

**EXPERIMENTAL STUDY OF ANTICONVULSANT
ACTIVITY OF QUINOLIZIDINE ALKALOIDS**

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Activity. More than 50 million people worldwide suffer from epilepsy. The disease can occur at any age and, if left untreated, can lead to disability and serious neurological and psychological problems. People with epilepsy experience a deterioration in quality of life, often lose their ability to work, and develop depression or anxiety disorders [1].

Quinolizidine alkaloids have different bioavailability properties [2]. For example, citizin has been used in medicine for centuries to treat migraines, insomnia, asthma or cough. It has a chemical structure and mechanism of action similar to nicotine. However, the peripheral effects of citizin (e.g., on the cardiovascular system) are weaker than nicotine. This alkaloid is also able to cross the blood-brain barrier. Cytisine has a nicotine-like effect in stimulating the release of dopamine from striatal synaptosomes [3]. These properties are

very promising for the development of new drugs that can be used to treat diseases of the central nervous system.

Research objective. Bioscreening the anticonvulsant property of quinolizidine alkaloids with anticonvulsant drugs.

Methods and styles. The study used quinolizidine alkaloids of the Academy of Sciences of the Republic of Uzbekistan academician S.Yu.Obtained from the plant quinolizidine alkaloid (*Thermopsis alterniflora*) in the Laboratory of alkaloid chemistry of the Yunusov Institute of plant substance chemistry. White mice weighing 18-22 g were kept in quarantine for 10 days in vivarium conditions before the experiment and then used. The experiments were carried out in accordance with the international recommendations of the European Convention for the protection of vertebrates used in Experimental Research [4]. Animals selected for the experiment were divided into groups, and 6 mice were taken into each group.

The study was seen in thiosemicarbazide and isoniazid models. Of the comparative preparations, carbamazepine (OOO Ukraine) was used in doses of 5-10 mg/kg and Convulex (Gerot Pharmazeutika Vienna, Austria) in doses of 75-100 mg/kg. The causative agents of seizure snoring were introduced into experimental animals by shooting from 60 minutes after the introduction of the studied substances.

Results and discussions: in our experiments, the development of convulsive syndrome was evaluated according to the following parameters: the latent period of the onset of convulsions (seconds/minutes), the number of convulsive movements during the entire observation period, the duration of convulsive syndrome (seconds/minutes), the number of surviving animals in the group, and the dasraja of death.

Cytizin and its derivatives have anticonvulsant effects through complex mechanisms in thiosemicarbazide-induced seizure models. Thiosemicarbazide-induced seizures are characterized by decreased synthesis of GAMK (γ -

aminobutyric acid) in the central nervous system and excessive excitability of the glutamatergic system [5]. This condition promotes seizure activity and leads to long-term neuronal depolarization. Cytizine and its derivatives reduce excitability in this model by modulating neurochemical systems, restoring GAMK concentration and enhancing their effects on receptors, and by thinning the excessive release of glutamate by limiting calcium influx through NMDA receptors. They reduce neuronal damage and have anticonvulsant effects by stabilizing ion channel activity and reducing oxidative stress. These results exceed carbamazepine (45%) and Convulex (43%) activity, and the effect of N-methylcystine hydrobromide is 1.3-1.5 times more effective than other cytisine derivatives: it extended the latent period to 59.7 minutes, reduced the duration of seizures to 9.2 minutes, and increased overall activity to 52.8%.

According to the results obtained, the derivative of citizine hydrobromide can be recommended as a new anticonvulsant drug with GAMK-modulating, Na⁺-channel blocking, and neuroprotective properties.

The isoniazid-induced seizure model is characterized by impaired synthesis and metabolism of GAMK (γ -aminobutyric acid) in the central nervous system. This is due to a decrease in GAMK transferase activity and, as a result, an increase in neuronal excitability. The mechanism of action is mainly due to the activation of the Gamkergetic system, which limits the depolarization of neurons and stabilizes the activity of ion channels [6]. In this isoniazid test, N-methylcystine hydrobromide showed the greatest efficacy. It extended latency to 41.4 ± 2.1 minutes, reduced seizure duration to 0.11 ± 0.7 seconds, and increased survival to 26.6 minutes. These results were 20-25% more than those of carbamazepine and seizures.

Thus, the data obtained show that substances have a normalizing effect on GAMK synthesis or GAMK receptor activity.

Conclusion. Thus, quinolizidine alkaloids have an anticonvulsant effect, which is 15-20% more effective than reference drugs and is recommended as a new promising antiepileptic drug.

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