Review Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2024.58.009110

Turmeric and Its Novel Properties in Healthcare

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ARTICLE INFO

Received: July 18, 2024

Published: August 09, 2024

Citation: Sana kanwal, Zoya Ahmed and Asma Saghir Khan. Turmeric and Its Novel Properties in Healthcare. Biomed J Sci & Tech Res 58(1)-2024. BJSTR. MS.ID.009110.

ABSTRACT

Since the development of mankind, turmeric has been used in traditional medicine. India is a leader in the production, marketing and export of turmeric and its value – added products. Curcuma longa (turmeric) is an Indian rhizome medicinal plant belonging to the Zingiberaceae family that is common and widely available worldwide. The Component of turmeric are curcumin, demethoxycurcumin and bisdemethoxycurcumin and are collecting called Curcuminoids. The scientific community has generally studied curcumin, the active ingredient of turmeric, its broad antioxidant activity, anti-inflammatory and anti-Cancer properties, anti-syndrom effect, neuroprotective effect, antimicrobial effect, anti-arthritic effect, antiviral effect, anti-asthma and anti-diabetic effect, anti-obesity, protection of heart and liver toxicity, anti-depressant and anti-anxiety effect. Turmeric has been widely used as a typical home remedy for cough, sore throat and respiratory diseases, and it can be an effective immune booster against SARS-Cov Of 2 during the current pandemic. Safety evaluation studies show that both turmeric and curcumin are well tolerated at very high doses without toxic effects. Thus, turmeric and its components have the potential to develop modern medicine to treat various diseases. So, in this review, we describe the various metabolic roles and effects of curcumin on human health [1-5].

Keywords: Turmeric; Health Benefits; Human Health; Novel Properties

Abbreviations: CAGR : Compound Annual Growth Rate; DMC: Demethoxycurcumin; BDMC: Bisdemethoxycurcumin; SOD: Superoxide Dismutase; GSH: Glutathione Peroxidase; TNF: Tumor Necrosis Factor; NF-B: Nuclear Factor; HBV: Hepatitis B Virus; HCV: Hepatitis C Virus; HuNoV: Human Norovirus; RSV: Respiratory Syncytial Virus; HSV: Herpes Simplex; IMPDH: Inosine Monophosphate Dehydrogenase; HO-1: Heme Oxygenase-11; NAFLD: Non-Alcoholic Fatty Liver Disease; BMI: Body Mass Index; GSH: Glutathione; GPx: Glutathione Peroxidase; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; ALP: Alkaline Phosphatase; MDCK: Madin-Darby Canine Kidney; HA: Hemagglutination

Introduction

Turmeric is used as a spice and traditional medicine to treat swelling, anxiety, chronic inflammation and digestive problems. Large preclinical studies have shown that turmeric and its biologically active Curcuminoid polyphenols can treat a variety of chronic diseases. Global production of turmeric is projected to increase to 1.5 million tons by 2027. The "Global Turmeric Industry "is reported to grow at a compound annual growth rate (CAGR) of approximately 3.9 percent during the period 2020-2027. Some of the divisions analyzed in the report are expected to register an average CAGR of 4 percent, reaching one million tons even at the end of the analysis period. According to forecasts, development of the pharmaceutical industry and other segments will increase to 3.6 percent over the next seven years The US Market is predicted to grow to perhaps 302.9 thousand tons, while China's CAGR is expected to be 7%. By 2027. China project a market size of 313.8 thousand tons, which represents a CAGR of 7% during the analysis period 2020-2027. Global Turmeric Market Forecasts 2012-2027. In 2016, the global Turmeric Market was valued at approximately $3.16 billion. Between 2020 and 2027, Japan is estimated to grow by 1.2 percent and Canada by 3 percent. While Germany is projected to have a CAGR of 2 percent. India has the largest number of turmeric growers, consumers and suppliers in the world. Due to the high quality of curcumin Indian turmeric is considered the best graded turmeric [6-15].

The export regions for turmeric India, Thailand, Taiwan and southeast Asia, Central and Latin America. Major importers of turmeric are Japan, SriLanka, Iran, the United Arab Emirates, the United States, the United Kingdom and Ethiopia. Telangana, Andhra Pradesh, Tamil Nadu, Karnataka, Odisha, West Bengal and Maharashtra are the major turmeric producing states in India. Statistics for 2018-2019 show that even in India, the turmeric –growing state of Telengana had 47.888 hectares, up from 44,956 hectares last year. The initial stocks were 2018-2019. Low production status. Possible incentive of the production, export and import of turmeric for pharmaceutical use may be due to active compounds such as curcumin, demethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC), collectively known as curcuminoidsm. These Curcuminoids were isolated from the rhizomes of the turmeric plant and were usually yellow in color. Curcumin with a low relative molecular weight, is one of the most interesting components of Curcuminoids and polyphenolic compound. At the acidic PH of the stomach, curcumin is stable [16-25]. Natural compounds. Including tumerone, atlantone, zingiberone, sugars, proteins and resins are other constituents. It is a tautomeric compound found in organic solvents and water as an enol and a keto. Turmeric is usually finger- like with bulbs and caps 2-8 cm long and 1.2cm wide. After harvesting, the rhizomes are dried and further processed to produce turmeric powder.

Nutritional and Chemical Composition of Turmeric

A rich source of carbohydrates and fiber is turmeric, which contains some protein and fat, but is completely free of cholesterol. In addition, it contains sufficient amounts of pyridoxine, vitamin C, potassium, calcium, magnesium and phosphorus, which are said to be a nutritionally effective natural food. Turmeric contains a wide variety of molecular components, each of which has a different biological effect. In total, approximately 326 biological activities have been identified for turmeric]. The most studied elements are curcuminoid polyphenols, which consisted of curcumin, bisdemethoxycurcumin and demethoxycurcumin [26]. Organic solvents are used to extract curcumin because it is insoluble in water. A method was developed to isolate curcumin from ground turmeric and thin-layer chromatography analysis was performed to confirm the presence of different components. They also showed that turmeric contains a large number of constituents Table 1.

Table 1: Turmeric -Nutritional Facts per 100g.

Nutrients	Amount	Percentage
Folates	39µg	10%
Niacin	5.140 mg	32%
Pyridoxine	1.80 mg	138%
Riboflavin	0.233mg	18%
Vitamin A	0.1U	0%
Vitamin C	25.9mg	43%
Vitamin E	3.10mg	21%
Vitamin K	13.4µg	11%
Sodium	38mg	2.5%
Potassium	2525mg	54%
Calcium	183mg	18%
Copper	603µg	67%
Iron	41.42mg	517%
Magnesium	193 mg	48%
Manganese	7.83 mg	340%
Phosphorus	268 mg	38%
Zinc	4.35 mg	39.5%

Benefits of Curcumin on Human Health

Antioxidants: Curcumin plays an important role in the repair of oxidative damage. There have been some studies showing that antioxidants such as superoxide dismutase (SOD) can increase serum activity. Some results of randomized controlled trials on the effectiveness of purified curcuminoid supplementation on oxidative stress markers showed that curcuminoid supplementation would have a significant effect on all investigated oxidative stress markers, such as SOD and catalase plasma behavior and glutathione peroxidase (GSH) serum. levels. It is important to note that all studies included in the meta-analysis used a specific formulation to address bioavailability concerns, and four of the six used piperine [27-35]. Thus many different mechanisms contribute to the action of curcumin on reactive oxygen species. Different forms of free radicals such as reactive oxygen

species and nitrogen species can be scavenged. This can impair the activity of oxidative neutral proteins such as GSH, catalase and SOD. it might as well. reduces ROS-producing enzymes such as lipoxygenase/cyclooxygenase and xanthine hydrogenase/oxidase.

Anti-Inflammatory Agent: In many human chronic diseases, the role of oxidative stress and its effective pathological processes are closely related to inflammation. Inflammatory cells are known to produce some free radicals at the site of inflammation, leading to inflammatory responses, suggesting a link between oxidative stress and inflammation. In addition, several reactive oxygen/nitrogen species can initiate an intracellular signaling pathway that increases proinflammatory gene expression. Inflammation has been implicated in the development of many cancers [36]. In most diseases, tumor necrosis factor (TNF) is an important regulator of inflammation, but this effect is regulated by stimulation of the transcription factor nuclear factor (NF-B), while TNF becomes the most powerful stimulator of NF-B. NF-B also controls TNF expression and is triggered by most inflammatory cytokines; gram negative bacteria; viruses that cause various diseases. Curcumin can inhibit NF-B activation and contributes to its mechanism of action as a potential anti-inflammatory agent [37-50].

Anti-Cancer Agent: About a fifth of all deaths are caused by various types of cancer worldwide. Genetic and epigenetic changes culminating in apoptosis, uncontrolled tumor growth, metastasis, and angiogenesis are the causal agents of cancer. The beneficial effects of curcumin on cancer have recently been widely investigated, with significant advances in gastrointestinal, breast and lung cancers. The anticancer effects of curcumin alone or in combination with conventional chemotherapy agents have been reported in several studies on cancer treatment. *In vitro* and *in vivo* experiments have also shown that curcumin inhibits carcinogenesis by affecting tumor growth and angiogenesis. Curcumin aptamers contain a sulfone that significantly inhibits tumor growth in human prostate, colon, lung, and pancreas [51].

Antimetabolic Syndrome: Beyond arthritis, the whole idea that curcumin can help alleviate systemic inflammation is directly related to the condition of various systems. Metabolic syndrome, characterized by insulin resistance, hyperglycemia, hypertension, cholesterol, high triglycerides, and obesity, especially visceral obesity, is one such disease. Curcumin has been shown to reduce several forms of cardiovascular disease by improving insulin sensitivity, reducing adipogenesis, and reducing blood pressure, Inflammation and oxidative stress [52-60]. Recent studies have shown that curcuminoids modulate gene coding and enzyme expression in lipid metabolism, ultimately resulting in a decrease in plasma triglyceride and cholesterol levels and an increase in high lipoprotein Cholesterol. Obesity and overweight are also associated with lower chronic inflammation; and although the exact mechanisms are not specific, the production of pro-inflammatory cytokines has been reported. These cytokines are believed to be at the heart of diabetes and cardiovascular problems.

Antimicrobial Agent: Turmeric is an antimicrobial agent for life-threatening bacterial infections. The use of essential oil obtained from turmeric leaves significantly reduces the growth of fungi, the production of aflatoxins B1 and G1. Although curcumin is a very active substance, its reduced solubility in water makes its use difficult. Nano-curcumin disrupts the cell wall and leads to complete bacterial death [61]. A combination of epigallocatechin gallate (EGCG) and turmeric can be added to the medication to prevent or control Acinetobacter baumannii infections. Elimination of Acanthamoeba castellanii is difficult because amoebae are resistant to anti-amoebic drugs. Amoebicidal activity of ethanolic extracts of plant varieties including narcissus, peanut and turmeric was evaluated on Acanthamoeba castellanii cysts [62]. The researchers found confirmed results of the inhibitory effect of the extract on the proliferation of Acanthamoeba cysts, but the effect was time- and dose-dependent [63].

In addition, a mouthwash with turmeric can be successfully used to prevent plaque and gingivitis. Additionally, turmeric mouthwash was found to significantly reduce total microbial counts. In addition, turmeric inhibits the growth of Bacillus subtilis and Escherichia coli by limiting the accumulation of temperature-sensitive Z mutants (Fts Z) by inhibiting Fts Z polymerization [64-70]. Curcumin also dose-dependently reduces adhesion and cell proliferation. It significantly reduces the cytotoxicity of Vibrio vulnificus to HeLa cells by inhibiting the growth of *V. vulnificus*. Curcumin impairs bacterial adhesion, and RTX toxin binding to host cells resulted in inhibition of host cell rounding and actin aggregation. Curcumin can reduce Vibrio vulnificus by inducing translocation in specific HeLa cells that proliferate abnormally. In addition, a wide range of antiviral effects of curcumin has also been reported. Several other studies have been conducted on its mechanisms against various human immunodeficiency viruses (HIV). Curcumin has been shown to inhibit HIV-1 integrase [71,72]. In addition, this polyphenol and its analogues can prevent the infection and reproduction of viral genes. They inhibit HIV protease and HIV-related kinases (eg, tyrosine kinase). Curcumin also interacts with biomedical drugs. In particular, curcumin inhibits the reducing activity of Apurinic/Apyrimidine endonuclease-1. As a result, it affects many different genes and pathways. It has been found that curcumin can inhibit the replication of the Kaposi's sarcoma-associated herpesvirus and ultimately control the resulting pathological processes (eg, angiogenesis). Researchers have also reported anti-influenza activity of organic components of the turmeric plant. It can fight influenza A virus (IAV) by preventing its adsorption and replication.

Arthritis Rheumatoid Arthritis (RA): It is a chronic inflammatory disease thought to be an overgrowth of joint fibroblasts. Curcumin is known for its powerful anti-inflammatory and anti-arthritic properties. Curcumin treatment was performed in real time in patients with active RA and compared with a diclofenac sodium control group. The curcumin group has the highest percentage of improvement in RA and these values are significantly improved compared to

diclofenac sodium patients [73-79]. The curcumin group was found to be safe and healthy compared to the diclofenac sodium group. The antioxidant, anti-inflammatory, anti-proliferative and immunosuppressive effects of curcumin are believed to be common in improving symptoms in patients with RA.

Antiviral Papillomavirus: (HPV), Hepatitis B Virus (HBV), Influenza Virus, Hepatitis C Virus (HCV), Adenovirus, Coxsackie Virus, Human Norovirus (HuNoV), Respiratory Syncytial Virus (RSV) and Herpes Simplex 1 (HSV)-1) can be improved by curcumin. Curcumin contains graphene oxide, which has synergistic antiviral activity against respiratory syncytial virus infection. Respiratory syncytial virus (RSV) occurs in the lower respiratory tract of infants and causes severe lung disease. Curcumin also has a dose-dependent antiviral effect. Curcumin inhibits the enzyme inosine monophosphate dehydrogenase (IMPDH) in either a noncompetitive or competitive manner. Viral entry or other steps in the life cycle involve the curcumin mechanism rather than viral RNA replication. Thus, IMPDH should be inhibited for curcumin to exert its potential antiviral, antiproliferative and antiparasitic effects [80-86].

Medications for Asthma and Diabetes: Curcumin reduced nasal congestion, relieving cough, cold and flu symptoms. It also increases IL-4, IL-8 and tumor necrosis factor-alpha, and increases IL-10 levels and soluble intercellular adhesion molecules. Curcumin prevented allergic airway nasal irritation and preserved structural integrity in allergic asthmatic mice. The antioxidant properties of curcumin may be associated with enhanced antidiabetic effects. In their study, the researchers looked at the beneficial effects of curcumin by reducing superoxide production and vascular protein kinase C reserve in the development of endothelial dysfunction induced by diabetes. New studies have already miraculously demonstrated the ability of curcumin to immediately quench reactive oxygen species (ROS), which can contribute to oxidative damage. Such a property has been recognized to enhance the specific protective properties of curcumin. Curcumin can alleviate oxidative stress-induced cell death by engaging and activating antioxidant/cytoprotective enzymes such as heme oxygenase-11 (HO-1). Some of the emerging therapeutic opportunities for HO-1 in the treatment of diabetic diseases may lie in the protective mechanisms of HO-1 in diabetes [87,88].

Protective Measures Against Obesity and Cardio-Hepatotoxicity: Promising findings that curcumin increases lipids and fat in preserved humans help understand that it actually helps improve obesity. They first investigated the effects of oral curcumin products on lipid profile parameters, basal metabolic rate and glucose levels in obese subjects. Findings showed significant changes only in triglyceride levels, while other parameters remained constant after 30 days of curcumin treatment. A study looking at such variables in patients with non-alcoholic fatty liver disease (NAFLD) also recorded body mass index (BMI) and weight loss. Results also showed that 4 weeks of 2.8 g/day turmeric supplementation does not actually change oxidative stress or inflammatory parameters in obese women with systemic inflammatory markers, nor cause significant changes in the metabolic Profile. Researchers use different animal models with physicochemical markers such as serum marker enzymes and antioxidants in peripheral tissues to evaluate the preventive effect of curcumin in confirmed hepatotoxicity and cardiotoxicity experimental data to evaluate increased lipid peroxidation, decreased glutathione (GSH), glutathione peroxidase (GPx) levels. and superoxide dismutase (SOD) marker enzymes, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) in edematous, granulomatous, liver, and cardiac tissues during liver injury and cardiac necrosis.

Depression and Anxiety: Different clinical trials have evaluated the effects of oral curcumin on mental health problems. In such studies, curcumin was taken orally at 500–1000 mg regularly, alone, with bioperine or even in combination with escitalopram venlafaxine or fluoxetine and conventional antipsychotics. The studied people showed a very clear improvement in depression-related diseases in all tests evaluated by the appropriate scales. The only exception was an approved study where curcumin administration reduced nervousness but not despair, which may have been a sign of the shortest administration time (30 days versus 5-8 weeks in other studies).

Possible Use of Turmeric and Its Extracts in the Treatment of SARS-CoV-2

Since December 2019, the epidemic of the disease SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus 2) has rapidly spread across the planet. There are hardly any specific medications or vaccines approved to treat or prevent it. Until now, both antiretroviral capsules and hydroxychloroquine, etc., have been used for treatment. Various curcumin derivatives have antiviral properties. A neuraminidase stimulation assay shows that five active derivatives of the curcumin supplement reduced H1N1-induced neuraminidase activation in H1N1-infected lung epithelial cells. This activation of the same nucleoprotein is even regulated by tetramethyl-l-curcumin and curcumin. Significant antiviral activity of turmeric against H5N1 virus is also determined in Madin-Darby canine kidney (MDCK) cells *in vitro* by inhibiting the activity of infectious hemagglutination (HA), which may be useful in recent outbreak conditions. The effects of H5N1 antiviral infection and turmeric extracts were demonstrated by upregulation of both TNF-alpha and IFN-β mRNA expression in MDCK cells examined as complete antiviral agents. Due to its inhibitory effect on HIV protease and integrase, curcumin is also useful in other viral problems such as AIDS. Other pathogens such as hepatitis B, hepatitis C, zika, chikungunya, dengue etc. also have an inhibitory effect on curcumin. The most common cause of mortality in COVID-19 is respiratory syndrome with fulminant hypercytokinemia and multiple organ failure. Curcumin has been reported to reduce lung tissue damage induced by influenza virus by suppressing NF-umB signaling and inhibiting the release of inflammatory cytokines [89-95].

Safety And Toxicity or Side Effects of Curcumin: The safety of curcumin has also been studied *in vitro*, in animal models, and in drug tests. According to a detailed review of this topic, the organism is not poisonous. Studies with cultured cells have shown that «curcumin can reduce the growth of probiotics and exert anti-proliferative effects on healthy cells.» There is really little evidence of genotoxicity and mutagenicity. In humans, the same curcumin is safe to take orally. Shortness of breath, red tongue, atrial fibrillation, and gastrointestinal problems (eg, flatulence, diarrhea, nausea, and constipation) have been reported in a small percentage of cases. Indeed, there is a problem of biocompatibility with intravenous curcumin, so it should be taken at a lower dose than orally [96]. It should be mentioned that curcumin can trigger pharmacokinetic changes of some types of cardiovascular drugs, antibiotics, antidepressants, chemotherapy drugs, immunosuppressants and corticosteroids. Therefore, its simultaneous availability with other collectivistic drugs should be regularly determined. Weight gain of F2 generation offspring is slightly reduced during the weight-bearing period when oral curcumin is about 1000 mg/kg of body weight as reported in one report [97].

The same safety of such modern mixtures must be considered when interpreting drug delivery techniques to enhance the bioactivity of turmeric. For example, if carriers or surfactants are used as a biocompatibility agenda, the product may be toxic. Although most of such innovative technologies appear to be safe, with no adverse effects on osteosarcoma patients or healthy populations, a solid lipid curcumin formulation has no adverse effects. Poly(N-isopropylacrylamide) delivery network is another different framework for expressing curcuminoids through the nose to the brain. Dipeptide curcumin nanomaterials are too safe [98]. The dipeptide is made of alpha-, beta-dehydrophenylalanine and methionine, which are conveniently and safely soluble in nature. In addition, curcumin-loaded serum albumin nanoparticles showed almost no toxic effects during arterial administration in all HCT116 tumor xenograft models. A new study on intravenous curcumin showed that rabbits in the total curcumin nanosuspension group were less likely to experience local irritation and phlebitis and red blood cell hemolysis than those in the curcumin solution group.

Conclusion

Curcumin is known worldwide for its antioxidant, anti-inflammatory properties and other potential public health benefits. It improves bioavailability together with curcumin and piperine. Curcumin can also treat oxidative, inflammatory, metabolic, arthritis, anxiety and hyperlipidemic diseases. Exercise-induced inflammation and muscle soreness are monitored and intensified by inactive individuals during rehabilitation and performance levels. It is also really helpful for people who have not yet successfully treated any disease. The root is the essence of turmeric and contains more than enough bioactive compounds, vitamins and minerals to make it the safest herb. It is also used during pregnancy and in case of kidney or liver failure in lactating women. It contains curcumin, the main bioactive element, which contains certain substances such as atlantocurcuminoid, demethoxycurcumin, diarylheptanoid, tumerone and the diferuloylmethane flavonoid curcumin. They have antibacterial, anti-inflammatory and antioxidant effects that protect against various cellular damages. In addition, turmeric successfully treats mental diseases such as Parkinson's and Alzheimer's. It is also effective in metabolic syndrome and various cancers. In conclusion, it can be added to the diet to control many human diseases. A large outbreak of the highly contagious novel coronavirus (COVID-19) in China in December 2019 has spread globally into a new pandemic [99,100].

It is caused by the new coronavirus SARS-CoV-2 (severe coronavirus 2 acute respiratory syndrome) from the Coronaviridae family. There is currently no specific antiviral treatment available for patients with COVID-19. Physicians in developing countries have considered combination therapy that includes antivirals, antibiotics, and anti-inflammatory drugs. The use, including hydroxychloroquine, was extensive. In addition, the role of curcumin in the action of RAAS components (renin-angiotensin-aldosterone system), through which antioxidant, anti-inflammatory and antimicrobial effects are known, has also been thoroughly studied. Animal models have suggested a role for curcumin in the regulation of ACE and AT1R in brain tissue and vascular smooth muscle cells, which normally result in blood pressure and oxidative stress effects in animals by inhibiting angiotensin II-AT1R, respectively. In order to achieve a better understanding and moral judgment of its use in medical care, further research is needed for its implementation in the future.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2024.58.009110

Asma Saghir Khan. Biomed J Sci & Tech Res

Submission Link: https://biomedres.us/submit-manuscript.php