REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 25, No. 1 (2024)
http://www.veterinaria.org
Article Received: Revised: Accepted:

An Extensive Analysis Of The Advantages Of Curcumin For The Treatment Of Viral Infections And Abnormal Blood Disorders: A Review

Krishma Kumari[1*], Deepshikha[2], Dr. Asha Gandhi[3], Ranju Marwaha[4], Amanjeet Singh[5], Rubal[6]

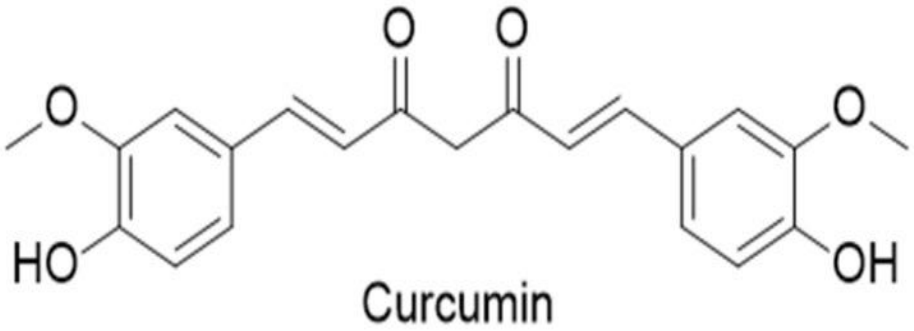
[1,2]Swami Devi Dyal Institute of Pharmacy, Panchkula,
[3]Sri Sukhmani Institute of Pharmacy, Derabassi,
[4]Sri Sukhmani Institute of Engineering & Technology, Derabassi,
[5]Sri Sukhmani Institute of Pharmacy, Derabassi,
[6]Swami Devi Dyal Institute of Pharmacy, Panchkula

ABSTRACT
The primary active ingredient in turmeric extracts is curcumin. Naturally occurring in plants, curcumin has drawn a lot of interest as a dietary supplement due to its apparent efficacy in treating a variety of human medical disorders. Curcumin exhibits pharmacological properties that are anti-inflammatory and antioxidative, as well as immunological modulation and anticancer properties, all of which are generally good for human health. We provide an overview of the current developments on curcumin as a biologically active agent in viral infectious illnesses and haematological disorders in this review article.

Keywords: curcumin, blood diseases, viral infectious diseases.

INTRODUCTION

The history of turmeric is extensive. Turmeric's therapeutic benefits were noted by Marco Polo in his Sino-Indian journey journal early in the 12th century, and Arab traders brought the spice to Europe in the 13th century. Curry powder was initially utilised for medicinal purposes in humans during the 15th century, when Britain was still ruling India. It was combined with turmeric and numerous other herbs. [**1**]. Turmeric is used in traditional Chinese medicine to alleviate blood stasis and encourage blood circulation. Due to its ability to grow in hot, humid settings, turmeric is often found in tropical and subtropical locations, particularly in Southeast Asia, China, and India. Yujin, zedoary, and turmeric are all members of the turmeric family according to modern botany. Curcumin components, such as curcumin, demethoxycurcumin, and bisdemethoxycurcumin, volatile oil, and resins make up the majority of turmeric. [**2**] Among them, curcumin, which has the chemical formula C21H20O6, is extracted from the dried rhizomes of turmeric and is the primary active ingredient (Figure 1). A colourless, orange-red, photosensitive powder known as curcumin is insoluble in water. Curcumin has demonstrated a variety of pharmacological actions to date, including anti-inflammation [**3**], antioxidation [**4**], antitumor [**5**] and immune regulation activities. Curcumin is therefore thought to have a broad variety of therapeutic potentials in the treatment of cerebral and cardiovascular diseases, mental and cognitive problems, and solid tumours. Terms that define curcumin and disease were utilised to conduct a literature search utilising databases like Web of Science, PubMed, Google Scholar, and CNKI. Studies spanning 2000 to 2022, including reviews and basic research, were included in the literature search. We discovered that only few literature papers expounded on curcumin's antiviral capacity, with most of the reports focusing on blood irregularities, AD, and malignant tumours. In this work, we examine the pharmacological effects and molecular approaches of curcumin, with particular attention to developments on its use for anticancer, AD, viral infection, and blood disease applications.**[6]**



Curcumin

.

VIRAL INFECTION:

Infectious microscopic viruses proliferate by invading live cells and causing persistent illnesses in people, including AIDS, hepatitis B and C, the flu, and others that can be fatal if left untreated. Various approaches have been employed to create novel and enhanced antiviral medications to combat viral infections. A virus is a microscopic organism that

cannot reproduce by itself outside the host body. The viruses carry either ribonucleic acid (RNA) or deoxyribonucleic acid (DNA) as their genetic material which can be single-stranded or double-stranded [**7**]. The infections by viruses in humans caused millions of deaths around the globe and are accountable for the human diseases like HIV/AIDS, hepatitis, influenza, herpes simplex, common cold, etc. [**8], [9], [10].** The infection process varies among viral species; however, they follow certain common steps in infecting the animal hosts. The typical stages of virus infection include (i) attachment and entry: initially, the glycoproteins on the envelope of virus attach to the receptor/co-receptor molecules on the host cell membrane, which facilitates the entry of virus inside the host cell through endocytosis (ii) Replication and transcription of viral genome: the viral genome comprising DNA or RNA is transported into the nucleus where its replication and transcription occurs to produce the multiple copies of genome and messenger RNA (mRNA) molecules, respectively.[**11]**

Table1: Pathways impacted by Curcumin and their effect on virus:

S.NO	Pathways	Antiviral activity	Virus	References
1.	Actin filament organization	Viral entry Replication	Viral hemorrhagic septicemia virus Dengue virus	**[12] [13]**
2.	Anti-inflammation	Replication	Human immunodeficiency virus	**[14]**
3.	APE1 redox reactions	Replication	Kaposi's sarcoma-associated herpesvirus	**[15]**
4.	Cleavage of eIF4G	Protein expression	Enterovirus 71	**[16]**
5.	NF-κB signalling	Replication	Influenza A virus	**[17]**
6.	ROS production	Viricidal	Norovirus	**[18]**
7.	Viral proteins	Viral entry Viral protein degradation	Porcine reproductive and respiratory syndrome virus Human immunodeficiency virus	**[19] [20]**

Blood disorders:

Diabestes Mellitus:

A person with diabetes mellitus (DM) has elevated blood sugar levels. DM is a chronic metabolic condition. In turn, polyuria, polydipsia, and polyphagia symptoms are brought on by the elevated blood sugar. Type 1, type 2, and gestational diabetes are the three main forms of the disease. Type 1 diabetes is caused by the body's inability to create insulin, whereas type 2 diabetes (T2DM) is caused by the body's improper use of insulin. Pro-inflammatory cytokines and oxidative stress have been linked to the pathophysiology of type 2 diabetes (T2DM) by a number of studies conducted over the past few years **[21]**. Curcumin exhibits anti-inflammatory properties, making it a potentially effective treatment for type 2 diabetes. The earliest evidence of curcumin's capacity to lower blood sugar levels in patients was published in 1972. After consuming 5 g of turmeric powder over a period of time, a 16-year-old male patient's fasting blood sugar dropped from 140 to 70 mg/dl. The blood sugar level was lowered when insulin and turmeric, or curcumin, were consumed together. Moreover, the anti-diabetic benefit of turmeric persisted even when the insulin dosage was reduced to the lowest possible level. It's interesting to note that random blood sugar levels rose to 140 mg/dl after curcumin and turmeric were stopped for a week. Consequently, the 5-g daily dose of turmeric was resumed, and the fasting blood sugar level was quickly lowered to 110 mg/dl. Following three months of turmeric medication, the patient's blood urea was between 20 and 22, and their ECG was within normal limits. The benefits of turmeric as a potent laxative and good appetite stimulant were noted, rather than any evident side effects linked to turmeric therapy **[22].**

Conventional Lipid Profiles

When assessing the risk of CVD, conventional lipid profiles—which contain LDL-C and HDL-C—are essential. The "bad cholesterol," or low-density lipoprotein (LDL-C), is a major cause of atherosclerosis. Extensive clinical trials like the Framingham Heart Study have conclusively demonstrated the link between elevated levels of low-density lipoprotein (LDL-C) and an increased cardiac disease (CVD) risk **[23]**. As a result, LDL-C remains the main target for medicinal interventions, and statins have demonstrated efficacy in lowering LDL-C levels and lowering cardiovascular events. HDL-C, or "good cholesterol," on the other hand, is associated with a lower risk of cardiovascular events. Reverse cholesterol transport, which involves transporting extra cholesterol from tissues outside the liver to the liver for excretion, is facilitated by HDL particles. Studies in epidemiology, like the Prospective Cardiovascular Münster project, have consistently demonstrated a negative correlation between HDL-C levels and the risk of cardiovascular disease. However, it has been challenging to convert this apparent relationship into effective treatment strategies because clinical studies have shown conflicting results from therapies aimed at raising HDL-C levels. Essential components of the traditional lipid profile, triglycerides and total cholesterol, provide additional information for assessing the risk of CVD. Elevated triglyceride levels are associated with an increased risk of atherosclerosis, particularly in the presence of conditions such as metabolic syndrome and diabetes. Total cholesterol, which is the sum of LDL, HDL, and VLDL cholesterol, provides a comprehensive picture of a person's lipid profile. Although traditional lipid profiles are essential for assessing risk levels, their shortcomings are now widely recognized. Significantly, they may need to

comprehensively depict the intricacy of lipid metabolism and consider changes in particle size and functionality. Consequently, there has been an increase in the pursuit of more sophisticated and all-encompassing biomarkers**. [24]**

TREATMENT:

CURCUMIN IN TREATMENT OF VIRAL INFECTION

With over six million deaths to date, the new coronavirus-caused worldwide pandemic has been getting worse since 2019. Despite the fact that a variety of immunisations have been given all over the world, COVID-19 vaccine development is quickly approaching because to the virus's highly varied mutations. Both bebtelovimab and paxlovid were recently approved for sale; nevertheless, there is a lack of clinical data and side effects related to the skeleton, and bebtelovimab is temporarily included in the NIH recommendations as an alternate therapy. Angiotensin-converting enzyme 2 (ACE2) inhibitors and spike (S) protein blocking are the primary potential targets of COVID-19 treatment **[25]**.The novel coronavirus S protein binds to the viral protein and cuts off the virus host pathway. The S-protein-neutralizing antibody prevents the virus from fusing with the human ACE2 receptor because it has a very high affinity for the ACE2 receptor on the human extracellular vesicle (EV).Wu and others **[26]** extracted EV-expressing ACE2 kidney cells, constructed a fake virus that carries S protein and can bind to ACE2 and found that EV can block infection by a fake virus in normal host cells; that is, too much ACE2 can competitively inhibit the binding of viral S protein to human ACE2. The researchers subsequently discovered that the EV released by the cells might express additional ACE2 after using curcumin to stimulate kidney cells that overexpressed ACE2. The new coronavirus and transmissible gastroenteritis virus (TGEV) have certain similarities and are both members of the coronavirus family's α-coronavirus genus. Before infecting cells with TGEV, Li et al. **[27]** treated them with curcumin. They found that curcumin inhibited the proliferation of TGEV and the synthesis of viral proteins in a manner that was dose-, temperature-, and time-dependent. The highly contagious nature of the novel coronavirus makes it difficult to use as a direct research subject; nonetheless, curcumin's potential to counteract the virus is beginning to show promise. There is evidence that curcumin inhibits other viruses, even though its impact on the novel coronavirus is yet unclear. Curcumin has been shown in early investigations to suppress influenza viruses, including H1N1, H3N3, and human respiratory syncytial virus **[28]**. Curcumin also exhibits some inhibitory activity against common infectious human pathogens. For instance, curcumin has been shown to considerably reduce the long terminal repeat (LTR) of the HIV gene, hence influencing the virus's pathogenicity and capacity for replication while having no effect on cell function [**29**]. By weakening the ubiquitin-proteasome system (UPS), decreasing viral titer, and lowering viral RNA expression and protein synthesis, curcumin can also suppress coxsackievirus [**30**]. According to Wei et al. , following curcumin intervention, the intracellular covalently closed circular DNA (cccDNA) and HBV DNA viral loads were both reduced. The expression levels of the hepatitis HBV surface antigen (HBsAg) and hepatitis HBV e-antigen (HBeAg) of the HBV stable mutant HepG2.2.15 were also significantly downregulated.[**31]** Curcumin can also downregulate HCV gene expression and viral replication by inducing heme oxygenase-1 expression or inhibiting the Akt-SREBP-1 pathway [**32**]. Oral and cervical cancer are largely caused by high-risk human papillomaviruses (HPVs) that express the E6 and E7 proteins. Curcumin has been shown in a study to specifically inhibit the transcription of the HPV-16/E6 proto-oncogene and downregulate the nuclear transcription factors AP-1 and NF-κB. [**33**]

Apart from the prevalent viral infections mentioned above, the disorders brought on by the herpes virus are especially significant. During the incubation phase, the herpes virus can cause a permanent infection and periodically reactivate [**34**]. Antiherpes medication side effects and drug resistance are common when taken for extended periods of time. One novel approach to treating herpes viruses is to concentrate on naturally occurring chemicals derived from plants. Curcumin has been shown to have excellent therapeutic potential in the treatment of herpes viruses. Curcumin inhibits IE gene expression and herpes simplex virus-1 (HSV-1) infection by affecting the recruitment of IE gene promoters by RNA polymerase II, which is mediated by viral transactivator protein vp16. This mechanism is independent of the activity of transcriptional coactivator protein p300/CBP histone acetyltransferase [**35**]. Curcumin has the potential to impede HSV-2 replication by suppressing NF-κB. Curcumin has also been shown to suppress other herpesviruses. Curcumin, for instance, may suppress the human cytomegalovirus by downregulating IEA, UL83A, and Hsp90, as well as the pseudorabies virus (PRV) by transcription of BZLF1 against the EBV virus, Kaposi's sarcoma-associated herpesvirus, and APE1-mediated redox function [**36**].

CURCUMIN IN TREATMENT OF ABNORMAL BLOOD CONDITIONS

Reduction in Blood Lipids

Unusual blood lipid levels, particularly elevated low-density lipoprotein (LDL), are acknowledged as pathogenic elements contributing to coronary atherosclerosis. Lower blood lipid levels can prevent plaque development or rupture and lower the number of cardiovascular events. Curcumin has no discernible impact on serum HDL levels, but it can dramatically lower serum levels of triglycerides and low-density lipoprotein (LDL) in patients with hyperlipidemia, according to a meta-analysis [**37**]. One efficient way to lower blood lipid levels is to regulate cholesterol absorption, accumulation, and transport. When ApoE −/− mice were fed a high-fat diet either by itself or in conjunction with curcumin, Zou et al. [**38**] observed that the degree of atherosclerosis, the amount of cholesterol accumulated in the aorta, and the amount of cholesterol absorbed in the small intestine all decreased by 56%, 51%, and 45%, respectively. In the

liver of rats given a high-fat diet, curcumin has been shown by Kim et al. [**39**] to boost the expression of CYP7A1, a rate-limiting enzyme for cholesterol production of bile acids. This decreases LDL, cholesterol, and the arteriosclerosis index by quickening the excretion of cholesterol. Curcumin may potentially have an indirect effect on blood lipid regulation by way of antioxidant and anti-inflammatory mechanisms. When Fan et al. added curcumin to rabbit coronary atherosclerosis models, the animals' blood cholesterol levels dramatically dropped—an outcome that was comparable to rosuvastatin's. SOD activity rose in these models whereas the inflammatory markers hs-CRP, TNF-α, and IL-6 declined**.[40]**

Reduction in Blood Sugar

While curcumin has no effect on blood sugar in healthy individuals, it can dramatically lower blood sugar levels during fasting and after meals in those with type II diabetes mellitus (T2DM) and drastically raise levels of glycosylated haemoglobin [**41**]. Insulin resistance and islet cell dysfunction are the primary causes of type 2 diabetes (T2DM), hence it makes sense to protect islet β cells in order to postpone the onset of the disease. Curcumin has been demonstrated in studies to improve insulin resistance and enhance skeletal muscle's absorption of glucose by blocking islet β-cell apoptosis [**42**]. Targeting enzymes associated with glucose intake is also crucial in the treatment of diabetes. Patients with type 2 diabetes mellitus experience elevated liver sugar production and insulin resistance due to increased activities of rate-limiting enzymes associated with liver gluconeogenesis, namely G-6-pase and PEPCK [**43**]. α -glucosidase and other carbohydrate hydrolases are activated, which quickens the absorption of glucose. In order to control glucose metabolism, curcumin can inhibit the functions of PEPCK, G-6-pase, and α-glucosidase in mice as well as lower the expression of PEPCK and G-6-pase proteins [**44**].

Diabetes-related chronic problems can also be cured with curcumin. Curcumin, for instance, has the ability to cure diabetic retinopathy through anti-angiogenic and antioxidant effects [**45**], diabetic cardiac disorders through inhibition of myocardial fibrosis, and diabetic nephropathy through reduction of inflammatory response [**46**].

Anticoagulation and Antiplatelet Aggregation

It is understood that platelet aggregation and activation are essential components of atherosclerotic thrombosis. A complex cascade that is triggered by factors such as collagen, arachidonic acid, adenosine diphosphate, platelet-activating factor, and adrenaline is responsible for the secretion and aggregation of platelets. Curcumin can influence the cascade by either directly preventing arachidonic acid from being deacetylated or indirectly preventing it from attaching to platelet phospholipids. It is known that atherosclerotic thrombosis is primarily caused by platelet aggregation and activation. The secretion and aggregation of platelets are caused by a complicated cascade that is initiated by various substances, including collagen, arachidonic acid, adenosine diphosphate, platelet-activating factor, and adrenaline. Through direct inhibition of arachidonic acid's deacetylation or indirect inhibition of its attachment to platelet phospholipids, curcumin can affect the cascade. **[47]**

CONCLUSION

Over the past three decades, pharmacological research has validated the health advantages of plant-derived curcumin, which is still commonly present at Asian dining tables. Because of its multitarget and multichannel properties, curcumin appears to be a cure-all. It exhibits a broad range of pharmacological properties in the areas of treating antiviral diseases, treating AD, controlling blood lipids and blood glucose, and treating malignant tumours. The surprising thing is that curcumin may potentially suppress the new coronavirus.

A growing number of curcumin complexes have been discovered in recent years, with an emphasis on the deficiencies of curcumin's low water solubility and bioavailability. These complexes are theoretically combined with other compounds or embedded in unique materials to increase the bioavailability of curcumin and potentially enhance its pharmacological effects.

REFERENCES:

1. Esatbeyoglu T., Huebbe P., Ernst I.M.A., Chin D., Wagner A.E., Rimbach G. Curcumin--from molecule to biological function. Angew. Chem. Int. Ed. Engl. 2012.
2. Qi Y., Zhang H.B., Guo H. Research progress of turmeric and prediction analysis of quality marker (Q-Marker) Chin. Herb. Med. 2021.
3. Vallée A., Lecarpentier Y. Curcumin and Endometriosis. Int. J. Mol. Sci. 2020.
4. Abrahams S., Haylett W.L., Johnson G., Carr J.A., Bardien S. Antioxidant effects of curcumin in models of neurodegeneration, aging, oxidative and nitrosative stress: A review. Neuroscience. 2019.
5. Giordano A., Tommonaro G. Curcumin and Cancer. Nutrients. 2019.
6. Yang M., Akbar U., Mohan C. Curcumin in Autoimmune and Rheumatic Diseases. Nutrients. 2019.
7. H. Lodish, A. Berk, S.L. Zipursky, P. Matsudaira, D. Baltimore, J. Darnell, Molecular Cell Biology. 4 ed., W.H. Freeman & Co. Ltd, New York, 2000.
8. Boggian K., Piffaretti J.C., Hirschel B., Janin P., Francioli P., Flepp M., Telenti A. Clinical progression, survival, and
8. Greub G., Ledergerber B., Battegay M., Grob P., Perrin L., Furrer H., Burgisser P., Erb P., immune recovery

during antiretroviral therapy in patients with HIV-1 and hepatitis C virus coinfection: the Swiss HIV cohort study. *Lancet.* 2000;356(9244):1800–1805. doi: 10.1016/s0140-6736(00)032323 [PubMed] [CrossRef] [Google Scholar] [Ref list]

9. CDC, HIV/AIDs Surveillance Report, US Department of Health and Human Services, Public Health Service . Center for Infectious Diseases; Division of HIV/AIDS: 1990. Centers for Disease Control; pp. 1–18. [Google Scholar] [Ref list]
10 A.S. Evans, Viral Infections of Humans: Epidemiology and Control, 3 ed., Springer Science & Business Media2013.
11. Fenner F., Bachmann P.A., Gibbs E.P.J., Murphy F.A., Studdert M.J., White D.O. Viral replication. *Veterinary Virology.* 1987:55–88. doi: 10.1016/B978-0-12-253055-5.500086 [CrossRef] [Google Scholar]
12. A., Pilankatta R., Teramoto T., Sajith A.M., Nwulia E., Kulkarni A., Padmanabhan R. Inhibition of dengue virus by curcuminoids. Antivir. Res. 2019;162:71–78. doi: 10.1016/j.antiviral.2018.12.002. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
13 . Jeong E.-H., Vaidya B., Cho S.-Y., Park M.-A., Kaewintajuk K., Kim S.R., Oh M.-J., Choi J.-S., Kwon J., Kim D. Identification of regulators of the early stage of viral hemorrhagic septicemia virus infection during curcumin treatment. Fish Shellfish Immunol. 2015;45:184–193. doi: 10.1016/j.fsi.2015.03.042. [PubMed] [CrossRef] [Google Scholar]
14 Ferreira V.H., Nazli A., Dizzell S.E., Mueller K., Kaushic C. The anti-inflammatory activity of curcumin protects the genital mucosal epithelial barrier from disruption and blocks replication of HIV-1 and HSV-2. PLoS ONE. 2015;10:e0124903. doi: 10.1371/journal.pone.0124903. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
15. Li H., Zhong C., Wang Q., Chen W., Yuan Y. Curcumin is an APE1 redox inhibitor and exhibits an antiviral activity against KSHV replication and pathogenesis. *Antivir. Res.* 2019;**167**:98–103. doi: 10.1016/j.antiviral.2019.04.011. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
16. Lin C.-J., Chang L., Chu H.-W., Lin H.-J., Chang P.-C., Wang R.Y.L., Unnikrishnan B., Mao J.-Y., Chen S.-Y., Huang C.-C. High Amplification of the Antiviral Activity of Curcumin through Transformation into Carbon Quantum Dots. *Small.* 2019;**15**:1902641. doi: 10.1002/smll.201902641. [PubMed] [CrossRef] [Google Scholar]
17. Dai J., Gu L., Su Y., Wang Q., Zhao Y., Chen X., Deng H., Li W., Wang G., Li K. Inhibition of curcumin on influenza A virus infection and influenzal pneumonia via oxidative stress, TLR2/4, p38/JNK MAPK and NF-κB pathways. *Int. Immunopharmacol.* 2018;**54**:177–187. doi: 10.1016/j.intimp.2017.11.009. [PubMed] [CrossRef] [Google Scholar]
18. Wu J., Hou W., Cao B., Zuo T., Xue C., Leung A.W., Xu C., Tang Q.J. Virucidal efficacy of treatment with photodynamically activated curcumin on murine norovirus bio-accumulated in oysters. *Photodiagnosis Photodyn. Ther.* 2015;**12**:385–392. doi: 10.1016/j.pdpdt.2015.06.005. [PubMed] [CrossRef] [Google Scholar]
19. Du T., Shi Y., Xiao S., Li N., Zhao Q., Zhang A., Nan Y., Mu Y., Sun Y., Wu C., et al. Curcumin is a promising inhibitor of genotype 2 porcine reproductive and respiratory syndrome virus infection. *BMC Vet. Res.* 2017;**13**:298. doi: 10.1186/s12917-017-1218-x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
20. Ali A., Banerjea A.C. Curcumin inhibits HIV-1 by promoting Tat protein degradation. *Sci. Rep.* 2016;**6**:27539. doi: 10.1038/srep27539. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
21 Sathyapalan T, Atkin SL. Is there a role for immune and anti-in-flammatory therapy in type 2 diabetes? *Minerva Endocrinol.* 2011;36(2):147–156. [PubMed] [Google Scholar]
22. Srinivasan M. Effect of curcumin on blood sugar as seen in a diabetic subject. *Indian J Med Sci.* 1972;26(4):269–270. [PubMed] [Google Scholar]
23. Dyslipidaemia. Durrington P. *Lancet.* 2003;12:717–731. [PubMed] [Google Scholar] [Ref list]
24. Monogenic hypercholesterolemia: new insights in pathogenesis and treatment. Rader DJ, Cohen J, Hobbs HH. *J Clin Investig.* 2003;6:1795–1803. [PMC free article] [PubMed] [Google Scholar]
25 Muralidar S., Ambi S.V., Sekaran S., Krishnan U.M. The emergence of COVID-19 as a global pandemic: Understanding the epidemiology, immune response and potential therapeutic targets of SARS-CoV-2. *Biochimie.* 2020.
26 Wu C.H. *Master's Thesis.* Guangzhou University of Chinese Medicine; Guangzhou, China: 2021. Inhibition of SARS-CoV-2 Infection by Extracellular Vesicles and the Effect of Curcumin on Extracellular Vesicles.
27 Li Y., Wang J., Liu Y., Luo X., Lei W., Xie L. Antiviral and virucidal effects of curcumin on transmissible gastroenteritis virus in vitro. *J. Gen. Virol.* 2020.
28. Liu Ni Meng Y.R., Zhang J.L., Zhu Y.T., Huang Z.C. Experimental study of curcumin against influenza viruses H1N1 and H3N2 in vitro. *Zhejiang J. Integr. Tradit. Chin. West. Med.* 2008.
29. Balasubramanyam K., Varier R.A., Altaf M., Swaminathan V., Siddappa N.B., Ranga U., Kundu T.K. Curcumin, a novel p300/CREB-binding protein-specific inhibitor of acetyltransferase, represses the acetylation of histone/nonhistone proteins and histone acetyltransferase-dependent chromatin transcription. *J. Biol. Chem.* 2004.
30. Si X., Wang Y., Wong J., Zhang J., McManus B.M., Luo H. Dysregulation of the ubiquitin-proteasome system by curcumin suppresses coxsackievirus B3 replication. *J. Virol.* 2007.
31. Wei Z., Zhang Y., Ke C., Chen H., Ren P., He Y., Hu P., Ma D., Luo J., Meng Z. Curcumin inhibits hepatitis B virus infection by down-regulating cccDNA-bound histone acetylation. *World J. Gastroenterol.* 2017

32. Chen M.H., Lee M.Y., Chuang J.J., Li Y.Z., Ning S.T., Chen J.C., Liu Y.W. Curcumin inhibits HCV replication by induction of heme oxygenase-1 and suppression of AKT. *Int. J. Mol. Med.* 2012.
33. Mishra A., Kumar R., Tyagi A., Kohaar I., Hedau S., Bharti A.C., Sarker S., Dey D., Saluja D., Das B. Curcumin modulates cellular AP-1, NF-kB, and HPV16 E6 proteins in oral cancer. *Ecancermedicalscience.* 2015.
34. Šudomová M., Hassan S. Nutrace utical Curcumin with Promising Protection against Herpesvirus Infections and Their Associated Inflammation: Mechanisms and Pathways. *Microorganisms.* 2021.
35. Kutluay S.B., Doroghazi J., Roemer M.E., Triezenberg S.J. Curcumin inhibits herpes simplex virus immediate-early gene expression by a mechanism independent of p300/CBP histone acetyltransferase activity. *Virology.* 2008.
36. Chen T.-Y., Chen D.-Y., Wen H.-W., Ou J.-L., Chiou S.-S., Chen J.-M., Wong M.-L., Hsu W.-L. Inhibition of enveloped viruses infectivity by curcumin. *PLoS ONE.* 2013.
37. Qin S., Huang L., Gong J., Huang J., Ren H., Hu H. Efficacy and safety of turmeric and curcumin in lowering blood lipid levels in patients with cardiovascular risk factors: A meta-analysis of randomized controlled trials. *Nutr. J.* 2017.
38. Zou J., Zhang S., Li P., Zheng X., Feng D. Supplementation with curcumin inhibits intestinal cholesterol absorption and prevents atherosclerosis in high-fat diet–fed apolipoprotein E knockout mice. *Nutr. Res.* 2018.
39. Kim M., Kim Y. Hypocholesterolemic effects of curcumin via up-regulation of cholesterol 7a-hydroxylase in rats fed a high fat diet. *Nutr. Res. Pract.* 2010.
40. Fan A.Y., Wu X.J., Shao A.M., Chen G. Effects of curcumin on blood lipid, inflammatory factors and endothelial function in atherosclerotic rabbits. *Sci. Technol. Tradit. Chin. Med.* 2020.
41. Zhang T., He Q., Liu Y., Chen Z., Hu H. Efficacy and Safety of Curcumin Supplement on Improvement of Insulin Resistance in People with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Evid.-Based Complement. Altern. Med.*2021.
42 Zhu Y.J., Cheng J.L., Gao Z.G., Cui X., Li X.C., Chang B.C. Curcumin promotes skeletal muscle GLUT4 translocation and improves insulin resistance in diabetic rats. *Chin. J. Endocrinol. Metab.* 2021.
43. Du G.H., Liu B.W., Yin F.Z., Qi X.M., Fan D.M. Effect of liraglutide on the expression and mechanism of liver glycosuria key enzymes PEPCK and G6pase in diabetic mice. *Chin. J. Comp. Med.* 2020.
44. Qian W.L., Gao X.B., Yu Z.W., Nan L.H. Study on the improvement effect and mechanism of curcumin central administration on insulin resistance mice. *Fujian Tradit. Chin. Med.* 2019.
45. Radomska-Leśniewska D.M., Osiecka-Iwan A., Hyc A., Góźdź A., Dąbrowska A.M., Skopiński P. Therapeutic potential of curcumin in eye diseases. *Cent. Eur. J. Immunol.* 2019.
46. Boarescu P.M., Boarescu I., Bocșan I.C., Gheban D., Bulboacă A.E., Nicula C., Pop R.M., Râjnoveanu R.-M., Bolboacă S.D. Antioxidant and Anti-Inflammatory Effects of Curcumin Nanoparticles on Drug-Induced Acute Myocardial Infarction in Diabetic Rats. *Antioxidants.*2019.
47. Keihanian F., Saeidinia A., Bagheri R.K., Johnston T.P., Sahebkar A. Curcumin, hemostasis, thrombosis, and coagulation. *J. Cell Physiol.* 2018.