EURASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
Innovative Academy Research Support Center
IF = 9.2 www.in-academy.uz/index.php/ejmns

EXPERIMENTAL STUDY OF THE ACUTE TOXICITY OF FILM-COATED ETORICOXIB-BASED «ETICOX» TABLETS

Maksudova F.Kh.
Rakhimova M.A.
Tashkent Pharmaceutical Institute, Tashkent.
Tel: (99)5257701; e-mail: muxlisaraximova@gmail.uz
https://doi.org/10.5281/zenodo.22043133

ARTICLE INFO

Received: 24th April 2026
Accepted: 29th April 2026
Online: 30th April 2026

KEYWORDS

Etoricoxib, selective COX-2 inhibitor, non-steroidal anti-inflammatory drugs, acute toxicity, LD_{50}, toxicological safety, reference drug.

ABSTRACT

This study involved a comparative assessment of the acute toxicity of «Eticox» (film-coated tablets in dosages of 60, 90, and 120 mg)—a selective cyclooxygenase-2 (COX-2) inhibitor manufactured by «NOVUGEN PHARMA» LLC (Uzbekistan)—and the reference drug «Arcoxia®» (film-coated tablets in dosages of 60, 90, and 120 mg; Merck Sharp & Dohme, Netherlands). Studies were conducted on white outbred mice to evaluate clinical signs, mortality, and LD_{50} values following a single oral administration of the drugs. The results demonstrated that the LD_{50} values and toxicological parameters of the drug «Eticox» (at doses of 60, 90, and 120 mg) were comparable to the corresponding parameters of the reference drug «Arcoxia®». The results obtained demonstrated that the developed topical preparation exhibits an acute toxicity safety profile comparable to that of the comparator drug.

ЭКСПЕРИМЕНТАЛЬНОЕ ИССЛЕДОВАНИЕ ОСТРОЙ ТОКСИЧНОСТИ ТАБЛЕТОК «ЭТИКОКС», ПОКРЫТЫХ ПЛЁНОЧНОЙ ОБОЛОЧКОЙ, НА ОСНОВЕ ЭТОРИКОКСИБА

Maksudova Ф.Х., Рахимова М.А.
Ташкентский фармацевтический институт, г. Ташкент
Тел.: (99) 525-77-01; e-mail: muxlisaraximova@gmail.com
https://doi.org/10.5281/zenodo.22043133

ARTICLE INFO

Received: 24th April 2026
Accepted: 29th April 2026
Online: 30th April 2026

KEYWORDS

эторикоксиб, селективный ингибитор ЦОГ-2, нестероидные противовоспалительные препараты, острая токсичность, LD_{50}, токсикологическая

ABSTRACT

В настоящем исследовании проведено сравнительное изучение острой токсичности лекарственного препарата «Этикокс» (таблетки, покрытые плёночной оболочкой, 60 мг, 90 мг и 120 мг), являющегося селективным ингибитором циклооксигеназы-2 (ЦОГ-2) и выпускаемого ООО «NOVUGEN PHARMA» (Узбекистан), с референтным препаратом Аркоксиа® (таблетки, покрытые плёночной оболочкой, 60 мг, 90 мг и 120 мг, Merck Sharp & Dohme, Нидерланды).

безопасность, референтный препарат.

Исследования проводились на беспородных белых мышах. Препараты вводили однократно перорально (per os), после чего оценивали клинические признаки интоксикации, летальность животных, а также показатели средней летальной дозы (LD_{50}). По результатам исследования установлено, что значения LD_{50} и токсикологические показатели препарата «Этикокс» в дозировках 60 мг, 90 мг и 120 мг сопоставимы с аналогичными показателями референтного препарата Аркоксиа®. Полученные данные свидетельствуют о том, что разработанный отечественный препарат обладает токсикологическим профилем безопасности при острой токсичности, аналогичным референтному препарату.

Introduction. Etoricoxib (a derivative of 5-chloro-3-(4-methylsulfonylphenyl)-6-methyl-[2,3′-bipyridinyl]) is a selective non-steroidal anti-inflammatory drug (NSAID) in which a 4-methylsulfonylphenyl group is attached to the central ring of the molecule. This functional group ensures the highly selective binding of the drug to the active site of the cyclooxygenase-2 (COX-2) enzyme and serves as a key structural element determining its pharmacological activity [1,2].

Etoricoxib selectively binds to the hydrophilic side channel of the COX-2 enzyme, forming a stable complex and blocking the interaction of arachidonic acid with the enzyme's active site. As a result, prostaglandin biosynthesis is inhibited, leading to a reduction in inflammation, pain, and edema [5, 6].

Its interaction with the COX-1 enzyme is relatively weak and reversible, and it does not significantly affect the synthesis of physiological prostaglandins. Consequently, etoricoxib is less likely to cause adverse effects on the gastrointestinal mucosa and platelet function. Etoricoxib demonstrates approximately 106-fold greater selectivity for COX-2 compared to COX-1—a figure that exceeds even the corresponding value for celecoxib [3, 4].

Scientists from the Tashkent Pharmaceutical Institute, in collaboration with «NOVUGEN PHARMA» LLC, have developed film-coated etoricoxib tablets in 60 mg, 90 mg, and 120 mg dosages under the trade name «Eticox».

This drug is intended for the treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, spondyloarthritis, other inflammatory diseases of the musculoskeletal system, pain syndromes associated with spinal pathology, and acute gout attacks, as well as for the relief of post-traumatic and postoperative inflammation and pain syndromes [4–6].

The aim of this study is to evaluate the acute toxicity of the developed film-coated «Eticox» tablets under experimental conditions and to

determine their toxicological safety profile.

Materials and methods. The acute toxicity of the drug «Eticox»—film-coated etoricoxib tablets at doses of 60, 90, and 120 mg (developed during the initial stage of the study)—was evaluated in experimental toxicology studies. The aim of the study was to determine the drug's safety profile and assess the LD_{50} value.

Experimental animals. The study was conducted on 60 outbred white mice of both sexes weighing 19–21 g.

Comparator drugs. «Arcoxia®» (Merck Sharp & Dohme, Netherlands) was used as the comparator drug in the study, while film-coated «Eticox» tablets («NOVUGEN PHARMA» LLC, Uzbekistan) served as the investigational drug. Prior to the experiment, the animals underwent a 14-day quarantine period. During the study, they were housed in an animal facility under standard conditions: an air temperature of 20–22°C, relative humidity not exceeding 50%, a specific air exchange rate (exhaust-to-supply ratio of 8:10), and a natural day-night light cycle. The mice were kept in standard plastic cages and provided with a standard laboratory diet and drinking water ad libitum [7].

Preparation of aqueous solutions: to study acute toxicity and determine the LD50, a 9% suspension of the reference preparations was prepared (6 tablets + 4 ml H_2O).

Conducting the experiment: The experiment to study the acute toxicity of the compared preparations was conducted in two series [7].

Methodology for studying acute toxicity. The study was conducted in two series. In the first series, outbred white mice were randomly assigned to five groups of six animals each. A 9% suspension of the test drug «Eticox» (film-coated tablets in dosages of 60, 90, and 120 mg; «NOVUGEN PHARMA» LLC, Uzbekistan) was prepared and administered to the animals as a single oral dose. The drug was administered at the following doses:

- Group 1 (n = 6) – 900 mg/kg (0.2 mL);
- Group 2 (n = 6) – 1800 mg/kg (0.4 mL);
- Group 3 (n = 6) – 2250 mg/kg (0.5 mL);
- Group 4 (n = 6) – 2700 mg/kg (0.6 mL);
- Group 5 (n = 6) – 3600 mg/kg (0.8 mL).

In the second series of experiments conducted according to the same protocol, a 9% suspension of the reference drug «Arcoxia®» (film-coated tablets in dosages of 60, 90, and 120 mg; Merck Sharp & Dohme, Netherlands) was used. The drug was administered to the animals orally as a single dose at levels of 900, 1800, 2250, 2700, and 3600 mg/kg (in volumes of 0.2, 0.4, 0.5, 0.6, and 0.8 mL, respectively).

Following drug administration, all animals were monitored under laboratory conditions at hourly intervals during the first 24 hours of the experiment. Assessments included general condition, behavior, locomotor activity and coordination, skeletal muscle tone, presence of convulsions, response to external stimuli, respiratory rate and depth, color of mucous membranes, pupil status, food intake and

body weight, as well as the quantity and consistency of feces [7].

Subsequent observations were conducted daily for 14 days under vivarium conditions. During the observation period, the following parameters were recorded: the animals' general clinical condition, locomotor activity and behavioral characteristics, reactions to painful, auditory, and visual stimuli, respiratory and cardiac function, the condition of the coat and skin, the state of the tail, patterns of urination and defecation, changes in body weight, and other clinical signs indicative of potential toxic effects of the drug.

Throughout the study, all experimental animals were kept under identical vivarium conditions and fed a standard laboratory diet, with free access to drinking water and food.

Based on the results obtained at the end of the study, the median lethal dose (LD_{50}) of the preparations was calculated, and their toxicity class was determined in accordance with the current toxicological classification [7].

Results obtained: The results of the acute toxicity study of the drug «Eticox» (film-coated tablets, 60 mg, 90 mg, and 120 mg; «NOVUGEN PHARMA» LLC, Uzbekistan) are presented in Table 1.

During the observation period, no significant changes in general condition, behavior, or physiological parameters were observed in mice treated with the drug at a dose of 900 mg/kg. The animals remained active and consumed food and water normally; their coat and skin condition remained normal. No animal deaths were recorded during the 14-day observation period [7].

Following administration of the drug at a dose of 1800 mg/kg, some mice exhibited transient lethargy and reduced locomotor activity. Two animals were observed lying on their sides; they died within the first 24 hours of the experiment.

In the remaining mice, the general condition began to recover from the second day onwards; food and water consumption normalized, and no pathological changes or additional deaths were recorded during the subsequent observation period.

At a dose of 2250 mg/kg, lethargy and reduced locomotor activity were observed in the test animals. Three mice developed signs of severe intoxication and died within the first 24 hours. Although a temporary deterioration in the general condition of the surviving animals was observed on the second day, their behavior and physiological parameters normalized starting from the third day. No animal deaths were recorded during the subsequent observation period (Table 1).

At a dose of 2700 mg/kg, signs of severe intoxication were observed in all mice. Five animals died within the first 24 hours. Although the surviving mouse exhibited persistent lethargy on the second and third days, its general condition and physiological parameters normalized starting from the fourth day. No further animal deaths were recorded during the remainder of the observation period (Table 1).

However, at a dose of 3600 mg/kg, a pronounced toxic effect of the drug was observed, and all experimental animals died.

Based on the results obtained, the median lethal dose (LD_{50}) of the drug «Eticox» was 2080 mg/kg (95% confidence interval: 1739–2487 mg/kg).

Similar results were obtained for the drug «Arcoxia®» (Merck Sharp & Dohme, Netherlands), used as a comparator (Table 1). The LD_{50} value for this drug was 2200 mg/kg (95% confidence interval: 1938–2497 mg/kg) [7].

Table 1

Determination of the acute toxicity (LD_{50}) of the preparation «Eticox» 60 mg.

№	«Eticox» tablets, «NOVUGEN PHARMA» LLC (Uzbekistan)				«Arcoxia®» tablets (Merck Sharp and Dohme, Netherlands)			
	Dose		Input method	Result	Dose		Input method	Result
	mg/kg	ml			mg/kg	ml		
1	900	0,2	oral	0/6	900	0,2	Oral	0/6
2	1800	0,4		2/6	1800	0,4		1/6
3	2250	0,5		3/6	2250	0,5		3/6
4	2700	0,6		5/6	2700	0,6		5/6
5	3600	0,8		6/6	3600	0,8		6/6
LD_{50}	2080(1739 ÷ 2487) mg/kg				2200 (1938÷2497) mg/kg			

Results of the acute toxicity study of the drug at a dose of 90 mg.

In the study of the acute toxicity of «Eticox» 90 mg (film-coated tablets; «NOVUGEN PHARMA» LLC, Uzbekistan) and the reference drug «Arcoxia®» 90 mg (Merck Sharp & Dohme, Netherlands), the species and number of experimental animals, the method of preparing the drug suspensions, and the study methodology were the same as those used in the experiments involving the 90 mg dosage. The observation results are generally consistent with the data obtained using the 60 mg dose; differences were observed only in the results for the 2700 mg/kg dose (Group 4) [7, 8, 9].

In mice treated with the drug at a dose of 900 mg/kg, no changes in general condition, behavior, or physiological parameters were observed during the 14-day observation period, nor were any deaths recorded.

At a dose of 1800 mg/kg, transient lethargy and reduced locomotor activity were observed in some animals. Two mice died on the first day of the experiment; however, the general condition of the remaining animals normalized starting from the second day, and no pathological changes were detected during the subsequent observation period.

At a dose of 2250 mg/kg, three mice exhibited signs of severe intoxication and died within the first 24 hours. The clinical condition of the surviving animals normalized starting from the third day, and no further deaths were recorded (Table 2).

Following administration of the drug at a dose of 2700 mg/kg, signs of severe intoxication were observed in all animals. Four mice died within the first 24 hours; although the two remaining animals exhibited lethargy, their general condition and physiological parameters

normalized starting from the fourth day. No further deaths occurred during the observation period (Table 2).

At a dose of 3600 mg/kg, all test animals died as a result of intoxication.

Based on the obtained results, the LD_{50} value of the drug «Eticox» (90 mg) was 2200 mg/kg (95% confidence interval: 1582–3058 mg/kg).

Similar results were obtained for the comparator drug «Arcoxia®» 90 mg (Table 2). The LD_{50} value for this drug was 2100 mg/kg (95% confidence interval: 1567–2814 mg/kg) [7].

Table 2

Determination of the acute toxicity (LD_{50}) of the drug «Eticox» 90 mg.

№	«Eticox» tablets, «NOVUGEN PHARMA» LLC (Uzbekistan)				«Arcoxia®» tablets (Merck Sharp and Dohme, Netherlands)			
	Dose		Input method	Result	Dose		Input method	Result
	mg/kg	ml			mg/kg	ml		
1	900	0,2	oral	0/6	900	0,1	oral	0/6
2	1800	0,4		2/6	1800	0,2		2/6
3	2250	0,5		3/6	2250	0,3		4/6
4	2700	0,6		4/6	2700	0,4		4/6
5	3600	0,8		6/6	3600	0,5		6/6
LD_{50}	2200 (1582 ÷ 3058) mg/kg				2100 (1567÷2814) mg/kg			

Results of the acute toxicity study of the drug at a dose of 120 mg.

A study on the acute toxicity of the drug «Eticox» 120 mg (film-coated tablets; «NOVUGEN PHARMA» LLC, Uzbekistan) and the reference drug «Arcoxia®» 120 mg (Merck Sharp & Dohme, Netherlands) was conducted using the methodology employed in previous experiments. The study was conducted without altering the species or number of experimental animals, the method of preparing the drug suspension, or the administration procedure [7].

No significant changes in general condition, behavior, or physiological parameters were observed in mice treated with the drug at a dose of 900 mg/kg. The animals remained active and consumed food and water normally; no deaths were recorded during the 14-day observation period.

At a dose of 1800 mg/kg, transient lethargy and reduced locomotor activity were observed in some animals. Two mice died within the first 24 hours. The general condition of the surviving animals returned to normal starting from the second day; no pathological changes were detected during the subsequent observation period.

At a dose of 2250 mg/kg, three mice developed signs of severe intoxication and died within the first 24 hours. In the remaining animals, clinical condition and physiological parameters normalized starting from the third day, and no further deaths occurred during the observation period (Table 3).

Following the administration of a 2700 mg/kg dose, signs of severe intoxication were observed in all animals. Five mice died within the first 24 hours. Although the surviving animal remained lethargic on the second and

third days, its general condition and physiological parameters normalized starting from the fourth day. No further deaths occurred during the remainder of the observation period (Table 3).

At a dose of 3600 mg/kg, all test animals died due to intoxication. Based on the results obtained, the LD_{50} value for the preparation «Eticox» (120 mg) was 2100 mg/kg (95% confidence interval: 1750–2520 mg/kg).

Similar results were obtained for the comparator drug «Arcoxia®» at a dose of 120 mg (Table 3). The LD_{50} value for this drug was 2050 mg/kg (95% confidence interval: 1767–2378 mg/kg) [9, 10, 11].

Table 3

Determination of the acute toxicity (LD_{50}) of the preparation «Eticox» (120 mg).

№	«Eticox» tablets, «NOVUGEN PHARMA» LLC (Uzbekistan)				«Arcoxia®» tablets (Merck Sharp and Dohme, Netherlands)			
	Dose		Input method	Result	Dose		Input method	Result
	mg/kg	ml			mg/kg	Ml		
1	900	0,2	oral	0/6	900	0,2	Oral	0/6
2	1800	0,4		2/6	1800	0,4		2/6
3	2250	0,5		3/6	2250	0,5		4/6
4	2700	0,6		5/6	2700	0,6		5/6
5	3600	0,8		6/6	3600	0,8		6/6
LD_{50}	2100 (1750 ÷ 2520) mg/kg				2050 (1767÷2378) mg/kg			

Conclusion: Experimental studies were conducted to evaluate the acute toxicity of the drug «Eticox» (film-coated tablets in dosages of 60 mg, 90 mg, and 120 mg; manufacturer: «NOVUGEN PHARMA» LLC, Uzbekistan). It was determined that the obtained LD_{50} values and the observed signs of toxicity are consistent with data from domestic and international literature regarding etoricoxib.

When compared with the reference drug «Arcoxia®» (film-coated tablets, 60 mg, 90 mg, and 120 mg; Merck Sharp & Dohme, Netherlands), the LD_{50} values for all doses of «Eticox» were comparable, and no significant differences in the toxicological safety profile were observed.

The obtained results confirm that the acute toxicity of the developed drug «Eticox» is comparable to that of the reference drug «Arcoxia®» and demonstrate the toxicological safety of the drug.

References:

1. Е.Д.Семивеличенко, Л.В.Эриванова, Д.Ю.Ивкин, А.С.Ивкина, Г.А.Плиско, Е.И.Елецкая, А.С.Дзюба, А.И.Тюкавин. Сравнительный анализ эффективности обзора по доклиническим и клиническим исследованиям и собственных

исследований как инструмента для регистрации генерика// Санкт-Петербург. Laboratory animals for science - 2019.- С.40-54.
2. Беленький М.Л. Элементы количественной оценки фармакологического эффекта. Л., 1963,- С.81-90.
3. А.Т.Бурбелло., А.В.Шабров. Современные лекарственные средства. Москва, 2007. – С. 284.
4. А.Е. Каратеев. Эторикоксиб — новый селективный ингибитор циклооксигеназы 2// Современная ревматология №2.-2019-С.64-72.
5. Нуридуллаева К.Н., Кариева Ё.С., Халилов Р.М. Разработка промышленной технологии производства инулина из корней одуванчика лекарственного (Taraxacum officinale Wigg.) // Химико-фармацевтический журнал. 2023. Т. 57, №8. С. 67–72. https://doi.org/10.30906/0023-1134 -2023-57-8-67-72
6. Максудова Ф.Х., Кариева Ё.С., Турсунова М.Х. Изучение фармакологи-ческих свойств комбинированного геля диклофенака натрия и бензкето-зона// Инфекция, иммунитет и фармакология. – Ташкент. - 2015. -№5.- С. 160-163.
7. F.X.Maksudova., M.A.Raximova. O'zbekiston Respublikasida qayd etilgan nosteroid yallig'lanishga qarshidori vositalari nomenklaturasining kontent-tahlili//Farmatsiya №2.-2025.-B.58-63.
8. Т.А.Гуськова. Токсикология лекарственных средств. Москва, 2008. – с.27-30.
9. Методические указания по изучению общетоксического действия фармакологических веществ. /В Руководстве по экспериментальному (доклиническому) изучению новых фармакологических веществ. Под общей редакцией члена-корреспондента РАМН, профессора Р. У. ХАБРИЕВА. Издание второе, переработанное и дополненное/. М.: - 2005. - М.: ОАО «Издательство «Медицина», 2005.— С. 41-54.
10. Методические указания по изучению новых нестероидных противовоспалительных препаратов. /В Руководстве по экспериментальному (доклиническому) изучению новых фармакологических веществ Под общей редакцией члена-корреспондента РАМН, профессора Р. У. ХАБРИЕВА. Издание второе, переработанное и дополненное/. М.: - 2005. - М: ОАО «Издательство «Медицина», 2005.— С. 695 – 710
11. Основные методы статистической обработки результатов фарма кологических экспериментов. /В Руководстве по экспериментальному (доклиническому) изучению новых фармакологических веществ Под общей редакцией члена-корреспондента РАМН, профессора Р. У. ХАБРИЕВА. Издание второе, переработанное и дополненное/. М.: - 2005. - М: ОАО «Издательство «Медицина», 2005.— С. 763-774.
1. А.В.Стефанова Доклинические исследования лекарственных средств., Киев 2002. – с. 91.