The American Journal of Medical Sciences and Pharmaceutical Research ISSN 2689-1026 Volume 08 - 2026

Acute Toxicity and Antitoxic Effect of Compositions of Cytisine N-Alkyl (Aryl) Derivatives with Succinic Acid

Latipova Shaxla Bekdurdiyevna
Assistant of the Department of Pharmacology and Clinical Pharmacology, Urgench state medical university, Urgench, Uzbekistan

Azamatov Azizbek Azamat o‘g‘li
PhD, Senior researcher at the Department of Pharmacology and Toxicology of the Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan

Tursunkhodzhaeva Firuza Muratovna
DSc, professor, Head of the Department of Pharmacology and Toxicology of the Institute of Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan

Aytmuratova Urkhiya Kallibekovna
PhD student, Department of Pharmacology and Toxicology, the Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan

Received: 31 Dec 2025 | Received Revised Version: 25 Jan 2026 | Accepted: 12 Feb 2026 | Published: 28 Feb 2026

Volume 08 Issue 02 2026 | Crossref DOI: 10.37547/tajmspr/Volume08Issue02-31

Abstract

In the article, the acute toxicity, resorptive effects, and antitoxic activity of N-alkyl (aryl) derivatives of cytisine and their compositions with succinic acid were studied in experimental animals using models of alcohol- and hypnotic-induced intoxication. The results demonstrated that these compositions possess relatively low acute toxicity and exhibit antitoxic effects under conditions of narcotic intoxication by reducing the duration of sleep.

Keywords: Cytisine derivatives, succinic acid, antitoxic effect, acute toxicity, antihypoxants, narcotic sleep.

Cite This Article: Latipova Shaxla Bekdurdiyevna, Azamatov Azizbek Azamat o‘g‘li, Tursunkhodzhaeva Firuza Muratovna, & Aytmuratova Urkhiya Kallibekovna. (2026). Acute Toxicity and Antitoxic Effect of Compositions of Cytisine N-Alkyl (Aryl) Derivatives with Succinic Acid. The American Journal of Medical Sciences and Pharmaceutical Research, 8(2), 207–210. https://doi.org/10.37547/tajmspr/Volume08Issue02-31

1. Introduction

Intoxication, hypoxia, and disturbances of central nervous system activity represent significant challenges in clinical

medicine and experimental pharmacology. In such conditions, the use of metabolic correctors that support energy metabolism, as well as antihypoxic and neurotropic agents, is considered one of the effective therapeutic approaches [1,2,3].

Succinic acid (succinate) is a natural metabolite involved in mitochondrial energy processes; under hypoxic conditions, it stimulates energy production, reduces metabolic acidosis, and enhances cellular adaptation. Cytisine and its derivatives belong to a group of biologically active compounds that exert effects on the central nervous system [4].

In this context, investigating the toxicological and antitoxic properties of combinations of cytisine derivatives with succinic acid is of considerable scientific and practical importance.

2. Methods

N-derivatives of cytisine were synthesized in the Laboratory of Alkaloid Chemistry at the Institute of the Chemistry of Plant Substances of the Academy of Sciences of the Republic of Uzbekistan by V.I. Vinogradova and Sh.B. Rakhimov.

Acute alcohol intoxication was induced by intraperitoneal administration of a 24% ethanol solution at a dose of 4.8 g/kg [5] to mice weighing 18–22 g. The test substances were administered subcutaneously 10–15 minutes prior to ethanol injection. The effects of the compounds were evaluated based on the duration of the lateral position (narcotic sleep) in the animals, and the time spent in the lateral position was recorded.

The studied compounds were administered orally at the doses indicated in the table, 30 minutes before ethanol administration.

The effect of combinations of N-benzyl derivatives of cytisine with succinic acid (1:1) on the duration of narcotic sleep was evaluated using models of sleep induced by intraperitoneal administration of urethane (1300.0 mg/kg) and sodium ethaminal (50.0 mg/kg) [5].

The obtained results were statistically processed using OriginPro 9.0 (MicroCal Software, Northampton, MA), with calculation of the arithmetic mean, standard error of the mean, and Student's t-test. Differences were considered statistically significant at $p < 0.05$.

3. Results

Acute toxicity and resorptive effect: Following subcutaneous administration of the composition at a dose of 50.0 mg/kg, animals exhibited increased motor activity, respiration rate, heart rate, and heightened responses to external sounds and pain stimuli. No mortality was observed within 24 hours.

At a dose of 100.0 mg/kg, a decrease in motor activity was noted after 15 minutes; however, pain perception and response to external sounds remained normal, and no deaths were recorded.

At a dose of 125.0 mg/kg, 15 minutes after administration, the animals demonstrated decreased motor activity, grooming behavior, partial eyelid closure, mild tremor, and increased sensitivity to external sounds and pain stimuli. One out of six mice died within 37 minutes after administration, while no additional mortality was observed among the remaining animals during the following 24 hours.

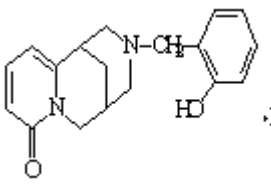
Following administration of the composition at a dose of 140.0 mg/kg, a decrease in motor activity was observed within 10 minutes, accompanied by reduced sensitivity to external sounds and pain stimuli. After 13 minutes, tremor developed, and all animals showed diminished responses to pain and auditory stimuli. Two out of six animals died at this dose. The surviving animals were maintained in the vivarium with adequate access to food and water for 14 days, during which no additional mortality was observed.

After subcutaneous administration at a dose of 170.0 mg/kg, motor activity in the experimental animals decreased within 3–5 minutes, and responses to external sounds and pain stimuli disappeared. After 9 minutes, persistent tremor and a lateral position developed, and within 24 hours, mortality was observed in 5 out of 6 animals.

At a dose of 175.0 mg/kg, animals receiving the composition exhibited decreased motor activity after 5 minutes and reduced perception of external sounds and pain after 12 minutes. Tremor developed, followed by prolonged mild clonic movements. One mouse died after 29 minutes, two mice after 38 minutes, three mice after 54 minutes, four mice after 76 minutes, five mice after 103 minutes, and six mice after 152 minutes. Following subcutaneous administration, the LD_{50} in mice was 150.0 mg/kg (95% CI: 130.4–172.5 mg/kg) [6].

Table 1.

Study of the Acute Toxicity of the N-(2-Hydroxybenzyl) Cytisine Hydrochloride and Succinic Acid Composition (1:1)

№	Compound	Chemical formula	Dose, mg/kg	Animal mortality/ survival	LD_{50}, mg/kg
1	N-(2-hydroxybenzyl) cytisine hydrochloride		50.0 100.0 125.0 140.0 150.0 160.0 170.0 175.0	0/6 0/6 1/5 2/4 3/3 4/2 5/1 6/0	150.0 (130.4±172.5)

Alcohol intoxication model: In the control group, ethanol-induced narcotic sleep lasted on average 107.6 minutes. According to the experimental results, succinic acid at a dose of 10 mg/kg reduced sleep duration by approximately 40%. Cytisine at a dose of 0.1 mg/kg demonstrated an effect of 66.5%. The combination of cytisine with succinic acid exhibited the highest antitoxic efficacy (≈74.6%). The N-(2-hydroxybenzyl) cytisine:succinic acid composition showed an efficacy ranging from 24% to 47%.

Urethane-induced narcotic sleep model: The compositions significantly reduced the duration of narcotic sleep. In particular, the N-(2-hydroxybenzyl) cytisine:succinic acid combination at a dose of 0.1 mg/kg demonstrated an efficacy of approximately 68.7%. At other tested doses, the effectiveness ranged from 50% to 70%.

Sodium ethaminal-induced narcotic sleep: The composition also demonstrated high antitoxic activity in this model. At a dose of 0.5 mg/kg, the efficacy exceeded 75%, and the duration of narcotic sleep was reduced approximately 6.5-fold compared to the control group.

4. Discussion

The obtained results indicate that the combination of cytisine derivatives with succinic acid exerts a complex pharmacological effect. Succinic acid activates mitochondrial energy processes and improves cellular energy supply under hypoxic conditions.

In combination with cytisine derivatives, these effects may enhance neurometabolic protective mechanisms in the central nervous system and reduce the consequences of intoxication. The shortening of narcotic sleep duration confirms the antitoxic potential of this combination.

5. Conclusion

1. The composition of the N-(2-hydroxybenzyl) derivative of cytisine with succinic acid demonstrated moderate acute toxicity, with an LD_{50} of approximately 150 mg/kg.

2. The composition significantly reduced the duration of narcotic sleep under conditions of alcohol intoxication, exhibiting a pronounced antitoxic effect.

3. High efficacy was also observed in models of narcotic sleep induced by urethane and sodium ethaminal.

4. The antihypoxic properties of succinic acid, when

combined with cytisine derivatives, may enhance metabolic protection and potentiate the antitoxic effect.

References

1. Zakusov V.V. Pharmacology of the central nervous system. - Moscow: Meditsina, 2004.
2. Lukyanova L.D. Antihypoxants: Achievements and Prospects. Moscow: Russian Academy of Medical Sciences, 2010.
3. Afanasyev V.V. Metabolic correctors in clinical practice. - St. Petersburg: SpetsLit, 2008.
4. Kulinsky V.I., Olkhovsky I.A. Succinate in the system of metabolic correction of hypoxic conditions // Experimental and clinical pharmacology. - 2011. - No. 4. - P. 3-8.
5. Mironov A.N. Guidelines for conducting preclinical studies of medicinal products. Part one. Moscow: Grif i K, 2012. - 944 p.
6. IBM SPSS Statistics 27 Documentation. https://www.ibm.com/support/pages/ibm-spss-statistics-27-documentation