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Synthesis and anticancer properties of *N*-(5-R-benzyl-1,3-thiazol-2-yl)-2,5-dimethyl-3-furamides

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Aim. Study of the synthesis and anticancer activity of a series of *N*-(5-R-benzyl-1,3-thiazol-2-yl)-2,5-dimethyl-3-furamides. **Methods.** Organic synthesis, analytical and spectral methods, pharmacological screening. **Results.** *N*-(5-R-benzyl-1,3-thiazol-2-yl)-2,5-dimethyl-3-furamides 7a-g have been prepared in good yields by the reaction of 2-amino-5-(R-benzyl)thiazoles with 2,5-dimethyl-3-furoylchloride. Their structure was confirmed by ^{1}H NMR spectroscopy and microanalyses. The synthesized compounds have been evaluated for their anticancer activity against 60 cancer lines in the concentration of 10 μM. The human tumour cell lines were derived from nine different cancer types: leukemia, melanoma, lung, colon, CNS, ovarian, renal, prostate, and breast cancers. It was found that compounds 7d,e,g exhibit a high activity with GP = 29.05–35.02 % whereas 7a-c,f – moderate activity with GP = 60.31–67.36 %. The most active compound 7g showed a high inhibition activity (GI_{50}<10 μM) against 54 of 58 human tumor cell lines with average GI_{50} values of 4.22 μM and the colon cancer subpanel demonstrated the highest sensitivity with [a] mean GI_{50} value of 2.53 μM. The most sensitive line was T-47D (BreastCancer, GI_{50} = 0.088 μM). [The] MG-MID values for the most active compound 7g are less compared with those for 5-fluorouracil, curcumin and cisplatin when testing in the same manner. **Conclusions.** A series of new *N*-(5-R-benzyl-1,3-thiazol-2-yl)-2,5-dimethyl-3-furamides were prepared. The compounds with high anticancer activity have been identified.

K e y w o r d s: organic synthesis, arylation, acylation, 2-amino-5-arylmetylthiazole, anticancer activity.

Introduction

The diazonim salts are very important as starting materials in organic synthesis. In our previous works we have developed [the] methods of synthesis of furane [1,2], thiophene [3],

pyrazole [4], thiazole[5-7], triazole [8] derivatives based on using diazonium salt as starting reagents. The condensed compounds were also prepared [9-11]. The advantage of the proposed method is that the synthesis of arenediazonium salts from low-cost aromatic amines abundantly available in the market is very simple. It means that the variety of different substitutes in organic molecules can be introduced, which is very important for the purposes of medical chemistry. One of the heterocyclic core prepared by this strategy was 2-aminothiazole [5-7, 12], a privileged structure in medical chemistry[13-16].

The present work is devoted to the synthesis and evaluation of anticancer activity [of] *N*-(5-R-benzyl-1,3-thiazol-2-yl)-2,5-dimethyl-3-furamides using diazonium salts as a starting material. Noteworthy, *N*-1,3-thiazol-2-yl furamides display biological activity of different kind such as antivarial [17] and antibacterial [18], they are effective against both replicative and latent mycobacterium tuberculosis [19, 20], malaria parasites [21], as well as the ligands of adenosine receptors [22], allosteric glucokinase activators [23]and the inhibitors of the Src family kinase p56Lck [24]. The anticancer properties of *N*-1,3-thiazol-2-yl furamides were also reported [25–28]. Considering the above, the synthesis of *N*-(1,3-thiazol-2-yl)-2,5-dimethyl-3-furamides and the investigation of their biological properties are [an] actual task.

Materials and Methods

All starting materials were purchased from Merck and used without purification. NMR spectra were determined with Varian Mercury 400 (400 MHz) spectrometer, in DMSO-d_6. Melting points were determinated in open capillary tubes and are uncorrected. The purity of the compounds was checked by thin-layer chromatography performed with Merck Silica Gel 60 F254 aluminum sheets.

5-R-benzylthiazol-2-ylamines **5a-g** were prepared according [to the] procedure described in [12].

N-(5-R-benzyl-1,3-thiazol-2-yl)-2,5-dimethylfuran-3-carboxamides(7a-g)

General procedure. To a solution of 0.01 mol of 2-aminothiazole **5a-g** and 1 ml of triethylamine in 30 ml of anhydrous dioxane we added under stirring 1.59g (0.01 mol) of 2,5-dimethyl-3-furoyl chloride **6**. The mixture was left for 0.5 h and diluted with water, and the precipitate was filtered off, washed with water, and recrystallized from mixture alcohol – DMF.

***N-(5-benzyl-1,3-thiazol-2-yl)-2,5-dimethylfuran-3-carboxamide* (*7a*).** Yield80 %, m.p. 157-158 °C. ^{1}HNMR (400 MHz, [D_6]DMSO): δ = 11.90 (s, 1H, NH), 7.38–7.25 (m, 5H, C_6H_4, thiazole), 7.22 (t, *J* = 7.0 Hz, 1H, C_6H_4), 6.81 (s, 1H, furane), 4.08 (s, 2H, CH_2), 2.49 (s, 3H, CH_3), 2.22 (s, 3H, CH_3). Anal. Calcd. for $C_{17}H_{16}N_2O_2S$: C, 65.36; H, 5.16; N, 8.97. Found: C, 65.22; H, 5.09; N, 8.88.

2,5-Dimethyl-N-[5-(3-methylbenzyl)-1,3-thiazol-2-yl]furan-3-carboxamide (7b). Yield76 %, m.p. 116-117 °C. ^{1}HNMR (400 MHz, [D_6]DMSO): δ = 11.90 (s, 1H, NH), 7.27 (s, 1H, thiazole), 7.19 (t, *J* = 7.4 Hz, 1H, C_6H_4), 7.12–6.99 (m, 3H, C_6H_4), 6.81 (s, 1H, furane), 4.03 (s, 2H, CH_2), 2.49 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 2.22 (s, 3H, CH_3). Anal. Calcd. for $C_{18}H_{18}N_2O_2S$: C, 66.23; H,

5.56; N, 8.58. Found: C, 66.06; H, 5.49; N, 8.41.

2,5-Dimethyl-N-[5-(4-methylbenzyl)-1,3-thiazol-2-yl]furan-3-carboxamide (7c). Yield 84 %, m.p. 155-156 °C. ^{1}HNMR (400 MHz, [D_6]DMSO): δ = 11.89 (s, 1H, NH), 7.25 (s, 1H, thiazole), 7.15 (d, *J* = 7.9 Hz, 2H, C_6H_4), 7.11 (d, *J* = 7.9 Hz, 2H, C_6H_4), 6.80 (s, 1H, furane), 4.02 (s, 2H, CH_2), 2.49 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 2.22 (s, 3H, CH_3). Anal. Calcd. for $C_{18}H_{18}N_2O_2S$: C, 66.23; H, 5.56; N, 8.58. Found: C, 66.11; H, 5.48; N, 8.47.

N-[5-(4-Ethylbenzyl)-1,3-thiazol-2-yl]-2,5-dimethylfuran-3-carboxamide (7d). Yield74 %, m.p. 123-124 °C. ^{1}HNMR (400 MHz, [D_6]DMSO): δ = 11.89 (s, 1H, NH), 7.26 (s, 1H, thiazole), 7.17 (d, *J* = 8.1 Hz, 2H, C_6H_4), 7.14 (d, *J* = 8.2 Hz, 2H, C_6H_4), 6.81 (s, 1H, furane), 4.03 (s, 2H, CH_2), 2.56 (q, *J* = 7.6 Hz, 2H, CH_2), 2.49 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 1.15 (t, *J* = 7.6 Hz, 3H, CH_3) Anal. Calcd. for $C_{19}H_{20}N_2O_2S$: C, 67.03; H, 5.92; N, 8.23. Found: C, 66.88; H, 5.80; N, 8.11.

N-[5-(4-Methoxybenzyl)-1,3-thiazol-2-yl]-2,5-dimethylfuran-3-carboxamide (7e): Yield 88 %, m.p. 155-156 °C. ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 11.88 (s, 1H, NH), 7.24 (s, 1H, thiazole), 7.18 (d, *J* = 8.5 Hz, 2H, C_6H_4), 6.87 (d, *J* = 8.6 Hz, 2H, C_6H_4), 6.80 (s, 1H, furane), 4.00 (s, 2H, CH_2), 3.72 (s, 3H, OCH_3), 2.49 (s, 3H, CH_3), 2.22 (s, 3H, CH_3). Anal. Calcd. for $C_{18}H_{18}N_2O_3S$: C, 63.14; H, 5.30; N, 8.18. Found: C, 63.01; H, 5.22; N, 8.19.

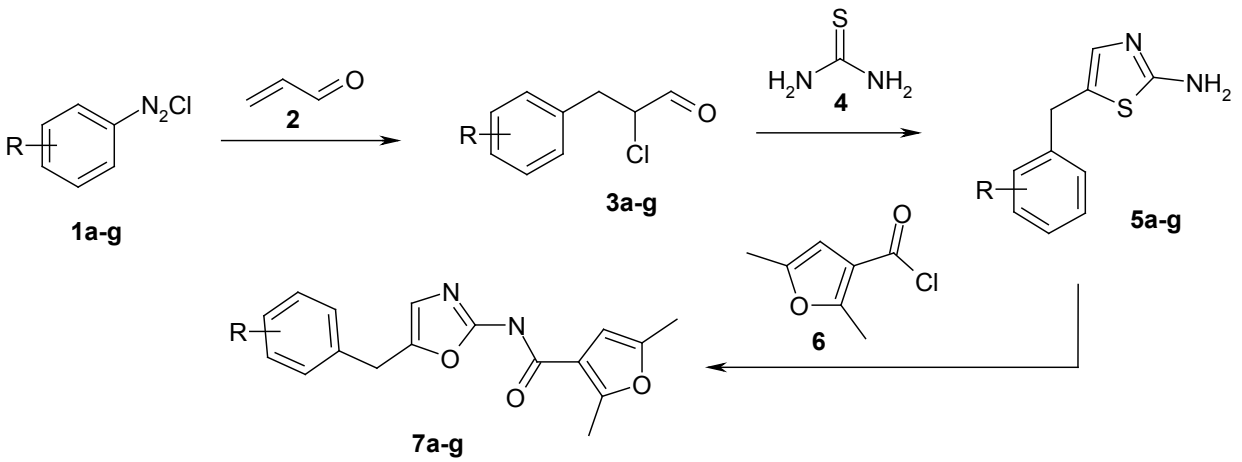
N-[5-(4-Fluorobenzyl)-1,3-thiazol-2-yl]-2,5-dimethylfuran-3-carboxamide (7f). Yield91 %, m.p. 146-147 °C.^{1}HNMR (400 MHz, [D_6]DMSO): δ = 11.91 (s, 1H, NH), 7.31 (dd, J_{HH} = 8.1, J_{HF} =5.7 Hz, 2H, C_6H_4), 7.27 (s, 1H, thiazole), 7.13 (t, *J* = 8.8 Hz, 2H, C_6H_4), 6.81 (s, 1H, furane), 4.08 (s, 2H, CH_2), 2.49 (s, 3H, CH_3), 2.22 (s, 3H, CH_3). Anal. Calcd for $C_{17}H_{15}FN_2O_2S$: C, 61.80; H, 4.58; N, 8.48. Found: C, 61.63; H, 4.51; N, 8.37.

N-[5-(4-Chlorobenzyl)-1,3-thiazol-2-yl]-2,5-dimethylfuran-3-carboxamide (7g). Yield 93 %, m.p. 140-141°C. ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 11.90 (s, 1H, NH)7.35 д (2H, *J* = 8.3 Гц, ClC_6H_4), 7.30-7.25 м (3H, ClC_6H_4 +thiazole),6.81 (s, 1H, furane) 4.94 с (2H, CH_2), 2.49 (s, 3H, CH_3), 2.22 (s, 3H, CH_3). Anal. Calcd for $C_{17}H_{15}FN_2O_2S$: C, 61.73; H, 4.57; N, 8.47. Found: C, 61.60; H, 4.53; N, 8.35.

Results and Discussion

A series of new *N*-(5-R-benzyl-1,3-thiazol-2-yl)-2,5-dimethyl-3-furamides were prepared according to the scheme. The diazonium salts were used as starting material. They react with acroleine under the Meerwein reaction condition [29] to form 3-aryl-2-chloropropanales [12]. These aldehydes were converted into 5-R-benzyl-thiazol-2-ylamines with high yields according to the previously reported synthetic protocols [12]. The acylation of 5-(R-benzyl)-1,3-thiazole-2-amines was carried out by the classical method using 2,5-dimethyl-3-furoyl chloride. The obtained amides **7a-g** are high-melted substances of white or grey colour, poorly soluble in non-polar solvents, good in DMSO and DMF.

The structure of synthesized compounds was confirmed by ^{1}H NMR and microanalyses. In [the] ^{1}H NMR spectra, the signals for the protons of all the structural units were observed in their characteristic ranges. The protons of thiazole and furan rings were recorded



1,**3**,**5**,**7** R = H(**a**), 3-CH_3(**b**), 4-CH_3(**c**), 4-C_2H_5(**d**), 4-CH_3O(**e**), 4-F(**f**), 4-Cl(**g**)

Scheme. Synthesis of *N*-(5-R-benzyl-1,3-thiazol-2-yl)-2,5-dimethyl-3-furamides **7a-g.**

as singlet at δ 7.24–7.27 ppm and 6.80–6.81ppm respectively. H–N amide protons appeared as a singlet at δ11.88–11.91 ppm and methylene groups at 4.00–4.08 ppm. Two other singlets at δ 2.49 and 2.22 ppm indicated methyl groups of furan rings.

Anticancer activity. The synthesized compounds were selected by the National Cancer Institute (NCI) Developmental Therapeutic Program (www.dtp.nci.nih.gov) for the *in vitro* cell line screening. The primary anticancer assay was performed at approximately sixty human tumor cell lines panel derived from nine neoplastic diseases, in accordance with the protocol of the Drug Evaluation Branch, National Cancer Institute, Bethesda [30-33]. The tested compounds were added to the culture at a single concentration (10^{-5}M) and the cultures were incubated for 48 h. Determination of the endpoint was made with a protein binding dye, sulforhodamine B (SRB). [The] Results for each tested compound were reported as the percent of growth of the treated cells when compared to the untreated control cells. The percentage growth was evaluated spectrophotometrically versus controls not treated with test agents.

The screening results are shown in Table 1. The synthesized compounds display different levels of activity in the *in vitro* screening on the tested cell lines. Compounds **7d,e,g** showed [a] high activity with GP = 29.05–35.02 % whereas **7a-c,f** – [a] moderate [activity] with GP = 60.31–67.36 %. Compouds **7d,e** were very sensitive to the cell lines MDA-MB-435 (Melanoma), HL-60(TB) (Leukemia), SNB-75 (CNS Cancer) and compounds **7g** – to MDA-MB-435 (Melanoma), UACC-62 (Melanoma). In all mentioned cases the cytotoxic effect was observed. Noteworthy also, compounds **7a-c** stimulate the activity of COLO 205 (Colon Cancer) cell line with GP = 113.99–115.05 %.

Table 1. **Cytotoxic activity of the tested compounds in the concentration 10^{-5} M against 60 cancer cell lines**

Test compounds	Average growth, %	Range of growth, %	Most sensitive cell line (cancer line/type) GP, %
7a	65.63	19.92–113.99	KM12 (Colon Cancer) 19.92 NCI-H460 (Non-Small Cell Lung Cancer) 24.52 UACC-62 (Melanoma) 24.89
7b	63.22	20.37–115.05	SF-295 (CNS Cancer) 20.37 KM12 (Colon Cancer) 21.59 NCI-H460 (Non-Small Cell Lung Cancer) 21.65 CAKI-1 (Renal Cancer) 26.52 MCF7 (Breast Cancer) 28.62
7c	67.36	4.22–115.04	MDA-MB-435 (Melanoma) 4.22 K-562 (Leukemia) 29.51
7d	35.02	-21.46 –66.34	MDA-MB-435 (Melanoma) – 21.46 HL-60(TB) (Leukemia) – 21.31 SNB-75 (CNS Cancer) – 4.36 A498 (Renal Cancer) 8.18 MDA-MB-468 (Breast Cancer) 9.50 HT29 (Colon Cancer) 10.83
7e	35.02	-9.34 –70.68	HL-60(TB) (Leukemia) – 9.34 SNB-75 (CNS Cancer) – 8.41 MDA-MB-435 (Melanoma)-0.62 K-562 (Leukemia) 11.41 HT29 (Colon Cancer) 13.61 SR (Leukemia) 14.05
7f	60.31	17.47–112.78	KM12 (Colon Cancer) 17.47 SF-295 (CNS Cancer) 17.79 UACC-62 (Melanoma) 20.18 NCI-H460 (Non-Small Cell Lung Cancer) 21.75 MCF7 (Breast Cancer) 26.90 CAKI-1 (Renal Cancer) 27.69
7g	29.05	-6.27 –68.99	MDA-MB-435 (Melanoma)-6.27 UACC-62 (Melanoma) – 0.02 SR (Leukemia) 1.38 NCI-H460 (Non-Small Cell Lung Cancer) 7.63 K-562 (Leukemia) 8.25 MDA-MB-468 (Breast Cancer) 9.96

Finally, compound **7g** was selected for an advanced assay against a panel of approximately sixty tumor cell lines at 10-fold dilutions of five concentrations (100 μM, 10 μM, 1.0 μM, 0.1 μM and 0.01 μM) (Table 2). The percentage growth was evaluated spectrophotometrically versus controls not treated with the test agents after 48-h exposure using the SRB protein assay to estimate the cell viability or growth. The dose–response parameters were calculated for each cell line: GI_{50} – molar concentration of the compound leading to

the 50 % inhibition of net cell growth; TGI – molar concentration of the compound leading to the total inhibition; and LC_{50}– molar concentration of the compounds leading to [the] 50 % net cell death. Furthermore, the mean graph midpoints (MG_MID) were calculated for GI_{50}, giving an average activity parameter over all cell lines for the tested compound. For the calculation of MG_MID, the insensitive cell lines were included with the highest concentration tested.

The most active compound **7g** showed [a] high inhibition activity (GI_{50}<10 μM) against 54 of 58 human tumor cell lines with [the] average GI_{50} values of 4.22 μM and the colon cancer subpanel demonstrated the highest sensitivity with [the] mean GI_{50} value of 2.53 μM (Table 2). The most sensitive line was T-47D

Table 2. **Influence of compound 7g on the growth of tumor cell lines**

Disease	Cell line	GI_{50}, μM	Disease	Cell line	GI_{50}, μM
Leukemia	CCRF-CEM	5.84	**Melanoma**	LOX IMVI	3.31
	HL-60(TB)	3.03		MALME-3M	6.12
	K-562	1.31		M14	2.83
	MOLT-4	3.18		MDA-MB-435	1.58
	RPMI-8226	4.97		SK-MEL-2	1.70
	SR	0.657		SK-MEL-28	6.77
Non-Small Cell Lung Cancer	A549/ATCC	1.22		SK-MEL-5	0.398
	EKVX	4.15		UACC-257	5.01
	HOP-62	4.63		UACC-62	0.481
	HOP-92	4.83	**Ovarian Cancer**	IGROV1	7.82
	NCI-H226	21.8		OVCAR-3	3.76
	NCI-H23	3.87		OVCAR-4	1.02
	NCI-H322M	11.9		OVCAR-5	-
	NCI-H460	0.432		OVCAR-8	5.75
	NCI-H522	2.64		NCI/ADR-RES	2.21
Colon Cancer	COLO 205	4.90		SK-OV-3	12.1
	HCC-2998	0.740	**Renal Cancer**	786-0	2.42
	HCT-116	3.54		A498	2.96
	HCT-15	0.728		ACHN	-
	HT29	3.64		CAKI-1	0.798
	KM12	0.893		RXF 393	4.88
	SW-620	3.24		SN12C	5.07
CNS Cancer	SF-268	3.73		TK-10	9.80
	SF-295	0.589		UO-31	1.93
	SF-539	3.85	**Breast Cancer**	MCF7	0.659
	SNB-19	9.37		MDA-MB-231/ATCC	1.51
	SNB-75	12.6			
	U251	3.58		HS 578T	12.8
Prostate Cancer	PC-3	5.92		BT-549	3.70
	DU-145	3.21		T-47D	0.088
				MDA-MB-468	1.70

(Breast Cancer, GI_{50} = 0.088 μM). [The] Values of TGI and LC_{50} were above the 100 μM except [the] data of TGI for Non-Small Cell Lung Cancer cell lines HOP-92(TGI = 62.5μM), CNS Cancer cell lines SF-295 (TGI = 40.0μM) and SNB-75 (TGI = 90.1μM), Melanoma cell lines MDA-MB-435 (TGI = 5.10 μM), SK-MEL-5(TGI = 31.3μM) and UACC-62 (TGI = 90.1 μM), Renal Cancer cell line MDA-MB-468 (TGI = 56.8μM), RXF 393(TGI= 63.7 μM) and Breast Cancer cell line MDA-MB-468 (TGI= 8.29μM).

The selectivity index (SI) obtained by dividing the full panel MG-MID (μM) of the compound **7g** by its individual subpanel MG-MID (μM) was considered as a measure of compound's selectivity.The value between 3 and 6 refers to moderate selectivity. The index SI greater than 6 indicates a high selectivity toward the corresponding cell line, whereas the compounds meeting neither of the criteria are rated as non-selective [34]. In this context, the active compound **7g** does not demonstrate any selectivity toward all tested cell lines (Table 3).

Table 4 demonstrates that the tested compound **7g** is effective against all of the cell lines, as it is shown by the full panel mean-graph. MG-MID (μM) values for **7g** are less than those for 5-fluorouracyl, curcumin and cisplatin when tested in the same manner.

Conclusions

A series of novel *N*-(5-R-benzyl-1,3-thiazol-2-yl)-2,5-dimethylfuran-3-carboxamides were synthesized and their anticancer activity was investigated. The compounds with significant levels of anticancer activity towards the selected cancer cell lines have been found and may be used for the further optimization.

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Table 3. **Anticancer selectivity pattern of the most active compound 7g at the GI_{50} (C, μM) levels**

Cpd	Parameters	Subpanel tumor cell lines								
		L	NSCLC	ColC	CNSC	M	OV	RC	PC	BC
7g	GI_{50}	3.17	6.16	2.53	5.62	3.13	5.44	3.98	4.57	3.41
	SI	1.33	0.69	1.67	0.75	1.35	0.78	1.06	0.92	1.24

L – leukemia, NSCLCC – non-small cell lung cancer, ColC – colon cancer, CNSC – CNS cancer, M – melanoma, OV– ovarian cancer, RC – renal cancer, PC – prostate cancer, BC – breast cancer.

Table 4. **Mean growth inhibitory concentration (GI_{50}, μM) of compound 7g in comparison with 5-FU, Cisplatin and Curcumin**

	Subpanel tumor cell lines									
Cpd	L	NSCLC	ColC	CNSC	M	OV	RC	PC	BC	MG-MID
7g	3.17	6.16	2.53	5.62	3.13	5.44	3.98	4.57	3.41	4.22
5-FU	15.1	>100	8.4	72.1	70.6	61.4	45.6	22.7	76.4	52.5
Cisplatin	6.3	9.4	21.0	4.7	8.5	6.3	10.2	5.6	13.3	9.48
Curcumin	3.7	9.2	4.7	5.8	7.1	8.9	10.2	11.2	5.9	7.41

USA, for *in vitro* evaluation of [the] anticancer activity.

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Синтез і протипухлинні властивості *N*-(5-R-бензил-1,3-тіазол-2-іл)-2,5-диметил-3-фурамідів

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Мета. Синтез та дослідження протипухлинної активності *N*-(5-R-бензил-1,3-тіазол-2-іл) – 2,5-диметил-3-фурамідів. **Методи.** Органічний синтез, аналітичні та спектральні методи, фармакологічний скринінг.

Результати. У результаті взаємодії 2-аміно-5-(R-бензил) тіазолів з 2,5-диметил-3-фуроїлхлоридом було отримано відповідні *N*-5-R-бензил-1,3-тіазол-2-іл)-2,5-диметил-3-фураміди **7a-g** з хорошими виходами. Структуру синтезованих сполук підтверджено ^{1}H ЯМР спектроскопією та мікроаналізом. Протипухлинну активність синтезованих сполук вивчали *invitro* на 60 лініях ракових клітин у концентрації 10 мкМ. Лінії пухлинних клітин людини отримували з дев'яти різних типів раку: лейкемії, меланоми, легенів, товстої кишки, ЦНС, яєчників, нирки, простати та молочної залози. Встановлено, що сполуки **7d, e, g**проявляють високу активність з GP = 29,05 – 35,02 %, тоді як **7a-c, f**–помірну при GP = 60,31–67,36 %. Найактивніша сполука**7g** виявила високу інгібуючу активність (GI_{50}<10 мкМ) проти 54 з 58 клітинних ліній пухлин людини із середніми значеннями GI_{50}= 4,22 мкМ, а субпанель раку товстої кишки продемонструвала найвищу активність із середнім значенням GI_{50}= 2,53 мкМ. Найбільш чутливою лінією була T-47D (Рак молочної залози, GI_{50} = 0,088 мкм). Значення MG-MID для найбільш активної сполуки **7g**є меншим, у порівнянні з 5-фторурацилом, куркуміном та цисплатином при тестуванні аналогічним чином. **Висновки.** Отримано ряд нових *N*-(5-R-бензил-1,3-тіазол-2-іл)-2,5-диметил-3-фурамідів. Виявлено сполуки з високою протиракковою активністю.

Ключові слова: органічний синтез, арилювання, ацилювання, 2-аміно-5-арилметилтіазоли, протипухлинна активність.

Синтез и противоопухолевые свойства *N*-(5-R-бензил-1,3-тиазол-2-ил)-2,5-диметил-3-фурамидов

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Цель. Синтез и исследование противоопухолевой активности *N*-(5-R-бензил-1,3-тиазол-2-ил)-2,5-диметил-3-фурамидов. **Методы.** Органический синтез, аналитические и спектральные методы, фармакологический скрининг. **Результаты.** В результате взаимодействия 2-амино-5-(R-бензил)тиазолов с 2,5-диметил-3-фуроилхлоридом было получено соответствующие *N*-5-R-бензил-1,3-тиазол-2-ил)-2,5-диметил-3-фурамиды **7a-g** с хорошими выходами. Структуру синтезированных соединений подтверждено методом спектроскопии^{1}H ЯМР и микроанализом. Противоопухолевую активность синтезированных соединений изучали *in vitro* на 60 линияхраковых клеток в концентрации 10 мкм. Линии опухолевых клеток человека получали из девяти различных типов рака: лейкемии, меланомы, легких, толстой кишки, ЦНС, яичников, почки, простаты и молочной железы. Установлено, что соединения **7d**, **e**, **g** проявляют высокую активность с GP = 29,05–35,02 %, тогда как **7a-c**, **f**– умеренную при GP = 60,31–67,36 %. Для соединения**7g** обнаружено высокую ингибирующую активность (GI_{50}<10 мкм) против 54 из 58 клеточных линий опухолей человека со средними значениями GI_{50}= 4,22 мкм, а субпанель рака толстой кишки продемонстрировала самую высокую активность со средним значением GI_{50}= 2,53 мкМ. Наиболее чувствительной линией была T-47D (Рак молочной железы, GI_{50} = 0,088 мкМ). Значение MG-MID для наиболее активного соединения **7g** меньше, по сравнению с 5-фторурацилом, куркумином и цисплатином при тестировании аналогичным образом. **Выводы.** Получен ряд новых *N*-(5-R-бензил-1,3-тиазол-2-ил)-2,5-диметил-3-фурамидов. Обнаруженосоединения с высокой противоопухолевойактивностью.

Ключевые слова: органический синтез, арилирование, ацилирование, 2-амино-5-арилметилтиазолы, противоопухолевая активность.

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