J Vet Pharmacol Ther. 2011 Apr;34(2):120-9. doi: 10.1111/j.1365-2885.2010.01200.x.

Silybin inhibits interleukin-1β-induced production of pro-inflammatory mediators in canine hepatocyte cultures.

Au AY, Hasenwinkel JM, Frondoza CG.

Source

Research and Development, Nutramax Laboratories, Inc., Edgewood, MD 21040, USA.

Abstract

Hepatocytes are highly susceptible to cytokine stimulation and are fundamental to liver function. We established primary canine hepatocyte cultures to study effects of anti-inflammatory agents with hepatoprotective properties. Hepatocyte cultures were incubated with control media alone, silybin (SB), or the more bioavailable silybin-phosphatidylcholine complex (SPC), followed by activation with interleukin-1 beta (IL-1β; 10 ng/mL). Inflammatory response was measured by prostaglandin E2 (PGE(2)), interleukin-8 (IL-8), and monocyte chemotactic protein-1 (MCP-1) production and also nuclear factor-kappa B (NF-κB) translocation. Hepatocyte cultures continued production of the phenotypic marker albumin for more than 7 days in culture. IL-1β exposure increased PGE(2) , IL-8, and MCP-1 production, which was paralleled by NF-κB translocation from the cytoplasm to the nucleus. Pretreatment with SB and SPC significantly inhibited IL-1β-induced production of pro-inflammatory markers and attenuated NF-κB nuclear translocation. We demonstrate for the first time that primary canine hepatocyte cultures can be maintained in culture without phenotypic loss. The observation that hepatocyte cultures respond to pro-inflammatory IL-1β activation indicates hepatocytes as primary cellular targets of extrinsic IL-1β. The ability of SB and SPC to inhibit hepatocyte culture activation by IL-1β reinforces the notion of their hepatoprotective effects. Our primary canine hepatocyte culture model facilitates identification of hepatoprotective agents and their mechanism of action.

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21395602
[PubMed - indexed for MEDLINE]

Natl Toxicol Program Tech Rep Ser. 2011 May;(565):1-177.

Toxicology and carcinogenesis studies of milk thistle extract (CAS No. 84604-20-6) in F344/N rats and B6C3F1 mice (Feed Studies).

National Toxicology Program.

Collaborators (45)

Abstract

Milk thistle extracts have been used as medicinal herbs in the treatment of liver cirrhosis, chronic hepatitis (liver inflammation), and gallbladder disorders. Treatment claims also include lowering cholesterol levels; reducing insulin resistance; reducing the growth of cancer cells in breast, cervical, and prostate gland cancers; and antiviral activity. Other reported uses of milk thistle in folk medicine include as a treatment for malarial fever, bronchitis, gallstones, jaundice, peritonitis, uterine congestion, varicose veins, and as a milk production stimulant for nursing mothers. The roots soaked in water overnight are used in food, and the despined leaves are added to salads. Roasted milk thistle fruit has been used as a coffee substitute. Milk thistle extract was nominated for study by the National Institute of Environmental Health Sciences because it is one of the most widely used herbs in the United States. Male and female F344/N rats and B6C3F1 mice were exposed to an ethanol/water extract of milk thistle fruit (milk thistle extract) containing approximately 65% silymarin in feed for 3 months or 2 years. Genetic toxicology studies were conducted in Salmonella typhimurium and Escherichia coli and mouse peripheral blood erythrocytes. 3-MONTH STUDY IN RATS: Groups of 10 male and 10 female rats were fed diets containing 0, 3,125, 6,250, 12,500, 25,000, or 50,000 ppm milk thistle extract (equivalent to average daily doses of approximately 260, 525, 1,050, 2,180, or 4,500 mg milk thistle extract/kilogram body weight to males and 260, 510, 1,050, 2,150, or 4,550 mg/kg to females) for 14 weeks. All rats survived to the end of the study. Mean body weights of exposed groups were within 10% of those of the controls. Feed consumption by exposed and control groups was similar. The sperm motility in 12,500, 25,000, and 50,000 ppm males was decreased by 5%, 11%, and 9%, respectively, relative to that of the controls; the total number of spermatid heads per testis decreased by 11%, 21%, and 9% in 12,500, 25,000, and 50,000 ppm males. No significant differences in estrous cyclicity were observed between exposed and control groups of female rats. No exposure-related histopathologic lesions were observed. 3-MONTH STUDY IN MICE: Groups of 10 male and 10 female mice were fed diets containing 0, 3,125, 6,250, 12,500, 25,000, or 50,000 ppm milk thistle extract (equivalent to average daily doses of approximately 640, 1,340, 2,500, 5,280, or 11,620 mg/kg to males and 580, 1,180, 2,335, 4,800, or 9,680 mg/kg to females) for 14 weeks. All mice survived to the end of the study. Mean body weights and feed consumption of all exposed groups were similar to those of the controls. Absolute and relative thymus weights were significantly decreased in 25,000 and 50,000 ppm males. No significant differences were observed between exposed and control groups, for sperm parameters of male mice, for estrous cyclicity of female mice, or for reproductive organ weights of male or female mice, when mice were administered

milk thistle extract in feed at 12,500, 25,000, or 50,000 ppm. No exposure-related histopathologic lesions were observed. 2-YEAR STUDY IN RATS: Groups of 50 male and 50 female rats were fed diets containing 0, 12,500, 25,000, or 50,000 ppm milk thistle extract (equivalent to average daily doses of approximately 570, 1,180, or 2,520 mg/kg to males and 630, 1,300, or 2,750 mg/kg to females) for 105 to 106 weeks. Exposure to milk thistle extract had no effect on survival of male or female rats. Mean body weights of all exposed groups were similar to those of the controls throughout the study. Feed consumption by exposed groups of males and females was generally similar to that by the controls throughout the study. Significantly decreased incidences of mammary gland fibroadenoma, adenoma, or carcinoma (combined) occurred in females exposed to 25,000 or 50,000 ppm. Significantly increased incidences of clear cell and mixed cell focus of the liver occurred in 25,000 and 50,000 ppm females. The incidences of bile duct hyperplasia were significantly decreased in 50,000 ppm males and in all exposed groups of females, and the incidence of mixed inflammatory cell infiltration was significantly decreased in 50,000 ppm males. 2-YEAR STUDY IN MICE: Groups of 50 male and 50 female mice were fed diets containing 0, 12,500, 25,000, or 50,000 ppm milk thistle extract (equivalent to average daily doses of approximately 1,610, 3,530, or 7,770 mg/kg to males and 1,500, 3,175, or 7,180 mg/kg to females) for 105 to 106 weeks. Exposure to milk thistle extract had no effect on survival of male or female mice. The mean body weights of the 25,000 ppm groups were less than those of controls after week 25; mean body weights of 50,000 ppm groups were less than those of controls after week 12. Feed consumption by exposed groups of males and females was generally similar to that by the controls throughout the study. Significantly decreased incidences of hepatocellular adenoma and hepatocellular carcinoma occurred in 50,000 ppm males, and decreased incidences of hepatocellular adenoma or carcinoma (combined) occurred in 25,000 and 50,000 ppm males. GENETIC TOXICOLOGY: Five milk thistle extracts were tested independently in bacterial mutagenicity studies using a variety of S. typhimurium tester strains and one E. coli strain. Results were negative in three of the five studies, with and without exogenous metabolic activation. In two studies, milk thistle extract was mutagenic in S. typhimurium strain TA98 in the presence of exogenous metabolic activation enzymes. Silymarin, a major constituent of milk thistle extract, was positive in S. typhimurium strains TA98 and TA100, when testing occurred in the presence of exogenous metabolic activation enzymes. Silybin, another component of milk thistle extract, was negative in a S. typhimurium gene mutation assay, with and without liver S9 activation enzymes. Administration of milk thistle extract in feed for 3 months did not increase the frequencies of micronucleated normochromatic erythrocytes, an indication of chromosomal abnormalities, in the peripheral blood of male or female B6C3F1 mice. CONCLUSIONS: Under the conditions of these 2-year feed studies, there was no evidence of carcinogenic activity of milk thistle extract in male or female F344/N rats or B6C3F1 mice exposed to 12,500, 25,000, or 50,000 ppm. Exposure to milk thistle extract resulted in increased incidences of clear cell and mixed cell foci in the liver of female rats and decreases in body weights of exposed groups of male and female mice. Decreased incidences of mammary gland neoplasms occurred in exposed groups of female rats, and decreased incidences of hepatocellular neoplasms occurred in exposed groups of male mice.

PMID:
21685957

KATT
Am J Vet Res. 2009 Jan;70(1):57-62.

Assessment of oxidative stress in leukocytes and granulocyte function following oral administration of a silibinin-phosphatidylcholine complex in cats.

Webb CB, McCord KW, Twedt DC.

Source

Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO 80523, USA.

Abstract

OBJECTIVE:

To determine the effect of oral administration of a silibinin-phosphatidylcholine complex (SPC) on oxidative stress in leukocytes and granulocyte function in healthy cats.

ANIMALS:

10 purpose-bred adult cats.

PROCEDURES:

Cats were administered SPC (10 mg/kg/d) orally for 5 days; blood samples were collected prior to and immediately after the 5-day treatment period. Leukocytes were incubated with monochlorobimane for detection of reduced glutathione (GSH) via flow cytometry. Leukocytes were also incubated with dihydrorhodamine 123 and mixed with Escherichia coli conjugated to a fluorescent marker to measure E coli phagocytosis and the subsequent oxidative burst via flow cytometry. Activities of the antioxidant enzymes superoxide dismutase and glutathione peroxidase, along with the reduced glutathione-to-oxidized glutathione (GSH:GSSG) ratio and a measure of lipid peroxidation (malondialdehyde concentration [micromol/L of blood]), were measured spectrophotometrically.

RESULTS:

The mean fluorescence intensity (MFI), representing GSH content, increased significantly in feline lymphocytes and granulocytes following 5 days of oral administration of SPC. Mean +/- SD lymphocyte MFI significantly increased from 27.8 +/- 9.0 to 39.6 +/- 6.7, and the granulocyte MFI increased from 508.6 +/- 135.6 to 612.1 +/- 122.9. Following 5 days of SPC administration, the percentage of phagocytic cells that were responding optimally significantly increased (from 37 +/- 11.8% to 45 +/- 17.5%). Other measures of oxidative stress did not change significantly.

CONCLUSIONS AND CLINICAL RELEVANCE:

In cats, oral administration of supplemental SPC appears to increase granulocyte GSH content and phagocytic function, both of which would be potentially beneficial in cats with diseases associated with oxidative stress.

PMID:
19119949 [PubMed - indexed for MEDLINE]

J Anim Physiol Anim Nutr (Berl). 2012 Feb 9. doi: 10.1111/j.1439-0396.2012.01275.x. [Epub ahead of print]

Hepatoprotective effects of S-adenosylmethionine and silybin on canine hepatocytes in vitro.

Au AY, Hasenwinkel JM, Frondoza CG.

Source

Research and Development, Nutramax Laboratories, Inc., Edgewood, MD, USA Department of Biomedical and Chemical Engineering, Syracuse University, Syracuse, NY, USA Department of Orthopaedic Surgery, Johns Hopkins University, Baltimore, MD, USA College of Veterinary Medicine, Mississippi State University, Mississippi State, MS, USA.

Abstract

Inflammation and oxidative stress are associated with liver injury and development of liver disease. The transcription factors nuclear factor-kappa beta (NF-κB) and nuclear factor erythroid 2-related factor 2 (Nrf2) play critical roles in modulating liver injury and damage. Activation of NF-κB induces production of pro-inflammatory molecules including prostaglandin E2 (PGE(2)), interleukin-8 (IL-8) and macrophage chemotactic protein-1 (MCP-1). Nrf2 regulates genes controlling antioxidants. Our laboratory previously showed that hepatocytes, the primary functional cell type comprising liver tissue, respond to the cytokine interleukin-1 beta (IL-1β) by increased production of PGE(2) , IL-8 and MCP-1. This increase is associated with nuclear translocation of NF-κB. In this study, we evaluated whether primary canine hepatocytes pre-treated with the combination of S-adenosylmethionine (SAMe; 30 and 2000 ng/ml) and silybin (SB; 298 ng/ml), agents with known anti-inflammatory and antioxidant properties, could attenuate IL-1β-induced inflammation and oxidative stress. The SAMe and SB combination reduced cytokine-induced PGE(2) , IL-8 and MCP-1 production while also inhibiting NF-κB nuclear translocation. These changes were accompanied by increased antioxidant enzyme-reduced glutathione (GSH) comparable to control levels. The study shows for the first time that the SAMe and SB combination inhibits both inflammation and oxidative stress through two separate signalling pathways.

J Vet Pharmacol Ther. 2007 Apr;30(2):132-8.

Bioavailability of a silybin-phosphatidylcholine complex in dogs.

Filburn CR, Kettenacker R, Griffin DW.

Source

Veterinary Science Division, Nutramax Laboratories, Inc., Edgewood, MD 21040, USA.

Abstract

Liver dysfunction often is associated with an imbalance in the production and removal of free radicals derived from oxygen and nitrogen and has been managed clinically with antioxidant supplements, including silymarin extract derived from milk thistle. The potential for enhanced bioavailability of a phytosome complex containing phosphatidylcholine and silybin, the primary active flavonolignan in silymarin extract, was tested in dogs. A group of eight beagles (four males, four females) were dosed orally with a silybin-phosphatidylcholine complex (SPC) and a commercially available standardized silymarin extract containing equivalent levels of silybin. Dosing with the SPC resulted in Cmax, Tmax, and AUC0-24 h values (mean+/-SD) for total silybin of 1310+/-880 ng/mL, 2.87+/-2.23 h, and 11,200+/-6520 ng.h/mL, respectively; corresponding values for a standardized silymarin extract were 472+/-383 ng/mL, 4.75+/-2.82 h, and 3720+/-4970 ng.h/mL. A second, separate group of beagles were also dosed with the extract alone, yielding values of 449+/-402 ng/mL, 6.87+/-7.43 h, and 2520+/-2976 ng.h/mL. These data show that a phytosome complex of phosphatidylcholine and silybin markedly enhances bioavailability in dogs.

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17348898
[PubMed - indexed for MEDLINE]

US National Library of Medicine National Institutes of Health
Indian J Med Res. 2006 Nov;124(5):491-504.

Hepatoprotective herbal drug, silymarin from experimental pharmacology to clinical medicine.

Pradhan SC, Girish C.

Source

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Abstract

Silymarin, a flavonolignan from 'milk thistle' (Silybum marianum) plant is used almost exclusively for hepatoprotection and amounts to 180 million US dollars business in Germany alone. In this review we discuss about its safety, efficacy and future uses in liver diseases. The use of silymarin may replace the polyherbal formulations and will avoid the major problems of standardization, quality control and contamination with heavy metals or bacterial toxins. Silymarin consists of four flavonolignan isomers namely--silybin, isosilybin, silydianin and silychristin. Among them, silybin being the most active and commonly used. Silymarin is orally absorbed and is excreted mainly through bile as sulphates and conjugates. Silymarin offers good protection in various toxic models of experimental liver diseases in laboratory animals. It acts by antioxidative, anti-lipid peroxidative, antifibrotic, anti-inflammatory, membrane stabilizing, immunomodulatory and liver regenerating mechanisms. Silymarin has clinical applications in alcoholic liver diseases, liver cirrhosis, Amanita mushroom poisoning, viral hepatitis, toxic and drug induced liver diseases and in diabetic patients. Though silymarin does not have antiviral properties against hepatitis virus, it promotes protein synthesis, helps in regenerating liver tissue, controls inflammation, enhances glucuronidation and protects against glutathione depletion. Silymarin may prove to be a useful drug for hepatoprotection in hepatobiliary diseases and in hepatotoxicity due to drugs. The non traditional use of silymarin may make a breakthrough as a new approach to protect other organs in addition to liver. As it is having a good safety profile, better patient tolerability and an effective drug at an affordable price, in near future new derivatives or new combinations of this drug may prove to be useful.

Food Chem Toxicol. 2010 Jun;48(6):1632-7. Epub 2010 Mar 27.

In vitro and in vivo hepatoprotective effects of the aqueous extract from Taraxacum officinale (dandelion) root against alcohol-induced oxidative stress.

You Y, Yoo S, Yoon HG, Park J, Lee YH, Kim S, Oh KT, Lee J, Cho HY, Jun W.

Source

Department of Food and Nutrition, Chonnam National University, Gwangju, Republic of Korea.

Abstract

The protective effects of Taraxacum officinale (dandelion) root against alcoholic liver damage were investigated in HepG2/2E1 cells and ICR mice. When an increase in the production of reactive oxygen species was induced by 300 mM ethanol in vitro, cell viability was drastically decreased by 39%. However, in the presence of hot water extract (TOH) from T. officinale root, no hepatocytic damage was observed in the cells treated with ethanol, while ethanol-extract (TOE) did not show potent hepatoprotective activity. Mice, which received TOH (1 g/kg bw/day) with ethanol revealed complete prevention of alcohol-induced hepatotoxicity as evidenced by the significant reductions of serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and lactate dehydrogenase activities compared to ethanol-alone administered mice. When compared to the ethanol-alone treated group, the mice receiving ethanol plus TOH exhibited significant increases in hepatic antioxidant activities, including catalase, glutathione-S-transferase, glutathione peroxidase, glutathione reductase, and glutathione. Furthermore, the amelioration of malondialdehyde levels indicated TOH's protective effects against liver damage mediated by alcohol in vivo. These results suggest that the aqueous extract of T. officinale root has protective action against alcohol-induced toxicity in the liver by elevating antioxidative potentials and decreasing lipid peroxidation.

Acta Biol Hung. 2010 Jun;61(2):175-90.

Hepatocurative potential of sesquiterpene lactones of Taraxacum officinale on carbon tetrachloride induced liver toxicity in mice.

Mahesh A, Jeyachandran R, Cindrella L, Thangadurai D, Veerapur VP, Muralidhara Rao D.

Source

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Abstract

The hepatocurative potential of ethanolic extract (ETO) and sesquiterpene lactones enriched fraction (SL) of Taraxacum officinale roots was evaluated against carbon tetrachloride (CCl 4) induced hepatotoxicity in mice. The diagnostic markers such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin contents were significantly elevated, whereas significant reduction in the level of reduced glutathione (GSH) and enhanced hepatic lipid peroxidation, liver weight and liver protein were observed in CCl 4 induced hepatotoxicity in mice. Post-treatment with ETO and SL significantly protected the hepatotoxicity as evident from the lower levels of hepatic enzyme markers, such as serum transaminase (ALT, AST), ALP and total bilirubin. Further, significant reduction in the liver weight and liver protein in drug-treated hepatotoxic mice and also reduced oxidative stress by increasing reduced glutathione content and decreasing lipid peroxidation level has been noticed. The histopathological evaluation of the liver also revealed that ETO and SL reduced the incidence of liver lesions induced by CCl 4 . The results indicate that sesquiterpene lactones have a protective effect against acute hepatotoxicity induced by the administration of CCl 4 in mice. Furthermore, observed activity of SL may be due to the synergistic action of two sesquiterpene lactones identified from enriched ethyl acetate fraction by HPLC method.

Food Chem Toxicol. 2010 May;48(5):1255-61. Epub 2010 Feb 17.

TOP1 and 2, polysaccharides from Taraxacum officinale, attenuate CCl(4)-induced hepatic damage through the modulation of NF-kappaB and its regulatory mediators.

Park CM, Youn HJ, Chang HK, Song YS.

Source

Department of Smart Foods and Drugs, Biohealth Products Research Center, Inje University, Obang-dong 607, Gimhae, Gyeongnam, Republic of Korea.

Abstract

In this work, we estimate the inhibitory effect of two polysaccharides from Taraxacum officinale (TOP) on CCl(4)-induced oxidative stress and inflammation in Sprague-Dawley rats. TOP1 and 2 (304, 92 mg/kg bw) were administered for 7 days via a stomach sonde, and hepatitis was induced by a single dose of CCl(4) (50% CCl(4)/olive oil; 0.5 mL/kg bw) administration. CCl(4) significantly elevated serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities. Histopathological observation further revealed that CCl(4)-induced moderate levels of inflammatory cell infiltration, centrilobular fatty change, apoptosis, and necrosis. However, TOPs pretreatment markedly decreased AST and ALT activities as well as hepatic lesions. TOPs also increased free radical scavenging activity, as exhibited by a lowered TBARS concentration. TOPs pretreatment also reversed other hepatitis-associated symptoms, including GSH depletion, inhibited anti-oxidative enzyme activities, up-regulation of NF-kappaB and increased expression of its regulatory inflammatory mediators, such as inducible nitric oxide synthase (iNOS), cyclooxygenase (COX)-2, tumor necrosis factor (TNF)-alpha, and interleukin (IL)-1beta. These results suggest that TOPs have a hepatoprotective effect by modulating inflammatory responses and ameliorating oxidative stress.

PMID:
20170702
[PubMed - indexed for MEDLINE]

J Ethnopharmacol. 2011 Jan 27;133(2):834-42. doi: 10.1016/j.jep.2010.11.015. Epub 2010 Nov 11.

Taraxacum officinale Weber extracts inhibit LPS-induced oxidative stress and nitric oxide production via the NF-κB modulation in RAW 264.7 cells.

Park CM, Park JY, Noh KH, Shin JH, Song YS.

Source

Department of Smart Foods and Drugs, Inje University, Obang-dong 607, Gimhae, Gyeongnam 621-749, Republic of Korea.

Abstract

ETHNOPHARMACOLOGICAL RELEVANCE:

The common dandelion (Taraxacum officinale G.H. Weber ex Wiggers, Asteraceae) has been widely used in folklore medicine to treat dyspepsia, heartburn, and spleen and liver disorders.

AIM OF THE STUDY:

To compare the antioxidative and anti-inflammatory activities of Taraxacum officinale methanol extract (TOME) and water extract (TOWE) in lipopolysaccharide (LPS)-stimulated RAW 264.7 cells and assess their constitutional differences, including luteolin, chicoric acid, and total phenol content.

MATERIALS AND METHODS:

Antioxidative enzyme activities, nitric oxide (NO) production, and inducible NO synthase (iNOS) and nuclear factor (NF)-κB expression were estimated by biochemical analysis, the Griess reaction, reverse transcription-polymerase chain reaction, western hybridization, and electrophoretic mobility shift assay. High-performance liquid chromatography and the Folin-Ciocalteau method were used to analyze functional phytochemicals and total phenol content.

RESULTS:

TOME and TOWE significantly reduced NO production with an IC(50) of 79.9 and 157.5 μg/mL, respectively, without cytotoxicity. Depleted glutathione (GSH) and antioxidative enzyme activities, including superoxide dismutase, catalase, GSH-peroxidase, and GSH-reductase, were restored by dandelion extracts. Both extracts inhibited LPS-stimulated iNOS gene expression and that of its transcription factor, NF-κB, in parallel with nitrite reduction. TOME showed more potent antioxidative and anti-inflammatory capacities than TOWE, which was attributable to its high total phenol, luteolin, and chicoric acid content.

CONCLUSIONS:

These results indicate that TOME and TOWE inhibit oxidative stress and inflammatory responses through elevated de novo synthesis of antioxidative enzymes and suppression of iNOS expression by NF-κB inactivation.

Antioxidant properties of Taraxacum officinale leaf extract are involved in the protective effect against hepatoxicity induced by acetaminophen in mice.

Colle D, Arantes LP, Gubert P, da Luz SC, Athayde ML, Teixeira Rocha JB, Soares FA.

Source

Department of Chemistry, Natural and Exact Sciences Center, Federal University of Santa Maria, Santa Maria, Rio Grande do Sul, Brazil.

Abstract

Acetaminophen (APAP) hepatotoxicity has been related to several cases of hepatitis, cirrhosis, and hepatic transplant. As APAP hepatotoxicity is related to reactive oxygen species (ROS) formation and excessive oxidative stress, natural antioxidant compounds have been tested as an alternative therapy to diminish the hepatic dysfunction induced by APAP. Taraxacum officinale Weber (Family Asteraceae), commonly known as dandelion, is used for medicinal purposes because of its choleretic, diuretic, antioxidant, anti-inflammatory, and hepatoprotective properties. This study evaluated the hepatoprotective activity of T. officinale leaf extract against APAP-induced hepatotoxicity. T. officinale was able to decrease thiobarbituric acid-reactive substance levels induced by 200 mg/kg APAP (p.o.), as well as prevent the decrease in sulfhydryl levels caused by APAP treatment. Furthermore, histopathological alterations, as well as the increased levels of serum aspartate and alanine aminotransferases caused by APAP, were prevented by T. officinale (0.1 and 0.5 mg/mL). In addition, T. officinale extract also demonstrated antioxidant activity in vitro, as well as scavenger activity against 2,2-diphenyl-1-picrylhydrazyl and nitric oxide radicals. Our results clearly demonstrate the hepatoprotective effect of T. officinale against the toxicity induced by APAP. The possible mechanisms involved include its scavenger activities against ROS and reactive nitrogen species, which are attributed to the content of phenolic compounds in the extract.

J Ethnopharmacol. 2006 Oct 11;107(3):313-23. Epub 2006 Jul 22.

Taraxacum--a review on its phytochemical and pharmacological profile.

Schütz K, Carle R, Schieber A.

Source

Institute of Food Technology, Section Plant Foodstuff Technology, Hohenheim University, August-von-Hartmann-Strasse 3, D-70599 Stuttgart, Germany.

Abstract

The genus Taraxacum is a member of the family Asteraceae, subfamily Cichorioideae, tribe Lactuceae and widely distributed in the warmer temperate zones of the Northern Hemisphere. The perennial weed has been known since ancient times for its curative properties and has been utilized for the treatment of various ailments such as dyspepsia, heartburn, spleen and liver complaints, hepatitis and anorexia. However, its use has mainly been based on empirical findings. This contribution provides a comprehensive review of the pharmacologically relevant compounds of Taraxacum characterized so far and of the studies supporting its use as a medicinal plant. Particular attention has been given to diuretic, choleretic, anti-inflammatory, anti-oxidative, anti-carcinogenic, analgesic, anti-hyperglycemic, anti-coagulatory and prebiotic effects. Finally, research needs such as quantification of individual Taraxacum constituents and assessment of their pharmacological activities in humans have briefly been outlined.

PMID:

16950583

[PubMed - indexed for MEDLINE]

Nutr Rev. 2012 Sep;70(9):534-47. doi: 10.1111/j.1753-4887.2012.00509.x. Epub 2012 Aug 17.

Diverse biological activities of dandelion.

González-Castejón M, Visioli F, Rodriguez-Casado A.

Source

IMDEA Food Institute, CLAID-PCM Building c/Faraday 7, Campus de Cantoblanco, Madrid, Spain.

Abstract

Dandelion (Taraxacum officinale Weber) is a member of the Asteraceae (Compositae) family, native to Europe but widely distributed in the warmer temperate zones of the Northern Hemisphere. Dandelion and its parts are habitually consumed as plant foods in several areas of the world, where they are also employed in phytotherapy. Indeed, dandelion contains a wide array of phytochemicals whose biological activities are actively being explored in various areas of human health. In particular, emerging evidence suggests that dandelion and its constituents have antioxidant and anti-inflammatory activities that result in diverse biological effects. The present review provides a comprehensive analysis of the constituents of dandelion, an assessment of the pharmacological properties of dandelion, and a description of relevant studies that support the use of dandelion as a medicinal plant.

Phytother Res. 2010 Sep;24(9):1347-53. doi: 10.1002/ptr.3121.

Amelioration of oxidative stress by dandelion extract through CYP2E1 suppression against acute liver injury induced by carbon tetrachloride in Sprague-Dawley rats.

Park CM, Cha YS, Youn HJ, Cho CW, Song YS.

Source

Department of Smart Foods and Drugs, Food Sciences Institute, Biohealth Products Research Center, Inje University, Gimhae, Gyeongnam, 621-749, Korea.

Abstract

The protective effects of common dandelion leaf water extract (DLWE) were investigated by carbon tetrachloride (CCl4) induced hepatitis in Sprague-Dawley rats. The animals were divided into five groups: normal control, DLWE control, CCl4 control, and two DLWE groups (0.5 and 2 g/kg bw). After 1 week of administering corresponding vehicle or DLWE, a single dose of CCl4 (50% CCl4/olive oil; 0.5 mL/kg bw) was administered 24 h before killing in order to produce acute liver injury. The

DLWE treatment significantly decreased CCl4-induced hepatic enzyme activities (AST, ALT and LDH) in a dose dependent manner. Also, the obstructed release of TG and cholesterol into the serum was repaired by DLWE administration. Hepatic lipid peroxidation was elevated while the GSH content and antioxidative enzyme activities were reduced in the liver as a result of CCl4 administration, which were counteracted by DLWE administration. Furthermore, the hepatocytotoxic effects of CCl4 were confirmed by significantly elevated Fas and TNF-α mRNA expression levels, but DLWE down-regulated these expressions to the levels of the normal control. Highly up-regulated cytochrome P450 2E1 was also lowered significantly in the DLWE groups. These results indicate that DLWE has a protective effect against CCl4-induced hepatic damage with at least part of its effect being attributable to the attenuation of oxidative stress and inflammatory processes resulting from cytochrome P450 activation by CCl4.

J Ethnopharmacol. 2010 Aug 9;130(3):569-77. doi: 10.1016/j.jep.2010.05.046. Epub 2010 Jun 2.

Antifibrotic activity of Taraxacum officinale root in carbon tetrachloride-induced liver damage in mice.

Domitrović R, Jakovac H, Romić Z, Rahelić D, Tadić Z.

Source

Department of Chemistry and Biochemistry, School of Medicine, University of Rijeka, Rijeka, Croatia. robertd@medri.hr

Abstract

AIM OF THE STUDY:

Dandelion (Taraxacum officinale) has been traditionally used in the treatment of various liver disorders. The present study was aimed to assess the efficacy of dandelion root water-ethanol extract (DWE) in carbon tetrachloride (CCl(4))-induced hepatic fibrosis.

MATERIALS AND METHODS:

The mice were treated with CCl(4) dissolved in olive oil (20%, v/v, 2 ml/kg) intraperitoneally (i.p.), twice a week for 4 weeks. DWE was administered i.p. once daily for next 10 days, in doses of 200 and 600 mg/kg of body weight. The degree of hepatic fibrosis was determined by hydroxyproline content and Mallory trichrome staining. Oxidative stress was determined by measuring hepatic superoxide dismutase (Cu/Zn SOD) activity. The expression and specific tissue distribution of glial fibrillary acidic protein (GFAP), alpha-smooth muscle actin (alpha-SMA), and metallothionein (MT) I/II in the liver were determined by immunohistochemistry.

RESULTS:

Hepatic Cu/Zn SOD activity has been decreased in intoxicated mice and normalized in DWE treated groups. MT I/II immunopositivity was strongly reduced in the CCl(4) group. DWE treatment successfully decreased hepatic fibrinous deposits, restored histological architecture, and modulate the expression of GFAP and alpha-SMA. Concomitantly, MT I/II expression increased in the DWE treated groups.

CONCLUSIONS:

Our results suggest the therapeutic effect of DWE on CCl(4)-induced liver fibrosis by the inactivation of hepatic stellate cells and the enhancement of hepatic regenerative capabilities. The present results provide scientific evidence to substantiate the traditional use of Taraxacum officinale root in hepatic disorders.

PMID:

20561925

[PubMed - indexed for MEDLINE]

JPEN J Parenter Enteral Nutr. 2006 Jan-Feb;30(1):45-51.

Curcumin, an atoxic antioxidant and natural NFkappaB, cyclooxygenase-2, lipooxygenase, and inducible nitric oxide synthase inhibitor: a shield against acute and chronic diseases.

Bengmark S.

Source

Institute of Hepatology, University College, London Medical School, London, United Kingdom. s.bengmark@ucl.ac.uk

Abstract

BACKGROUND:

The world suffers a tsunami of chronic diseases, and a typhoon of acute illnesses, many of which are associated with the inappropriate or exaggerated activation of genes involved in inflammation. Finding therapeutic agents which can modulate the inflammatory reaction is the highest priority in medical research today. Drugs developed by the pharmaceutical industry have thus far been associated with toxicity and side effects, which is why natural substances are of increasing interest.

METHODS:

A literature search (PubMed) showed almost 1500 papers dealing with curcumin, most from recent years. All available abstracts were read. Approximately 300 full papers were reviewed.

RESULTS:

Curcumin, a component of turmeric, has been shown to be non-toxic, to have antioxidant activity, and to inhibit such mediators of inflammation as NFkappaB, cyclooxygenase-2 (COX-2), lipooxygenase (LOX), and inducible nitric oxide synthase (iNOS). Significant preventive and/or curative effects have been observed in experimental animal models of a number of diseases, including arteriosclerosis, cancer, diabetes, respiratory, hepatic, pancreatic, intestinal and gastric diseases, neurodegenerative and eye diseases.

CONCLUSIONS:

Turmeric, an approved food additive, or its component curcumin, has shown surprisingly beneficial effects in experimental studies of acute and chronic diseases characterized by an exaggerated inflammatory reaction. There is ample evidence to support its clinical use, both as a prevention and a treatment. Several natural substances have greater antioxidant effects than conventional vitamins, including various polyphenols, flavonoids and curcumenoids. Natural substances are worth further exploration both experimentally and clinically.

J Gastroenterol Hepatol. 2006 Feb;21(2):358-66.

Curcumin ameliorates acute thioacetamide-induced hepatotoxicity.

Shapiro H, Ashkenazi M, Weizman N, Shahmurov M, Aeed H, Bruck R.

Source

The Unit of Clinical Hypnosis, The E. Wolfson Medical Center, Holon and Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel.

Abstract

BACKGROUND AND AIM:

Increased production of reactive oxygen species and nitric oxide and activation of nuclear factor kappa B are implicated in the pathogenesis of various liver diseases, including fulminant hepatic failure. Curcumin is a naturally occurring anti-oxidant that reduces oxidative stress and inhibits nuclear factor kappa B and nitric oxide

formation. The aim of the present study is to assess curcumin's therapeutic potential in acute thioacetamide hepatotoxicity, a rat model of fulminant hepatic failure.

METHODS:

Fulminant hepatic failure was induced by two intraperitoneal (i.p.) injections of 300 mg/kg thioacetamide (TAA) at 24-h intervals. The experimental groups received a low-dose (200 mg/kg per day, i.p.) or a high-dose (400 mg/kg per day) of curcumin, initiated 48 h prior to the first TAA injection. A fourth group was administered neither TAA nor curcumin and served as a control.

RESULTS:

The survival rate was higher in both curcumin-treated groups compared to the TAA only treated group. Biochemical parameters of liver injury, blood ammonia and hepatic necroinflammation were lower in the low-dose curcumin group compared to TAA controls, and were further reduced in the high-dose group ($P < 0.05$ and $P < 0.01$, respectively). Curcumin treatment also reduced the TAA-induced elevated hepatic levels of thiobarbituric acid-reactive substances (TBARS), and inhibited the nuclear binding of nuclear factor kappa B (NFkappaB) and inducible nitric oxide (iNOS) protein expression.

CONCLUSIONS:

Curcumin improved survival and minimized oxidative stress, hepatocellular injury and hepatic necroinflammation, NFkappaB binding and iNOS expression in a rat model of FHF. These findings support the role of ROS, NFkappaB and iNOS in mediating liver insult due to TAA, and that of curcumin as a hepato-protectant.

Liver Int. 2009 Nov;29(10):1457-66. doi: 10.1111/j.1478-3231.2009.02086.x.

Pharmacological actions of curcumin in liver diseases or damage.

Rivera-Espinoza Y, Muriel P.

Source

Departamento de Graduados e Investigación en Alimentos, Escuela Nacional de Ciencias Biológicas, Instituto Politécnico Nacional, Carpio y Plan de Ayala, México City, México.

Abstract

Since 1900 bc, several therapeutic activities have been attributed to the rhizomes of the plant Curcuma longa for a variety of diseases, including liver disorders. Curcumin, the main active compound obtained from this plant, was first isolated two centuries ago and its structure as diferuloylmethane was determined in 1910. Curcumin has shown anti-inflammatory, anti-oxidant, antifungal, antibacterial and anticancer activities. The pharmacological properties of curcumin were reviewed recently and focused mainly on its anticancer properties. However, its beneficial activity on liver diseases (known centuries ago, and demonstrated recently utilizing animal models) has not being reviewed in depth until now. The curcumin ability to inhibit several factors like nuclear factor-kappaB, which modulates several pro-inflammatory and profibrotic cytokines as well as its anti-oxidant properties, provide a rational molecular basis to use it in hepatic disorders. Curcumin attenuates liver injury induced by ethanol, thioacetamide, iron overdose, cholestasis and acute, subchronic and chronic carbon tetrachloride (CCl(4)) intoxication; moreover, it reverses CCl(4) cirrhosis to some extent.

Biochim Biophys Acta. 2007 Jun;1770(6):989-96. Epub 2007 Feb 22.

Curcumin protects against acute liver damage in the rat by inhibiting NF-kappaB, proinflammatory cytokines production and oxidative stress.

Reyes-Gordillo K, Segovia J, Shibayama M, Vergara P, Moreno MG, Muriel P.

Source

Sección Externa de Farmacología, Cinvestav-IPN., Apdo. Postal 14-740. México 07000, D.F. Mexico.

Abstract

Curcumin, an anti-inflammatory and antioxidant compound, was evaluated for its ability to suppress acute carbon tetrachloride-induced liver damage. Acute hepatotoxicity was induced by oral administration of CCl4 (4 g/kg, p.o.). Curcumin treatment (200 mg/kg, p.o.) was given before and 2 h after CCl4 administration. Indicators of necrosis (alanine aminotransferase) and cholestasis (gamma-glutamyl transpeptidase and bilirubins) resulted in significant increases after CCl4 intoxication, but these effects were prevented by curcumin treatment. As an indicator of oxidative stress, GSH was oxidized and the GSH/GSSG ratio decreased significantly by CCl4, but was preserved within normal values by curcumin. In addition to its antioxidants properties, curcumin is capable of preventing NF-kappaB activation and therefore to prevent the secretion of proinflammatory cytokines. Therefore, in this study we determined the concentrations of tumor necrosis factor-alpha (TNF-alpha), interleukin-1beta (IL-1beta), and interleukin-6 (IL-6) mRNA, and NF-kappaB activation. CCl4-administered rats depicted significant increases in TNF-alpha, IL-1beta, and IL-6 production, while curcumin remarkably suppressed these mediators of inflammation in liver damage. These results were confirmed by measuring TNF-alpha, and IL-1beta protein production using Western Blot analysis. Accordingly,

these proteins were increased by CCl4 and this effect was abolished by curcumin. Administration of CCl4 induced the translocation of NF-kappaB to the nucleus; CCl4 induced NF-kappaB DNA binding activity was blocked by curcumin treatment. These findings suggest that curcumin prevents acute liver damage by at least two mechanisms: acting as an antioxidant and by inhibiting NF-kappaB activation and thus production of proinflammatory cytokines.

Fundam Clin Pharmacol. 2008 Aug;22(4):417-27. doi: 10.1111/j.1472-8206.2008.00611.x.

Curcumin prevents and reverses cirrhosis induced by bile duct obstruction or CCl4 in rats: role of TGF-beta modulation and oxidative stress.

Reyes-Gordillo K, Segovia J, Shibayama M, Tsutsumi V, Vergara P, Moreno MG, Muriel P.

Source

Sección Externa de Farmacología, Cinvestav-IPN., Apdo. Postal 14-740, México 07000, D.F. México.

Abstract

Curcumin is a phytophenolic compound, which is highly efficacious for treating several inflammatory diseases. The aim of this study was to evaluate the efficacy of curcumin in preventing or reversing liver cirrhosis. A 4-week bile duct ligation (BDL) rat model was used to test the ability of curcumin (100 mg/kg, p.o., daily) to prevent cirrhosis. To reverse cirrhosis, CCl(4) was administered chronically for 3 months, and then it was withdrawn and curcumin administered for 2 months. Alanine aminotransferase, gamma-glutamyl transpeptidase, liver histopathology, bilirubin, glycogen, reduced and oxidized glutathione, and TGF-beta (mRNA and protein) levels were assessed. Curcumin preserved normal values of markers of liver damage in BDL rats. Fibrosis, assessed by measuring hydroxyproline levels and histopathology, increased nearly fivefold after BDL and this effect was partially but significantly prevented by curcumin. BDL increased transforming growth factor-beta (TGF-beta) levels (mRNA and proteins), while curcumin partially suppressed this mediator of fibrosis. Curcumin also partially reversed the fibrosis induced by CCl(4). Curcumin was effective in preventing and reversing cirrhosis, probably by its ability of reducing TGF-beta expression. These data suggest that curcumin might be an effective antifibrotic and fibrolitic drug in the treatment of chronic hepatic diseases

J Pharm Pharmacol. 2013 Mar;65(3):423-9. doi: 10.1111/j.2042-7158.2012.01610.x. Epub 2012 Nov 15.

Dramatic increase in hepatic and biliary curcumin exposure by modulation of its elimination pathway in rats.

Lee JH, Kim HG, Oh JH, Lee YJ.

Source

College of Pharmacy, Kyung Hee University, Seoul, Korea.

Abstract

OBJECTIVES:

Curcumin, a major component of the food spice turmeric (Curcuma longa), has multiple beneficial effects on diseases of the liver and bile duct. We have investigated whether modulation of the curcumin elimination pathway could increase its hepatic and biliary exposure in rats.

METHODS:

Probenecid, an inhibitor of the metabolism and biliary excretion of curcumin, was used as a modulator. After intravenous administration of curcumin at a dose of 18 mg/kg/h without (control) or with co-infusion of probenecid (230 mg/kg/h) in rats, the pharmacokinetic parameters of curcumin were estimated.

KEY FINDINGS:

Coadministration of probenecid significantly increased the total area under the plasma (1.88-fold) and bile (6.73-fold) concentration-time curves from 0 to 80 min of curcumin relative to those in the controls. The tissue-to-plasma concentration ratio in the liver was also dramatically increased (69.3-fold) by probenecid. These results may be attributed to the dual inhibitory effects of probenecid, to a greater extent, on metabolism via glucuronidation, and to a lesser extent, on the biliary excretion of curcumin via the multidrug resistance-associated protein 2.

CONCLUSIONS:

The probenecid-mediated increase in hepatic and biliary exposure of curcumin suggested that the use of combination drug regimens involving curcumin and modulators of elimination may be an innovative approach for the therapeutic use of curcumin.

J Physiol Biochem. 2013 Feb 22. [Epub ahead of print]

Curcumin prevents liver fat accumulation and serum fetuin-A increase in rats fed a high-fat diet.

Oner-İyidoğan Y, Koçak H, Seyidhanoğlu M, Gürdöl F, Gülçubuk A, Yildirim F, Cevik A, Uysal M.

Source

Department of Biochemistry, Istanbul Faculty of Medicine, Istanbul University, Çapa, Istanbul, Turkey, iyidogan@istanbul.edu.tr.

Abstract

Fetuin-A is synthesized in the liver and is secreted into the bloodstream. Clinical studies suggest involvement of fetuin-A in metabolic disorders such as visceral obesity, insulin resistance, diabetes, and fatty liver. Curcumin is extracted from the rhizome Curcuma longa and has been shown to possess potent antioxidant, anticarcinogenic, anti-inflammatory, and hypoglycemic properties. In this study, we investigated the effect of curcumin treatment on serum fetuin-A levels as well as hepatic lipids and prooxidant-antioxidant status in rats fed a high-fat diet (HFD). Male Sprague-Dawley rats were divided into six groups. Group 1 was fed control diet (10 % of total calories from fat). Groups 2 and 3 were given curcumin (100 and 400 mg/kg bw/day, respectively) by gavage for 8 weeks and were fed control diet. Group 4 was fed with HFD (60 % of total calories from fat). Groups 5 and 6 received HFD together with the two doses of curcumin, respectively. Curcumin treatment appeared to be effective in reducing liver triglycerides and serum fetuin-A levels. These findings suggest that the reduction of fetuin-A may contribute to the beneficial effects of curcumin in the pathogenesis of obesity.

LoS One. 2012;7(1):e28784. doi: 10.1371/journal.pone.0028784. Epub 2012 Jan 9.

Curcumin prevents high fat diet induced insulin resistance and obesity via attenuating lipogenesis in liver and inflammatory pathway in adipocytes.

Shao W, Yu Z, Chiang Y, Yang Y, Chai T, Foltz W, Lu H, Fantus IG, Jin T.

Source

Division of Cell and Molecular Biology, Toronto General Research Institute, University Health Network, Toronto, Canada.

Abstract

BACKGROUND:

Mechanisms underlying the attenuation of body weight gain and insulin resistance in response to high fat diet (HFD) by the curry compound curcumin need to be further explored. Although the attenuation of the inflammatory pathway is an accepted mechanism, a recent study suggested that curcumin stimulates Wnt signaling pathway and hence suppresses adipogenic differentiation. This is in contrast with the known repressive effect of curcumin on Wnt signaling in other cell lineages.

METHODOLOGY AND PRINCIPAL FINDINGS:

We conducted the examination on low fat diet, or HFD fed C57BL/6J mice with or without curcumin intervention for 28 weeks. Curcumin significantly attenuated the effect of HFD on glucose disposal, body weight/fat gain, as well as the development of insulin resistance. No stimulatory effect on Wnt activation was observed in the mature fat tissue. In addition, curcumin did not stimulate Wnt signaling in vitro in primary rat adipocytes. Furthermore, curcumin inhibited lipogenic gene expression in the liver and blocked the effects of HFD on macrophage infiltration and the inflammatory pathway in the adipose tissue.

CONCLUSIONS AND SIGNIFICANCE:

We conclude that the beneficial effect of curcumin during HFD consumption is mediated by attenuating lipogenic gene expression in the liver and the inflammatory response in the adipose tissue, in the absence of stimulation of Wnt signaling in mature adipocytes.

Eur J Pharmacol. 2013 Jan 5;698(1-3):95-102. doi: 10.1016/j.ejphar.2012.10.013. Epub 2012 Oct 29.

Anti-tumor effect of germacrone on human hepatoma cell lines through inducing G2/M cell cycle arrest and promoting apoptosis.

Liu Y, Wang W, Fang B, Ma F, Zheng Q, Deng P, Zhao S, Chen M, Yang G, He G.

Source

The Genetic Engineering International Cooperation Base of Ministry of Science and Technology, Chinese National Center of Plant Gene HUST Part, College of Life Science and Technology, Huazhong University of Science & Technology, Luoyu Road 1037, Wuhan 430074, Hubei, China.

Abstract

Germacrone is one of the main bioactive components in the traditional Chinese medicine Rhizoma curcuma. In this study, the anti-proliferative effect of germacrone on the human hepatoma cell lines and the molecular mechanism underlying the cytotoxicity of germacrone were investigated. Treatment of human hepatoma cell lines HepG2 and Bel7402 with germacrone resulted in cell cycle arrest and apoptosis in a dose-dependent manner as measured by MTT assay, flow cytometric and fluorescent microscopy analysis, while much lower effect on normal human liver cell L02 was observed. Flow cytometric analysis revealed that germacrone induced G2/M arrest in the cell cycle progression that was associated with an obvious decrease in the protein expression of cyclin B1 and its activating partner CDK1 with concomitant inductions of p21. Hoechst 33258 and Annexin V/PI staining results showed that the total cell number in apoptosis associated with a dose-dependent up-regulation of Bax and down-regulation of Bcl-2/Bcl-xl was increased. In the meantime, the up-regulation of p53 and reactive oxygen species increase were observed, which suggested that germacrone might be a new potent chemopreventive drug candidate for liver cancer via regulating the expression of proteins related to G2/M cell cycle and apoptosis, and p53 and oxidative damage may play important roles in the inhibition of human hepatoma cells growth by germacrone.

BMC Complement Altern Med. 2012 Sep 16;12:156. doi: 10.1186/1472-6882-12-156.

Inhibition by curcumin of multiple sites of the transforming growth factor-beta1 signalling pathway ameliorates the progression of liver fibrosis induced by carbon tetrachloride in rats.

Yao QY, Xu BL, Wang JY, Liu HC, Zhang SC, Tu CT.

Source

Department of Gastroenterology and Hepatology, Zhongshan hospital, Fudan University, 180# Fenglin Road, Shanghai, 200032, People's Republic of China.

Abstract

BACKGROUND:

At present there is no effective and accepted therapy for hepatic fibrosis. Transforming growth factor (TGF)-β1 signaling pathway contributes greatly to hepatic fibrosis. Reducing TGF-β synthesis or inhibiting components of its complex signaling pathway represent important therapeutic targets. The aim of the study was to investigate the effect of curcumin on liver fibrosis and whether curcumin attenuates the TGF-β1 signaling pathway.

METHODS:

Sprague-Dawley rat was induced liver fibrosis by carbon tetrachloride (CCl4) for six weeks together with or without curcumin, and hepatic histopathology and collagen content were employed to quantify liver necro-inflammation and fibrosis. Moreover, the mRNA and protein expression levels of TGF-β1, Smad2, phosphorylated Smad2, Smad3, Smad7 and connective tissue growth factor (CTGF) were determined by quantitative real time-PCR, Western blot, or immunohistochemistry.

RESULTS:

Rats treated with curcumin improved liver necro-inflammation, and reduced liver fibrosis in association with decreased α-smooth muscle actin expression, and decreased collagen deposition. Furthermore, curcumin significantly attenuated expressions of TGFβ1, Smad2, phosphorylated Smad2, Smad3, and CTGF and induced expression of the Smad7.

CONCLUSIONS:

Curcumin significantly attenuated the severity of CCl4-induced liver inflammation and fibrosis through inhibition of TGF-β1/Smad signalling pathway and CTGF expression. These data suggest that curcumin might be an effective antifibrotic drug in the prevention of liver disease progression.

Phytomedicine. 2012 Apr 15;19(6):545-50. doi: 10.1016/j.phymed.2011.12.006. Epub 2012 Mar 23.

Curcumin prevents chronic alcohol-induced liver disease involving decreasing ROS generation and enhancing antioxidative capacity.

Rong S, Zhao Y, Bao W, Xiao X, Wang D, Nussler AK, Yan H, Yao P, Liu L.

Source

Department of Nutrition and Food Hygiene, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, 13 Hangkong Road, Wuhan 430030, PR China.

Abstract

Our previous study found that curcumin, a major active component of turmeric, could ameliorate ethanol-induced hepatocytes oxidative stress in vitro. The objective of this work was to investigate the effect of curcumin on chronic alcoholic liver disease (ALD) in vivo. Ethanol-exposed (2.4g/kg/day ethanol for the initial 4 weeks and 4g/kg/day for another 2 weeks) Balb/c mice were simultaneously treated with curcumin for 6 weeks. The results showed that curcumin attenuated ethanol-induced histopathological changes of the liver and ameliorated the evident release of cellular alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Ethanol exposure resulted in reactive oxygen species (ROS) generation, malondialdehyde (MDA) elevation, glutathione (GSH) depletion and antioxidant defense system impairment, which were significantly reversed by curcumin treatment. In conclusion, curcumin provided protection against chronic ALD and the mechanism might be related to the alleviation of oxidative damage.

Fundam Clin Pharmacol. 2009 Dec;23(6):735-45. doi: 10.1111/j.1472-8206.2009.00722.x. Epub 2009 Jul 28.

Hepatoprotective activity of picroliv, curcumin and ellagic acid compared to silymarin on paracetamol induced liver toxicity in mice.

Girish C, Koner BC, Jayanthi S, Ramachandra Rao K, Rajesh B, Pradhan SC.

Source

Department of Pharmacology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry, India. gcnx@rediffmail.com

Abstract

Oxidative stress is implicated as a common pathologic mechanism contributing to the initiation and progression of hepatic damage in a variety of liver disorders. Present study attempts to evaluate the hepatoprotective activity of picroliv, curcumin and ellagic acid in comparison to silymarin using paracetamol (PCM) induced acute liver damage. Hepatotoxicity was induced by administering a single oral dose of PCM (500 mg/kg) and was assessed by quantifying the serum enzyme activities, phenobarbitone induced sleeping time and histopathological analysis of liver tissues. The antioxidant parameters, malondialdehyde (MDA), reduced glutathione (GSH) and catalase of the liver tissue were also assessed. The herbal drugs were administered for 7 days by oral route at 50 and 100 mg/kg. PCM induced hepatic damage was manifested by a significant increase in the activities of marker enzymes (alanine transaminase, aspartate transaminase and alkaline phosphatase) in serum and MDA level in liver. There was also a significant decrease in activity of GSH and catalase levels. The histopathological examination on toxic models revealed centrizonal necrosis and fatty changes. Pretreatment of mice with picroliv, curcumin and ellagic acid reversed these altered parameters towards normal values, which were compared with silymarin. The normalization of phenobarbitone induced sleeping time suggests the restoration of liver cytochrome P450 enzymes. This study supports the use of these active phytochemicals against toxic liver injury, which may act by preventing the lipid peroxidation and augmenting the antioxidant defense system or regeneration of hepatocytes. These active phytochemicals may be developed as drugs for the treatment of liver diseases.

Clin Exp Pharmacol Physiol. 2012 Mar;39(3):283-99. doi: 10.1111/j.1440-1681.2011.05648.x.

Discovery of curcumin, a component of golden spice, and its miraculous biological activities.

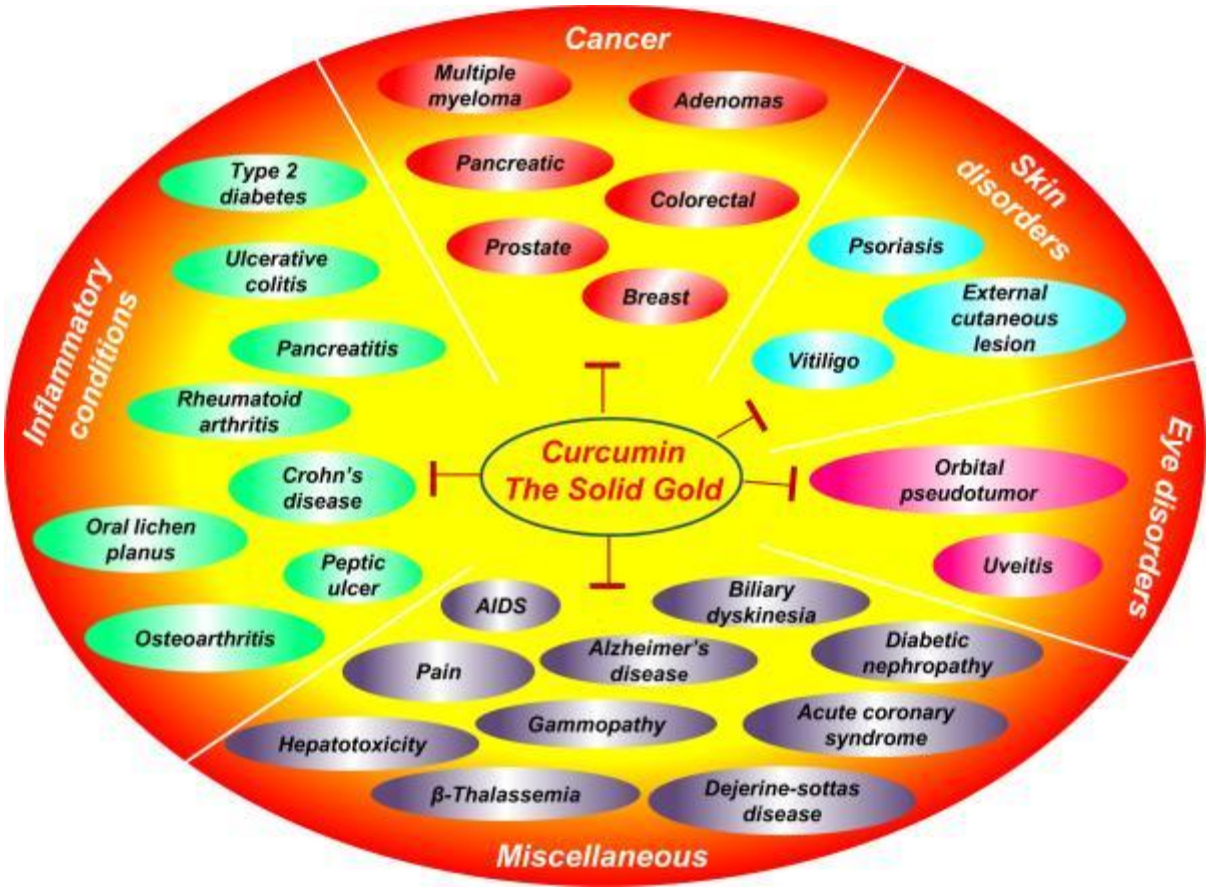
Gupta SC, Patchva S, Koh W, Aggarwal BB.

Source

Cytokine Research Laboratory, Department of Experimental Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA.

Abstract

1. Curcumin is the active ingredient of the dietary spice turmeric and has been consumed for medicinal purposes for thousands of years. Modern science has shown that curcumin modulates various signalling molecules, including inflammatory molecules, transcription factors, enzymes, protein kinases, protein reductases, carrier proteins, cell survival proteins, drug resistance proteins, adhesion molecules, growth factors, receptors, cell cycle regulatory proteins, chemokines, DNA, RNA and metal ions. 2. Because of this polyphenol's potential to modulate multiple signalling molecules, it has been reported to possess pleiotropic activities. First demonstrated to have antibacterial activity in 1949, curcumin has since been shown to have anti-inflammatory, anti-oxidant, pro-apoptotic, chemopreventive, chemotherapeutic, antiproliferative, wound healing, antinociceptive, antiparasitic and antimalarial properties as well. Animal studies have suggested that curcumin may be active against a wide range of human diseases, including diabetes, obesity, neurological and psychiatric disorders and cancer, as well as chronic illnesses affecting the eyes, lungs, liver, kidneys and gastrointestinal and cardiovascular systems. 3. Although many clinical trials evaluating the safety and efficacy of curcumin against human ailments have already been completed, others are still ongoing. Moreover, curcumin is used as a supplement in several countries, including India, Japan, the US, Thailand, China, Korea, Turkey, South Africa, Nepal and Pakistan. Although inexpensive, apparently well tolerated and potentially active, curcumin has not been approved for the treatment of any human disease. 4. In the present article, we discuss the discovery and key biological activities of curcumin, with a particular emphasis on its activities at the molecular and cellular levels, as well as in animals and humans.



Molecules. 2011 Jun 3;16(6):4567-98. doi: 10.3390/molecules16064567.

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.

PMID:
21642934
[PubMed - indexed for MEDLINE]
J Clin Immunol. 2007 Jan;27(1):19-35. Epub 2007 Jan 9.

"Spicing up" of the immune system by curcumin.

Jagetia GC, Aggarwal BB.

Source

Cytokine Research Laboratory, Department of Experimental Therapeutics, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, USA.

Abstract

Curcumin (diferuloylmethane) is an orange-yellow component of turmeric (Curcuma longa), a spice often found in curry powder. Traditionally known for its an antiinflammatory effects, curcumin has been shown in the last two decades to be a potent immunomodulatory agent that can modulate the activation of T cells, B cells, macrophages, neutrophils, natural killer cells, and dendritic cells. Curcumin can also downregulate the expression of various proinflammatory cytokines including TNF, IL-1, IL-2, IL-6, IL-8, IL-12, and chemokines, most likely through inactivation of the transcription factor NF-kappaB. Interestingly, however, curcumin at low doses can also enhance antibody responses. This suggests that curcumin's reported beneficial effects in arthritis, allergy, asthma, atherosclerosis, heart disease, Alzheimer's disease, diabetes, and cancer might be due in part to its ability to modulate the immune system. Together, these findings warrant further consideration of curcumin as a therapy for immune disorders.

PMID:
17211725
[PubMed - indexed for MEDLINE]

Trends Pharmacol Sci. 2009 Feb;30(2):85-94. doi: 10.1016/j.tips.2008.11.002. Epub 2008 Dec 26.

Pharmacological basis for the role of curcumin in chronic diseases: an age-old spice with modern targets.

Aggarwal BB, Sung B.

Source

Cytokine Research Laboratory, Department of Experimental Therapeutics, University of Texas M. D. Anderson Cancer Center, Houston, TX 77030, USA. aggarwal@mdanderson.org

Abstract

Curcumin (diferuloylmethane), a yellow pigment in the spice turmeric (also called curry powder), has been used for centuries as a treatment for inflammatory diseases. Extensive research within the past two decades has shown that curcumin mediates its anti-inflammatory effects through the downregulation of inflammatory transcription factors (such as nuclear factor kappaB), enzymes (such as cyclooxygenase 2 and 5 lipoxygenase) and cytokines (such as tumor necrosis factor, interleukin 1 and interleukin 6). Because of the crucial role of inflammation in most chronic diseases, the potential of curcumin has been examined in neoplastic, neurological, cardiovascular, pulmonary and metabolic diseases. The pharmacodynamics and pharmacokinetics of curcumin have been examined in animals and in humans. Various pharmacological aspects of curcumin in vitro and in vivo are discussed in detail here

Adv Exp Med Biol. 2007;595:105-25.

Antioxidant and anti-inflammatory properties of curcumin.

Menon VP, Sudheer AR.

Source

Department of Biochemistry & Center for Micronutrient Research, Annamalai University, Tamilnadu, India. biocmr@sify.com

Abstract

Curcumin, a yellow pigment from Curcuma longa, is a major component of turmeric and is commonly used as a spice and food-coloring agent. It is also used as a cosmetic and in some medical preparations. The desirable preventive or putative therapeutic properties of curcumin have also been considered to be associated with its antioxidant and anti-inflammatory properties. Because free-radical-mediated peroxidation of membrane lipids and oxidative damage of DNA and proteins are believed to be associated with a variety of chronic pathological complications such as

cancer, atherosclerosis, and neurodegenerative diseases, curcumin is thought to play a vital role against these pathological conditions. The anti-inflammatory effect of curcumin is most likely mediated through its ability to inhibit cyclooxygenase-2 (COX-2), lipoxygenase (LOX), and inducible nitric oxide synthase (iNOS). COX-2, LOX, and iNOS are important enzymes that mediate inflammatory processes. Improper upregulation of COX-2 and/or iNOS has been associated with the pathophysiology of certain types of human cancer as well as inflammatory disorders. Because inflammation is closely linked to tumor promotion, curcumin with its potent anti-inflammatory property is anticipated to exert chemopreventive effects on carcinogenesis. Hence, the past few decades have witnessed intense research devoted to the antioxidant and anti-inflammatory properties of curcumin. In this review, we describe both antioxidant and anti-inflammatory properties of curcumin, the mode of action of curcumin, and its therapeutic usage against different pathological conditions.

BMC Complement Altern Med. 2013 Mar 5;13:56. doi: 10.1186/1472-6882-13-56.

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.

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 livercirrhosis 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.

PMID:
23496995

Yao Xue Xue Bao. 2007 Sep;42(9):973-7.

BMC Complement Altern Med. 2013 Mar 5;13:56. doi: 10.1186/1472-6882-13-56.

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.

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Department of Molecular Medicine, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia.

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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.

Determination of curcumol in plasma by HPLC-MS/MS method and its pharmacokinetics in Beagle dogs

[Article in Chinese]

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Source

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Abstract

To establish a high performance liquid chromatography (HPLC) coupled with tandem mass spectrometry quantitative detection method for the determination of curcumol, the main ingredient of zedoary turmeric oil fat emulsion, and investigate its pharmacokinetics in Beagle dogs, nine healthy Beagle dogs were divided into three groups, and blood samples were collected at scheduled time points after intravenous injection of 7.5, 10 and 12.5 mg x kg(-1) zedoary turmeric oil fat emulsion. The concentrations of curcumol were determined and pharmacokinetics was calculated. A good linearity was obtained from 0.25 to 100 ng x mL(-1) in plasma. The relative recoveries were from 91.33% to 103.17%, and the absolute recoveries were from 31.61% to 37.20%. The intra-day and inter-day variances (RSD) were < 15%. The main pharmacokinetic parameters of curcumol after intravenous injection of 7.5, 10 and 12.5 mg x kg(-1) zedoary turmeric oil fat emulsion were as follows, T1/2 : (2.0 +/- 0.4), (1.7 +/- 0.2) and (2.3 +/- 0.8) h, AUC(0-infinity): (15.1 +/- 2.7), (18.3 +/- 2.0) and (29.5 +/- 4.0) ng x mL(-1) x h; MRT: (0.9 +/- 0.1), (0.8 +/- 0.2) and (0.8 +/- 0.1) h, CL: (21.9 +/- 4.0), (24.9 +/- 6.0) and (18.4 +/- 1.2) L x h(-1) x kg; Vd : (65.4 +/- 26.5), (62.0 +/- 13.4) and (61.2 +/- 19.8) L x kg(-1), respectively. The developed method was rapid, highly sensitive and specific and could be used in curcumol pharmacokinetic studies in vivo. A three-compartment model was best fit to the plasma concentration--time curves obtained in Beagle dogs and the plasma AUC was increased proportionally with doses.

Cynara Scolymus

Biol Trace Elem Res. 2010 Jun;135(1-3):264-74. Epub 2009 Aug 4.

Effect of artichoke leaf extract on hepatic and cardiac oxidative stress in rats fed on high cholesterol diet.

Küçükgergin C, Aydin AF, Ozdemirler-Erata G, Mehmetçik G, Koçak-Toker N, Uysal M.

Source

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Abstract

Hypercholesterolemia and lipid peroxidation play complementary roles in atherosclerosis. Artichoke (Cynara scolymus L., Asteraceae) leaf extract (ALE), rich in antioxidants, has cholesterol-reducing effect. We investigated the effect of ALE on serum and hepatic lipid levels and pro-oxidant-antioxidant balance in the liver and heart of hypercholesterolemic rats. Rats were fed on 4% (w/w) cholesterol and 1% cholic acid (w/w) supplemented diet for 1 month. ALE (1.5 g/kg/day) was given by gavage during the last 2 weeks. High cholesterol (HC) diet caused significant increases in serum and liver cholesterol and triglyceride levels. It increased malondialdehyde (MDA) and diene conjugate (DC) levels in both tissues. Hepatic vitamin E levels and hepatic and cardiac glutathione peroxidase (GSH-Px) activities decreased, but superoxide dismutase and glutathione transferase activities, glutathione, and vitamin C levels remained unchanged due to HC diet. Serum cholesterol and triglyceride levels and ratio of cholesterol to high-density lipoprotein (HDL)-cholesterol decreased in ALE plus HC-treated rats, but liver cholesterol and triglyceride levels remained unchanged. Significant decreases in hepatic and cardiac MDA and DC levels and increases in hepatic vitamin E and GSH-Px activities were observed in ALE-treated hypercholesterolemic rats. Our results indicate that ALE decreases serum lipids and hypercholesterolemia-induced pro-oxidant state in both tissues.

Phytother Res. 2010 Apr;24(4):565-70.

Artichoke leaf extract reduces oxidative stress and lipoprotein dyshomeostasis in rats fed on high cholesterol diet.

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Source

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Abstract

Hypercholesterolemia and lipid peroxidation play complementary role in atherosclerosis. Artichoke leaf extract (ALE) is rich in natural antioxidants and has a cholesterol-reducing effect. However, there is no study investigating the effect of ALE on lipid levels and lipid peroxidation in experimental hypercholesterolemic conditions. Rats were fed on 4% (w/w) cholesterol and 1% (w/w) cholic acid supplemented diet for 1 month. ALE (1.5 g/kg/day) was given by gavage during the last 2 weeks. Serum lipid composition, malondialdehyde (MDA) and diene conjugate (DC) levels and plasma antioxidant activity (AOA) were measured. In addition, endogenous DC and copper-induced MDA levels were determined in apo B-containing lipoproteins (LDL+VLDL fraction). Serum cholesterol and triglyceride levels and the ratio of cholesterol to HDL-cholesterol decreased due to ALE treatment in rats fed on HC diet. Significant decreases in serum MDA and DC levels and increases in plasma AOA were detected in serum in ALE-treated hypercholesterolemic rats. Endogenous DC and copper-induced MDA levels were also lower in LDL+VLDL fraction due to ALE-treatment in hypercholesterolemic rats. Our results indicate that ALE may be useful for the prevention of hypercholesterolemia-induced pro-oxidant state in LDL+VLDL fraction and the reduction of increased serum cholesterol and triglyceride levels.

PMID:
19777605
[PubMed - indexed for MEDLINE]

J Ethnopharmacol. 2003 Jun;86(2-3):203-11.

Efficacy of different Cynara scolymus preparations on liver complaints.

Speroni E, Cervellati R, Govoni P, Guizzardi S, Renzulli C, Guerra MC.

Source

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Abstract

Cynara scolymus leaves extracts have long been used in folk medicine for their choleretic and hepatoprotective activities, that are often related to the cynarin content. These therapeutic properties are also attributed to mono- and di-caffeoylquinic acids and since commercial C. scolymus preparations can differ for their activities, we studied four extracts to evaluate, if present, a relationship between the hepatobiliary properties of the different preparations and their content in phenolics. The antioxidant activity of the commercial preparations examined was also considered in an in vitro system. The results showed that the extract with the highest content in phenolic derivatives (GAE) exerted the major effect on bile flow and liver protection. Also the results of the antioxidant capacity (BR) of the different preparations are in good agreement with the results obtained in vivo. On the contrary, administering rats with doses of chlorogenic acid, equivalent to those present in this extract, we did not observe any choleretic or protective action. An histopathological analysis of liver sections confirmed the biochemical results. Perhaps caffeoyl derivatives have a role in the therapeutic properties of C. scolymus extracts, as reported in literature for "in vitro" studies, but when administered alone, they are not so effective in exerting this action.

PMID:
12738088
[PubMed - indexed for MEDLINE]

J Nat Prod. 1987 Jul-Aug;50(4):612-7.

Hepatoprotective activity of polyphenolic compounds from Cynara scolymus against CCl4 toxicity in isolated rat hepatocytes.

Adzet T, Camarasa J, Laguna JC.

Source

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Abstract

The hepatoprotective activity against CCl4 toxicity in isolated rat hepatocytes of some polyphenolic compounds, such as cynarin, isochlorogenic acid, chlorogenic acid, luteolin-7-glucoside, and two organic acids, caffeic and quinic, from Cynara scolymus, is tested. Only cynarine and, to a lesser extent, caffeic acid showed cytoprotective action. The possible relationship between the molecular structure and the protective effect found is discussed.

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3430163
[PubMed - indexed for MEDLINE]

Toxicol Appl Pharmacol. 1997 Jun;144(2):279-86.

Antioxidative and protective properties of extracts from leaves of the artichoke (Cynara scolymus L.) against hydroperoxide-induced oxidative stress in cultured rat hepatocytes.

Gebhardt R.

Source

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Abstract

Primary rat hepatocyte cultures exposed to tert-butylhydroperoxide (t-BHP) or cumene hydroperoxide were used to assess the antioxidative and protective potential of water-soluble extracts of artichoke leaves. Both hydroperoxides stimulated the production of malondialdehyde (MDA), particularly when the cells were pretreated with diethylmaleate (DEM) in order to diminish the level of cellular glutathione (GSH). Addition of artichoke extracts did not affect basal MDA production, but prevented the hydroperoxide-induced increase of MDA formation in a concentration-dependent manner when presented simultaneously or prior to the peroxides. The effective concentrations (down to 0.001 mg/ml) were well below the cytotoxic levels of the extracts which started above 1 mg/ml. The protective potential assessed by the LDH leakage assay and the MTT assay closely paralleled the reduction in MDA production and largely prevented hepatocyte necrosis induced by the hydroperoxides. The artichoke extracts did not affect the cellular level of glutathione (GSH), but diminished the loss of total GSH and the cellular leakage of GSSG resulting from exposure to t-BHP. Chlorogenic acid and cynarin accounted for only part of the antioxidative principle of the extracts which was resistant against tryptic digestion, boiling, acidification, and other treatments, but was slightly sensitive to alkalinization. These results demonstrate that artichoke extracts have a marked antioxidative and protective potential. Primary hepatocyte cultures seem suitable for identifying the constituents responsible for these effects and for elucidating their possible mode of action.