Kazcaine - A New Original Local Anaesthetic and Antiarrhythmic Agent

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Taking into account the need of medicine in new high-effective anaesthetics and antiarrhythmics the target synthesis of new substances with these kinds of pharmacological activity investigations are carried out with the number of mono- and diazaheterocycles. Among the synthesized variety of compounds 1-(2-ethoxyethyl)-4-ethynyl-4-benzoyloxypiperidine hydrochloride (named by us as *Kazcaine*) attracted our attention by high pharmacological action, low toxicity and simplicity of its synthesis. The synthesis of *Kazcaine* was made in the framework of the co-operation of three organizations: Institute of Chemical Sciences of MS-AS RK, Kazakh State Medicinal University and Novokuznetsk Scientific Research Chemical Pharmaceutical Institute, Russia.

Technological scheme of Kazcaine preparation includes the condensation of 1-(2-ethoxyethyl)-4-oxopiperidine with acetylene in liquid ammonia in the presence of potassium hydroxide in ethynyl alcohol. The interaction of the resulting product with benzoyl chloride leads to 1-(2-ethoxyethyl)-4-ethynyl-4-benzoyloxypiperidine hydrochloride, which was purified by the crystallization from *i*-propanol. This scheme is the base of production technology of *Kazcaine* (substance).

Flame- and explosion-dangerous diethylether was used as a solvent for piperidone-4 addition to the reaction mixture and extraction of formed ethynylpiperidole-4. Therefore, we had decided to use another solvent, which is safer than diethylether. Aminoketone was solved in toluene (m.p. –95.1°C) and added to the reaction mixture, since the reaction is carried out in liquid ammonia (b.p. -77,7^{0}C). After the hydrolysis of potassium ethynylide ethynyl alcohol is separated by extraction with benzene. The use of benzene and toluene leads to improve of the yield of the reaction product by 5-10 % alongside the increasing of safety.

Kazcaine possess local anaesthetical properties, which exceeds by 2-6 times effectiveness and duration of anaesthetical affect of *lidocaine, trimecaine* and *piromecaine* used in medical practice. *Kazcaine* was shown antiarrhythmical activity exceeding one of lidocaine, ethmozine and verapamile at the different models of cordial arrhythmics. The doses of *Kazcaine*, which possess local anaesthetical and antiarrhythmical affect, practically does not influence on breath, cause dose-dependence no less than one of lidocaine definite hipotensive affection, can increase cordial systoles frequency and elevation of cordial ejection (positive inotropic effect). *Kazcaine* has antihistaminic and spasmolytic effectiveness. Moreover, *Kazcaine* has not general toxic affect on functions and morphological construction of vitally important human systems and organs (cordial system, nervous system, liver, kidney, blood creative systems etc.). *Kazcaine* does not display tetragenic, embriotoxic, mutagenic and allergic effects.