

CHEMICAL AND TOXICOLOGICAL RESEARCHES OF CHLOROPYRAMINE IN THE ORGANS OF POISONED RATS

Mamina O. O., Kabachny V. I., Tomarovskaya T. O.
National University of Pharmacy, Kharkiv, Ukraine

Reliability, reproducibility and efficiency developed techniques of drugs isolation from biological material, purification of extracts from biogenic impurities, identification, quantitative determination are confirmed in studying of organs and body fluids of animals in conditions of acute poisoning. The choice of objects for chemical and toxicological analysis (CTA) is based on data on the distribution and localization of these substances in animal organisms.

For approbation of CTA-techniques of chloropyramine in bodies poisoned animals were used male rats, weighing 220–240 g. During the day rats did not receive food before entering the investigational drug. Chloropyramine hydrochloride was administered to rats in the stomach as a suspension in water, containing 218.5 ± 2.5 mg dose (LD_{50} for rats is 920 mg/kg by the oral application). After 5 hours the rats were decapitated.

For the study were taken blood, heart, brain, liver, kidneys, lungs, spleen, stomach and intestines with content. In parallel experiments were used control of the relevant organs. Isolation of a chloropyramine was conducted with application of modified methods of extraction with water, acidified with oxalic acid. For purification of extracts from impurities was used extraction with hexane. Quantitative determination of chloropyramine was performed by the most sensitive GLC/MS method on a gas chromatograph Hewlett Packard HP-6890/5972A with mass selective detector on capillary column Rxi-5MS (5% Diphenyl Methyl Siloxane), nominal length and diameter – 30 m x 250 μ m, nominal thickness phase – 0,25 μ m by method of absolute calibration. For reliable and reproducible results derivatization of extracts from organs and body fluids of poisoned rats was conducted in direction of double methylation.

As a result of preliminary investigations, were found optimal parameters GLC/MS - analysis chloropyramine: parameters of mass selective detector (temperature of ion source and interface lines – 280 °C, for detecting ions - scan mass numbers range – 45-450); parameters of gas chromatograph (carrier gas – helium, gas flow rate of carrier - 1 cm³ / min, the temperature of the evaporator – 280 °C, volume of sample introduction – 1 μ l, chromatography mode – without flow separation); temperature mode (initial temperature – 45 °C, time of chromatography at the initial temperature – 2 min, linear increase in temperature – 10 °C/min, the final temperature of – 280 °C, time of chromatography at the final temperature - 5 min).

Established that the mass spectrum chloropyramine in a standard solution for the retention time 22.814 min has a set of specific ion m/z: 58, 71, 79, 89, 99, 125, 219. According to the chromatograms were conducted searches using libraries of mass spectra "Nist 02 Spectra Lib" and "Wiley 138".

Found that the highest amount of chloropyramine was defined in the kidney, spleen and liver; much less of the substance was found in the intestines with content, stomach with contents, lungs, brain, heart and blood. Obtained results suggest the chloropyramine distribution in organs in acute poisoning animals, that substance is absorbed in the gastrointestinal tract and is localized in the organs of detoxification and excretion. If possible chloropyramine poisoning or mixtures chloropyramine with medicines and narcotics for CTA need to use kidneys, liver, spleen, intestines with content, stomach with contents, blood.