

Evaluation Of The Anti-Inflammatory Activity Of 1,4-Disubstituted 1h-1,2,3-Triazole Derivatives In Experimental Models

Aytmuratova Urkhiya Kallibekovna¹, Azamatov Azizbek Azamat o'g'li², Tursunkhodzhaeva Firuza Muratovna³, Ashurmetov Rustam Isayevich⁴, Aytbaeva Aygul Baxtiyarovna⁵, Ortikov Ilhomjon Sobirovich⁶, Jalilov Fazliddin Sodiqovich⁷

¹PhD doctoral student of the Department of Pharmacology and Toxicology of the Institute Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, <https://orcid.org/0009-0005-3565-8739> e-mail:

urxiyaaytmuratova@mail.ru

²PhD, 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, <https://orcid.org/0000-0001-5827-2103> e-mail: azizbek.azamatov@bk.ru

³DSc, 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, <https://orcid.org/0000-0002-8404-0952> e-mail: ftm40438@gmail.com

⁴Senior 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, <https://orcid.org/0009-0000-2991-6926> e-mail: rustam_5656@mail.ru

⁵PhD doctoral student of the Department of Pharmacology and Toxicology of the Institute Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, e-mail: aygulaytbaeva21@gmail.com

⁶Alfraganus University, Tashkent, Uzbekistan PhD, Docent of the Department of Pharmacology and Chemistry <https://orcid.org/0000-0003-1961-8639> ortikovilxomjon@gmail.com

⁷Alfraganus University, Tashkent, Uzbekistan DSc, professor, Head of the Department of Pharmacology and Chemistry <https://orcid.org/0000-0001-7379-8445> dr.fazliddin@gmail.com

*Corresponding author: E-mail: azizbek.azamatov@bk.ru

ABSTRACT

The anti-inflammatory activity of 1,4-disubstituted 1H-1,2,3-triazole derivatives was studied in the «formalin-induced edema», «carrageenan-induced edema», and «serotonin-induced aseptic arthritis» models. In these models, ketoprofen, used as a reference drug at a dose of 10.0 mg/kg, demonstrated anti-inflammatory activity of 73.4%, 75%, and 75.8%, respectively, while sodium diclofenac showed activity of 66.3%, 67.7%, and 70.3%. Among the studied compounds, substance 1 demonstrated anti-inflammatory activity at a dose of 50.0 mg/kg in the «formalin-induced edema» and «carrageenan-induced edema» models with an effect of 78%, while in the «serotonin-induced aseptic arthritis» model, at a dose of 150.0 mg/kg, it showed an effect of 79.8%. The experiment revealed that this compound has a significant impact on the dynamics of inflammatory and anti-inflammatory cytokines in the blood serum, surpassing the corresponding results of the reference drugs.

KEYWORDS: 1,4-disubstituted 1H-1,2,3-triazole derivatives, formalin-induced edema model, carrageenan-induced edema model, serotonin-induced aseptic arthritis model.

How to Cite: Aytmuratova Urkhiya Kallibekovna, Azamatov Azizbek Azamat o'g'li, Tursunkhodzhaeva Firuza Muratovna, Ashurmetov Rustam Isayevich, Aytbaeva Aygul Baxtiyarovna, Ortikov Ilhomjon Sobirovich, Jalilov Fazliddin Sodiqovich, (2025) Evaluation Of The Anti-Inflammatory Activity Of 1,4-Disubstituted 1h-1,2,3-Triazole Derivatives In Experimental Models, Vascular and Endovascular Review, Vol.8, No.7s, 111-116.

INTRODUCTION

Triazoles are compounds that contain a five-membered ring in their chemical structure, consisting of three nitrogen atoms and two carbon atoms. These compounds have garnered significant attention in the pharmaceutical industry due to their diverse pharmacological activity (Mohammed M. Matin et.al. 2022)¹⁰. Studies conducted by scientists worldwide have demonstrated that triazoles exhibit antimicrobial (Razaq, Ali & Nahi. Et.al. 2021)¹⁴, antifungal (Dong, Y et.al. 2023)⁵, antiviral (Kozan, A. A. Et.al. 2023)⁹, anticancer (Sujana Oggu et.al. 2023., Belay, Y et.al. 2024)^{17,3}, and anti-inflammatory (Teresa Glomb et.al. 2024)¹⁸ activities. One of the notable biological activities of triazoles is their antifungal activity. They inhibit the growth and replication of fungal cells by interfering with the synthesis of ergosterol, an essential structural component of fungal cell membranes (Veselov .B. 2015)¹⁹. Triazoles also have great potential as antiviral agents. They prevent the replication and spread of viruses by targeting specific enzymes and proteins in the viral cell (Smurova Natalia V et.al. 2021)¹⁵. Some triazole derivatives have demonstrated the ability to inhibit the growth of tumor cells and enhance the process of apoptosis, making them promising candidates for cancer treatment in the future (Mosa Alsehlhi. Et.al. 2025)¹¹. The anti-inflammatory activity of triazole derivatives is being studied as inhibitors of the enzyme cyclooxygenase-2 (COX-2). Their anti-inflammatory action is based on the inhibition of COX-2, which, from arachidonic acid, promotes the synthesis of inflammation mediators such as prostaglandins, bradykinin, and serotonin (Bushra Khan et.al. 2021)⁴. Overall, the universal nature of triazoles makes them a promising class of compounds for

pharmaceutical research and drug development.

The aim of the study is to investigate the anti-inflammatory activity of 1,4-disubstituted 1H-1,2,3-triazole derivatives using inflammation models.

MATERIALS AND METHODS.

The study focused on nine derivatives of 1,4-disubstituted 1H-1,2,3-triazole synthesized at the Department of Organic Synthesis of the Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan.

The experiments were conducted on male rats weighing 200–220 g, housed under standard vivarium conditions (controlled temperature and humidity, with free access to food and water).

An acute inflammatory response was induced by subplantar injection of phlogogenic agents into the right hind paw of the rats: 0.1 ml of 2% formalin, 0.1 ml of 0.1% carrageenan, and 0.1 ml of 1% serotonin.

Subplantar injection of phlogogenic agents into the rat paw causes cellular damage at the injection site, leading to the release of endogenous inflammatory mediators (histamine, serotonin, prostaglandins, bradykinin), which trigger proliferative inflammation. Such tissue damage in the rat's paw caused by phlogogenic agents leads to the development of chronic and localized inflammation. The maximum development of swelling in the paws is observed 180 minutes after the administration of the phlogogenic agent to the animals (Mironov A.N. 2012)¹².

Before the start of the experiment, all the animals underwent a 14-day adaptation period. The experimental groups were formed using a random selection method. The experimental animals were divided into the following groups: control group, comparison group, and experimental group. Six animals were selected for each group. The test substances were administered intragastrically in doses of 25.0, 50.0, 100.0, 150.0, and 200.0 mg/kg 60 minutes before the administration of the phlogogenic agent. In the conducted experiments, an aqueous solution of Tween-80 (Sigma Aldrich, USA) was used as a solvent for the test substances. The comparison drugs, Ketoprofen (Russia), were administered orally in doses of 1.0-5.0-10.0 mg/kg, and Sodium Diclofenac (Russia) was administered in doses of 8.0-10.0 mg/kg. The degree of swelling was measured using the oncometric method, based on changes in the volume of the paws of the experimental animals (Novikov V.E. et.al. 2015)¹³. The volume of the animals' paws was measured before the administration of the inflammatory agent and 180 minutes after its administration. The acute inflammatory response begins with the activation of tissue macrophages and the secretion of inflammatory cytokines, particularly tumor necrosis factor (TNF- α) and IL-6, which lead to multiple local and systemic changes in the development of the acute inflammatory response. However, some cytokines have an anti-inflammatory effect, one of which is IL-4. Interleukin-4 performs a number of important physiological functions: it is an anti-inflammatory cytokine, inhibits the synthesis of IL-1, IL-6, IL-8, and TNF- α ; blocks the activity of T cells and macrophages; regulates the synthesis of immunoglobulins (Invention patent No. IAP 7858 derivatives of 1H-1,2,3-triazole with analgesic and anti-inflammatory effects. 2024)⁸.

The acute inflammatory process was modeled by subcutaneously injecting 0.1 ml of a 2% formalin solution into the thigh area of male rats (n=306) weighing 200-220 g. The experimental animals were divided into 3 groups: Group I (control group, n=6) received 0.2 ml of a physiological sodium chloride solution orally for 7 days after the acute inflammatory process developed; Group II (comparison group, n=30) received Ketoprofen orally in doses of 1.0-5.0-10.0 mg/kg and Sodium Diclofenac in doses of 8.0-10.0 mg/kg for 7 days. Group III (experimental group, n=270) received the test substances orally in doses of 25.0, 50.0, 100.0, 150.0, and 200.0 mg/kg for 7 days. To determine the levels of major cytokines in the bodies of the experimental animals after modeling the acute inflammatory process, blood samples were taken before the start of the experiment and 7 days after its initiation.

The animal study was conducted by the International Convention for the Protection of Vertebrate Animals used for Experimental and Scientific Purposes (Strasbourg, 1986) (European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, ETS №123, Strasbourg 1986)⁶, and the ICPS Institutional Scientific Board approved the protocol based on an annual working plan of the Pharmacology and Toxicology Department (Protocol No. 1 from January 17 in 2024).

The concentration of major cytokines in the serum of rats, namely: interleukin-4, interleukin-6, and TNF- α , was determined by enzyme-linked immunosorbent assay (ELISA) on the Mindray MR-96a immunoassay analyzer (China) using reagent kits from Vector-Best LLC (Russia) according to the manufacturer's instructions. Data were shown as mean $\pm$ SD of different groups. The data of this study were statistically analyzed using OriginPro 9.0 (MicroCal Software, Northampton, MA). The $p < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION:

When studying the anti-inflammatory activity of 1,4-disubstituted derivatives of 1H-1,2,3-triazole in the «**formalin-induced edema**», «**carrageenan-induced edema**», and «**serotonin-induced aseptic arthritis**» models, the reference drugs demonstrated the following anti-inflammatory activity compared to the control group: ketoprofen at a dose of 10.0 mg/kg showed 73.4%, 75%, and 75.8% respectively, and sodium diclofenac showed 66.3%, 67.7%, and 70.3% respectively. Among the test substances, compound 1 demonstrated anti-inflammatory activity in the «**formalin-induced edema**» and «**carrageenan-induced edema**» models at a dose of 50.0 mg/kg with 78%, and in the «**serotonin-induced aseptic arthritis**» model at a dose of 150.0 mg/kg with

79.8%. Compounds 2, 3, 7, and 8 exhibited anti-inflammatory activity above 50% in all inflammation models at a dose of 150.0 mg/kg (Table 1).

Table 1 Anti-inflammatory activity of 1,4-disubstituted 1H-1,2,3-triazoles and comparison drugs ketoprofen and sodium diclofenac (n=6)

№	Compound	Dose, mg/kg	Formalin-induced paw edema model		Carrageenan-induced paw edema model		Serotonin-induced aseptic arthritis model	
			Percentage (%) increase in paw volume relative to baseline	Effect %	Percentage (%) increase in paw volume relative to baseline	Effect %	Percentage (%) increase in paw volume relative to baseline	Effect %
1	Intact	Phys. solution (Saline solution) 0.2 ml	74.3±0.63	-	71.4±0.54	-	86.3±0.78	-
2	Ketoprofen	1.0	51.7±0.41	30.4	49.6±0.31	30.5	58.3±0.62	32.5
		5.0	31.5±0.38	57.6	31.7±0.26	55.7	35.0±0.46	59.5
		10.0	19.7±0.54	73.4	25.0±0.23	75.0	20.9±0.25	75.8
3	Sodium Diclofenac	8.0	26.1±0.25	64.8	29.7±0.34	58.5	25.3±0.34	66.3
		10.0	25.0±0.49	66.3	23.1±0.39	67.7	29.1±0.38	70.3
4	1	25.0	23.4±0.68	68.5	23.8±0.25	66.7	29.7±0.35	65.6
		50.0	16.3±0.34	78.0	16.3±0.33	78.0	24.3±0.43	71.9
		100.0	23.8±0.42	67.9	23.8±0.26	67.9	21.0±0.27	75.7
		150.0	30.0±0.37	59.6	30.0±0.35	59.6	17.5±0.24	79.8
		200.0	31.1±0.52	58.2	29.8±0.37	58.3	20.2±0.31	76.6
5	2	25.0	53.6±0.43	27.8	45.1±0.42	36.8	54.6±0.43	36.7
		50.0	44.7±0.24	39.8	38.4±0.48	46.2	48.1±0.55	44.2
		100.0	43.7±0.35	41.1	37.5±0.33	47.4	45.4±0.47	47.3
		150.0	34.0±0.39	54.2	35.7±0.27	50.0	42.1±0.42	51.2
		200.0	37.5±0.48	49.5	36.6±0.46	48.7	45.0±0.38	47.8
6	3	25.0	47.6±0.51	35.9	47.5±0.52	33.4	52.5±0.54	39.1
		50.0	45.2±0.40	39.1	40.9±0.43	42.7	48.6±0.59	43.6
		100.0	38.2±0.33	48.5	38.0±0.39	46.7	46.6±0.51	46.0
		150.0	35.8±0.38	51.8	34.0±0.27	52.3	40.2±0.47	53.4
		200.0	41.3±0.45	44.4	40.4±0.34	43.4	46.8±0.32	45.7
7	4	25.0	42.3±0.57	43.6	43.6±0.46	38.9	56.0±0.68	35.1
		50.0	38.8±0.42	47.7	42.1±0.32	41.0	50.6±0.54	41.3
		100.0	37.8±0.35	49.1	35.5±0.44	50.2	46.8±0.61	45.7
		150.0	38.3±0.29	48.4	41.9±0.49	41.3	43.6±0.47	49.4
		200.0	40.6±0.64	45.3	43.0±0.51	39.7	52.6±0.34	39.0
8	5	25.0	44.8±0.53	39.7	46.3±0.36	35.1	58.6±0.49	32.0
		50.0	42.6±0.46	42.6	43.3±0.51	39.3	50.6±0.61	41.3
		100.0	36.9±0.57	50.3	36.9±0.27	48.3	48.6±0.40	43.6
		150.0	37.6±0.46	49.3	40.4±0.46	43.4	46.7±0.37	45.8
		200.0	44.3±0.37	40.3	44.4±0.31	37.8	47.5±0.49	44.9
9	6	25.0	46.6±0.52	37.2	47.1±0.44	34.0	56.0±0.66	35.1
		50.0	44.0±0.49	40.7	45.8±0.53	35.8	52.1±0.52	39.6
		100.0	40.2±0.55	45.8	37.0±0.35	48.1	46.8±0.37	45.7
		150.0	38.5±0.37	48.1	31.5±0.28	55.8	44.4±0.49	48.5
		200.0	44.4±0.48	40.2	39.7±0.41	44.3	55.4±0.46	35.8
10	7	25.0	45.6±0.59	38.6	48.8±0.56	31.6	57.1±0.61	33.8
		50.0	44.1±0.54	40.6	42.6±0.47	40.3	53.4±0.58	38.1
		100.0	41.9±0.46	43.6	38.3±0.38	46.3	46.1±0.45	46.5
		150.0	37.0±0.43	50.2	35.0±0.43	50.9	43.2±0.37	49.9
		200.0	39.7±0.51	46.5	36.4±0.29	49.0	46.0±0.54	46.6
11	8	25.0	45.0±0.64	39.4	46.3±0.51	35.1	53.7±0.39	37.7
		50.0	39.7±0.57	46.5	40.4±0.48	43.4	47.9±0.52	44.4
		100.0	37.8±0.50	49.1	37.6±0.34	47.3	44.7±0.43	48.2
		150.0	32.5±0.48	56.2	36.5±0.46	48.8	42.2±0.49	51.1
		200.0	44.4±0.61	40.2	37.9±0.37	46.9	43.7±0.41	49.3

12	9	25.0	50.6±0.56	31.8	50.6±0.42	29.1	52.7±0.53	38.9
		50.0	44.3±0.53	40.3	44.1±0.54	38.2	49.3±0.38	42.8
		100.0	40.2±0.39	45.8	38.4±0.26	46.2	45.2±0.47	47.6
		150.0	38.0±0.47	48.8	37.5±0.35	47.4	43.4±0.52	49.7
		200.0	41.8±0.52	43.7	40.9±0.47	42.7	45.6±0.49	47.1

Note: $P=0.05$ compared to the control group

The dynamics of cytokines in the serum of experimental animals during the acute inflammatory process were studied, and the following results were obtained (Table 2).

Table 2 Cytokine profile (interleukin-4, interleukin-6, and TNF- α) of rat serum during acute inflammation (n=6)

Nº	Drug	Dose, mg/kg	IL-4	IL-6	TNF- α
1	Intact	Phys. solution (Saline solution) 0.2 ml	0.16(0.45±0.75)	0.31(0.29±0.33)	3.10(2.93±3.26)
2	Ketoprofen	1.0	0.35(0.31±0.39)	0.13(0.11±0.15)	2.09(2.08±2.11)
		5.0	0.39(0.34±0.43)	0.12(0.11±0.15)	1.13(1.11±1.15)
		10.0	0.45(0.42±0.49)	0.09(0.07±0.11)	0.98(0.93±1.03)
3	Sodium Diclofenac	8.0	0.37(0.33±0.41)	0.11(0.14±0.17)	1.07(1.12±1.19)
		10.0	0.42(0.39±0.44)	0.08(0.04±0.12)	0.98(0.85±1.12)
4	1	25.0	0.41(0.38±0.44)	0.08(0.04±0.11)	1.02(0.97±1.07)
		50.0	0.52(0.49±0.55)	0.06(0.03±0.08)	0.96(0.88±1.04)
		100.0	0.44(0.40±0.48)	0.10(0.07±0.13)	1.09(1.05±1.13)
		150.0	0.37(0.33±0.40)	0.13(0.09±0.16)	1.14(1.10±1.18)
		200.0	0.31(0.27±0.36)	0.15(0.11±0.18)	1.15(1.13±1.19)
5	2	25.0	0.18(0.16±0.20)	0.23(0.19±0.27)	1.25(1.22±1.28)
		50.0	0.20(0.18±0.22)	0.21(0.18±0.24)	1.23(1.20±1.26)
		100.0	0.23(0.21±0.25)	0.19(0.17±0.21)	1.21(1.19±1.23)
		150.0	0.27(0.24±0.30)	0.16(0.14±0.18)	1.17(1.15±1.19)
		200.0	0.25(0.23±0.27)	0.17(0.13±0.21)	1.19(1.16±1.22)
6	3	25.0	0.19(0.17±0.21)	0.24(0.22±0.26)	1.33(1.30±1.36)
		50.0	0.21(0.18±0.24)	0.23(0.20±0.26)	1.31(1.29±1.33)
		100.0	0.25(0.22±0.28)	0.20(0.18±0.22)	1.26(1.24±1.28)
		150.0	0.26(0.24±0.28)	0.18(0.15±0.21)	1.24(1.21±1.27)
		200.0	0.23(0.21±0.25)	0.21(0.19±0.23)	1.28(1.25±1.31)
7	4	25.0	0.21(0.19±0.23)	0.25(0.23±0.27)	1.34(1.31±1.37)
		50.0	0.24(0.21±0.27)	0.22(0.20±0.24)	1.32(1.31±1.34)
		100.0	0.25(0.21±0.29)	0.20(0.18±0.22)	1.29(1.26±1.32)
		150.0	0.23(0.20±0.26)	0.23(0.20±0.26)	1.30(1.27±1.33)
		200.0	0.21(0.19±0.23)	0.26(0.23±0.29)	1.36(1.33±1.39)
8	5	25.0	0.20(0.17±0.23)	0.24(0.21±0.27)	1.22(1.20±1.24)
		50.0	0.24(0.20±0.28)	0.20(0.17±0.23)	1.19(1.16±1.22)
		100.0	0.27(0.23±0.31)	0.14(0.12±0.16)	1.14(1.12±1.16)
		150.0	0.25(0.23±0.27)	0.18(0.15±0.21)	1.17(1.13±1.20)
		200.0	0.23(0.20±0.26)	0.22(0.20±0.24)	1.23(1.20±1.26)
9	6	25.0	0.26(0.23±0.29)	0.23(0.20±0.26)	1.22(1.20±1.24)
		50.0	0.29(0.27±0.31)	0.20(0.17±0.23)	1.18(1.15±1.21)
		100.0	0.31(0.28±0.34)	0.18(0.16±0.20)	1.15(1.13±1.17)
		150.0	0.34(0.31±0.37)	0.14(0.11±0.17)	1.12(1.10±1.14)
		200.0	0.28(0.25±0.31)	0.19(0.17±0.21)	1.17(1.14±1.20)
10	7	25.0	0.25(0.23±0.27)	0.26(0.23±0.29)	1.24(1.21±1.27)
		50.0	0.28(0.25±0.31)	0.21(0.19±0.23)	1.21(1.19±1.23)
		100.0	0.30(0.27±0.33)	0.19(0.16±0.22)	1.17(1.14±1.20)
		150.0	0.34(0.31±0.37)	0.15(0.13±0.17)	1.14(1.11±1.17)
		200.0	0.32(0.30±0.34)	0.17(0.14±0.20)	1.16(1.14±1.18)
11	8	25.0	0.27(0.24±0.30)	0.24(0.21±0.27)	1.23(1.20±1.26)
		50.0	0.33(0.30±0.36)	0.18(0.15±0.21)	1.19(1.17±1.21)
		100.0	0.35(0.32±0.38)	0.14(0.12±0.16)	1.16(1.14±1.18)
		150.0	0.39(0.35±0.43)	0.11(0.09±0.13)	1.12(1.10±1.14)
		200.0	0.36(0.33±0.39)	0.13(0.11±0.15)	1.14(1.12±1.16)
12	9	25.0	0.24(0.22±0.26)	0.27(0.25±0.29)	1.25(1.21±1.29)
		50.0	0.27(0.24±0.30)	0.23(0.20±0.26)	1.21(1.19±1.23)

	100.0	0.31(0.28±0.34)	0.18(0.16±0.21)	1.18(1.15±1.21)
	150.0	0.34(0.31±0.37)	0.15(0.12±0.18)	1.15(1.13±1.18)
	200.0	0.29(0.27±0.31)	0.19(0.17±0.21)	1.20(1.18±1.22)

Note: $P=0.05$ compared to the control group

According to the results of the experiment, among the compounds studied, substance 1 demonstrated a more pronounced effect on cytokine dynamics (IL-4, IL-6, TNF- α) compared to the reference drugs. Relative to the control group, Ketoprofen at a dose of 10.0 mg/kg increased the IL-4 level by 2.81 times, Sodium Diclofenac at a dose of 8.0 mg/kg increased it by 2.62 times, and substance 1 increased it by 3.25 times. The IL-6 level decreased with Ketoprofen at a dose of 10.0 mg/kg by 3.44 times, Sodium Diclofenac at a dose of 8.0 mg/kg by 3.87 times, and substance 1 by 5.16 times. The TNF- α level decreased with Ketoprofen at a dose of 10.0 mg/kg by 3.16 times, Sodium Diclofenac at a dose of 8.0 mg/kg by 3.16 times, and substance 1 by 3.22 times.

In our previous studies, it was established that the derivatives of 1,4-disubstituted 1H-1,2,3-triazoles belong to the IV toxicity group according to GOST 12.1 007-76 (Interstate standard occupational safety standards system harmful substances classification and general safety requirements GOST 12.1.007-76. Moscow Standartinform, 2007).⁷ and the V class of low-toxic substances according to A.V. Stefanov's classification (Stefanova A.V. 2002)¹⁶, and also exhibit high analgesic activity (Aytmuratova U.K., et.al. 2024., Aytmuratova U.K., et.al. 2023)^{1,2}.

In conclusion, it can be noted that among the studied derivatives of 1,4-disubstituted 1H-1,2,3-triazoles, compound 1 exhibited more pronounced anti-inflammatory activity compared to the reference drugs. Conducting in-depth pharmacological studies on the mechanisms of this compound's effect on the inflammatory process holds promise for expanding the range of low-toxic drugs with analgesic and anti-inflammatory properties.

REFERENCES:

- [1] Aytmuratova U.K., Azamatov A.A., Ortikov I.S., Tursunkhodzhaeva F.M.. Investigation of the analgesic and anti-inflammatory activity of a newly synthesized 1,2,3-triazole derivative. *Frontiers in Health Informatics*. Vol.13 №6 (2024) P 686-693
- [2] Aytmuratova U.K., Azamatov A.A., Ortikov I.S., Tursunkhodzhaeva F.M., Elmurodov B.J.. Acute Toxicity and Analgesic Activity Of 4-(4-((4- (Methoxycarbonyl) Phenoxy) Methyl) -1H-1,2 ,3-Triazol-1-il) Benzoic Acid. 15th International Symposium on the Chemistry of Natural Compounds November 2-5, 2023-Antalya, Turkiye. p.87.
- [3] Belay, Y., Muller, A., Mokoena, F.S. *et al.* 1,2,3-triazole and chiral Schiff base hybrids as potential anticancer agents: DFT, molecular docking and ADME studies. *Sci Rep* 14, 6951 (2024). <https://doi.org/10.1038/s41598-024-57689-5>.
- [4] [Bushra Khan](#), [Abdullah Naiyer](#), [Fareeda Athar](#), [Shakir Ali](#), [Sonu Chand Thakur](#). Synthesis, characterization and anti-inflammatory activity evaluation of 1,2,4-triazole and its derivatives as a potential scaffold for the synthesis of drugs against prostaglandin-endoperoxide synthase. *J Biomol Struct Dyn*. 2021 Feb;39(2):457-475. doi: 10.1080/07391102.2019.1711193.
- [5] Dong, Y.; Li, M.; Hao, Y.; Feng, Y.; Ren, Y.; Ma, H. Antifungal Activity, Structure-Activity Relationship and Molecular Docking Studies of 1,2,4-Triazole Schiff Base Derivatives. *Chem. Biodivers.* 2023, 20, e202201107
- [6] European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, ETS №123, Strasbourg 1986.
- [7] Interstate standard occupational safety standards system harmful substances classification and general safety requirements GOST 12.1.007-76. Moscow Standartinform, 2007.
- [8] Invention patent No. IAP 7858 derivatives of 1H-1,2,3-triazole with analgesic and anti-inflammatory effects. 2024
- [9] Kozan, A. A., & Nahi, R. J. (2023). Synthesis and Molecular Docking Studies of New Pyrimidinone ring Containing 1, 2, 3-Triazole Derivatives. *Int. J. Drug Deliv. Technol*, 13(3), 1005-1010
- [10] Mohammed M. Matin, Priyanka Matin, Md. Rezaur Rahman, Taibi Ben Hadda, Faisal A. Almalki, Shafi Mahmud, Mohammed M. Ghoneim, Maha Alruwaily and Sultan Alshehri. Triazoles and Their Derivatives: Chemistry, Synthesis, and Therapeutic Applications *Front. Mol. Biosci.*, 25 April 2022
- [11] Mosa Alsehli, Adeeb Al Sheikh Ali, Mohamed S. Nafie, Sanaa Bardaweel, Ateyatallah Aljuhani, Khaled M. Darwish, Shaya Yahya Alraqa, Nadjet Rezki, Mohamed Reda Aouad. Discovery of novel tris-1,2,3-triazole-based hybrids as VEGFR2 inhibitors with potent anti-proliferative and cytotoxicity through apoptosis induction. *Bioorganic Chemistry*. Volume 155. February 2025, 108131
- [12] Mironov A.N. Guidelines for conducting preclinical studies of drugs. Part one. M: Grif i K, 2012.-944 p.
- [13] Novikov V.E., Pozhilova E.V., Ilyukhin S.A. Effect of antihypoxants on the development of acute formalin edema. *Reviews of clinical pharmacology and drug therapy*. Vol. 13/2015/1. pp. 41-44
- [14] Razzaq, Ali & Nahi, Riyadh. (2021). In vitro evaluation of antioxidant and antibacterial activities of new 1,2,3- triazole derivatives containing 1,2,4- triazole ring. *Systematic Reviews in Pharmacy*. 12. 196-200.
- [15] Smurova Natalia V., Mayboroda Elena I.. Antiviral activity of 1,2,4-triazole derivatives. *Chemistry of Heterocyclic Compounds* 2021, 57(4), 420-422
- [16] Stefanova A.V. "Preclinical studies of medicines", Kiev 2002, Part I, p. 91.
- [17] Sujana Oggu, Parameswari Akshinthala, Naresh Kumar Katari, Laxmi Kumari Nagarapu, Srimannarayana Malempati, Rambabu Gundla, Sreekantha Babu Jonnalagadda. Design, synthesis, anticancer evaluation and molecular docking studies of 1,2,3-triazole incorporated 1,3,4-oxadiazole-Triazine derivatives. *Heliyon* Volume 9, ISSUE 5, E15935, May 2023.

- [18] Teresa Glomb , Julia Minta , Michalina Nowosadko, Julia Radzikowska and Piotr Swiatek Search for New Compounds with Anti-Inflammatory Activity Among 1,2,4-Triazole Derivatives. *Molecules* 2024, 29, 6036. <https://doi.org/10.3390/molecules29246036>
- [19] Veselov .B. Isavuconazole is a new antifungal drug of the triazole class. *PROBLEMS OF MEDICAL MYCOLOGY*, 2015, VOL.17, No. 4, pp. 18-24.