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ACCEPTED MANUSCRIPT

Interactions of aliskiren, a direct renin inhibitor, with antiepileptic drugs in the test of maximal electroshock in mice

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Abstract

Experimental studies showed that certain angiotensin-converting enzyme inhibitors and angiotensin AT_1 receptor antagonists can decrease seizure severity in rodents. Additionally, some of these blockers of the renin-angiotensin system have been documented to enhance the anticonvulsant activity of antiepileptic drugs against maximal electroshock-induced seizures. The aim of the current study was to investigate the effect of aliskiren, a direct renin inhibitor and a novel antihypertensive drug, on the protective action of numerous antiepileptic drugs (carbamazepine, valproate, clonazepam, phenobarbital, oxcarbazepine, lamotrigine, topiramate and pregabalin) in the test of maximal electroshock in mice. The examined drugs were administered intraperitoneally. Aliskiren up to a dose of 75 mg/kg did not affect the threshold for electroconvulsions, however, aliskiren (75 mg/kg) enhanced the anticonvulsant action of clonazepam and valproate. Following aliskiren treatment, a higher brain

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