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# BOOK OF ABSTRACTS

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# CREDITS

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# Protective mechanism of xanthohumol against genotoxicity of heat generated compounds: PhIP and MeIQx in HepG2 cells

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An important class of heat generated compounds from the diet are heterocyclic aromatic amines (HAAs) classified by IARC as a dietary risk factor for human cancer [1]. Deleterious effects from HAAs can be minimized by the action of specific antioxidant compounds from diet.

Beer is rich in antioxidant compounds, including that xanthohumol (XN), a hop derived prenylflavonoid, characterized as a potential "broad-spectrum" chemo-preventive agent, very efficiently protects against genotoxicity and potential carcinogenicity of the HA 2-amino-3-methylimidazo[4,5-f]quinoline (IQ) [1]. However, studies on other HAs, namely, the most abundant HAs found in the diet, the 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) and 2-amino-3,8 dimethylimidazo[4,5-f]quinoxaline (MeIQx) are scarce [2].

In the present study we evaluated PhIP and MeIQx genotoxicity in the human hepatoma cell line, HepG2, analyzing the induction of DNA strand breaks, with the alkaline comet assay. In addition, changes in gene expression of the main enzymes involved in HAs metabolism were determined, using quantitative real-time PCR.

In HepG2 cells XN completely prevented PhIP and MeIQx induced DNA strand breaks at nanomolar concentrations. With the QRT-PCR gene expression analysis of the main enzymes involved in the biotransformation of HAs in HepG2 cells we found that XN up-regulates the expression of phase I (CYP1A1 and CYP1A2) and phase II (UGT1A1) enzymes. However, gene expression analysis in cells exposed to MeIQx and PhIP in combination with XN revealed that XN mediated up-regulation of UGT1A1 expression may be important mechanism of XN mediated protection against HAAs induced genotoxicity.

Results obtained confirm the evidence that XN displays strong chemopreventive effects against genotoxicity of heat generated compounds, and shed light for the first time the modulator effect of XN on the expression of genes involved in HAs biotransformation.

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