Abstract:
Preclinical evidence strongly implicates GABA_B receptors in the pathophysiology of several psychiatric disorders including anxiety and depression. In the present study, we investigated the effects of the selective GABA_B receptor agonists baclofen and SKF 97541, the GABA_B receptor positive allosteric modulator CGP 7930 and the GABA_B receptor antagonist SCH 50911 in the modified forced swimming test (FST) and in the elevated zero maze test (EZM), i.e. in animal models predictive of antidepressant and anxiolytic activities, respectively. The classical antidepressant imipramine and the anxiolytic diazepam were employed as control drugs in the FST and in the EZM, respectively.

In the FST, baclofen (0.25 mg/kg), SKF 97541 (0.01–0.05 mg/kg) or CGP 7930 (1–3 mg/kg) and SCH 50911 (1–3 mg/kg) showed antidepressant-like activity, significantly decreasing immobility time; these effects were not related to changes in locomotor activity. The antidepressant effects produced by the GABA_B receptor ligands were compared with that of imipramine (30 mg/kg). In the EZM, CGP 7930 (1 mg/kg) and SCH 50911 (1–3 mg/kg) produced anxiolytic-like effects, significantly increasing time spent in the open areas of the maze; those effects were comparable with the effects of diazepam (1–2 mg/kg).

Our results indicate that differential manipulation of GABA_B receptors can modify behaviors relevant to depression and anxiety. The GABA_B receptor positive allosteric modulator CGP 7930 and the antagonist SCH 50911 show both antidepressant and anxiolytic profile, while the GABA_B receptor agonists (baclofen and SKF 97541) produce effects that are characteristic of antidepressant drugs.

Key words:
GABA_B receptor ligands, elevated zero maze, forced swim test, rats