipoxygenase and glutathione S-transferase. [32]. This extraordinary herb has thought that it was route into the spotlight in the west because of its wide range of medicinal benefits. Curcumin has likewise shown protection against hepatic conditions, chronic arsenic exposure, and alcohol intoxication [33].

Curcumin, its principle dynamic constituent, is a powerful antioxidant as vitamins C, E and Beta-Carotene, making turmeric usage a consumer choice for cancer prevention, liver protection and premature aging [34]. Several distributed studies also show that turmeric inhibits the growth of several different types of cancer cells [35,36]. In addition, turmeric is a strong anti-inflammatory, easing conditions such as bursitis, arthritis and back pain [37]. Turmeric's anti-inflammatory action is likely due to a combination of three separate properties [38]. First, turmeric brings down the production of inflammation-inducing histamine [39]. Also, it increases and prolongs the action of the body's natural antiinflammatory adrenal hormone, cortisol, and finally, turmeric improves circulation, thereby flushing toxins out of small joints where cellular wastes and inflammatory compounds are frequently trapped [40]. Research has additionally affirmed the digestive benefits of turmeric. Turmeric acts as a cholagogue, stimulating bile production, thus, increasing the bodies' capability to digest fats, improving digestion and eliminating toxins from the liver [41].

CURCUMIN AND MALIGNANCY

Cancer is a multigene disease which emerges as a result of mutational and epigenetic changes coupled with activation of complex signaling networks [42]. There are four sorts of cancers; (a) carcinoma: arise from the epithelial sheet that covers the surfaces, e.g., skin, colon, etc. More or less 90% of all human cancers are carcinomas; (b) sarcoma: these include cancer of the connective tissues such as muscle, bone, cartilage, and fibrous tissue. Approximately 2% of all cancers are sarcomas; (c) leukemia and (d) lymphoma: they begin from blood forming cells and from cells of the immune system, respectively [43]. Approx. 8% of all cancers are leukemia and lymphomas. In light of metastatic potential, there are two classifications of cancers; (a) benign tumors or adenomas: when neoplastic growth remains clustered as a single mass, (b) malignant tumor or adenocarcinoma: when tumor invades normal tissue and spreads throughout the body [44].

Most drugs currently available for the treatment of cancer have constrained potential because they are very toxic, highly inefficient in treating cancer, or highly expensive and thus beyond the reach of the majority [45]. Treatments without these disadvantages are required. Herbal drugs or extracts themselves contain a combination of active constituents, which interact within themselves and also between other endorsed pharmaceutical drugs to either enhance (synergize) or decrease (antagonize) the therapeutic effect [46].Curcumin is one such agent; derived from turmeric (*Curcuma longa*), it has been utilized for thousands of years as a healing agent for variety of illnesses [47]. Research over the last few decades has indicated that curcumin is a potent antiinflammatory agent with strong therapeutic potential against a variety of cancers [48].

Prospective role of curcumin in carcinogenesis

Carcinogenesis is a complex process but may be largely recognized to be comprised of three phases: initiation, promotion, and progression. These nearly related steps: going from a normal cell to a transformed initiated cell (initiation); from initiated to pre-neoplastic cell (promotion); and from pre-neoplastic to neoplastic (progression); may confer them to curcumin intervention.

There is suggestive proof that inflammation may have a role in the three phases of carcinogenesis. Cancer initiation has been produced by oxidative stress and chronic inflammation. Inflammation acts a key controller in promotion of these initiated cells, possibly by providing them with proliferating signals and by preventing apoptosis [49]. The role of inflammation in tumor induction and subsequent malignant progression has been examined. Inflammatory response produces cytokines which act as growth or angiogenic factors leading transformed cells to proliferate and undergo development [50]. Leukocytes induce cytokines, angiogenic factors as well as matrix-degrading proteases that allow the tumor cells to proliferate, invade, and metastasize.

Tumor-infiltrating lymphocytes discharge matrix-degrading proteinases like matrix metallopeptidase 9 (MMP-9), thus promoting neoplastic proliferation, angiogenesis, and invasion [51].These details exhibit the role of inflammation in all three stages of carcinogenesis. Substantial confirmation for the role of inflammation in cancer may be seen by the frequent up regulation of inflammatory mediators like NF-κB [52]. The pathways enacted by NF-κB up regulators are implicated not only in tumor growth and progression but also in cancer cell development of resistance to anti-cancer drugs, radiation and death cytokines. NF-κB is a top notch target for anti-cancer therapy. The impact of curcumin on carcinogenesis is felt to be through inhibition of NF-κB as well as other molecular targets.

Impact on tumor initiation by curcumin

Inflammation may initiate carcinogenesis all the way through the production of reactive oxygen species (ROS) and reactive nitrogen species by activated neutrophils and macrophages that lead to cancer causing mutations. Curcumin has established significant reduction of levels of inducible nitric oxide synthesis (iNOS). Curcumin inhibits the stimulation of nitric oxide synthase and is a potent scavenger of free radicals like nitric oxide [53]. NF-κB has been concerned in the induction of iNOS which produces oxidative stress, one of the causes of tumor initiation [54]. Curcumin counteracts phosphorylation and degradation of inhibitor κ Bα, thereby blocking NF-κB activation which down regulates iNOS gene transcription.

Deregulatory imbalances between adaptive and innate immunity brings about chronic inflammation which is associated with epithelial tumor genesis, the prominent mechanism being NF-κB activation [55]. Curcumin was found to hinder cell proliferation and cytokine production by inhibiting NF-κB target genes included in this mitogen induction of T-cell proliferation, interleukin IL-2 production and nitric oxide generation [56,57]. Reduction induced over expression of cytokines, such as IL-10, IL-6, and IL-18, is accompanied by NF-κB induction which is regulated by and inhibited by curcumin [58,59].

Curcumin has been exhibited to increase expression of conjugation enzymes (phase II). These have been demonstrated to suppress ROS-mediated NF-κB, AP-1 and mitogen-activated protein kinases (MAPK) activation [60]. These enzymes, such as sulfotransferase and glutathiones- transferase, conjugate toxic metabolites (through phase I enzymatic action) and then excrete them. Curcumin regulates cytochrome p450 function and has been showed to reduce aflatoxin B1-DNA adduct formation, an inhibitory step important in chemical carcinogenesis [61]. In various cancer models, curcumin was seen to further balance ROS by increasing ornithine decarboxylase, glutathione, antioxidant enzymes and phase II metabolizing enzymes. Heme oxygenase-1 (HO-1) has been seen to counteract oxidative stress, balance apoptosis and inhibit cancer cell proliferation [62]. Curcumin induces HO-1 expression by signaling through nuclear factor (erythroid derived 2)-related factor 2 (NRF-2) and NF-κB and subsequently has the potential to reduce oxidative stress [63]. NRF-2 is a transcription factor that regulates the expression of conjugatory enzymes like glutathione-s-transferase through an anti-oxidant response element (ARG) [64]. Curcumin prevents initiation of tumors either by curtailing the proinflammatory pathway or by prompting phase II enzymes [65].

Tumor proliferation and progression inhibition by curcumin

Evidence suggests NF-κB has an imperative part in cancer initiation, promotion and progression. NF-κB binds to DNA and results in transcription of genes leading to tumor genesis: inflammation, anti-apoptosis and positive regulators of cell proliferation and angiogenesis [66]. NF-κB initiation occur primary via inhibitor κ B kinase (IKK)-mediated phosphorylation of inhibitory molecules [67]. Curcumin inhibits NF-κB signaling and blocks IKK activation. Suppression is noted on cell survival and cell proliferation genes, including Bcl-2, cyclin D1, IL-6, COX-2 and MMP [68,69]. Curcumin also initiates apoptosis by caspase activation of a poly (ADP-ribose) polymerase (PARP) cleavage. Regulation of NF-κB by curcumin is linked with activation of caspase 3 and 9, decreasing Bcl-X (L) messenger RNA (mRNA) and increasing Bcl-X (S) and c-IAP-2 mRNA.

COX-2 is the inducible form of cyclooxygenase that catalyzes the role limiting step in prostaglandin synthesis from arachidonic acid and plays a significant role in cancer and tumor promotion [70]. Over expression of COX-2 results in malignant cell proliferation and invasion and the effect is reversed by non-steroidal anti-inflammatory agents, elucidating the importance of COX-2 inhibitors in cancer chemotherapy [71]. It has been recommended that COX-2 induction is mediated by NF-κB intracellular signaling pathway. Curcumin has been noted to decrease proliferation of various cancer cells, especially in the colon by down-regulating COX-2 [72]. Curcumin represses COX-2 but not COX-1 in colon cancer cells, demonstrating its selectivity [73]. It has been indicated to inhibit COX-2 expression by repressing degradation of the inhibitory unit inhibitor κ B α and hindering the nuclear translocation of the functionally active subunit of NF-κB, thereby blocking improper NF-κB activation [74].

Curcumin has been found to lessen the invasion and subsequent metastasis of cancer cells. Curcumin suppresses MMP expression which is assumed to play a major role in mediating neovascularization and is increased during tumor progression [75]. MMPs play a vital role in endothelial cell migration and tube formation [76]. Two determinants of neovascularization that aid in forming new capillaries from preexisting blood vessels are MMP-2 and MMP-9 [77,78]. These two MMPs are known to be involved in tumor angiogenesis primarily through their matrix degrading capacity. Curcumin down regulates expression of MMP-9 by inhibiting NF-κB and AP-1 binding to the DNA promoter region [79]. Adhesion molecules, such as vascular cell adhesion molecules (VCAM), are concerned with cancer progression and they are elevated in patients with advanced disease.

Curcumin has been prominent to cause significant inhibition of tumor necrosis factor α induced VCAM-1 expression, related to the activation of the MAPK NF-κB pathway. Curcumin has been revealed to reduce cell migration and invasion induced by Osteopontin, an extracellular matrix protein, through the NF-κB pathway [80]. Curcumin might inhibit cancer cell growth through down regulation of IL-1 and IL-8 induced receptor internalization. Curcumin controls malignancy progression by either blocking tumor growth or

inhibiting its invasive and aggressive potential. Most of the effects in either case are exerted by curcumin-induced NF-κB inhibition.

Certain molecular targets of curcumin's chemoprotective action are β-catenin, β-catenin/T cell factor (TCF), and lymphoid enhance factor (LEF) which are regularly disrupted in many cancer cells, especially colorectal carcinoma [81]. Dysregulated β-catenin (TCF) is concerned with cancer progression and poor prognosis. β-catenin with the cytoplasmic pool is phosphorylated by the axin adenomatous polyposis coli-glycogen synthase kinase 3β complex and exposed to degradation by the ubiquitin proteasome pathway [82]. Non-degraded β-catenin either enters the nucleus to transactivate the TCF/LEF transcription factors, leading to the up regulation of several genes responsible for cell proliferation, or binds to the E-cadherin adhesion complex [83]. Reduction or loss of E-cadherin and/or increased localization of β-catenin in the nucleus is linked to the invasive metastatic cancer progression and poor prognosis.

Curcumin has been found to decrease nuclear β-catenin and TCF4 and hence inhibit β-catenin /TCF signaling in a variety of cell cancer lines. Curcumin activated G2/M phase arrest in the cell cycle and apoptosis in colon cancer cells by impairing Wnt signaling and decreasing transactivation of β-catenin/TCF/LEF, subsequently alternating tumor progression [84]. The anti-tumor impact of curcumin was confirmed by its capacity to decrease intestinal tumors in an animal model of FAP by reducing the expression of the oncoprotein β-catenin. Some human β-catenin /TCF target genes, including cyclin D, MMP7, OPN, IL-8 and matrilysin, assume a part in tumor promotion and progression [85]. NF-κB repression and decreased β-catenin signaling are some of the ways by which curcumin suppresses the promotion and progression of cancer [86].

Antioxidant effects

Curcumin exerts antioxidant activity in a direct and an indirect way by scavenging reactive oxygen species and triggering an antioxidant response, respectively [87]. Water and fat soluble extracts of turmeric and its curcumin component display strong antioxidant activity, similar to vitamins C and E [88]. Several human and animal studies show protection against carcinogenesis with the consumption of high amounts of antioxidants [89]. A study of ischemia in the feline heart established that curcumin pretreatment decreased ischemia-induced changes in the heart [90]. In particular, curcumin, a powerful antioxidant derived from the curry spice turmeric, has evolved as a strong inducer of the heat shock response [91]. In light of this discovering, curcumin supplementation has been recently considered as an alternative, nutritional approach to reduce oxidative damage [92].

Hepatoprotective effects

In battling liver sicknesses, it appears to be clear that curcumin pushes a hypolipidic impact, which avoids the fatty acid accumulation in the hepatocytes that may result from metabolic imbalances, and which may cause nonalcoholic steatohepatitis [93]. Animal studies have shown turmeric's hepatoprotective effects from a variety of hepatotoxic insults, including carbon tetrachloride (CCl_4), galactosamine, and acetaminophen (paracetamol), and *Aspergillus* aflatoxin [94]. Turmeric's hepatoprotective effect is chiefly a result of its antioxidant properties, as well as its ability to decrease the formation of pro-inflammatory cytokines [95]. In rats with CCl_4 induced acute and subacute liver injury, curcumin administration altogether decreased liver injury in test animals compared to controls. Turmeric extract repressed fungal aflatoxin production by 90 percent when given to ducklings infected with *Aspergillus parasiticus* [96]. Turmeric and curcumin reversed biliary hyperplasia, fatty changes, and necrosis induced by aflatoxin production [97]. Sodium curcuminate, a salt of curcumin, also exerts choleretic effects by increasing biliary excretion of bile salts, cholesterol, and bilirubin, as well as increasing bile solubility, subsequently possibly preventing and treating cholelithiasis.

Anti-inflammatory effects

Traditionally curcumin is known for its antiinflammatory effects, curcumin has been indicated in the last two decades to be a potent immunomodulatory agent that can modulate the activation of T cells, B cells, macrophages, neutrophils, natural killer cells, and dendritic cells [98]. Oral administration of curcumin in instances of acute inflammation was found to be as efficient as cortisone or phenylbutazone, and one-half as effective in cases of chronic inflammation. In rats with Freund's adjuvant-induced arthritis, oral administration of *Curcuma longa* considerably reduced inflammatory swelling compared to controls. In monkeys, curcumin inhibited neutrophil aggregation coupled with inflammation [99]. *C. longa's* anti-inflammatory properties may be certified to its ability to inhibit both biosynthesis of inflammatory prostaglandins from arachidonic acid, and neutrophil function during inflammatory states. Curcumin may also be applied topically to neutralize inflammation and irritation associated with inflammatory skin conditions and allergies, although care must be used to prevent staining of clothing from the yellow pigment [100].

Antimicrobial effects

Turmeric extract and the essential oil of *Curcuma longa* inhibit the development of a variety of bacteria, parasites, and pathogenic fungi [101]. Animal was treated by means of curcumin and cotrimoxazole. Ileum, spleen, and liver of all animals were isolated and cultured. We found that curcumin-cotrimoxazole combination treatment lowered the antimicrobial effectivity of cotrimoxazole in both intraintestinal and extraintestinal organs [102]. Another animal study, in which guinea pigs were infected with either dermatophytes, pathogenic molds, or yeast, establish that topically applied turmeric oil inhibited dermatophytes and pathogenic fungi, but neither curcumin nor turmeric oil affected the yeast isolates [103]. Improvements in lesions were noted in the dermatophytes and fungi-infected guinea pigs, and at seven days of post-turmeric application the lesions disappeared [104]. Curcumin has also been originated to have moderate activity against *Plasmodium falciparum* and *Leishmania sp.* [105].

Cardiovascular effects

Turmeric's shielding 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 [106]. Curcumin is a potent anti-inflammatory agent that averts the release of TNFalpha and protects against the pulmonary and cardiovascular effects [107]. A study conducted on atherosclerotic rabbits given low-dose turmeric extract demonstrated decreased vulnerability of LDL to lipid peroxidation, in addition to lower plasma cholesterol and triglyceride levels [108]. The higher dose did not decrease lipid peroxidation of LDL, but cholesterol and triglyceride level decreases were noted, though to a lesser degree than with the lower dose [109]. Turmeric extract's effect on cholesterol levels might 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 [110].

Gastrointestinal effects

Constituents of *Curcuma longa* exert several defensive effects on the gastrointestinal tract [111]. Sodium curcuminate repressed intestinal spasm and p-tolymethylcarbinol, a turmeric component, increased gastrin, secretin, bicarbonate, and pancreatic enzyme secretion. An Indian dietary subordinate (curcumin), a yellow pigment found in the rhizome of *Curcuma longa*, has been widely used for the treatment of numerous diseases. Epidemiologically, it was recommended that curcumin might reduce the risk of inflammatory disorders, such as cancer and ulcer. These biological effects are certified to its anti-inflammatory and antioxidant activities. It can, hence, be accounted from the literature that curcumin prevents gastrointestinal-induced ulcer and can be recommended as a novel drug for ulcer treatment.

Curcumin boost immunity

Curcumin, a natural polyphenolic antioxidant compound, exerts immunomodulatory effects, the latter which can manipulate the

activation of immune cells including T cells [112]. In addition to this localized immune stimulation, curcumin also enhances immunity in common. Curcumin work against cancers through modulation of the immune system and regulates pro-inflammatory mediator production [113]. Researchers in India have recorded increased antibodies and more immune action in mice given curcumin.

Safety and tolerance of curcumin

Published studies on a variety of animals such as rats, guinea pigs etc and clinical trials on human volunteers have established that curcumin is safe and well tolerated in animals and humans even at high doses [114]. Curcumin is being used in many diseases for several years without any serious adverse effects [115,116]. Although many studies have recommended that curcumin induces apoptosis through p53 pathways, a study has suggested that curcumin inhibits apoptosis, which is induced by tumor suppressor protein p53 in cultured human colon cancer cells, suggesting that curcumin exhibits a modest carcinogenic risk [117,118]. In the prevention and treatment of cancer antioxidants therapies play vital role [119,120]. A current dose study of curcumin has determined that curcumin is well tolerated and safe even in high single oral dose of 12000 mg.

CONCLUSION

To sum up, although classy modern methods and treatments against many fatal diseases are being invented day-by-day the average life expectancy of cancer patient has not increased significantly. Hence, preventive measures should be taken to minimize the risk of developing cancer, curcumin acts as a potential chemopreventive agent and because of its cost effectiveness it can be easily administered with a variety of foods that people consume daily. Curcumin is proven to exhibit good tolerance even when administered in high doses. More clinical trials should be needed for better establishment of its potency in the treatment of cancer and to ensure safety.

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