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PROTECTIVE EFFECTS OF SCHIFF BASE CYCLIC AMINO ACID DERIVATIVES AGAINST MYCOTOXINS GENO- AND CYTOTOXICITY

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The objective of this study was to investigate the protective effects of Schiff base cyclic amino acid derivatives picolinyl-L-phenylalanine (PLP), picolinyl-L-tryptophan (PLT) and nicotinyl-L-tryptophan (NLT) against genotoxicity and cytotoxicity of mycotoxins aflatoxin B1 (AFB1) and ochratoxin A (OTA) in rat blood and bone marrow using comet assay and trypan blue exclusion test in vivo. Additionally molecular-cytogenetic effects of AFB1 on copy number variants (CNVs) was studied in vitro in human leukocytes. Oral administration of AFB1 and OTA at concentration of 25 μg/kg/day over 21 days leads to increased levels of DNA damage but does not show the cytotoxic effect. PLP, NLT and PLT (5 and 10 mg/kg/day, 10 days of administration) demonstrated weak genotoxic activity, with exception for PLT which was non-genotoxic at concentration 5 mg/kg/day. PLP, PLT and NLT had no impact on cell viability. AFB1-induced DNA damage was reduced by 50% after treatment with PLT (10 mg/kg/day). OTA-induced DNA damage was reduced by 34% after treatment with NLT (5 mg/kg/day). It was revealed that genotoxic and protective activities of substances investigated are tissue-dependent. Thus, the PLT demonstrated the lowest genotoxicity and highest protective activity and requires further surveys. Additionally the influence of AFB1 on CNVs was studied in vitro in human leukocytes using parental origin determination fluorescence in situ hybridization. The obtained results indicate that AFB1 can induce CNVs instability in 8p21.2 and 15q11.2 regions which was a consequence of deletions. This first study on influence of AFB1 on CNVs requires further systematic trials in future.