GB

"Protection of chlorophyllin against oxidative damage by inducing HO-1 and NQO1 expression mediated by PI3K/Akt and Nrf2."

DE

Schutz von Chlorophyllin gegen oxidative Schäden durch per PI3K/Akt und Nrf2 vermittelte Induktion der HO-1- und NQO1-Expression.

GR

Προστασία της χλωροφυλλίνης ενάντια στις οξειδωτικές βλάβες προκαλώντας την έκφραση HO-1 και NQO1 με μεσολάβηση PI3K/Akt και Nrf2.

FR

Protection offerte par la chlorophylline contre les lésions oxydatives en induisant une expression de HO-1 et NQO1 médiatisée par PI3K/Akt et Nrf2.

CZ

Ochrana chlorofylinu před oxidačním poškozením navozením exprese HO-1 a NQO1 zprostředkované signální dráhou PI3K/Akt a transkripčním faktorem Nrf2.

Free Radic Res. 2008 Apr;42(4):362-71. doi: 10.1080/10715760801993076.

Protection of chlorophyllin against oxidative damage by inducing HO-1 and NQO1 expression mediated by PI3K/Akt and Nrf2.

Zhang Y, Guan L, Wang X, Wen T, Xing J, Zhao J.

Source Research Center of Occupational Medicine, Third Hospital of Peking University, Peking, PR China.

Abstract

Green vegetables are thought to have a chemoprotective effect on the basis of epidemiologic evidence. This study investigated whether chlorophyllin (CHL) could induce antioxidant enzymes and confer protection against oxidative damage. The results showed that CHL could induce HO-1 and NQO1 expression in human umbilical vein endothelial cell (HUVEC) in a time- and dose-dependent manner and protect them against hydrogen peroxide caused oxidative damage. The induction of HO-1 and NQO1 by CHL was accompanied with the accumulation of transcription factor Nrf2 in nucleus and the activation of PI3K/Akt signalling pathway. Additionally, the specific inhibitor of PI3K/Akt could obviously decrease not only the induced expression of HO-1 and NQO1 but also the antioxidant effect of CHL. **In conclusion, this study proved that CHL exerts antioxidant effect by inducing HO-1 and NQO1 expression mediated by PI3K/Akt and Nrf2. One thinks CHL may have promise to be prophylactic pharmaceuticals without adverse effects.**

PMID: 18404535

GB

„Inhibitory effects of chlorophyllin, hemin and tetrakis(4-benzoic acid)porphyrin on oxidative DNA damage and mouse skin inflammation induced by 12-Otetradecanoylphorbol-13-acetate as a possible anti-tumor promoting mechanism.“

DE

Inhibitorische Wirkung von Chlorophyllin, Hämin und Tetrakis(4-Benzoesäure)porphyrin auf oxidative DNA-Schäden und Maushautentzündung induziert durch 12-O-Tetradecanoylphorbol-13-acetat als möglicher anti-tumorfördernder Mechanismus.

GR

„του και (4-βενζοϊκό οξύ) πορφυρίνης πάνω σε οξειδωτικές βλάβες του DNA και δερματικές φλεγμονές που προκλήθηκαν από 12-Otetradecanoylphorbol-13-acetate ως πιθανό μηχανισμό κατά της καρκινογένεσης.“

FR

Effets inhibiteurs de la chlorophylline, de l‘hémine et de la tétrakis(4-acide benzoïque)porphyrine sur les lésions oxydatives de l‘ADN et l‘inflammation de la peau de la souris induite par du 12-otétradécanoylphorbol-13-acétate en tant que possible mécanisme promoteur anti-tumoral.

CZ

Inhibiční účinky chlorofylinu, heminu a tetrakis (kyselina 4-benzoová) porfyrinu na oxidační poškození DNA a zánět kůže myší vyvolané 12-O-tetradekanoylforbol-13-acetátem jako možný mechanismus protinádorového působení.

Mutat Res. 2003 Dec 9;542(1-2):89-97.

Inhibitory effects of chlorophyllin, hemin and tetrakis(4-benzoic acid)porphyrin on oxidative DNA damage and mouse skin inflammation induced by 12-O-tetradecanoylphorbol-13-acetate as a possible anti-tumor promoting mechanism.

Park KK, Park JH, Jung YJ, Chung WY.

Source Department of Oral Biology, Yonsei University College of Dentistry, 134 Shinchon-Dong, Seodaemoon-Ku, Seoul 120-752, South Korea.

Abstract

Reactive oxygen species (ROS) from both endogenous and exogenous sources can cause oxidative DNA damage and dysregulated cell signaling, which are involved in the multistage process of carcinogenesis such as tumor initiation, promotion and progression. A number of structurally different anticarcinogenic agents inhibit inflammation and tumor promotion as they reduce ROS production and oxidative DNA damage. Evidence suggests that porphyrins can interfere with the actions of various carcinogens and mutagens by forming face-to-face complexes and their antimutagenic or antigenotoxic effects may also be attributed to their antioxidant activities. However, little is known regarding the anti-tumor promoting potential and mechanism of the porphyrin compounds. Based on our previous results on the inhibitory effects of chlorophyllin (CHL), hemin and tetrakis(4-benzoic acid)porphyrin (TBAP) against two-stage mouse skin carcinogenesis, we have investigated their anti-tumor promoting mechanisms. In the present work, CHL, hemin and TBAP reduced superoxide anion generation by 12-O-tetradecanoylphorbol-13-acetate (TPA) in differentiated HL-60 cells and the production of hydroxyl radicals by Fenton reaction. Porphyrins exert a dose-related inhibition of his(+) reversion in Salmonella typhimurium TA102 induced by tert-butylhydroperoxide (t-BOOH). DNA strand breaks by ROS derived from H(2)O(2)/Cu(II) and the formation of 8-hydroxydeoxyguanosine (8-OH-dG) in calf thymus DNA treated with H(2)O(2)/UV also were inhibited markedly by porphyrins in a concentration-dependent manner. Furthermore, CHL, hemin and TBAP

decreased myeloperoxidase (MPO) activity and H(2)O(2) formation as well as epidermal ornithine decarboxylase (ODC) activity in mouse skin treated with TPA. **These results demonstrate that the antioxidative properties of porphyrins are important for inhibiting TPA-induced tumor promotion.**

PMID: 14644357

GB

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

DE

Wirkung von Chlorophyll und Chlorophyllin auf die Pharmakokinetik von niedrig dosiertem Aflatoxin B(1) bei menschlichen Probanden.

GR

„Αποτελέσματα της χλωροφύλλης και της χλωροφυλλίνης στις φαρμακοκινητικές ιδιότητες χαμηλής δοσολογίας αφλατοξίνης B(1) σε εθελοντές.“

FR

Effets de la chlorophylle et de la chlorophylline sur la pharmacocinétique de l‘aflatoxine B(1) à faible dose chez des volontaires humains.

CZ

Účinky chlorofylu a chlorofylinu na farmakokinetika aflatoxinu B(1) v malých dávkách u zdravých dobrovolníků.

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.

Jubert C, Mata J, Bench G, Dashwood R, Pereira C, Tracewell W, Turteltaub K, Williams D, Bailey G.

Source

Linus Pauling Institute, Oregon State University, Corvallis, OR 97331, USA.

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.**

PMID: 19952359

GB

„Natural chlorophyll inhibits aflatoxin B1-induced multiorgan carcinogenesis in the rat.“

DE

Natürliches Chlorophyll hemmt durch Aflatoxin B1 induzierte Multiorgankarzinogenese der Ratte.

GR

Η φυσική χλωροφύλλη εμποδίζει την πολυοργανική καρκινογένεση που προκαλείται από την αφλατοξίνη Β1 σε ποντίκια.

FR

Chez le rat, la chlorophylle naturelle inhibe la carcinogenèse multi-organes induite par l‘aflatoxine B1.

CZ

Přírodní chlorofyl brání multiorgánové karcinogenezi vyvolané aflatoxinem B1 u potkanů.

Carcinogenesis. 2007 Jun;28(6):1294-302. Epub 2007 Feb 8.

Natural chlorophyll inhibits aflatoxin B1-induced multi-organ carcinogenesis in the rat.

Simonich MT, Egner PA, Roebuck BD, Orner GA, Jubert C, Pereira C, Groopman JD, Kensler TW, Dashwood RH, Williams DE, Bailey GS.

Source Linus Pauling Institute, Oregon State University, Corvallis, OR 97331, USA.

Chemoprevention by chlorophyll (Chl) was investigated in a rat multi-organ carcinogenesis model. Twenty-one male F344 rats in three gavage groups (N = 7 rats each) received five daily doses of 250 microg/kg [(3)H]-aflatoxin B(1) ([(3)H]-AFB(1)) alone, or with 250 mg/kg chlorophyllin (CHL), or an equimolar amount (300 mg/kg) of Chl. CHL and Chl reduced hepatic DNA adduction by 42% (P = 0.031) and 55% (P = 0.008), respectively, AFB(1)-albumin adducts by 65% (P < 0.001) and 71% (P < 0.001), respectively, and the major AFB-N(7)-guanine urinary adduct by 90% (P = 0.0047) and 92% (P = 0.0029), respectively. To explore mechanisms, fluorescence quenching experiments established formation of a non-covalent complex in vitro between AFB(1) and Chl (K(d) = 1.22 +/- 0.05 microM, stoichiometry = 1Chl:1AFB(1)) as well as CHL (K(d) = 3.05 +/- 0.04 microM; stoichiometry = 1CHL:1AFB(1)). The feces of CHL and Chl co-gavaged rats contained 137% (P = 0.0003) and 412% (P = 0.0048) more AFB(1) equivalents, respectively, than control feces, indicating CHL and Chl inhibited AFB(1) uptake. However, CHL or Chl treatment in vivo did not induce hepatic quinone reductase (NAD(P)H:quinone oxidoreductase) or glutathione S-transferase (GST) above control levels. These results are consistent with a mechanism involving complex-mediated reduction of carcinogen uptake, and do not support a role for phase II enzyme induction in vivo under these conditions. In a second study, 30 rats in three experimental groups were dosed as in study 1, but for 10 days. At 18 weeks, CHL and Chl had reduced the volume percent of liver occupied by GST placental form-positive foci by 74% (P < 0.001) and 77% (P < 0.001), respectively compared with control livers. CHL and Chl reduced the mean number of aberrant crypt foci per colon by 63% (P = 0.0026) and 75% (P = 0.0004), respectively. **These results show Chl and CHL provide potent chemoprotection against early biochemical and late pathophysiological biomarkers of AFB(1) carcinogenesis in the rat liver and colon.**

PMID:17290047

Free full text

GB
„Heme and Chlorophyll Intake and Risk of Colorectal Cancer in the Netherlands Cohort Study“

DE
Häm- und Chlorophyllaufnahme und das Risiko von Kolorektalkrebs in der Netherlands Cohort Study

GR
Πρόσληψη Αίμης και Χλωροφύλλης και Κίνδυνος Ορθοκολικού Καρκίνου στη μελέτη Netherlands Cohort Study

FR
Prise d‘hème et de chlorophylle, et risque de cancer colorectal dans l‘étude de cohorte aux Pays-Bas.

CZ
Příjem hemu a chlorofylu a riziko kolorektálního karcinomu v holandské kohortové studii

Heme and Chlorophyll Intake and Risk of Colorectal Cancer in the Netherlands Cohort Study

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Abstract

Background: The evidence for red meat as a determinant of colorectal cancer remains equivocal, which might be explained by differences in heme content. Heme is the pro-oxidant, iron-containing porphyrin pigment of meat and its content depends on the type of meat. Chlorophyll from green vegetables might modify this association.

Methods: The Netherlands Cohort Study was initiated in 1986 when a self-administered questionnaire on risk factors for cancer was completed by 120,852 subjects ages 55 to 69 years. After 9.3 years of follow-up through the Cancer Registry, 1,535 incident colorectal cancer cases (869 men and 666 women) were available. Nineteen of the 150 items in the validated dietary questionnaire related to consumption of specific types of fresh and processed meat. Heme iron content was calculated as a type-specific percentage of the total iron content and chlorophyll content of vegetables was derived from the literature.

Results: Multivariate rate ratios for quintiles of heme iron intake and colon cancer were 1.00, 0.98, 1.04, 1.13, and 1.29 (P_{trend} = 0.10) among men and 1.00, 1.31, 1.44, 1.18, and 1.20 (P_{trend} = 0.56) among women, respectively. No consistent associations were observed for rectal cancer. Rate ratios for colon cancer increased across successive quintiles of the ratio of heme/chlorophyll among men only (1.00, 1.08, 1.01, 1.32, and 1.43; P_{trend} = 0.01). No associations were observed between fresh meat and colorectal cancer.

Conclusion**: Our data suggest an elevated risk of colon cancer in men with increasing intake of heme iron and decreasing intake of chlorophyll.** Further research is needed to confirm these results. (Cancer Epidemiol Biomarkers Prev 2006;15(4):717–25)

GB

„Green vegetables, red meat and colon cancer: chlorophyll prevents the cytotoxic and hyperproliferative effects of haem in rat colon.“

DE

Grünes Gemüse, rotes Fleisch und Kolonkarzinom: Chlorophyll verhindert die zytotoxische und hyperproliferative Wirkung von Häm im Rattenkolon.

GR

Πράσινα λαχανικά, κόκκινο κρέας και καρκίνος του παχέος εντέρου: η χλωροφύλλη εμποδίζει τα κυτταροτοξικά και υπερπολλαπλασιαστικά αποτελέσματα της αίμης στο παχύ έντερο αρουραίων.

FR

Légumes verts, viande rouge et cancer du côlon : la chlorophylle prévient les effets cytotoxiques et hyperprolifératifs de l‘hème dans le côlon du rat.

CZ

Zelenina, červené maso a karcinom tlustého střeva: Chlorofyl brání cytotoxickým a hyperproliferativním účinkům hemu v tlustém střevě potkanů.

Carcinogenesis. 2005 Feb;26(2):387-93. Epub 2004 Nov 18.

Green vegetables, red meat and colon cancer: chlorophyll prevents the cytotoxic and hyperproliferative effects of haem in rat colon.

de Vogel J, Jonker-Termont DS, van Lieshout EM, Katan MB, van der Meer R.

Source Nutrition and Health Programme, Wageningen Centre for Food Sciences and NIZO Food Research, PO Box 20, 6710 BA Ede, The Netherlands.

Abstract

Diets high in red meat and low in green vegetables are associated with increased colon cancer risk. This association might be partly due to the haem content of red meat. In rats, dietary haem is metabolized in the gut to a cytotoxic factor that increases colonic cytotoxicity and epithelial proliferation. Green vegetables contain chlorophyll, a magnesium porphyrin structurally analogous to haem. We studied whether green vegetables inhibit the unfavourable colonic effects of haem. First, rats were fed a purified control diet or purified diets supplemented with 0.5 mmol haem/kg, spinach (chlorophyll concentration 1.2 mmol/kg) or haem plus spinach (n = 8/group) for 14 days. In a second experiment we also studied a group that received haem plus purified chlorophyll (1.2 mmol/kg). Cytotoxicity of faecal water was determined with a bioassay and colonic epithelial cell proliferation was quantified in vivo by [methyl-(3)H]thymidine incorporation into newly synthesized DNA. Exfoliation of colonocytes was measured as the amount of rat DNA in faeces. In both studies haem increased cytotoxicity of the colonic contents approximately 8-fold and proliferation of the colonocytes almost 2-fold. Spinach or an equimolar amount of chlorophyll supplement in the haem diet inhibited these haem effects completely. Haem clearly inhibited exfoliation of colonocytes, an effect counteracted by spinach and chlorophyll. **Finally, size exclusion chromatography showed that chlorophyll prevented formation of the cytotoxic haem metabolite. We conclude that green vegetables may decrease colon cancer risk because chlorophyll prevents the detrimental, cytotoxic and hyperproliferative colonic effects of dietary haem.**

PMID:15550456 Free full text

GB
Chlorophylls as anticarcinogens (review).

DE
Chlorophylle als Antikarzinogene (Review).

GR
Η χλωροφύλλη ως αντικαρκινική ουσία (επιθεώρηση).

FR
Les chlorophylles en tant que substances anti-cancéreuses (passage en revue).

CZ
Chlorofyly jako antikarcinogeny (studie).

Int J Oncol. 1997 Apr;10(4):721-7.

Chlorophylls as anticarcinogens (review).

Dashwood R.

Abstract

Chlorophylls, chlorins, and other porphyrins have been used clinically for many years, including photodynamic therapy of tumors. More recently, the cancer chemopreventive properties of chlorophylls have come to be recognized. Chlorophylls exhibit anti-mutagenic activity in short-term genotoxicity assays, and protect against various intermediate biomarkers of cancer in vivo. The anticarcinogenic activity of sodium-copper chlorophyllin (CHL), a clinically-used water soluble salt of chlorophyll, has been studied in several species. Collectively, the results from these studies support a chemopreventive role for CHL against aromatic carcinogens (aflatoxins, polycyclic aromatic hydrocarbons, heterocyclic amines) in various target organs of rats, mice, and rainbow trout. In vivo mechanism studies indicate that inhibition is most effective when CHL is administered simultaneously with the carcinogen, thereby allowing direct interaction (molecular complex formation) between CHL and the carcinogen. Studies of post-initiation treatment with CHL have provided conflicting results, with evidence for inhibition or promotion of carcinogenesis. **These findings are discussed in terms of the inhibitory and promotional mechanisms of CHL, the relevance of such mechanisms to natural chlorophylls present in the diet, and the current use of CHL as a health supplement.**

PMID: 21533436