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Comparative study of analgesic effect of N-decyltropine (IEM-1556), adenosine and mecamylamine

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Mecamylamine, nonselective antagonist of cholinergic nicotinic receptors after intramuscular (i.m.) and intragastric (i.g.) administration causes maximal analgesia in the tail-flick test in only 30% of the rats, and also reduces time of paw licking in the formalin test of only 30% compared with the control, suggesting relatively weak analgesic activity of mecamylamine in both tests. Adenosine in a dose of 25-30 mg/kg and IEM-1556 (N-decyltropin chloride) in a dose of 1-3 mg/kg after intramuscular and intragastric administration cause maximal analgesic effect in the tail-flick test and formalin test in 80-100% of the rats. Dipyridamole inhibiting reuptake of adenosine, in 9-12 times reduces ED50 of adenosine and IEM-1556, and antagonist of adenosine receptors of 1,3-dipropyl-8-phenylxanthine (DPX) in 3.8-4.5 times increases ED50 of adenosine and IEM-1556 in both tests. The received results, evidence in favor of participation of endogenous adenosine in the mechanism of the analgesic action IEM-1556. Preliminary anesthesia of the gastric mucosa with 1% lidocaine and subdiaphragmatic gastric vagotomy almost equally in 3.7-4.4-fold increase ED50 IEM-1556 and adenosine in both tests, indicating the involvement of vagal afferents in gastric mucosa in the development of analgesic action both IEM-1556, and adenosine. Coincidence of mechanisms of the vagus-stimulating and analgesic action of exogenous adenosine and IEM-1556 demonstrates that IEM-1556 as a probable liberator of endogenous adenosine after system and oral administration in a low dose of 1-3 mg/kg causes development of analgesia as a result of stimulation of adenosine -sensitive vagal afferents in gastric mucosa. In higher doses the analgesic effect of IEM-1556 (which isn't eliminated by DPX, vagotomy and lidocaine) is presumably explained by additional blockade of cholinergic nicotinic receptors in CNS.

Biography

Valery Gmiro is the leading Researcher of Institute of Experimental Medicine (Russia). He has published more than 150 papers in reputed journals. The main scientific interest concerns the Chemistry and Pharmacology of biologically active compounds. He is the USSR State Prize Winner for the investigations in the field of Physiology of Synaptic Transmission. During the last years, he has been working on the problem of the creation of adaptogenic drugs acting through activation of afferent nerves. These drugs were shown to be effective tools to study the mechanisms of transmission of afferent signals and may be of interest in clinical usage.

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