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Turmeric (*Curcuma longa* L.): Chemical Components and Their Effective Clinical Applications

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Abstract: Turmeric (*Curcuma longa* L.) is widely utilized as a spice, food colorant, and preservative in India, China, and South-East Asia. With containing potential turmeric extracts and compounds, it has been utilized in traditional medicine for various diseases counting diabetes, hepatitis, hemorrhoids, hysteria, indigestion, skin disease, inflammation, anorexia, hepatic disorders, cough, and sinusitis, etc. So far, a large number of work has been conducted to find and prove biological activities and pharmacological applications of turmeric and its extracts in both animals and humans. In particular, curcumin (diferuloylmethane), a characteristic component with major yellow bioactive turmeric feature, has been found to possess numerous biological actions. Nonetheless, the polyphenol compound in curcumin has been limited for human disease treatments even though adequate studies are utilized in animal trials. Plenty of ongoing studies are also contributing significantly to this promising molecule that to the forefront of human therapeutics as well as its activities in health benefits. Thus, curcumin and some turmeric extracts are considered as non-toxic and highly promising compounds with a lot of potentially biological functions based on an appropriately used dose. It is expected that curcumin and some turmeric extracts can be explored in novel medical applications in the future to effectively against or treat various diseases. Here, we hope that it is likely a good and right approach for using and encouraging this product, and its chemical components and effective clinical applications will be briefly summarized in disease treatments.

Keywords: Turmeric, *Curcuma longa* L., curcumin, curcuminoids, disease.

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INTRODUCTION

There is a consecutive increase in treating various diseases based on natural products (herbs) in recent years. Primarily, *Curcuma longa* L. (Zingiberaceae – Ginger family) is known to be turmeric that is native to India, as well as which is cultivated and assigned everywhere tropical/subtropical regions and South East Asia (1, 2) (Figure 1). For *Curcuma longa* plant, it has ovate or oblong leaves with light green and a spicy aroma while its flowers' color are lilac–white (3). Besides, its rhizomes accord flavorful yellow powder after dried and crushed (4), which have been extensively served with a long history in Chinese and Ayurvedic medicines (Indian system of Medicine, as a "cleanser of the body") (5) (Figure 1). It was probably cropped at first as a dye and later on, which was employed as cosmetic (i.e., aromatic food product). Similar to other herbal foods, people first utilized it as a food and later explored that it has effective medicinal actions; therefore, Curcuma longa L. has also attracted significant attention because of its colorant nature (6). This natural pigment is considered as a food colorant and as a material that enhances health or even healing diseases (7, 8), instead of synthetic dyes that can weaken the hepatic function and induce oxidative stress. There is currently numerous turmeric products marketed with various concentrations of extracted bioactive compounds (9), as well as plenty of studies demonstrated the high performance of bioactive compounds contained in this plant utilizing like anti-bacterial, anti-inflammatory, anti-oxidant and anti-carcinogenic agents. They were employed to be a herbal medicine to prevent premature aging and diseases (10-12). In particular, natural curcuminoids curcumin (i.e., diferuloylmethane, demethoxycurcumin, and bis-demethoxycurcumin) in turmeric are essentially found in rhizomes, natural monoterpenes are often in essential oils from flowers and leaves, and natural sesquiterpenes are essentially contained from roots and rhizomes. The curcuminoid curcumin contents are often different with various conditions (i.e., sources, locations, varieties, and cultivations), resulting in that the quality and quantity of commercial turmeric products can be significantly varied.

Additionally, *Curcuma longa* L. has found several biological and pharmacological activities leading to becoming an engaging nutraceutical for chemoprevention purposes or disease treatments (13), which have been attributed to natural curcuminoids; curcumin-containing phenolic compounds counted mainly of curcumin I, II, and III (i.e., diferuloylmethane, demethoxycurcumin, and bis-demethoxycurcumin) (14) (Figure 2). Nonetheless, in the curcuminoids, curcumin is poorly stable as well as reach low aqueous solubility (15). Actually, curcumin is unstable in basic solutions that break down easily (especially for non-solubility in acidic solutions), yielding mainly feruloylmethane, ferulic acid, and yellow-brown products (16), which induces its invalidation in pharmaceutical actions as well as its limitation in food industries (17, 18). This often confuses the solubility concept of curcumin; besides, curcumin can be changed to free-flowing micro-particles that support improving its solubility in both acidic media and aqueous stability overcome the above-mentioned problems (19).

In addition to the above, the combination of turmeric extracts and chitosan films [i.e., anti-microbial, biocompatible, biodegradable, and eco-friendly features (20, 21)] was also investigated to evaluate the anti-bacterial and physical properties. Notably, biopolymers-based wound-healing materials have attached a significant consideration that can combine with curcumin or bioactive turmeric extracts for wound-healing applications to enhance their excellent performances (22). Theoretically, wound healing relates to multiple factors (i.e., growth factors and cytokines), such as cell populations, extracellular matrix, and soluble mediators. It can induce chronic wound growth if healing does not evolve a stepwise procedure. Especially, curcumin is one of them, used to treat dermal injury (23, 24) as well as a variety of diseases (i.e., asthma, hepatic disorders, diabetes, respiratory diseases, etc.). From *in vitro* or *in vivo* tests, curcumin prodded fibroblast proliferation, granulation tissue development and collagen deposition in cutaneous wound healing (23-25).

As known, coronavirus disease 2019 (COVID-19) was found first in Wuhan (China) at the end of 2019 like an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), handwashing (soap and water/lukewarm water-based handwashing, or alcohol-based hand sanitizers) and wearing masks (cloth masks, medical masks, N95 respirators, and surgical masks) are currently one of the ways that can prevent the influenza virus infection (26, 27). Remarkably, turmeric is served as one of functional foods that can strengthen the immune system and treat respiratory diseases. People in the world are now self-isolating at their homes, the use of turmeric products may support enhancing the immune system and prevent SARS-CoV-2 infection through the daily diet, that may reduce the COVID-19 infection risk and a recovery in SARS-CoV-2 infection cases (28). Therefore, it is imperative to clearly understand its available chemical components and activities to can be utilized in bioactive and pharmacological applications after demonstrated its reliability. Herein, we hope that it is likely a good and right approach for using and encouraging this product, and its chemical components and effective clinical applications with appropriately used doses will be briefly summarized in disease treatments.

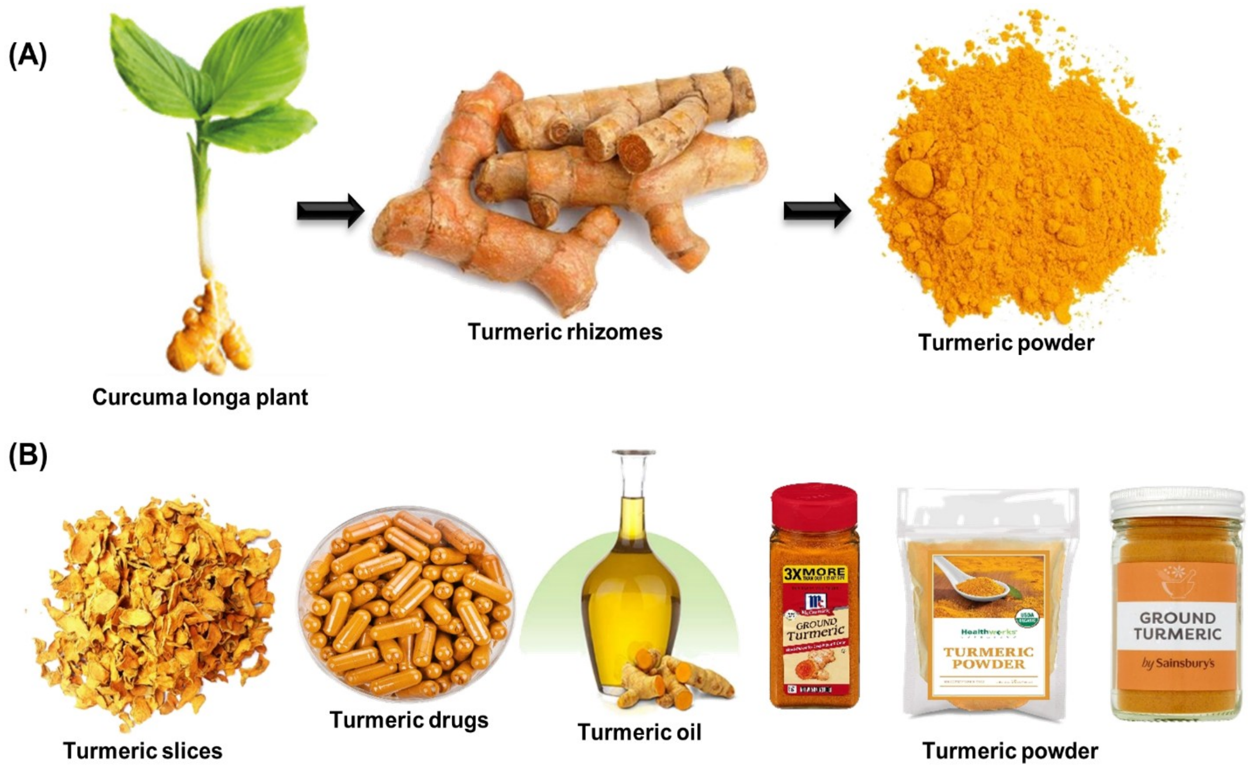

Figure 1: *Curcuma longa* L. – turmeric rhizomes and powder (A); and possibly commercial turmeric products (B).

CHEMICAL COMPONENTS

Curcuma longa L. was known as turmeric that was extensively served as a food colorant; nonetheless, it was considered to be plenty of possible biological and medicinal activities, such as anticancer, antioxidant, anti-inflammatory properties, *etc*. (Possible biological and medicinal activities of compounds/extracts from turmeric rhizomes are summarized in Table 1). The chemical structures of some available compounds (natural curcuminoids curcumin) are presented in Figure 2.

The quality and quantity of curcuminoids and chemical components of turmeric are significantly noticed to their performance in human disease treatments, for instance, the major bioactive properties in the turmeric rhizome are curcuminoids (14), phenolic acid and flavonoids (29). To maintain the quality of turmeric during storage and usage processes, dehydration (moisture removal) is suggested as a main method for turmeric preservation (30), such as freeze-drying, low-temperature drying, and microwave-vacuum drying methods (31, 32). Among them, the common hot-air drying method is a good selection, owing to being a simple and easy process; however, if this method is conducted during a long time with high temperatures, it can degrade color, flavor, and bioactive compounds. For the freeze drying method, it is the most effective approach to maintain turmeric quality, but its disadvantages are high cost, long drying time, and high energy consumption. For the sun-drying method, it is known a traditional approach, which takes a long time that can reduce the product quality and bioactive compounds (32). Thereby, a more effective drying method is required to maintain expected quality as well as to preserve the major bioactive compounds in turmeric.

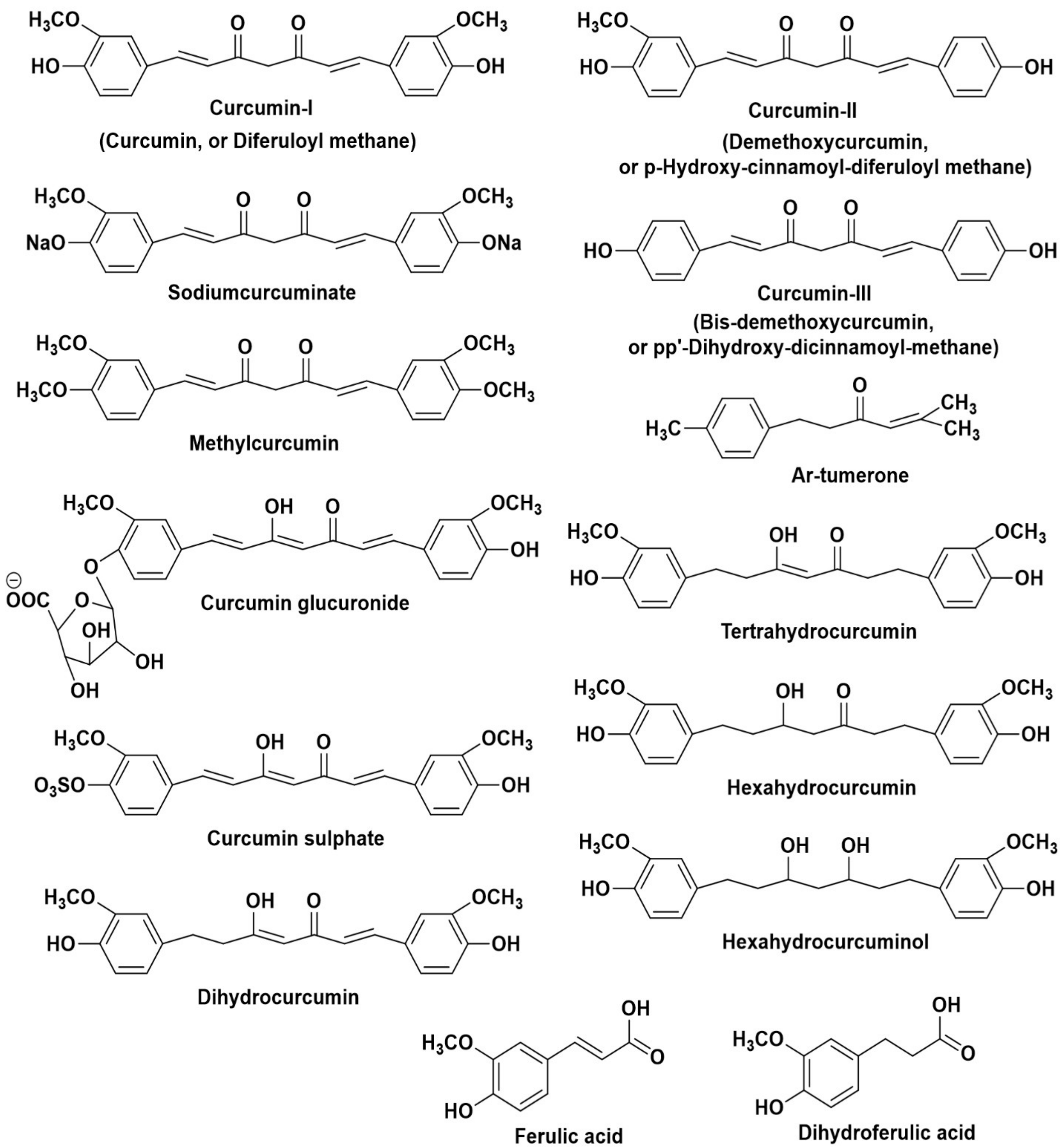

Figure 2: Chemical structures of natural curcuminoids and metabolites of curcumin.

Actually, turmeric from *Curcuma longa* L. contained carbohydrates (69.4%), protein (6.3%), fat (5.1%), minerals (3.5%), and moisture (13.1%), as well as its oil, could attain ~5.8% through steam distillation of turmeric rhizomes with borneol (0.5%), α-phellandrene (1%), zingiberene (25%), sabinene (0.6%), cineole (1%), and sesquiterpenes (53%) (33). In particular, curcumin is a mixture of three curcuminoids [i.e., curcumin I ($C_{21}H_{20}O_6$, diferuloylmethane, 94%), curcumin II ($C_{20}H_{18}O_5$, demethoxycurcumin, 6%) and curcumin III ($C_{19}H_{16}O_4$, bis-demethoxycurcumin, 0.3%)] (14, 34) (Figure 2), which is considered a characteristic for its yellow color. Besides, curcumin I ($C_{21}H_{20}O_6$, curcumin, diferuloylmethane) is a major curcuminoid, as well as phenolic -OH and -CH_2 groups in β-diketone moiety contained in these turmeric compounds, have been revealed to possess anti-inflammatory (35) and antioxidant (36) properties, and other effective bio-activities as shown in Table 1, leading to becoming an engaging nutraceutical for chemopreventive purposes or disease treatments.

Moreover, it is dissolved well in some organic solvents (methanol, ethanol, acetone, and dimethyl sulfoxide, *etc*.) that can reach various derivatives/extracts, but they are insoluble in water. The use of solvents in extraction processes is one of important factors to achieve high performance and environment. To attain anti-oxidative extracts in *Curcuma longa* L., it is performed with conventional solvents (methanol, ethanol, and acetonitrile) (37, 38). In recent years, deep eutectic solvents (i.e., solvents based on an incorporation of a hydrogen bond acceptor and a hydrogen bond donor) (39, 40) are considered to be one of new classes of green solvents have emerged that is owing to non-toxic and biocompatible extraction procedures, which can cause less influence to environment and available nature of these bioactive compounds. In fact, the deep eutectic solvents can be prepared from the required purpose, especially for the extraction of bioactive compounds that are known as designer solvents. From solvent characteristics, there are current various hydrogen bond donors and hydrogen bond acceptors used to synthesize these deep eutectic solvents, such as choline chloride (41), menthol, and betaine (42), that for their combination can be sugars, carboxylic acids, alcohols, amines, or other compounds containing hydrogen bonds (41, 42). Other parameters are important in this approach, i.e., solute/solvent ratio, extraction temperature and time (43, 44). Particularly, some studies have conducted the extraction processes to attain bioactive compounds from turmeric based on the use of green solvents (45-47). For example, Oliveira et al. (48) investigated the deep eutectic solvents and various process conditions to extract bioactive compounds from the parts of *Curcuma longa* plant (i.e., leaves, rhizome, and flowers) that could be used as flavonoids, antioxidant, antimicrobial, chelation with Fe^{2+}, inhibition of the cholinesterase enzymes, cytotoxicity, and genotoxicity in *Allium cepa* cells. As a result, these extracts showed non-cytotoxicity, non-genotoxicity, chelation with iron and anti-bacterial features indicating a high potential application in the pharmaceutical industries.

In order to reach highly effective curcumin and some turmeric extracts in biological applications, it depends significantly on suitably used doses. Specifically, dietary use of curcumin/turmeric extracts with appropriate doses has also been indicated to inhibit tumor induction in various organs of mice (49-51) and rats (52). The use of curcumin (53) and turmeric extracts (54) with high doses on mice have not shown an increase in mortality as well; in contrast, those of turmeric oleoresin to pigs has been lowered the food-conversion efficiency (or weight gain) as well as raised the weight of the liver and thyroid leading to having histological changes in their kidney, liver, and urinary bladder (55). Besides, the use of turmeric extracts with high doses on mice has also been impacted strongly to the tissue weights, bodily weight gain, and levels of their red blood cells and white blood cells (54). Thereby, curcumin and some turmeric extracts are served as non-toxic and highly promising compounds with plenty of potentially biological functions based on an appropriately used dose. In addition to above-mentioned biological activities, turmeric has been found in traditional medicine and currently medicinal applications, such as anemia, indigestion, diabetes, hemorrhoids, edema, hepatitis, atherosclerosis, hysteria, wound and bruise healing, urinary disease, psoriasis, rheumatism, anorexia, dermal disease, inflammation, hepatic disorders, cough, sinusitis, *etc*. (56).

Table 1: Biological activities of turmeric compounds and extracts.

Compounds/extracts	Biological activities
Turmeric powder	Wound-healing (57)
Alcoholic extract	Anti-bacterial (58)
Aqueous extract	Anti-fertility (59)
Ar-turmerone	Anti-venom (60)
Bis-demethoxycurcumin or Demethoxycurcumin	Anti-oxidant (61)
Crude etheric or Chloroform extracts	Antifungal (62)
Curcumin	Anti-bacterial (63), anti-protozoan (58), anti-viral (64), hypolipemic (65), hypoglycemic (66), anti-coagulant (67), anti-oxidant (36), anti-tumor (68), anti-carcinogenic (69)
Ethanolic extract	Anti-inflammatory (70), hypolipemic (71), anti-tumor (72), anti-protozoan (73)
Methyl curcumin	Anti-protozoan (74)
Petroleum ether extract	Anti-inflammatory (70), anti-fertility (59)
Sodium curcuminate	Anti-inflammatory (70), anti-bacterial (58)
Volatile oil	Anti-inflammatory, anti-bacterial (58), anti-fungal (75)

EFFECTIVE CLINICAL STUDIES

Turmeric has been utilized much in Chinese and Ayurvedic medicines, at same time that various biological and pharmaceutical characterization (i.e., anti-inflammatory, antioxidant, anti-diabetic, anti-carcinogenic, anti-coagulant, anti-bacterial, anti-ulcer, antifungal, anti-fibrotic, hypotensive, antiviral, *etc*.) of curcumin and some turmeric extracts can contribute to being effective against or treating human diseases. Wherein, crude extracts from turmeric have reached high evaluations in numerous medicinal and clinical applications to can be applied in more extensive studies grounded on their bioactivity, mechanism of action, pharmacological effects, and toxic features. Also, curcumin can exist in a pure compound that shows lots of biological activities, which contribute to developing and expanding novel drugs from this compound based on its mechanism of action and pharmacological effects. Concomitantly, plenty of studies based on animal models have also contributed to building up a solid foundation that can evaluate well the safety and efficacy of curcumin to prevent and treat human diseases (Table 2).

Among them, turmeric extracts and curcumin have revealed possible activities that were utilized for both prevention and treatment of human diseases counting cancer (colorectal cancer, multiple myeloma, prostate cancer, oral cancer, pulmonary cancer, pancreatic cancer, etc.), peptic ulcer, ulcerative proctitis, atherosclerosis, gastric ulcer/inflammation, diabetes, diabetic nephropathy/micro-angiopathy, chronic bacterial prostatitis, *etc*. (56). As such, turmeric extracts and curcumin have used effectively in the treatment of human diseases, but their bioavailability are poor that can be due to poor absorption, rapid metabolism/systemic elimination inducing some restrictions of their therapeutic efficacies (76). On that basis, there were lots of approaches grounding on combinations of curcumin and several various appropriate components to can be served more effectively in the treatment of human diseases (76-79). Especially, the bioavailability of curcumin has been investigated to be significantly enhanced by considering curcumin and non-curcuminoid compounds of turmeric (80). The polyphenol compound in turmeric also causes several disadvantages in used curcumin doses, and its safety, efficacy, and a non-toxicity at appropriate doses have been suggested through human clinical trials.

In particular, Cheng et al. (81) conducted evaluations of the effectively used curcumin dose (8.0 g/day) in the pharmacokinetics, toxicology, and biological characterization of 25 patients with uterine cervical intraepithelial neoplasm, Bowen disease of the skin, oral leucoplakia, cancer of the resected urinary bladder, or intestinal metaplasia of the stomach through the oral curcumin for 3 months. Besides, Dhillon *et al*. and Kanai *et al*. (82, 83) also investigated a combination of curcumin (8.0 g/day) and gemcitabine that was safe and effectively applied in >20 patients with pancreatic cancer. Curcumin containing polyphenol lowered the aberrant crypt foci formation (i.e., colorectal polyps' precursor) (84) in 44 smokers through oral curcumin for 30 days (2.0-4.0 g/day), as well as which indicated the effect of curcumin against and prevented an aberrant crypt formation of foci on smokers (84). In addition, 360.0 mg of curcumin in capsules was used for patients with colorectal cancer for 10–30 days (three times a day) (85), suggested that the use of curcumin in the colorectal cancer treatment could improve the patients' health (85). Polasa *et al*. (86) studied the treatment of pulmonary cancer in smokers based on the use of turmeric, resulting in that the urinary excretion of mutagens lowered significantly in these smokers.

Curcumin has not been only used alone, but also combined with other agents. For instance, oral curcumin and piperine have been combined effectively to treat pains and oxidative stress markers (malondialdehyde) in patients with tropical pancreatitis (60), resulting in the plasma malondialdehyde and erythrocyte glutathione levels lowered and increased, respectively; however, the pains were not improved (87). Curcumin also prevented prostate-specific antigen productions in men with high prostate-specific antigens (88); besides, 1.0 g of a curcumin pill for one week could enhance levels of vitamins C/E and reduce the contents of 8-hydroxydeoxyguanosine / malondialdehyde in patients with precancerous lesions (89). Furthermore, curcumin could be used as a maintenance medication for 89 patients with ulcerative colitis (90, 91), indicating that relapse rates in the curcumin-treated group (4.65%) were lower much than that in the placebo group (20.51%) (90, 91). Kedia et al. (92) conducted oral curcumin investigation according to mild-to-moderate level of ulcerative colitis (150 mg/thrice/day; 8 weeks), indicating that low dose was ineffective in inducing remission in mild to moderate cases of ulcerative colitis, while oral curcumin (500.0 mg/day) and prednisone have been combined well together to treat a patient with ulcerative colitis by Lahiff et al. (93). Concomitantly, tetrahydrocurcuminoid and narrow-band ultraviolet B have been coupled together to against and treat vitiligo – a skin disorder (94), resulting significant improvements in the overall re-pigmentation degree of the combination group (94). Crohn's disease is a chronic relapsing inflammatory intestinal disease, which influences to the gastrointestinal tract (oral-anal). Holt *et al*. (95) investigated this disease through the use of curcumin, manifesting that there are significant reduction in symptoms as well as inflammatory indices in all patients. In the case of gallbladder contraction, the use of curcumin could also impact to gallbladder through the studies of Rasyid *et al*. (96, 97). As a result, the gallbladder sizes lowered through an appropriately used curcumin dose (20.0-80.0 mg; 0.5-2 h). Niederau *et al*. (98) showed a faster reduction in dumpy and colicky pain of patients with biliary dyskinesia. For the cases of inflammatory diseases, use of curcumin also achieved effective performances in the recurrent and chronic anterior uveitis treatments. Ocular discomfort reduced after 12-18 months of the recurrent anterior uveitis treatment in more than 80.0% of patients (106 patients) (99), as well as there were not any adverse effect with efficacy and recurrent of disease (100). Besides, oral curcumin was applied for patients with peptic ulcer (101), gastric ulcer (102), and postoperative inflammation (103), resulting in that the ulcer formation reduced significantly (101, 102), as well as the anti-inflammatory property, exhibited superior comparing with phenylbutazone (103). Notably, a standardized preparation of curcuminoids was used in type 2 diabetes treatment of different oxidative stress (malondialdehyde) and inflammatory markers (104), leading to much improving for those markers in these patients. Particularly, the use of curcumin can show a promising and potential treatment for Alzheimer’s disease (105, 106). Multiple myeloma (107) was also treated by use of curcumin for 6 months (4.0 g/day), indicating that para-protein load and urinary N-telopeptide of type I collagen in 26 patients decreased much; additionally, theracurmin (i.e., a well absorptive curcumin) dispersed well in colloidal nanoparticles that could inhibit alcoholic intoxication in humans (77).

In general, the use of curcumin has shown beneficial activities that could against or treat human diseases through the above mentions. Nonetheless, there were also several reported restrictions toward the uses of this polyphenol compound. Specifically, it could inhibit the activity of metabolizing enzymes in vitro/animal (108-110); in contrast, the use of curcumin to human-like drugs metabolized (i.e., acetaminophen, digoxin, and morphine) by these enzymes could lead to undesired results of them that might induce to toxic features. Curcumin could induce DNA damage in cells (111), leading to a common occurrence in carcinogenesis; concomitantly, it also served as an iron chelator that induced anemia in rats and mice (112). Furthermore, use of curcumin with high doses (0.45-3.6 g/day or 0.9-3.6 g/day) could induce nausea/diarrhea, as well as which raised lactate dehydrogenase and alkaline phosphatase amounts in humans (113, 114); besides, the used doses of curcumin was unallowable at a higher level of 8.0 g/day in patients with premalignant lesions (81).

Remarkably, curcumin has been also suggested as a COVID-19 disease treatment to prevent the lethal influences of SARS-CoV-2 (115), which may be helpful to be a supportive part for other drugs that can probably prevent or treat the COVID-19 disease (116). A respiratory syncytial virus is recently noticed as a major threatening remark to human with various ages that induces acute respiratory infections. Chen et al. (117) demonstrated the influenza virus yield lowering >90.0% in cell culture through the use of curcumin (C_o = 30 μM) that could be due to the influences of viral protein synthesis (i.e., neuraminidase, hemagglutinins, and matrix protein). Likewise, curcumin could also inhibit the budding and replication in the nasal epithelial cells of humans leading to the improvement of the activities of an epithelial barrier to be effective against respiratory syncytial virus (118), as well as the oral curcumin effectively inhibited the inflammatory prostaglandin synthesis and neutrophil functions (119) reducing well desired-inflammation. Simultaneously, several curcumin derivatives have indicated with anti-viral properties; for example, a surveyed-neuraminidase process manifested that curcumin derivatives could reduce influenza A virus subtype H1N1 (H1N1) activation caused neuraminidase in lung cells with infected H1N1 (120). Moreover, turmeric compounds and extracts were also used to be effective against influenza A virus subtype H5N1 (H5N1) virus in Madin-Darby dog renal cells through intervening infectious hem-agglutination activities (in vitro) (121), or both the up-regulation of mRNA expressions (IFN-β and TNF-α) (122, 123) to be beneficial for recent disease outbreak cases. The use of curcumin is truly helpful in other viral troubles (i.e., acquired immunodeficiency syndrome, AIDS) (124) that regards to its inhibition activity on both human immunodeficiency virus type 1 (HIV) integrase and protease (125), and which was demonstrated to reduce the influenza virus-infected pulmonary tissue by hampering the NF-umB signals and preventing the inflammatory cytokines release (126, 127).

For the wound healing, oral administration and topical applications are the most common usages. Actually, the wound healing procedure is known a very complex approach, that regards to substance coagulation, inflammation, accumulation, formation of fibers tissues and collagen proliferation, contraction of wound, and granulation tissue and scar formation (128). In the case of treatment, curcumin has manifested a limitation in pharmaceutical feature, a low absorption in oral bioavailability, quick metabolism, and short half-life (76, 129). Concomitantly, curcumin has a very poor solubility in aqueous solution (nature of a hydrophobic compound) that leads to be not appropriate for topical applications at wound regions, which can also induce a toxic response from the use of high concentrations (characterization of a polyphenolic compound) (130). Therefore, the therapeutic usefulness of curcumin in topical wound-healing applications has been developed on effective delivery systems, which is based on better curcumin solubilization to build a principle for stable and slow release of the soluble drug form. Curcumin can combine with several biopolymers to enhance the wound healing performance. Zhang et al. (131) conducted a chemical modification for curcumin compounds to apply effectively in the wound healing standardized in streptozotocin-induced diabetic rats, which achieved high performances through daily topical applications (C_o = 1.0% and 3.0%, over 7-10 days) or administered systemically (oral intubation; 30.0 mg/kg). Nano-formulated curcumin has also well inhibited methicillin-resistant S. aureus, and noticeably accelerated the wound healing process on wound mice (7.5 mg/mL, over 7 days) (132). Chereddy *et al*. (133) showed a potential capacity of poly(lactide-*co*-glycolide) nanoparticles loaded with curcumin in the wound healing evaluation, as well as improved both the stability and solubility of curcumin. The gel-core hyalurosomes loaded curcumin also indicated a high healing performance for the burn wound on wound rats (134). These proposed that the nano-formulated curcumin can be utilized for preclinical applications in the future. The used curcumin doses have been proved to be similar effects in humans and remain to be explained. Additionally, a large number of studies have indicated in detail the safety and efficacy of this polyphenol in animals (i.e., monkeys, rodents, horses, cats, *etc*.) to offer a solid foundation for effective surveys in human clinical trials. In other words, this polyphenol's efficacy is needed more investigated before it can be applied for human disease treatment. In summary, the efficacy of curcumin and some turmeric extracts have prevented and treated human diseases that seem promising and potential. It is expected that quantities of ongoing studies can contribute significantly and reveal a detailed and more precise understanding of turmeric efficacy and its action to prevent and treat human diseases.

Table 2: Accomplished clinical studies using biological activities of turmeric.

Diseases	Number of patients	Dosages	Durations
Colorectal cancer (84, 85)	44 (84) 126 (85)	2.0-4.0 g/day (84) 1.08 g/day (85)	1 month (84) 10-30 days (85)
Cancer lesions (81, 89)	25 (81) 75 (89)	8.0 g/day (81) 1.0 g/day (89)	3 months (81) 7 days (89)
Diabetes (104, 135)	72 (104) 14 (135)	0.6 g/day (104) 6.0 g (135)	8 weeks (104) 15-120 min (135)
Diabetic micro-angiopathy (136)	25	1.0 g/day	4 weeks
Pancreatic cancer (82, 83, 87)	25 (82) 21 (83) 20 (87)	8.0 g/day (82) 8.0 g/day (83) 1.5 g/day (87)	3 months 3 months 6 weeks (87)
Prostatic cancer (88)	85	0.1 g/day	6 months
Pulmonary cancer (86)	16	1.5 g/day	30 days
Ulcerative colitis (90-93)	89 (90, 91) 1 (93) 29 (92)	2.0 g/day (90, 91) 0.5 g/day (93) 150 mg/thrice/day (92)	6 months (90, 91) 2-10 months (93) 8 weeks (92)
Vitiligo (94)	10	Twice/day	12 weeks
Alcohol intoxication (77)	7	0.03 g/once	--
Alzheimer's disease (105, 106)	34 (105) 33 (106)	1.0-4.0 g/day (105) 2.0-4.0 g/day (106)	6 months (105) 24 weeks (106)
Peptic ulcer (101)	45	3.0 g/day	4 weeks
Gastric ulcer (102)	60	1.0 g/day	6-12 weeks
Postoperative inflammation (103)	46	1.2 g/day	6 days
Multiple myeloma (107)	26	4.0 g/day	6 months
Gallbladder contraction (96, 97)	12	20.0-80.0 mg	0.5-2 h
Acquired immunodeficiency syndrome (124)	40	2.5 g/day	8 weeks
Lupus nephritis (137)	24	500.0 mg/day	3 months
Atherosclerosis (138)	10	0.5 g/day	7 days
Acute coronary syndrome (139)	70	0.045-0.18 g/day	2 months
Dejerine-Sottas' disease (140)	1	1.5 g/day	4 months

		2.5 g/day	8 months
Crohn's disease (95, 141)	5 (95) 31 (141)	1.08-1.44 g/day (95) 3.0 g/day (141)	1-2 months (95) 6 months (141)
Ulcerative proctitis (95)	5	1.1 g/day 1.65 g/day	1 month 1 month
Recurrent anterior uveitis (99)	106	1.2 g/day	12-18 months
***H. pylori* infection (142)**	8	1.125 g/day	6-22 months
Chronic anterior uveitis (100)	53	1.125 g/day	12 weeks
Rheumatoid arthritis (143-145)	8 (143) 18 (144) 45 (145)	0.5 g in food (143) 1.2 g/day (144) 0.5 g/day (145)	2 weeks (144) 8 weeks (145)
Osteoarthritis (146, 147)	50 (146) 100 (147)	0.2 g/day (146) 1.0 g/day (147)	3 months (146) 8 months (147)

CONCLUSION

In summary, turmeric (Curcuma long L.) has been directly employed in curries and other spicy dishes from India, China, and South East Asia, which has been proved the correlative bio-activities of curcumin in its possibly pharmaceutical applications that against or treat animal/human diseases. In addition to studies using curcumin in animal trials, it has already been revealed to be safe and effective at appropriately used doses through plenty of clinical trials; however, the polyphenolic compound has also been limited to treat or prevent some human diseases. Numerous studies regarded to absorption, metabolism, distribution, and excretion of curcumin indicated its poor absorption and fast metabolism that gravely restricts its available bioavailability; therefore, plenty of approaches based on a variety of combination between curcumin and several various appropriate components to can be applied in the effective treatment of human diseases. Simultaneously, a large number of ongoing studies can contribute significantly to this promising molecule at the forefront of human therapeutics. Thereby, curcumin and some turmeric extracts are considered as non-toxic and highly promising compounds with a lot of potentially biological functions that based on an appropriately used dose. For further understanding and suitable judgment in medical care, it is expected that curcumin and some turmeric extracts can be explored in novel medical applications in the future to effectively against or treat various human diseases.

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