Experimental study on the analgesic and anti-seizure activity of newly synthesised hydrazide-hydrazone derivatives bearing 2H-chromene and coumarin scaffold

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Despite the plethora of anti-epileptic drugs (AEDs) available, in one third of patients with epilepsy the seizure control remains poor. Due to the similarity between the mechanisms of epileptogenesis and neuropathic pain, some AEDs have an indication for pain treatment. All of them, however, show adverse effects. There has been a recent strengthening of the specific regulatory restrictions for some AEDs, due to the recognised risk of fetal harm. The aim of the present study is to investigate the anti-convulsive and analgesic activity of newly synthesised hydrazide-hydrazone derivatives bearing 2H-chromene and coumarin scaffold in ICR mice.

Male ICR mice were used (8 per group). Maximal electroshock (MES) test was applied to study anti-convulsive activity. Two tests were used to assess analgesic activity, i.e. the hot plate test and the formalin test.

Antiseizure activity has been observed for p-chlorophenyl, 2-furyl and p-methoxyphenyl substituted derivatives of coumarin-hydrazide/hydrazones (4a, 4c) (ED₅₀ 99.71mg/kg, 81.29 mg/kg respectively, MES test), and for p-chlorophenyl and 2-furyl substituted derivatives of 2H-chromene based hydrazide/hydrazone (8a, 8b) (ED₅₀ 87.63 mg/kg and 12.51 mg/kg, respectively, MES test). During the hot plate test, 8b significantly increased the latency time when compared to the control group (median values 53.5 vs. 25 sec, $p < 0.05$). During the first phase of the formalin test, 4a and 4c significantly shortened the licking time (median values 15 and 25 sec, respectively) when compared to the control group (51 sec, $p < 0.05$). The investigated substances did not demonstrate anti-nociceptive effects during the second phase of the formalin test.

The results from this study indicate that 4a, 4c and 8b possess anti-nociceptive and anti-convulsive effects. The connection between the chemical structure of the investigated compounds and the observed is to be elucidated by ongoing studies. These studies will also reveal certain molecular mechanisms of action.