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CYTOTOXICITY AND ACUTE TOXICITY OF A NEW COMPOUND COMPRISING IODINE ADDUCTS IN MICE

Abstract. The cytotoxicity and acute toxicity were studied after oral and intraperitoneal administration of a new compound (R8) comprising iodine adducts to mice. The median cytotoxic concentration (CC_{50}) was determined in the six cell lines, and ranged from 2.1 to 3.9 mg/ml. The median lethal dose of the compound R8 in mice when administered orally was 1000 mg/kg, intraperitoneally – 200 mg/kg. According to the international system of classification for toxicity of chemicals GHS, the compound R8 may be assigned to Toxicity Category IV.

Keywords: iodine, adducts, cytotoxicity, acute toxicity, mice.

Introduction. The prevalence of resistance to colistin and carbapenems in bacteria actually disarms the modern anti-infectious therapy [1]. For this reason, the urgent is the search for new approaches and strategies for the treatment of drug-resistant infections [2]. Currently, iodine is among the few substances that have retained antimicrobial properties [3-6]. The preparations comprising complexes of iodine with organic macromolecules such as povidone-iodine and cadexomers, have become widespread in human and veterinary medicine [5, 7]. In addition, the complexes of iodine with dextran increase expression of IL-1β, IL-8, TNF-α, and VEGF mRNA and do not affect IL-6, IL-10, IL-12 and bFGF mRNA, which indicates the specific immunotropic activity [8]. At the same time, their use is limited to relatively high chemical activity and toxicity of povidone-iodine [7,9]. One of the ways to reduce iodine toxicity lies in its combining with carbohydrates and producing a complex with dextrin (cadexomers). A comparative study on the effect of various complex compounds of iodine on the blood vessels in the chick embryo chorioallantoic membrane showed that povidone-iodine at 1% concentration is characterized by strong irritating activity, whereas cadexomer at a concentration up to 1.8% had a moderate activity with an exposure for 60 minutes [9]. This approach was used in the synthesis of a new stable iodine-containing substance. A new coordination iodine compound (R8) has been synthesized in the Scientific Center for Anti-Infectious Drugs [10]. To carry out initial assessment of toxicity of the compound R8, the cytotoxicity was studied in various mammalian cell cultures, and acute toxicity studies were performed in mice.

Materials and Methods. *Test substance*. Coordination iodine compound with molecular weight of 458.11 and the chemical formula $C_{18}H_{23}I_3N_2O_4$. The substance at 20°C and 101.3 kPa is a solid crystalline gray-green powder with a faint iodine odor. It is readily soluble in water. Immediately before performing assays, the R8 substance was dissolved in sterile water.

Cell cultures. RD - human embryonic rhabdomyosarcoma cells, BHK-21 - newborn Syrian hamster kidney fibroblasts, MDCK - dog kidney cell line, Hep G2 - human hepatocellular carcinoma cells (ATCC). The subinoculated suspension cell cultures: H9 – human cutaneous T-cell lymphoma (ATCC), K562 - human erythroblastoid leukemic cells (ATCC).