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Effects of some new antiepileptic drugs and progabide on glucocorticoid receptor-mediated gene transcription in LMCAT cells

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Abstract:
Antiepileptic drugs affect endocrine and immune system activity, however, it is not clear whether these effects are indirect, *via* interference with neurotransmitters, membrane receptors and ion channels or maybe independent of neuronal mechanisms. In order to shed more light on this problem, in the present study, we evaluated effects of some new-generation antiepileptic drugs and progabide as a GABA-mimetic on the corticosterone-induced chloramphenicol acetyltransferase (CAT) activity in mouse fibroblast cells stably transfected with mouse mammary tumor virus (MMTV)-CAT plasmid. Treatment of cells with felbamate for five days inhibited in a concentration-dependent manner (3–100 μM) the corticosterone-induced reporter gene transcription. Progabide and loreclezole also inhibited the corticosterone-induced CAT activity, but with lower potency, and significant effects were observed at 10 to 100 μM concentration. Tiagabine and stiripentol showed less potent inhibitory effect on functional activity of glucocorticoid receptors (GR). In contrast, topiramate and lamotrigine (3–100 μM) failed to affect the corticosterone-induced gene transcription. These data indicate that some new antiepileptic drugs and progabide may suppress glucocorticoid effects via the inhibition of GR-mediated gene transcription. In turn, attenuation of GR function could influence antiepileptic drug effect on seizures, neuronal degeneration and immune system activity.

Key words:
antiepileptic drugs, progabide, glucocorticoid-mediated gene transcription, fibroblast cells