March 27, 2023

Re: Purifí: Curated Blend and Cellular Absorption Technology Clinical Dossier

Here at THREE, we provide curated proactive wellness solutions using our proprietary Cellular Absorption Technology, proven to help you live a life of greater health and purpose.

This dossier contains peer-reviewed clinical studies both on the curated blend and the Cellular Absorption Technologies used in Purifí that validates its ability to do the following:

- Detoxify and cleanse 5 organs (liver, lungs, colon, kidneys, and skin).
- Support the body's elimination organs to remove toxins.
- Increase nutrient absorption in the body.
- Help support a healthy weight.
- Eliminate heavy metal toxins.

One thing that you can expect from us here at THREE is that we are always in the process of running clinical studies in elucidating new mechanisms of action by which our products work along with discovering additional areas in which our products can promote human health. We have several exciting clinical studies in the pipeline and will announce these when they are completed.

The clinical studies contained herein, and others that will follow, explain why our products provide the powerful health benefits our customers from all around the world experience every time they use a THREE product.

Thank you for joining us on this journey and for trusting us with your proactive wellness needs.

Be well,

Dr. Dan Gubler
Chief Scientific Officer
Three International

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Lehi, UT 84043

Cell Mol Neurobiol. 2015 Apr;35(3):335-344. doi: 10.1007/s10571-014-0129-7.
Epub 2014 Oct 29.

Protective effects of Arctium lappa L. roots against hydrogen peroxide-induced cell injury and potential mechanisms in SH-SY5Y cells

Xing Tian [1] [2], Li-Ping Guo [1], Xiao-Long Hu [1], Jin Huang [1], Yan-Hua Fan [1], Tian-Shu Ren [1], Qing-Chun Zhao [3] [4]

Affiliations
PMID: 25352420 DOI: 10.1007/s10571-014-0129-7

Abstract

Accumulated evidence has shown that excessive reactive oxygen species (ROS) have been implicated in neuronal cell death related with various chronic neurodegenerative disorders. This study was designed to explore neuroprotective effects of ethyl acetate extract of Arctium lappa L. roots (EAL) on hydrogen peroxide (H2O2)-induced cell injury in human SH-SY5Y neuroblastoma cells. The cell viability was significantly decreased after exposure to 200 μM H2O2, whereas pretreatment with different concentrations of EAL attenuated the H2O2-induced cytotoxicity. Hoechst 33342 staining indicated that EAL reversed nuclear condensation in H2O2-treated cells. Meanwhile, TUNEL assay with DAPI staining showed that EAL attenuated apoptosis was induced by H2O2. Pretreatment with EAL also markedly elevated activities of antioxidant enzyme (GSH-Px and SOD), reduced lipid peroxidation (MDA) production, prevented ROS formation, and the decrease of mitochondrial membrane potential. In addition, EAL showed strong radical scavenging ability in 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) assays. Furthermore, EAL inhibited H2O2-induced apoptosis by increases in the Bcl-2/Bax ratio, decreases in cytochrome c release, and attenuation of caspase-3, caspase-9 activities, and expressions. These findings suggest that EAL may be regarded as a potential antioxidant agent and possess potent neuroprotective activity against H2O2-induced injury.

Related information

PubChem Compound (MeSH Keyword)

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Full Text Sources

Springer

Other Literature Sources

scite Smart Citations

Cancer Prev Res (Phila). 2009 Dec;2(12):1015-22. doi: 10.1158/1940-6207.CAPR-09-0099. Epub 2009 Dec 1.

Effects of chlorophyll and chlorophyllin on low-dose aflatoxin B(1) pharmacokinetics in human volunteers

Carole Jubert [1], John Mata, Graham Bench, Roderick Dashwood, Cliff Pereira, William Tracewell, Kenneth Turteltaub, David Williams, George Bailey

Affiliations

PMID: 19952359 PMCID: PMC5314947 DOI: 10.1158/1940-6207.CAPR-09-0099

Free PMC article

Abstract

Chlorophyll (Chla) and chlorophyllin (CHL) were shown previously to reduce carcinogen bioavailability, biomarker damage, and tumorigenicity in trout and rats. These findings were partially extended to humans, where CHL reduced excretion of aflatoxin B(1) (AFB(1))-DNA repair products in Chinese unavoidably exposed to dietary AFB(1). However, neither AFB(1) pharmacokinetics nor Chla effects were examined. We conducted an unblinded crossover study to establish AFB(1) pharmacokinetic parameters among four human volunteers, and to explore possible effects of CHL or Chla cotreatment in three of those volunteers. For protocol 1, fasted subjects received an Institutional Review Board-approved dose of 14C-AFB(1) (30 ng, 5 nCi) by capsule with 100 mL water, followed by normal eating and drinking after 2 hours. Blood and cumulative urine samples were collected over 72 hours, and 14C- AFB(1) equivalents were determined by accelerator mass spectrometry. Protocols 2 and 3 were similar except capsules also contained 150 mg of purified Chla or CHL, respectively. Protocols were repeated thrice for each volunteer. The study revealed rapid human AFB(1) uptake (plasma k(a), 5.05 + or - 1.10 h(-1); T(max), 1.0 hour) and urinary elimination (95% complete by 24 hours) kinetics. Chla and CHL treatment each significantly impeded AFB(1) absorption and reduced Cmax and AUCs (plasma and urine) in one or more subjects. These initial results provide AFB(1) pharmacokinetic parameters previously unavailable for humans, and suggest that Chla or CHL co-consumption may limit the bioavailability of ingested aflatoxin in humans, as they do in animal models.

Figures

Environ Mol Mutagen. 2009 Mar;50(2):134-44. doi: 10.1002/em.20449.

Chlorophyllin significantly reduces benzo[a]pyrene-DNA adduct formation and alters cytochrome P450 1A1 and 1B1 expression and EROD activity in normal human mammary epithelial cells

Channa Keshava [1], Rao L Divi, Tracey L Einem, Diana L Richardson, Sarah L Leonard, Nagalakshmi Keshava, Miriam C Poirier, Ainsley Weston

Affiliations

PMID: 19152381 PMCID: PMC2637934 DOI: 10.1002/em.20449

Free PMC article

Abstract

We hypothesized that chlorophyllin (CHLN) would reduce benzo[a]pyrene-DNA (BP-DNA) adduct levels. Using normal human mammary epithelial cells (NHMECs) exposed to 4 microM BP for 24 hr in the presence or absence of 5 microM CHLN, we measured BP-DNA adducts by chemiluminescence immunoassay (CIA). The protocol included the following experimental groups: BP alone, BP given simultaneously with CHLN (BP+CHLN) for 24 hr, CHLN given for 24 hr followed by BP for 24 hr (preCHLN, postBP), and CHLN given for 48 hr with BP added for the last 24 hr (preCHLN, postBP+CHLN). Incubation with CHLN decreased BPdG levels in all groups, with 87% inhibition in the preCHLN, postBP+CHLN group. To examine metabolic mechanisms, we monitored expression by Affymetrix microarray (U133A), and found BP-induced up-regulation of CYP1A1 and CYP1B1 expression, as well as up-regulation of groups of interferon-inducible, inflammation and signal transduction genes. Incubation of cells with CHLN and BP in any combination decreased expression of many of these genes. Using reverse transcription real time PCR (RT-PCR) the maximal inhibition of BP-induced gene expression, >85% for CYP1A1 and >70% for CYP1B1, was observed in the preCHLN, postBP+CHLN group. To explore the relationship between transcription and enzyme activity, the ethoxyresorufin-O-deethylase (EROD) assay was used to measure the combined CYP1A1 and CYP1B1 activities. BP exposure caused the EROD levels to double, when compared with the unexposed controls. The CHLN-exposed groups all showed EROD levels similar to the unexposed controls. Therefore, the addition of CHLN to BP-exposed cells reduced BPdG formation and CYP1A1 and CYP1B1 expression, but EROD activity was not significantly reduced.

Figures

Comparative Study Mutat Res. 2008 Apr 2;640(1-2):145-52.
doi: 10.1016/j.mrfmmm.2008.01.003. Epub 2008 Feb 2.

Transcriptional profiles of benzo(a)pyrene exposure in normal human mammary epithelial cells in the absence or presence of chlorophyllin

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Affiliations
PMID: 18336845 DOI: 10.1016/j.mrfmmm.2008.01.003

Abstract

Benzo(a)pyrene (BP) exposure causes alterations in gene expression in normal human mammary epithelial cells (NHMECs). This study used Affymetrix Hu-Gene133A arrays, with 14,500 genes represented, to evaluate modulation of BP-induced gene expression by chlorophyllin in six NHMEC strains derived from different donors. A major goal was to seek potential biomarkers of carcinogen exposure and how they behave in the presence of a chemopreventive agent. NHMECs (passage 6 and 70% confluence) were exposed for 24h to either vehicle control, or BP, or chlorophyllin followed by BP and chlorophyllin together. BP exposure resulted in approximately 3-fold altered expression of 49 genes in at least one of the six NHMEC strains. When cells were exposed to chlorophyllin pre-treatment followed by BP plus chlorophyllin, expression of 125 genes was similarly altered. Genes in the functional categories of xenobiotic metabolism, cell signaling, cell motility, cell proliferation, cellular transcription, metabolism, cell cycle control, apoptosis and DNA repair were identified. Only CYP1B1 and ALDH1A3 were consistently up-regulated by approximately 3-fold in most of the cell strains (at least 4) when exposed to BP. Cluster analysis identified a suite of 13 genes induced by BP where induction was mitigated in the presence of chlorophyllin. Additionally, cluster analysis identified a suite of 16 genes down-regulated by BP where induction was partially restored in the presence of chlorophyllin.

Related information

MedGen
PubChem Compound
PubChem Compound (MeSH Keyword)
PubChem Substance

LinkOut - more resources

Full Text Sources
Elsevier Science

Cancer Lett. 2010 Jun 28;292(2):254-60. doi: 10.1016/j.canlet.2009.12.008. Epub 2010 Feb 16.

CYP1A1 and CYP1B1 gene expression and DNA adduct formation in normal human mammary epithelial cells exposed to benzo[a]pyrene in the absence or presence of chlorophyllin

Kaarthik John [1], Rao L Divi, Channa Keshava, Christine C Orozco, Marie E Schockley, Diana L Richardson, Miriam C Poirier, Joginder Nath, Ainsley Weston

Affiliations

PMID: 20163913 PMCID: PMC3475201 DOI: 10.1016/j.canlet.2009.12.008

Free PMC article

Abstract

Benzo[a]pyrene (BP) is a potent pro-carcinogen and ubiquitous environmental pollutant. Here, we examined the induction and modulation of CYP1A1 and CYP1B1 and 10-(deoxyguanosin-N(2)-yl)-7,8,9-trihydroxy-7,8,9,10-tetrahydrobenzo[a]pyrene (BPdG) adduct formation in DNA from 20 primary normal human mammary epithelial cell (NHMEC) strains exposed to BP (4muM) in the absence or presence of chlorophyllin (5muM). Real-time polymerase chain reaction (RT-PCR) analysis revealed strong induction of both CYP1A1 and CYP1B1 by BP, with high levels of inter-individual variability. Variable BPdG formation was found in all strains by r7, t8-dihydroxy-t-9, 10 epoxy-7,8,9,10-tetrahydrobenzo[a]pyrene (BPDE)-DNA chemiluminescence assay (CIA). Chlorophyllin mitigated BP-induced CYP1A1 and CYP1B1 gene expression in all 20 strains when administered with BP. Chlorophyllin, administered prior to BP-exposure, mitigated CYP1A1 expression in 18/20 NHMEC strains ($p<0.005$) and CYP1B1 expression in 17/20 NHMEC strains ($p<0.005$). Maximum percent reductions of CYP1A1 and CYP1B1 gene expression and BPdG adduct formation were observed when cells were pre-dosed with chlorophyllin followed by administration of the carcinogen with chlorophyllin ($p<0.005$ for CYP1A1 and CYP1B1 expression and $p<0.0005$ for BPdG adducts). Therefore, chlorophyllin is likely to be a good chemoprotective agent for a large proportion of the human population.

Figures

Food Chem Toxicol. 2020 Nov;145:111706. doi: 10.1016/j.fct.2020.111706. Epub 2020 Aug 29.

A strategy for repression of arsenic toxicity through nuclear factor E2 related factor 2 activation mediated by the (E)-2-alkenals in Coriandrum sativum L. leaf extract

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Affiliations

PMID: 32871193 DOI: 10.1016/j.fct.2020.111706

Abstract

Activation of the Kelch-like ECH-associated protein 1 (Keap1)/nuclear factor E2 related factor 2 (Nrf2) system plays a role in repression of xenobiotic toxicity. The Coriandrum sativum L. leaf extract (CSLE) contains various aliphatic electrophiles such as (E)-2-decenal and (E)-2-dodecenal. In the present study, we examined the activation of Nrf2 coupled to chemical modification of Keap1 mediated by (E)-2-alkenals in CSLE, and the protective role of CSLE and (E)-2-alkenals against inorganic arsenite (iAsIII) cytotoxicity. Ultra-performance liquid chromatography-elevated collision energy mass spectrometry analysis revealed that (E)-2-decenal modified recombinant Keap1 at Cys241, Cys249, Cys257 and His274. Exposure of HepG2 cells to CSLE, (E)-2-decenal, or (E)-2-dodecenal upregulated Nrf2-related downstream signaling such as expression of phase-II xenobiotic-metabolizing enzymes and phase-III transporters involved in cytoprotection against iAsIII. Pretreatment with CSLE or (E)-2-butenal, a prototype of (E)-2-alkenal, prior to iAsIII exposure suppressed accumulation of iAsIII significantly and reduced iAsIII-induced cytotoxicity in cells. Oral administration of CSLE to C57BL/6 mice upregulated downstream proteins of Nrf2 and reduced accumulation of arsenic in liver tissue. The present study indicates that CSLE containing (E)-2-alkenals activates Nrf2, leading to a reduction in arsenic accumulation in vivo.

Keywords: Alkenal; Arsenite; Cilantro; Coriandrum sativum L.; Decenal; Nrf2.

Related information

MedGen

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Full Text Sources

Elsevier Science

Chemosphere. 2020 Apr;244:125543. doi: 10.1016/j.chemosphere.2019.125543. Epub 2019 Dec 4.

Biochar efficacy for reducing heavy metals uptake by Cilantro (Coriandrum sativum) and spinach (Spinaccia oleracea) to minimize human health risk

Amir Zeb Khan [1], Xiaodong Ding [2], Sardar Khan [3], Tehreem Ayaz [4], Rivka Fidel [5], Muhammad Amjad Khan [6]

Affiliations

PMID: 32050340 DOI: 10.1016/j.chemosphere.2019.125543

Abstract

Environmentally friendly and cost-effective techniques are required to reclaim land degraded during mining activities. Bioaccumulation of heavy metals (HMs) in vegetables grown on contaminated soils can increase human health risks. The potential effects of hardwood biochar (HWB) was assessed for chromium (Cr), zinc (Zn), copper (Cu), manganese (Mn) and lead (Pb) bioavailability in mine-contaminated soils and their subsequently bioaccumulation in crops and associated health risk. HWB was applied to chromium-manganese mine contaminated soils at the rate of 3% to investigate the efficiency of HWB for the second crop in crop rotation technique. Cilantro (Coriandrum sativum) and spinach (Spinaccia oleracea) were grown as second crop in the same pots which were already used for rice cultivation as first crop (without adding further amendments). Application of HWB decreased the concentrations of Cr, Zn, Cu, Mn, and Pb in cilantro by 25.5%, 37.1%, 42.5%, 34.3%, and 36.2%, respectively as compared to control. In spinach, the reduction in concentrations of Cr was 75.0%, Zn 24.1%, Cu 70.1%, Mn 78.0%, and Pb 50.5% as compared to control. HWB significantly ($P < 0.01$) reduced the HMs uptake in spinach cultivated in the amended soils as compared to the spinach in control. Bioaccumulation factor results also indicate that HWB decreased the bioaccumulation of selected HMs in cilantro and spinach, thus reducing health risks. Results of the study clearly demonstrate that the use of HWB can significantly reduce HMs in vegetables, associated health risk and improve food quality, therefore can be used as soil amendment for reclamation of mine-degraded soils.

Keywords: Crop rotation technique; Hard wood biochar (HWB); Health risk; Heavy metals (HMs); Vegetables.

Related information

PubChem Compound (MeSH Keyword)

J Pept Sci. 2023 Jan;29(1):e3447. doi: 10.1002/psc.3447. Epub 2022 Aug 19.

Ameliorative effect of dandelion (Taraxacum officinale) peptides on benzo(a)pyrene-induced oxidative stress and inflammation in human umbilical vein endothelial cells

Zhixiang Cai [1], Tao Yan [2], Siwen Li [3], Jianyi Zhang [1], Xianyue Wang [2], Li Li [4], Huailing Wang [5], Hanwei Chen [4], Yukuan Tang [4]

Affiliations
PMID: 35940823 DOI: 10.1002/psc.3447

Abstract

Dandelion (Taraxacum officinale) is widely consumed as a health food and a traditional medicine. However, the protective effect of dandelion bio-active peptides (DPs) against polycyclic aromatic hydrocarbon-induced blood vessel inflammation and oxidative damage is not well documented. In the current study, four novel DPs were isolated using an activity tracking method. The protective activity of the DPs against benzo(a)pyrene (Bap)-induced human umbilical vein endothelial cell (HUVEC) damage was explored. The results indicated that DP-2 [cycle-(Thr-His-Ala-Trp)] effectively inhibited Bap-induced reactive oxygen species (ROS) and malondialdehyde (MDA) overproduction and reinforced antioxidant enzyme activity while inhibiting the production of inflammatory factors in HUVECs. Moreover, DP-2 increased NAD(P)H:quinone oxidoreductase 1, heme oxygenase-1, and nuclear factor E2-releated factor 2 expression levels by activating the PI3K/Akt signaling pathway. In addition, DP-2 attenuated Bap-induced HUVEC apoptosis via the Bcl-2/Bax/cytochrome c apoptotic pathway. These results suggest that DP-2 is a promising compound for protecting HUVECs from Bap-induced inflammatory and oxidative damage.

Keywords: benzo(a)pyrene; cycle-peptide; dandelion; inflammatory; oxidative stress.

Related information

PubChem Compound (MeSH Keyword)

LinkOut - more resources

Research Materials

NCI CPTC Antibody Characterization Program

Int J Mol Sci. 2018 Apr 7;19(4):1112. doi: 10.3390/ijms19041112.

Dandelion Root Extract Induces Intracellular Ca^{2+} Increases in HEK293 Cells

Andrea Gerbino [1], Daniela Russo [2], Matilde Colella [3], Giuseppe Procino [4], Maria Svelto [5], Luigi Milella [6], Monica Carmosino [7]

Affiliations

PMID: 29642457 PMCID: PMC5979456 DOI: 10.3390/ijms19041112

Free PMC article

Abstract

Dandelion *(Taraxacum officinale* Weber ex F.H.Wigg.) has been used for centuries as an ethnomedical remedy. Nonetheless, the extensive use of different kinds of dandelion extracts and preparations is based on empirical findings. Some of the tissue-specific effects reported for diverse dandelion extracts may result from their action on intracellular signaling cascades. Therefore, the aim of this study was to evaluate the effects of an ethanolic dandelion root extract (DRE) on Ca^{2+} signaling in human embryonic kidney (HEK) 293 cells. The cytotoxicity of increasing doses of crude DRE was determined by the Calcein viability assay. Fura-2 and the fluorescence resonance energy transfer (FRET)-based probe ERD1 were used to measure cytoplasmic and intraluminal endoplasmic reticulum (ER) Ca^{2+} levels, respectively. Furthermore, a green fluorescent protein (GFP)-based probe was used to monitor phospholipase C (PLC) activation (pleckstrin homology [PH]-PLCδ-GFP). DRE (10-400 µg/mL) exposure, in the presence of external Ca^{2+}, dose-dependently increased intracellular Ca^{2+} levels. The DRE-induced Ca^{2+} increase was significantly reduced in the absence of extracellular Ca^{2+}. In addition, DRE caused a significant Ca^{2+} release from the ER of intact cells and a concomitant translocation of PH-PLCδ-GFP. In conclusion, DRE directly activates both the release of Ca^{2+} from internal stores and a significant Ca^{2+} influx at the plasma membrane. The resulting high Ca^{2+} levels within the cell seem to directly stimulate PLC activity.

Keywords: Ca2+ fluorescent sensors; Ca2+ influx; Ca2+ signaling; Fura-2; bioactive compounds; endoplasmic reticulum; herbal extract; phospholipase C; plasma membrane.

Figures

Meta-Analysis Phytother Res. 2020 Aug;34(8):1947-1955. doi: 10.1002/ptr.6659.
Epub 2020 Mar 5.

Effects of garlic supplementation on liver enzymes: A systematic review and meta-analysis of randomized controlled trials

Asieh Panjeshahin [1 2], Mehdi Mollahosseini [1 2], Monireh Panbehkar-Jouybari [1 2], Mojtaba Kaviani [3], Farhang Mirzavandi [1 2], Mahdieh Hosseinzadeh [1 2]

Affiliations
PMID: 32135032 DOI: 10.1002/ptr.6659

Abstract

Current evidence on the beneficial effects of garlic on liver enzymes is contradictory. Therefore, the aim of this systematic review and meta-analysis is to evaluate the effect of garlic supplementation on human liver enzymes, such as Alanine Transaminase (ALT/SGPT) and Aspartate Transaminase (AST/SGOT). To collect the required data, PubMed, Scopus, ISI Web of Science, and Google scholar databases were systematically searched from inception to June 2019. A meta-analysis was conducted using the random-effects model to evaluate the effects of garlic supplementation on ALT and AST levels. The Cochran's Q-test and inconsistency index were also used to evaluate heterogeneity among the studies. Among a total of 15,514 identified articles, six studies (containing 301 participants) met the inclusion criteria. Results of the meta-analysis showed that garlic supplementation significantly decreased AST level (Hedges' g = -0.36, 95% confidence interval [CI]: -0.72, -0.004, p = .047); whereas, it had no significant effect on ALT level (Hedges' g = -0.22, 95% CI: -0.64, 0.20, p = .310). Results showed that garlic supplementation reduced AST levels significantly; however, had no significant effect on ALT levels. Further studies are still needed to confirm the results.

Keywords: ALT; AST; garlic; liver enzyme; meta-analysis; systematic review.

Related information

MedGen
PubChem Compound (MeSH Keyword)

LinkOut - more resources

Full Text Sources
Ovid Technologies, Inc.

Int J Biol Sci. 2013;9(3):237-45. doi: 10.7150/ijbs.5549. Epub 2013 Feb 20.

Garlic oil attenuated nitrosodiethylamine-induced hepatocarcinogenesis by modulating the metabolic activation and detoxification enzymes

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Affiliations

PMID: 23494807 PMCID: PMC3596709 DOI: 10.7150/ijbs.5549

Free PMC article

Abstract

Nitrosodiethylamine (NDEA) is a potent carcinogen widely existing in the environment. Our previous study has demonstrated that garlic oil (GO) could prevent NDEA-induced hepatocarcinogenesis in rats, but the underlying mechanisms are not fully understood. It has been well documented that the metabolic activation may play important roles in NDEA-induced hepatocarcinogenesis. Therefore, we designed the current study to explore the potential mechanisms by investigating the changes of hepatic phase I enzymes (including cytochrome P450 enzyme (CYP) 2E1, CYP1A2 and CYP1A1) and phase II enzymes (including glutathione S transferases (GSTs) and UDP- Glucuronosyltransferases (UGTs)) by using enzymatic methods, real-time PCR, and western blotting analysis. We found that NDEA treatment resulted in significant decreases of the activities of CYP2E1, CYP1A2, GST alpha, GST mu, UGTs and increases of the activities of CYP1A1 and GST pi. Furthermore, the mRNA and protein levels of CYP2E1, CYP1A2, GST alpha, GST mu and UGT1A6 in the liver of NDEA-treated rats were significantly decreased compared with those of the control group rats, while the mRNA and protein levels of CYP1A1 and GST pi were dramatically increased. Interestingly, all these adverse effects induced by NDEA were simultaneously and significantly suppressed by GO co-treatment. These data suggest that the protective effects of GO against NDEA-induced hepatocarcinogenesis might be, at least partially, attributed to the modulation of phase I and phase II enzymes.

Keywords: Cytochrome P450 enzyme; Garlic oil; Glutathione S transferase; Nitrosodiethylamine; UDP-glucuronosyltransferase..

Figures

Review Curr Clin Pharmacol. 2016;11(3):159-167.
doi: 10.2174/1574884711666160813233225.

Humic Acids as Therapeutic Compounds in Lead Intoxication

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Affiliations

PMID: 27526696 DOI: 10.2174/1574884711666160813233225

Abstract

Background: The toxicity of lead and its compounds is well known, causing anemia by inhibiting the synthesis of porphyrins. The neurotoxic effects, particularly in the young, alter the structure of cell membranes and DNA. Chronic exposure to lead has adverse effects on the body by disrupting the mechanisms of energy production and tissue damage, in particular in its links with thiol groups and competition for binding sites with zinc.

Objective: This review is therefore a description of the mechanism of lead toxicity as well as of possible interventions for the detoxification of the body. Part of the clinical intervention is the provision of chelates that form insoluble complexes with lead and eliminate the load in tissues. Most of these chelating agents have a number of side effects. It is therefore not surprising that active compounds with distinctive antioxidant and chelating properties are being sought after.

Conclusion: The possibility of administering lower amounts, and the corresponding decrease in side effects, would be important for clinical practice. Both prospective studies and our initial studies on humic acids have highlighted positive effects based on their antioxidant and chelating properties.

Related information

MedGen
PubChem Compound (MeSH Keyword)

LinkOut - more resources

Full Text Sources

Bentham Science Publishers Ltd.
Ingenta plc

Other Literature Sources

Int J Mol Sci. 2020 Mar 30;21(7):2369. doi: 10.3390/ijms21072369.

Modulatory Effects of Silymarin on Benzo[a]pyrene-Induced Hepatotoxicity

Seung-Cheol Jee [1], Min Kim [1], Jung-Suk Sung [1]

Affiliations

PMID: 32235460 PMCID: PMC7177818 DOI: 10.3390/ijms21072369

Free PMC article

Abstract

Benzo[a]pyrene (B[a]P), a polycyclic aromatic hydrocarbon, is a group 1 carcinogen that introduces mutagenic DNA adducts into the genome. In this study, we investigated the molecular mechanisms underlying the involvement of silymarin in the reduction of DNA adduct formation by B[a]P-7,8-dihydrodiol-9,10-epoxide (BPDE), induced by B[a]P. B[a]P exhibited toxicity in HepG2 cells, whereas co-treatment of the cells with B[a]P and silymarin reduced the formation of BPDE-DNA adducts, thereby increasing cell viability. Determination of the level of major B[a]P metabolites in the treated cells showed that BPDE levels were reduced by silymarin. Nuclear factor erythroid 2-related factor 2 (Nrf2) and pregnane X receptor (PXR) were found to be involved in the activation of detoxifying genes against B[a]P-mediated toxicity. Silymarin did not increase the expression of these major transcription factors, but greatly facilitated their nuclear translocation. In this manner, treatment of HepG2 cells with silymarin modulated detoxification enzymes through NRF2 and PXR to eliminate B[a]P metabolites. Knockdown of Nrf2 abolished the preventive effect of silymarin on BPDE-DNA adduct formation, indicating that activation of the Nrf2 pathway plays a key role in preventing B[a]P-induced genotoxicity. Our results suggest that silymarin has anti-genotoxic effects, as it prevents BPDE-DNA adduct formation by modulating the Nrf2 and PXR signaling pathways.

Keywords: BPDE-DNA adduct; Nrf2; PXR; benzo[a]pyrene; detoxification; silymarin.

Figures

Int J Pharm. 2014 Aug 25;471(1-2):173-81. doi: 10.1016/j.ijpharm.2014.05.026. Epub 2014 May 22.

Phyto-liposomes as nanoshuttles for water-insoluble silybin-phospholipid complex

Ruggero Angelico [1], Andrea Ceglie [2], Pasquale Sacco [3], Giuseppe Colafemmina [4], Maria Ripoli [5], Alessandra Mangia [5]

Affiliations

PMID: 24858381 DOI: 10.1016/j.ijpharm.2014.05.026

Abstract

Among various phospholipid-mediated drug delivery systems (DDS) suitable for topic and oral administration, phytosome technology represents an advanced innovation, widely used to incorporate standardized bioactive polyphenolic phytoconstituents into phospholipid molecular complexes. In order to extend their potential therapeutic efficiency also to other routes of administration, we proposed a novel phytosome carrier-mediated vesicular system (phyto-liposome) as DDS for the flavonolignan silybin (SIL), a natural compound with multiple biological activities related to its hepatoprotective, anticancer and antioxidant (radical scavenging) effects. We screened the optimum fraction of its phytosome, available in the market as Siliphos™, into liposomes prepared by extrusion, such that vesicle sizes and charges, monitored through dynamic light scattering and laser doppler velocimetry, satisfied several quality requirements. Special emphasis was placed on the study of host-guest interaction by performing UV-vis absorption, spectrofluorimetry and NMR experiments both in aqueous and non-polar solvents to probe the effect of the presence of phospholipids on the electronic properties of SIL and its propensity to engage H bonding with the lipid headpolar groups. Finally, fluorescence microscopy observations confirmed the ability of phyto-liposomes to be internalized in human hepatoma cells, which was promising for their potential application in the treatment of acute or chronic liver diseases.

Keywords: Physicochemical properties; Phyto-liposome; Phytosome; Silybin; Silybin–phospholipids interactions.

Related information

MedGen
PubChem Compound (MeSH Keyword)

LinkOut - more resources

Full Text Sources

Review Altern Med Rev. 2005 Sep;10(3):193-203.

A review of the bioavailability and clinical efficacy of milk thistle phytosome: a silybin-phosphatidylcholine complex (Siliphos)

Parris Kidd [1], Kathleen Head

Affiliations
PMID: 16164374

Abstract

Certain of the water-soluble flavonoid molecules can be converted into lipid-compatible molecular complexes, aptly called phytosomes. Phytosomes are better able to transition from a hydrophilic environment into the lipid-friendly environment of the outer cell membrane, and from there into the cell, finally reaching the blood. The fruit of the milk thistle plant (Silybum marianum, Family Asteraceae) contains flavonoids that are proven liver protectants. The standardized extract known as silymarin contains three flavonoids of the flavonol subclass. Silybin predominates, followed by silydianin and silychristin. Although silybin is the most potent of the flavonoids in milk thistle, similar to other flavonoids it is not well-absorbed. Silybin-phosphatidylcholine complexed as a phytosome provides significant liver protection and enhanced bioavailability over conventional silymarin.

Related information

MedGen
PubChem Compound
PubChem Compound (MeSH Keyword)
PubChem Substance

LinkOut - more resources

Other Literature Sources
The Lens - Patent Citations

Medical
ClinicalTrials.gov

Basic Clin Pharmacol Toxicol. 2007 Jun;100(6):414-9. doi: 10.1111/j.1742-7843.2007.00069.x.

Silymarin protection against major reactive oxygen species released by environmental toxins: exogenous H2O2 exposure in erythrocytes

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Free article

Abstract

Silymarin is a polyphenolic plant flavonoid (a mixture of flavonoid isomers such as silibinin, isosilibinin, silidianin and silichristin) derived from Silymarin marianum that has anti-inflammatory, hepatoprotective and anticarcinogenic effects. Our earlier studies have shown that silymarin plays a protective role against the oxidative damage induced by environmental contaminants like benzo(a)pyrene in erythrocyte haemolysates. During the detoxification of these environmental contaminants, the major reactive oxygen species generated is hydrogen peroxide (H(2)O(2)). Because H(2)O(2)can easily penetrate into the cell and cause damage to biomolecules, the protective role of silymarin was further assessed against this cytotoxic agent in vitro in erythrocyte haemolysates. The protective effect was monitored by assessing the levels of the antioxidant enzymes superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, glutathione-s-transferase, glutathione peroxidase and malondialdehyde (LPO) in three groups: vehicle control, H(2)O(2)-exposed groups and drug co-incubation group (H(2)O(2) + silymarin). The protective effect of silymarin on the non-enzymic antioxidant glutathione and haemolysis, methaemoglobin content and protein carbonyl content were also assessed. It was observed that the activities of antioxidant enzymes and glutathione were reduced and the malondialdehyde levels were elevated after H(2)O(2)exposure. There were also alterations in haemolysis, methaemoglobin content and protein carbonyl content, whereas after the administration of silymarin, the antioxidant enzyme activities reversed to near normal with reduced malondialdehyde content and normalized haemolysis, methaemoglobin content and protein carbonyl content. The results suggest that silymarin possesses substantial protective effect and free radical scavenging mechanism against exogenous H(2)O(2)-induced oxidative stress damages, hence, can be used as a protective drug against toxicity induced by environmental contaminants.

Related information

PubChem Compound
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PubChem Substance

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A study of the hepatoprotective effect of Plantago psyllium L. seed extract against Carbon tetrachloride induced hepatic injury in rats

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Abstract

Background: The liver is the main metabolic organ involved in disposal and detoxification of various molecules. Plantago psyllium L. seed has been reported to exert positive effects in some pathological conditions. The current study aims to assess the hepatoprotective effect of Plantago psyllium L. seed extract against carbon tetrachloride-induced hepatotoxicity.

Methods: Male albino Wistar rats were randomly divided into five groups of 10 rats each. Hepatotoxicity was induced by orally administered carbon tetrachloride (CCl4) for nine weeks with or without the different treatments which were utilized daily for the whole nine weeks. Serum and tissue samples were then withdrawn and different liver biomarkers were investigated.

Results: Treatment of rats with Psyllium seed ethanolic extract significantly alleviated the toxic effects of CCl4. This was evidenced by its ability to restore liver biomarkers levels. Moreover, treatment with Psyllium seed extract normalized levels of oxidative biomarkers such as lipid peroxidation, hepatic content of reduced glutathione and catalase activity, as well as the expression level of the inflammatory marker TNF-α. Histopathological examination reflected the protective effect of the extract on liver architecture and confirmed the observed biochemical data.

Conclusions: The presented data demonstrates a potential hepatoprotective effect of Psyllium seed extract compared to the standard hepatoprotective drug silymarin. This effect can be attributed to the antioxidant and anti-inflammatory effects of Psyllium extract.

Keywords: Anti-oxidant activity; CCl4; Hepatoprotective activities; Plantago psyllium L.; TNF-α.

Related information

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