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Study into a possible mechanism responsible for the antidepressant-like activity of the selective 5-HT_6 receptor antagonist SB-399885 in rats

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Abstract:
The mechanism of the antidepressant-like activity of the selective 5-hydroxytryptamine$_6$ (5-HT_6) receptor antagonist *N*-[3,5-dichloro-2-(methoxy)phenyl]-4-(methoxy)-3-(1-piperazinyl)benzenesulfonamide (SB-399885) was studied in the forced swim test in rats. SB-399885 administered intraperitoneally at a single dose of 10 mg/kg potently shortened the immobility time in rats. That potential antidepressant-like effect of SB-399885 was not modified in animals with a lesion of the 5-HT system produced by *p*-chloroamphetamine (*p*-CA, 2 × 10 mg/kg). The anti-immobility effect of SB-399885 was blocked by the dopamine D_1- and D_2-like receptor antagonists SCH 23390 (0.063 mg/kg) and sulpiride (10 mg/kg), respectively, as well as by the α_2-adrenoceptor antagonist idazoxan (4 mg/kg), but it was not changed by the α_1-adrenoceptor antagonist prazosin (1 mg/kg). Neither sulpiride (10 mg/kg) or idazoxan (4 mg/kg) nor SCH-23390 (0.063 mg/kg) administered jointly with SB-399885 (10 mg/kg) noticeably changed the exploratory locomotor activity of rats evaluated by the open field test. The results described in the present paper indicate that the anti-immobility activity of SB-399885 is not connected with 5-HT innervation, and that D_1- and D_2-like receptors and α_2-adrenoceptors are involved in this action.

Key words:
5-HT_6 receptor antagonist, SCH 23390, sulpiride, idazoxan, prazosin, forced swim test, rats