Published Online: 2025 February 4

Review Article

Curcumin as a Natural Therapeutic Agent: A Rapid Review of Potential Clinical Uses and Mechanisms of Action

Mohammad Mohajeri [1], Reza Momenai [2], Somayyeh Karami-Mohajeri [1], Mandana Ohadi [3,*], Mohammad Amin Raeisi Estabragh [4,**]

[1] Department of Pharmacology and Toxicology, School of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran
[2] Nimeh Shaaban Hospital, Kerman, Iran
[3] Pharmaceutics Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
[4] Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran

[*] ***Corresponding Author:*** Pharmaceutics Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran. Email: mandanaohady@gmail.com
[**] ***Corresponding Author:*** Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran. Email: aminr374@yahoo.com

Received: 12 October, 2024; **Revised:** 17 December, 2024; **Accepted:** 2 January, 2025

Abstract

Context: Curcumin, a natural compound derived from the rhizome of the turmeric plant, exhibits various pharmacological and therapeutic effects through distinct cellular and molecular mechanisms.

Evidence Acquisition: Given the therapeutic applications and pharmacological properties of curcumin, it is essential to explore its pharmacological effects for potential use in clinical research. Notably, curcumin demonstrates significant antioxidant, anti-inflammatory, and anti-cancer properties. Importantly, no side effects or specific toxicity have been reported for curcumin.

Results: Curcumin, as a natural compound, can be utilized as a drug supplement in treatment regimens for various diseases. Numerous clinical studies have indicated that curcumin enhances the efficacy of chemotherapy drugs or mitigates their side effects when used concurrently.

Conclusions: This review presents an overview of studies conducted on the pharmacological effects and therapeutic properties of curcumin.

Keywords: Curcumin, Pharmacological Effects, Therapeutic Properties, Antioxidant, Anti-inflammatory, Anti-cancer

1. Context

The use of medicinal plants in disease treatment is on the rise. The extraction and analysis of herbal compounds for their effects on various diseases, including cancer, have garnered significant attention (1). Curcumin, chemically known as diferuloylmethane, is an active compound found in the rhizome of the turmeric plant (*Curcuma longa*) (2) (Figure 1). The yellow and golden hue of turmeric is primarily attributed to curcumin, which constitutes approximately 2% to 8% of its compounds, contributing to many of turmeric's properties (3, 4).

Curcumin was first extracted and purified from turmeric in 1815, with its structure identified as diferuloylmethane in 1910 (5). It was determined that curcumin is formed through a bond between two chromophore groups of aryl butene-2-anne (feruloy) and a methylene group (3, 5, 6). Curcumin possesses both phenolic groups and conjugated bonds, rendering it a lipophilic fluorescent substance (1, 2).

Curcumin exhibits extensive pharmacological activities, including antioxidant, anti-inflammatory, antimicrobial, and anti-cancer properties, despite its low intrinsic toxicity (2, 6, 7). Additional activities attributed to curcumin include hypolipidemic effects (8), liver protection (9), inhibition of lipoxygenase (LOX) (10) and cyclooxygenase (COX) (11), protease inhibition (12), free radical scavenging (13), inhibition of lipid peroxidation (14), cholesterol reduction (15), reduction

Copyright © 2025, Mohajeri et al. This open-access article is available under the Creative Commons Attribution 4.0 (CC BY 4.0) International License (https://creativecommons.org/licenses/by/4.0/), which allows for unrestricted use, distribution, and reproduction in any medium, provided that the original work is properly cited.

How to Cite: Mohajeri M, Momenai R, Karami-Mohajeri S, Ohadi M, Raeisi Estabragh M A. Curcumin as a Natural Therapeutic Agent: A Rapid Review of Potential Clinical Uses and Mechanisms of Action. Iran J Pharm Res. 2025; 24 (1): e156983. https://doi.org/10.5812/ijpr-156983.

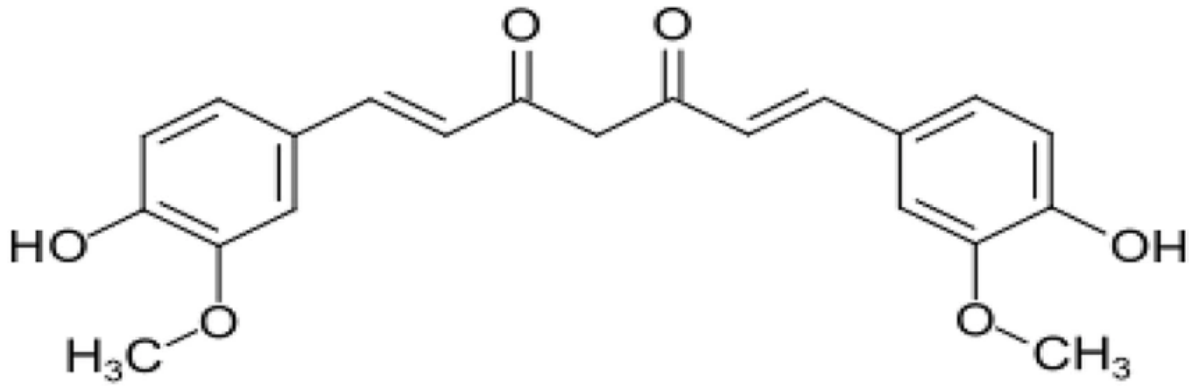

Figure 1. The chemical structure of curcumin

of platelet aggregation (16), reduction of cancer cell proliferation (17), enhancement of food digestion through increased bile flow (18), and modulation of cytokines and other inflammatory factors (19, 20).

Currently, it is believed that an imbalance of inflammatory reactants contributes to many chronic diseases (21, 22). Turmeric, particularly curcumin, has demonstrated a significant anti-inflammatory effect across multiple systems, as evidenced by recent scientific studies. Consequently, turmeric and curcumin are extensively used in the treatment of numerous diseases (23-27).

2. Evidence Acquisition

2.1. The Main Mechanisms of Curcumin

Curcumin exerts its effects on various cells through multiple cellular pathways and by influencing different receptors and messengers. In the following sections, we will discuss and review some of the mechanisms and molecules involved in the effects of curcumin.

2.1.1. Pre-oxidant and Antioxidant Effects of Curcumin

While pro-oxidants are believed to act as mediators in various diseases, antioxidants are commonly employed to delay or prevent disease progression. Numerous reports indicate that curcumin can function as both a pro-oxidant and an antioxidant (28). Regarding the mechanism of curcumin's pro-oxidant effects: (1) It stimulates the expression of reactive oxygen species (ROS) within cells, playing a crucial role in inducing the cellular anti-proliferative effects of this compound; (2) it binds with thioredoxin reductase (TR), leading to the overproduction of ROS in cancer cells (29-33).

Curcumin exhibits significant antioxidant and free radical scavenging effects in both living and non-living environments (34). This compound protects normal cells from oxidative damage by neutralizing ROS. It is inferred that the antioxidant and scavenging activities of curcumin arise from the phenolic OH groups and the CH_2 group of the beta-ketone part of the molecule (35). Free radicals are neutralized and inactivated by receiving protons from curcumin or by accepting electrons from this compound (36). Curcumin has also demonstrated the ability to accept electrons and regenerate. In a study conducted by the authors on the oxidation-reduction behavior of curcumin on the surface of a hanging mercury drop electrode and its oxidation-reduction mechanism, it was found that curcumin can readily accept electrons from reducing species and regenerate through a four-electron mechanism (37).

Curcumin also exhibits its antioxidant effects primarily by inhibiting superoxide radicals, hydrogen peroxide, and nitric oxide (38). It has been shown to increase the activity of various antioxidant enzymes, such as catalase (39), superoxide dismutase (40), co-oxygenase (26), and glutathione peroxidase, thereby preventing lipid peroxidation (41). Additionally, curcumin enhances the activity of detoxifying enzymes in the liver and kidneys, protecting normal cells against

carcinogenesis processes (9, 15, 33). It also boosts the activity of other enzymes, such as glutathione transferase (42), increases the levels of reduced glutathione and free sulfhydryl groups, and ultimately raises the antioxidant capacity of the living environment (14, 43).

2.1.2. Anti-inflammatory Effects

Curcumin has demonstrated anti-inflammatory properties in numerous studies. Oxidative stress is a major contributor to chronic inflammatory diseases, and antioxidants have been shown to possess anti-inflammatory properties (28, 44). Curcumin exhibits high antioxidant activity, which may underlie its anti-inflammatory effects (45). The anti-inflammatory properties of curcumin are manifested through multiple mechanisms, including the inhibition of nuclear factor-κB (NF-κB) activation, which induces the expression of pro-inflammatory gene products (46-49).

Curcumin modulates the expression of inflammatory enzymes such as cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS), both of which play roles in various inflammatory processes (50, 51). Another pro-inflammatory enzyme inhibited by curcumin is 5-lipoxygenase (5-LOX); curcumin inhibits 5-LOX activity by binding to its active site (52). Curcumin reduces the expression of several cell surface molecules that bind to inflammatory mediators (12, 19, 25, 41). It also decreases the expression of C-reactive protein (CRP) and various inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-8 (IL-8), interleukin-6 (IL-6), and chemokines (53, 54). Curcumin inhibits the activity of TNF-α, one of the most important pro-inflammatory mediators (55). Additionally, curcumin inhibits the proliferation and migration of T lymphocytes (56).

2.1.3. Regulatory Effects on Cytokines and Growth Factors

Curcumin has been shown to regulate the cellular activity of cytokines and various growth factors (57). Firstly, curcumin modulates the effect of epidermal growth factor (EGF) by reducing the expression and activity of EGF receptors (58). Secondly, curcumin modulates the activity of human epidermal growth factor receptor 2 (HER2/neu), a growth factor receptor closely associated with breast, lung, kidney, and prostate cancers. Thirdly, curcumin suppresses IL-6 activity by modulating signal transducer and activator of transcription 3 (STAT3) (10, 58, 59). Additionally, curcumin inhibits transforming growth factor-beta 1 (TGF-β1) and reduces the production of several pro-inflammatory cytokines, such as TNF-α and monocyte chemoattractant protein-1 (MCP-1) (60-62).

2.1.4. Roles in Angiogenesis

Angiogenesis is a critical stage in tissue development, playing a vital role in the progression of solid tumors (63). Numerous molecules are involved in angiogenesis, including vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), COX-2, and TNF-α (64, 65). Firstly, curcumin modulates VEGF expression by inhibiting NF-κB expression and disrupting its signaling role in angiogenesis (66). Secondly, curcumin modulates FGF-dependent angiogenesis (67). Thirdly, curcumin negatively modulates COX-2 expression (68-70). Fourthly, it inhibits the expression and activity of TNF-α. Curcumin also inhibits angiogenesis by reducing the expression of proteins involved in angiogenesis, such as matrix metalloproteinase-2 (MMP-2), matrix metalloproteinase-9 (MMP-9), and protein kinase C-alpha (PKC-α). Based on this evidence, curcumin can inhibit angiogenesis through several pathways (55, 71-73).

Figure 2 illustrates several pathways affected by curcumin. Curcumin inhibits the phosphoinositide 3-kinase (PI3K)/AKT/mTOR (PAM) signaling pathway by downregulating IKKβ, AKT, glycogen synthase kinase 3 beta (GSK3β), and HER2, potentially reducing cellular growth, invasion, and metastasis. It also affects the Janus kinase/signal transducer and activator of transcription 3 (JAK/STAT3) pathway by lowering STAT, JAK, and IL-6 levels and preventing STAT translocation into the nucleus, thereby suppressing proliferation and invasion in hormone receptor contexts. Additionally, curcumin modulates the mitogen-activated protein kinase (MAPK) pathway, targeting transforming growth factor (TGF), epidermal growth factor receptor (EGFR), extracellular signal-regulated kinases 1/2 (ERK1/2), mitogen-activated protein kinase kinase 4/7 (MKK4/7), c-Jun N-terminal kinase (JNK), and p38, and reducing nuclear c-Myc, c-Fos, and c-Jun, leading to decreased proliferation, migration, and induced apoptosis. Lastly, curcumin upregulates IκB and miR181b while downregulating NF-κB and IKK, preventing NF-κB nuclear translocation, which in turn inhibits proliferation, survival, metastasis, and angiogenesis (74).

3. Results

3.1. Potential Clinical Uses of Curcumin and Mechanisms of Action

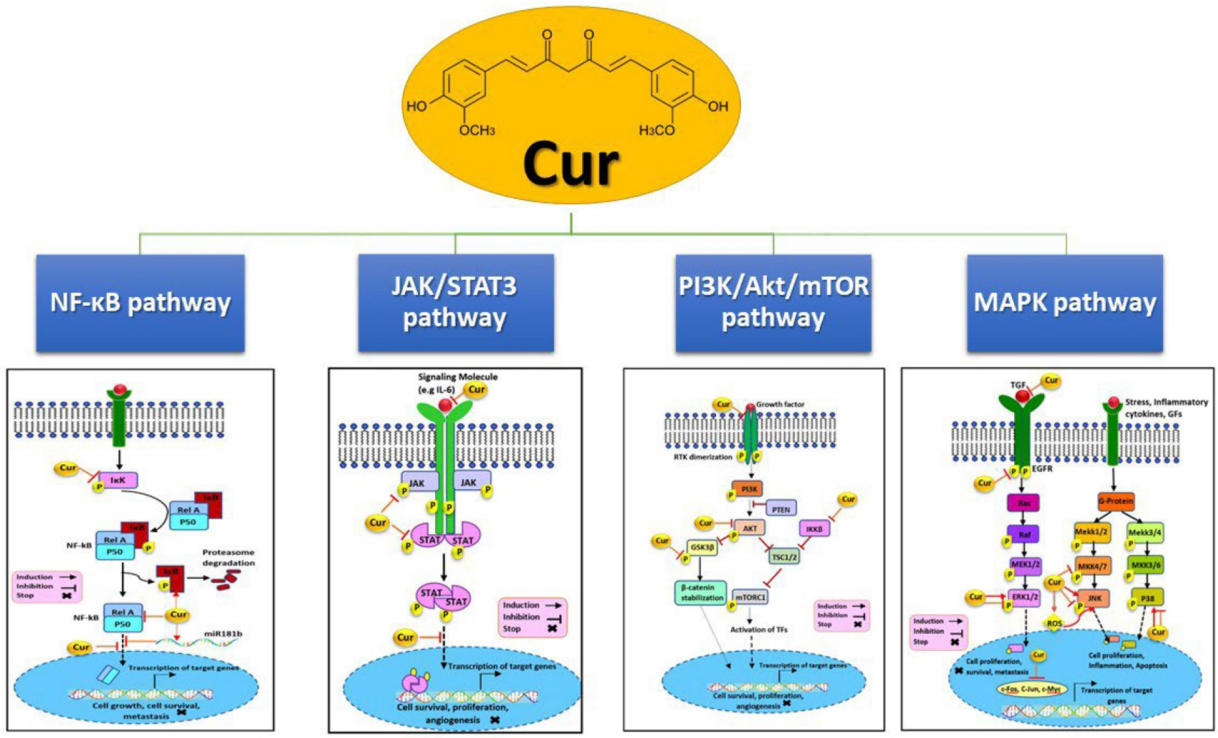

Figure 2. Some pathways that curcumin effects on them, with some changes from the article of Farghadani and Naidu (74).

Considering the mechanisms and cellular pathways discussed above, some of the clinical potentials of curcumin are outlined below.

3.1.1. Cancer

Curcumin has demonstrated preventive and therapeutic effects in various cancers (75). The formation or spread of tumors can be prevented or reduced by this compound, as evidenced by numerous studies (76, 77). The cell proliferation cycle is impacted by antiangiogenic effects, induction of apoptosis, and interference (78-80). Curcumin can exhibit its anti-cancer effects through several mechanisms (Table 1).

Firstly, curcumin can inhibit and suppress cell proliferation in a wide range of cancer cells by modulating anti-apoptotic gene products, activating caspases, and stimulating cancer-suppressing genes such as p53 (97, 98). This compound demonstrates its antiangiogenic effects by inhibiting VEGF, angiopoietin I and II, and tyrosine kinase receptors such as Flk-1/KDR (one of the VEGF receptors). Additionally, curcumin activates apoptosis by activating Bcl-2 and Bcl-XL proteins, inducing caspases 3, 8, and 9, releasing cytochrome c, and activating peroxisome proliferator-activated receptor gamma (PPAR-γ) (99-101).

Secondly, curcumin inhibits tumor invasion through the modulation of matrix metalloproteinases (MMPs), cell surface adhesion molecules, AP-1, NF-κB, TNF-α, LOX, COX, chemokines, and growth factors such as EGFR and HER-2, as well as the inhibition of terminal deoxynucleotidyl transferase (TdT) activity and protein tyrosine kinase (102, 103). Exposure of various human gastrointestinal cell lines to curcumin inhibits lipid peroxidation, COX-2 expression, and prostaglandin E2 (PGE2) production, while increasing the level of glutathione S-transferase enzyme (104, 105).

Thirdly, the suppression of angiogenic cytokines such as interleukin-23 (IL-23), IL-6, and interleukin-1 beta (IL-1β) contributes to curcumin's inhibition of angiogenesis in certain tumors (106-108).

Fourthly, curcumin's anti-tumor effects are partly due to its ability to reduce inflammation, given the

Table 1. Summary of the Study on the Role of Curcumin in Cellular Signaling Pathways in Different Types of Cancer

Cell Signaling Pathways	Models	Curcumin Administered Doses	Effects	References
Wnt/β-catenin (μM)	Human cell line A549	60	Downregulation/inhibition	(81)
VEGF (mg/kg)	Nude mice	100	Downregulation/inhibition	(82)
NOTCH 1 (μM)	Human lung cancer cell lines	6	Downregulation/inhibition	(83)
ERK ½ (ng/mL)	Human NCI-H1975 line	10	Downregulation/inhibition	(84)
Akt/mTOR (μM)	Human breast cell lines	10 or 30	Downregulation/inhibition	(85)
NF-κB (μM)	Human breast cell lines	20 or 25	Downregulation/inhibition	(86)
Bcl-2 and Bcl-XL and Autocrine GH (μM)	T47D human breast cells	20	Downregulation/inhibition	(87)
MDR-1 (μM)	MCF-7 breast cancer cell line	1.3	Downregulation/inhibition	(88)
FEN1 (μM/L)	MCF-7 breast cancer cell line	0 - 50	Downregulation/inhibition	(89)
STAT3 and IAP (μM)	Human GBM stem cells	25	Downregulation/inhibition	(90)
Platelet-derived growth factor (μM)	Rat pancreatic stellate cells	25	Downregulation/inhibition	(91)
PI3 K/Akt (μM)	Panc-1 human pancreatic cells	20	Downregulation/inhibition	(92)
IAP (μM)	Panc-1 human cells	10/50/100	Downregulation/inhibition	(93)
Cdc20 (μM)	Patu8988 and Panc-1 human cell lines	10 or 20	Downregulation/inhibition	(94)
PI3K (μM)	Human SGC-7901 and BGC-823 cells	10/20/40	Downregulation/inhibition	(95)
Wnt3 and a/β-catenin/EMT and Bcl-2 (μM)	Human gastric cell lines	20	Downregulation/inhibition	(96)

Abbreviations: VEGF, vascular endothelial growth factor; NF-κB, nuclear factor-κB; STAT3, signal transducer and activator of transcription 3; PI3K, phosphoinositide 3-kinase.

connection between inflammation and cancer. This compound reduces the production of inflammatory mediators, such as cytokines, COX-2, LOX-2, inducible iNOS, and related cytokines, thereby preventing several types of cancer (109, 110).

Fifthly, curcumin has a chemopreventive effect that can suppress tumor spread, which is one of the possible mechanisms for its action. Its topical application strongly inhibits inflammation caused by 12-O-tetradecanoylphorbol-13-acetate (TPA), cell proliferative hyperplasia, ornithine decarboxylase (ODC) activity, production of ROS, DNA oxidative changes, and papilloma formation (111-113). Since the production of ROS is involved in carcinogenic processes, part of the anti-cancer effects of curcumin is related to its antioxidant and ROS-scavenging effects (29, 35).

Another mechanism for the anticancer effects of curcumin is its involvement in the cell cycle and reduced expression of cyclin-dependent kinases (CDKs). The CDKs are serine-threonine kinases that control cell cycle progression (114). Curcumin also inhibits STAT3 phosphorylation, which is responsible for signaling carcinogenic pathways (115).

3.1.2. Diabetes

Curcumin plays a role in the treatment of type II diabetes, a condition characterized by insulin resistance (116) Oxidative stress caused by hyperglycemia, alterations in energy metabolism, and inflammatory mediators significantly contribute to the pathology of diabetes, depletion of cellular antioxidant defense systems, and induction of ROS production (117, 118). Oxidative stress, along with hyperglycemia, impairs cellular, vascular, and neuronal functions. High glucose concentrations induce free radical production through mechanisms involving advanced glycation end products (AGEs), activation of protein kinase C, and the aldose reductase pathway (119).

Another critical factor contributing to increased ROS is TNF, which is linked to obesity and diabetes and is associated with insulin resistance and diabetes complications (120). Since NF-κB and TNF are involved in the induction of insulin resistance, and curcumin can modulate NF-κB activity and TNF expression, curcumin may be effective in reducing the incidence of type II diabetes (119). Curcumin also aids in the management of diabetes (121).

Curcumin exhibits several effects, including proteasome inhibition (a protein complex that regulates the levels of proteins involved in apoptosis), neuroprotective, antioxidant, anti-inflammatory, hypoglycemic, lipid-lowering, and hemoglobin A1c-reducing effects, which collectively slow down or halt the progression of type II diabetes. Table 2 presents various diabetic animal models used to study the effect of curcumin on blood glucose levels.

3.1.3. Cardiovascular Diseases

Table 2. Diabetic Animal Models to Study the Effect of Curcumin on Blood Sugar

Curcumin (Route and Dose)	Time of Treatment	Animal Models	References
Oral, 60 mg/kg·BW	14 days	Wistar rats	(122)
0.02% curcumin in diet	42 days	db/db mice	(123)
Oral, 60 mg/kg·BW	14 days	Wistar rats	(124)
Oral, 150 mg/kg·BW	42 days	Wistar rats	(125)
Oral, 80 mg/kg·BW	15 and 60 days	SD rats	(126)
Oral, 100 mg/kg·BW	28 days; 56 days	SD rats	(127)
0.5% curcumin in diet	16 weeks	Wistar rats	(128)
Oral, 300 mg/kg·BW	56 days	Wistar rats	(129)
Oral, 80 mg/kg·BW	21 days	Wistar rats	(130)
I.P., 10 mM	28 days	Swiss mice	(131)
Oral, 50 mg/kg·BW	15 days	C57BL/6J mice	(132)

Curcumin has been shown to prevent myocardial infarction and other cardiovascular diseases (133). Atherosclerosis, the most common heart disease, involves the buildup of fat, cholesterol, carbohydrate complexes, and fibrin (which causes blood clots) within the inner walls of major arteries, forming plaques. These plaques can completely or partially obstruct a blood vessel and impede arterial blood flow, potentially leading to clot formation on the plaque's surface (134, 135). If such conditions occur and blood flow in the coronary arteries is interrupted, it can result in a heart attack.

Controllable mechanisms of atherosclerotic proliferation include low-density lipoprotein (LDL) oxidation, abnormal platelet aggregation, and inflammation. Curcumin possesses anti-platelet aggregation and antioxidant properties (136, 137). Its ability to control platelet aggregation appears to be directly dependent on the inhibition of thromboxane and the increased activity of prostacyclin (138).

Curcumin is a potent antioxidant and free radical scavenger, reducing cellular damage. It also lowers blood lipid levels, including triglycerides and cholesterol, particularly LDL and very-low-density lipoprotein (VLDL), while increasing high-density lipoprotein (HDL) levels (27, 29, 81-83, 114, 115). This compound reduces the incidence of cardiovascular diseases by inhibiting or preventing oxidative stress processes and exhibiting direct cardioprotective effects (8, 139, 140). Additionally, curcumin can prevent vascular disorders by reducing the calcification levels of the vascular wall (141).

3.1.4. Neurodegenerative Disorders

Curcumin has demonstrated neuroprotective effects in neurological diseases such as Alzheimer's disease (AD), dyskinesia, depression, epilepsy, and several other neurological disorders (142). Oxidative stress is one of the mechanisms leading to neuronal damage in the brain. Alzheimer's disease is a progressive disorder associated with cognitive and memory impairments, speech difficulties, and personality changes (143). Although the underlying cause of AD is not fully understood, there is substantial evidence that oxidative stress and impaired protein metabolism contribute to its pathogenesis.

The neuroprotective ability of curcumin has been demonstrated in studies investigating its protective effects against the side effects of high alcohol doses (144). Various research studies have explored the beneficial effects of curcumin on AD and Parkinson's disease using laboratory animals. These studies have shown that curcumin reduces amyloid pathology (145). Curcumin is believed to prevent the onset and progression of AD by exerting beneficial effects on amyloid metabolism, as well as through its anti-inflammatory and antioxidant properties (146).

Given the widespread use of curcumin as a food additive, whose safety has been established in short-term studies, curcumin is considered a promising agent in the treatment and prevention of AD (147, 148). Some studies have demonstrated that curcumin can prevent blood-brain barrier damage, cerebral edema, cerebral circulatory disorders, and tissue and chemical changes in the central nervous system (CNS). These effects are attributed to the antioxidant and anti-inflammatory properties of curcumin (149, 150).

3.1.5. Hepatic Fibrosis

Liver fibrosis and cirrhosis, often resulting from chronic liver damage and disorders, pose significant therapeutic challenges worldwide (151). Currently, liver

transplantation is the only treatment for end-stage cirrhosis. Oxidative stress and inflammation play crucial roles in the development of alcohol-induced hepatic fibrosis and the metabolism of multiple polyunsaturated fatty acids (PUFAs). Due to its antioxidant and anti-inflammatory properties, curcumin inhibits liver fibrosis (152).

Curcumin is recognized as a potent hepatic anti-fibrosis agent by inducing the expression of MMPs in the liver (153). Overall, curcumin exerts a protective effect on the liver and can prevent MMP activity. This compound also aids in improving liver damage (154). The primary protective and therapeutic effects of curcumin on liver tissue are attributed to its anti-inflammatory, antioxidant, and anti-fibrogenic activities (155).

Curcumin increases the levels of glutathione and superoxide dismutase enzymes in liver tissue, reduces lipid peroxidation, enhances the levels of detoxifying enzymes, boosts the liver's overall antioxidant capacity, and ultimately inhibits the production of ROS (156). Additionally, curcumin can help improve liver damage by lowering serum levels of fat and uric acid (157).

3.1.6. AIDS and Psoriasis

Curcumin has recently been shown to inhibit HIV transcription (158). Mazumder reported that curcumin inhibited P24 antigen production and Tat-dependent transcription. They also demonstrated that curcumin inhibited HIV-1 integrase (159). The anti-AIDS effects of curcumin are attributed to two phenyl rings attached to adjacent molecules through hydroxyl groups (158). Curcumin is also considered a moderate inhibitor of HIV-1 and HIV-2 proteases (160). This compound can inhibit HIV-1 through Tat protein degradation (161).

Similar to AIDS, psoriasis involves modulation of immune system activity. Curcumin has beneficial effects on psoriasis in mice through its anti-inflammatory and antioxidant properties (162). In psoriasis, curcumin exhibits its anti-inflammatory effects by reducing the expression of cytokines such as interleukin-17A (IL-17A), interleukin-17F (IL-17F), interleukin-22 (IL-22), IL-6, IL-1β, and TNF-α, and by inhibiting NF-κB activation (163). Curcumin has been shown to improve psoriasis by inhibiting keratinocyte proliferation (164).

Heng et al. (as cited by Thangapazham et al.) revealed that topical treatment with curcumin yielded favorable results, confirmed by immunological, histological, and clinical criteria. According to their findings, these effects of curcumin were associated with the modulation of phosphorylase kinase (PhK) activity in the calcium-calmodulin signaling pathway. This pathway is involved in glycogenolysis and ATP-dependent phosphorylation, providing the necessary energy for cell proliferation and migration (164). The effectiveness of curcumin is partly due to the reduction of PhK levels, as PhK activity is elevated in untreated psoriasis (165).

4. Conclusions

The use of curcumin has proven effective in treating various diseases in both animal and human studies. Curcumin is a natural compound with potent anti-inflammatory and antioxidant properties. These properties have led to its application in gastrointestinal and liver diseases, cancer, arthritis, allergies, asthma, atherosclerosis, AD, and hyperglycemia. However, it is important to note that the use of curcumin as a therapeutic agent for the prevention and treatment of diseases requires further clinical trials.

Acknowledgements

This article is the result of a research project approved by the Student Research Committee of Kerman University of Medical Sciences No. 403000584 which was carried out with the financial support of the Vice-Chancellor for Research and Technology of the University.

Footnotes

Authors' Contribution: M. M., M. A. R. E., and M. O. had the idea for the article. M. M., R. M., and S. K. performed the literature search and data analysis. M. M., and M. O. drafted and M. A. R. E. critically revised the work.

Conflict of Interests Statement: The authors declared no conflict of interest.

Funding/Support: This study was carried out with the financial support of the Vice-Chancellor for Research and Technology of the Kerman University of Medical Sciences (No. 403000584).

References

1. Mohajeri M, Rezaee M, Sahebkar A. Cadmium-induced toxicity is rescued by curcumin: A review. *Biofactors*. 2017;**43**(5):645-61. [PubMed ID: 28719149]. https://doi.org/10.1002/biof.1376.
2. Mohajeri M, Bianconi V, Avila-Rodriguez MF, Barreto GE, Jamialahmadi T, Pirro M, et al. Curcumin: a phytochemical modulator of estrogens and androgens in tumors of the reproductive system. *Pharmacol Res*. 2020;**156**:104765. [PubMed ID: 32217147]. https://doi.org/10.1016/j.phrs.2020.104765.

3. Mohajeri M, Behnam B, Cicero AFG, Sahebkar A. Protective effects of curcumin against aflatoxicosis: A comprehensive review. *J Cell Physiol*. 2018;**233**(4):3552-77. [PubMed ID: 29034472]. https://doi.org/10.1002/jcp.26212.
4. Shakeri A, Cicero AFG, Panahi Y, Mohajeri M, Sahebkar A. Curcumin: A naturally occurring autophagy modulator. *J Cell Physiol*. 2019;**234**(5):5643-54. [PubMed ID: 30239005]. https://doi.org/10.1002/jcp.27404.
5. Gupta SC, Patchva S, Koh W, Aggarwal BB. Discovery of curcumin, a component of golden spice, and its miraculous biological activities. *Clin Exp Pharmacol Physiol*. 2012;**39**(3):283-99. [PubMed ID: 22118895]. [PubMed Central ID: PMC3288651]. https://doi.org/10.1111/j.1440-1681.2011.05648.x.
6. Mohajeri M, Sahebkar A. Protective effects of curcumin against doxorubicin-induced toxicity and resistance: A review. *Crit Rev Oncol Hematol*. 2018;**122**:30-51. [PubMed ID: 29458788]. https://doi.org/10.1016/j.critrevonc.2017.12.005.
7. Harikrishnan A, Khanna S, Veena V. Design of New Improved Curcumin Derivatives to Multi-targets of Cancer and Inflammation. *Curr Drug Targets*. 2021;**22**(5):573-89. [PubMed ID: 32753008]. https://doi.org/10.2174/1389450121666200804113745.
8. Hussein SA, El-Senosi YA, Ragab MR, Hammad MM, Apo A. Hypolipidemic effect of curcumin in hyper-cholesterolemic rats. *Benha Vet Med J*. 2014;**27**(2):277-89.
9. Naik RS, Mujumdar AM, Ghaskadbi S. Protection of liver cells from ethanol cytotoxicity by curcumin in liver slice culture in vitro. *J Ethnopharmacol*. 2004;**95**(1):31-7. [PubMed ID: 15374604]. https://doi.org/10.1016/j.jep.2004.06.032.
10. Skrzypczak-Jankun E, Zhou K, McCabe NP, Selman SH, Jankun J. Structure of curcumin in complex with lipoxygenase and its significance in cancer. *Int J Mol Med*. 2003;**12**(1):17-24. [PubMed ID: 12792803].
11. Selvam C, Jachak SM, Thilagavathi R, Chakraborti AK. Design, synthesis, biological evaluation and molecular docking of curcumin analogues as antioxidant, cyclooxygenase inhibitory and anti-inflammatory agents. *Bioorg Med Chem Lett*. 2005;**15**(7):1793-7. [PubMed ID: 15780608]. https://doi.org/10.1016/j.bmcl.2005.02.039.
12. Zahedipour F, Hosseini SA, Sathyapalan T, Majeed M, Jamialahmadi T, Al-Rasadi K, et al. Potential effects of curcumin in the treatment of COVID-19 infection. *Phytother Res*. 2020;**34**(11):2911-20. [PubMed ID: 32430996]. [PubMed Central ID: PMC7276879]. https://doi.org/10.1002/ptr.6738.
13. Kassim M, Ibrahim MIM, Mansor M, Hasan MS, Al-abd NM. Curcumin Scavenges Peroxynitrite in RAW 264.7 Macrophages through Phenolic Hydroxyl Groups. *J Pharm Res Int*. 2021;**33**:66-77. https://doi.org/10.9734/jpri/2021/v33i23A31414.
14. Iqbal M, Shah MD, Vun-Sang S, Okazaki Y, Okada S. The therapeutic potential of curcumin in alleviating N-diethylnitrosamine and iron nitrilotriacetate induced renal cell tumours in mice via inhibition of oxidative stress: Implications for cancer chemoprevention. *Biomed Pharmacother*. 2021;**139**:111636. [PubMed ID: 33957566]. https://doi.org/10.1016/j.biopha.2021.111636.
15. Peschel D, Koerting R, Nass N. Curcumin induces changes in expression of genes involved in cholesterol homeostasis. *J Nutr Biochem*. 2007;**18**(2):113-9. [PubMed ID: 16713233]. https://doi.org/10.1016/j.jnutbio.2006.03.007.
16. Tabeshpour J, Hashemzaei M, Sahebkar A. The regulatory role of curcumin on platelet functions. *J Cell Biochem*. 2018;**119**(11):8713-22. [PubMed ID: 30098070]. https://doi.org/10.1002/jcb.27192.
17. Hussein Y, Loutfy SA, Kamoun EA, El-Moslamy SH, Radwan EM, Elbehairi SEI. Enhanced anti-cancer activity by localized delivery of curcumin form PVA/CNCs hydrogel membranes: Preparation and in vitro bioevaluation. *Int J Biol Macromol*. 2021;**170**:107-22. [PubMed ID: 33358954]. https://doi.org/10.1016/j.ijbiomac.2020.12.133.
18. Lee JH, Oh JH, Lee YJ. Biliary excretion of curcumin is mediated by multidrug resistance-associated protein 2. *Biol Pharm Bull*. 2012;**35**(5):777-80. [PubMed ID: 22687416]. https://doi.org/10.1248/bpb.35.777.
19. Valizadeh H, Abdolmohammadi-Vahid S, Danshina S, Ziya Gencer M, Ammari A, Sadeghi A, et al. Nano-curcumin therapy, a promising method in modulating inflammatory cytokines in COVID-19 patients. *Int Immunopharmacol*. 2020;**89**(Pt B):107088. [PubMed ID: 33129099]. [PubMed Central ID: PMC7574843]. https://doi.org/10.1016/j.intimp.2020.107088.
20. Hadizadeh-Bazaz M, Vaezi G, Khaksari M, Hojati V. Curcumin attenuates spatial memory impairment by anti-oxidative, anti-apoptosis, and anti-inflammatory mechanism against methamphetamine neurotoxicity in male Wistar rats: Histological and biochemical changes. *Neurotoxicology*. 2021;**84**:208-17. [PubMed ID: 33819551]. https://doi.org/10.1016/j.neuro.2021.03.011.
21. Hamer M, Williams E, Vuonovirta R, Giacobazzi P, Gibson EL, Steptoe A. The effects of effort-reward imbalance on inflammatory and cardiovascular responses to mental stress. *Psychosom Med*. 2006;**68**(3):408-13. [PubMed ID: 16738072]. https://doi.org/10.1097/01.psy.0000221227.02975.a0.
22. Grange PA, Weill B, Dupin N, Batteux F. Does inflammatory acne result from imbalance in the keratinocyte innate immune response? *Microbes Infect*. 2010;**12**(14-15):1085-90. [PubMed ID: 20691803]. https://doi.org/10.1016/j.micinf.2010.07.015.
23. He Y, Yue Y, Zheng X, Zhang K, Chen S, Du Z. Curcumin, inflammation, and chronic diseases: how are they linked? *Molecules*. 2015;**20**(5):9183-213. [PubMed ID: 26007179]. [PubMed Central ID: PMC6272784]. https://doi.org/10.3390/molecules20059183.
24. Rahmani S, Asgary S, Askari G, Keshvari M, Hatamipour M, Feizi A, et al. Treatment of Non-alcoholic Fatty Liver Disease with Curcumin: A Randomized Placebo-controlled Trial. *Phytother Res*. 2016;**30**(9):1540-8. [PubMed ID: 27270872]. https://doi.org/10.1002/ptr.5659.
25. Hatamipour M, Ramezani M, Tabassi SAS, Johnston TP, Sahebkar A. Demethoxycurcumin: A naturally occurring curcumin analogue for treating non-cancerous diseases. *J Cell Physiol*. 2019;**234**(11):19320-30. [PubMed ID: 31344992]. https://doi.org/10.1002/jcp.28626.
26. Sahebkar A. Why it is necessary to translate curcumin into clinical practice for the prevention and treatment of metabolic syndrome? *Biofactors*. 2013;**39**(2):197-208. [PubMed ID: 23239418]. https://doi.org/10.1002/biof.1062.
27. Panahi Y, Fazlolahzadeh O, Atkin SL, Majeed M, Butler AE, Johnston TP, et al. Evidence of curcumin and curcumin analogue effects in skin diseases: A narrative review. *J Cell Physiol*. 2019;**234**(2):1165-78. [PubMed ID: 30073647]. https://doi.org/10.1002/jcp.27096.
28. Sandur SK, Ichikawa H, Pandey MK, Kunnumakkara AB, Sung B, Sethi G, et al. Role of pro-oxidants and antioxidants in the anti-inflammatory and apoptotic effects of curcumin (diferuloylmethane). *Free Radic Biol Med*. 2007;**43**(4):568-80. [PubMed ID: 17640567]. [PubMed Central ID: PMC2754304]. https://doi.org/10.1016/j.freeradbiomed.2007.05.009.
29. Lee YJ, Kim NY, Suh YA, Lee C. Involvement of ROS in Curcumin-induced Autophagic Cell Death. *Korean J Physiol Pharmacol*. 2011;**15**(1):1-7. [PubMed ID: 21461234]. [PubMed Central ID: PMC3062078]. https://doi.org/10.4196/kjpp.2011.15.1.1.
30. Giordano A, Tommonaro G. Curcumin and Cancer. *Nutrients*. 2019;**11**(10). [PubMed ID: 31590362]. [PubMed Central ID: PMC6835707]. https://doi.org/10.3390/nu11102376.
31. Hsu CH, Cheng AL. Clinical studies with curcumin. *Adv Exp Med Biol*. 2007;**595**:471-80. [PubMed ID: 17569225]. https://doi.org/10.1007/978-0-387-46401-5_21.

32. Pari L, Tewas D, Eckel J. Role of curcumin in health and disease. *Arch Physiol Biochem*. 2008;**114**(2):127-49. [PubMed ID: 18484280]. https://doi.org/10.1080/13813450802033958.
33. Pulido-Moran M, Moreno-Fernandez J, Ramirez-Tortosa C, Ramirez-Tortosa M. Curcumin and Health. *Molecules*. 2016;**21**(3):264. [PubMed ID: 26927041]. [PubMed Central ID: PMC6273481]. https://doi.org/10.3390/molecules21030264.
34. Dahl TA, Bilski P, Reszka KJ, Chignell CF. Photocytotoxicity of curcumin. *Photochem Photobiol*. 1994;**59**(3):290-4. [PubMed ID: 8016207]. https://doi.org/10.1111/j.1751-1097.1994.tb05036.x.
35. Barzegar A, Moosavi-Movahedi AA. Intracellular ROS protection efficiency and free radical-scavenging activity of curcumin. *PLoS One*. 2011;**6**(10). e26012. [PubMed ID: 22016801]. [PubMed Central ID: PMC3189944]. https://doi.org/10.1371/journal.pone.0026012.
36. Pedersen JZ, Oliveira C, Incerpi S, Kumar V, Fiore AM, De Vito P, et al. Antioxidant activity of 4-methylcoumarins. *J Pharm Pharmacol*. 2007;**59**(12):1721-8. [PubMed ID: 18053335]. https://doi.org/10.1211/jpp.59.12.0015.
37. Barik A, Mishra B, Shen L, Mohan H, Kadam RM, Dutta S, et al. Evaluation of a new copper(II)-curcumin complex as superoxide dismutase mimic and its free radical reactions. *Free Radic Biol Med*. 2005;**39**(6):811-22. [PubMed ID: 16109310]. https://doi.org/10.1016/j.freeradbiomed.2005.05.005.
38. Unnikrishnan MK, Rao MN. Curcumin inhibits nitrogen dioxide induced oxidation of hemoglobin. *Mol Cell Biochem*. 1995;**146**(1):35-7. [PubMed ID: 7651374]. https://doi.org/10.1007/BF00926878.
39. Mofidi Najjar F, Taghavi F, Ghadari R, Sheibani N, Moosavi-Movahedi AA. Destructive effect of non-enzymatic glycation on catalase and remediation via curcumin. *Arch Biochem Biophys*. 2017;**630**:81-90. [PubMed ID: 28668706]. https://doi.org/10.1016/j.abb.2017.06.018.
40. Shen LR, Xiao F, Yuan P, Chen Y, Gao QK, Parnell LD, et al. Curcumin-supplemented diets increase superoxide dismutase activity and mean lifespan in Drosophila. *Age (Dordr)*. 2013;**35**(4):1133-42. [PubMed ID: 22653297]. [PubMed Central ID: PMC3705117]. https://doi.org/10.1007/s11357-012-9438-2.
41. Saeidinia A, Keihanian F, Butler AE, Bagheri RK, Atkin SL, Sahebkar A. Curcumin in heart failure: A choice for complementary therapy? *Pharmacol Res*. 2018;**131**:112-9. [PubMed ID: 29550354]. https://doi.org/10.1016/j.phrs.2018.03.009.
42. Tejo J. Chapter 45 - Curcumin, antioxidant activity, and paracetamol toxicity. In: Patel VB, Preedy VR, editors. *Toxicology*. Academic Press; 2021. p. 469-77. https://doi.org/10.1016/B978-0-12-819092-0.00046-7.
43. Hu G, Batool Z, Cai Z, Liu Y, Ma M, Sheng L, et al. Production of self-assembling acylated ovalbumin nanogels as stable delivery vehicles for curcumin. *Food Chem*. 2021;**355**:129635. [PubMed ID: 33780798]. https://doi.org/10.1016/j.foodchem.2021.129635.
44. Rodrigues FC, Kumar NA, Thakur G. The potency of heterocyclic curcumin analogues: An evidence-based review. *Pharmacol Res*. 2021;**166**:105489. [PubMed ID: 33588007]. https://doi.org/10.1016/j.phrs.2021.105489.
45. Shi Y, Liang X, Chi L, Chen Y, Liang L, Zhao J, et al. Ethanol extracts from twelve Curcuma species rhizomes in China: Antimicrobial, antioxidative and anti-inflammatory activities. *South African J Botany*. 2021;**140**:167-72. https://doi.org/10.1016/j.sajb.2021.04.003.
46. Memarzia A, Khazdair MR, Behrouz S, Gholamnezhad Z, Jafarnezhad M, Saadat S, et al. Experimental and clinical reports on anti-inflammatory, antioxidant, and immunomodulatory effects of Curcuma longa and curcumin, an updated and comprehensive review. *Biofactors*. 2021;**47**(3):311-50. [PubMed ID: 33606322]. https://doi.org/10.1002/biof.1716.
47. Kuadkaew S, Ungphaiboon S, Phdoongsombut N, Kaewsuwan S, Mahattanadul S. Efficacy of a Chitosan-curcumin Mixture in Treating Indomethacininduced Acute Gastric Ulcer in Rats. *Curr Pharm Biotechnol*. 2021;**22**(14):1919-31. [PubMed ID: 33504303]. https://doi.org/10.2174/1389201022666210127115427.
48. Gao X, Yi X, Liu Z, Dong X, Xia G, Zhang X, et al. Comparative Study on Curcumin Loaded in Golden Pompano (Trachinotus blochii) Head Phospholipid and Soybean Lecithin Liposomes: Preparation, Characteristics and Anti-Inflammatory Properties. *Molecules*. 2021;**26**(8). [PubMed ID: 33923773]. [PubMed Central ID: PMC8073247]. https://doi.org/10.3390/molecules26082328.
49. Kunchandy E, Rao MNA. Oxygen radical scavenging activity of curcumin. *Int J Pharm*. 1990;**58**(3):237-40. https://doi.org/10.1016/0378-5173(90)90201-E.
50. Goel A, Boland CR, Chauhan DP. Specific inhibition of cyclooxygenase-2 (COX-2) expression by dietary curcumin in HT-29 human colon cancer cells. *Cancer Lett*. 2001;**172**(2):111-8. [PubMed ID: 11566484]. https://doi.org/10.1016/s0304-3835(01)00655-3.
51. Bengmark S. Curcumin, an atoxic antioxidant and natural NFkappaB, cyclooxygenase-2, lipooxygenase, and inducible nitric oxide synthase inhibitor: a shield against acute and chronic diseases. *JPEN J Parenter Enteral Nutr*. 2006;**30**(1):45-51. [PubMed ID: 16387899]. https://doi.org/10.1177/014860710603000145.
52. D'Cunha NM, Seddon N, Mellor DD, Georgousopoulou EN, McKune AJ, Panagiotakos DB, et al. Curcumin for Cognition: Is It Just Hype, Based on Current Data? *Adv Nutr*. 2019;**10**(1):179-81. [PubMed ID: 30624556]. [PubMed Central ID: PMC6370263]. https://doi.org/10.1093/advances/nmy066.
53. Sung S, Kwon D, Um E, Kim B. Could Polyphenols Help in the Control of Rheumatoid Arthritis? *Molecules*. 2019;**24**(8). [PubMed ID: 31013659]. [PubMed Central ID: PMC6515230]. https://doi.org/10.3390/molecules24081589.
54. Kim KI, Shin KS, Jun WJ, Hong BS, Shin DH, Cho HY, et al. Effects of polysaccharides from rhizomes of Curcuma zedoaria on macrophage functions. *Biosci Biotechnol Biochem*. 2001;**65**(11):2369-77. [PubMed ID: 11791707]. https://doi.org/10.1271/bbb.65.2369.
55. Singh S, Aggarwal BB. Activation of transcription factor NF-kappa B is suppressed by curcumin (diferuloylmethane) [corrected]. *J Biol Chem*. 1995;**270**(42):24995-5000. [PubMed ID: 7559628]. https://doi.org/10.1074/jbc.270.42.24995.
56. Sikora E, Bielak-Zmijewska A, Piwocka K, Skierski J, Radziszewska E. Inhibition of proliferation and apoptosis of human and rat T lymphocytes by curcumin, a curry pigment. *Biochem Pharmacol*. 1997;**54**(8):899-907. [PubMed ID: 9354590]. https://doi.org/10.1016/s0006-2952(97)00251-7.
57. Ashrafizadeh M, Zarrabi A, Hushmandi K, Zarrin V, Moghadam ER, Hashemi F, et al. Toward Regulatory Effects of Curcumin on Transforming Growth Factor-Beta Across Different Diseases: A Review. *Front Pharmacol*. 2020;**11**:585413. [PubMed ID: 33381035]. [PubMed Central ID: PMC7767860]. https://doi.org/10.3389/fphar.2020.585413.
58. Chen A, Xu J, Johnson AC. Curcumin inhibits human colon cancer cell growth by suppressing gene expression of epidermal growth factor receptor through reducing the activity of the transcription factor Egr-1. *Oncogene*. 2006;**25**(2):278-87. [PubMed ID: 16170359]. https://doi.org/10.1038/sj.onc.1209019.
59. Shanmugam MK, Rane G, Kanchi MM, Arfuso F, Chinnathambi A, Zayed ME, et al. The multifaceted role of curcumin in cancer prevention and treatment. *Molecules*. 2015;**20**(2):2728-69. [PubMed ID: 25665066]. [PubMed Central ID: PMC6272781]. https://doi.org/10.3390/molecules20022728.
60. Baj T, Seth R. Role of Curcumin in Regulation of TNF-alpha Mediated Brain Inflammatory Responses. *Recent Pat Inflamm Allergy Drug Discov*. 2018;**12**(1):69-77. [PubMed ID: 29972106]. https://doi.org/10.2174/1872213X12666180703163824.

61. Sikora E, Scapagnini G, Barbagallo M. Curcumin, inflammation, ageing and age-related diseases. *Immun Ageing*. 2010;**7**(1):1. [PubMed ID: 20205886]. [PubMed Central ID: PMC2827376]. https://doi.org/10.1186/1742-4933-7-1.
62. Hatami M, Abdolahi M, Soveyd N, Djalali M, Togha M, Honarvar NM. Molecular Mechanisms of Curcumin in Neuroinflammatory Disorders: A Mini Review of Current Evidences. *Endocr Metab Immune Disord Drug Targets*. 2019;**19**(3):247-58. [PubMed ID: 30488803]. https://doi.org/10.2174/1871530319666181129103056.
63. Mirzaei H, Bagheri H, Ghasemi F, Khoi JM, Pourhanifeh MH, Heyden YV, et al. Anti-Cancer Activity of Curcumin on Multiple Myeloma. *Anticancer Agents Med Chem*. 2021;**21**(5):575-86. [PubMed ID: 32951583]. https://doi.org/10.2174/1871520620666200918113625.
64. Bae M, Kim S, Jeong J, Lee Y, Kim H, Kim S, et al. Curcumin inhibits hypoxia-induced angiogenesis via down-regulation of HIF-1. *Oncol Rep*. 2006;**15**(6):1557-62. https://doi.org/10.3892/or.15.6.1557.
65. Bhandarkar SS, Arbiser JL. Curcumin as an inhibitor of angiogenesis. *Adv Exp Med Biol*. 2007;**595**:185-95. [PubMed ID: 17569211]. https://doi.org/10.1007/978-0-387-46401-5_7.
66. Binion DG, Otterson MF, Rafiee P. Curcumin inhibits VEGF-mediated angiogenesis in human intestinal microvascular endothelial cells through COX-2 and MAPK inhibition. *Gut*. 2008;**57**(11):1509-17. [PubMed ID: 18596194]. [PubMed Central ID: PMC2582343]. https://doi.org/10.1136/gut.2008.152496.
67. Wang TY, Chen JX. Effects of Curcumin on Vessel Formation Insight into the Pro- and Antiangiogenesis of Curcumin. *Evid Based Complement Alternat Med*. 2019;**2019**:1390795. [PubMed ID: 31320911]. [PubMed Central ID: PMC6607718]. https://doi.org/10.1155/2019/1390795.
68. Shishodia S. Molecular mechanisms of curcumin action: gene expression. *Biofactors*. 2013;**39**(1):37-55. [PubMed ID: 22996381]. https://doi.org/10.1002/biof.1041.
69. Shehzad A, Lee YS. Molecular mechanisms of curcumin action: signal transduction. *Biofactors*. 2013;**39**(1):27-36. [PubMed ID: 23303697]. https://doi.org/10.1002/biof.1065.
70. Lee YK, Lee WS, Hwang JT, Kwon DY, Surh YJ, Park OJ. Curcumin exerts antidifferentiation effect through AMPKalpha-PPAR-gamma in 3T3-L1 adipocytes and antiproliferatory effect through AMPKalpha-COX-2 in cancer cells. *J Agric Food Chem*. 2009;**57**(1):305-10. [PubMed ID: 19093868]. https://doi.org/10.1021/jf802737z.
71. Banerji A, Chakrabarti J, Mitra A, Chatterjee A. Effect of curcumin on gelatinase A (MMP-2) activity in B16F10 melanoma cells. *Cancer Lett*. 2004;**211**(2):235-42. [PubMed ID: 15219947]. https://doi.org/10.1016/j.canlet.2004.02.007.
72. Saja K, Babu MS, Karunagaran D, Sudhakaran PR. Anti-inflammatory effect of curcumin involves downregulation of MMP-9 in blood mononuclear cells. *Int Immunopharmacol*. 2007;**7**(13):1659-67. [PubMed ID: 17996675]. https://doi.org/10.1016/j.intimp.2007.08.018.
73. Mahmmoud YA. Modulation of protein kinase C by curcumin; inhibition and activation switched by calcium ions. *Br J Pharmacol*. 2007;**150**(2):200-8. [PubMed ID: 17160011]. [PubMed Central ID: PMC2042896]. https://doi.org/10.1038/sj.bjp.0706970.
74. Farghadani R, Naidu R. Curcumin: Modulator of Key Molecular Signaling Pathways in Hormone-Independent Breast Cancer. *Cancers (Basel)*. 2021;**13**(14). [PubMed ID: 34298639]. [PubMed Central ID: PMC8307022]. https://doi.org/10.3390/cancers13143427.
75. Jahanbakhshi F, Maleki Dana P, Badehnoosh B, Yousefi B, Mansournia MA, Jahanshahi M, et al. Curcumin anti-tumor effects on endometrial cancer with focus on its molecular targets. *Cancer Cell Int*. 2021;**21**(1):120. [PubMed ID: 33602218]. [PubMed Central ID: PMC7891161]. https://doi.org/10.1186/s12935-021-01832-z.
76. Darvesh AS, Aggarwal BB, Bishayee A. Curcumin and liver cancer: a review. *Curr Pharm Biotechnol*. 2012;**13**(1):218-28. [PubMed ID: 21466422]. https://doi.org/10.2174/138920112798868791.
77. Bar-Sela G, Epelbaum R, Schaffer M. Curcumin as an anti-cancer agent: review of the gap between basic and clinical applications. *Curr Med Chem*. 2010;**17**(3):190-7. [PubMed ID: 20214562]. https://doi.org/10.2174/092986710790149738.
78. Naksuriya O, Okonogi S, Schiffelers RM, Hennink WE. Curcumin nanoformulations: a review of pharmaceutical properties and preclinical studies and clinical data related to cancer treatment. *Biomaterials*. 2014;**35**(10):3365-83. [PubMed ID: 24439402]. https://doi.org/10.1016/j.biomaterials.2013.12.090.
79. Wang Y, Yu J, Cui R, Lin J, Ding X. Curcumin in Treating Breast Cancer: A Review. *J Lab Autom*. 2016;**21**(6):723-31. [PubMed ID: 27325106]. https://doi.org/10.1177/2211068216655524.
80. Di Martino RM, Luppi B, Bisi A, Gobbi S, Rampa A, Abruzzo A, et al. Recent progress on curcumin-based therapeutics: a patent review (2012-2016). Part I: Curcumin. *Expert Opin Ther Pat*. 2017;**27**(5):579-90. [PubMed ID: 28024125]. https://doi.org/10.1080/13543776.2017.1276566.
81. Wang JY, Wang X, Wang XJ, Zheng BZ, Wang Y, Wang X, et al. Curcumin inhibits the growth via Wnt/beta-catenin pathway in non-small-cell lung cancer cells. *Eur Rev Med Pharmacol Sci*. 2018;**22**(21):7492-9. [PubMed ID: 30468498]. https://doi.org/10.26355/eurrev_201811_16290.
82. Li X, Ma S, Yang P, Sun B, Zhang Y, Sun Y, et al. Anticancer effects of curcumin on nude mice bearing lung cancer A549 cell subsets SP and NSP cells. *Oncol Lett*. 2018;**16**(5):6756-62. [PubMed ID: 30405819]. [PubMed Central ID: PMC6202465]. https://doi.org/10.3892/ol.2018.9488.
83. Wu GQ, Chai KQ, Zhu XM, Jiang H, Wang X, Xue Q, et al. Anti-cancer effects of curcumin on lung cancer through the inhibition of EZH2 and NOTCH1. *Oncotarget*. 2016;**7**(18):26535-50. [PubMed ID: 27049834]. [PubMed Central ID: PMC5041997]. https://doi.org/10.18632/oncotarget.8532.
84. Li X, He S, Tian Y, Weiss RM, Martin DT. Synergistic inhibition of GP130 and ERK signaling blocks chemoresistant bladder cancer cell growth. *Cell Signal*. 2019;**63**:109381. [PubMed ID: 31374291]. https://doi.org/10.1016/j.cellsig.2019.109381.
85. Hu S, Xu Y, Meng L, Huang L, Sun H. Curcumin inhibits proliferation and promotes apoptosis of breast cancer cells. *Exp Ther Med*. 2018;**16**(2):1266-72. [PubMed ID: 30116377]. [PubMed Central ID: PMC6090267]. https://doi.org/10.3892/etm.2018.6345.
86. Coker-Gurkan A, Celik M, Ugur M, Arisan ED, Obakan-Yerlikaya P, Durdu ZB, et al. Curcumin inhibits autocrine growth hormone-mediated invasion and metastasis by targeting NF-kappaB signaling and polyamine metabolism in breast cancer cells. *Amino Acids*. 2018;**50**(8):1045-69. [PubMed ID: 29770869]. https://doi.org/10.1007/s00726-018-2581-z.
87. Coker-Gurkan A, Bulut D, Genc R, Arisan ED, Obakan-Yerlikaya P, Palavan-Unsal N. Curcumin prevented human autocrine growth hormone (GH) signaling mediated NF-kappaB activation and miR-183-96-182 cluster stimulated epithelial mesenchymal transition in T47D breast cancer cells. *Mol Biol Rep*. 2019;**46**(1):355-69. [PubMed ID: 30467667]. https://doi.org/10.1007/s11033-018-4479-y.
88. Attia YM, El-Kersh DM, Ammar RA, Adel A, Khalil A, Walid H, et al. Inhibition of aldehyde dehydrogenase-1 and p-glycoprotein-mediated multidrug resistance by curcumin and vitamin D3 increases sensitivity to paclitaxel in breast cancer. *Chem Biol Interact*. 2020;**315**:108865. [PubMed ID: 31628941]. https://doi.org/10.1016/j.cbi.2019.108865.
89. Zou J, Zhu L, Jiang X, Wang Y, Wang Y, Wang X, et al. Curcumin increases breast cancer cell sensitivity to cisplatin by decreasing FEN1 expression. *Oncotarget*. 2018;**9**(13):11268-78. [PubMed ID: 29541412]. [PubMed Central ID: PMC5834274]. https://doi.org/10.18632/oncotarget.24109.

90. Gersey ZC, Rodriguez GA, Barbarite E, Sanchez A, Walters WM, Ohaeto KC, et al. Curcumin decreases malignant characteristics of glioblastoma stem cells via induction of reactive oxygen species. *BMC Cancer*. 2017;**17**(1):99. [PubMed ID: 28160777]. [PubMed Central ID: PMC5292151]. https://doi.org/10.1186/s12885-017-3058-2.

91. Masamune A, Suzuki N, Kikuta K, Satoh M, Satoh K, Shimosegawa T. Curcumin blocks activation of pancreatic stellate cells. *J Cell Biochem*. 2006;**97**(5):1080-93. [PubMed ID: 16294327]. https://doi.org/10.1002/jcb.20698.

92. Zhao Z, Li C, Xi H, Gao Y, Xu D. Curcumin induces apoptosis in pancreatic cancer cells through the induction of forkhead box O1 and inhibition of the PI3K/Akt pathway. *Mol Med Rep*. 2015;**12**(4):5415-22. [PubMed ID: 26166196]. https://doi.org/10.3892/mmr.2015.4060.

93. Diaz Osterman CJ, Gonda A, Stiff T, Sigaran U, Valenzuela MM, Ferguson Bennit HR, et al. Curcumin Induces Pancreatic Adenocarcinoma Cell Death Via Reduction of the Inhibitors of Apoptosis. *Pancreas*. 2016;**45**(1):101-9. [PubMed ID: 26348467]. [PubMed Central ID: PMC4679699]. https://doi.org/10.1097/MPA.0000000000000411.

94. Zhang Y, Xue YB, Li H, Qiu D, Wang ZW, Tan SS. Inhibition of Cell Survival by Curcumin Is Associated with Downregulation of Cell Division Cycle 20 (Cdc20) in Pancreatic Cancer Cells. *Nutrients*. 2017;**9**(2). [PubMed ID: 28165402]. [PubMed Central ID: PMC5331540]. https://doi.org/10.3390/nu9020109.

95. Fu H, Wang C, Yang D, Wei Z, Xu J, Hu Z, et al. Curcumin regulates proliferation, autophagy, and apoptosis in gastric cancer cells by affecting PI3K and P53 signaling. *J Cell Physiol*. 2018;**233**(6):4634-42. [PubMed ID: 28926094]. https://doi.org/10.1002/jcp.26190.

96. Liu WH, Yuan JB, Zhang F, Chang JX. [Curcumin inhibits proliferation,migration and invasion of gastric cancer cells via Wnt3a/beta-catenin/EMT signaling pathway]. *Zhongguo Zhong Yao Za Zhi*. 2019;**44**(14):3107-15. ZH. [PubMed ID: 31602860]. https://doi.org/10.19540/j.cnki.cjcmm.20190304.002.

97. Choudhuri T, Pal S, Agwarwal ML, Das T, Sa G. Curcumin induces apoptosis in human breast cancer cells through p53-dependent Bax induction. *FEBS Lett*. 2002;**512**(1-3):334-40. [PubMed ID: 11852106]. https://doi.org/10.1016/s0014-5793(02)02292-5.

98. Jee SH, Shen SC, Tseng CR, Chiu HC, Kuo ML. Curcumin induces a p53-dependent apoptosis in human basal cell carcinoma cells. *J Invest Dermatol*. 1998;**111**(4):656-61. [PubMed ID: 9764849]. https://doi.org/10.1046/j.1523-1747.1998.00352.x.

99. Wang JB, Qi LL, Zheng SD, Wu TX. Curcumin induces apoptosis through the mitochondria-mediated apoptotic pathway in HT-29 cells. *J Zhejiang Univ Sci B*. 2009;**10**(2):93-102. [PubMed ID: 19235267]. [PubMed Central ID: PMC2644749]. https://doi.org/10.1631/jzus.B0820238.

100. Woo JH, Kim YH, Choi YJ, Kim DG, Lee KS, Bae JH, et al. Molecular mechanisms of curcumin-induced cytotoxicity: induction of apoptosis through generation of reactive oxygen species, down-regulation of Bcl-XL and IAP, the release of cytochrome c and inhibition of Akt. *Carcinogenesis*. 2003;**24**(7):1199-208. [PubMed ID: 12807727]. https://doi.org/10.1093/carcin/bgg082.

101. Zhu L, Han MB, Gao Y, Wang H, Dai L, Wen Y, et al. Curcumin triggers apoptosis via upregulation of Bax/Bcl-2 ratio and caspase activation in SW872 human adipocytes. *Mol Med Rep*. 2015;**12**(1):1151-6. [PubMed ID: 25760477]. https://doi.org/10.3892/mmr.2015.3450.

102. Hassan ZK, Daghestani MH. Curcumin effect on MMPs and TIMPs genes in a breast cancer cell line. *Asian Pac J Cancer Prev*. 2012;**13**(7):3259-64. [PubMed ID: 22994744]. https://doi.org/10.7314/apjcp.2012.13.7.3259.

103. Troselj KG, Kujundzic RN. Curcumin in combined cancer therapy. *Curr Pharm Des*. 2014;**20**(42):6682-96. [PubMed ID: 25341940]. https://doi.org/10.2174/1381612820666140826154601.

104. Susan M, Rao MN. Induction of glutathione S-transferase activity by curcumin in mice. *Arzneimittelforschung*. 1992;**42**(7):962-4. [PubMed ID: 1418063].

105. Goud VK, Polasa K, Krishnaswamy K. Effect of turmeric on xenobiotic metabolising enzymes. *Plant Foods Hum Nutr*. 1993;**44**(1):87-92. [PubMed ID: 8332589]. https://doi.org/10.1007/BF01088486.

106. Baliga MS, Joseph N, Venkataranganna MV, Saxena A, Ponemone V, Fayad R. Curcumin, an active component of turmeric in the prevention and treatment of ulcerative colitis: preclinical and clinical observations. *Food Funct*. 2012;**3**(11):1109-17. [PubMed ID: 22833299]. https://doi.org/10.1039/c2fo30097d.

107. Abdollahi E, Momtazi AA, Johnston TP, Sahebkar A. Therapeutic effects of curcumin in inflammatory and immune-mediated diseases: A nature-made jack-of-all-trades? *J Cell Physiol*. 2018;**233**(2):830-48. [PubMed ID: 28059453]. https://doi.org/10.1002/jcp.25778.

108. Jain A, Doppalapudi S, Domb AJ, Khan W. Tacrolimus and curcumin co-loaded liposphere gel: Synergistic combination towards management of psoriasis. *J Control Release*. 2016;**243**:132-45. [PubMed ID: 27725194]. https://doi.org/10.1016/j.jconrel.2016.10.004.

109. Rao CV. Regulation of COX and LOX by curcumin. *Adv Exp Med Biol*. 2007;**595**:213-26. [PubMed ID: 17569213]. https://doi.org/10.1007/978-0-387-46401-5_9.

110. Oyagbemi AA, Saba AB, Ibraheem AO. Curcumin: from food spice to cancer prevention. *Asian Pac J Cancer Prev*. 2009;**10**(6):963-7. [PubMed ID: 20192567].

111. Lin JK, Pan MH, Lin-Shiau SY. Recent studies on the biofunctions and biotransformations of curcumin. *Biofactors*. 2000;**13**(1-4):153-8. [PubMed ID: 11237176]. https://doi.org/10.1002/biof.5520130125.

112. Liao YF, Hung HC, Hour TC, Hsu PC, Kao MC, Tsay GJ, et al. Curcumin induces apoptosis through an ornithine decarboxylase-dependent pathway in human promyelocytic leukemia HL-60 cells. *Life Sci*. 2008;**82**(7-8):367-75. [PubMed ID: 18187158]. https://doi.org/10.1016/j.lfs.2007.11.022.

113. Pescatello LS, Turner D, Rodriguez N, Blanchard BE, Tsongalis GJ, Maresh CM, et al. Dietary calcium intake and renin angiotensin system polymorphisms alter the blood pressure response to aerobic exercise: a randomized control design. *Nutr Metab (Lond)*. 2007;**4**:1. [PubMed ID: 17204161]. [PubMed Central ID: PMC1779272]. https://doi.org/10.1186/1743-7075-4-1.

114. Song X, Zhang M, Dai E, Luo Y. Molecular targets of curcumin in breast cancer (Review). *Mol Med Rep*. 2018;**19**(1):23-9. https://doi.org/10.3892/mmr.2018.9665.

115. Bharti AC, Donato N, Aggarwal BB. Curcumin (diferuloylmethane) inhibits constitutive and IL-6-inducible STAT3 phosphorylation in human multiple myeloma cells. *J Immunol*. 2003;**171**(7):3863-71. [PubMed ID: 14500688]. https://doi.org/10.4049/jimmunol.171.7.3863.

116. Chuengsamarn S, Rattanamongkolgul S, Luechapudiporn R, Phisalaphong C, Jirawatnotai S. Curcumin extract for prevention of type 2 diabetes. *Diabetes Care*. 2012;**35**(11):2121-7. [PubMed ID: 22773702]. [PubMed Central ID: PMC3476912]. https://doi.org/10.2337/dc12-0116.

117. Pivari F, Mingione A, Brasacchio C, Soldati L. Curcumin and Type 2 Diabetes Mellitus: Prevention and Treatment. *Nutrients*. 2019;**11**(8). [PubMed ID: 31398884]. [PubMed Central ID: PMC6723242]. https://doi.org/10.3390/nu11081837.

118. Zhang DW, Fu M, Gao SH, Liu JL. Curcumin and diabetes: a systematic review. *Evid Based Complement Alternat Med*. 2013;**2013**:636053. [PubMed ID: 24348712]. [PubMed Central ID: PMC3857752]. https://doi.org/10.1155/2013/636053.

119. Nabavi SF, Thiagarajan R, Rastrelli L, Daglia M, Sobarzo-Sanchez E, Alinezhad H, et al. Curcumin: a natural product for diabetes and its

complications. *Curr Top Med Chem*. 2015;**15**(23):2445-55. [PubMed ID: 26088351]. https://doi.org/10.2174/1568026615666150619142519.

120. Stefanska B. Curcumin ameliorates hepatic fibrosis in type 2 diabetes mellitus - insights into its mechanisms of action. *Br J Pharmacol*. 2012;**166**(8):2209-11. [PubMed ID: 22452372]. [PubMed Central ID: PMC3448887]. https://doi.org/10.1111/j.1476-5381.2012.01959.x.
121. Rashid K, Sil PC. Curcumin enhances recovery of pancreatic islets from cellular stress induced inflammation and apoptosis in diabetic rats. *Toxicol Appl Pharmacol*. 2015;**282**(3):297-310. [PubMed ID: 25541178]. https://doi.org/10.1016/j.taap.2014.12.003.
122. Peeyush KT, Gireesh G, Jobin M, Paulose CS. Neuroprotective role of curcumin in the cerebellum of streptozotocin-induced diabetic rats. *Life Sci*. 2009;**85**(19-20):704-10. [PubMed ID: 19804785]. https://doi.org/10.1016/j.lfs.2009.09.012.
123. Seo KI, Choi MS, Jung UJ, Kim HJ, Yeo J, Jeon SM, et al. Effect of curcumin supplementation on blood glucose, plasma insulin, and glucose homeostasis related enzyme activities in diabetic db/db mice. *Mol Nutr Food Res*. 2008;**52**(9):995-1004. [PubMed ID: 18398869]. https://doi.org/10.1002/mnfr.200700184.
124. Xavier S, Sadanandan J, George N, Paulose CS. beta(2)-adrenoceptor and insulin receptor expression in the skeletal muscle of streptozotocin induced diabetic rats: antagonism by vitamin D(3) and curcumin. *Eur J Pharmacol*. 2012;**687**(1-3):14-20. [PubMed ID: 22579915]. https://doi.org/10.1016/j.ejphar.2012.02.050.
125. Na LX, Zhang YL, Li Y, Liu LY, Li R, Kong T, et al. Curcumin improves insulin resistance in skeletal muscle of rats. *Nutr Metab Cardiovasc Dis*. 2011;**21**(7):526-33. [PubMed ID: 20227862]. https://doi.org/10.1016/j.numecd.2009.11.009.
126. El-Moselhy MA, Taye A, Sharkawi SS, El-Sisi SF, Ahmed AF. The antihyperglycemic effect of curcumin in high fat diet fed rats. Role of TNF-alpha and free fatty acids. *Food Chem Toxicol*. 2011;**49**(5):1129-40. [PubMed ID: 21310207]. https://doi.org/10.1016/j.fct.2011.02.004.
127. Soetikno V, Sari FR, Veeraveedu PT, Thandavarayan RA, Harima M, Sukumaran V, et al. Curcumin ameliorates macrophage infiltration by inhibiting NF-kappaB activation and proinflammatory cytokines in streptozotocin induced-diabetic nephropathy. *Nutr Metab (Lond)*. 2011;**8**(1):35. [PubMed ID: 21663638]. [PubMed Central ID: PMC3123175]. https://doi.org/10.1186/1743-7075-8-35.
128. Chougala MB, Bhaskar JJ, Rajan MG, Salimath PV. Effect of curcumin and quercetin on lysosomal enzyme activities in streptozotocin-induced diabetic rats. *Clin Nutr*. 2012;**31**(5):749-55. [PubMed ID: 22445558]. https://doi.org/10.1016/j.clnu.2012.02.003.
129. Patumraj S, Wongeakin N, Sridulyakul P, Jariyapongskul A, Futrakul N, Bunnag S. Combined effects of curcumin and vitamin C to protect endothelial dysfunction in the iris tissue of STZ-induced diabetic rats. *Clin Hemorheol Microcirc*. 2006;**35**(4):481-9. [PubMed ID: 17148847].
130. Arun N, Nalini N. Efficacy of turmeric on blood sugar and polyol pathway in diabetic albino rats. *Plant Foods Hum Nutr*. 2002;**57**(1):41-52. [PubMed ID: 11855620]. https://doi.org/10.1023/a:1013106527829.
131. El-Azab MF, Attia FM, El-Mowafy AM. Novel role of curcumin combined with bone marrow transplantation in reversing experimental diabetes: Effects on pancreatic islet regeneration, oxidative stress, and inflammatory cytokines. *Eur J Pharmacol*. 2011;**658**(1):41-8. [PubMed ID: 21349269]. https://doi.org/10.1016/j.ejphar.2011.02.010.
132. He HJ, Wang GY, Gao Y, Ling WH, Yu ZW, Jin TR. Curcumin attenuates Nrf2 signaling defect, oxidative stress in muscle and glucose intolerance in high fat diet-fed mice. *World J Diabetes*. 2012;**3**(5):94-104. [PubMed ID: 22645638]. [PubMed Central ID: PMC3360224]. https://doi.org/10.4239/wjd.v3.i5.94.
133. Kang JY, Kim H, Mun D, Yun N, Joung B. Co-delivery of curcumin and miRNA-144-3p using heart-targeted extracellular vesicles enhances the therapeutic efficacy for myocardial infarction. *J Control Release*. 2021;**331**:62-73. [PubMed ID: 33460670]. https://doi.org/10.1016/j.jconrel.2021.01.018.
134. Noubiap JJ, Kamtchum-Tatuene J, Fitzgerald JL, Sanders P. Stroke risk associated with carotid and aortic atherosclerosis in patients with atrial fibrillation: A systematic review. *J Neurol Sci*. 2021;**425**:117444. [PubMed ID: 33862399]. https://doi.org/10.1016/j.jns.2021.117444.
135. Benson JC, Cheek H, Aubry MC, Lanzino G, Huston Iii J, Rabinstein A, et al. Cervical Carotid Plaque MRI : Review of Atherosclerosis Imaging Features and their Histologic Underpinnings. *Clin Neuroradiol*. 2021;**31**(2):295-306. [PubMed ID: 33398451]. https://doi.org/10.1007/s00062-020-00987-y.
136. Momtazi-Borojeni AA, Zabihi NA, Bagheri RK, Majeed M, Jamialahmadi T, Sahebkar A. Intravenous Curcumin Mitigates Atherosclerosis Progression in Cholesterol-Fed Rabbits. *Adv Exp Med Biol*. 2021;**1308**:45-54. [PubMed ID: 33861436]. https://doi.org/10.1007/978-3-030-64872-5_5.
137. Pourbagher-Shahri AM, Farkhondeh T, Ashrafizadeh M, Talebi M, Samargahndian S. Curcumin and cardiovascular diseases: Focus on cellular targets and cascades. *Biomed Pharmacother*. 2021;**136**:111214. [PubMed ID: 33450488]. https://doi.org/10.1016/j.biopha.2020.111214.
138. Salehi B, Del Prado-Audelo ML, Cortes H, Leyva-Gomez G, Stojanovic-Radic Z, Singh YD, et al. Therapeutic Applications of Curcumin Nanomedicine Formulations in Cardiovascular Diseases. *J Clin Med*. 2020;**9**(3). [PubMed ID: 32164244]. [PubMed Central ID: PMC7141226]. https://doi.org/10.3390/jcm9030746.
139. Hatamipour M, Jamialahmadi T, Ramezani M, Tabassi SAS, Simental-Mendia LE, Sarborji MR, et al. Protective Effects of Curcumin Phytosomes Against High-Fat Diet-Induced Atherosclerosis. *Adv Exp Med Biol*. 2021;**1308**:37-44. [PubMed ID: 33861435]. https://doi.org/10.1007/978-3-030-64872-5_4.
140. Soliman GZ. Effect of Curcumin, Mixture of Curcumin and Piperine and Curcum (Turmeric) on Lipid Profile of Normal and Hyperlipidemic Rats. *Egypt J Hospital Med*. 2005;**21**(1):145-61. https://doi.org/10.21608/ejhm.2005.18057.
141. Takano K, Tatebe J, Washizawa N, Morita T. Curcumin Inhibits Age-Related Vascular Changes in Aged Mice Fed a High-Fat Diet. *Nutrients*. 2018;**10**(10). [PubMed ID: 30309028]. [PubMed Central ID: PMC6213737]. https://doi.org/10.3390/nu10101476.
142. Monroy A, Lithgow GJ, Alavez S. Curcumin and neurodegenerative diseases. *Biofactors*. 2013;**39**(1):122-32. [PubMed ID: 23303664]. [PubMed Central ID: PMC3578106]. https://doi.org/10.1002/biof.1063.
143. Mohajeri M, Behnam B, Barreto GE, Sahebkar A. Carbon nanomaterials and amyloid-beta interactions: potentials for the detection and treatment of Alzheimer's disease? *Pharmacol Res*. 2019;**143**:186-203. [PubMed ID: 30943430]. https://doi.org/10.1016/j.phrs.2019.03.023.
144. Chin D, Huebbe P, Pallauf K, Rimbach G. Neuroprotective properties of curcumin in Alzheimer's disease–merits and limitations. *Curr Med Chem*. 2013;**20**(32):3955-85. [PubMed ID: 23931272]. https://doi.org/10.2174/09298673113209990210.
145. Cole GM, Teter B, Frautschy SA. Neuroprotective effects of curcumin. *Adv Exp Med Biol*. 2007;**595**:197-212. [PubMed ID: 17569212]. [PubMed Central ID: PMC2527619]. https://doi.org/10.1007/978-0-387-46401-5_8.
146. Palmal S, Maity AR, Singh BK, Basu S, Jana NR, Jana NR. Inhibition of amyloid fibril growth and dissolution of amyloid fibrils by curcumin-gold nanoparticles. *Chemistry*. 2014;**20**(20):6184-91. [PubMed ID: 24691975]. https://doi.org/10.1002/chem.201400079.
147. Ryu EK, Choe YS, Lee KH, Choi Y, Kim BT. Curcumin and dehydrozingerone derivatives: synthesis, radiolabeling, and evaluation for beta-amyloid plaque imaging. *J Med Chem*. 2006;**49**(20):6111-9. [PubMed ID: 17004725]. https://doi.org/10.1021/jm0607193.

148. Lim GP, Chu T, Yang F, Beech W, Frautschy SA, Cole GM. The curry spice curcumin reduces oxidative damage and amyloid pathology in an Alzheimer transgenic mouse. *J Neurosci*. 2001;**21**(21):8370-7. [PubMed ID: 11606625]. [PubMed Central ID: PMC6762797]. https://doi.org/10.1523/JNEUROSCI.21-21-08370.2001.

149. Chibhabha F, Yang Y, Ying K, Jia F, Zhang Q, Ullah S, et al. Non-invasive optical imaging of retinal Abeta plaques using curcumin loaded polymeric micelles in APP(swe)/PS1(DeltaE9) transgenic mice for the diagnosis of Alzheimer's disease. *J Mater Chem B*. 2020;**8**(33):7438-52. [PubMed ID: 32662804]. https://doi.org/10.1039/d0tb01101k.

150. Maiti P, Bowers Z, Bourcier-Schultz A, Morse J, Dunbar GL. Preservation of dendritic spine morphology and postsynaptic signaling markers after treatment with solid lipid curcumin particles in the 5xFAD mouse model of Alzheimer's amyloidosis. *Alzheimers Res Ther*. 2021;**13**(1):37. [PubMed ID: 33557949]. [PubMed Central ID: PMC7871397]. https://doi.org/10.1186/s13195-021-00769-9.

151. Cao Y, Ji C, Lu L. Mesenchymal stem cell therapy for liver fibrosis/cirrhosis. *Ann Transl Med*. 2020;**8**(8):562. [PubMed ID: 32775363]. [PubMed Central ID: PMC7347778]. https://doi.org/10.21037/atm.2020.02.119.

152. Nouri-Vaskeh M, Malek Mahdavi A, Afshan H, Alizadeh L, Zarei M. Effect of curcumin supplementation on disease severity in patients with liver cirrhosis: A randomized controlled trial. *Phytother Res*. 2020;**34**(6):1446-54. [PubMed ID: 32017253]. https://doi.org/10.1002/ptr.6620.

153. Mogharrabi M, Rahimi HR, Hasanzadeh S, Dastani M, Kazemi-Oskuee R, Akhlaghi S, et al. The effects of nanomicelle of curcumin on the matrix metalloproteinase (MMP-2, 9) activity and expression in patients with coronary artery disease (CAD): A randomized controlled clinical trial. *ARYA Atheroscler*. 2020;**16**(3):136-45. [PubMed ID: 33447259]. [PubMed Central ID: PMC7778509]. https://doi.org/10.22122/arya.v16i3.1938.

154. Wang X, Chang X, Zhan H, Zhang Q, Li C, Gao Q, et al. Curcumin and Baicalin ameliorate ethanol-induced liver oxidative damage via the Nrf2/HO-1 pathway. *J Food Biochem*. 2020;**44**(10). https://doi.org/10.1111/jfbc.13425.

155. Moradi Kelardeh B, Rahmati-Ahmadabad S, Farzanegi P, Helalizadeh M, Azarbayjani MA. Effects of non-linear resistance training and curcumin supplementation on the liver biochemical markers levels and structure in older women with non-alcoholic fatty liver disease. *J Bodyw Mov Ther*. 2020;**24**(3):154-60. [PubMed ID: 32825982]. https://doi.org/10.1016/j.jbmt.2020.02.021.

156. Farzaei MH, Zobeiri M, Parvizi F, El-Senduny FF, Marmouzi I, Coy-Barrera E, et al. Curcumin in Liver Diseases: A Systematic Review of the Cellular Mechanisms of Oxidative Stress and Clinical Perspective. *Nutrients*. 2018;**10**(7). [PubMed ID: 29966389]. [PubMed Central ID: PMC6073929]. https://doi.org/10.3390/nu10070855.

157. Panahi Y, Kianpour P, Mohtashami R, Jafari R, Simental-Mendia LE, Sahebkar A. Curcumin Lowers Serum Lipids and Uric Acid in Subjects With Nonalcoholic Fatty Liver Disease: A Randomized Controlled Trial. *J Cardiovasc Pharmacol*. 2016;**68**(3):223-9. [PubMed ID: 27124606]. https://doi.org/10.1097/FJC.0000000000000406.

158. Jordan WC, Drew CR. Curcumin--a natural herb with anti-HIV activity. *J Natl Med Assoc*. 1996;**88**(6):333. [PubMed ID: 8691490]. [PubMed Central ID: PMC2608099].

159. Mazumder A, Raghavan K, Weinstein J, Kohn KW, Pommier Y. Inhibition of human immunodeficiency virus type-1 integrase by curcumin. *Biochem Pharmacol*. 1995;**49**(8):1165-70. [PubMed ID: 7748198]. https://doi.org/10.1016/0006-2952(95)98514-a.

160. da Silva TAL, Medeiros RMV, de Medeiros DC, Medeiros R, de Medeiros JA, de Medeiros G, et al. Impact of curcumin on energy metabolism in HIV infection: A case study. *Phytother Res*. 2019;**33**(3):856-8. [PubMed ID: 30648299]. https://doi.org/10.1002/ptr.6258.

161. Prasad S, Tyagi AK. Curcumin and its analogues: a potential natural compound against HIV infection and AIDS. *Food Funct*. 2015;**6**(11):3412-9. [PubMed ID: 26404185]. https://doi.org/10.1039/c5fo00485c.

162. Kang D, Li B, Luo L, Jiang W, Lu Q, Rong M, et al. Curcumin shows excellent therapeutic effect on psoriasis in mouse model. *Biochimie*. 2016;**123**:73-80. [PubMed ID: 26826458]. https://doi.org/10.1016/j.biochi.2016.01.013.

163. Mao KL, Fan ZL, Yuan JD, Chen PP, Yang JJ, Xu J, et al. Skin-penetrating polymeric nanoparticles incorporated in silk fibroin hydrogel for topical delivery of curcumin to improve its therapeutic effect on psoriasis mouse model. *Colloids Surf B Biointerfaces*. 2017;**160**:704-14. [PubMed ID: 29035818]. https://doi.org/10.1016/j.colsurfb.2017.10.029.

164. Thangapazham RL, Sharma A, Maheshwari RK. Beneficial role of curcumin in skin diseases. *Adv Exp Med Biol*. 2007;**595**:343-57. [PubMed ID: 17569219]. https://doi.org/10.1007/978-0-387-46401-5_15.

165. Goel A, Kunnumakkara AB, Aggarwal BB. Curcumin as "Curecumin": from kitchen to clinic. *Biochem Pharmacol*. 2008;**75**(4):787-809. [PubMed ID: 17900536]. https://doi.org/10.1016/j.bcp.2007.08.016.