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Curcumin: A pharmacologically functional active ingredient from nature

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Abstract
Curcumin is a widely used Indian rhizomatous medicinal plant from the family Zingiberaceae, an orange-yellow polyphenolic and hydrophobic phytochemical element of the turmeric herb (*Curcuma longa* Linn.), has been shown to have strong immunomodulatory properties varieties of nutritional value in both animals and humans. Science technology, a relatively recent scientific research field, is commonly used in medical sciences, but it has limited implementations in fish nutrition at the present day. Many experiments have shown that curcumin and its derivatives have beneficial effects on animal nutrition when used as medicinal agents as well as nutritional agents. Although curcumin shows beneficial effects, studies have shown that ingestion of curcumin or its derivatives has even less impact on animal efficiency or welfare due to its poor bioavailability, rapid metabolism, and removal from the animal body; thus, advanced curcumin formulations are required. This study focuses on the health advantages of curcumin and its derivatives, as well as its possible use in fish growth. Furthermore, this study discusses curcumin as well as its derivatives, as well as their uses in fish nutrition, in the future.

Keywords: Curcumin, antioxidant, anticancer, antimicrobial

Introductions
Turmeric, or *Curcuma longa*, is an herbaceous plant in the Zingiberaceae family that has long been used in Indian and Chinese traditional medicine as well as nutrients. India produces and uses almost all of the turmeric crop in the globe. It is mostly grown in tropical and subtropical climates [1]. Temperatures between 20 °C to 30 °C are required for the turmeric plant to grow, as well as a significant quantity of yearly rainfall. Individual plants can reach 1 m in height and have long oblong leaves. Plants are harvested for their rhizomes once a year, and some of the rhizomes are reseeded the next season. Turmeric has about 100 components that have been identified. Turmeric has a volatile oil that contains turmerone, as well as additional colouring compounds called curcuminoids. Curcuminoids are natural antioxidants that include curcumin desmethoxycurcumin, 5'-methoxycurcumin, and dihydro curcumin [2, 3]. Nutritional analysis revealed that 100 g of turmeric contains 2500 mg potassium, 69.9 g total carbohydrates, 50 mg ascorbic acid, 47.5 mg iron, 21 g dietary Fiber, 10 mg sodium, 10 g total fat, 8 g protein, 4.8 mg niacin, 3 g sugars, 3 g saturated fat, 0.9 mg thiamine, 0.26 g phosphorous, 0.2 g calcium, 0.19 mg riboflavin, and 0 mg cholesterol [4] (Figure 1).Turmeric also contains good amount of -linolenic acid and -3 fatty acid [5]. The main curcuminoids in commercial curcumin are 3% bisdemethoxycurcumin (curcumin III), and cyclocurcumin (curcumin IV), 17% desmethoxycurcumin (curcumin II), 77% curcumin (curcumin I), as well as 5.1% fat, 5.8% essential oils, 6.3% protein, and 36% curcuminoids and 69.4% carbohydrates [6].

Curcumin work as antioxidant agent
As an antioxidant, curcumin has a wide range of biological and pleiotropic effects [7, 8]. They're also useful in cooking and in-home cures, and they have powerful antioxidant properties at various degrees of activity. According to studies, significant amounts of turmeric can be ingested *in vivo* from curries to provide effective antioxidant protection [9]. When applied as an antioxidant, turmeric extracts can reduce oxidative stress, increase antioxidant enzymes, and minimise lipid peroxidation. When incubated with cells for 3 hours, turmeric (100 g/mL) reduces lipid peroxidation in renal cells and protects them against hydrogen peroxide-induced damage [10].

Curcumin work as antibacterial

Curcumin and its derivatives have antibacterial properties. To analyse the influence of curcumin I on bacterial morphology, curcumin I treated S. Aureus samples were examined in a scanning electron microscope (SEM) and the images of treated cells were compared to the images of untreated control specimens. They represented the pictures of S. aureus cells treated with 25 M, 50 M, and 100 M curcumin, respectively. As a result of exposure to curcumin I, they saw a deformation in the shape of cells, as well as depressions on the surface. At greater concentrations (i.e., 100 M of curcumin I exposure), the frequency of dead and injured cells was found to be higher. The untreated control cells, on the other hand, were shown to be completely unaffected. After comparing curcumin, I-treated bacterial samples to control (untreated) samples, the percentage of survival was measured. Curcumin I was shown to have a high killing power against all the microorganisms examined. The killing rate increased when the dose of curcumin I and the exposure duration were increased. When comparing percentage survival vs concentration, the variation in curcumin I killing effectiveness at different concentrations and exposure periods was determined to be statistically significant ($p < 0.05$)[1] (Figure 2).

Curcumin work as Anti cancerous agent

They also play a key role in antineoplastic [11, 12] and antiproliferative treatment [13]. Turmeric has been shown lower rate of reaction to decrease the cell growth of skin cancer [14], oral cancer [15], stomach cancer [14, 16], breast cancer [17]. It inhibits mutation [18], detoxifies carcinogens [19], decreases cell proliferation, and help in tumour cell death [20]. Dalton's lymphoma causes malignancy in animals, but turmeric extract reduces the reaction rate of malignancy [21]. Mice were given Dalton's lymphoma cells intraperitoneally and turmeric supplement (10–40 mg/animal) for 10 days. In comparison to non-treated mice, tumour development was reduced by up to 80% after 30 days, according to scientists. They also discovered that after 30 days of treatment, up to 75% of mice survived and 50% survived after 60 days. Inhibition of DMBA-induced expression of the Ras oncogene product, induction of p21 and its downstream targets, reduction of proliferating cell nuclear antigen and Bcl-2 expression as well as induction of p21 and its downstream targets, mitogen-activated protein kinases, were all involved in Anti carcinogenesis. Turmeric also increased apoptosis (by increasing caspase-3, Bax, and the apoptotic index) while lowering inflammation (by lowering COX-2, PGE2 and the downstream target of activator protein-1/nuclear factor KB [NF-KB]) [20]. Curcumin may potentially be used to reduce the risk of colorectal cancer in those who have Familial Adenomatous Polyposis (FAP), an autosomal dominant disorder that causes the formation of hundreds or thousands of polyps. If three doses of 480 mg curcumin combined with 20 mg quercetin (a popular supplementary flavanol) may prevent adenoma development in FAP patients. In a study of five patients with FAP who had previously colectomy, the number and mean size of polyps had decreased by 60.4% and 50.9%, respectively, after six months [22].

Curcumin play a role to prevent neurogenerative disorder

Curcumin is also hypothesized to have a role in avoiding the etiologic of various mental disorders, and there is some evidence that it can bind beta-amyloid plaques and lower plaque load, reducing the course of early Alzheimer's disease [23]. In one research of Asians with no substantial cognitive problems, those who consumed curry (curcumin) on a regular basis scored much higher on the mini-mental status test (a screening questionnaire intended to detect early indications of dementia) than those who did not. Curcumin's effectiveness and safety in the treatment of mild and moderate Alzheimer's dementia have now been studied in another way [24]. In addition, they have an impact in preventing IIR-induced lung damage (intestinal ischemia-reperfusion injury). As a result, they have therapeutic potential for neurodegenerative disorders [25, 26], cardiovascular illnesses [27, 28], hepatic damage [29, 30].

Curcumin work as anti-inflammatory and antifungal agent

Curcumin's anti-inflammatory properties were identified through blocking the NF-Kb pathway [31]. Curcumin ethanolic extracts show antifungal action against Trichophyton longifusus [32]. Using the agar disc diffusion method to determine antifungal activity, an ethanolic extracts infusion of turmeric cleared all diagnostic strains of dermatophytes. The inhibition zone for this extract was 6.1–26.0 mm [33]. It also shows therapeutic potential for neurodegenerative disorders [25, 26], cardiovascular diseases [27, 28], hepatic damage [29], and diabetes [29, 30].

Curcumin work as hepatoprotective agent

Turmeric has been shown to be hepatoprotective, with turmeric extract diets suppressing increases in alanine aminotransferase (ALT), and aspartate aminotransferase (AST) lactate dehydrogenase (LDH), produced by D-galactosamine-induced liver damage in rat [34].

Curcumin plays a role to cure chronic disease

Another major medical problem aided by curcumin is the condition of atherosclerosis, which is very widespread in Western societies. Although there are many possible causes for this pattern of atherosclerosis, one aspect that may play a role is the Western diet's decreasing consumption of natural plant-based compounds like curcumin. They have shown some effectiveness in the treatment of hypercholesterolemia. In one small trial, daily treatment of 500 mg of curcumin for one week resulted in a substantial 33% reduction in lipid peroxides, a 29% rise in HDL cholesterol, and a 12% reduction in total body cholesterol. Another research found that taking 10 mg of curcumin twice a day reduced blood LDL while increasing HDL level [35], renal disease [7, 36, 37], and diabetes mellitus [38, 39, 40].

Curcumin work as anti-depressing agent

Turmeric can also reduce anxiety [41, 42, 43]. Stress-induced reductions in 5-hydroxyindoleacetic acid, noradrenaline, dopamine concentrations and serotonin, as well as increased serotonin turnover, are mediated by its ethanolic extract. Additionally, Aquatic stress-induced increases in blood corticotropin-releasing factor and cortisol levels in mice were significantly decreased by this extract, regulating their neurochemical and neuroendocrine systems [43]. Platelet aggregation is inhibited, and eicosanoid production is modulated. Because of their eicosanoid-modulating properties and their ability to prevent platelet aggregation caused by arachidonate, adrenaline, and collagen [44].

Curcumin plays effective role on carbohydrate metabolism

Curcumin has gotten a lot of interest in the recent decade for its anti-diabetic characteristics [1], which has led to a lot of study, mostly in *in vitro* and *in vivo* animal models. Curcumin's ability to interact with a number of important molecules and processes involved in diabetes mellitus pathophysiology and its consequences has been linked to its wide spectrum of beneficial effects. Theracurmin (a formulation that increases the bioavailability of curcumin when given orally to rats [45] was recently discovered to improve glucose intolerance in rats, this effect was accompanied by increased plasma GLP-1 levels [46]. GW1000 is a G protein-coupled receptor (GPR) 40/120 antagonist, as well as the phospholipase C inhibitor neomycin, both blocked the enhanced secretion of GLP-1, showing that the increased secretion of GLP-1 is likely mediated by a cAMP-independent GPR40/120 pathway. GLP-1 secretion would result in insulin release, which would reduce glucose levels[47]. Curcumin's effectiveness has been studied in a number of *in vivo* and *in vitro* insulin resistance models; for example, curcumin reduced insulin resistance in rats with metabolic syndrome and polycystic ovarian syndrome [47] and in cultured human liver HepG2 cells [48]. Curcumin has also been examined in animal models of the disease, with results indicating that it can reduce insulin resistance by activating the IRS/PI3K/Akt pathway and increasing insulin receptor expression [49]. Insulin's effect on its receptor usually promotes this pathway, which is important for glucose metabolism and transport [49]. The PI3K/Akt/GSK-3b pathway is important in glucose metabolism, and its dysfunction is linked to the development of metabolic diseases [50]. GSK-3b, in example, is an enzyme that inhibits glycogen synthase via phosphorylation, and it is considered to be a potential curcumin target since curcumin fits into the enzyme's binding pocket, according to simulated docking tests [51]. This binding inhibits GSK-3b in a dose-dependent manner, resulting in increased glycogen synthesis in the liver of fasting mice [51]. Curcumin has also been shown to protect cultured new-born rat cardiomyocytes from apoptosis caused by high glucose levels by increasing phosphorylation of Akt and GSK-3b [50]. Curcumin lowered glucose blood levels and cardiac dysfunction in a rat model of type 2 diabetes, as well as other heart parameters like fibrosis, oxidative stress, inflammation, and apoptosis; all of these results were related to curcumin-induced activation of Akt and GSK-3b [52]. Obesity is recognised to be connected to diabetes mellitus [53], and adipokines released by adipose tissue are linked to insulin resistance and glucose homeostasis/ dyshomeostasis [54]. In this aspect, leptin is a hormone that, among other things, acts on the brain to reduce appetite and improve insulin sensitivity [55]. However, a condition known as leptin resistance can be present in the characteristics of obesity/hyperleptinemia/diabetes mellitus, resulting to overeating, fat storage, and a variety of changes in lipid and glucose metabolism[55]. Another technique has been to combine curcumin (150 mg/kg for 45 days) with zinc, which resulted in the complex having greater anti-diabetic characteristics than curcumin or zinc alone when given to diabetic rats [56]. In a model of streptozotocin-induced diabetes in rats, this formulation was tested and compared to "native curcumin". It was shown to be more resistant to deterioration and to give a higher quality product. *In vitro* tests showed that it was more effective than "natural curcumin" at lowering fasting glucose levels in rats, and it was also superior in the oral glucose tolerance test[57]. Both formulations analysed lowered triglyceride and cholesterol levels in the same way, but had no effect on insulin levels in pancreatic tissue. Both of these transcription [57] factors are required for the survival, proliferation, and functioning of b-pancreatic cells [58, 59]. Curcumin nano formulations increased gene expression of pancreatic duodenal homeobox-1 (Pdx-1) and NK6 homeobox-1 (Nkx6.1) to greater levels than controls [57].

Curcumin paly effective on lipid metabolism

In numerous *in vitro* and animal models, curcumin has been demonstrated to block leptin activities and reduce its levels [60]. In adipocytes treated to an ethanolic turmeric extract [61], found a reduction in fat formation and leptin levels, as well as enhanced lipolysis and expression of adipose triglyceride lipase and hormone-sensitive lipase. In comparison to controls, rats fed a high-fat cholesterol diet increased their leptin plasma levels and body weight [61]. Curcumin inhibits the phosphorylation of extracellular signal-regulated kinases (ERK), JNK, and p38, as well as the transcription factors CCAAT-enhancer-binding protein a (C/ EBP a) and peroxisome proliferator-activated receptor g (PPARg), all while stimulating the Wnt/b-catenin signalling pathway [62]. Because curcumin inhibited fatty acid synthase and increased hepatic fatty acid b-oxidation [60], hypothesised that these activities were responsible for preventing hyperlipidaemia. Curcumin has been shown to inhibit the transcription factors sterol regulatory element-binding proteins (SREBPs) in the liver and adipose tissue *in vivo* and *in vitro* [63] because SREBPs regulate genes involved in lipid biosynthesis and clearance [64], treatment with curcumin improved the lipid profile and reduced body weight gain in mice fed a high-fat diet [63]. Because the coadjutants were employed at sub-optimal levels, the researchers attribute the observed benefits to improved bioavailability of curcumin rather than a pharmacological impact of the coadjutants [65] Regardless of the kind of formulation studied, a longer period of treatment is required, and the observed changes correspond to the lipid profile, emphasizing the potential of curcumin as a hypolipidemic drug. Because curcumin lowers triglycerides and cholesterol, this potential has been highlighted [66], and both of them could be used together as part of an integrated treatment for hyperlipidaemia-related conditions.

Curcumin plays effective role on blood parameter

Blood smear analysis of A. testudineus showed nucleated RBCs as the major cell type. RBCs in their mature state were round in form. The immature cells were spherical. Platelets (thrombocytes) were nucleated cells with a tiny size. Their cytoplasm was in the form of prolonged spikes on opposing ends. Lymphocytes, monocytes, and granulocytes were among the WBCs (eosinophils, basophils, and neutrophils). The mature lymphocytes were spherical and sparsely cytoplasmic, with a big round nucleus. The cytoplasm was more numerous in the immature ones. Furthermore, macrophages with big vacuoles in the cytoplasm were frequently seen, and these vacuoles were almost always phagosomes. The shape and structure of the cells in the blood smears of negative control

and curcumin-fed fish were identical. Curcumin-fed fish had higher haemoglobin content, RBC count, and haematocrit than control fish, but WBC count, platelet count, MCV, MCH, and MCHC were unchanged. Curcumin-fed fish had a lower WBC-to-RBC ratio. The erythrocytes and their nuclei did not alter following curcumin administration, according to cytometric studies. In Giemsa's, Schiff's, and acridine orange staining, there was no sign of hematopathology in the curcumin-fed fish. Cyclophosphamide treatment resulted in a significant rise in the frequency of MN in the positive control fish, but the negative control and curcumin-fed fish exhibited a reduction in MN frequency. The increased RBC count and haemoglobin concentration in curcumin-treated fish may aid in the effective delivery of oxygen to the tissues. Haemoglobin is known to be protected against oxidation by curcumin [67]. Curcumin can be a safe feed supplement in the aquaculture, according to data on haematocrit (the percentage of blood by the volume occupied by red cells), MCV (the average size of RBC expressed in femtoliters), MCH (average amount of Hb inside an RBC expressed in pictograms), and MCHC (the average concentration of Hb in RBCs expressed as a percent). WBCs play an important part in the fish defence, and a rise in WBC count might suggest a pathologic state [68]. In Aeromonas hydrophile-infected Cyprinus carpio [69], found that WBC numbers increased whereas RBC, haemoglobin (Hb), and haematocrit/packed cell volume (PCV) counts declined dramatically. The WBC count remained unaffected in this investigation, ruling out the possibility of infection. Azadirachta is an example of a single and combined medicinal plant ingredient. Turmeric use may boost the non-specific immune system and provide long-term protection [70].

Conclusion

Curcumin has long been used as a flavour and food colouring agent, as well as a component in a variety of Ayurvedic and Chinese medicine therapeutic treatments. It Curcumin has gotten a lot of coverage because of its numerous health advantages, which appear to be mostly due to its positive biological processes. Science has demonstrated over time that curcumin has a variety of beneficial impacts on human health. Curcumin is still consumed as a culinary ingredient today, but contemporary technology has allowed it to be applied in a variety of food and health-related applications. According to study, curcumin may improve in the treatment of inflammatory and oxidative illnesses, hyperlipidaemia and arthritis, metabolic syndrome anxiety. It may also effectively treat muscle soreness and letting athletes and exercise-induced inflammation to recover more quickly and perform better. Furthermore, even a little dosage can give health advantages to persons who do not have a recognised health problem.

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