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# Effects of selective σ receptor ligands on glucocorticoid receptor-mediated gene transcription in LMCAT cells

Grażyna Skuza[1], Zofia Rogóż[1], Magdalena Szymańska[2], Bogusława Budziszewska[2]

[1]Department of Pharmacology, [2]Department of Experimental Neuroendocrinology, Institute of Pharmacology, Polish Academy of Sciences, Smętna 12, PL 31-343 Kraków, Poland

**Correspondence:** Grażyna Skuza, e-mail: skuza@if-pan.krakow.pl

**Abstract:**
It has been shown previously that σ receptor agonists reveal potential antidepressant activity in experimental models. Moreover, some data indicate σ receptor contribution to stress-induced responses (e.g., conditioned fear stress in mice), though the mechanism by which σ ligands can exert their effects, remains unclear. Recent studies have indicated that antidepressant drugs (ADs) inhibit glucocorticoid receptor (GR) function *in vitro*. The aim of the present study was to find out whether σ receptor ligands are able to directly affect GR action. To this end, we evaluated the effect of σ receptor agonists and antagonists on GR function in mouse fibroblast cells (L929) stably transfected with mouse mammary tumor virus-chloramphenicol acetyltransferase (MMTV-CAT) plasmid (LMCAT cells). For this study, we chose SA 4503, PRE 084, DTG (selective $\sigma_1$ or $\sigma_{1/2}$ receptor agonists) and BD 1047, SM 21, rimcazole (σ receptor antagonists). Fluvoxamine, the selective serotonin reuptake inhibitor with $\sigma_{1/2}$ receptor affinity, was used for comparison. It was found that SM 21 (at 1, 3, 10 and 30 μM), BD 1047 (3, 10 and 30 μM) rimcazole (10 μM), and fluvoxamine (at 3, 10 and 30 μM) significantly inhibited corticosterone-induced gene transcription, while DTG, SA 4503 and PRE 084 remained ineffective. Thus, the σ receptor agonists that predominantly showed antidepressant-like activity in behavioral models, were without effect in this *in vitro* model. These results suggest that antidepressant-like activity of σ receptor agonists is independent of corticosterone-induced gene transcription. Therefore, the attenuation of GR function induced by σ receptor antagonists remains ambiguous and requires further study.

**Key words:**
selective σ ligands, glucocorticoid-mediated gene transcription, fibroblast cells