SYNTHESIS, MOLECULAR DOCKING AND ANTI-INFLAMMATORY ACTIVITY 2,4-DIMETHYL-\(N\)-(2-ARYL)-3-FURAMIDES

Y. Matiichuk,[a] Y. Horak,[b] T. Chaban,[a] V. Ogurtsov,[a] L. Kostyshyn,[a] and V. Matiychuk[b]*

Keywords: Furamides, acylation, molecular docking, anti-inflammatory activity.

2,4-Dimethyl-N-aryl-3-furamides were synthesized by the reaction of 2,4-dimethyl-furan-3-carbonyl chloride with aromatic amines in dry dioxane in the presence of triethylamine. The structures of the obtained substances were confirmed by \(^1\)H NMR spectroscopy and elemental analysis. The synthesized compounds were preselected via molecular docking to be tested for their anti-inflammatory activity. The results have shown that the some novel furamides demonstrated considerable anti-inflammatory effect.

* Corresponding Authors
Fax: 38032260039
E-Mail: v_matiychuk@ukr.net
[a] DanyloHalytskyLviv National Medical University, Pekarska 69, Lviv, 79010, Ukraine
[b] Ivan Franko National University of Lviv, 6 Kyryla and Mefodia, Lviv, 79005, Ukraine

INTRODUCTION

Inflammation is a protective attempt by the organism to remove the injurious stimuli and to initiate the healing. This process may vary from a localized to a generalized response characterized by the accumulation of fluids and leukocytes leading to edema and pain.\(^1\) The non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most common therapeutic groups of agents used worldwide for the treatment of inflammation. However, NSAIDs have high incidence of serious side effects.\(^2\) Although drug treatment has been improved to some extent yet, it is still a challenge for the pharmaceutical chemists to explore the more effective and potent therapeutic agents to treat inflammation and reduce the signs and symptoms of acute inflammation and chronic inflammatory diseases.\(^3\)

Furan derivatives are an important class of heterocyclic compounds that possess important biological properties. During last few decades a considerable amount of attention has been focussed on synthesis of furan derivatives and screening them for different pharmacological activities. Amides of furan-3-carboxylic acids are also promising compounds with a broad spectrum of biological activity. Fenfuram, furcarbanil and methfuroxam are used as agrochemical fungicides. About of the activity of analogues of these drugs was reported in the works.\(^4\) Furan-3-carboxamides exhibit antiproliferative\(^5\) activities also. They are inhibitors of carboxylesterase,\(^6\) glycosidase,\(^7\) \(\beta\)-galactosidase\(^7\) and HCV NS5B Polymerase.\(^8\)

In a previous work\(^9\) we have described the synthesis and anti-inflammatory activities of some 2,5-dimethyl-3-furan-3-carboxamides and 5-aryl-2-methyl-3-furan-3-carboxamides. In this article which is the part of our project on of biologically active heterocycles\(^10-23\) we describe synthesis, molecular docking and anti-inflammatory activities of 2,4-dimethyl-N-(2-aryl)-3-furamides.

EXPERIMENTAL

All chemicals were of analytical grade and commercially available. All reagents and solvents were used without further purification and drying. Ibuprofen was purchased from a medical store.

All the melting points were determined in an open capillary and are uncorrected. \(^1\)H NMR spectra were recorded on a Varian Mercury 400 (400 MHz for \(^1\)H) instrument with TMS or deuterated solvent as an internal reference. Satisfactory elemental analyses were obtained for new compounds (C\(\pm\)0.17, H\(\pm\)0.21, N\(\pm\)0.19).

Syntheses

**Ethyl 2,4-dimethyl-3-furoate (3)**

To a solution of 6.5 g (0.05 mol) of ethyl acetoacetate (1), in 100 mL of 0.5 M alcoholic solution of sodium ethoxide, was added a solution of 9.05 g (0.05 mol) of dimethyl-2-propynylsulfonyl bromide in 100 mL of ethanol. The mixture was refluxed for 6-7 h and the ethanol was distilled off in a water bath. To the residue was added 200 mL of ether and the suspension was filtered. The ether was distilled off from the filtrate under atmospheric pressure. The residue was distilled at 130–132 °C/20 Torr.

**2,4-Dimethyl-3-furoic acid (4)**

To a solution of 8.5 g (0.05 mol) of 3 in 30 mL of alcohol was added a solution of 4.5 g (0.08 mol) of potassium hydroxide in 20 mL of alcohol. The mixture was refluxed for 30 min, then dissolved in an equal amount of water and
acidified with diluted (1:1) hydrochloric acid. The precipitate was filtered off, washed with water and recrystallized. Yield 82 %, m.p. 119–120 °C (m.p. [d1] 118–119 °C).24

2,4-Dimethyl-3-furoyl chloride(5)

A mixture of 2.8 g (0.02 mol) of 4 and 3 mL of thionyl chloride in 50 mL of dry benzene was refluxed until complete dissolution of the acid. After cooling, the benzene was distilled off and the residue was distilled in vacuum at 115–118 °C/20 Torr.

General procedure for preparation of 2,4-dimethyl-N-(2-aryl)-3-furamides (7a–n)

To a mixture of 0.01 mol of corresponding amine 6a-n and 0.12 mL of triethylamine in 10 mL of dry dioxane a solution of 1.58 g (0.01 mol) of 5 in 10 mL of dry dioxane was added with stirring. The reaction mixture was left overnight and then was poured into water. The formed precipitate was filtered and recrystallized from alcohol.

2,4-Dimethyl-N-(2-methylphenyl)-3-furamide (7a)

Yield 83 %, m.p. 131–132 °C. 1H NMR (400 MHz, DMSO) δ = 9.02 (s, 1H, NH), 7.45 (d, J = 8.1 Hz, 1H, C6H3), 7.26 – 7.04 (m, 4H, C6H4 + 5-Hfurane), 2.46 (s, 3H, CH3), 2.26 (s, 3H, CH3), 2.12 (s, 3H, CH2). Anal. Calcd. for C13H12NO2: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.45; H, 6.64; N, 6.02.

2,4-Dimethyl-N-(3-methylphenyl)-3-furamide (7b)

Yield 84 %, m.p. 104–105 °C. 1H NMR (400 MHz, DMSO) δ = 9.56 (s, 1H, NH), 7.50 (s, 1H, C6H3), 7.43 (d, J = 8.1 Hz, 1H, C6H3), 7.19 (s, 1H, 5-Hfurane), 7.13 (t, J = 7.8 Hz, 1H, C6H3), 6.83 (d, J = 7.7 Hz, 1H, C6H4), 2.40 (s, 3H, CH3), 2.32 (s, 1H, CH2), 2.07 (s, 3H, CH3). Anal. Calcd. for C13H12NO2: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.21; H, 6.60; N, 6.22.

2,4-Dimethyl-N-(4-methylphenyl)-3-furamide (7c)

Yield 90 %, m.p. 115–116 °C. 1H NMR (400 MHz, DMSO) δ = 9.55 (s, 1H, NH), 7.53 (d, J = 8.0 Hz, 2H, C6H4), 7.19 (s, 1H, 5-Hfurane), 7.06 (d, J = 8.4 Hz, 1H, C6H3), 2.40 (s, 3H, CH3), 2.29 (s, 3H, CH3), 2.07 (s, 3H, CH3). Anal. Calcd. for C13H12NO2: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.43; H, 6.51; N, 6.03.

N-(3,4-dimethylphenyl)-2,4-dimethyl-3-furamide (7d)

Yield 82 %, m.p. 119–120 °C. 1H NMR (400 MHz, DMSO) δ = 9.46 (s, 1H, NH), 7.42 (s, 1H, C6H3), 7.35 (d, J = 8.2 Hz, 1H, C6H3), 7.18 (s, 1H, 5-Hfurane), 6.99 (d, J = 8.1 Hz, 1H, C6H4), 2.40 (s, 3H, CH3), 2.23 (s, 3H, CH3), 2.20 (s, 3H, CH3), 2.07 (s, 3H, CH3). Anal. Calcd. for C14H15NO2: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.91; H, 7.12; N, 5.85.

N-(3,5-dimethylphenyl)-2,4-dimethyl-3-furamide (7f)

Yield 92 %, m.p. 164–165 °C. 1H NMR (400 MHz, DMSO) δ = 9.46 (s, 1H, NH), 7.27 (s, 2H, C6H4), 7.19 (s, 1H, 5-Hfurane), 6.65 (s, 1H, C6H3), 2.39 (s, 3H, CH3), 2.27 (s, 6H, 2*CH3), 2.07 (s, 3H, CH3). Anal. Calcd. for C15H17NO2: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.94; H, 7.02; N, 5.68.

N-(3-chlorophenyl)-2,4-dimethyl-3-furamide (7g)

Yield 91 %, m.p. 77–78 °C. 1H NMR (400 MHz, DMSO) δ = 9.54 (s, 1H, NH), 7.89 (t, J = 2.0 Hz, 1H, C6H4), 7.64 – 7.58 (m, 1H, C6H4), 7.25 (t, J = 8.1 Hz, 1H, C6H4), 7.03 – 6.98 (m, 1H, C6H4), 6.59 (s, 1H, 5-Hfurane), 2.51 (s, 3H, CH3), 2.28 (s, 3H, CH3). Anal. Calcd. for C13H12ClNO2: C, 62.53; H, 4.84; N, 5.61. Found: C, 62.65; H, 4.73; N, 5.75.

N-(4-chlorophenyl)-2,4-dimethyl-3-furamide (7b)

Yield 87 %, m.p. 152–153 °C. 1H NMR (400 MHz, DMSO) δ = 9.80 (s, 1H, NH), 7.69 (d, J = 8.9 Hz, 2H, C6H4), 7.26 (d, J = 8.8 Hz, 2H, C6H4), 7.21 (t, J = 8.1 Hz, 1H, C6H4), 7.03 (d, J = 8.8 Hz, 1H, C6H4), 6.59 (s, 1H, 5-Hfurane), 2.49 (s, 3H, CH3), 2.40 (s, 3H, CH3). Anal. Calcd. for C13H12ClNO2: C, 62.53; H, 4.84; N, 5.61. Found: C, 62.65; H, 4.91; N, 5.54.

N-(3,4-dichlorophenyl)-2,4-dimethyl-3-furamide (7i)

Yield 85 %, m.p. 151–152 °C. 1H NMR (400 MHz, DMSO) δ = 9.93 (s, 1H, NH), 8.02 (d, J = 2.4 Hz, 1H, C6H4), 7.59 (dd, J = 8.8, 2.4 Hz, 1H, C6H4), 7.42 (d, J = 8.8 Hz, 1H, C6H3), 7.22 (s, 1H, 5-Hfurane), 2.40 (s, 3H, CH3), 2.07 (s, 3H, CH3). Anal. Calcd. for C13H12ClNO2: C, 54.95; H, 3.90; N, 4.93. Found: C, 55.06; H, 3.81; N, 5.04.

N-(4-bromophenyl)-2,4-dimethyl-3-furamide (7j)

Yield 89 %, m.p. 158–159°C. 1H NMR (400 MHz, DMSO) δ = 9.80 (s, 1H, NH), 7.64 (d, J = 8.8 Hz, 2H, C6H4), 7.39 (d, J = 7.3 Hz, 1H, C6H4), 7.21 (s, 1H, 5-Hfurane), 2.40 (s, 3H, CH3), 2.07 (s, 3H, CH3). Anal. Calcd. for C13H12BrNO2: C, 53.08; H, 4.11; N, 4.76. Found: C, 53.19; H, 4.02; N, 4.84.

N-(4-methoxyphenyl)-2,4-dimethyl-3-furamide (7k)

Yield 95 %, m.p. 123–124 °C. 1H NMR (400 MHz, DMSO) δ = 9.50 (s, 1H, NH), 7.56 (d, J = 8.7 Hz, 2H, C6H4), 7.18 (s, 1H, 5-Hfurane), 6.81 (d, J = 8.3 Hz, 2H, C6H4), 3.74 (s, 3H, CH3O), 2.40 (s, 3H, CH3), 2.07 (s, 3H, CH3).
Anal. Calcd. for C_{16}H_{15}NO_6: C, 61.25; H, 5.71; N, 4.20. Found: C, 61.34; H, 5.69; N, 4.31.

N-(4-ethoxyphenyl)-2,4-dimethyl-3-furamide (7l)

Yield 84 %, m.p. 191−192 °C. 1H NMR (400 MHz, DMSO) δ = 9.71 (s, 1H, NH), 9.58 (s, 1H, NH), 7.55 (d, J = 8.9 Hz, 2H, C_6H_4), 7.46 (d, J = 8.8 Hz, 2H, C_6H_4), 7.19 (s, 1H, 5-Hfuran), 2.40 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.01 (s, 3H, CH_3). Anal. Calcd. for C_{15}H_{16}N_2O_3: C, 66.16; H, 5.92; N, 10.29. Found: C, 66.27; H, 6.01; N, 10.18.

Methyl 2-[(2,4-dimethyl-3-furoyl)amino]-4,5-dimethoxybenzoate (7n)

Yield 87 %, m.p. 146−147 °C. 1H NMR (400 MHz, DMSO) δ = 11.11 (s, 1H, NH), 8.44 (s, 1H, C_6H_4), 7.41 (s, 1H, C_6H_4), 7.24 (s, 1H, 5-Hfuran), 3.90 (s, 3H, CH_3O), 3.86 (s, 3H, CH_3O), 3.79 (d, J = 8.8 Hz, 2H, C_6H_4), 2.51 (s, 3H, CH_3), 2.18 (s, 3H, CH_3). Anal. Calcd. for C_{16}H_{17}NO_6: C, 64.16; H, 6.01; N, 4.20. Found: C, 64.27; H, 6.01; N, 10.18.

RESULTS AND DISCUSSION

The starting material, 5, was prepared according scheme 1. In the first stage, 2 was reacted with an acetoacetic ester 1 to form etyl 2,4-dimethyl-3-furoate 3 which was hydrolyzed with an aqueous solution of sodium hydroxide. Next 2,4-dimethyl-3-furoyl chloride 5 was prepared by the reaction of acid 4 with thionyl chloride.

Scheme 1. Synthesis 2,4-dimethyl-3-furoyl chloride.

The target 2,4-dimethyl-N-aryl-3-furamides 7a-n were synthesized by the reaction of 2,4-dimethyl-furan-3-carbonyl chloride 5 with aromatic amines 6a-n in dry dioxane in the presence of triethylamine (Scheme 2). Yields of the reaction products were 84−92 %.

Scheme 2. Synthesis 2,4-dimethyl-N-aryl-3-furamides.

Eur. Chem. Bull. 2020, 9(12), 410-415 http://dx.doi.org/10.17628/ecb.2020.9.410-415 412
Table 1. Values of the Chemgauss 4 score of 2,4-dimethyl-N-(2-aryl)-3-furamides derivatives and reference compounds.

| Compound ID or reference compound | Chemgauss 4 score | Compound ID or reference compound | Chemgauss 4 score |
|-----------------------------------|-------------------|-----------------------------------|-------------------|
|                                   | 1HT5 (COX-1) | 3MQE (COX-2) | 1HT5 (COX-1) | 3MQE (COX-2) |
| 7a                                | -9.003030     | -10.270514 | Aspirin     | -7.977182     | -8.933105 |
| 7b                                | -8.843842     | -10.332836 | Diclofenac  | -8.298965     | -10.573636 |
| 7c                                | -8.943698     | -10.325527 | Etoricoxib  | 0.489733      | -9.833112 |
| 7d                                | -9.316087     | -10.865539 | Flurbiprofen| -12.727644    | -12.073698 |
| 7e                                | -7.995869     | -11.244852 | Ibuprofen   | -12.126113    | -10.477378 |
| 7f                                | -7.564784     | -10.768264 | Indomethacin| -8.843241     | -11.326180 |
| 7g                                | -7.970945     | -10.427266 | Isoxicam    | -7.356161     | -9.013797  |
| 7h                                | -9.477314     | -10.019304 | Ketoprofen  | -10.003001    | -11.834192 |
| 7i                                | -7.862546     | -10.936769 | Ketorolac   | -9.982499     | -12.177383 |
| 7j                                | -9.574938     | -10.233967 | Lumiracoxib | -10.311695    | -12.314234 |
| 7k                                | -8.871384     | -10.072598 | Meloxicam   | -6.610479     | -9.254274  |
| 7l                                | -8.582786     | -10.723902 | Parecoxib   | -8.273745     | -11.163197 |
| 7m                                | -7.314748     | -9.674338  |             |               |            |
| 7n                                | -9.126192     | -11.325491 |             |               |            |

Figure. Compound 7a docked in the active site of COX-1 (a) and COX-2 (b) in comparison with inhibitor Ibuprofen (c and d) docked in the active site of COX-1 and COX-2 correspondingly.
The structures of the obtained compounds were confirmed by $^1$H NMR 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 (1HT5 and 3MQE correspondingly) were obtained from Protein Data Bank (www.rcsb.org). As research objects: 2,4-dimethyl-N-(2-aryl)-3-furamides derivatives, common NSAIDs (aspirin, mefenamic acid, diclofenac, ibuprofen, indomethacin, ketoprofen, ketorolac and others) and well-known selective COX-2 inhibitors, such as parecoxib, lumiracoxib, etoricoxib and others, were chosen. To estimate *in silico* COX-2-compound and COX-1-compound binding scoring function values were calculated. Chemgauss 4 scoring function ranking allowed us to select compounds, which could prospectively be selective COX-2 inhibitors. Make Receptor program allows to extract the active sites (biotarget) of COX-2 and COX-1 from crystallographic models for molecular docking.

Molecular docking studies included generation of R-, S- and cys-trans isomers of ligands and them conformers using program were generated via Omega 2 with Flipper parameter. Further program Hybrid that uses elements of ligand based design to enhance performance. Typically, the 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. Ranking property of the scoring function allowed to analyze the results easily (table 1).

Ranking and analysis of the molecular docking results were obtained using the selected compounds and crystallographic model of COX-2 and COX-1 with scoring function (Chemgauss 4). Results allowed us to select compounds, which could prospectively be COX inhibitors at the level of Ibuprofen for future (in-depth) pharmacological studies for further evaluation of in vitro anti-inflammatory activity. The interactions between COX-1 and COX-2 active site and the most active compound 7n in comparison with Ibuprofen (non-selective inhibitor of COX-1&2) is shown in Figure. Moreover, it should be noted that results predicted via docking correlate quite well with that obtained in the in vitro assay. The selected “lead” compound 7n based on the *in vitro* screening results was also predicted to be the most active in the docking studies.

**Pharmacology**

Carrageenan-induced paw edema is a 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 2,4-dimethyl-N-(aryl)-3-furamides 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 induce various anti-inflammatory activity – from almost complete absence to a pronounced anti-inflammatory effect. Evaluation indicated that 11 compounds (7a, 7b, 7c, 7d, 7e, 7f, 7g, 7j, 7k, 7l, 7m) showed no significant decrease in carrageenan-induced rat paw edema, as their inhibition rates were only 7.2-35.6%, as compared to the control group. The anti-inflammatory effect for compounds 7h and 7i is approximately equivalent to that of the reference drug. However, the anti-inflammatory activity of the for compound 7n gave the result at the level of 45.4 % inhibition indicating the methyl 2-[(2,4-dimethyl-3-furyl)amino]-4,5-dimethoxybenzoate were more potent than Ibuprofen.

### Table 2. Anti-inflammatory effect of 2,4-dimethyl-N-(aryl)-3-furamides on carrageenan-induced rat paw edema (mL) in vivo evaluation, % protection from inflammation.

| Compound ID | Paw edema volume (mL)±SEM* | % Inhibition | Activity relative to Ibuprofen, % |
|-------------|---------------------------|--------------|----------------------------------|
| Control     | 2.20 ± 0.050              | -            | -                                |
| 7a          | 1.71± 0.040               | 22.3         | 55.5                             |
| 7b          | 1.93± 0.045               | 12.1         | 30.1                             |
| 7c          | 1.84± 0.045               | 16.2         | 40.3                             |
| 7d          | 2.04 ± 0.050              | 7.2          | 17.9                             |
| 7e          | 1.58 ± 0.040              | 28.3         | 70.4                             |
| 7f          | 1.90 ± 0.045              | 13.5         | 33.6                             |
| 7g          | 1.42± 0.035               | 35.6         | 88.6                             |
| 7h          | 1.31± 0.035               | 40.5         | 100.8                            |
| 7i          | 1.29± 0.035               | 41.2         | 102.5                            |
| 7j          | 1.51± 0.035               | 31.2         | 77.6                             |
| 7k          | 1.86± 0.045               | 15.6         | 38.8                             |
| 7l          | 1.65 ± 0.040              | 25.1         | 62.4                             |
| 7m          | 1.71 ± 0.040              | 22.3         | 55.5                             |
| 7n          | 1.20 ± 0.030              | 45.4         | 112.9                            |
| Ibuprofen   | 1.32 ± 0.035              | 40.2         | 100                              |

**CONCLUSION**

In summary, we have presented an efficient approach of the synthesis of 2,4-dimethyl-N-(2-aryl)-3-furamides. The synthesized compounds were preselected via molecular docking for further testing of their anti-inflammatory activity in vitro. During the study of synthesized substances anti-inflammatory effect in the carrageenan model of inflammatory oedema of white rats paws, we found three highly active compounds with a pronounced anti-inflammatory effect. Evaluation indicated the methyl 2-[(2,4-dimethyl-3-furyl)amino]-4,5-dimethoxybenzoate were more potent than Ibuprofen.

**ACKNOWLEDGEMENTS**

This work was financially supported by the National Research Foundation of Ukraine (project 2020.01/0166). We are grateful Department of Pharmacology, DanyloHalytskyLviv National Medical University for in vivo evaluation of the anti-inflammatory activity.
REFERENCES

1Pirlamarla, P., Bond, R. M., FDA labeling of NSAIDs: Review of nonsteroidal anti-inflammatory drugs in cardiovascular disease, Trends Cardiovasc. Med., 2016, 26 (8), 675. doi: 10.1016/j.tcm.2016.04.011

2Kileen, M. J., Linder, M., Pontoniere, P., Crea, R., NF-κB signaling and chronic diseases: exploring the potential of natural products to drive new therapeutic opportunities, Drug Discov. Today, 2014, 19, 373. doi: 10.1016/j.drudis.2013.11.002

3Bacchi, S., Palumbo, P., Sponta, A., Coppolino, M., Clinical pharmacology of non-steroidal anti-inflammatory drugs: a review, Antinflamm. Antiallergy Agents Med. Chem., 2012, 11, 52–64. doi: 10.2174/187152312803476255

4Wen, F., Jin, H., Tao, K., Hou, T., Design, synthesis and antiinflammatory activity of novel furancarboxamide derivatives, Eur. J. Med. Chem., 2016, 120, 244. doi: 10.1016/j.ejmech.2016.04.060

5Hee J. K., Chang-Hyun, O., Kyung H. Y., Synthesis of New Pyrimidinylaminobenzene Derivatives and Their Antiproliferative Activities Against Melanoma Cell Line, Bull. Korean Chem. Soc., 2013, 34 (8), 2311. doi:10.5120/bks.2013.34.8.2311

6Young, B. M., Hyatt, J. L., Bouck, D. C., Chen, T., Hanumesh, P., Price, J., Boyd, A., Potter, P. M., Webb, T. R., Structure–Activity Relationships of Stabilized 1-Pyryld-2-phenyl-1,2-ethanediones: Potent, Selective Carboxylesterase Inhibitors, J. Med. Chem., 2010, 53 (24), 8709. doi:10.1021/jm101011q

7Moreno-Vargas, A. J., Raynald, I. R., Vogel, D. P., Synthesis and Glycosidase Inhibitory Activities of 5′-(1′′'-Dideoxy-1′,4′-iminocarbonylsulfonyl-2-phenyl-1,2-ethanediyl)-2′-methyl-3-azido-3′-(35,4R)-3,4-dihydroxypropanoyl-2-yl)-2-methylfuranyl-3-carboxylic Acid Derivatives: New Leads as Selective α-L-Fucosidase and β-L-Galactosidase Inhibitors, Helv. Chim. Acta, 2003, 86 (6), 1894. doi:10.1002/hch.200309152

8Cheng, C. C., Huang, X., Gerald, W., Shipps, Jr., Wang, Y., Wyss, D. F., Soucy, K. A., Jiang, C., Cravalho, S., Ferrari, E., He, Z., Huang, H. C., ACS Med. Chem. Lett., 2010, 1(9), 466. doi:10.1021/ml100128h

9Matiychuk, Y., Ogurtsov, V., Ostopiuk, Y., Chaban, T., Matiychuk, V., Pyridine Carboxamides: Potent Palm Site Inhibitors of HCV NS5B Polymerase, Bioinorganic Res. Appl. Chem., 2020, 10 (4), 5809. doi:10.33263/BRIAC104.809814

10Chaban, T., Ogurtsov, V., Matiychuk, V., Tymoshuk, O., Byczyński, Ł., Synthesis, structural characterization and thermal studies of a novel reagent 1-[5-benzyl-1,3-thiazol-2(3H)-yl]diazenyl]naphthalhene-2-ol, J. Therm. Anal. Calorim., 2017, 127, 2233. doi:10.1007/s10973-016-5784-0

11Chaban, T., Klenina, O., Chaban, I., Ogurtsov, V., Harkov, S., Lelyukh, M., Thiazolo[5,4-d]pyrimidines and thiazolo[4,5-d]pyrimidines: a review on synthesis and pharmacological importance of their derivatives, Pharmacia, 2018, 65 (2), 54.http://bsphs.org/?magasine=thiazolo54-dpyrimidines-and-thiazolo45-dpyrimidines-a-review-on-synthesis-and-pharmacological-importance-of-their-derivatives

12Pokhodylo, N. T., Teslenko, Y. O., Matiychuk, V. S., Obushak, M. D., Synthesis of 2,1-Benzisoxazoles by Nucleophilic Substitution of Hydrogen in Nitroarenes Activated by the Azole Ring, Synthesis, 2009, 16, 2741. doi:10.1055/s-0029-1216875

13Chaban, T., Ogurtsov, V., Mahlovanyy, A., Sukhodolska, N., Chaban, I., Harkov, S., Matiychuk, V., Antioxidant properties of some novel derivatives thiazolo[4,5-b] pyridine, Pharmacia, 2019, 66(4), 171. doi:10.3897/pharmacia.66.e36764

14Pokhodylo, N. T., Matiychuk, V. S., Obushak, N. D., Synthesis of 1H,1,2,3-triazole derivatives by the cyclization of aryl azides with 2-benzothiazolylacetonone, 1,3-benz-thiazol-2-ylacetonitrile, and (4-aryl-1,3-thiazol-2-yl)acetonitriles, Chem. Heterocycl. Compd., 2009, 45 (4), 483. doi: 10.1007/s10593-009-0287-6

15Lozynska, L., Tymoshuk, O., Chaban, T. Spectrophotometric Studies of 4-[N-[4(3-methoxybenzylidene)-benzenesulfonfyl as a Reagent for the Determination of Palladium, Acta Chimica Slovenica, 2015, 62(3), 159. doi:10.17344/acs.2014.866

16Chaban, T., Ogurtsov, V., Chaban, I., Myrko, I., Harkov, S., Lelyukh, M., Synthesis of some new 4-iminothiazolidine-2-ones as possible antioxidants agents, Pharmacia, 2019, 66 (1), 27. doi:10.3897/pharmacia.66.e35131

17Tymoshuk, O., Oleksiv, L., Khvalbota, L., Chaban, T., Patsay, I., (4′-[(4′-flavone–3′-benzyl-1,3-thiazol-2′-yl)diazenyl]naphthalene-2-yl)acyclohexane: a new reagent 1-([(5-benzyl-1,3-thiazol-2-yl)diazenyl]naphthalhene-2-ol, Ukr. Biochem. J., 2010, 82 (1), 63. doi:10.17344/ubj92.02.132

18Byczyński, Ł., Design, synthesis, and SAR studies of some novel analogs of 5,7-dimethyl-6-phenylazo-thiazolo[4,5-b]pyrimidine: a novel reagent 1-[5-benzyl-1,3-thiazol-2(3H)-yl]diazenyl]naphthalhene-2-ol, J. Heterocycl. Chem., 2010, 47, 415. doi:10.1002/jhet.321

19Chaban, T., Matiychuk, V., Ogurtsov, V., Chaban, I., Harkov, S., Nektgaevec, I., Synthesis and biological activity of some novel derivatives 5,7-dimethyl-6-phenylazo-3H-thiazolo[4,5-b]pyridine-2-one, Pharmacia, 2018, 65 (4), 51. http://bsphs.org/?magasine=synthesis-and-biological-activity-of-some-novel-derivatives-57-dimethyl-6-phenylazo-3Hthiazolo45-bpyridine-2one

Received: 07.11.2020. Accepted: 22.11.2020.