Anti-inflammatory Action of Curcumin and Its Use in the Treatment of Lifestyle-related Diseases

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Abstract
Chronic inflammation plays a significant role in lifestyle-related diseases, such as cardiovascular diseases and obesity/impaired glucose tolerance. Curcumin is a natural extract that possesses numerous physiological properties, as indicated by its anti-inflammatory action. The mechanisms underlying these effects include the inhibition of nuclear factor-kappaB and Toll-like receptor 4-dependent signalling pathways and the activation of a peroxisome proliferator-activated receptor-gamma pathway. However, the bioavailability of curcumin is very low in humans. To resolve this issue, several drug delivery systems have been developed and a number of clinical trials have reported beneficial effects of curcumin in the management of inflammation-related diseases. It is expected that evidence regarding the clinical application of curcumin in lifestyle-related diseases associated with chronic inflammation will accumulate over time.

Keywords
Inflammation, curcumin, lifestyle-related diseases, cardiovascular risk factor, natural product

Inflammation involves an array of processes in response to tissue damage resulting from oxidative stress or other causes and triggers repair, such as subsequent extracellular matrix remodelling and fibrosis.1–3 Chronic inflammation continues for a prolonged period, lasting from several months to several years, and is characterised by tissue invasion by inflammatory macrophages. This induces the expression of inflammatory cytokines or growth factors, which is associated with the pathophysiology of various lifestyle-related diseases including cardiovascular disease, obesity, diabetes, chronic obstructive pulmonary disease (COPD) and other related diseases, such as dementia.4–6 Atherosclerosis is a chronic illness associated with inflammation and is a major cause of cardiovascular disease.7–10

Curcumin is a polyphenol found in the spice turmeric that is used as a natural drug.11–13 Curcumin exhibits various physiological activities, including anti-inflammatory, antioxidant and anticancer activities.4,12–16 It inhibits signalling pathways, such as nuclear factor kappa-B (NF-kappaB) and myeloid differentiation protein 2-Toll-like receptor 4 co-receptor pathways, activates peroxisome proliferator-activated receptor-gamma (PPAR-gamma) and inhibits the production of proinflammatory cytokines, such as tumour necrosis factor-alpha (TNF-alpha) and interleukin (IL)-1beta (Figure 1).4,15

The US Food and Drug Administration has approved curcumin as a compound that is “generally recognised as safe” and a clinical trial reported that it was well tolerated and safe at doses as high as 4,000–8,000 mg/kg per day.11 Trials in humans have reported beneficial effects of curcumin and it appears to have a role in treating lifestyle-related diseases associated with inflammation.

Curcumin and Atherosclerosis
Risk factors for atherosclerosis, including hypertension, diabetes and smoking, cause a chronic inflammatory response. Oxidative stress can cause atherosclerotic plaques to become unstable and rupture, possibly triggering thrombosis. Statins are drugs with anti-inflammatory effects that are used for treating high cholesterol and various studies have demonstrated their effectiveness in the primary and secondary prevention of cardiovascular events.16

Risk factors associated with atherosclerosis lead to the production of inflammatory cytokines IL-1beta and TNF-alpha in the arterial walls via an increase in lipid peroxides and free radicals. These inflammatory cytokines produce IL-6 and are related to the adhesion and accumulation of inflammatory cells in the vessel walls.14 Macrophages are the most abundant immune cells in atherosclerotic lesions and they play an important role in every stage of the disease, from lesion formation to plaque rupture. Macrophages are involved in the production of inflammatory cytokines, chemokines and proteases as well as having a role in foam cell formation.17 Numerous prospective cohort studies have reported that various inflammatory markers in the blood, such as C-reactive protein (CRP), are associated with the onset of cardiovascular disease.18
mice were fed a high-fat diet. They found that TNF-alpha induction of TNF-alpha and IL-6 expression. Wang et al. studied a rat rodent model of MI, considerably increased expression of inflammatory cytokines, such as TNF-alpha, IL-6 and IL-1beta, both systemically and in the myocardium; thus, reducing the inflammatory response.20 Hemández et al. evaluated a mouse model of myocarditis caused by the protozoan parasite Trypanosoma cruzi and reported that curcumin inhibited the expression of cyclooxygenase-2 and microsomal prostaglandin E synthase-1 in the myocardium as well as inhibiting inflammation in the myocardium and increased the survival rate of mice.21 TNF-alpha and IL-6 are inflammatory cytokines, whereas IL-4 and IL-13 are anti-inflammatory cytokines. Curcumin inhibited the expression of TNF-alpha and IL-6 and increased the expression of IL-4 and IL-13 in autoimmune acute myocarditis induced by cardiac myosin.22 Moreover, curcumin enhanced signal transducer and activator of transcription 6 phosphorylation and induced M2 macrophage polarisation, thus inhibiting myocarditis progression.22

The impact of curcumin in myocarditis has been studied using a number of rodent models. In coxsackievirus B3-induced myocarditis, curcumin inhibited the phosphatidylinositol-3 kinase–Akt–NF-kappaB signalling pathway and inhibited the expression of inflammatory cytokines, such as TNF-alpha, IL-6 and IL-1beta, both systemically and in the myocardium; thus, reducing the inflammatory response.20 The high level of the inflammatory cytokine TNF-alpha has been reported in the blood of patients with chronic heart failure.29

The impact of curcumin on lifestyle-related conditions is significant. Curcumin inhibits p300 histone acetyltransferase activity, thus inhibiting the development of left ventricular hypertrophy and left ventricular systolic dysfunction.21 In a rat model of doxorubicin-induced heart failure, curcumin inhibited the expression of atrial natriuretic factor, brain natriuretic peptide and beta-myosin heavy chain.24 The inhibition of heart failure by curcumin may thus be associated with its anti-inflammatory action.

Curcumin and Ischaemic Myocardial Damage
The death of myocytes due to MI temporarily causes an intense inflammatory response via the activation of Toll-like receptors.21 In a rodent model of MI, considerably increased expression of inflammatory cytokines, such as TNF-alpha, IL-1beta and IL-6, was evident after a few hours in some cases (several hours to 1 day).21 In addition, the generation of reactive oxygen species due to ischaemia is essential in activating inflammatory responses.21

Several studies suggest that curcumin has an inhibitory effect on NF-kappaB, which is a pivotal mediator of inflammatory responses. Lv et al. assessed a rat model of MI in which they ligated the left anterior descending artery. They found that administering 150 mg/kg curcumin on the day after ligation significantly inhibited an increase in NF-kappaB expression as a result of MI and increased the PPAR-gamma expression, which is involved in anti-inflammatory signalling, consequently reducing the infarct size.21 In a rabbit model of myocardial ischaemia–reperfusion injury during cardiopulmonary bypass, Saeidinia et al. reported that curcumin inhibited NF-kappaB activation in the nucleus of cardiomyocytes, thus reducing TNF-alpha, IL-6 and IL-8 levels in the blood, and that it inhibited monocyte apoptosis.24

Early growth response 1 plays a key role in the pathophysiology of acute and chronic cardiovascular disease and is associated with induction of TNF-alpha and IL-6 expression. Wang et al. studied a rat model of myocardial ischaemia–reperfusion injury and found that previous administration of curcumin inhibited early growth response 1 expression and reduced the infarct size.25

Curcumin and Myocarditis and Heart Failure
Myocarditis is often induced by a viral infection but has non-infectious causes, including autoimmune disorders.26,27 Heart failure is the final stage of cardiovascular disease. Chronic inflammation and subsequent myocyte death are associated with heart failure. Patients with heart failure have an abnormal immune response that disrupts wound healing and prolongs inflammation, consequently worsening heart failure.28 A high level of the inflammatory cytokine TNF-alpha has been reported in the blood of patients with chronic heart failure.29

Smoking is a common comorbidity in patients with mild-to-moderate COPD. Morimoto et al. studied two rat models of heart failure caused by hypertension and MI and showed that curcumin inhibits p300 histone acetyltransferase activity, thus inhibiting the development of left ventricular hypertrophy and left ventricular systolic dysfunction.21 In a rat model of doxorubicin-induced heart failure, curcumin inhibited the expression of atrial natriuretic factor, brain natriuretic peptide and beta-myosin heavy chain.24 The inhibition of heart failure by curcumin may thus be associated with its anti-inflammatory action.

Curcumin and Chronic Obstructive Pulmonary Disease
COPD is a family of diseases mainly characterised by airflow obstruction due to airway inflammation and remodelling. Several clinical studies have demonstrated the relationship between COPD and an increase in inflammatory markers, such as TNF-alpha, IL-6 and CRP.28,29 Smoking is the primary cause of COPD, and can cause systemic inflammation, but this is further exacerbated in people with COPD.28,29 COPD causes various complications, including MI, stroke and lung cancer. The most common comorbidity in patients with mild-to-moderate COPD is cardiovascular disease. One study suggested that chronic inflammation due to COPD exacerbates atherosclerosis, both directly and indirectly, and promotes thrombosis by weakening plaque.22

Several studies have demonstrated the possible benefits of curcumin in COPD. Moghaddam et al. used a mouse model of K-ras-induced lung cancer in which Haemophilus influenzae induced COPD-like airway inflammation and showed that curcumin inhibited neutrophil...
| Study | Subjects and Treatment | Purpose | Endpoint | Results |
|-------|------------------------|---------|----------|---------|
| Panahi et al., 2015 | 117 subjects with metabolic syndrome | To study the effectiveness of supplementation with a curcuminoid-piperine preparation on measures of systemic oxidative burden in people with knee osteoarthritis | | Curcuminoids induced significant elevation in serum malondialdehyde, hs-CRP, IL-6, and SAA-LDL concentrations (p<0.001) compared with placebo and a significant reduction in malondialdehyde (p=0.044) and C-reactive protein (p=0.064) and a borderline significant elevation in glutathione concentrations (p=0.036). | Significant increase in markers of oxidative stress and inflammation compared with placebo. |
| Panahi et al., 2016 | 40 patients with mild-to-moderate primary knee osteoarthritis | To investigate the effects of unformulated curcumin and placebo on measures of biomarkers in people with type 2 diabetes | | Curcuminoids 500 mg/day co-administered with 15 mg piperine per day or placebo did not show any significant differences in hs-CRP concentrations compared with placebo. | No significant differences in biomarker levels compared with placebo. |
| Mohammadi et al., 2018 | 120 patients with metabolic syndrome | To evaluate the efficacy of curcumin using dispersion technology in patients with mild COPD by examining its effect on the postprandial inflammatory response | | Curcuminoids 1 g curcumin, phospholipidated curcumin per day or placebo for 6 weeks did not show any significant differences in markers of inflammatory biomarkers compared with placebo. | No significant differences in inflammatory biomarkers compared with placebo. |
| Panahi et al., 2019 | 48 subjects with elevated serum transaminase and fatty liver disease | To investigate the effects of unformulated curcumin and placebo on measures of oxidative stress in alcoholics | | Compared with placebo, nanocurcumin significantly decreased the percentage change in alpha1-antitrypsin-LDL level and the cumulative postprandial response of soluble E-selectin compared with placebo. | Nanocurcumin significantly decreased markers of oxidative stress compared with placebo. |
| Adibian et al., 2019 | 44 people with type 2 diabetes | To investigate the effects of curcumin supplementation on measures of inflammatory biomarkers in obese non-alcoholic fatty liver disease patients | | Compared with control, curcumin decreased hs-CRP (p<0.05), TNF-alpha, IL-6, and IL-8. | Curcumin significantly decreased inflammatory markers compared with control. |
| Krishnareddy et al., 2019 | 1 g curcumin, phospholipidated curcumin on anti-Hsp27 in patients with Type 2 diabetes | To investigate the effects of unformulated curcumin and placebo on anti-Hsp27 | | Curcumin and phospholipidated curcumin did not modify anti-Hsp27 concentration compared with placebo. | No significant changes in anti-Hsp27 concentration compared with placebo. |
Table 2: Results of Studies of Curcumin using Drug Delivery Systems to Increase Bioavailability

| Study                  | Formulation                                                      | Advantage                                      | Application                        | Outcome                                      |
|------------------------|------------------------------------------------------------------|-----------------------------------------------|------------------------------------|----------------------------------------------|
| El-Naggar et al. 2010  | Biodegradable curcumin encapsulated in poly lactide-poly(ethylene glycol) copolymer nanoparticles | • Better solubility and stability              | Streptozotocin-induced diabetic rats | Enhanced the suppressive effect on markers of hepatitis and oxidative stress |
| Karri et al. 2016      | Curcumin in chitosan nanoparticles impregnated into a collagen-alginate scaffold | • Better solubility and stability; • Controlled release; • Prevention from rapid clearance | Streptozotocin-induced diabetic rats | Promoted wound healing                        |
| Hu et al. 2018         | Inhalable curcumin-loaded poly(lactic-co-glycolic) acid large porous microparticles | • Suitable aerodynamic diameters for inhalation; • Prevention from phagocytosis | Rat pulmonary fibrosis models       | Enhanced antifibrotic activity                |
| Qiao et al. 2017       | Amphiphilic curcumin polymer                                     | • Better solubility and stability; • Targeting for colonic reducing environment | Dextran sulphate sodium-induced     | Suppressed the progression of inflammation in the colon |
| Young et al. 2014      | Nano-emulsion curcumin                                           | • Better solubility                           | Lipopolysaccharide-induced acute    | Suppressed lipopolysaccharide-induced blood monocyte accumulation |
| Li et al. 2019         | E-selectin-modified atorvastatin calcium and curcumin-loaded liposome | • Targeted for endothelial cells; • Co-delivery | Apoe−/− mice                       | Suppressed atherosclerosis                    |
| Funamoto et al. 2016   | Curcumin dispersed with colloidal nanoparticles                  | • Better stability and solubility             | People with mild chronic obstructive pulmonary disease | Suppressed an increase in alpha-antitrypsin LDL |

migration to the lungs.²⁹ Yuan et al. studied a mouse model of COPD induced by lipopolysaccharide and cigarette smoke, reporting that curcumin inhibited the degradation of iNOS-α protein and the expression of cyclooxygenase-2, thus reducing airway inflammation and remodelling.²⁹ Funamoto et al. conducted a clinical trial including patients with mild COPD in which the oxidised LDL – α1-antitrypsin LDL – was significantly decreased in those taking highly absorbable curcumin compared with those taking a placebo.³⁰

Curcumin, Obesity and Diabetes

Adipose tissue is a multifunctional endocrine organ that releases various inflammatory and anti-inflammatory cytokines and physiologically active peptides.⁴¹,⁴² Obesity is a risk factor for cardiovascular disease.⁴³,⁴⁴ The accumulation of pericardial fat and myocardial steatosis is associated with the progression of coronary artery atherosclerosis. In obese patients, the secretion of inflammatory adipocytokines, such as TNF-α and IL-6, is increased and the secretion of anti-inflammatory adipocytokines is inhibited in enlarged mast cells in the visceral adipose tissue.⁴²,⁴³

Several rodent studies have assessed the effects of curcumin in models of obesity. In a mouse model of obesity due to a high-fat diet and in a model of genetic obesity, curcumin reduced macrophage invasion of adipose tissue, increased adiponectin production (which has anti-inflammatory and anti-atherosclerotic actions) and inhibited adipose tissue inflammation.⁴⁴

Pan et al. evaluated a mouse model of obesity due to a high-fat diet and reported that ingestion of curcumin inhibited weight gain, reduced fat accretion due to a high-fat diet and significantly improved the serum lipid profile (including serum levels of triglycerides, total cholesterol, LDL-cholesterol, HDL-cholesterol and free fatty acids).⁴⁵ In addition, curcumin increased the adipose triglyceride lipase and hormone-sensitive lipase protein expression by activating PPAR-gamma/alpha and CCAAT/enhancer binding protein alpha in adipose tissue. Further, curcumin broke down lipids and improved glycolipid metabolism.⁴⁶ Curcumin administration via percutaneous absorption in obese rats improved serum leptin levels and reduced adipose tissue volume to a level comparable with that in normal rats.⁴⁶

Jazayeri-Tehrani et al. conducted a clinical trial involving 84 overweight or obese patients who were diagnosed with non-alcoholic steatohepatitis.⁴⁷ They noted a decrease in TNF-α, high-sensitivity CRP, IL-6 and LDL-cholesterol as well as an increase in HDL-cholesterol in the blood. There was also increased absorption efficiency in patients taking nanocurcumin compared to those taking placebo. Nesfatin, an appetite-regulating protein, is significantly increased in patients taking nanocurcumin. When patients taking placebo were compared with those taking nanocurcumin, the two groups had a similar percentage decrease in BMI, but those taking nanocurcumin had a significantly greater percentage decrease in abdominal circumference.⁴⁷

In people with type 2 diabetes, trials have shown that curcumin decreased leptin and increased adiponectin in the blood and resulted in improved lipid metabolism.⁴⁸,⁴⁹

Curcumin and Dementia

Over the past few years, the role of inflammation has been recognised in the onset and progression of dementia.⁵⁰,⁵¹ One study reported that dementia onset may be related to conditions such as hypertension, dyslipidaemia and diabetes, independent of cardiovascular risk factors.⁵²

The onset of Alzheimer’s-type dementia is closely correlated with inflammation and oxidative stress in the brain.⁵³ NF-kappaB activation in the glial cells of Alzheimer’s patients induces increased expression of inflammatory cytokines and contributes to neuronal degeneration in the brain.⁵⁴ Levels of CRP, IL-6 and alpha-1-antichymotrypsin in the blood are significantly correlated with the degree of dementia.⁵⁵
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Figure 2: The Mechanisms of Curcumin Action on Inflammation

Curcumin

COX2 = cyclooxygenase-2; kβ = inhibitor of kappab; IL- = interleukin; mPGES-1 = microsomal prostaglandin E synthase-1; NF-kB = nuclear factor-kappab; PPAR = peroxisomal proliferator-activated receptor-gamma; TL4 = toll-like receptor 4; TNF-alpha = tumour necrosis factor-alpha

1. Libby P. Inflammatory mechanisms: the molecular basis of inflammation and disease. Nutr Rev 2007;65:51406. https://doi.org/10.1111/j.1753-4877.2007.00203.x; PMID: 18240338.
2. Chereh P, Kim SL, Nalapiss S, et al. Oxidative stress and pulmonary fibrosis. Biochim Biophys Acta 2013;1832:1028-40. https://doi.org/10.1016/j.bbadis.2012.11.021; PMID: 23219955.
3. Frangogiannis NG. The extracellular matrix in myocardial injury, repair, and remodeling. Circ Res 2017;121:1600-12. https://doi.org/10.1161/CIRCRESAHA.117.315573; PMID: 28459429.
4. Xu XY, Meng X, Li J, et al. Bioactivity, health benefits, and related molecular mechanisms of curcumin: current progress, challenges, and perspectives. Nutrients 2018;10:61153. https://doi.org/10.3390/nu10051153; PMID: 30347782.
5. Aggarwal BB, Ichikawa S, and Ramesh R. Targeting inflammatory pathways for prevention and therapy of cancer. Cell Death Dis 2012;3:645-50. https://doi.org/10.1038/cddis.2012.9; PMID: 22884744.
6. Patel R, Jailal A. Chronic inflammation. StorVita. 2018. Available at: https://www.mds.nimh.nih.gov/books/NBK491737 (accessed 11 June 2019).
7. Najiri S, Daida H. Atherosclerotic cardiovascular risk in Japan. J Clin Med 2017;6:11796601771213. https://doi.org/10.1177/11796601771213. PMID: 28680271.
8. Frostell G. J. Immunology, atherosclerosis and cardiovascular disease. BMJ 2016;355:i6098. https://doi.org/10.1136/bmj.i6098; PMID: 26833242.
9. Zhao TX, Mallat Z. Targeting the immune system in atherosclerosis. JACC: state-of-the-art review. J Am Coll Cardiol 2019;73:1691-706. https://doi.org/10.1016/j.jacc.2018.12.083; PMID: 30497923.
10. Hansson GK. Inflammation and atherosclerosis: the end of a controversy. Circulation 2017;136:1875-7. https://doi.org/10.1161/CIRCULATIONAHA.117.030944; PMID: 28916447.
11. Tsuda T. Curcumin as a functional food-derived factor: degradation products, metabolites, bioactivity, and future perspectives. Food Funct 2019;8:705-14. https://doi.org/10.1039/c9fo012422; PMID: 29282654.
12. Raut A, Imam M, Endoag-Mohan J, et al. Health perspective of a bioactive compound curcumin: a review. Trends Food Sci Technol 2016;54:33-45. https://doi.org/10.1016/j.tifs.2016.01.016.
13. Liu X, Zhu L, Gao X, et al. Magnetic molecularly imprinted polymers for spectrophotometric quantification of curcumin in food. J Food Chem 2016;202:309-15. https://doi.org/10.1016/j.jfoodchem.2016.02.015; PMID: 26502099.
14. Hewings SJ, Kalman DS. Curcumin: a review of its effects on human health. Foods 2017;6:929. https://doi.org/10.3390/foods6090929; PMID: 29056946.
15. Ghosh S, Banejee S, Syl PC. The beneficial role of curcumin in inflammation, diabetes and neurodegenerative disease: A recent update. Food Chem Toxicol 2015;82:111-24. https://doi.org/10.1016/j.fct.2015.05.022; PMID: 26066364.
16. Willerson JT, Rider PM. Inflammation as a cardiovascular risk factor. Circulation 2004;109:12-10. https://doi.org/10.1161/01.HTA.0000129535.04194.38; PMID: 15173056.
17. Cochan G, Zmerek A. Macrophages in vascular inflammation and atherosclerosis. Pilot Acta 2017;49:945-99. https://doi.org/10.1007/s12285-014-1915-y; PMID: 27818320.
18. Welsh F, Drusano G, Beith S, et al. Targeting inflammation to reduce cardiovascular disease risk: a realistic clinical prospect? V J PAMMARS 2017;17:389-913. https://doi.org/10.1111/1471-6975.12818; PMID: 28409625.
19. Zhang S, Zou L, Li P, et al. Curcumin protects against atherosclerosis in apolipoprotein E knockout mice by inhibiting toll-like receptor 4 expression. J Agric Food Chem 2018;66:449-56. https://doi.org/10.1021/acs.jafc.8b03420; PMID: 29224313.
20. Ghosh SS, Right S, Krieg R, et al. High-fat high cholesterol diet (Western diet) aggravates atherosclerosis, hyperglycemia and renal failure in nephrectomized LDL receptor knockout mice: role of intestinal derived lipopolysaccharide. Kidr Ore 2015;10:61401109. https://doi.org/10.1371/journal. pone.0141109; PMID: 26385687.
21. Frankogniss NS. The inflammatory response in myocardial injury, repair, and remodeling. Nat Rev Cardiol 2014:11-25. https://doi.org/10.1038/nrcardio.2014.28; PMID: 24463091.
22. Nian M, Lee P, Kheper N, et al. Inflammatory cytokines and postinfarction remodeling. Circ Res 2004;94:1543-53. https://doi.org/10.1161/01.RES.0000130526.20814.44; PMID: 15217919.

Trials on Anti-inflammatory Effects of Curcumin

The anti-inflammatory effect of curcumin forms the basis for its potential clinical applications (Figure 2). A large body of clinical evidence is expected to accumulate in the future. Among trials registered at Clinicaltrials.gov, 162 studies are related to the anti-inflammatory effect of curcumin. Of these, 50 are currently on-going, 70 are complete and 42 have been withdrawn, have unknown status or have been terminated. Of the 50 completed studies, the 10 randomised double-blind and placebo-controlled comparative studies are listed in Table 1. The results of eight of these studies were significant. As the absorption of curcumin is very poor, most studies that reported significant effects used a large dose of curcumin (>1.5 g/day) or employed strategies to increase its absorption, such as using a drug delivery system.

Drug Delivery Systems

Curcumin has beneficial effects on the status of various diseases involving chronic inflammation. However, the absorption of curcumin is poor, and even if absorbed into the body it is rapidly metabolised and excreted in faeces. To overcome its low bioavailability, various drug delivery systems have been developed (Table 2). These include polymer nanoparticles, chitosan nanoparticles, colloidal nanoparticles, nanoemulsion and ligand-targeted liposomes.

The beneficial effects of these drug delivery systems on curcumin bioavailability have been reported in streptozotocin-induced diabetic rats, a pulmonary fibrosis rat model, a dextran sulphate sodium-induced inflammatory bowel disease mouse model and a lipopolysaccharide-stimulated acute inflammation mouse model. E-selectin-modified liposomes was effective for ApoE−/− mice. Moreover, Funamoto et al. reported that curcumin dispersed with colloidal nanoparticles (Theracurmin) suppressed an increase in alpha1-antitrypsin LDL levels in people with mild COPD. The improvement in the bioavailability of curcumin through the development of drug delivery systems may contribute to the successful clinical application of curcumin.

Conclusion

A number of studies have reported the efficacy of curcumin and the mechanisms by which its anti-inflammatory activity could treat various lifestyle-related conditions associated with chronic inflammation, including atherosclerosis, heart failure, obesity, diabetes and other related diseases, such as dementia. Most of these studies have involved animal experiments; however, there are several reports on the benefits of curcumin use in humans. Because curcumin has extremely low bioavailability in humans, an appropriate drug delivery system is necessary for its clinical application.

It is important to study the relationship between the structure and activity of curcumin and to develop novel compounds that are more effective than natural curcumin. Additional clinical trials involving drug delivery systems for curcumin in humans need to be conducted to determine the benefits of curcumin treatment in conditions associated with inflammation.
absorptive curcumin reduces serum atherosclerotic low-density lipoprotein levels in patients with mild COPD. Int J Clin Pract 2016;11:2309-34. https://doi.org/10.1177/1742124116635437

23. Lu FH, Yin H, Che YQ, et al. Effects of curcumin on the apoptosis of cardiomyocytes and the expression of NF-κB, PPAR-γ and Bcl-2 in rats with myocardial infarction injury. J Exp Clin Med 2015;9:53-60. https://doi.org/10.1386/jecm.15.2.S1-53

24. Wang N, Peng XF, Zhang LH, et al. Attenuation of inflammatory response and reduction in size by postconditioning in rats associated with downregulation of early growth response 1 during reperfusion in rat heart. Stock 2014;41:346-54. https://doi.org/10.1017/S1351071613000102

25. Feldman AM, Mcnamara O, Myocarditis. N Engl J Med 2000;343:1988-98. https://doi.org/10.1056/NEJM200010053431401

26. Fung G, Luo H, Qu J, et al. Myocarditis. Cir Res 2016;118:496-514. m AF. https://doi.org/10.1161/CIRCRESAHA.116.3056773

27. Frideres J, Shaw SM, Yonan N, et al. The immune system and chronic heart failure: is the heart in control? J Am Coll Cardiol 2009;53:1013-20. doi:10.1016/j.jacc.2008.11.046; PMID: 19299913

28. Yendrade V, Damak K, Die E, et al. Role of inflammation in the progression of the heart failure. Curr Cardiol Rep 2007;9:236-41. doi:10.1007/s11895-007-9046-3; PMID: 18423638

29. Song Y, Ge W, Chai H, et al. Curcumin protects mice from coxsackievirus B3-induced myocarditis by inhibiting the phosphatidylinositol 3-kinase/Akt/mTOR/m-2 pathway. J Cardiovasc Pharmacol Ther 2013;18:569-75. https://doi.org/10.1089/jcpt.2012.0183

30. Hernández M, Wilcz S, Corral RS. Cardioprotective actions of curcumin, kaempferol and gentisin against postischaemic injury in rat heart. J Mol Cell Cardiol 2018;129:262-73. https://doi.org/10.1016/j.yjmcc.2018.03.009; PMID: 29708289

31. Aylett WR, Aravintakis AD, Ebrahimi-Hosseini Z, Bhatia-Zarni A, et al. In vivo anti-obesity efficacy of curcumin loaded nanofibers transitional patches in high-fat diet induced obese rats. Meter Sci Eng C Mater Biol Appl 2016;62:193-200. https://doi.org/10.1016/j.msec.2016.08.030; PMID: 30184739.

32. Jayaprakasha GK, Nandargi SM, Jaganath S, et al. Nanoparticle delivery of curcumin: improvement of its oral bioavailability and delivery to target organs. J Agric Food Chem 2013;61:2607-13. https://doi.org/10.1021/jf304362j; PMID: 23076487

33. Chawla SP, Rattanamukkala S, Phirorankit N, et al. Reduction of atherogenic risk in patients with type 2 diabetes with curcumin loaded microemulsion: a randomized, double-blind randomized placebo-controlled clinical trial. Nutr Metab Cardiovasc Dis 2019;19:618-27. https://doi.org/10.1016/j.numecd.2019.05.013; PMID: 32444538.

34. Panahi Y, Kheiri H, Sadeghi E, et al. Curcuminoids modify lipid profile in type 2 diabetes mellitus: a randomized controlled trial. Complement Ther Med 2018;33:1-5. https://doi.org/10.1016/j.ctim.2018.04.005; PMID: 29148437.

35. Morimoto T, Sunagawa Y, Kasaumi T, et al. The dietary consumption of curcumin nanoemulsion improves inflammatory activity and prevents heart failure in rats. J Innt 2018;45:44-8. https://doi.org/10.1007/s11376-017-1373-3; PMID: 19292869.

36. Saedehinia A, Kheirfam F, Butler AE, et al. Curcumin in heart failure: a brief review of the basic science and clinical literature. Acta Med Iran 2018;56:112-9. https://doi.org/10.1016/j.jalz.2018.02.014; PMID: 29436043

37. DarWEEN SK, Wolters F, Iram MA, et al. Inflammatory markers and the risk of chronic obstructive pulmonary disease: a systematic review and meta-analysis. PLoS One 2018;13:2015. doi:10.1371/journal.pone.0200354; PMID: 29305835

38. Barnes PS, Celli BR. Systematic manifestations and comorbidities of COPD. Eur Respir J 2009;33:1165-85. doi:10.1183/09031936.09.00126608; PMID: 19407001.

39. Su B, Liu Y, Fan K, et al. Inflammatory markers and the risk of chronic obstructive pulmonary disease: a systematic review and meta-analysis. J Int Med 2016;11:150586. doi:10.1177/1515166016631015; PMID: 27104349.

40. Sn DD, MacNeil WC. Chronic obstructive pulmonary disease and cardiovascular disease: a "vulnerable" relationship. Am J Respir Crit Care Med 2015;192:2-4. https://doi.org/10.1164/rccm.201506-1093RD; PMID: 25231347.

41. Moghadam SJ, Rama P, Mirabolghanlou SG, et al. Curcumin inhibits COPD-like airway inflammation and lung cancer progression in mice. Cingonics 2009;30:1949-56. https://doi.org/10.1007/s11596-009-0082-9; PMID: 19797980.

42. Yuan J, Liu R, Ma Y, et al. Curcumin attenuates airway inflammation and airway remodeling by inhibiting NF-κB signaling and COX-2 in cigarette smoke-induced COPD mice. Inflammation 2014;41:1804-14. https://doi.org/10.1007/s10753-014-0131-z; PMID: 25154033

43. Funamoto M, Sunagawa Y, Katayama Y, et al. Highly