

## EFFECTS OF SUBACUTE DIBUTYL PHTHALATE EXPOSURE ON UDP-GLUCURONOSYLTRANSFERASE 1A9 EXPRESSION IN RAT LIVER

**Ivana Ivelja, Jelena Vukčević, Nebojša Andrić, Jelena Marković Filipović**

*Department of biology and ecology, Faculty of Science, University of Novi Sad, 21000 Novi Sad, Trg Dositeja Obradovića 3, Serbia  
e-mail: ivana.ivelja@dbe.uns.ac.rs*

### **Abstract**

Di-n-butyl phthalate (DBP) is a plastic additive known for its endocrine-disrupting and reproductive toxicity. DBP is metabolized by UDP-glucuronosyltransferase 1A9 (UGT1A9) in a glucuronidation reaction that takes place in the liver. The aim of our study was to determine whether DBP exposure disturbs UGT1A9 expression in rat hepatic tissue. A total of 24 female *Wistar* rats were divided into four groups and exposed to different DBP doses (100, 500, or 5000 mg/kg diet) over 28 days. Formalin-fixed, paraffin-embedded liver tissue was cut into 5 µm thin sections and immunostained with anti-UGT1A9 antibody. We assessed UGT1A9 levels using ImageJ software, measuring both the optical density (OD) of the immunolabeled UGT1A9, which indicates staining intensity, and the total number of positive cells through the ImageJ plugin IHC profiler. During the sections examination, UGT1A9 was found in abundance in cytoplasm of hepatocytes across all treated groups, as well as, in control group. Interestingly, while the OD remained unaffected by DBP treatment, we found significant changes in the percentage of cells exhibiting high positive and positive UGT1A9 expression. The number of positive cells decreased in the group treated with 500 mg DBP/kg diet while the reduction of high positive cells was observed in all experimental groups. Nevertheless, the total number of positive cells remained consistent. Our results indicate that subacute DBP treatment by changing the percent of high positive and positive immunopositive cells may have the ability to affect UGT1A9 expression.

### **Acknowledgements**

This work was supported by the Provincial Secretariat for Higher Education and Scientific Research of the Autonomous Province of Vojvodina [Grant No. 142-451-3164/2023-01].