# A novel anticonvulsant drug prototype with high inhibition effect on ERK1/2 pathway

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An effective treatment for epilepsy is one of the most important social and medical problems of our time. Up to 30% of cases of epilepsy are characterized by pronounced pharmacoresistance, which requires a search for a new drug. GIZH-298 is a new 4-benzoilpiridine oxime derivative which prevents convulsions and protects 100% of experimental animals against death (90% death in the control group) in a dose-dependent manner in the maximal electroshock seizure test in mice. This compound exhibits higher protection than valproic acid, routinely used anticonvulsant drug. Moreover, GIZH-298 has a pronounced anticonvulsant effect in the chronic cobalt and D,L-homocysteine thiolactone induced epilepsy model which generates seizure activity in various brain structures in rats with a predominant effect in the cortex and hypothalamus. The protection is realized in the decrease of motor manifestations and in elimination of EEG discharges as well as in protection against the death of treated animals. Using the maximal electroshock model in mice, we showed that administration of GIZH-298 at a dose of 60 mg/kg significantly reduces the phosphorylation of extracellular signal-regulated kinases (ERK1/2) and synapsin I, which plays an important role in seizure. This ERK1/2 inhibition effect of GIZH-298 was comparable to that of valproic acid. Exploring neuroblastoma SH-SY5Y cell culture we demonstrated that GIZH-298 also reduces ERK1/2 phosphorylation level in a dose-dependent manner *in vitro*. The data obtained suggest that the mechanism of GIZH-298 protective effect is based on a decrease of the ERK1/2 phosphorylation by direct inhibition of the upstream components of the ERK1/2 cascade. The obtained results enable to conclude that GIZH-298 can be recommended for further study as a promising anticonvulsant drug in humans.
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