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N-decyltropine (iem-1556) - perspective anti-parkinsonian and antiepileptic drug

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Rotenone-induced parkinsonism in rats is a common animal model of parkinsonism. N-decyltropine (IEM-1556) when administered orally in a dose of 10 mg/kg significantly exceeds the anti-parkinsonian activity of levodopa in a dose of 20 mg/kg, since 3 times more than levodopa reduces the number of rats with severe oligokinesia, and in contrast to levodopa completely eliminate severe catalepsy in rats with rotenone-induced parkinsonism. IEM-1556 can be proposed as a potential alternate for levodopa in Parkinsonism patients' resistant to levodopa.

The corazal kindling is a generally accepted chronic preclinical model of temporal epilepsy in rats. The standard antiepileptic sodium valproate in a dose of 200 mg/kg after oral chronic administration suppresses development of generalized clonic-tonic pentylenetetrazol kindling seizures in 100% of rats, but prevents local clonic kindling seizures only in 57% of rats. In the specified dose sodium valproate by 1.7 times in comparison with control reduces the average severity of pentylenetetrazol kindling seizures. IEM-1556 in a dose of 10 mg/kg has in 1.6 times higher than that of sodium valproate, anticonvulsant activity, as it reduces the average severity of pentylenetetrazol kindling seizures in 2.6 times compared with the control and prevents local clonic kindling seizures in 86% of rats.

IEM-1556 is adenosine liberator and combines central (nicotinic-blocking) and peripheral (vagus-stimulating) components. The principal difference of IEM-1556 from the known CNS agents (morphine, benzodiazepines, etc.) that stimulate vagal afferents is that vagal stimulation caused by morphine causes side effects associated with activation of efferent vagus (bradycardia, bronchospasm). IEM-1556 is a selective blocker of the parasympathetic ganglia, and therefore turns off the pathological morphine-like efferent vagal impulsation, and the afferent branch of the vagus, on the contrary, stimulates. IEM-1556 is the first selective stimulator of vagal afferents, which, in principle, is not capable of causing peripheral efferent vagal complications.

References: [1] Gmiro V.E. et al., Russian Journal of Physiology. V. 103. N 10. P. 1106-1113. 2017 (in Russian). [2] Patent of the Russian Federation No. 2597616.

Biography

Valery Gmiro is the leading researcher of Institute Experimental Medicine (Russia). He has published more than 150 papers in reputed journals. He is the USSR State Prise Winner for the investigations in the field of physiology of synaptic transmission. He was the first to discover selective inhibitors of subtype of AMPA receptors such as IEM-1460, combined antagonists of NMDA- and AMPA glutamate receptors, synthesized and published the results of successful preclinical studies of drugs for the treatment of epilepsy (IEM-2062, IEM-1913), parkinsonism (IEM-2151, IEM-1913), pain (IEM-1556), multiple sclerosis (IEM-1556), and potentiation of the effects of CNS drugs while eliminating their side effects.

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