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## MEETING ABSTRACTS

# THE EFFECT OF POTENTIAL CARCINOGEN HARMAN ON SELECTED CYTOCHROME P450 ENZYMES IN RATS

**Eva Klásková [1], Markéta Strakošová [1], Jan Juřica [1,2,3], Ondřej Zendulka [1]**
Presenting author: Eva Klásková (eva.klaskova@med.muni.cz)

[1] Department of Pharmacology, Faculty of Medicine, Masaryk University, Kamenice 753/5, 625 00 Brno, Czechia
[2] Institutional Pharmacy, Masaryk Memorial Cancer Institute, Žlutý kopec 7, 656 53 Brno, Czechia
[3] Department of Pharmacology and Toxicology, Faculty of Pharmacy, Masaryk University, Palackého třída 1946/1, 612 00, Brno, Czechia

Harman is a heterocyclic aromatic amine discovered in coffee, cigarette smoke, roasted meat, or fish (1). However, carcinogenic properties of harmane were proved - partly explained by its interaction via the AhR receptor and induction of CYP1A1 (2). Cytochrome P450 (CYP) enzymes are responsible for the metabolism of 75 % of drugs used in clinical practice (3). Our study aimed to determine the effects of harman on the most important CYP variants in a preclinical experiment.

Harman was administered to Wistar Albino rats intragastrically at the doses of 25, 40, and 64 mg/kg/day for 8 days (control group - 66% propylene-glycol). Microsomes were prepared from liver samples via differential ultracentrifugation. The content of total protein and CYP was measured in isolated microsomes. To evaluate the metabolic activity, the microsomes were incubated in vitro with CYP specific substrates: diclofenac (CYP2C6), dextromethorphan (CYP2D1/2), phenacetin (CYP1A2), testosterone (CYP2A, CYP3A, CYP2C).

Harman significantly decreased the metabolic activity of rat CYP2B, CYP3A, CYP2D1/2 (40 and 64 mg/kg/day) and CYP2C11 (25, 40 and 64 mg/kg/day). The metabolic activity of CYP1A2, CYP2A or CYP2C6 was not affected. Our results did not confirm the potential of harmane to induce liver CYP450 in rat. Nevertheless, significant inhibition of various CYP enzymes was proved. To exclude the risk of serious interactions, the effect of harmane on CYP in humans should be studied.

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*Keywords: Cytochrome P450; harmane; metabolic activity; drug-drug interactions*

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