Evaluating of novel thiazolidinone compounds with hypnotic effects

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Abstract

Introduction: Insomnia is a common problem among the people all over the world. This problem affects both sleep's quantity and quality. Among sedative-hypnotic drugs, barbiturates are more toxic than benzodiazepines. Besides, current benzodiazepines have many side effects like dependence, muscle relaxation, and withdrawal syndrome. Attention to synthesize novel benzodiazepine like derivatives, which have fewer side effects, has been improved. Thiazolidinone derivatives are novel benzodiazepine-like compounds that have all pharmacophores like lipophilic group and aromatic ring for binding to the benzodiazepine receptor (GABA).

Methods and Results: In this research hypnotic effect of two novel thiazolidinone derivatives were evaluated, using pentobarbital-induced loss of righting reflex test. Open field test, was used to evaluate the locomotor activity of the mice in all groups. Male mice in the range of 18-25 g of weight were used in all tests. Moreover, diazepam and flumazenil were used as an agonist and antagonist of GABA-A receptor respectively to indicate that the novel compounds show their effects through interacting with benzodiazepine receptors. Compound SM4 at the dose of 20, 30, and 40 mg/kg (i.p.) and compound SM6 at the dose of 30 and 40 mg/kg (i.p.) increased the sleeping time dose-dependently and showed significant hypnotic effects compared to the control group in the righting reflex test. Also, the sleeping time was decreased by the injection of flumazenil as an antagonist of GABA-A receptor after the injection of each compound. In the open field test, both compounds at the dose of 20, 30, and 40 mg/kg (i.p.) decreased the total distance moved which indicates sedative effect of the novel compounds.

Conclusions: The results indicate that both compounds (SM4 and SM6) have sedative-hypnotic effects, which may be due to an interaction between novel benzodiazepine-like compounds and GABA-A receptor. We recommend further studies to determine the exact mechanism of action and toxicity of the novel compounds.

Key words: Benzodiazepines, Thiazolidinone, Righting reflex test, Open field test, Mice