Pharmacological Profile for the Contribution of NO/cGMP Pathway on Chlorpheniramine Antidepressant-like Effect in Mice Forced Swim Test

Shakiba, S. (Saeed)[1] , Dehpour, A.R. (Ahmad Reza)[2]

1 Experimental Medicine Research Center, Tehran University of Medical Science, Tehran, Iran Department of Pharmacological, School of Medicine, Tehran University of Medical Science, Tehran, Iran

2 Experimental Medicine Research Center, Tehran University of Medical Science, Tehran, Iran

Objective: Chlorpheniramine, a first generation antihistamine, is widely used for allergic reactions. Previous studies showed the interaction between antidepressant activity and nitric oxide and cyclic guanosine monophosphate (NO/cGMP) pathway. Thus, we aimed to assess the possible involvement of NO/cGMP pathway in this effect using forced swim test (FST) in male mice.

Methods: To evaluate the locomotor activity and immobility time we performed open field test (OFT) and FST on each mouse. Chlorpheniramine was administered intraperitoneally (i.p.) (0.1, 0.3, 1, 10 mg/kg) 30 minute before FST. To assess the involvement of NO/cGMP pathway, a non-selective nitric oxide synthase (NOS) inhibitor, L-NAME (10mg/kg, i.p.), a selective inducible NOS (iNOS) inhibitor, animoguanidine (50 mg/kg, i.p.), a selective neural NOS (nNOS) inhibitor, 7-nitroindazole (7-NI, 30mg/kg, i.p.), a NO precursor, L-arginine (750 mg/kg, i.p.) and a selective phosphodiesterase-5 (PDE-5) inhibitor, sildenafil (5mg/kg, i.p.) was co-administered with chlorpheniramine.

Results: chlorpheniramine significantly decreased the immobility time at doses of 1mg/kg ($p < 0.01$) and 10 mg/kg ($p<0.001$). Administration of L-NAME ($p<0.01$) and 7-NI enhanced the anti-immobility activity of chlorpheniramine ($p<0.001$), while animoguanidine did not have any significant effects on the immobility time ($p>0.05$). Moreover, pretreatment with L-arginine ($p<0.01$) and sildenafil ($p<0.001$) significantly reduced the anti-immobility effect of chlorpheniramine. These treatments did not alter the locomotor activity of mice in OFT.

Conclusion: Our results revealed that the antidepressant-like the effect of chlorpheniramine is mediated through inhibition of NO/cGMP pathway.

Keywords: Chlorpheniramine, Nitric oxide, Cyclic Guanosine Monophosphate, Forced swim test, Mice