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DEVELOPMENT OF EFFECTIVE ANTI-INFLAMMATORY DRUG CANDIDATES AMONG NOVEL THIAZOLOPYRIDINES

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*In an effort to develop novel anti-inflammatory agents, a series of thiazolo[4,5-b]pyridines were synthesized and modified at the N^3 position. The structures of the obtained compounds were confirmed by ^{1}H NMR spectroscopy and elemental analysis. The synthesized substances were preselected via molecular docking to be tested for their anti-inflammatory activity in vitro. Evaluation of compounds using the carrageenan-induced rat paw edema method showed strong anti-inflammatory action of some compounds (**1**, **2**, **8**) which exceeded that of ibuprofen.*

K e y w o r d s: organic synthesis, thiazolo[4,5-b]pyridines, molecular docking, anti-inflammatory activity.

Introduction

Inflammation is one of the common events in the majority of acute as well as chronic debilitating diseases and represents a chief cause of morbidity in the contemporary era of modern lifestyles. Current approaches to overcome inflammation include the use of nonsteroidal anti-inflammatory drugs (NSAIDs), immune selective anti-inflammatory derivatives, selective glucocorticoid receptor agonists, resolvins/protectins, and TNF inhibitors. Although drug treatment has been improved to some extent, it is still yet a challenge for pharmaceutical chemists to explore more effective and potent therapeutic agents to treat inflammation and reduce the signs and symptoms of acute inflammation and chronic inflammatory diseases [1].

The use of scientific and technological innovations as a research tool combining multidisciplinary knowledge in informatics, biotechnology, chemistry and biology are essential for optimizing time and reducing costs in drug design [2]. The integration of these *in silico* techniques makes it possible to search for new anti-inflammatory drugs available drugs.

The combination of two heterocyclic systems, both of which are of high priority in modern medicinal chemistry, can be considered as a systematic approach for rational molecular design of drug candidates [3-5]. Thiazolopyridines, as purine bioisosteres, are an important type of heterocyclic system that are being intensively studied because of both their considerable range of pharmacological activities and possibilities at different molecular positions for functionalization of synthetic derivatives. Among the thiazolopyridines, substances have been identified with antioxidant [6-9], fungicidal [10], anti-inflammatory [11-13], anti-mitotic [14], tuberculostatic [15], herbicidal [16], and antitumor [17], activities, as well as agonists of H3-histamine receptors [18], antagonists of metabotropic glutamate receptors 5 (mGluR5) [19], substances with high inhibitory activity against epidermal growth factor receptors [20] and several other enzymes [21].

The present work is devoted to the synthesis of a series of novel thiazolo[4,5-*b*]pyridine-2-ones for further pharmacological *in vivo* anti-inflammatory activity assay based on the results obtained from computer simulation of molecular docking.

Methods

All chemicals were of analytical grade and commercially available. All reagents and solvents

were used without further purification and drying. Ibuprofen was purchased from the medical store.

Chemistry. All melting points were determined in an open capillary. The elemental analysis experimental data on contents of sulfur and nitrogen were within ±0.3% of the theoretical values. ^{1}H NMR spectra of synthesized compounds in dimethyl sulfoxide (DMSO)-d6 solutions were recorded on a spectrometer Varian Mercury VX-400 [Agilent Technologies, San Francisco, USA] (400 MHz) at 298 K. Chemical shifts are reported as δ (ppm) relative to tetramethylsilane (TMS) as an internal standard. The coupling constant J is expressed in Hz.

*3-(5-Hydroxy-7-methyl-2-oxo-thiazolo[4,5-b]pyridin-3-yl)-propionitrile (Compound **1**):* A mixture of pyridine (50 ml) and water (10 ml) with acrylonitrile (3 ml) was added to 5-hydroxy-7-methylthiazolo[4,5-b]pyridin-2(3H)-one (10 mmol). The reaction mixture was refluxed for 5 h. Upon cooling, precipitation was achieved with a petroleum ether-water mixture (3:1). The precipitate was recrystallized from ethanol, filtered off, and dried. This compound was isolated as a white crystalline solid, well soluble in ethanol, chloroform, dioxane, dimethyl formamide (DMF) and acetic acid. White solid; Yield: 74%; mp 105 ºC; ^{1}H NMR: δ_H = 2.27 (s, 3H, CH_3), 3.04 (t, *J* = 6.5 Hz, 2H, CH_2), 4.15 (t, *J* = 6.5 Hz, 2H, CH_2), 6.41 (s,1H, Py), 11.09 (s, 1H, OH); anal. calcd. for $C_{10}H_9N_3O_2S$: C 51.05, H 3.86, N 17.86; found: C 50.97, H 3.89, N 17.77.

*3-(5-Hydroxy-7-methyl-2-oxothiazolo[4,5-b]pyridin-3(2H)-yl)-propanoic acid (Compound **2**):* A mixture of the propanenitrile compound **1** (10 mmol), acetic acid (30 ml), and hydrochloric acid (15 ml) was placed into the round-bottomed flask. The reaction mixture was refluxed 3 h and the product was precipitated with water. The mixture was left standing for 24 h at ambient temperature, the precipitate was filtered off and treated with toluene. The precipitate was recrystallized from ethanol, filtered off, and dried. This compound was isolated as a white crystalline powdered solid, well soluble in ethanol, chloroform, dioxane, DMF, and acetic acid. White solid; Yield: 66%; mp 111 ºC; ^{1}H NMR: δ_H = 2.25 (s, 3H, CH_3), 2.68 (t, *J* = 7.5 Hz, 2H, CH_2), 4.10 (t, *J* = 7.6 Hz, 2H, CH_2), 6.38 (s,1H, Py), 11.05 (s, 1H, OH), 12.07 (s, 1H, COOH); anal. calcd. for $C_{10}H_{10}N_2O_4S$: C 47.24, H 3.96, N 11.02; found: C 47.88, H 3.98, N 11.21.

*General procedure for the synthesis of 3-(5-hydroxy-7-methyl-2-oxothiazolo[4,5-b]pyridin-3(2H)-yl)-N-aryl-l propanamides (Compounds **3-10**).* A mixture of the propanoic acid (Compound **2,** 10 mmol), thionyl chloride (57 mmol), and dioxane (30 ml) was placed into the round-bottomed flask. The reaction mixture was refluxed for 30 min and the product was precipitated with n-hexane, then the precipitate was filtered off. The resulting acyl chlorides are used for further transformations without further purification. The obtained 3-(5-hydroxy-7-methyl-2-oxothiazolo[4,5-*b*]pyridin-3(*2H*)-yl) propanoyl chloride (10 mmol) was dissolved in anhydrous dioxane (10 ml), an appropriate aromatic amine (10 mmol), and triethylamine (10 mmol) were added to the solution. The reaction mixture was refluxed for 15 min. Upon cooling, the mixture was diluted with water, the precipitated crystalline solid was filtered off, washed with methanol and dried. The obtained compounds were recrystallized from acetic acid.

*3-(5-Hydroxy-7-methyl-2-oxothiazolo[4,5-b]pyridin-3(2H)-yl)-N-phenylpropanamide (Compound **3**):* White solid; Yield: 48%; mp 214 ºC; ^{1}H NMR: δ_H = 2.28 (s, 3H, CH_3), 2.71 (t, 2H, *J* = 7.1 Hz, CH_2), 4.13 (t, 2H, *J* = 7.2 Hz, CH_2), 6.42 (s, 1H, Py), 7.21-7.26 (m, 2H, C_6H_5), 7.40-7.48 (m, 3H, C_6H_5), 9.96 (s, 1H, NH), 11.09 (s, 1H, OH); anal. calcd. for $C_{16}H_{15}N_3O_3S$: C 58.35, H 4.59, N 12.76; found: C 58.43, H 4.67, N 12.88.

*3-(5-Hydroxy-7-methyl-2-oxo-thiazolo[4,5-b]pyridin-3-yl)-N-p-tolyl-propionamide (Compound **4**):* White solid; Yield: 44%; mp 218 ºC; ^{1}H NMR: δ_H = 2.18 (s, 3H, C_6H_4-CH_3), 2.29 (s, 3H, CH_3), 2.80 (t, 2H, *J* = 7.1 Hz, CH_2), 4.13 (t, 2H, *J* = 7.1 Hz, CH_2), 6.49 (s, 1H, Py), 7.33-7.40 (m, 2H, C_6H_4), 7.60-7.67 (m, 2H, C_6H_4), 10.08 (s, 1H, NH), 11.14 (s, 1H, OH); anal. calcd. for $C_{17}H_{17}N_3O_3S$: C 59.46, H 4.99, N 12.24; found: C 59.60, H 5.08, N 12.55.

4-[3-(5-Hydroxy-7-methyl-2-oxo-thiazolo[4,5-b]pyridin-3-yl)-propionylamino]-benzoic acid (Compound 5): White solid; Yield: 51%; mp 228 ºC; ^{1}H NMR: δ_H = 2.18 (s, 3H, C_6H_4-CH_3), 2.29 (s, 3H, CH_3), 2.80 (t, 2H, J = 7.1 Hz, CH_2), 4.13 (t, 2H, *J* = 7.1 Hz, CH_2), 6.49 (s, 1H, Py), 7.33-7.40 (m, 2H, C_6H_4), 7.60-7.67 (m, 2H, C_6H_4), 10.08 (s, 1H, NH), 11.14 (s, 1H, OH); anal. calcd. for $C_{17}H_{15}N_3O_5S$: C 54.69, H 4.05, N 11.25; found: C 54.44, H 4.12, N 11.33.

N-(4-Chloro-phenyl)-3-(5-hydroxy-7-methyl-2-oxo-thiazolo[4,5-b]pyridin-3-yl)-propionamide (Compound 6): White solid; Yield: 39%; mp 231 ºC; ^{1}H NMR: δ_H =2.28 (s, 3H, CH_3), 2.77 (t, 2H, *J* = 7.2 Hz, CH_2), 4.11 (t, 2H, J = 7.2 Hz, CH2), 6.39 (s, 1H,

Py), 7.28-7.34 (m, 2H, C_6H_4), 7.49-7.55 (m, 2H, C_6H_4), 10.01 (s, 1H, NH), 11.11 (s, 1H, OH); anal. calcd. for $C_{16}H_{11}ClN_3O_3S$: C 52.82, H 3.88, N 11.55; found: C 53.02, H 3.85, N 11.49.

*N-(4-Fluoro-phenyl)-3-(5-hydroxy-7-methyl-2-oxo-thiazolo[4,5-b]pyridin-3-yl)-propionamide (Compound **7**):* White solid; Yield: 42%; mp 219 ºC; ^{1}H NMR: δ_H = 2.31 (s, 3H, CH3), 2.82 (t, 2H, *J* = 7.2 Hz, CH2), 4.15 (t, 2H, J = 7.2 Hz, CH2), 6.44 (s, 1H, Py), 7.31-7.37 (m, 2H, C6H4), 7.52-7.59 (m, 2H, C6H4), 10.12 (s, 1H, NH), 10.98 (s, 1H, OH); anal. calcd. for $C_{16}H_{11}FN_3O_3S$: C 55.32, H 4.06, N 12.10 found: C 55.47, H 4.11, N 12.25.

*N-(2-Chloro-phenyl)-3-(5-hydroxy-7-methyl-2-oxo-thiazolo[4,5-b]pyridin-3-yl)-propionamide (Compound **8**):* White solid; Yield: 46%; mp 222 ºC; ^{1}H NMR: δ_H = 2.33 (s, 3H, CH3), 2.82 (t, 2H, *J* = 7.0 Hz, CH_2), 4.18 (t, 2H, *J* = 7.0 Hz, CH_2), 6.51 (s, 1H, Py), 7.15 (d, 1H, *J* = 7.0 Hz, C_6H_4), 7.27 (t, 1H, *J* = 8.0 Hz, C_6H_4), 7.41 (d, 1H, J = 7.8 Hz, C_6H_4), 7.72-7.75 (m, 1H, C_6H_4), 10.13 (s, 1H, NH), 11.11 (s, 1H, OH); anal. calcd. for $C_{16}H_{11}ClN_3O_3S$: C 52.82, H 3.88, N 11.55; found: C 52.56, H 3.96, N 11.44.

N-(2-Fluoro-phenyl)-3-(5-hydroxy-7-methyl-2-oxo-thiazolo[4,5-b]pyridin-3-yl)-propionamide (Compound 9): White solid; Yield: 42%; mp 209 ºC; ^{1}H NMR: δ_H = 2.28 (s, 3H, CH_3), 2.76 (t, 2H, *J* = 7.0 Hz, CH_2), 4.14 (t, 2H, *J* = 7.0 Hz, CH_2), 6.45 (s, 1H, Py), 7.11 (d, 1H, *J* = 7.1 Hz, C_6H_4), 7.21 (t, 1H, *J* = 7.9 Hz, C_6H_4), 7.38 (d, 1H, *J* = 7.9 Hz, C_6H_4), 7.69-7.72 (m, 1H, C_6H_4), 10.06 (s, 1H, NH) 11.06 (s, 1H, OH); anal. calcd. for $C_{16}H_{11}FN_3O_3S$: C 55.32, H 4.06, N 12.10 found: C 55.74, H 4.18, N 12.05.

*3-(5-Hydroxy-7-methyl-2-oxo-thiazolo[4,5-b] pyridin-3-yl)-N-(2-trifluoromethyl-phenyl)-propionamide (Compound **10**):* White solid; Yield: 55%; mp 239 ºC; ^{1}H NMR: δ_H = 2.31 (s, 3H, CH_3), 2.79 (t, 2H, *J* = 7.0 Hz, CH_2), 4.17 (t, 2H, *J* = 7.0 Hz, CH_2), 6.48 (s, 1H, Py), 7.13 (d, 1H, *J* = 6.9 Hz, C6H4), 7.24 (t, 1H, *J* = 8.1 Hz, C_6H_4), 7.37 (d, 1H, *J* = 7.8 Hz, C6H4), 7.70-7.73 (m, 1H, C_6H_4), 10.11 (s, 1H, NH) 11.08 (s, 1H, OH); anal. calcd. for $C_{17}H_{14}F_3N_3O_3S$: C 51.38, H 3.55, N 10.57 found: C 51.55, H 3.48, N 10.46.

Molecular docking. Molecular docking was conducted with the OpenEye Scientific Software program [Software, Santa Fe, New Mexico, USA] as a computer based approach to the search of molecules with affinity to certain biotargets. Other software used included Fred Receptor, Vida, Omega 2 and Hybrid programs [Software, Santa Fe, New Mexico, USA].

Pharmacology. Anti-inflammatory activity [22] was evaluated using the carrageenan-induced rat paw edema method in Wistar rats (weight 180-220 g). The experiments were carried out in accordance with the requirements of the European convention for the protection of vertebrate animals used for experimental and other scientific purposes. The experimental protocol was approved by the Danylo Halytsky Lviv National Medical University ethics committee, constituted by the Ministry of Health of Ukraine. Ethical Committee or Institutional Animal Care and Use Committee Approval: 18/03/2013 No 3.

Animals were divided into 12 groups comprising five rats per group. One group was kept as the control and the remaining 11 groups (test groups) were used to determine the anti-inflammatory activity elicited by ibuprofen and the 10 compounds. Rats were kept in the animal house under standard conditions of light and temperature on a standard diet prior to the experiment.

The standard drug, ibuprofen (50 mg/kg body weight) and the test compounds (50 mg/kg body weight) were dissolved in DMSO and administered through an intraperitoneal route. DMSO was injected into the control group. At 30 minutes later, 0.1 ml of a 2% carrageenan solution in saline was injected in the sub-plantar region of the right hind paw of each rat. At 4 h after the carrageenan injection, the volume of paw edema (in ml) was measured using a water plethysmometer [Orchid Scientific, Mumbai, India] and decrease in paw edema was compared between the control group and the test groups.

Results of decreased paw edema were expressed as the mean ± standard deviation and compared statistically with the control group using Student's *t*-test. A level of $P < 0.05$ was considered to be significant. The inflammatory reaction inhibition was expressed as a percent reduction of paw volume and was calculated using the following formula:

$$\% \text{ Inhibition} = \frac{V_{\text{control}} - V}{V_{\text{control}}} \cdot 100\,\%$$

where V_{control} is the increase in paw volume in control group animals; *V* is the increase in paw volume in animals injected with the test substances.

Results and Discussion

With the view of continuing the systematic study of thiazolo[4,5-*b*]pyridines as potential drug candidates, we introduced synthesis and anti-inflam-

matory activity evaluation of some thiazolo[4,5-*b*] pyridin-2-ones. An efficient synthetic approach for the 3H-thiazolo[4,5-*b*]pyridine-2-one system construction had been developed earlier [23] as the protocol based on [3+3] cyclocondensation of 4-iminothiazolidone-2 because of its N,C-binucleophilic properties with dielectrophilic reagents. By using 4-iminothiazolidin-2-one as the initial compound that was reacted with acetoacetic ester, it was possible to obtain 5-hydroxy-7-methyl-3H-thiazolo[4,5-*b*] pyridin-2-one [13] (Scheme 1).

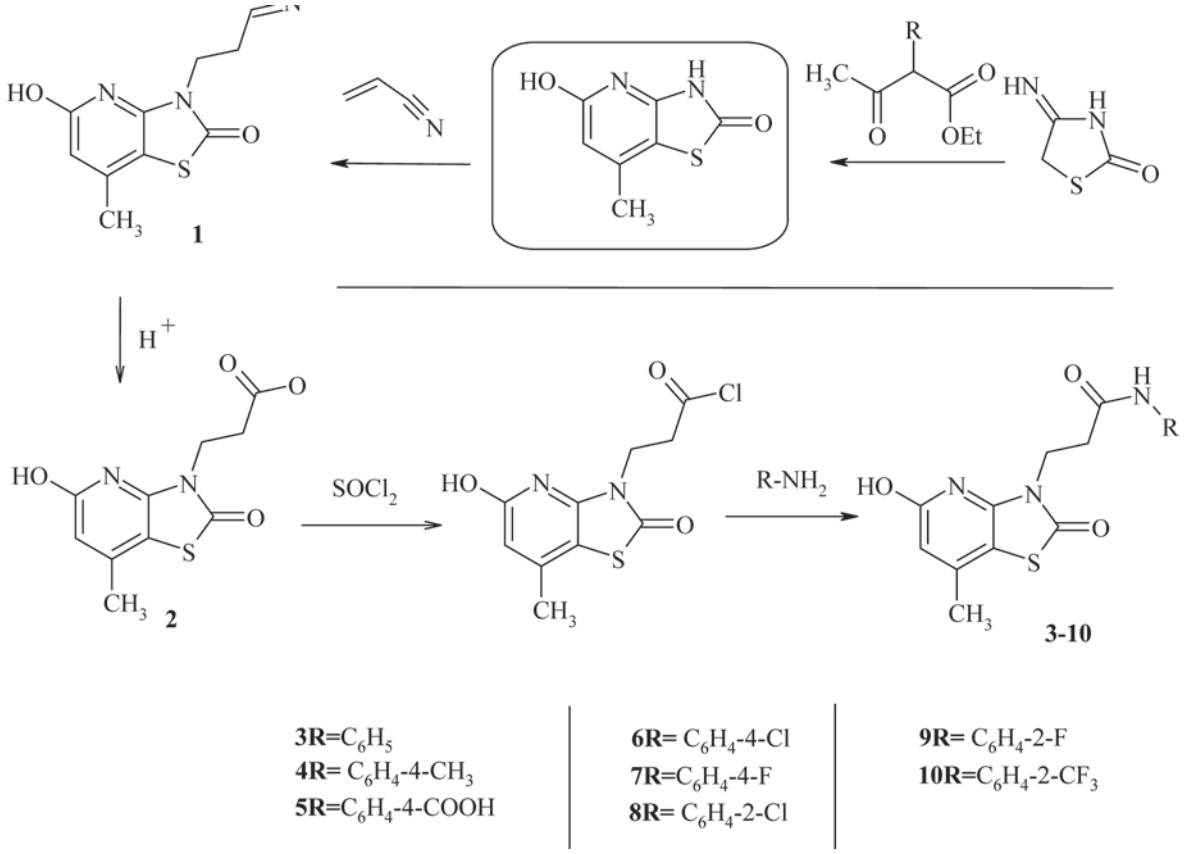
The high electrophilicity of the basic scaffold N^3 position makes it possible to use its functionalization as a fairly convenient method for obtaining a variety of N^3-substituted derivatives, thereby extending the number of thiazolo[4,5-*b*]pyridines.

Therefore, the functionalization of thiazolo[4,5-*b*]pyridine could be easily performed by the addition reaction to acrylonitrile. We discovered that the high yield of the product (compound **1**) could be achieved while treating equimolar amounts of 5-hydroxy-7-methyl-3*H*-thiazolo[4,5-*b*]pyridin-2-one with acrylonitrile in a pyridine – water medium (5:1). 3-(5-Hydroxy-7-methyl-2-oxothiazolo[4,5-*b*]pyridin-3(2*H*)-yl) propanenitrile (compound **1**) prepared in this way was subjected to hydrolysis leading to the formation of 3-(5-hydroxy-7-methyl-2-oxothiazolo[4,5-*b*]pyridin-3(2*H*)-yl) propanoic acid (compound **2**) (Scheme 1).

For the compound **2** carboxyl group transformation, the corresponding chloranhydride was obtained, which belongs to unstable highly reactive reagents, so its application in further transformations was carried out without isolation by introducing aromatic amine acylation. The above conversion allowed us to obtain a number of suitable propionamides (compounds **3-10**) (Scheme). Powders of these products are well soluble in DMF, DMSO, and acetic acid but sparingly soluble in water and other organic solvents.

The structures of the obtained compounds were confirmed by ^{1}H spectroscopy and elemental analysis. All these new compounds gave spectroscopic data in accordance with the proposed structures.

Molecular docking. Crystallographic models of COX-1 and COX-2 (3N8Y and 1PXX, respectively)



Scheme. Synthesis of some thiazolo[4,5-b]pyridines

were obtained from the Protein Data Bank (www.rcsb.org). The following were chosen as research objects: thiazolo[4,5-*b*]pyridine derivatives, common NSAIDs (aspirin, mefenamic acid, diclofenac, ibuprofen, indomethacin, ketoprofen, ketorolac, others) and well-known selective COX-2 inhibitors (parecoxib, lumiracoxib, etoricoxib and others). To estimate *in silico* COX-1-compound and COX-2-compound binding, values of the scoring function were calculated. The Chemgauss 4 scoring function ranking allowed us to select compounds which could prospectively be selective COX-2 inhibitors. The Fred receptor program allowed us to extract the active sites (biotargets) of COX-1 and COX-2 from crystallographic models for molecular docking.

Molecular docking studies included generation of R-, S- and cys-trans isomers of ligands and then conformers were generated using the Omega 2 program with Flipper parameter. In addition, the Hybrid program that uses elements of ligand based design was used to enhance performance. Typically, protein structure is determined with X-ray crystallography in the presence of a known binding ligand (or bound ligand). The Hybrid program uses the information present in both the structure of the protein and the bound ligand to enhance docking performance. Values of the scoring function (Chemgauss 4) were obtained as a result. The ranking property of the scoring function allowed us to easily analyze the results (Table 1).

Ranking and analysis of the molecular docking results were obtained using the selected compounds and crystallographic model of COX-2 with scoring function (Chemgauss 4). The results allowed us to select compounds, which could prospectively be selective COX-2 inhibitors at the level of diclofenac and ibuprofen for future (in-depth) pharmacological studies to further evaluate *in vitro* anti-inflammatory activity. The interactions between the COX-2 active site and the most active compound 1 in comparison with the COX-2 inhibitor diclofenac are shown in Figure.

Moreover, it should be noted that results predicted by molecular docking correlate quite well with that obtained in the *in vitro* assay. The selected "lead" compound **1** based on the *in vitro* screening results was also predicted to be the most active in the docking studies.

In contrast, the generated conformations of thiazolo[4,5-*b*]pyridine derivatives did not possess the necessary parameters for successful binding to the target COX-1 active site and were found to be bad substrates for cyclooxygenase-1 during the docking experiment.

Evaluation of the anti-inflammatory activity in vivo. Carrageenan-induced paw edema is a

Table 1. Values of the Chemgauss 4 score of thiazolo[4,5-b]pyridine-2-ones and reference compounds

Compound ID or reference compound	Chemgauss 4 score		Compound ID or reference compound	Chemgauss 4 score	
	3N8Y (COX-1)	1PXX (COX-2)		3N8Y (COX-1)	1PXX (COX-2)
1	-8.2392	-11.8320	Etoricoxib	-2.6886	-10.5080
2	-7.5129	-10.3840	Flurbiprofen	-12.7735	-11.4541
3	-6.3490	-8.8240	Ibuprofen	-11.1124	-11.7179
4	-6.3490	-8.8240	Indomethacin	-7.9776	-11.9668
5	-5.9252	-9.7765	Isoxicam	-7.3339	-9.0114
6	-5.6768	-9.3958	Ketoprofen	-10.9859	-12.4525
7	-6.0150	-10.0712	Ketorolac	-8.5278	-12.5004
8	-6.6819	-9.6173	Lumiracoxib	-8.8057	-11.8814
9	-6.9729	-10.1682	Mefenamic acid	-9.3569	-13.0445
10	-5.5237	-9.5894	Meloxicam	-7.8126	-11.7675
Aspirin	-8.9541	-10.3855	Parecoxib	-6.2776	-10.0099
Diclofenac	-9.3414	-13.2157			

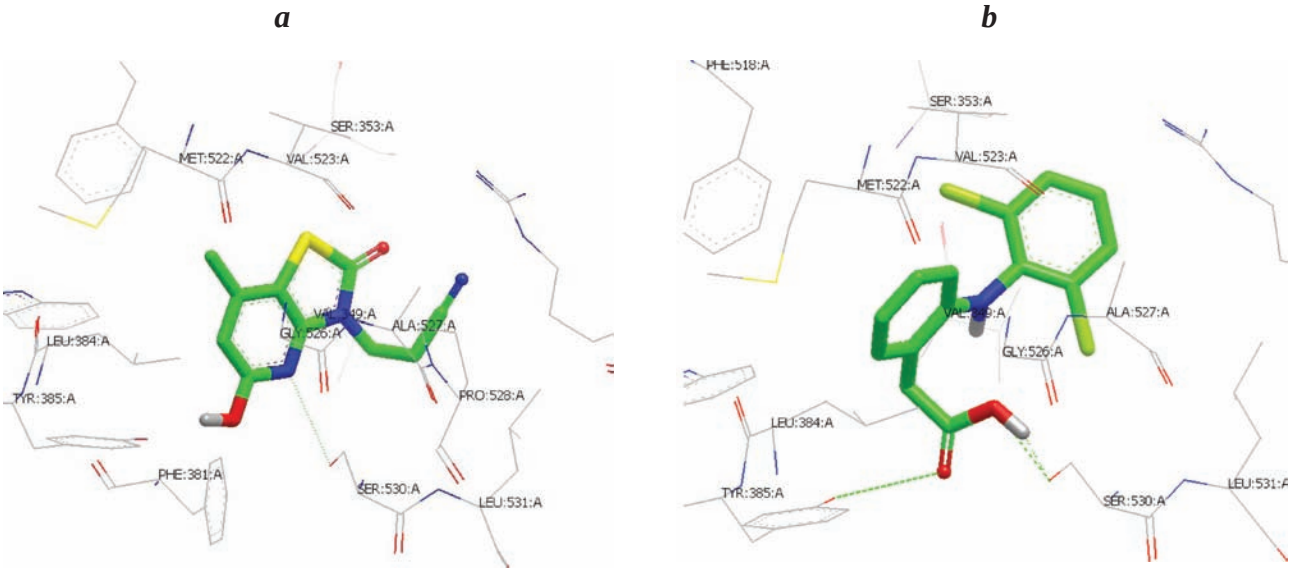


*Figure. (**a**) Compound 1 docked in the active site of COX-2 in comparison with (**b**) diclofenac docked in the active site of COX-2*

well-known animal model of acute inflammation, and is the most widely used in the search for new anti-inflammatory drugs. *In vivo* studies of novel thiazolo[4,5-*b*]pyridine-2-one derivatives were performed for anti-inflammatory activity. The results of the anti-inflammatory activity of the synthesized compounds and ibuprofen are shown in Table 2.

The synthesized compounds possess a range of anti-inflammatory activity - from its almost complete absence to a distinct anti-inflammatory effect. Evaluation indicated that 6 compounds (**3**, **4**, **5**, **7**, **9**, **10**) showed no significant decrease in carrageenan-induced rat paw edema, as their inhibition rates were only 20.0-36.2%, as compared to the control group (Table 2). The anti-inflammatory effect for compound **6** is approximately equivalent to that of the reference drug (ibuprofen). The anti-inflammatory effect for compounds **1**, **2** and **8** resulted in inhibi-

Table 2. In vivo evaluation of anti-inflammatory effect of thiazolo[4,5-b]pyridine-2-ones on carrageenan-induced rat paw edema volume, expressed as % inhibition

Compound ID	Paw edema volume (ml) ± SEM*	% Inhibition	Activity relative to Ibuprofen, %
Control	2.20 ± 0.050	-	
1	1.13± 0.020	**48.8**	121.4
2	1.20 ± 0.025	**45.3**	112.7
3	1.65 ± 0.040	**25.2**	62.7
4	1.66 ± 0.040	**24.8**	61.7
5	1.76 ± 0.045	**20.0**	49.8
6	1.27± 0.030	**42.5**	105.7
7	1.41± 0.035	**35.8**	89.1
8	1.23± 0.030	**44.0**	109.5
9	1.40± 0.035	**36.2**	90.0
10	1.54± 0.040	**30.2**	75.1
Ibuprofen	1.32 ± 0.035	**40.2**	100

*SEM denotes standard error of mean.

tion rates of 44.0-48.8%, indicating that these compounds were more potent than ibuprofen.

Conclusion

The core thiazolo[4,5-b]pyridine heterocyclic system may be regarded as a promising scaffold for the development of effective anti-inflammatory drug candidates.

Conflict of interest. Authors have completed the Unified Conflicts of Interest form at http://ukrbiochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

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РОЗРОБКА ЕФЕКТИВНИХ КАНДИДАТІВ ПРОТИЗАПАЛЬНИХ ПРЕПАРАТІВ СЕРЕД НОВИХ ТІАЗОЛОПІРИДИНІВ

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З метою пошуку нових протизапальних засобів було синтезовано та модифіковано у позиції N^3 ряд тіазоло[4,5-*b*]піридинів. Структури отриманих сполук підтверджено методом ^{1}H ЯМР-спектроскопії та елементного аналізу. Синтезовані речовини були попередньо відібрані за допомогою молекулярного докінгу для перевірки їх протизапальної активності *in vitro*. Результати дослідження на спричинений карагеніном набряк лапи щура виявили вищу протизапальну дію деяких сполук порівняно з ібупрофеном.

Ключові слова: органічний синтез, тіазоло[4,5-*b*]піридини, молекулярний докінг, протизапальна активність.

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