DAPK1 modulates a curcumin-induced G2/M arrest and apoptosis by regulating STAT3, NF-κB, and caspase-3 activation.

Wu B, Yao H, Wang S, Xu R.

Abstract

Curcumin, an active polyphenol extracted from the perennial herb Curcuma longa, controls various molecules involved in tumor cell death. In this study, we found that the tumor suppressor death-associated protein kinase 1 (DAPK1) plays a vital role in the anti-carcinogenic effects of curcumin. We found that curcumin increased DAPK1 expression at the mRNA and protein levels in U251 cells, and that the siRNA-mediated knockdown of DAPK1 attenuated the curcumin-induced inhibition of STAT3 and NF-κB. Moreover, DAPK1 suppression diminished curcumin-induced caspase-3 activation. In addition, we confirmed that DAPK1 was required for a curcumin-induced G2/M cell cycle arrest and apoptosis. Thus, DAPK1 is involved in curcumin-mediated death pathways. Our data suggest novel mechanisms for curcumin in cancer therapy.

Curcumin Inhibits Transforming Growth Factor-β1-Induced EMT via PPARγ Pathway, Not Smad Pathway in Renal Tubular Epithelial Cells.


Abstract

Tubulointerstitial fibrosis (TIF) is the final common pathway in the end-stage renal disease. Epithelial-to-mesenchymal transition (EMT) is considered a major contributor to the TIF by increasing the number of myofibroblasts. Curcumin, a polyphenolic compound derived from rhizomes of Curcuma, has been shown to possess potent anti-fibrotic properties but the mechanism remains elusive. We found that curcumin inhibited the EMT as assessed by reduced expression of α-SMA and PAI-1, and increased E-cadherin in TGF-β1 treated proximal tubular epithelial cell HK-2 cells. Both of the conventional TGF-β1/Smad pathway and non-Smad pathway were investigated. Curcumin reduced TGF-β receptor type I (TβR-I) and TGF-β receptor type II (TβR II), but had no effect on phosphorylation of Smad2 and Smad3. On the other hand, in non-Smad pathway curcumin reduced TGF-β1-induced ERK phosphorylation and PPARγ phosphorylation, and promoted nuclear translocation of PPARγ. Further, the effect of curcumin on α-SMA, PAI-1, E-cadherin, TβR I and TβR II were reversed by ERK inhibitor U0126 or PPARγ inhibitor BADGE, or PPARγ shRNA. Blocking PPARγ signaling pathway by inhibitor BADGE or shRNA had no effect on the phosphorylation of ERK whereas the suppression of ERK signaling pathway inhibited the phosphorylation of PPARγ. We conclude that curcumin counteracted TGF-β1-induced EMT in renal tubular epithelial cells via ERK-dependent and then PPARγ-dependent pathway.


Nutraceuticals as new treatment approaches for oral cancer: II. Green tea extracts and resveratrol.

Zlotogorski A, Dayan A, Dayan D, Chaushu G, Salo T, Vered M.

Abstract

Tubulointerstitial fibrosis (TIF) is the final common pathway in the end-stage renal disease. Epithelial-to-mesenchymal transition (EMT) is considered a major contributor to the TIF by increasing the number of myofibroblasts. Curcumin, a polyphenolic compound derived from rhizomes of Curcuma, has been shown to possess potent anti-fibrotic properties but the mechanism remains elusive. We found that curcumin inhibited the EMT as assessed by reduced expression of α-SMA and PAI-1, and increased E-cadherin in TGF-β1 treated proximal tubular epithelial cell HK-2 cells. Both of the conventional TGF-β1/Smad pathway and non-Smad pathway were investigated. Curcumin reduced TGF-β receptor type I (TβR-I) and TGF-β receptor type II (TβR II), but had no effect on phosphorylation of Smad2 and Smad3. On the other hand, in non-Smad pathway curcumin reduced TGF-β1-induced ERK phosphorylation and PPARγ phosphorylation, and promoted nuclear translocation of PPARγ. Further, the effect of curcumin on α-SMA, PAI-1, E-cadherin, TβR I and TβR II were reversed by ERK inhibitor U0126 or PPARγ inhibitor BADGE, or PPARγ shRNA. Blocking PPARγ signaling pathway by inhibitor BADGE or shRNA had no effect on the phosphorylation of ERK whereas the suppression of ERK signaling pathway inhibited the phosphorylation of PPARγ. We conclude that curcumin counteracted TGF-β1-induced EMT in renal tubular epithelial cells via ERK-dependent and then PPARγ-dependent pathway.


Nutraceuticals as new treatment approaches for oral cancer: II. Green tea extracts and resveratrol.

Zlotogorski A, Dayan A, Dayan D, Chaushu G, Salo T, Vered M.

Abstract

Tubulointerstitial fibrosis (TIF) is the final common pathway in the end-stage renal disease. Epithelial-to-mesenchymal transition (EMT) is considered a major contributor to the TIF by increasing the number of myofibroblasts. Curcumin, a polyphenolic compound derived from rhizomes of Curcuma, has been shown to possess potent anti-fibrotic properties but the mechanism remains elusive. We found that curcumin inhibited the EMT as assessed by reduced expression of α-SMA and PAI-1, and increased E-cadherin in TGF-β1 treated proximal tubular epithelial cell HK-2 cells. Both of the conventional TGF-β1/Smad pathway and non-Smad pathway were investigated. Curcumin reduced TGF-β receptor type I (TβR-I) and TGF-β receptor type II (TβR II), but had no effect on phosphorylation of Smad2 and Smad3. On the other hand, in non-Smad pathway curcumin reduced TGF-β1-induced ERK phosphorylation and PPARγ phosphorylation, and promoted nuclear translocation of PPARγ. Further, the effect of curcumin on α-SMA, PAI-1, E-cadherin, TβR I and TβR II were reversed by ERK inhibitor U0126 or PPARγ inhibitor BADGE, or PPARγ shRNA. Blocking PPARγ signaling pathway by inhibitor BADGE or shRNA had no effect on the phosphorylation of ERK whereas the suppression of ERK signaling pathway inhibited the phosphorylation of PPARγ. We conclude that curcumin counteracted TGF-β1-induced EMT in renal tubular epithelial cells via ERK-dependent and then PPARγ-dependent pathway.


Nutraceuticals as new treatment approaches for oral cancer: II. Green tea extracts and resveratrol.

Zlotogorski A, Dayan A, Dayan D, Chaushu G, Salo T, Vered M.

Abstract

Tubulointerstitial fibrosis (TIF) is the final common pathway in the end-stage renal disease. Epithelial-to-mesenchymal transition (EMT) is considered a major contributor to the TIF by increasing the number of myofibroblasts. Curcumin, a polyphenolic compound derived from rhizomes of Curcuma, has been shown to possess potent anti-fibrotic properties but the mechanism remains elusive. We found that curcumin inhibited the EMT as assessed by reduced expression of α-SMA and PAI-1, and increased E-cadherin in TGF-β1 treated proximal tubular epithelial cell HK-2 cells. Both of the conventional TGF-β1/Smad pathway and non-Smad pathway were investigated. Curcumin reduced TGF-β receptor type I (TβR-I) and TGF-β receptor type II (TβR II), but had no effect on phosphorylation of Smad2 and Smad3. On the other hand, in non-Smad pathway curcumin reduced TGF-β1-induced ERK phosphorylation and PPARγ phosphorylation, and promoted nuclear translocation of PPARγ. Further, the effect of curcumin on α-SMA, PAI-1, E-cadherin, TβR I and TβR II were reversed by ERK inhibitor U0126 or PPARγ inhibitor BADGE, or PPARγ shRNA. Blocking PPARγ signaling pathway by inhibitor BADGE or shRNA had no effect on the phosphorylation of ERK whereas the suppression of ERK signaling pathway inhibited the phosphorylation of PPARγ. We conclude that curcumin counteracted TGF-β1-induced EMT in renal tubular epithelial cells via ERK-dependent and then PPARγ-dependent pathway.


Nutraceuticals as new treatment approaches for oral cancer: II. Green tea extracts and resveratrol.

Zlotogorski A, Dayan A, Dayan D, Chaushu G, Salo T, Vered M.
Nutraceuticals with anti-neoplastic potential are suitable candidates for extending the range of therapeutic options for several types of cancers. One of these malignancies is oral cancer of the squamous cell carcinoma type, for which current treatment approaches have not succeeded in improving long-term clinical outcome. We recently reviewed the beneficial effects of curcumin for the treatment of oral cancer. In the current review, we focused on the beneficial effects of other two nutraceuticals, green tea extracts [especially (-)-epigallocatechin-3-gallate (EGCG)] and resveratrol, in the treatment of oral cancer. In vivo and in vitro studies as well as clinical trials were reviewed, focusing on the beneficial effect of each of these plant-derived dietary agents, either alone or in combination with various pharmacological agents. We also presented the anti-cancer effects against cancer cells and against components of the tumor microenvironment. It emerged that the poor bioavailability of these nutraceuticals poses an obstacle to their exerting adequate anti-cancer potential. Ground-breaking studies employing new nanotechnology-based therapeutic approaches were presented.

Caloric restriction favorably impacts metabolic and immune/inflammatory profiles in obese mice but curcumin/piperine consumption adds no further benefit.


Abstract

BACKGROUND:
Obesity is associated with low-grade inflammation and impaired immune response. Caloric restriction (CR) has been shown to inhibit inflammatory response and enhance cell-mediated immune function. Curcumin, the bioactive phenolic component of turmeric spice, is proposed to have anti-obesity and anti-inflammation properties while piperine, another bioactive phenolic compound present in pepper spice, can enhance the bioavailability and efficacy of curcumin. This study sought to determine if curcumin could potentiate CR's beneficial effect on immune and inflammatory responses in obesity developed in mice by feeding high-fat diet (HFD).

METHODS:
Mice were fed a HFD for 22 wk and then randomized into 5 groups: one group remained on HFD ad libitum and the remaining 4 groups were fed a 10% CR (reduced intake of HFD by 10% but maintaining the same levels of micronutrients) in the presence or absence of curcumin and/or piperine for 5 wk, after which CR was increased to 20% for an additional 33 wk. At the end of the study, mice were sacrificed, and spleen cells were isolated. Cells were stimulated with T cell mitogens, anti-CD3/CD28 antibodies, or lipopolysaccharide to determine T cell proliferation, cytokine production, and CD4+ T cell subpopulations.

RESULTS:
Compared to HFD control group, all CR mice, regardless of the presence of curcumin and/or piperine, had lower body weight and fat mass, lower levels of blood glucose and insulin, and fewer total spleen cells but a higher percentage of CD4+ T cells. Additionally, they demonstrated lower production of pro-inflammatory cytokines IL-1beta and TNF-alpha, a trend toward lower IL-6, and lower production of PGE2, a lipid molecule with pro-inflammatory and T cell-suppressive properties. Mice with CR alone had higher splenocyte proliferation and IL-2 production, but this effect of CR was diminished by spice supplementation. CR alone or in combination with spice supplementation had no effect on production of cytokines IL-4, IL-10, IFN-gamma, and IL-17, or the proportion of different CD4+ T cell subsets.

CONCLUSION:
CR on an HFD favorably impacts both metabolic and immune/inflammatory profiles; however, the presence of curcumin and/or piperine does not amplify CR's beneficial effects.
Comparative evaluation of the pain-relieving properties of a lecithinized formulation of curcumin (Meriva®), nimesulide, and acetaminophen.

Francesco DP, Giuliana R, Eleonora AD, Giovanni A, Federico F, Stefano T.
Source Velleja Research.
Abstract
In addition to its anti-inflammatory activity, Meriva®, a proprietary lecithin formulation of curcumin, has been anecdotally reported to decrease acute pain in patients with various chronic diseases. Given that curcumin can desensitize transient receptor potential A1, a nociceptor seemingly also mediating the analgesic effect of acetaminophen, as well as inhibiting and downregulating the expression of cyclo-oxygenase 2, the selective target of nimesulide, a nonsteroidal anti-inflammatory agent, we carried out a pilot comparative study of the acute pain-relieving properties of these three agents. At a dose of 2 g (corresponding to 400 mg of curcumin), Meriva showed clear analgesic activity, comparable with that of a standard dose (1 g) of acetaminophen, but lower than that of a therapeutic (100 mg) dose of nimesulide. The analgesic activity of lower (1.5 g) doses of Meriva was less satisfactory, and the onset of activity was longer than that of nimesulide for both doses. On the other hand, gastric tolerability was significantly better than that of nimesulide and comparable with that of acetaminophen. Taken together, our results show that the preclinical analgesic properties of curcumin have clinical relevance, at least at a dose of 2 g as the Meriva formulation. While this dose is significantly higher than that used to relieve chronic inflammatory conditions (1-1.2 g/day), its pain-relieving activity could benefit from the general downregulation of the inflammatory response induced by curcumin, considering that the transient receptor potential channel-mediated mechanisms of analgesia are magnified by attenuation of inflammation. In patients on treatment with Meriva, this would also translate into better control of acute pain, providing a rationale for the analgesic properties associated with this curcumin formulation.
Intestinal I/R induced marked bowel injuries. Curcumin treatment significantly improved animal survival and reduced the pathologic injuries in the intestines. Furthermore, the elevated intestinal water content and levels of malondialdehyde, interleukin 1β (IL-1β) and IL-6 were significantly decreased, but levels of superoxide dismutase increased. Interestingly, we found that the decreased leptin and its receptor Ob-Rb were restored by curcumin administration. In addition, in vitro studies showed that curcumin increased leptin expression and release after hypoxia/reoxygenation-induced cell injuries. Moreover, curcumin treatment restored decreased ERK1/2 phosphorylation (p-ERK1/2) and inhibited overactive p38 (p-p38) after injuries, and the effect was reversed by a leptin-specific antibody or Ob-R blocker.

CONCLUSION: These data suggest that leptin and Ob-Rb-dependent ERK and p38 MAPK signaling pathways may be involved in curcumin protection against intestinal I/R injury, and leptin may be a potential target of curcumin in intestinal I/R injury and other related acute diseases.

Curcumin attenuates allergic airway inflammation by regulation of CD4+CD25+ regulatory T cells (Tregs)/Th17 balance in ovalbumin-sensitized mice.
Ma C, Ma Z, Fu Q, Ma S.
Source
Department of Pharmacology of Chinese Materia Medica, China Pharmaceutical University, Nanjing 210009, PR China.
Abstract
The present study aimed to determine the protective effects and the underlying mechanisms of curcumin on ovalbumin (OVA)-induced allergic inflammation in a mouse model of allergic asthma. Asthma mice model was established by ovalbumin-induced. A total of 60 mice were randomly assigned to six experimental groups: control, model, dexamethasone (2mg/kg), and curcumin (50mg/kg, 100mg/kg, 200mg/kg). Airway resistance (Raw) was measured by the forced oscillation technique, differential cell count in BAL fluid (BALF) was measured by Wright-Giemsa staining, histological assessment was measured by hematoxylin and eosin (HE) staining, BALF levels of Treg/Th17 cytokines were measured by enzyme-linked immunosorbent assay, Treg cells and Th17 cells were evaluated by flow cytometry (FCM). Our study demonstrated that curcumin inhibited OVA-induced increases in eosinophil count; interleukin (IL)-17A level were recovered in bronchoalveolar lavage fluid increased IL-10 level in bronchoalveolar lavage fluid. Histological studies demonstrated that curcumin substantially inhibited OVA-induced eosinophilia in lung tissue. Flow cytometry (FCM) studies demonstrated that curcumin remarkably inhibited Th17 cells and significantly increased Treg cells. The results in vivo show ovalbumin-induced significantly broke Treg/Th17 balance; curcumin treatments markedly attenuated the inflammatory in asthma model by regulating Treg/Th17 balance. Our findings support the possible use of curcumin as a therapeutic drug for patients with allergic asthma.

Modulation of adipose tissue inflammation by bioactive food compounds.
Siriwardhana N, Kalupahana NS, Cekanova M, Lemieux M, Greer B, Moustaid-Moussa N.
Source
Nutritional Sciences, College of Human Sciences, Texas Tech University, Lubbock, TX, 79409-1240, USA. Electronic address: naima.moustaid-moussa@ttu.edu.
Abstract
Adipose tissue has an important endocrine function in the regulation of whole-body metabolism. Obesity leads to a chronic low-grade inflammation of the adipose tissue, which disrupts this endocrine function and results in metabolic derangements, such as type-2 diabetes. Dietary
bioactive compounds, such as polyphenols and certain fatty acids, are known to suppress both systemic and adipose tissue inflammation and have the potential to improve these obesity-associated metabolic disorders. Mechanistically, polyphenolic compounds including non-flavonoids, such as curcumin and resveratrol, and flavonoids, such as catechins (tea-polyphenols), quercetin and isoflavones, suppress nuclear factor-κB (NF-κB) and mitogen-activated protein (MAP) kinases (MAPK) pathways while activating the 5′ adenosine monophosphate-activated protein kinase (AMPK) pathway in adipose tissue. Dietary polyunsaturated fatty acids, such as eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), conjugated linoleic acid (CLA) and monounsaturated fatty acids (MUFA), such as oleic acid, also impart anti-inflammatory effects through several mechanisms. These include activation of AMPK and peroxisome proliferator-activated receptor gamma (PPAR-γ), as well as suppression of toll-like receptors (TLRs) and NF-κB pathway. This review discusses the major molecular mechanisms of dietary polyphenols and fatty acids, alone or in combination, which are responsible for adipose tissue-associated anti-inflammatory effects.


Interaction of curcumin with phosphocasein micelles processed or not by dynamic high-pressure.

Benzaria A, Maresca M, Taieb N, Dumay E.

Source
Université Montpellier 2, UMR 1208, Ingénierie des Agropolymères et Technologies Emergentes, Equipe de Biochimie et Technologie Alimentaires cc023, 2, Place Eugène Bataillon, 34095 Montpellier Cedex 5, France.

Abstract
The binding of curcumin to native-like phosphocaseins (PC) dispersed in simulated milk ultrafiltrate at pH 6.6 was assessed by fluorescence spectrophotometry. Curcumin binds to native-like PC micelles with ~1 binding site per casein molecule, and a binding constant of 0.6-5.6×10^4 M⁻¹. Dynamic high pressure (or ultra-high pressure homogenisation, UHPH) at 200MPa did not affect the binding parameters of curcumin to processed PC. UHPH-processing of PC dispersions at 300MPa was followed by a slight but significant (p=0.05) increase in the binding constant of curcumin to processed PC, which may result from the significant UHPH-induced dissociation of initial PC micelles into neo-micelles of smaller sizes, and from the corresponding 1.5-2-fold increase in micelle surface area. PC-curcumin complexes were resistant to pepsin but were degraded by pancreatin, providing the possibility of a spatiotemporally controlled release and protection of bound biomolecules. UHPH-processed PC did not induce TC7-cell damage or major inflammation as assessed by LDH release or IL-8 secretion, respectively, compared with native-like PC. PC micelles could provide a valuable submicron system to vectorise drugs and nutrients.


Targeted delivery of curcumin for treating type 2 diabetes.

Maradana MR, Thomas R, O’Sullivan BJ.

Source
Diamantina Institute for Cancer, Immunology and Metabolic Medicine, University of Queensland, Princess Alexandra Hospital, Brisbane, Queensland, Australia.

Abstract
Type 2 diabetes is a chronic condition in which cells have reduced insulin signalling, leading to hyperglycemia and long-term complications, including heart, kidney and liver disease. Macrophages activated by dying or stressed cells, induce the transcription factor nuclear factor kappa-B leading to the production of pro-inflammatory cytokines including TNF and IL-6. These inflammatory macrophages in liver and adipose tissue promote insulin resistance, and medications which reduce inflammation and enhance insulin signalling improve glucose control. Curcumin is an anti-oxidant and nuclear factor kappa-B inhibitor derived from turmeric. A number of studies have shown that dietary curcumin reduces inflammation and delays or prevents obesity-induced insulin
resistance and associated complications, including atherosclerosis and immune-mediated liver disease. Unfortunately, dietary curcumin is poorly absorbed by the digestive system and undergoes glucuronidation and excretion rather than being released into the serum and systemically distributed. This confounds understanding of how dietary curcumin exerts its beneficial effects in type 2 diabetes and associated diseases. New improved methods of delivering curcumin are being developed, including nanoparticles and lipid/liposome formulations that increase absorption and bioavailability of curcumin. Development and refinement of these technologies will enable cell-directed targeting of curcumin and improved therapeutic outcome.


Is there a role for curcumin in the treatment of bipolar disorder?

Brietzke E, Mansur RB, Zugman A, Carvalho AF, Macêdo DS, Cha DS, Abílio VC, McIntyre RS.

Source
Department of Psychiatry, Universidade Federal de São Paulo, São Paulo, Brazil.

**Abstract**
Curcumin is a polyphenolic nonflavonoid compound extracted from the rhizome of turmeric (Curcuma longa), a plant commonly used in Indian and Chinese traditional medicine to treat rheumatism, cough, inflammation, and wounds. Curcumin putative targets, known based on studies of diverse central nervous system disorders other than bipolar disorders (BD) include several proteins currently implicated in the pathophysiology of BD. These targets include, but are not limited to, transcription factors activated by environmental stressors and pro-inflammatory cytokines, protein kinases (PKA, PKC), enzymes, growth factors, inflammatory mediators, and anti-apoptotic proteins (Bcl-XL). Herein, we review previous studies on the anti-inflammatory and anti-oxidant properties of curcumin and discuss its therapeutic potential in BD.


Curcumin: An Orally Bioavailable Blocker of TNF and Other Pro-inflammatory Biomarkers.

Aggarwal BB, Gupta SC, Sung B.

Source
Cytokine Research Laboratory, Department of Experimental Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, Texas.

**Abstract**
Because tumor necrosis factors (TNFs) are major mediators of inflammation and inflammation-related diseases, the United States Food and Drug Administration (FDA) has approved blockers of the cytokine, TNF-α, which include chimeric TNF antibody (Infliximab), humanized TNF-α antibody (Humira), and soluble TNF receptor-II (Enbrel). TNF blockers are now being used for the treatment of osteoarthritis, inflammatory bowel disease, psoriasis, and ankylosis at a total cumulative market value of more than $20 billion/year. Besides being expensive ($15,000-20,000/person/year), these drugs must be injected and have enough adverse effects to be given a black label warning by the FDA. In the current report, we describe an alternative, curcumin (diferuloylmethane), a component of turmeric (Curcuma longa) that is very inexpensive, orally bioavailable, and highly safe in humans, yet can block TNF-α action and production in in vitro models, in animal models, and in humans. In addition, we provide evidence for curcumin's activities against all of the diseases for which TNF blockers are being used. Mechanisms by which curcumin inhibits the production and the cell signaling pathways activated by this cytokine are also discussed. With health care costs and safety being major issues today, this golden spice may help provide the solution.


Curcumin and obesity.

Bradford PG.

Source
Department of Pharmacology and Toxicology, School of Medicine and Biomedical Sciences, State University of New York at Buffalo, Buffalo, NY. pgb@buffalo.edu.
Abstract
Turmeric has been long recognized for its anti-inflammatory and health-promoting properties. Curcumin is one of the principal anti-inflammatory and healthful components of turmeric comprising 2-8% of most turmeric preparations. Experimental evidence supports the activity of curcumin in promoting weight loss and reducing the incidence of obesity-related diseases. With the discovery that obesity is characterized by chronic low-grade metabolic inflammation, phytochemicals like curcumin which have anti-inflammatory activity are being intensely investigated. Recent scientific research reveals that curcumin directly interacts with white adipose tissue to suppress chronic inflammation. In adipose tissue, curcumin inhibits macrophage infiltration and nuclear factor κB (NF-κB) activation induced by inflammatory agents. Curcumin reduces the expression of the potent proinflammatory adipokines tumor necrosis factor-α (TNFα), monocyte chemoattractant protein-1 (MCP-1), and plasminogen activator inhibitor type-1 (PAI-1), and it induces the expression of adiponectin, the principal anti-inflammatory agent secreted by adipocytes. Curcumin also has effects to inhibit adipocyte differentiation and to promote antioxidant activities. Through these diverse mechanisms curcumin reduces obesity and curtails the adverse health effects of obesity. © 2013 BioFactors, 39(1):78-87, 2013.

Molecular mechanisms of hypolipidemic effects of curcumin.
Zingg JM, Hasan ST, Meydani M.
Source
Vascular Biology Laboratory, Jean Mayer USDA-Human Nutrition Research Center on Aging, Tufts University, Boston, MA. Jean-Marc.Zingg@tufts.edu.

Abstract
Recent evidence suggests potential benefits from phytochemicals and micronutrients in reducing the elevated oxidative and lipid-mediated stress associated with inflammation, obesity, and atherosclerosis. These compounds may either directly scavenge reactive oxygen or nitrogen species or they may modulate the activity of signal transduction enzymes leading to changes in the expression of antioxidant genes. Alternatively, they may reduce plasma lipid levels by modulating lipid metabolic genes in tissues and thus reduce indirectly lipid-mediated oxidative and endoplasmic reticulum stress through their hypolipidemic effect. Here we review the proposed molecular mechanisms by which curcumin, a polyphenol present in the rhizomes of turmeric (Curcuma longa) spice, influences oxidative and lipid-mediated stress in the vascular system. At the molecular level, mounting experimental evidence suggests that curcumin may act chemically as scavenger of free radicals and/or influences signal transduction (e.g., Akt, AMPK) and modulates the activity of specific transcription factors (e.g., FOXO1/3a, NRF2, SREBP1/2, CREB, CREBH, PPARγ, and LXRα) that regulate the expression of genes involved in free radicals scavenging (e.g., catalase, MnSOD, and heme oxygenase-1) and lipid homeostasis (e.g., aP2/FABP4, CD36, HMG-CoA reductase, and carnitine palmitoyltransferase-I (CPT-1)). At the cellular level, curcumin may induce a mild oxidative and lipid-metabolic stress leading to an adaptive cellular stress response by hormetic stimulation of these cellular antioxidant defense systems and lipid metabolic enzymes. The resulting lower oxidative and lipid-mediated stress may not only explain the beneficial effects of curcumin on inflammation, cardiovascular, and neurodegenerative disease, but may also contribute to the increase in maximum life-span observed in animal models. © 2013 BioFactors, 39(1):101-121, 2013.


2a, a novel curcumin analog, sensitizes cisplatin-resistant A549 cells to cisplatin by inhibiting thioredoxin reductase concomitant oxidative stress damage.
Zhou B, Huang J, Zuo Y, Li B, Guo Q, Cui B, Shao W, Du J, Bu X.
Source
School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou, PR China.
(1E,4Z,6E)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(5-methylfuran-2-yl)hepta-1,4,6-trien-3-one (2a), a novel curcumin analog, was previously synthesized in our laboratory as a potential thioredoxin reductase (TrxR) inhibitor with excellent growth inhibitory effects on several TrxR over-expressed cancer cells. In this study, our further studies show that 2a is able to inhibit the growth of cisplatin-resistant A549 (A549/CDDP) cells much more effectively in a dose-dependent manner than that of A549 cells in antiproliferative activity experiments. Moreover, 2a-pretreated A549/CDDP cells are sensitive to cisplatin treatment, which is accompanied by the inhibition of TrxR activity in A549/CDDP cells. As a consequence of targeting TrxR, 2a in turn remarkably up-regulates intracellular reactive oxygen species level, depletes glutathione (GSH), and reduces the GSH/GSSG ratio, suggesting that the intracellular redox balance is shifted to a more oxidative state. Consequently, concomitant with the cell growth inhibition of 2a, apoptosis is induced by 2a probably through increased oxidative stress in A549/CDDP cells. In conclusion, these observations demonstrated that TrxR inhibitors would be promising drugs to achieve a successful combinatory or single cancer chemotherapy.

Muglikar S, Patil KC, Shivswami S, Hegde R.

Abstract

Purpose: To evaluate the efficacy of curcumin mouthwash as an adjunct to scaling and root planing in the treatment of chronic gingivitis and to compare curcumin to chlorhexidine in terms of its anti-inflammatory and anti-microbial properties. Materials and Methods: Thirty patients aged 20-40 years with generalised chronic gingivitis were included in the study. They were randomly divided into 3 groups of 10 each. In group 1, patients underwent scaling and root planing followed by chlorhexidine mouthwash (SRP/CHX Gr-1); in group 2, patients underwent scaling and root planing followed by curcumin mouthwash (SRP/CUR Gr-2); in group 3, patients underwent only scaling and root planing (SRP Gr-3). Gingival and plaque indices were recorded at baseline (day 0) and 7, 14 and 21 days. Differences between the groups were statistically analysed. Results: The clinical parameters showed improvement in all the three groups compared to baseline. When compared to the scaling and root planing group (Gr-3), both curcumin and chlorhexidine groups were found to have statistically significantly better results (P < 0.05). However, when curcumin and chlorhexidine groups were compared, the gingival (Löe and Silness) and plaque index (Silness and Löe) scores were not found to be statistically significant (P > 0.05). Conclusion: Curcumin is comparable to chlorhexidine as an anti-inflammatory mouthwash. Thus, it can be considered as an effective adjunct to mechanical periodontal therapy.

Dietary regulation of histone acetylases and deacetylases for the prevention of metabolic diseases.
Pham TX, Lee J.

Source
Department of Nutritional Sciences, University of Connecticut, Storrs, CT 06269, USA.
Tho.Phama@uconn.edu

Abstract

Age-related diseases such as type 2 diabetes, cardiovascular disease, and cancer involve epigenetic modifications, where accumulation of minute changes in the epigenome over time leads to disease manifestation. Epigenetic changes are influenced by life style and diets. This represents an avenue whereby dietary components could accelerate or prevent age-related diseases through their effects on epigenetic modifications. Histone acetylation is an epigenetic modification that is regulated through the opposing action of histone acetylases (HATs) and deacetylases (HDACs). These two families of enzymes play critical roles in metabolic processes and their dysregulation is associated with pathogenesis of several diseases. Dietary components, such as butyrate, sulforaphane, and curcumin, have been shown to affect HAT and HDAC activity, and their health benefits are
attributed, at least in part, to epigenetic modifications. Given the decades that it takes to accumulate epigenetic changes, it is unlikely that pharmaceuticals could undo epigenetic changes without side effects. Therefore, long term consumption of dietary components that can alter the epigenome could be an attractive means of disease prevention. The goal of this review is to highlight the roles of diets and food components in epigenetic modifications through the regulation of HATs and HDACs for disease prevention.

Curcumin in inflammatory diseases.
Shehzad A, Rehman G, Lee YS.
Source
School of Life Sciences, College of Natural Sciences, Kyungpook National University, Daegu 702-701, Korea.
Abstract
Curcumin (diferuloylmethane), a yellow coloring agent extracted from turmeric is also used as a remedy for the treatment and prevention of inflammatory diseases. Acute and chronic inflammation is a major factor in the progression of obesity, type II diabetes, arthritis, pancreatitis, cardiovascular, neurodegenerative and metabolic diseases, as well as certain types of cancer. Turmeric has a long history of use in Ayurvedic medicine for the treatment of inflammatory disorders. Recent studies on the efficacy and therapeutic applicability of turmeric have suggested that the active ingredient of turmeric is curcumin. Further, compelling evidence has shown that curcumin has the ability to inhibit inflammatory cell proliferation, invasion, and angiogenesis through multiple molecular targets and mechanisms of action. Curcumin is safe, non-toxic, and mediates its anti-inflammatory effects through the down-regulation of inflammatory transcription factors, cytokines, redox status, protein kinases, and enzymes that all promote inflammation. In addition, curcumin induces apoptosis through mitochondrial and receptor-mediated pathways, as well as activation of caspase cascades. In the current study, the anti-inflammatory effects of curcumin were evaluated relative to various chronic inflammatory diseases. Based on the available pharmacological data obtained from in vitro and in vivo research, as well as clinical trials, an opportunity exists to translate curcumin into clinics for the prevention of inflammatory diseases in the near future. © 2012 BioFactors, 39(1):69-77, 2013.

Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases.
Aggarwal BB, Harikumar KB.
Source
Department of Experimental Therapeutics, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA. aggarwal@mdanderson.org
Abstract
Although safe in most cases, ancient treatments are ignored because neither their active component nor their molecular targets are well defined. This is not the case, however, with curcumin, a yellow-pigment substance and component of turmeric (Curcuma longa), which was identified more than a century ago. For centuries it has been known that turmeric exhibits anti-inflammatory activity, but extensive research performed within the past two decades has shown that this activity of turmeric is due to curcumin (diferuloylmethane). This agent has been shown to regulate numerous transcription factors, cytokines, protein kinases, adhesion molecules, redox status and enzymes that have been linked to inflammation. The process of inflammation has been shown to play a major role in most chronic illnesses, including neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. In the current review, we provide evidence for the potential role of curcumin in the prevention and treatment of various proinflammatory chronic diseases. These features, combined with the pharmacological safety and negligible cost, render curcumin an attractive agent to explore further.
Curcuma longa (turmeric) has a long history of use in Ayurvedic medicine as a treatment for inflammatory conditions. Turmeric constituents include the three curcuminoids: curcumin (diferuloylmethane; the primary constituent and the one responsible for its vibrant yellow color), demethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins. While numerous pharmacological activities, including antioxidant and antimicrobial properties, have been attributed to curcumin, this article focuses on curcumin's anti-inflammatory properties and its use for inflammatory conditions. Curcumin's effect on cancer (from an anti-inflammatory perspective) will also be discussed; however, an exhaustive review of its many anticancer mechanisms is outside the scope of this article. Research has shown curcumin to be a highly pleiotropic molecule capable of interacting with numerous molecular targets involved in inflammation. Based on early cell culture and animal research, clinical trials indicate curcumin may have potential as a therapeutic agent in diseases such as inflammatory bowel disease, pancreatitis, arthritis, and chronic anterior uveitis, as well as certain types of cancer. Because of curcumin's rapid plasma clearance and conjugation, its therapeutic usefulness has been somewhat limited, leading researchers to investigate the benefits of complexing curcumin with other substances to increase systemic bioavailability. Numerous in-progress clinical trials should provide an even deeper understanding of the mechanisms and therapeutic potential of curcumin.

Curcumin: an anti-inflammatory molecule from a curry spice on the path to cancer treatment.
Basnet P, Skalko-Basnet N.
Source
Drug Transport and Delivery Research Group, Department of Pharmacy, University of Tromsø, Tromsø N-9037, Norway. purusotam.basnet@uit.no
Abstract
Oxidative damage and inflammation have been pointed out in preclinical studies as the root cause of cancer and other chronic diseases such as diabetes, hypertension, Alzheimer's disease, etc. Epidemiological and clinical studies have suggested that cancer could be prevented or significantly reduced by treatment with anti-oxidant and anti-inflammatory drugs, therefore, curcumin, a principal component of turmeric (a curry spice) showing strong anti-oxidant and anti-inflammatory activities, might be a potential candidate for the prevention and/or treatment of cancer and other chronic diseases. However, curcumin, a highly pleiotropic molecule with an excellent safety profile targeting multiple diseases with strong evidence on the molecular level, could not achieve its optimum therapeutic outcome in past clinical trials, largely due to its low solubility and poor bioavailability. Curcumin can be developed as a therapeutic drug through improvement in formulation properties or delivery systems, enabling its enhanced absorption and cellular uptake. This review mainly focuses on the anti-inflammatory potential of curcumin and recent developments in dosage form and nanoparticulate delivery systems with the possibilities of therapeutic application of curcumin for the prevention and/or treatment of cancer.

Curcumin-targeting Pericellular Serine Protease Matriptase Role in Suppression of Prostate Cancer Cell Invasion, Tumor Growth and Metastasis.
Cheng TS, Chen WC, Lin YY, Tsai CH, Liao CI, Shyu HY, Ko CJ, Tzeng SF, Huang CY, Yang PC, Hsiao PW, Lee MS.

Source
1Department of Biochemistry and Molecular Biology, College of Medicine, National Taiwan University.

Abstract
Curcumin has been shown to possess potent chemopreventive and antitumor effects on prostate cancer. However, the molecular mechanism involved in curcumin's ability to suppress prostate cancer cell invasion, tumor growth and metastasis is not yet well understood. In this study, we showed that curcumin can suppress EGF- and heregulin-stimulated PC-3 cell invasion, as well as androgen-induced LNCaP cell invasion. Curcumin treatment significantly resulted in reduced MMP-9 activity and down-regulation of cellular matriptase, a membrane-anchored serine protease with oncogenic roles in tumor formation and invasion. Our data further show that curcumin is able to inhibit the induction effects of androgens and EGF on matriptase activation, as well as to reduce the activated levels of matriptase after its overexpression, thus suggesting that curcumin may interrupt diverse signal pathways to block the protease. Furthermore, the reduction of activated matriptase in cells by curcumin was also partly due to curcumin's effect on promoting the shedding of matriptase into an extracellular environment, but not via altering matriptase gene expression. Additionally, curcumin significantly suppressed the invasive ability of PCa cells induced by matriptase overexpression. In xenograft model, curcumin not only inhibits PCa tumor growth and metastasis but also down-regulates matriptase activity in vivo. Overall, the data indicate that curcumin exhibits a suppressive effect on prostate cancer cell invasion, tumor growth and metastasis, at least in part via down-regulating matriptase function.


Polyphenols inhibit indoleamine 3,5-dioxygenase-1 enzymatic activity--a role of immunomodulation in chemoprevention.

Chen SS, Corteling R, Stevanato L, Sinden J.

Source
Department of Research and Development, Ovarian and Prostate Cancer Research Trust Laboratory, Guildford, Surrey GU2 7YG, United Kingdom. s.chen@opcart-lab.org

Abstract
Metastasis is one of the cancer hallmarks described by Hanahan and Weinberg. Emerging evidence shows that it requires interplays between cancer cells and micro-environmental biofactors. Indoleamine 3,5-dioxygenase-1 (IDO-1) produced by cancer, local lymph nodes, and satellite cells have been demonstrated as one of the biofactors. Aberrant IDO-1 activity has partially contributed to immunosuppressive environment by repressing T lymphocyte and natural killer cell activities, and activating regulatory T cells (Treg, CD4+CD25+). Clinical investigations further show a negative correlation between the enzyme activity and prognosis in patients with various cancer types. The findings suggest a possible role of IDO-1 inhibitor in restoring host anti-tumor immunity and attenuating cancer metastasis. Data from preclinical and phase I/II clinical studies with IDO-1 inhibitors support this hypothesis. Polyphenols as antioxidants are shown to exhibit anticancer activities. However, the underlying mechanism has not been entirely characterized. We recently found that certain flavone molecules profoundly inhibit the enzymatic activity of IDO-1 but not mRNA expression in human neuronal stem cells (hNSC) confirmed by cell-based assay and qRT-PCR. To further the investigation, we studied additional anti-cancer phytochemicals including chalcone, flavonol, isoflavone, and diterpene. Here we summarize the results and show that the inhibitory sensitivity depends on the molecular structure in the following order: apigenin > wogonin > chrysin > biacalein ~ genistein > quercetin. Curcumin and isoliquiritigenin (a chalcone) exhibited toxicity to hNSCs. Although oridonin (a diterpene) showed a null toxicity toward hNSCs, it repressed the enzymatic function only marginally in contrast to its potent cytotoxicity in various cancer cell lines. While the mode of action of the enzyme-polyphenol complex awaits to be
investigated, the sensitivity of enzyme inhibition was compared to the anti-proliferative activities toward three cancer cell lines. The IC50s obtained from both sets of the experiments indicate that they are in the vicinity of micromolar concentration with the enzyme inhibition slightly more active. These results suggest that attenuation of immune suppression via inhibition of IDO-1 enzyme activity may be one of the important mechanisms of polyphenols in chemoprevention or combinatorial cancer therapy.


Source
Cytokine Research Laboratory, Department of Experimental Therapeutics, The University of Texas MD Anderson Cancer Center, 1901 East Road, Unit # 1950, Houston, TX 77054, USA.

Abstract
Extensive research over the past half century has shown that curcumin (diferuloylmethane), a component of the golden spice turmeric (Curcuma longa), can modulate multiple cell signaling pathways. Extensive clinical trials over the past quarter century have addressed the pharmacokinetics, safety, and efficacy of this nutraceutical against numerous diseases in humans. Some promising effects have been observed in patients with various pro-inflammatory diseases including cancer, cardiovascular disease, arthritis, uveitis, ulcerative proctitis, Crohn's disease, ulcerative colitis, irritable bowel disease, tropical pancreatitis, peptic ulcer, gastric ulcer, idiopathic orbital inflammatory pseudotumor, oral lichen planus, gastric inflammation, vitiligo, psoriasis, acute coronary syndrome, atherosclerosis, diabetes, diabetic nephropathy, diabetic microangiopathy, lupus nephritis, renal conditions, acquired immunodeficiency syndrome, β-thalassemia, biliary dyskinesia, Dejerine-Sottas disease, cholecystitis, and chronic bacterial prostatitis. Curcumin has also shown protection against hepatic conditions, chronic arsenic exposure, and alcohol intoxication. Dose-escalating studies have indicated the safety of curcumin at doses as high as 12 g/day over 3 months. Curcumin's pleiotropic activities emanate from its ability to modulate numerous signaling molecules such as pro-inflammatory cytokines, apoptotic proteins, NF-κB, cyclooxygenase-2, 5-LOX, STAT3, C-reactive protein, prostaglandin E(2), prostate-specific antigen, adhesion molecules, transforming growth factor-β, triglyceride, ET-1, creatinine, HO-1, AST, and ALT in human participants. In clinical trials, curcumin has been used either alone or in combination with other agents. Various formulations of curcumin, including nanoparticles, liposomal encapsulation, emulsions, capsules, tablets, and powder, have been examined. In this review, we discuss in detail the various human diseases in which the effect of curcumin has been investigated.


Source
Department of Urology, Teikyo University School of Medicine, Tokyo, Japan.

Abstract
The burden of increasing morbidity and mortality due to prostate cancer imposes a need for new, effective measures of prevention in daily life. The influence of lifestyle on carcinogenesis in Asian men who migrate to Western cultures supports a causal role for dietary, environmental, and genetic factors in the epidemiology of prostate cancer. Chemoprevention, a prophylactic approach that uses nontoxic natural or synthetic compounds to reverse, inhibit, or prevent cancer by targeting specific steps in the carcinogenic pathway, is gaining traction among health care practitioners. Soy isoflavones and curcumin, staples of the Asian diet, have shown promise as functional factors for the chemoprevention of prostate cancer because of their ability to modulate multiple intracellular signaling pathways, including cellular proliferation, apoptosis, inflammation, and androgen receptor signaling. Recent evidence has revealed the DNA damage response (DDR) to be one of the earliest
events in the multistep progression of human epithelial carcinomas to invasive malignancy. Soy isoflavones and curcumin activate the DDR, providing an opportunity and rationale for the clinical application of these nutraceuticals in the chemoprevention of prostate cancer.


Curcumin inhibits prostate cancer metastasis in vivo by targeting the inflammatory cytokines CXCL1 and -2.

Killian PH, Kronski E, Michalik KM, Barbieri O, Astigiano S, Sommerhoff CP, Pfeffer U, Nerlich AG, Bachmeier BE.

Source
Institute of Laboratory Medicine (former Dept. of Clin. Chemistry and Biochemistry), Ludwig-Maximilians-University, Munich, Germany.

Abstract
In America and Western Europe, prostate cancer is the second leading cause of death in men. Emerging evidence suggests that chronic inflammation is a major risk factor for the development and metastatic progression of prostate cancer. We previously reported that the chemopreventive polyphenol curcumin inhibits the expression of the proinflammatory cytokines CXCL1 and -2 leading to diminished formation of breast cancer metastases. In this study, we analyze the effects of curcumin on prostate carcinoma growth, apoptosis and metastasis. We show that curcumin inhibits translocation of NFκB to the nucleus through the inhibition of the IκB-kinase (IKKβ, leading to stabilization of the inhibitor of NFκB, IκBα, in PC-3 prostate carcinoma cells. Inhibition of NFκB activity reduces expression of CXCL1 and -2 and abolishes the autocrine/paracrine loop that links the two chemokines to NFκB. The combination of curcumin with the synthetic IKKβ inhibitor, SC-541, shows no additive or synergistic effects indicating that the two compounds share the target. Treatment of the cells with curcumin and siRNA-based knockdown of CXCL1 and -2 induce apoptosis, inhibit proliferation and downregulate several important metastasis-promoting factors like COX2, SPARC and EFEMP. In an orthotopic mouse model of hematogenous metastasis, treatment with curcumin inhibits statistically significantly formation of lung metastases. In conclusion, chronic inflammation can induce a metastasis prone phenotype in prostate cancer cells by maintaining a positive proinflammatory and prometastatic feedback loop between NFκB and CXCL1/-2. Curcumin disrupts this feedback loop by the inhibition of NFκB signaling leading to reduced metastasis formation in vivo.


The Three Dimensional Quantitative Structure Activity Relationships (3D-QSAR) and Docking Studies of Curcumin Derivatives as Androgen Receptor Antagonists.

Xu G, Chu Y, Jiang N, Yang J, Li F.

Source
School of Pharmacy, Nanjing Medical University, Nanjing 210029, China; E-Mails: xghchem@hotmail.com (G.X.); chuyanyan1@hotmail.com (Y.C.); jiangnan792000@163.com (N.J.); alley79@163.com (J.Y.).

Abstract
Androgen receptor antagonists have been proved to be effective anti-prostate cancer agents. 3D-QSAR and Molecular docking methods were performed on curcumin derivatives as androgen receptor antagonists. The bioactive conformation was explored by docking the potent compound 29 into the binding site of AR. The constructed Comparative Molecular Field Analysis (CoMFA) and Comparative Similarity Indices Analysis (CoMSIA) models produced statistically significant results with the cross-validated correlation coefficients q(2) of 0.658 and 0.567, non-cross-validated correlation coefficients r(2) of 0.988 and 0.978, and predicted correction coefficients r(2) (pred) of 0.715 and 0.793, respectively. These results ensure the CoMFA and CoMSIA models as a tool to guide the design of novel potent AR antagonists. A set of 30 new analogs were proposed by utilizing the results revealed in the present study, and were predicted with potential activities in the developed models.
Pathogenic role of HIF-1α in prostate hyperplasia in the presence of chronic inflammation.


Source
Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Republic of Korea.

Abstract
Benign prostatic hyperplasia (BPH) commonly occurs in older men with chronic prostatitis. Although BPH is frequently accompanied by inflammation, it is unclear whether inflammation underlies prostate enlargement. Recently, we reported that hypoxia-inducible factor 1α (HIF-1α), which is known to be induced by proinflammatory cytokines, is involved in testosterone-induced prostate hyperplasia. Therefore, we hypothesized that cytokines secreted from infiltrated macrophages under inflammatory conditions stimulate prostate enlargement by up-regulating HIF-1α. In the present study, we injected lipopolysaccharide (LPS) into rat prostates to mimic prostatitis and evaluated prostate hyperplasia 14 days later. Epithelial cells of LPS-treated prostates were found to be highly proliferative and HIF-1α levels in prostate tissues to be elevated. When prostate epithelial cells were incubated in conditioned medium from macrophages activated with LPS, they robustly expressed HIF-1α, and under these conditions IL-1β, IL-6, and TNF-α cytokines were found to mediate HIF-1α induction. In addition, HIF-1α was found to enhance the expression of Twist, which initiates epithelial-mesenchymal transition (EMT). Furthermore, profound EMT features were observed in LPS-treated rat prostates, and the natural HIF-1α inhibitors ascorbate and curcumin were found to attenuate EMT and prostate hyperplasia both in vivo and in vitro. Based on these results, we propose that HIF-1α mediates prostate enlargement under inflammatory conditions, and we suggest that HIF-1α be viewed as a promising target for blocking the transition from prostatitis to BPH.

Curcumin modulates DNA methylation in colorectal cancer cells.

Link A, Balaguer F, Shen Y, Lozano JJ, Leung HC, Boland CR, Goel A.

Source
Gastrointestinal Cancer Research Laboratory, Division of Gastroenterology, Baylor Research Institute, Baylor University Medical Center, Dallas, Texas, United States of America; Department of Gastroenterology, Hepatology and Infectious Diseases, Otto-von-Guericke University, Magdeburg, Germany.

Abstract
AIM: Recent evidence suggests that several dietary polyphenols may exert their chemopreventive effect through epigenetic modifications. Curcumin is one of the most widely studied dietary chemopreventive agents for colon cancer prevention, however, its effects on epigenetic alterations, particularly DNA methylation, remain unclear. Using systematic genome-wide approaches, we aimed to elucidate the effect of curcumin on DNA methylation alterations in colorectal cancer cells.

MATERIALS AND METHODS:
To evaluate the effect of curcumin on DNA methylation, three CRC cell lines, HCT116, HT29 and RKO, were treated with curcumin. 5-aza-2′-deoxycytidine (5-aza-CdR) and trichostatin A treated cells were used as positive and negative controls for DNA methylation changes, respectively. Methylation status of LINE-1 repeat elements, DNA promoter methylation microarrays and gene expression arrays were used to assess global methylation and gene expression changes. Validation was performed using independent microarrays, quantitative bisulfite pyrosequencing, and qPCR.

RESULTS:
As expected, genome-wide methylation microarrays revealed significant DNA hypomethylation in 5-aza-CdR-treated cells (mean β-values of 0.12), however, non-significant changes in mean β-
values were observed in curcumin-treated cells. In comparison to mock-treated cells, curcumin-induced DNA methylation alterations occurred in a time-dependent manner. In contrast to the generalized, non-specific global hypomethylation observed with 5-aza-CdR, curcumin treatment resulted in methylation changes at selected, partially-methylated loci, instead of fully-methylated CpG sites. DNA methylation alterations were supported by corresponding changes in gene expression at both up- and down-regulated genes in various CRC cell lines.

CONCLUSIONS:
Our data provide previously unrecognized evidence for curcumin-mediated DNA methylation alterations as a potential mechanism of colon cancer chemoprevention. In contrast to non-specific global hypomethylation induced by 5-aza-CdR, curcumin-induced methylation changes occurred only in a subset of partially-methylated genes, which provides additional mechanistic insights into the potent chemopreventive effect of this dietary nutraceutical.

Curcumin combined with turmerones, essential oil components of turmeric, abolishes inflammation-associated mouse colon carcinogenesis.
Murakami A, Furukawa I, Miyamoto S, Tanaka T, Ohigashi H.
Source
Division of Food Science and Biotechnology, Graduate School of Agriculture, Kyoto University, Kyoto 606-8502, Japan. cancer@kais.kyoto-u.ac.jp.
Abstract
Curcumin (CUR), a yellow pigment in turmeric, has marked potential for preventing colon cancer. We recently reported that ar-turmerone (ATM) suppressed nitric oxide (NO) generation in macrophages. In the present study, we explored the molecular mechanisms by which ATM attenuates NO generation and examined the anti-carcinogenesis activity of turmerones (TUR, a mixture of 5 sesquiterpenes including ATM). Both CUR and ATM inhibited lipopolysaccharide (LPS)-induced expression of inducible forms of both nitric oxide synthase and cyclooxygenase (iNOS and COX-2, respectively). A chase experiment using actinomycin D revealed that ATM accelerated the decay of iNOS and COX-2 mRNA, suggesting a post-transcriptional mechanism. ATM prevented LPS-induced translocation of HuR, an AU-rich element-binding protein that determines mRNA stability of certain inflammatory genes. In a colitis model, oral administration of TUR significantly suppressed 2% dextran sulfate sodium (DSS)-induced shortening of the large bowel by 52-58%. We also evaluated the chemopreventive effects of oral feeding of TUR, CUR, and their combinations using a model of dimethylhydrazine-initiated and DSS-promoted mouse colon carcinogenesis. At the low dose, TUR markedly suppressed adenoma multiplicity by 73%, while CUR at both doses suppressed adenocarcinoma multiplicity by 63-69%. Interestingly, the combination of CUR and TUR at both low and high doses abolished tumor formation. Collectively, our results led to our hypothesis that TUR is a novel candidate for colon cancer prevention. Furthermore, we consider that its use in combination with CUR may become a powerful method for prevention of inflammation-associated colon carcinogenesis Cochrane Database Syst Rev. 2012 Oct 17;10:CD008424. doi: 10.1002/14651858.CD008424.pub2.
Curcumin for maintenance of remission in ulcerative colitis.
Kumar S, Ahuja V, Sankar MJ, Kumar A, Moss AC.
Source
Division of Basic and Translational Research, Department of Surgery, University of Minnesota, Minneapolis, USA.
Abstract
BACKGROUND:
Ulcerative colitis (UC) is a chronic inflammatory condition of the colon characterized by episodes of disease activity and symptom-free remission. There is paucity of evidence regarding the efficacy and safety of complementary or alternative medicines for the management of UC. Curcumin, an anti-inflammatory agent, has been used in many chronic inflammatory conditions such as
rheumatoid arthritis, esophagitis and post-surgical inflammation. The efficacy of this agent for maintenance of remission in patients with UC has not been systematically evaluated.

OBJECTIVES:
The primary objective was to systematically review the efficacy and safety of curcumin for maintenance of remission in UC.

SEARCH METHODS:
A computer-assisted literature search of MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, and the Cochrane Inflammatory Bowel Disease Specialized Trial Register was performed on July 11, 2012 to identify relevant publications. Proceedings from major gastroenterology meetings and references from published articles were also searched to identify additional studies.

SELECTION CRITERIA:
Randomized placebo-controlled trials (RCT) of curcumin for maintenance of remission in UC were included. Studies included patients (of any age) who were in remission at the time of recruitment. Co-interventions were allowed.

DATA COLLECTION AND ANALYSIS:
Two authors independently extracted data and assessed the methodological quality of the included studies using the Cochrane risk of bias tool. Data were analyzed using Review Manager (RevMan 5.1). We calculated the relative risk (RR) and 95% confidence interval (95% CI) for each dichotomous outcome. For continuous outcomes we calculated the mean difference (MD) and 95% CI.

MAIN RESULTS:
Only one trial (89 patients) fulfilled the inclusion criteria. This trial randomized 45 patients to curcumin and 44 patients to placebo. All patients received treatment with sulfasalazine or mesalamine. The study was rated as low risk of bias. Curcumin was administered orally in a dose of 2 g/day for six months. Fewer patients relapsed in the curcumin group than the placebo group at six months. Four per cent of patients in the curcumin group relapsed at six months compared to 18% of patients in the placebo group (RR 0.24, 95% CI 0.05 to 1.09; P = 0.06). There was no statistically significant difference in relapse rates at 12 months. Twenty-two per cent of curcumin patients relapsed at 12 months compared to 32% of placebo patients (RR 0.70, 95% CI 0.35 to 1.40; P = 0.31). A total of nine adverse events were reported in seven patients. These adverse events included sensation of abdominal bulging, nausea, transient hypertension, and transient increase in the number of stools. The authors did not report which treatment group the patients who experienced adverse events belonged to. The clinical activity index (CAI) at six months was significantly lower in the curcumin group compared to the placebo group (1.0 + 2.0 versus 2.2 + 2.3; MD -1.20, 95% CI -2.14 to -0.26). The endoscopic index (EI) at six months was significantly lower in the curcumin group than in the placebo group (0.8 + 0.6 versus 1.6 + 1.6; MD -0.80, 95% CI -1.33 to -0.27).

AUTHORS’ CONCLUSIONS:
Curcumin may be a safe and effective therapy for maintenance of remission in quiescent UC when given as adjunctive therapy along with mesalamine or sulfasalazine. However, further research in the form of a large scale methodologically rigorous randomized controlled trial is needed to confirm any possible benefit of curcumin in quiescent UC.

Free Radic Res. 2013 Mar 11. [Epub ahead of print]
Antioxidants and cataract.
Thiagarajan R, Manikandan R.
Source
Department of Bioengineering, School of Chemical and Biotechnology, SASTRA University, Thanjavur, India.
Abstract
The major causes for cataract formation are free radicals, and these free radicals are neutralized by the presence of endogenous antioxidants in the eye. Using xenobiotics, it has been confirmed that
free radicals mediate the formation of cataract. Two cataract model-selenite model and the diabetic cataract model-have been developed to study the pathophysiology of cataract formation due to free radicals and the role of antioxidants during the process of cataractogenesis. This review focuses on natural compounds with antioxidant properties that could actually be applied as an interventional strategy on a large scale and are also relatively inexpensive. A brief overview of plants with antioxidant properties that in addition possess potential anti-cataract properties has been discussed. In addition to plants, three natural compounds (curcumin, vitamin C and vitamin E), on which a lot of data exist showing anti-cataract and antioxidant activities, have also been discussed. These antioxidants can be supplemented in the diet for a better defence against free radicals. Studies on vitamin C and vitamin E have proved that they are capable of preventing lipid peroxidation, thereby preventing the generation of free radicals, but their efficacy as anti-cataract agent is questionable. Unlike vitamins C and E, curcumin is well established as an anti-cataract agent, but the issue of curcumin bioavailability is yet to be addressed. Nanotechnology proves to be a promising area in increasing the curcumin bioavailability, but still a lot more research needs to be done before the use of curcumin as an effective anti-cataract agent for humans.

Curcuminoids distinctly exhibit antioxidant activities and regulate expression of scavenger receptors and heme oxygenase-1.
Kou MC, Chiu SY, Weng CY, Wang L, Ho CT, Wu MJ.
Source
Department of Biotechnology, Chia Nan University of Pharmacy and Science, Tainan, Taiwan.
Abstract
SCOPE:
Curcumin (CUR), demethoxycurcumin (DMC), and bisdemethoxycurcumin (BDMC) have been demonstrated as having antioxidant, anticarcinogenic, and hypocholesterolemic activities. We report the diverse antiatherogenic effects and mechanisms of curcuminoids.
METHODS AND RESULTS:
We found that CUR was the most potent antioxidant against copper-mediated LDL oxidation as measured by thiobarbituric acid-reactive substances assay, oxidized LDL (oxLDL) ELISA, and electrophoretic mobility. CUR upregulated heme oxygenase-1, modifier subunit of glutamate-cysteine ligase (GCLM), and CD36 expression in undifferentiated THP-1 cells, supporting the possible involvement of Nrf2 pathway in CD36 expression. Monocyte-to-macrophage differentiation plays a vital role in early atherogenesis. BDMC reduced oxLDL uptake most effectively, while CUR was the best inhibitor for CD36, scavenger receptor A, and lectin-like oxidized LDL receptor-1 expression during phorbol 12-myristate 13-acetate (PMA)-induced THP-1 differentiation. In PMA-differentiated THP-1 macrophages, CUR and DMC effectively induced heme oxygenase-1 expression, but attenuated oxLDL-induced CD36 expression, leading to decreased oxLDL uptake.
CONCLUSION:
This result indicates curcuminoids, despite structural similarities, exert different atheroprotective effects. Curcuminoids, especially CUR and DMC, are hormetic compounds, which induce Phase II enzyme expression and confer resistance to PMA- and oxLDL-induced scavenger receptor expression and activity.
Synthesis and biological evaluation of asymmetric indole curcumin analogs as potential anti-inflammatory and antioxidant agents.
Bandgar BP, Kinkar SN, Chavan HV, Jalde SS, Shaikh RU, Gacche RN.
Source
Medicinal Chemistry Research Laboratory, School of Chemical Sciences, Solapur University, Solapur, India.
Abstract
Abstract A series of asymmetric indole curcumin analogs were synthesized and evaluated as possible inhibitors of pro-inflammatory enzymes such as COX-2, pro-inflammatory cytokines as TNF-α and IL-6, trypsin and β-glucuronidase. They were also tested for antioxidant activities. The results showed that compounds 5e and 5h were found to be the most potent inhibitors of COX-2 (83.33%, 82.50%) and β-glucuronidase (67.80%, 64.12%). All the synthesized compounds exhibited promising activity against IL-6 in a range of 71-100% at 10 µM concentration. Compounds 5f, 5h, 5e, 5c and 5d showed significant inhibition against TNF-α (28-51%) and IL-6 (87-98%) with low toxicity (45-51%) against CCK-8 cells. With few exceptions, all other compounds were found to be good to excellent inhibitors of IL-6 and moderate inhibitors of TNF-α; however, the toxicity profiles of these compounds need to be ameliorated in further optimization studies. Amongst the tested compounds, 5c, 5b, 5j and 5g were found to possess excellent reducing activity and 5b, 5c and 5h were moderate DPPH (1,1-diphenyl-2-picryl hydrazine) radical scavengers.


Anti-inflammatory and apoptotic effects of the polyphenol curcumin on human fibroblast-like synoviocytes.

Kloesch B, Becker T, Dietersdorfer E, Kiener H, Steiner G.

Source
Ludwig Boltzmann Cluster Rheumatology, Balneology and Rehabilitation, Ludwig Boltzmann Institute of Rheumatology and Balneology, Kurbadstrasse 14, 1100 Vienna, Austria. Electronic address: burkhard.kloesch@gmx.at.

Abstract
BACKGROUND:
It has recently been reported that the polyphenol curcumin has pronounced anti-carcinogenic, anti-inflammatory and pro-apoptotic properties. This study investigated possible anti-inflammatory and apoptotic effects of curcumin on the human synovial fibroblast cell line MH7A, and on fibroblast-like synoviocytes (FLS) derived from patients with rheumatoid arthritis (RA).

METHODS:
MH7A cells and RA-FLS were stimulated either with interleukin (IL)-1β or phorbol 12-myristate 13 acetate (PMA), and treated simultaneously or sequentially with increasing concentrations of curcumin. Release of interleukin (IL)-6 and vascular endothelial growth factor (VEGF)-A was quantified by enzyme-linked immunosorbent assays (ELISAs). In MH7A cells, modulation of the transcription factor nuclear factor kappa-B (NF-κB) and mitogen-activated protein kinases (MAPKs) such as p38 and extracellular-signal regulated kinase (ERK1/2) were analysed by a reporter gene assay and Western blot, respectively. Pro-apoptotic events were monitored by Annexin-V/7-AAD based assay. Cleavage of pro-caspase-3 and -7 was checked with specific antibodies.

RESULTS:
Curcumin effectively blocked IL-1β and PMA-induced IL-6 expression both in MH7A cells and RA-FLS. VEGF-A expression could only be detected in RA-FLS and was induced by PMA, but not by IL-1β. Furthermore, curcumin inhibited activation of NF-κB and induced dephosphorylation of ERK1/2. Treatment of FLS with high concentrations of curcumin was associated with a decrease in cell viability and induction of apoptosis.

CONCLUSION:
The natural compound curcumin represents strong anti-inflammatory properties and induces apoptosis in FLS. This study provides an insight into possible molecular mechanisms of this substance and suggests it as a natural remedy for the treatment of chronic inflammatory diseases like RA.
Proniosomal formulation of curcumin having anti-inflammatory and anti-arthritic activity in different experimental animal models.
Kumar K, Rai AK.
Source
Institute of Pharmacy NIMS University, Jaipur, Rajasthan, India. kapil5november@gmail.com
Abstract
Curcumin, the active ingredient of the spice turmeric, has a long history as an herbal remedy for a variety of diseases. Transdermal drug delivery has been recognized as an alternative route to oral delivery. Proniosomes offer a versatile vesicle delivery concept with the potential for drug delivery via the transdermal route. In this study, different proniosomal gel bases were prepared by the ether injection method, using Span 60 and Span 80, Tween 20, cholesterol, and formulation PA2. They were characterized by scanning electron microscopy, revealing vesicular structures, and assessed for stability and effect on in vitro skin permeation using rat skin. Anti-inflammatory and anti-arthritic effects of formulation PA2 and PB1 were compared with a standard market product containing indomethacin. The effect of formulation PA2 and PB1 was evaluated for acute inflammation in carrageenan induced rat paw edema and for chronic inflammation in complete Freud's adjuvant (CFA) induced arthritis in rats. Further histopathological and radiographic evaluation was performed. The investigated curcumin loaded proniosomal formula proved to be non-irritant, non-toxic, but had lower anti-inflammatory and anti-arthritic effects than the marketed indomethacin products.

Hepatoprotective effect of ethanolic extract of Curcuma longa on thioacetamide induced liver cirrhosis in rats.
Salama SM, Abdulla MA, Alrashdi AS, Ismail S, Alkiyumi SS, Golbabapour S.
Source
Department of Molecular Medicine, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia. ammeen@um.edu.my.
Abstract
BACKGROUND:
Hepatology research has focused on developing traditional therapies as pharmacological medicines to treat liver cirrhosis. Thus, this study evaluated mechanisms of the hepatoprotective activity of Curcuma longa rhizome ethanolic extract (CLRE) on thioacetamide-induced liver cirrhosis in rats.
METHODS:
The hepatoprotective effect of CLRE was measured in a rat model of thioacetamide-induced liver cirrhosis over 8 weeks. Hepatic cytochrome P450 2E1 and serum levels of TGF-β1 and TNF-α were evaluated. Oxidative stress was measured by malondialdehyde, urinary 8-hydroxyguanosine and nitrotyrosine levels. The protective activity of CLRE free-radical scavenging mechanisms were evaluated through antioxidant enzymes. Protein expression of pro-apoptotic Bax and anti-apoptotic Bcl-2 proteins in animal blood sera was studied and confirmed by immunohistochemistry of Bax, Bcl2 proteins and proliferating cell nuclear antigen.
RESULTS:
Histopathology, immunohistochemistry and liver biochemistry were significantly lower in the Curcuma longa-treated groups compared with controls. CLRE induced apoptosis, inhibited hepatocytes proliferation but had no effect on hepatic CYP2E1 levels.
CONCLUSION:
The progression of liver cirrhosis could be inhibited by the antioxidant and anti-inflammatory activities of CLRE and the normal status of the liver could be preserved.

Inhibitory effect of hexahydrocurcumin on human platelet aggregation.
Dong HP, Yang RC, Chunag IC, Huang LJ, Li HT, Chen HL, Chen CY.
Source
Department of Physical Therapy, Fooyin University, Kaohsiung, Taiwan.

Abstract
The effects of hexahydrocurcumin on adenosine diphosphate (ADP)-induced human platelet aggregation were studied. Treatment of human platelet-rich plasma with hexahydrocurcumin resulted in an inhibitory effect on platelet aggregation, suggesting the potential of this compound as an anti-atherosclerogenic agent in humans.

Inhibitory effect of curcumin, a food spice from turmeric, on platelet-activating factor- and arachidonic acid-mediated platelet aggregation through inhibition of thromboxane formation and Ca2+ signaling.
Source
Department of Physiology and Pharmacology, The Aga Khan University, Karachi, Pakistan.

Abstract
Curcumin, a dietary spice from turmeric, is known to be anti-inflammatory, anticarcinogenic, and antithrombotic. Here, we studied the mechanism of the antiplatelet action of curcumin. We show that curcumin inhibited platelet aggregation mediated by the platelet agonists epinephrine (200 microM), ADP (4 microM), platelet-activating factor (PAF; 800 nM), collagen (20 microg/mL), and arachidonic acid (AA; 0.75 mM). Curcumin preferentially inhibited PAF- and AA-induced aggregation (IC50; 25-20 microM), whereas much higher concentrations of curcumin were required to inhibit aggregation induced by other platelet agonists. Pretreatment of platelets with curcumin resulted in inhibition of platelet aggregation induced by calcium ionophore A-23187 (IC50; 100 microM), but curcumin up to 250 microM had no inhibitory effect on aggregation induced by the protein kinase C (PKC) activator phorbol myristate acetate (1 microM). Curcumin (100 microM) inhibited the A-23187-induced mobilization of intracellular Ca2+ as determined by using fura-2 acetoxymethyl ester. Curcumin also inhibited the formation of thromboxane A2 (TXA2) by platelets (IC50; 70 microM). These results suggest that the curcumin-mediated preferential inhibition of PAF- and AA-induced platelet aggregation involves inhibitory effects on TXA2 synthesis and Ca2+ signaling, but without the involvement of PKC.

Optimized turmeric extract reduces β-Amyloid and phosphorylated Tau protein burden in Alzheimer's transgenic mice.
Source
Center for Excellence in Aging and Brain Repair, Dept. of Neurosurgery, University of South Florida College of Medicine, Tampa, FL 33612, USA.

Abstract
In a previous in vitro study, the standardized turmeric extract, HSS-888, showed strong inhibition of Aβ aggregation and secretion in vitro, indicating that HSS-888 might be therapeutically important. Therefore, in the present study, HSS-888 was evaluated in vivo using transgenic 'Alzheimer' mice (Tg2576) over-expressing Aβ protein. Following a six-month prevention period where mice received extract HSS-888 (5mg/mouse/day), tetrahydrocurcumin (THC) or a control through ingestion of customized animal feed pellets (0.1% w/w treatment), HSS-888 significantly reduced brain levels of soluble (~40%) and insoluble (~20%) Aβ as well as phosphorylated Tau protein (~80%). In addition, primary cultures of microglia from these mice showed increased expression of the cytokines IL-4 and IL-2. In contrast, THC treatment only weakly reduced phosphorylated Tau
protein and failed to significantly alter plaque burden and cytokine expression. The findings reveal that the optimized turmeric extract HSS-888 represents an important step in botanical based therapies for Alzheimer's disease by inhibiting or improving plaque burden, Tau phosphorylation, and microglial inflammation leading to neuronal toxicity.


Curcumin: a new paradigm and therapeutic opportunity for the treatment of osteoarthritis: curcumin for osteoarthritis management.

**Henrotin Y, Priem F, Mobasher A.**

Source
Bone and Cartilage Research Unit, University of Liège, Institute of Pathology, Level +5, CHU Sart-Tilman, Liège, 4000 Belgium ; Physical Therapy and Rehabilitation Department, Vivalia, Princess Paola Hospital, Marche-en-Famenne, Belgium.

Abstract
The management of osteoarthritis represents a real challenge. This complex and multi-factorial disease evolves over decades and requires not only the alleviation of symptoms, i.e. pain and joint function but also the preservation of articular structure without side effects. Nutraceuticals are good candidates for the management of OA due to their safety profile and potential efficacy. However, they are not part of the treatment guidelines and published recommendations. Curcumin is the yellow pigment isolated from the rhizomes of Curcuma longa, commonly known as turmeric. Curcumin is a highly pleiotropic molecule with an excellent safety profile. Strong molecular evidence has been published for its potency to target multiple inflammatory diseases. However, naturally occurring curcumin cannot achieve its optimum therapeutic outcomes due to its low solubility and poor bioavailability. Nevertheless, curcumin presents great potential for treating OA and has been categorized as having preclinical evidence of efficacy. This review aimed at gathering most of the available information to document the potential efficacy of curcumin based on the results obtained in in vitro models of cartilage and osteoarthritis and in other diseases.


Hypocholesterolemic effects of curcumin via up-regulation of cholesterol 7a-hydroxylase in rats fed a high fat diet.

**Kim M, Kim Y.**

Source
Department of Nutritional Science and Food Management, Ewha Womans University, 11-1 Daehyn-dong, Seodaemun-gu, Seoul 120-750, Korea.

Abstract
There is an increasing interest in curcumin (Curcuma longa L.) as a cardiovascular disease (CVD) protective agent via decreased blood total cholesterol and low-density lipoprotein-cholesterol (LDL-cholesterol) level. The aim of this study was to investigate further the potential mechanism in the hypocholesterolemic effect of curcumin by measuring cholesterol 7a-hydroxylase (CYP7A1), a rate limiting enzyme in the biosynthesis of bile acid from cholesterol, at the mRNA level. Male Sprague-Dawley rats were fed a 45% high fat diet or same diet supplemented with curcumin (0.1% wt/wt) for 8 weeks. The curcumin diet significantly decreased serum triglyceride (TG) by 27%, total cholesterol (TC) by 33.8%, and LDL-cholesterol by 56%, respectively as compared to control group. The curcumin-supplemented diet also significantly lowered the atherogenic index (AI) by 48% as compared to control group. Hepatic TG level was significantly reduced by 41% in rats fed with curcumin-supplemented diet in comparison with control group (P < 0.05). Conversely, the curcumin diet significantly increased fecal TG and TC. The curcumin diet up-regulated hepatic CYP7A1 mRNA level by 2.16-fold, compared to control group p (P < 0.05). These findings suggested that the increases in the CYP7A1 gene expression may partially account for the hypocholesterolemic effect of curcumin.
Curcumin ( diferuloylmethane) is the yellow-orange pigment of dried Curcuma longa L. rhizomes (turmeric). During the past two decades, there has been a large volume of published studies describing the biological and pharmacological properties of this phytochemical including anticancer, anti-inflammatory, antioxidant, antithrombotic, antiatherosclerotic, cardioprotective, neuroprotective, memory enhancing, antiparkinsonism, antirheumatic, anti-infectious, antiaging, antipsoriatic, and anticonvulsant activities. In addition, curcumin has been shown to be extremely safe and interact with multiple molecular targets that are involved in the pathogenesis of metabolic syndrome. Curcumin could favorably affect all leading components of metabolic syndrome including insulin resistance, obesity, hypertriglyceridemia, decreased HDL-C and hypertension, and prevent the deleterious complications of MetS including diabetes and cardiovascular disease. Owing to its antioxidant and anti-inflammatory properties, curcumin can also exert several pleiotropic effects and improve endothelial dysfunction, adipokine imbalances, and hyperuricemia which usually accompany MetS. Despite the potential tremendous benefit of this multifaceted phytopharmaceutical, no trial result has yet been publicized on this issue. This review seeks to briefly summarize the ample scientific evidence that supports the therapeutic efficacy of curcumin, at least as an adjunctive treatment, in patients with MetS. © 2012 BioFactors, 2013.