106 Abstracts

211. IN VITRO STUDIES ON THE BIOTRANSFORMATION OF CURCUMINOIDS Simone I. Höhle¹, Erika Pfeiffer^{*1}, Anikó M. Sólyom², Barbara N. Timmermann², and Manfred Metzler^{*1}

¹Institute of Food Chemistry and Toxicology, University of Karlsruhe, Karlsruhe, Germany;
²Arizona Center for Phytomedicine Research, University of Arizona, Arizona, USA

Curcuminoids constitute the yellow pigments of turmeric obtained from the rhizomes of the plant Curcuma longa. They exhibit anti-inflammatory and anti-oxidant activities, and are recently discussed as potential chemopreventive agents. Although in vivo studies have disclosed that the systemic bioavailability of curcumin is low and that its biotransformation may play an important role, information about curcumin metabolites is scarce and inconsistent. We have therefore studied the phase I and phase II metabolism of curcumin and of the related compounds demethoxycurcumin and bisdemethoxycurcumin in microsomes, cytosol and precision-cut tissue slices from rat liver. No oxidative but reductive phase I metabolites were demonstrated in these in vitro systems. Hexahydrocurcuminoids were identified by GC/MS and UV/VIS-spectra as the major products together with dihydro- and tetrahydrocurcuminoids. Liver slices from male and female rats generated the same reductive metabolites but in different quantities. Except for one dihydrocurcuminoid, all of the reductive metabolites formed hydrophilic conjugates. Despite of the known instability of curcuminoids in aqueous systems, the recovery in tissue slices was about 80%, mostly in the form of the more stable metabolites. The extensive metabolism suggests that the pharmacological activity of curcuminoids is mediated, in part, by reductive and conjugated metabolites.

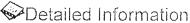
212. THE ANTIOXIDANT-ACTIVATED TRANSCRIPTION FACTOR NRF2 CONTROLS BOTH THE ARE- AND DRE-DEPENDENT INDUCTION OF NAD(P)H:QUINONE OXIDOREDUCTASE: CROSS-INTERACTION BETWEEN NRF2 AND AHR SIGNAL TRANSDUCTION

Qiang Ma, Krista Kinneer, and Yongyi Bi

Receptor Biology Laboratory, Toxicology and Molecular Biology Branch, Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, 1095 Willowdale Rd., Morgantown, WV 26505, USA

NAD(P)H:quinone oxidoreductase (NQOR, DT-diaphorase) is inducible by phenolic antioxidants via ARE-mediated gene transcription, and by 2,3,7,8-tetrachlorodibenzo-p-dioxin through DRE-dependent signal transduction. In this study, we examined the interaction between ARE-and DRE-dependent pathways. Treatment with cycloheximide blocks the basal, tBHQ-inducible, and TCDD-inducible expression of NQOR in hepalc1c7 cells. The inhibition is time and concentration-dependent, requires inhibition of protein synthesis, and occurs at the level of NQOR gene transcription. Examining Nrf2 protein stability reveals that Nrf2 is a labile protein; inhibition of the 26S proteasome mediated protein degradation by MG132 enhances the induction of NQOR by both tBHQ and TCDD. Lastly, analyses of the induction in Nrf2 –/— embryonic fibroblast cells derived from Nrf2 knockout mice demonstrate that Nrf2 is required for basal, tBHQ-inducible, and TCDD-inducible expression of NQOR. These findings reveal that Nrf2 serves as a mater regulator of mouse NQOR gene expression and implicate cross-interaction between ARE- and DRE-dependent pathways in the induction of phase II enzymes.

Doc Express CDC Information Center Information for healthy people



Exit to Main Menu

Return to List

Status

Viewing detailed information for Transaction Number 720274.

Detailed Request Information

Journal Title: Drug metabolism reviews

Volume: 35 Issue: suppl 1 Month: Year: 2003

Inclusive Pages: 106

Article Author: Ma; Kinneer

Article Title: The antioxidant-activated transcription factor Nrf

Item Author: Item Place: Item Publisher: Item Edition:

ISSN/ISBN: 0360-2532

Cited In: Cited Title: Cited Date: Cited Volume: Cited Pages:

Not Wanted After: 08/02/2008 Accept Non English: Yes Accept Alternate Edition: No

Due Date:

Renewals Allowed?:

Max Cost:

Notes Information

Transaction #	Date/Time	Added By	Note
720274	7/3/2007 8:19:38 AM	wdb1	Meeting Abstract

Item Tracking Information

Transaction #	Date/Time	Status	Changed By
720274	7/3/2007 8:19:38 AM	Submitted by Customer	wdb1
720274	7/3/2007 8:19:39 AM	Awaiting Copyright Clearance	wdb1
720274	7/9/2007 7:54:23 AM	Awaiting Request Processing	enq3
720274	7/11/2007 1:32:02 PM	Request in Processing	enq3
720274	7/11/2007 1:32:31 PM	Awaiting Docline Processing	enq3
720274	7/17/2007 11:59:16 AM	Request in Processing	eok3
720274	7/17/2007 12:02:07 PM	Request Sent	eok3
720274	7/18/2007 4:32:22 PM	In Electronic Delivery Processing	kir1
720274	7/24/2007 2:33:51 PM	Delivered to Web	kir1
720274	8/23/2007 7:00:09 PM	Request Finished	ILLiad