Anticonvulsant effect of 2-ethylthio-7-methyl-4-(4-methylphenyl) pyrazolo[1,5-a][1,3,5]triazine

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The anticonvulsant activity of some 4-aryl-2-ethylthio-7-methylpyrazolo[1,5-a][1,3,5]triazines was evaluated by two methods namely, maximal electroshock seizure (MES) and subcutaneous pentylenetetrazole (scPTZ) models. Phenytoin (20 mg/Kg) and clonazepam (0,5 mg/Kg) were used as standard drugs for comparison. ICR male mice weighing 25-30 g were used as experimental animals.

The maximal electroshock seizures were elicited by delivering a 60 Hz, 50 mA electrical stimuli via corneal electrodes for 0,1 s. Abolition of tonic hind limb extensor component of convulsion was considered as positive criterion.

The scPTZ test was performed by administering PTZ (80 mg/Kg) dissolved in 0,9% NaCl dissolution. A time of 30 min consequent to the administration of PTZ was used for detection seizures lasting for a period of at least five seconds.

Test compounds were orally administered at a dose of 100 mg/Kg 60 minutes before the administration of PTZ and at 30 and 300 mg/Kg where positive results were observed. The compounds were prepared as suspension in tween 80, propyleneglycol, glicerine and water (5, 10, 10 and 75%)

Among compounds evaluated, only 2-ethylthio-7-methyl-4-(4-methylphenyl) pyrazolo[1,5-a][1,3,5]triazine was effective against MES test (0.7 and 0.9 index protection at doses of 100 and 300 mg/Kg, respectively).

Neurotoxicity was evaluated in the rotarod test. The mice were trained to stay on a rotarod of 3 cm diameter, rotating at 12 rpm for a period of 30 seconds. Control animals were administered with vehicle. The average time of each group at 0, 60 and 120 minutes after administration were compared to establish the toxic effects of the compounds. No differences were observed between the test compounds and the vehicle.