OP12. PHARMACOLOGICAL PROPERTIES AND TECHNOLOGY OF THE DITERPENOID ALKALOID RANACONITINE FROM RHIZOMES WITH ROOTS OF THE *ACONITUM* GENUS PLANTS

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Plants of the *Aconitum* genus contain a significant amount of diterpenoid alkaloids, the main of them is the alkaloid lappaconitine, on the basis of which a new antiarrhythmic drug allapinin was developed. In *A. septentrionale* and *A. sinomontanum* plants alkaloids composition contains a significant amount of ranaconitine. During the production process of the drug substance allapinin from these plants, ranaconitine accumulates as a waste product. Ranaconitin is similar in structure to lappaconitine, unlike the latter, it contains an additional hydroxyl group at C-7.

We have developed a technology for obtaining the alkaloid ranaconitine from the waste of the drug allapinin. Methods for the analysis of the drug substance have been developed, stable samples of the alkaloid ranaconitine of high purity have been obtained.

Our pharmaco-toxicological studies of the alkaloid ranaconitine showed that the $LD_{50}$of ranaconitine in mice *intravenous* was 5.8 mg/kg, intraperitoneally - 11.6 mg/kg, and in rats intravenously - 6.2 mg/kg. Ranaconitine at doses of 0.05-0.5 mg/kg (i.v.) has apronounced antiarrhythmic and antifibrillatory effect in supraventricular and ventricular forms of arrhythmias of various origins and mechanisms of occurrence caused in various animals by aconitine, barium chloride, electrical stimulation of the atria and ventricles, and coronary artery occlusion. The ED_{50} of antiarrhythmic action *i.v.* is 0.05 mg/kg, which is not inferior to lappaconitine. The mechanism of antiarrhythmic action is associated with the blocking of fast sodium channels. On isolated rabbit intestine, ranaconitine at a concentration of 10^{-5}-10^{-4} reduces tone, the amplitude of spontaneous contractions and suppresses spasm caused by barium chloride and aconitine with an EC_{50} of $2 \cdot 10^{-5}$ g/ml.

Thus, the alkaloid ranaconitine is close to lappaconitine in antiarrhythmic activity and toxicity.

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