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Novel indole derivatives as melatonin receptor agonists with anticonvulsant action

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The study presents a series of novel indole derivates synthesized and explored *in vivo* for anticonvulsant activity and neurotoxicity. The pharmacophore model was constructed according to spatial data from available drug structures targeting the MT1 receptor. Obtained model was used for the preliminary selection of potent structures for synthesis. The formation of indole hydrazide–hydrazones was accomplished by the reaction of 5-methoxyindole-3-carboxaldehyde with hydrazides in the presence of ethanol. The compound with p-Cl-phenyl fragment was the most active in the 6Hz test (ED50=13.98 mg.kg-1, PI>21.46), while the derivative with 2-thienyl fragment demonstrated potency both in the MES test (ED50=108.7mg.kg-1, PI>2.76) and in the 6Hz test (ED50=96.36mg.kg-1, PI>3.11), respectively. The compound with 2-furyl fragment showed activity in the 6Hz test (ED50=38.8mg.kg-1, PI>7.89). The effects of the active compounds were higher or comparable to that of melatonin in the MES test (ED50=160.3mg.kg-1, PI>1.87) and in the 6Hz test (ED50=49.76mg.kg-1, PI>6.03), respectively. None of the compounds displayed neurotoxicity in the rota-rod test. The results suggest that the novel indole derivates deserve further evaluation in models of epilepsy and derivatization.

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