

ISSN Online: 2158-2750 ISSN Print: 2158-2742

The Golden Spice Turmeric (Curcuma longa) and Its Feasible Benefits in Prospering Human Health—A Review

Jyoti Prakash Sahoo¹*, Laxmipreeya Behera¹*, Jannila Praveena², Shraddha Sawant³, Ankita Mishra⁴, Siddhartha Shankar Sharma⁵, Lipi Ghosh⁶, Ambika Prasad Mishra⁻, Asit Ranjan Sahoo¹, Pranay Pradhan⁶, Subhasmita Sahu⁶, Ankit Moharana¹ჿ, Kailash Chandra Samal¹

How to cite this paper: Sahoo, J.P., Behera, L., Praveena, J., Sawant, S., Mishra, A., Sharma, S.S., Ghosh, L., Mishra, A.P., Sahoo, A.R., Pradhan, P., Sahu, S., Moharana, A. and Sama, K.C. (2021) The Golden Spice Turmeric (*Curcuma longa*) and Its Feasible Benefits in Prospering Human Health—A Review. *American Journal of Plant Sciences*, 12, 455-475.

https://doi.org/10.4236/ajps.2021.123030

Received: February 8, 2021 Accepted: March 28, 2021 Published: March 31, 2021

Abstract

From the evolution of the mankind, Turmeric has been used in conventional medication. India is in lead for producing, marketing and exporting the Turmeric and its value added products. *Curcuma longa* (Turmeric) is an Indian rhizomatous medicinal herb from the Zingiberaceae family that is common and widely available across the globe. The components of Turmeric are curcumin, demethoxycurcumin and bisdemethoxycurcumin and these are collectively known as curcuminoids. Curcumin, the active ingredient of Turmeric is generally investigated by the scientific community for its wide range of antioxidant activity, anti-Inflammatory properties and anti-cancer activity, anti-metabolic syndrome activities, neuroprotective activity, antimicrobial effects, anti-arthritis effects, anti-viral effects, anti-asthma and anti-diabetic effects, anti-obesity, cardio and liver toxicity protection activity, anti-depression

¹Department of Agricultural Biotechnology, Odisha University of Agriculture and Technology, Bhubaneswar, India

 $^{^2} Department \ of \ Fruit \ Science \ and \ Horticulture \ Technology, \ Odisha \ University \ of \ Agriculture \ and \ Technology, \ Bhubaneswar, \ India$

³Department of Plant Pathology, Odisha University of Agriculture and Technology, Bhubaneswar, India

⁴Department of Plant Breeding and Genetics, Odisha University of Agriculture and Technology, Bhubaneswar, India

⁵Department of Genetics and Plant Breeding and Seed Science & Technology, Centurion University of Technology and Management, Parlakhemundi, India

⁶School of Development Studies, Tata Institute of Social Sciences, Mumbai, India

⁷Department of Soil Science and Agricultural Chemistry, Faculty of Agriculture, Sri Sri University, Cuttack, India

⁸Department of Nematology, Odisha University of Agriculture and Technology, Bhubaneswar, India

⁹Department of Floriculture and Landscaping, Odisha University of Agriculture and Technology, Bhubaneswar, India

 $^{^{10}} Department \ of \ Seed \ Science \ and \ Technology, \ Odisha \ University \ of \ Agriculture \ and \ Technology, \ Bhubaneswar, \ India \ Email: \ "jyotiprakashsahoo 2010@gmail.com, \ "klaxmipreeyal@gmail.com"$

Copyright © 2021 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

http://creativecommons.org/licenses/by/4.0/





and anxiety activities. Turmeric has been widely used as a typical household treatment for cough, sore throat, respiratory ailments and could be an effective immunity booster against SARS-CoV-2 therapy during the ongoing pandemic situation. Safety evaluation studies indicate that both turmeric and curcumin are well tolerated at a very high dose without any toxic effects. Thus, turmeric and its constituents have the potential for the development of modern medicine for the treatment of various diseases. So in this review, we describe the various metabolic roles of curcumin and activities for the benefit of human health.

Keywords

Turmeric, Plant Extracts, Curcumin, Medicinal Properties, SARS-CoV-2, Immunity

1. Introduction

Turmeric is being used as a spice and a traditional medicine for the treatment of swelling, distress, chronic inflammation and gastrointestinal problems. Significant preclinical studies have shown that a variety of chronic conditions could be addressed by Turmeric and its biologically active curcuminoid polyphenols. Global turmeric output is projected to reach 1.5 million metric tonnes by 2027. It has been reported over the period 2020-2027 (https://www.reportlinker.com/ p05960349/Global-Turmeric-Industry.html) that, the "International Turmeric Industry" will grow at a compound annual growth rate (CAGR) of around 3.9 percent. An average 4 percent CAGR is expected to be recorded by a few of the divisions analysed in the report and reaches 1 million metric tonnes even by end of the analysis duration. The development in the pharmaceuticals & other segments are projected to be updated to a 3.6 percent CAGR over the next 7 years. It is projected that perhaps the U.S. market will grow at 302.9 thousand metric tonnes, while China is expected to grow at 7% CAGR (https://www.reportlinker.com/p05960349/Global-Turmeric-Industry.html). By 2027, China has projected the size of the market of 313.8 thousand metric tonnes, which represents a 7 percent increase in CAGR over the 2020 to 2027 analysis period. The 2012-2027 turmeric global market projections (Figure 1) show the value of the international turmeric market in 2012 and 2016 and provide a forecast for 2027. The global turmeric market was valued at about US\$3.16 billion in 2016 (https://www.statista.com/statistics/ 740259/global-turmeric-market-volume/). In Japan and Canada, over the 2020-2027 period, growth is estimated at 1.2 percent and 3 percent, respectively, whereas Germany is projected to grow at 2 percent CAGR. India has the world's largest number of farmers, consumers and suppliers of turmeric. Because of the condition of elevated curcumin quality, Indian Turmeric is regarded as the best graded (https://www.reportlinker.com/p05960349/Global-Turmeric-Industry. html). The main Turmeric exporting areas are India, Thailand, Taiwan, and

Southeast Asia, Central, and Latin America (https://economictimes.indiatimes. com/topic/Turmeric-market). The largest importers of Turmeric are in Japan, Sri Lanka, Iran, the UAE, the United States, the United Kingdom and Ethiopia (https:// economictimes.indiatimes.com/topic/Turmeric-market). Telangana, Andhra Pradesh, Tamil Nadu, Karnataka, Odisha, West Bengal and Maharashtratra are the major turmeric producing states in India. The 2018-2019 statistics show that even in India, 47,888 hectares were covered by government of Telengana growing turmeric compared to 44,956 hectares last year. The beginning stocks were reported to be around 1.32 lakh tonnes as per Turmeric supply figures presented in Figure 2 for 2018-19, while end stocks were only about 0.71 lakh tonnes due to increase in the number of internal demand and export for the year 2018 under a low production condition (https://economictimes.indiatimes.com/topic/Turmericmarket). The potential incentives for the production, exports and imports of Turmeric for pharmaceutical usage could be attributed to the presence of active compounds such as curcumin, demethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC) which are collectively known as curcuminoids [1] [2]. These curcuminoids were isolated from rhizomes of Turmeric plant and generally vellow in colour [3]. Curcumin, which has a small relative molecular mass, is one of the most interesting components of the curcuminoid, and is a polyphenolic compound. At the acidic pH of the stomach, curcumin is stable. Natural compounds, including tumerone, atlantone, zingiberone, sugars, proteins and resins are the other constituents present [4] [5]. It is a tautomeric compound found in organic solvents and water within the enolic and keto form. Turmeric is usually like fingers with bulbs and splits, 2 to 8 cm long and 1 to 2 cm wide. After harvesting, rhizomes are dried and further refined in order to acquire the Turmeric in powder form.

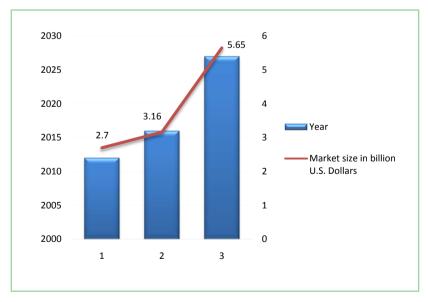


Figure 1. Global market value of Turmeric from the period 2012 to 2027 (in billion U.S. dollars).

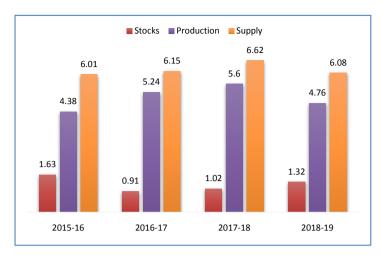


Figure 2. Status of Turmeric in India during 2018-19 marketing year (in lakh tonnes).

For its various benefits, curcumin has been used as a traditional medicine: antioxidant, anti-inflammatory, antimutagenic, antimicrobial and a number of other pharmaceutical properties [6]. Several substances are being used to increase curcumin's bioavailability, like piperine, which increases its biocompatibility by suppressing its metabolic pathway [6] [7]. Within the root extracts of turmeric, curcumin is an important component. This has been used in Asian countries as a flavouring agent and coloration agent for food and medicine [8]. There are several formulations of curcumin currently available, like pills, tablets and ointments [9]. Curcuminoids were approved as "Generally Accepted as Safe" (GRAS) [10] by the Food and Drug Administration (FDA) of the United States. Turmeric is often used in herbal based treatment for atrophic arthritis, chronic anterior uveitis, conjunctivitis, carcinoma, smallpox, chickenpox, wound healing, tract infections, and liver diseases, strengthening the body's general capacity, dissipating worms, controlling menstruation, breaking down gallstones, washing wounds, and even for various gastrointestinal issues, among many other conditions. Turmeric's chemical makeup consists of 3 percent of curcumin, 1.4 percent of demethoxycurcumin and 1.2 percent of bisdemethoxycurcumin [11] [12] [13]. Turmeric has a long history of using it as a spice in Asian cuisines, and in many other areas of the globe. Turmeric is used in countries such as China, India, Iran and Indonesia to cure human diseases and to be used as a tonic for an extended period. Curcumin has three major complexes of curcumin, i.e. curcumin I, curcumin II, and curcumin III [14] [15] [16]. The dry root portion of Turmeric has been observed to contain up to 8 curcumin [17]. The goal of this review is to have a brief overview of the health benefits of curcumin and its capacity for boosting immunity against the ongoing COVID-19 pandemic.

2. Nutritional and Chemical Composition of Turmeric

A rich source of carbohydrates and fibre is Turmeric which includes some pro-

tein and fat, but there is still a complete absence of cholesterol. In addition, this has an adequate amount of pyridoxine, vitamin C, potassium, calcium, magnesium, and phosphorus, which is reported as a natural food product which is nutritionally efficient. The brief nutritional composition of Turmeric is shown in Table 1 [18]. Turmeric has a broad variety of molecular components, each with a range of biological activities. Overall, Turmeric is identified for approximately 326 biological activities [19]. Curcuminoid polyphenols are the most researched elements consisted of curcumin, bisdemethoxycurcumin, and demethoxycurcumin (Figure 3). For the extraction of curcumin, organic solvents are used as it is insoluble in water. For the isolation of curcumin from grounded Turmeric, a methodology was designed [19] and thin layer chromatography analysis was performed to verify the presence of different components which have also shown that turmeric contains a large number of ingredients and Figure 4 indexes their percentage [20].

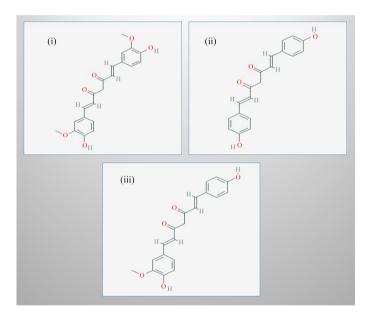


Figure 3. Curcuminoids available in Turmeric: (i) Curcumin; (ii) Bisdemethoxycurcumin; (iii) Demethoxycurcumin (https://pubchem.ncbi.nlm.nih.gov/).

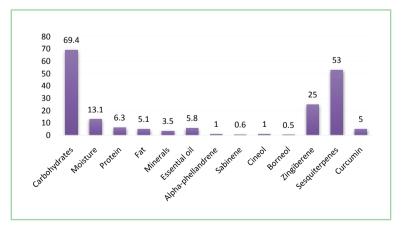
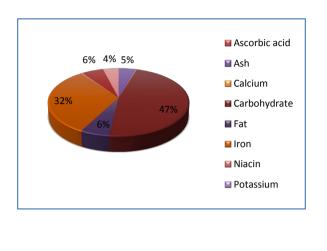


Figure 4. Percentage (%) of chemical constituents available in Turmeric.

Table 1. Nutritional composition of Turmeric.

0	0
Constituents	Quantity (g) per 100 g
Ascorbic acid	0.05
Ash	6.8
Calcium	0.2
Carbohydrate	69.9
Fat	8.9
Iron	47.5
Niacin	0.0048
Potassium	0.2
Phosphorus	0.26
Protein	8.5
Riboflavin	0.00019
Sodium	0.03
Water	6



Curcumin is likewise called diferuloylmethane and the IUPAC name of Curcumin is (1E-6E)-1,7-bis(4-hydroxy-3-methoxy phenyl)-1,6-heptadiene-3,5-dione with compound recipe C₂₁H₂₀O₆ and sub-atomic mass 368.385 g/mole [21]. In the curcumin structure, there are two oxy-subbed aryl moieties containing ortho-methoxy phenolic OH gatherings, which is connected by a seven carbon chain comprising of a β -unsaturated β -diketone moiety in which the methoxy bunch is missing from both aryl rings [22]. The reaction of hydrogen-atom donation which contributes to the curcumin oxidation process, the process of nucleophilic addition reactions, the process of hydrolysis, the degradation process and the essential enzymatic reactions are the prominent chemical reactions associated with the biological functional activity of curcumin [23]. Curcumin is hydrophobic in nature with a log P value of 3.43, but is generally not soluble in aqueous medium [24]. In polar solvents like DMSO, methanol, acetone and ethanol, the curcumin is soluble [25]. It can function as a hydrophobic reducing agent and scavenge various reactive oxygen species (ROS) and is better at suppressing the oxidative stress [26] [27]. Pharmacokinetic tests have shown that curcumin is digested to deliver sulfate and glucuronide metabolites upon oral ingestion [28].

3. Medicinal Attributes of Curcumin

3.1. Antioxidant

Curcumin plays a significant role in oxidative damage improvement [29] [30]. A few studies have been conducted that demonstrate that antioxidant such as superoxide dismutase (SOD) can increase serum activity [31]. Some results of the randomised controlled evidence relating to the effectiveness of purified curcu-

minoid reinforcement on oxidative stress markers indicated that curcuminoid reinforcement would have a significant effect on all oxidative stress markers examined, like SOD and catalase plasma behaviors, and also glutathione peroxidase (GSH) serum levels [30]. It is significant to note that certain formulation was being used by all of the studies included in meta-analysis to resolve bioavailability challenges, and four out of the six utilized piperine. So many different mechanisms affect the impact of curcumin on reactive oxygen species. Various forms of free radicals, such as reactive oxygen species and nitrogen species, could be scavenged [30]. It can attenuate the function of the oxidative neutralisation proteins such as GSH, catalase, and SOD [31]; it could also reduce the growth of ROS-generating enzymes such as lipoxygenase/cyclooxygenase and xanthine hydrogenase/oxidase [32]. A schematic view of the medicinal attributes of turmeric can be seen in Figure 5.

3.2. Anti-Inflammatory Agent

In many chronic illnesses of human beings, role of oxidative stress, as well as its effective pathological processes are closely linked to that of inflammation. Inflammatory cells are known to generate several free radicals at the inflammation site leading to inflammatory responses that shows the relationship among oxidative stress and inflammation [33]. Furthermore, an intracellular signalling pathway which improves pro-inflammatory gene expression could be initiated by a number of reactive oxygen/nitrogen species. The development of many types of cancers has identified inflammation [34]. In most disorders, tumour necrosis factor (TNF) is an important regulator of inflammation, but this effect is regulated by the stimulation of the nuclear factor (NF-B) transcription factor, whereas TNF is said to become the most powerful NF-B stimulator, TNF expression is also controlled by NF-B and triggered by most inflammatory cytokines; gram-negative bacteria; various viruses that cause disease. Curcumin has the potential to block the activation of NF-B [35] and promotes its mode of action as a potential anti-inflammatory factor.

3.3. Anti-Cancer Agent

Around one-fifth of the mortality are caused by different types of cancers globally. Genetic and epigenetic changes culminating to apoptosis, uncontrolled tumor growth, metastasis, and angiogenesis are the drivers of cancer [36]. The beneficial effect of curcumin on cancer has been extensively researched recently and important improvements resulted in gastrointestinal cancers, breast cancers and lung cancers [37]. The anti-cancer actions of curcumin alone or in combination with traditional chemotherapeutic agents are being reported in several studies for the cancer therapy [38]. *In vitro* and *in vivo* experiments have also shown that curcumin prevents carcinogenesis by influencing tumour growth and angiogenesis [39]. Curcumin aptamers contain sulfone, which greatly prevents the tumor growth in the human prostate, colon, lung and pancreas [40].

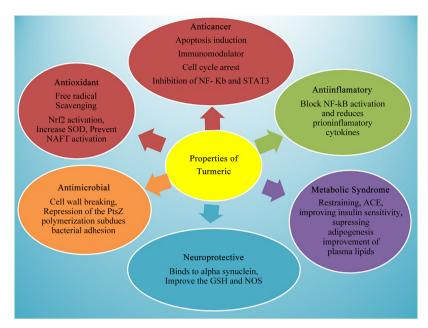


Figure 5. Schematic view of major medicinal attributes of Turmeric.

3.4. Anti-Metabolic Syndrome

Apart from arthritis, the entire concept that curcumin can help to mitigate systemic inflammation is also linked directly with the condition of various systems. Metabolic syndrome, that involves insulin resistance, hyperglycemia, high blood pressure, cholesterol, high triglyceride levels, and obesity, especially visceral obesity, is one such condition. By improving insulin sensitivity [41] [42], reducing adipogensis [43], and reducing blood pressure [44], inflammation [45], and oxidative stress [46] [47], curcumin was shown to reduce several forms of cardiovascular disease. Recent studies have shown that the curcuminoids modulate gene encoding and enzymatic expression in lipid metabolism, ultimately leading to plasma-decreased triglycerides and cholesterol as well as a boost in high cholesterol of lipoprotein [48] [49]. Obesity and overweight also are linked to lower chronic inflammation; and although precise mechanisms are not specific, pro-inflammatory cytokines are reported to be produced. These cytokines are thought to have been at the centre of diabetes and cardiovascular disease-related problems.

3.5. Antimicrobial Effects

Turmeric is an antimicrobial agent for life-threatening bacterial infections [50]. The application of essential oil derived from turmeric leaves significantly reduces fungal growth, the production of aflatoxins B1 and G1 [50]. Although curcumin is a highly active agent, its reduced water solubility impedes its applications. The nano-curcumin breaks the cell wall and leads to the complete death of the bacteria [51]. The combination of epigallocatechin gallate (EGCG) and turmeric may be incorporated into medicine to prevent or control *Acinetobacter baumannii* infections [52]. Elimination of *Acanthamoeba castellanii* is complicated

as the amoebas encyst it defiant to antiamoebic drugs. The amoebicidal activity of ethanol extracts of plant variants, including daffodil, groundnut, and turmeric has been evaluated on the Acanthamoeba castellanii cysts. The scientists found confirmed results for the inhibitory effect of the extract on the reproduction of Acanthamoeba cysts, but the effect was time and dose dependent [53]. In addition, turmeric mouth rinse can be successfully used to prevent plaque and gingivitis. Furthermore, turmeric mouthwash has been found to significantly diminish total microbial count [54]. Moreover, turmeric inhibits the growth of Bacillus subtilis and Escherichia coli by limiting the assembly of temperature-sensitive Z mutants (Fts Z) by suppressing the polymerization of Fts Z [55]. Curcumin also dose-dependently decreases infectivity and cell proliferation. It considerably reduces the cytotoxicity of Vibrio vulnificus for HeLa cells by preventing the growth of V. vulnificus. Curcumin subdues bacterial adhesion and binding of RTX toxin to host cells have resulted in inhibition of host cell rounding and actin aggregation [56]. Curcumin can decrease the Vibrio vulnificus which induces translocation in the specific HeLa cells which proliferates abnormally [57]. Furthermore, a wide-range of anti-viral activity of curcumin also reported [58]. There are several other studies concerning its different mechanisms against the human immunodeficiency viruses (HIVs). Curcumin has been shown to inhibit HIV-1 integrase [59]. Moreover, this polyphenol and its analogues can inhibit the infection and replication of viral genes. They inhibit HIV protease and HIV associated kinases (e.g., tyrosine kinase). Curcumin also has a collaborative effect with bio-medicinal drugs. It is noteworthy that curcumin inhibits the Apurinic/ apyrimidinic endonuclease-1 redox function. As a consequence, a large variety of genes and pathways are affected. It has been found that curcumin can retards Kaposi's sarcoma-associated herpesvirus replication and finally control the consequent pathologic processes (e.g., angiogenesis) [60] [61]. Scientists also reported anti-influenza activity of organic components of the Turmeric plant [62]. It can fight against the influenza-A virus (IAV) by inhibiting its adsorption and replication [63].

3.6. Anti-Arthritis

Rheumatoid arthritis (RA) is a chronic inflammatory disease considered a hyperplasia of synovial fibroblasts. Curcumin is well known for its strong anti-inflammatory and anti-arthritic properties [64]. Curcumin treatment was performed in real time in patients with active rheumatoid arthritis and compared to the diclofenac sodium reference group. The curcumin group has seen the highest percentage improvement of rheumatoid arthritis overall, and these values have improved significantly compared to Diclofenac sodium patients [64] [65]. The Curcumin group was found to be safe and healthy relative to the Diclofenac sodium group [65]. It is believed that curcumin antioxidant, anti-inflammatory, anti-proliferative, and immune-suppressive activities are shared in the upgrading of symptoms to patients who have rheumatoid arthritis [66].

3.7. Anti-Viral

Papillomavirus virus (HPV), Hepatitis B virus (HBV), influenza virus, Hepatitis C virus (HCV), adenovirus, coxsackievirus, Human norovirus (HuNoV), Respiratory syncytial virus (RSV) and Herpes simplex 1 (HSV-1) can be cured by curcumin [67]. Curcumin contains graphene oxide that shows synergistic anti-viral effect against the respiratory syncytial virus infection. Respiratory syncytial virus (RSV) present in the lower respiratory tract of infants and results in severe lung disease. Curcumin also shows the anti-viral effect in a dose-dependent manner [68]. Inosine-mono phosphate dehydrogenase (IMPDH) enzyme in either non-competitive or competitive manner is retarded by curcumin. Viral entry or other life cycle stages contain curcumin mechanism rather than viral RNA replication. So, for becoming potential anti-viral, anti-proliferative, and antiparasitic effects of curcumin, IMPDH should be inhibited [69].

3.8. Anti-Asthma and Anti-Diabetic

Curcumin reduced nasal air flow resistance by mitigating coughing, rhinorrhea and cold symptoms. It also overwhelms the factor alpha of IL-4, IL-8, and tumour necrosis and enhances IL-10 levels and solvable intercellular grip molecules. Curcumin suppressed allergic airline irritations thru the nasal route and retained structural reliability in the framework of allergic asthma mice [70]. The antioxidant properties of curcumin [71] can be related to the enhanced anti-diabetic action. In their study, researchers examined beneficial curcumin outcomes by decreasing superoxide production and vascular protein kinase C reserve thru the development of diabetes-persuaded endothelial dysfunction. New research have already shown, wondrously, the capacity of curcumin to immediately slake reactive oxygen species (ROS) which can make a contribution to oxidative damage [72]. It is identified that such a property adds to the particular defending characteristics of curcumin. Curcumin can weaken oxidative stress-induced cell death by the implementation and activation of antioxidant/cytoprotective enzymes, such as heme oxygenase-11 (HO-1). Some emerging therapeutic choices for the appearance of HO-1 in the administration of diabetic diseases may be present in the defensive devices of HO-1 in diabetes [73] [74] [75].

3.9. Anti-Obesity and Cardio and Liver Toxicity Protection Activity

Promising findings wherein curcumin enhances the lipid and fat content of preserved people help in understanding that this really helps in curing obesity. They first investigate the impact of Curcumin oral products in obese people on lipid profile parameters, basal metabolic rate and glucose levels. The findings indicated significant changes only in triglyceride concentrations, while other parameters stayed constant after 30 days of treatment with curcumin [76]. In the study that examined such variables in non-alcoholic fatty liver disease (NAFLD)

patients, body mass index (BMI) and body weight reduction also were recorded [77]. The outcomes have also shown that 4-week supplementation with 2.8 g/day Turmeric doesn't really change oxidative stress or inflammatory parameters in obese systemic inflammation females, nor would it cause a major transformation in the metabolic profile [78] [79]. Researchers use different animal models with physicochemical markers like serum marker enzymes and antioxidants in peripheral tissue to evaluate the preventive effects of curcumin on experimental data persuaded hepatotoxicity and cardio poisonousness to assess increased lipid peroxidation, decreased glutathione (GSH), glutathione peroxidase (GPx) and superoxide dismutase (SOD) marker enzymes, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) in edematous, granulomatous, liver and heart tissues during liver injury and cardiac necrosis [80].

3.10. Depression and Anxiety

Through various clinical studies, the impact of Curcumin oral path on mental illness was assessed. In such research, curcumin was taken orally at doses ranging from 500 - 1000 mg regularly, alone [81], with bioperine [82], or even in a combination of escitalopram venlafaxine or fluoxetine with conventional antipsychotic agents. The researched people demonstrated highly clear advancement in depression-linked illnesses throughout all experiments, evaluated using appropriate scales [83]. The only exclusion was the approved trial in which the direction of curcumin reduced nervousness, but not despair, that could be a sign of the shortest time of administration (30 days vs. 5 - 8 weeks in other studies) [83].

4. The Potential Use of Turmeric and Its Extracts in SARS-CoV-2 Treatment

Since December 2019, disease outbreak SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2) has rapidly spread all throughout entire planet. Hardly any specific drug or vaccine has been approved for its remedy or preventative measures. So far, even though anti-retroviral capsules as well as hydroxylchloroquine etc. have been used for the cure [84]. Various derivatives of curcumin have proof of anti-viral properties. The stimulation assay of neuraminidase demonstrates that five active derivatives of the curcumin additive reduced the activation of H1N1 induced neuraminidase in H1N1 infected lung epithelial cells [85]. This same activation of nucleoproteins becomes even down-regulated by Tetramethyl l curcumin and curcumin. Substantial antiviral activity of Turmeric against H5N1 virus is also determined in Madin-Darby dog kidney (MDCK) cells in vitro by interfering with the activity of infectious hemagglutination (HA) [86], that may be advantageous for recent disease outbreak circumstances. With both the up-regulation of TNF-alpha and IFN- β mRNA expressions within the investigated MDCK cells, that are comprehensive anti-viral agents, the impacts

of the anti-H5N1 viral infection with both the assistance of turmeric extracts have been demonstrated [87] [88]. Due to its inhibition activity on HIV protease and integrase, Curcumin is also beneficial in other viral problems like AIDS. Other pathogens also have an inhibition activity due to curcumin, such as hepatitis B, hepatitis C, zika, chikungunya, dengue, etc. The leading cause of COVID-19 death rates is respiratory illness syndrome with fulminant hypercyto-kinemia and multi-organ failure [89] [90]. Curcumin was reported to reduce lung tissue injuries sustained by influenza virus by obstructing the signalling of NF-umB and preventing the release of inflammatory cytokines.

5. Safety and Toxicity or Side-Effects of Curcumin

The safety of Turmeric has also been researched in vitro, animal models, as well as drug testing. As per a detailed review on this topic, the organism is not toxic. Cultured cells studies have shown that "curcumin can decrease the growth of probiotic and prove anti-proliferative impacts in healthy cells". There's really, even so, hardly any evidence of genotoxicity and mutagenicity. In human beings, this same oral use of curcumin is secure. In a small percentage of cases, gagging, tongue redness, atrial fibrillation, and gastrointestinal problems (e.g., flatulence, diarrhoea, nausea, and constipation) have been observed. There is indeed a biocompatibility issue with intravenous curcumin, so this should be consumed at a dose lesser than oral administration [91]. This should be mentioned that certain sorts of pharmacokinetic modification of cardiovascular medications, antibiotics, antidepressants, chemotherapy drugs, immunosuppressants and corticosteroids may well be triggered by curcumin. Consequently, its simultaneous accessibility with other collectivist medications must be routinely laid out [92]. A slight reduction throughout weight gain in F2 generation chicks has been triggered by oral curcumin of around 1000 mg/kg body mass, as published in one report [93]. This same security of such modern mixtures must be regarded with respect to the interpretation of drug transfer technologies for improving Turmeric bioactivity. For instance, if carriers or surfactants are being used as a biocompatibility action plan the product could be toxic [94]. Even though most of such innovative technologies occur to also be safe, there are no negative effects in patients with osteosarcoma and also in healthy populations, there are no detrimental effects on solid lipid curcumin formulation [95]. As yet another different framework expressing curcuminoids nasally to the brain, the poly (N-isopropylacrylamide) distribution network demonstrates hardly any noxiousness [96]. Dipeptide curcumin nanomaterials are too safe. A dipeptide is formulated from alpha, beta-dehydro phenylalanine and methionine amino acids which are comfortable and safe to dissolve in nature [96]. In additament, curcumin-loaded blood serum albumin nanoparticles showed hardly any toxic effects during arterial use throughout HCT116 tumour xenograft models [97]. A new intravenous curcumin study showed that rabbits throughout the curcumin nanosuspension group would have a reduced chance of local irritation and phlebitis and erythrocyte hemolysis than those from the curcumin solution group [98].

6. Conclusion

Globally, curcumin is recognised because of its antioxidant, anti-inflammatory characteristics and other potential benefits which are helpful for public health. It improves bioavailability in conjunction with curcumin and piperin. Curcumin also might deal with oxidative, inflammatory, metabolic, arthritis, anxiousness and hyperlipidemic diseases. Exercise-induced inflammation and sore muscles are monitored as well as enhanced by inactive individuals throughout rehabilitation and performance level. In addition, for people who have not yet been successfully treated with any disease, it's indeed beneficial. The root is the core aspect of Turmeric and includes more than enough bioactive compounds, vitamins and minerals, trying to make this the safest therapeutic herb. It is also used in pregnancy as well as during renal or hepatic failure in lactating women. It includes curcumin, the most main bioactive element, accompanied by certain substances like atlantone curcuminoid, dimethoxycurcumin, diarylheptanoid, tumerone, and diferuloylmethane flavonoid curcumin. These have antibacterial, anti-inflammatory, and antioxidant activity which safeguard against different cellular injuries. In addition, psychological diseases such as Parkinson's and Alzheimer's diseases also are successfully treated by Turmeric. It is also efficient against metabolic syndrome and different forms of cancer. In summary, to regulate a wide range of human illnesses, this can be added to dietary foods. A major emergence in China in December 2019 of the highly contagious novel coronavirus (COVID-19), spread across the world to a new pandemic [99]. It is caused by the novel SARS-CoV-2 Corona virus (severe coronavirus 2 acute respiratory syndrome) from the Coronaviridae family. No special antiviral treatment for COVID-19 patients is available to date. The clinicians, including antivirals, antibiotics and anti-inflammatory drugs [99], have considered combination therapy in developing countries. Including hydroxychloroquine, the use has been extensive. In addition, the role of curcumin in the influence of the RAAS (rennin-angiotensin-aldosterone system) components through which anti-oxidant, anti-inflammatory and antimicrobial effects are known has also been thoroughly researched. The role of curcumin in ACE and AT1R downregulation of brain tissue and vascular smooth muscle cells was impacted by animal models, which usually results in the mediated effects of hypertension and oxidative stress on animals, respectively, of the inhibition of angiotensin II-AT1R [100]. For greater understanding and moral judgement over its usage in medical care, even more investigation is essential for implementation throughout the future.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Panpatil, V.V., Tattari, S., Kota, N., Nimgulkar, C. and Polasa, K. (2013) In-Vitro

- Evaluation on Antioxidant and Antimicrobial Activity of Spice Extracts of Ginger, Turmeric and Garlic. *Journal of Pharmacognosy and Phytochemistry*, **2**, 143-148.
- [2] Aggarwal, B.B., Kumar, A. and Bharti, A.C. (2003) Anticancer Potential of Curcumin: Preclinical and Clinical Studies. *Anticancer Research*, **23**, 363-398.
- [3] Bhutya, R. (2011) Ayurvedic Medicinal Plants of India, Vol. 1. Scientific Publishers, 25-27.
- [4] Kharat, M., Du, Z., Zhang, G. and McClements, D.J. (2017) Physical and Chemical Stability of Curcumin in Aqueous Solutions and Emulsions: Impact of pH, Temperature and Molecular Environment. *Journal of Agricultural and Food Chemistry*, 65, 1525-1532. https://doi.org/10.1021/acs.jafc.6b04815
- [5] Panahi, Y., Hosseini, M.S., Khalili, N., Naimi, E., Majeed, M. and Sahebkar, A. (2015) Antioxidant and Anti-Inflammatory Effects of Curcuminoid-Piperine Combination in Subjects with Metabolic Syndrome: A Randomized Controlled Trial and an Updated Meta-Analysis. *Clinical Nutrition*, 34, 1101-1108. https://doi.org/10.1016/j.clnu.2014.12.019
- [6] Prasad, S. and Aggarwal, B.B. (2011) Turmeric, the Golden Spice. In: Benzie, I.F.F. and Wachtel-Galor, S. (Eds.), *Herbal Medicine*. *Biomolecular and Clinical Aspects*, 2nd Edition, CRC Press, Boca Raton.
- [7] Rheim, F.A., Ragab, A.A., Hamdy, H.E.D. and Hammam, F.M. (2015) Evaluation of DNA Damage *In Vivo* by Comet Assay and Chromosomal Aberrations for Pyrethroid Insecticide and the Antimutagenic: Role of Curcumin. *The Egyptian Journal of Hospital Medicine*, 59, 172-181. https://doi.org/10.12816/0012174
- [8] Hu, S., Maiti, P., Ma, Q., Zuo, X., Jones, M.R., Cole, G.M. and Frautschy, S.A. (2015) Clinical Development of Curcumin in Neurodegenerative Disease. *Expert Review of Neurotherapeutics*, 15, 629-637. https://doi.org/10.1586/14737175.2015.1044981
- [9] Kocaadam, B. and Şanlier, N. (2017) Curcumin, an Active Component of Turmeric (*Curcuma longa*), and Its Effects on Health. *Critical Reviews in Food Science and Nutrition*, 57, 2889-2895. https://doi.org/10.1080/10408398.2015.1077195
- [10] Chuengsamarn, S., Rattanamongkolgul, S., Luechapudiporn, R., Phisalaphong, C. and Jirawatnotai, S. (2012) Curcumin Extract for Prevention of Type 2 Diabetes. *Diabetes Care*, 35, 2121-2127. https://doi.org/10.2337/dc12-0116
- [11] Akbik, D., Ghadiri, M., Chrzanowski, W. and Rohanizadeh, R. (2014) Curcumin as a Wound Healing Agent. *Life Sciences*, **116**, 1-7. https://doi.org/10.1016/j.lfs.2014.08.016
- [12] Li, S. (2011) Chemical Composition and Product Quality Control of Turmeric (*Curcuma longa* L.). *Pharmaceutical Crops*, **5**, 28-54. https://doi.org/10.2174/2210290601102010028
- [13] Riva, A., Franceschi, F., Togni, S., Eggenhoffner, R. and Giacomelli, L. (2017) Health Benefits of Curcumin and Curcumin Phytosome in Bone Density Disorders. *JSM Bone Marrow Research*, **1**, 1006.
- [14] Delgado-Vargas, F. (2002) Natural Colorants for Food and Nutraceutical Uses. CRC Press, Boca Raton, FL. https://doi.org/10.1201/9781420031713
- [15] Ruby, A.J., Kuttan, G., Dinesh Babu, K., Rajasekharan, K.N. and Kuttan, R. (1995) Anti-Tumour and Antioxidant Activity of Natural Curcuminoids. *Cancer Letters*, **94**, 79-83. https://doi.org/10.1016/0304-3835(95)03827-J
- [16] Aggarwal, B.B., Kumar, A. and Bharti, A.C. (2003) Anticancer Potential of Curcumin: Preclinical and Clinical Studies. *Anticancer Research*, 23, 363-398.

- [17] Gul, P. and Bakht, J. (2015) Antimicrobial Activity of Turmeric Extract and Its Potential Use in Food Industry. *Journal of Food Science and Technology*, 52, 2272-2279. https://doi.org/10.1007/s13197-013-1195-4
- [18] Pradeep, K.U., Geervani, P. and Eggum, B.O. (1993) Common Indian Spices: Nutrient Composition, Consumption and Contribution to Dietary Value. *Plant Foods for Human Nutrition*, 44, 137-148. https://doi.org/10.1007/BF01088378
- [19] Anderson, A.M., Mitchell, M.S. and Mohan, R.S. (2000) Isolation of Curcumin from Turmeric. *Journal of Chemical Education*, 77, 359-360. https://doi.org/10.1021/ed077p359
- [20] Bagchi, A. (2012) Extraction of Curcumin. *IOSR Journal of Environmental Science*, *Toxicology and Food Technology*, **1**, 1-16.
- [21] Fanti, F., Conti, S., Campani, L., Morace, G., Dettori, G. and Polonelli, L. (1989) Studies on the Epidemiology of Aspergillus fumigatus Infections in a University Hospital. European Journal of Epidemiology, 5, 8-14. https://doi.org/10.1007/BF00145038
- [22] Nelson, K.M., Dahli, J.L., Bisson, J., Graham, J., Pauli, G.F. and Walters, M.A. (2017) The Essential Medicinal Chemistry of Curcumin. *Journal of Medicinal Chemistry*, 60, 1620-1637. https://doi.org/10.1021/acs.jmedchem.6b00975
- [23] Sharma, O.P. (1976) Antioxidant Activity of Curcumin and Related Compounds. Biochemical Pharmacology, 25, 1811-1812. https://doi.org/10.1016/0006-2952(76)90421-4
- [24] Goel, A., Kunnumakkara, A.B. and Aggarwal, B.B. (2008) Curcumin as "Curecumin": From Kitchen to Clinic. Biochemical Pharmacology, 75, 787-809. https://doi.org/10.1016/j.bcp.2007.08.016
- [25] Shishodia, S., Sethi, G. and Aggarwal, B.B. (2005) Curcumin: Getting Back to the Roots. Annals of the New York Academy of Sciences, 1056, 206-217. https://doi.org/10.1196/annals.1352.010
- [26] Griesser, M., Pistis, V., Suzuki, T., Tejera, N., Pratt, D.A. and Schneider, C. (2011) Autoxidative and Cyclooxygenase-2 Catalyzed Transformation of the Dietary Chemopreventive Agent Curcumin. *The Journal of Biological Chemistry*, 286, 1114-1124. https://doi.org/10.1074/jbc.M110.178806
- [27] Tamvakopoulos, C., Dimas, K. and Sofianos, Z.D. (2007) Metabolism and Anticancer Activity of the Curcumin Analogue, Dimethoxycurcumin. *Clinical Cancer Research*, **13**, 1269-1277. https://doi.org/10.1158/1078-0432.CCR-06-1839
- [28] Robinson, T.P. and Hubbard, R.B. (2005) Synthesis and Biological Evaluation of Aromatic Enones Related to Curcumin. *Bioorganic & Medicinal Chemistry*, **13**, 4007-4013. https://doi.org/10.1016/j.bmc.2005.03.054
- [29] Lin, Y.G., Kunnumakkara, A.B., Nair, A., Merritt, W.M., Han, L.Y., Armaiz-Pena, G.N., Kamat, A.A., Spannuth, W.A., Gershenson, D.M., Lutgendorf, S.K., *et al.* (2007) Curcumin Inhibits Tumor Growth and Angiogenesis in Ovarian Carcinoma by Targeting the Nuclear Factor-κB Pathway. *Clinical Cancer Research*, 13, 3423-3430. https://doi.org/10.1158/1078-0432.CCR-06-3072
- [30] Sahebkar, A., Serbanc, M.C., Ursoniuc, S. and Banach, M. (2015) Effect of Curcuminoids on Oxidative Stress: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Journal of Functional Foods*, 18, 898-909. https://doi.org/10.1016/j.iff.2015.01.005
- [31] Banach, M., Serban, C., Aronow, W.S., Rysz, J., Dragan, S., Lerma, E.V., Apetrii, M. and Covic, A. (2014) Lipid, Blood Pressure and Kidney Update. *International Urol-*

- ogy and Nephrology, 46, 947-961. https://doi.org/10.1007/s11255-014-0657-6
- [32] Priyadarsini, K.I., Maity, D.K., Naik, G.H., Kumar, M.S., Unnikrishnan, M.K., Satav, J.G. and Mohan, H. (2003) Role of Phenolic O-H and Methylene Hydrogen on the Free Radical Reactions and Antioxidant Activity of Curcumin. *Free Radical Biology & Medicine*, **35**, 475-484. https://doi.org/10.1016/S0891-5849(03)00325-3
- [33] Biswas, S.K. (2016) Does the Interdependence between Oxidative Stress and Inflammation Explain the Antioxidant Paradox? *Oxidative Medicine and Cellular Longevity*, **2016**, Article ID: 5698931. https://doi.org/10.1155/2016/5698931
- [34] Jurenka, J.S. (2009) Anti-Inflammatory Properties of Curcumin, a Major Constituent of *Curcuma longa*: A Review of Preclinical and Clinical Research. *Alternative Medicine Review: A Journal of Clinical Therapeutic*, **14**, 141-153.
- [35] Panahi, Y., Hosseini, M.S., Khalili, N., Naimi, E., Simental-Mendia, L.E., Majeed, M. and Sahebkar, A. (2016) Effects of Curcumin on Serum Cytokine Concentrations in Subjects with Metabolic Syndrome: A Post-Hoc Analysis of a Randomized Controlled Trial. *Biomedicine & Pharmacotherapy*, 82, 578-582. https://doi.org/10.1016/j.biopha.2016.05.037
- [36] Eric, J.T., Brosens, R.P., Delis-van Diemen, P.M., Bril, H., Tijssen, M., van Essen, D. F. and Meijer, G.A. (2012) Cell Cycle Proteins Predict Recurrence in Stage II and III Colon Cancer. *Annals of Surgical Oncology*, 19, 682-692. https://doi.org/10.1245/s10434-012-2216-7
- [37] Duvoix, A., Blasius, R., Delhalle, S., Schnekenburger, M., et al. (2003) Chemopreventive and Therapeutic Effects of Curcumin. Cancer Letters, 223, 181-190. https://doi.org/10.1016/j.canlet.2004.09.041
- [38] Bayomi, S.M., El-Kashef, H.A., El-Ashmawy, M.B., Nasr, M.N., El-Sherbeny, M.A., Abdel-Aziz, N.I., et al. (2015) Synthesis and Biological Evaluation of New Curcumin Analogues as Antioxidant and Antitumor Agents: Molecular Modeling Study. European Journal of Medicinal Chemistry, 101, 584-594. https://doi.org/10.1016/j.eimech.2015.07.014
- [39] Rubagotti, S., Croci, S., Ferrari, E., Orteca, G., Iori, M., Capponi, P.C., Versari, A. and Asti, M. (2017) Uptake of Ga-Curcumin Derivatives in Different Cancer Cell Lines: Toward the Development of New Potential ⁶⁸Ga-Labelled Curcumino-ids-Based Radiotracers for Tumour Imaging. *Journal of Inorganic Biochemistry*, 173, 113-119. https://doi.org/10.1016/j.jinorgbio.2017.05.002
- [40] Allegra, A., Innao, V., Russo, S., Gerace, D., Alonci, A. and Musolino, C. (2017) Anticancer Activity of Curcumin and Its Analogues Preclinical and Clinical Studies. *Cancer Investigation*, **35**, 1-22. https://doi.org/10.1080/07357907.2016.1247166
- [41] Na, L.X., Li, Y., Pan, H.Z., Zhou, X.L., Sun, D.J., Meng, M., Li, X.X. and Sun, C.H. (2013) Curcuminoids Exert Glucose-Lowering Effect in Type 2 Diabetes by Decreasing Serum Free Fatty Acids: A Double-Blind, Placebo-Controlled Trial. *Molecular Nutrition & Food Research*, 57, 1569-1577. https://doi.org/10.1002/mnfr.201200131
- [42] Chuengsamarn, S., Rattanamongkolgul, S., Luechapudiporn, R., Phisalaphong, C. and Jirawatnotai, S. (2012) Curcumin Extract for Prevention of Type 2 Diabetes. *Diabetes Care*, **35**, 2121-2127. https://doi.org/10.2337/dc12-0116
- [43] Bradford, P.G. (2013) Curcumin and Obesity. *BioFactors*, 39, 78-87. https://doi.org/10.1002/biof.1074
- 44] Hlavackova, L., Janegova, A., Ulicna, O., Janega, P., Cerna, A. and Babal, P. (2011) Spice up the Hypertension Diet—Curcumin and Piperine Prevent Remodeling of Aorta in Experimental L-NAME Induced Hypertension. *Nutrition & Metabolism*, 8,

- Article No. 72. https://doi.org/10.1186/1743-7075-8-72
- [45] Sahebkar, A. (2013) Are Curcuminoids Effective C-Reactive Protein-Lowering Agents in Clinical Practice? Evidence from a Meta-Analysis. *Phytotherapy Research*, **28**, 633-642. https://doi.org/10.1002/ptr.5045
- [46] Ak, T. and Gulcin, I. (2008) Antioxidant and Radical Scavenging Properties of Curcumin. *Chemico-Biological Interactions*, 174, 27-37. https://doi.org/10.1016/j.cbi.2008.05.003
- [47] Sahebkar, A., Mohammadi, A., Atabati, A., Rahiman, S., Tavallaie, S., Iranshahi, M., Akhlaghi, S., Ferns, G.A. and Ghayour-Mobarhan, M. (2013) Curcuminoids Modulate Pro-Oxidant-Antioxidant Balance but Not the Immune Response to Heat Shock Protein 27 and Oxidized LDL in Obese Individuals. *Phytotherapy Research*, 27, 1883-1888. https://doi.org/10.1002/ptr.4952
- [48] Mohammadi, A., Sahebkar, A., Iranshahi, M., Amini, M., Khojasteh, R., Ghayour-Mobarhan, M. and Ferns, G.A. (2013) Effects of Supplementation with Curcuminoids on Dyslipidemia in Obese Patients: A Randomized Crossover Trial. *Phytotherapy Research*, 27, 374-379. https://doi.org/10.1002/ptr.4715
- [49] DiSilvestro, R.A., Joseph, E., Zhao, S. and Bomser, J. (2012) Diverse Effects of a Low Dose Supplement of Lapidated Curcumin in Healthy Middle-Aged People. *Nutrition Journal*, 11, Article No. 79. https://doi.org/10.1186/1475-2891-11-79
- [50] Mythri, R.B. and Srinivas Bharath, M.M. (2012) Curcumin: A Potential Neuroprotective Agent in Parkinson's Disease. *Current Pharmaceutical Design*, 18, 91-99. https://doi.org/10.2174/138161212798918995
- [51] Ji, H.F. and Shen, L. (2014) A Multiple Pharmaceutical Potential of Curcumin in Parkinson's Disease. CNS & Neurological Disorders—Drug Targets, 13, 369-373. https://doi.org/10.2174/18715273113129990077
- [52] Mythri, R.B., Veena, J., Harish, G., Shankaranarayana, B.S. and Srinivas Bharath, M.M. (2011) Chronic Dietary Supplementation with Turmeric Protects against 1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine-Mediated Neurotoxicity *In Vivo*. Implications for Parkinson's Disease. *British Journal of Nutrition*, 106, 63-72. https://doi.org/10.1017/S0007114510005817
- [53] Harish, G., Venkateshappa, C., Mythri, R.B., et al. (2010) Bioconjugates of Curcumin Display Improved Protection against Glutathione Depletion Mediated Oxidative Stress in a Dopaminergic Neuronal Cell Line: Implications for Parkinson's Disease. Bioorganic & Medicinal Chemistry, 18, 2631-2638. https://doi.org/10.1016/j.bmc.2010.02.029
- [54] Wang, R., Li, Y.H., Xu, Y., et al. (2010) Curcumin Produces Neuroprotective Effects via Activating Brain-Derived Neurotrophic Factor/TrkB-Dependent MAPK and PI-3K Cascades in Rodent Cortical Neurons. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 34, 147-153. https://doi.org/10.1016/j.pnpbp.2009.10.016
- [55] Yanagisawa, D., Ibrahim, N.F., Taguchi, H., et al. (2015) Curcumin Derivative with the Substitution at C-4 Position, but Not Curcumin, Is Effective against Amyloid Pathology in APP/PS1 Mice. Neurobiology of Aging, 36, 201-210. https://doi.org/10.1016/j.neurobiolaging.2014.07.041
- [56] Doggui, S., Sahni, J.K., Arseneault, M., Dao, L. and Ramassamy, C. (2012) Neuronal Uptake and Neuroprotective Effect of Curcumin-Loaded PLGA Nanoparticles on the Human SK-N-SH Cell Line. *Journal of Alzheimer's Disease*, 30, 377-392. https://doi.org/10.3233/JAD-2012-112141
- [57] Dohare, P., Varma, S. and Ray, M. (2008) Curcuma Oil Modulates the Nitric Oxide System Response to Cerebral Ischemia/Reperfusion Injury. *Nitric Oxide*, **19**, 1-11.

https://doi.org/10.1016/j.niox.2008.04.020

- [58] Zhang, Z.J., Zhao, L.X., Cao, D.L., Zhang, X., Gao, Y.J. and Xia, C. (2012) Curcumin Inhibits LPS-Induced CCL2 Expression via JNK Pathway in C6 Rat Astrocytoma Cells. Cellular and Molecular Neurobiology, 32, 1003-1010. https://doi.org/10.1007/s10571-012-9816-4
- [59] Kulkarni, S., Akula, K.K. and Deshpande, J. (2012) Evaluation of Antidepressant-Like Activity of Novel Water-Soluble Curcumin Formulations and St. John's Wort in Behavioral Paradigms of Despair. *Pharmacology*, 89, 83-90. https://doi.org/10.1159/000335660
- [60] Keshavarzi, Z., Shakeri, F., Barreto, G.E., Bibak, B., Sathyapalan, T. and Sahebkar, A. (2019) Medicinal Plants in Traumatic Brain Injury: Neuroprotective Mechanisms Revisited. *BioFactors*, 45, 517-535. https://doi.org/10.1002/biof.1516
- [61] Sindhu, K., Indra, R., Rajaram, A., Sreeram, K.J. and Rajaram, R. (2011) Investigations on the Interaction of Gold-Curcumin Nanoparticles with Human Peripheral 12 Evidence-Based Complementary and Alternative Medicine Blood Lymphocytes. *Journal of Biomedical Nanotechnology*, 7, 56. https://doi.org/10.1166/jbn.2011.1199
- [62] Basniwal, R.K., Buttar, H.S., Jain, V. and Jain, N. (2011) Curcumin Nanoparticles: Preparation, Characterization, and Antimicrobial Study. *Journal of Agricultural and Food Chemistry*, 59, 2056-2061. https://doi.org/10.1021/jf104402t
- [63] Betts, J.W. and Wareham, D.W. (2014) In Vitro Activity of Curcumin in Combination with Epigallocatechin Gallate (EGCG) versus Multidrug-Resistant Acinetobacter baumannii. BMC Microbiology, 14, Article No. 172. https://doi.org/10.1186/1471-2180-14-172
- [64] El-Sayed, N.M., Ismail, K.A., Ahmed, S.A.E.G. and Hetta, M.H. (2012) In Vitro Amoebicidal Activity of Ethanol Extracts of Arachis hypogaea L., Curcuma longa L. and Pancratium maritimum L. on Acanthamoeba castellanii Cysts. Parasitology Research, 110, 1985-1992. https://doi.org/10.1007/s00436-011-2727-3
- [65] Waghmare, P., Chaudhari, A., Karhadkar, V. and Jamkhande, A. (2011) Comparative Evaluation of Turmeric and Chlorhexidinegluconate Mouthwash in Prevention of Plaque Formation and Gingivitis: A Clinical and Microbiological Study. *The Journal of Contemporary Dental Practice*, 12, 221-224. https://doi.org/10.5005/jp-journals-10024-1038
- [66] Kaur, C.D. and Saraf, S. (2011) Topical Vesicular Formulations of *Curcuma longa* Extract on Recuperating the Ultraviolet Radiation-Damaged Skin. *Journal of Cosmetic Dermatology*, 10, 260-265. https://doi.org/10.1111/j.1473-2165.2011.00586.x
- [67] Khalafalla, R.E., Muller, U., Shahiduzzaman, M., *et al.* (2011) Effects of Curcumin (Diferuloylmethane) on *Eimeria tenella* Sporozoites *In Vitro. Parasitology Research*, **108**, 879-886. https://doi.org/10.1007/s00436-010-2129-y
- [68] Na, H.S., Cha, M.H., Oh, D.R., Cho, C.W., Rhee, J.H. and Kim, Y.R. (2011) Protective Mechanism of Curcumin against *Vibrio vulnificus* Infection. *FEMS Immunology & Medical Microbiology*, 63, 355-362. https://doi.org/10.1111/j.1574-695X.2011.00855.x
- [69] Kim, J., Lee, H.J. and Lee, K.W. (2010) Naturally Occurring Phytochemicals for the Prevention of Alzheimer's Disease. *Journal of Neurochemistry*, 112, 1415-1430. https://doi.org/10.1111/j.1471-4159.2009.06562.x
- [70] Fu, W., Zhuang, W., Zhou, S. and Wang, X. (2015) Plant-Derived Neuroprotective Agents in Parkinson's Disease. *American Journal of Translational Research*, **7**, 1189-1202.
- [71] Ghosh, N., Ghosh, R. and Mandal, S.C. (2011) Antioxidant Protection a Promising

- Therapeutic Intervention in Neurodegenerative Disease. *Free Radical Research*, **45**, 888-905. https://doi.org/10.3109/10715762.2011.574290
- [72] Sayer, A. (2015) Yeast Is A Cause of Cancer and Turmeric Can Kill Both. *Research Confirms. Research*, **4**, 339.
- [73] Zhang, Q., Li, D., Liu, Y., Wang, H., et al. (2016) Potential Anticancer Activity of Curcumin Analogs Containing Sulfone on Human Cancer Cells. Archives of Biological Sciences, 68, 125-133. https://doi.org/10.2298/ABS150323134Z
- [74] Siegel, R., Ma, J., Zou, Z. and Jemal, A. (2014) Cancer Statistics, 2014. *CA: A Cancer Journal for Clinicians*, **64**, 9-29. https://doi.org/10.3322/caac.21208
- [75] Subhashini, Chauhan, P.S., Kumari, S., Kumar, J.P., Chawla, R., Dash, D., et al. (2013) Intranasal Curcumin and Its Evaluation in Murine Model of Asthma. *International Immunopharmacology*, 17, 733-743. https://doi.org/10.1016/j.intimp.2013.08.008
- [76] Wise, R., Hart, T., Cars, O., Streulens, M., Helmuth, R., Huovinen, P. and Sprenger, M. (1998) Antimicrobial Resistance Is a Major Threat to Public Health. *British Medical Journal*, 317, 609. https://doi.org/10.1136/bmj.317.7159.609
- [77] Samy, P.R. and Gopalakrishnakone, P. (2010) Therapeutic Potential of Plants as Anti-Microbials for Drug Discovery. Evidence-Based Complementary and Alternative Medicine, 7, 283-294. https://doi.org/10.1093/ecam/nen036
- [78] Panchatcharam, M., Miriyala, S., Gayathri, V.S. and Suguna, L. (2006) Curcumin Improves Wound Healing by Modulating Collagen and Decreasing Reactive Oxygen Species. *Molecular and Cellular Biochemistry*, 290, 87-96. https://doi.org/10.1007/s11010-006-9170-2
- [79] Chereddy, K.K., Coco, R., Memvanga, P.B., Ucakar, B., des Rieux, A., Vandermeulen, G. and Préat, V. (2013) Combined Effect of PLGA and Curcumin on Wound Healing Activity. *Journal of Controlled Release*, 171, 208-215. https://doi.org/10.1016/j.jconrel.2013.07.015
- [80] Aggarwal, B.B. and Harikumar, K.B. (2009) Potential Therapeutic Effects of Curcumin, the Anti-Inflammatory Agent, against Neurodegenerative, Cardiovascular, Pulmonary, Metabolic, Autoimmune and Neoplastic Diseases. *The International Journal of Biochemistry and Cell Biology*, 41, 40-59. https://doi.org/10.1016/j.biocel.2008.06.010
- [81] Sahebkar, A., Mohammadi, A., Atabati, A., Rahiman, S., Tavallaie, S., Iranshahi, M., Akhlaghi, S., Ferns, G.A. and Ghayour-Mobarhan, M. (2013) Curcuminoids Modulate Pro-Oxidant-Antioxidant Balance but Not the Immune Response to Heat Shock Protein 27 and Oxidized LDL in Obese Individuals. *Phytotherapy Research*, 27, 1883-1888. https://doi.org/10.1002/ptr.4952
- [82] Rahmani, S., Asgary, S., Askari, G., Keshvari, M., Hatamipour, M., et al. (2016) Treatment of Non-Alcoholic Fatty Liver Disease with Curcumin: A Randomized Placebo-Controlled Trial. Phytotherapy Research, 30, 1540-1548. https://doi.org/10.1002/ptr.5659
- [83] Nieman, D.C., Cialdella-Kam, L., Knab, A.M. and Shanely, R.A. (2012) Influence of Red Pepper Spice and Turmeric on Inflammation and Oxidative Stress Biomarkers in Overweight Females: A Metabolomics Approach. *Plant Foods for Human Nutri*tion, 67, 415-421. https://doi.org/10.1007/s11130-012-0325-x
- [84] Di Pierro, F., Bressan, A., Ranaldi, D., Rapacioli, G., Giacomelli, L. and Bertuccioli, A. (2015) Potential Role of Bioavailable Curcumin in Weight Loss and Omental Adipose Tissue Decrease: Preliminary Data of a Randomized, Controlled Trial in Overweight People with Metabolic Syndrome. Preliminary Study. European Review

- for Medical and Pharmacological Sciences, 19, 4195-4202.
- [85] Scannell, J.W., Blanckley, A., Boldon, H. and Warrington, B. (2012) Diagnosing the Decline in Pharmaceutical R and D Efficiency. *Nature Reviews Drug Discovery*, 11, 191-200. https://doi.org/10.1038/nrd3681
- [86] Yu, Y.Y., Pei, L.B., Zhang, Y., Wen, Z.Y. and Yang, J.L. (2015) Chronic Supplementation of Curcumin Enhances the Efficacy of Antidepressants in Major Depressive Disorder: A Randomized, Double-Blind, Placebo-Controlled Pilot Study. *Journal of Clinical Psychopharmacology*, 35, 406-410. https://doi.org/10.1097/ICP.0000000000000352
- [87] Esmaily, H., Sahebkar, A., Iranshahi, M., Ganjali, S., Mohammadi, A., Ferns, G. and Ghayour-Mobarhan, M. (2015) An Investigation of the Effects of Curcumin on Anxiety and Depression in Obese Individuals: A Randomized Controlled Trial. *Chi*nese Journal of Integrative Medicine, 21, 332-338. https://doi.org/10.1007/s11655-015-2160-z
- [88] Bergman, J., Miodownik, C., Bersudsky, Y. and Sokolik, S. (2013) Curcumin as an Add-On to Antidepressive Treatment: A Randomized, Double-Blind, Placebo-Conntrolled, Pilot Clinical Study. *Clinical Neuropharmacology*, 36, 73-77. https://doi.org/10.1097/WNF.0b013e31828ef969
- [89] Gupta, H., Gupta, M. and Bhargava, S. (2020) The Potential Use of Turmeric in COVID-19. Clinical and Experimental Dermatology, 45, 902-903. https://doi.org/10.1111/ced.14357
- [90] Lai, Y., Yan, Y., Liao, S., Li, Y., Ye, Y., Liu, N. and Xu, P. (2020) 3D-Quantitative Structure—Activity Relationship and Antiviral Effects of Curcumin Derivatives as Potent Inhibitors of Influenza H1N1 Neuraminidase. *Archives of Pharmacal Research*, 43, 489-502. https://doi.org/10.1007/s12272-020-01230-5
- [91] Soleimani, V., Sahebkar, A. and Hosseinzadeh, H. (2018) Turmeric (*Curcuma longa*) and Its Major Constituent (Curcumin) as Nontoxic and Safe Substances: Review. *Phytotherapy Research*, **32**, 985-995. https://doi.org/10.1002/ptr.6054
- [92] Bahramsoltani, R., Rahimi, R. and Farzaei, M.H. (2017) Pharmacokinetic Interactions of Curcuminoids with Conventional Drugs: A Review. *Journal of Ethnopharmacology*, 209, 1-12. https://doi.org/10.1016/j.jep.2017.07.022
- [93] Sun, M., Su, X., Ding, B., et al. (2012) Advances in Nanotechnology-Based Delivery Systems for Curcumin. Nanomedicine, 7, 1085-1100. https://doi.org/10.2217/nnm.12.80
- [94] Gota, V.S., Maru, G.B., Soni, T.G., Gandhi, T.R., Kochar, N. and Agarwal, M.G. (2010) Safety and Pharmacokinetics of a Solid Lipid Curcumin Particle Formulation in Osteosarcoma Patients and Healthy Volunteers. *Journal of Agricultural and Food Chemistry*, 58, 2095-2099. https://doi.org/10.1021/jf9024807
- [95] Ahmad, N., Ahmad, I., Umar, S., Iqbal, Z., Samim, M. and Ahmad, F.J. (2016) PNIPAM Nanoparticles for Targeted and Enhanced Nose-to-Brain Delivery of Curcuminoids: UPLC/ESIQ-ToF-MS/MS-Based Pharmacokinetics and Pharmacodynamics Evaluation in Cerebral Ischemia Model. *Drug Delivery*, 23, 2095-2114. https://doi.org/10.3109/10717544.2014.941076
- [96] Subramani, P.A., Panati, K., Lebaka, V.R., Reddy, D.D. and Narala, V.R. (2017) Nanostructures for Curcumin Delivery: Possibilities and Challenges. In: Grume-zescu, A.M., Ed., *Nano- and Micro-Scale Drug Delivery Systems*, Elsevier, Amsterdam, Netherlands, 393-418. https://doi.org/10.1016/B978-0-323-52727-9.00021-2
- [97] Kim, T.H., Jiang, H.H., Youn, Y.S., *et al.* (2011) Preparation and Characterization of Water-Soluble Albumin-Bound Curcumin Nanoparticles with Improved Antitumor

- Activity. *International Journal of Pharmaceutics*, **403**, 285-291. https://doi.org/10.1016/j.ijpharm.2010.10.041
- [98] Gao, Y., Li, Z., Sun, M., et al. (2011) Preparation and Characterization of Intravenously Injectable Curcumin Nanosuspension. Drug Delivery, 18, 131-142. https://doi.org/10.3109/10717544.2010.520353
- [99] Sahoo, J.P., Mohapatra, U., Mahapatra, S., Panda, K., Ganesh, P., Mishra, A., Samal, K. and Behera, S. (2020) An Immunological Outlook on SARS Coronavirus (SARS-CoV-2) and Its Current Clinical Status. *Journal of Pharmaceutical Research International*, 32, 37-59. https://doi.org/10.9734/ipri/2020/v32i2630838
- [100] Sahoo, J.P., Mohapatra, U., Mishra, A. and Samal, K. (2020) Turmeric (Haldi)—A Strapping Strategy for Enhancing the Immune System to Reduce the Effect of SARS-CoV-2. *Food and Scientific Reports*, **1**, 10-12.