DOI: 10.46991/JISEES.2025.SI1.151

Nuclear and Nucleolar Alterations in Rat Hepatocytes Following Combined Mycotoxin Exposure

Anna Karapetyan*, Anna Grigoryan, Tamara Abgaryan

Faculty of Biology, Yerevan State University, Yerevan, Armenia

ABSTRACT

Chronic exposure to multiple foodborne mycotoxins poses a significant health risk, yet the nuclear and nucleolar morphological responses of hepatocytes remain insufficiently characterized. This study investigated the cytomorphometric changes in hepatocyte nuclei and nucleoli of rats administered a combination of three common mycotoxins: aflatoxin B1, ochratoxin A, and zearalenone. Experimental animals were divided into three groups receiving daily contaminated feed for 15, 30, or 60 days. Cytological preparations from liver tissues were analyzed using DNA cytophotometry and morphometric methods to quantify nuclear and nucleolar DNA content and area. Results showed that by day 15, the nuclear and nucleolar area and DNA content had significantly increased compared to controls ($p<0.01$), suggesting enhanced transcriptional activity. This trend continued with reduced intensity by day 30. At day 60, while nuclear size and DNA content slightly decreased, nucleolar indices remained elevated, indicating sustained transcriptional activation. The frequency of mononucleolar and binucleolar hepatocytes increased, along with occasional trinucleolar cells (1–2%). Ploidy analysis revealed the presence of subdiploid nuclei by day 30, representing ~25% of hepatocytes, whereas by day 60, the ploidy profile approached control values, implying a partial restoration. These data indicate that dietary exposure to aflatoxin B1, ochratoxin A, and zearalenone induces early nuclear hypertrophy and nucleolar activation in hepatocytes, followed by potential adaptive responses over time. Understanding such adaptive plasticity may offer insights into hepatocellular resilience under toxic stress.

Keywords: mycotoxins, hepatocyteu, nucleolus, cytomorphometry, genotoxicity, ploidy

References:

1. Magakyan, Yu.A.; Karalova, E.M. Cytophotometry of DNA. **1989**. Moscow.
2. Wang, Y.; Wang, X.; Li, Q. Aflatoxin B_1 in poultry liver: Toxic mechanism. *Toxicon* **2023**, *233*, 107262. DOI:10.1016/j.toxicon.2023.107262
3. Ye, L.; Chen, H.; Wang, J.; Tsim, K.W.K.; Wang, Y.; Shen, X.; Lei, H.; Liu, Y. Aflatoxin B_1–induced liver pyroptosis is mediated by disturbing the gut microbial metabolites: The roles of pipecolic acid and norepinephrine. *J. Hazard. Mater.* **2024**, *474*, 134822. DOI:10.1016/j.jhazmat.2024.134822

*Corresponding Author:

Anna Karapetyan, Chair of Human and Animal Physiology, Faculty of Biology, Yerevan State University, 1 Alex Manoogian str., Yerevan, 0025, Armenia.
Email: annakarapetyan@ysu.am