CELLULAR UPTAKE AND CYTOTOXICITY *IN VITRO* AND TOXICITY *IN VIVO* OF DNA AND RNA INTERCALATOR ADAP

Marczi, S.[1]; Stojkovic, R.[2]; Belovari, T.[3]; Šeric, V.[1];
Piantanida, I.[2]; Glavaš-Obrovac, Lj.[1,3]
[1]Clinical Hospital Osijek; [2]Ruder Boškovic Institute, Zagreb;
[3]School of Medicine Osijek, Osijek, Croatia

Introduction: 4-Metyl-2,7-diamino-5,10-diphenyl-4,9-diazapyrenium hydrogensulfate (ADAP) is a potential antitumor and antiparasitic compound because of its DNA and RNA intercalating ability. The **objectives** of this study were to monitor uptake and intracellular distribution of ADAP, to investigate cytotoxic effects on human normal cells and various human, and mouse tumor cell lines, as well as to examine toxicity of ADAP on mouse model. **Results:** The ADAP entered into MIAPaCa-2 cell's cytoplasm in five minutes and into nuclei in sixty minutes after administration. MTT test showed that ADAP (0.1 – 100 μM) strongly inhibited growth of both mouse (FsaR, SCCVII) and human tumor cells (HeLa, Caco-2, HT-29, MIAPaCa-2, HBL, HEp-2, SW620, MCF-7) compared to its weak cytotoxic effects on controls and normal cells (WI38). Toxic effects of single and multiple LD_{10} doses of ADAP were not detected in treated mice (C3Hf/BuZGr) using hematological and clinical-chemical analysis of blood and histopathological examinations. **Conclusions:** Obtained findings indicate antitumor activity of ADAP. Based on DNA intercalating feature of this compound and due to absence of of its toxic effects on mice, we intend to examine antiparasitic activity of ADAP.

Key Words: 4,9-diazapyrenium, DNA intercalation, uptake, cytotoxicity, toxicity