Phenylephrine potentiates antidepressive and eliminates sedative action of amitriptyline in rats

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Abstract

Porsolt test is a widely used animal model of depression in rats. Amitriptyline is a standard antidepressive drug used in high doses causing strong sedative side effect. Phenylephrine in high dose produced antidepressive effects without side sedative action. The aim of present work was to study the antidepressive and sedative effects of the combination amitriptyline in high and low doses with phenylephrine in threshold noneffective alone doses. Single i. m. injection of amitriptyline in rats in high doses of 10—30 mg/kg causes a weak antidepressive effect because only in 1.3—1.7 times decrease immobilization in Porsolt test. In the specified doses amitriptyline exhibits appreciable sedative effect because in 3—6 times decrease horizontal activity, and also in 2—2.5 times decrease vertical activity of rats in the open field test. Combined single i.m. injection of amitriptyline in a small dose of 3 mg/kg and high dose of 30 mg/kg with phenylephine in threshold, noneffective alone dose of 0.02 mg/kg, causes the maximal antidepressive effect because decreases immobilization in Porsolt test, accordingly, in 3 and 4.6 times, but does not produce side sedative effect in the open field test. The mechanism of potentiation of the antidepressive effect and elimination of the sedative side effect of amitriptyline is based on stimulation of gastric vagal mucosa afferents by phenylephine.

Biography

V E Gmiro is the leading researcher of Institute Experimental Medicine (Russia). He has published more than 100 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. Since couple of years he is 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 use.

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