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RESEARCH ARTICLE

Synthesis of new pyrrolo[2,3-*d*]pyrimidine and thieno[2,3-*d*]pyrimidine derivatives of piperazin-1-yl-1,3-oxazole-4-carbonitriles, prediction and evaluation of their ADMET properties

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Abstract: The discovery of nucleoside antibiotics gave impetus to the development of the chemistry of pyrrolo[2,3-*d*]pyrimidines and thieno[2,3-*d*]pyrimidines as biologically active compounds. This work describes a universal and efficient approach to the synthesis of new pyrrolo[2,3-*d*]pyrimidine and thieno[2,3-*d*]pyrimidine derivatives of piperazin-1-yl-1,3-oxazole-4-carbonitriles. Their potential as biologically active compounds is considered and ADMET-score is predicted to assess their further application as pharmaceutical substances.

Keywords: pyrrolo[2,3-*d*]pyrimidine; thieno[2,3-*d*]pyrimidine; 1,3-oxazole; prediction ADMET.

Introduction

The discovery of nucleoside antibiotics has sparked sustained interest in pyrrolo[2,3-d]pyrimidines and thieno[2,3-d]pyrimidines as valuable scaffolds for the development of biologically active compounds. The presence of nitrogen atoms in heterocycle not only confer altered electronic properties but also add a hydrogen bond acceptors, lead to changing the physicochemical and biological properties of a substance.

A particularly interesting group of these molecules are amino-substituted pyrrolo[2,3-*d*]pyrimidines and thieno-[2,3-*d*]pyrimidines, which appear in a variety of biologically active molecules (Figure 1), can be particularly challenging or lengthy to prepare *via* reported methods.

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A series of piperazine-substituted pyrrolo[2,3-*d*]pyrimidine and thieno[2,3-*d*]pyrimidine derivatives were found as antiviral [1] and anticancer [2] agents. Pyrrolo[2,3-*d*]pyrimidine and thieno[2,3-*d*]pyrimidine fragments are the parts of molecules – inhibitors of adenosine kinase [3, 4], tyrosine kinases [5, 6], calcium channel blockers [7] and modulators of aldehyde dehydrogenase (ALDH) enzymatic activity [8].

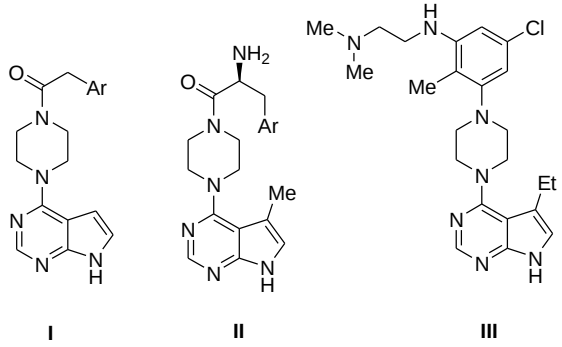

Figure 1. Biologically active piperasine-substituted pyrrolo-[2,3-*d*]pyrimidines and thieno[2,3-*d*]pyrimidines.

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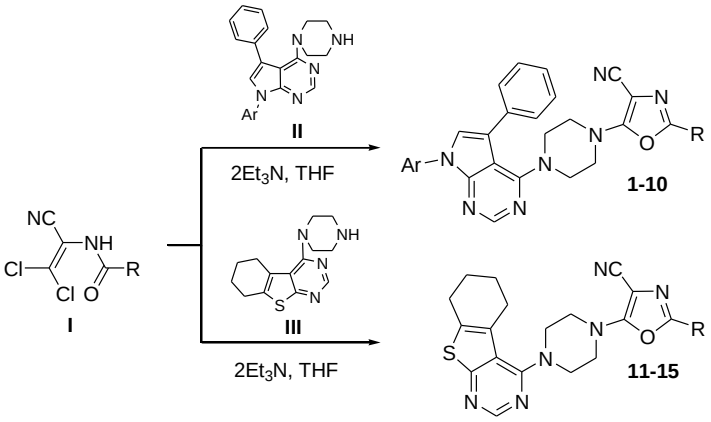
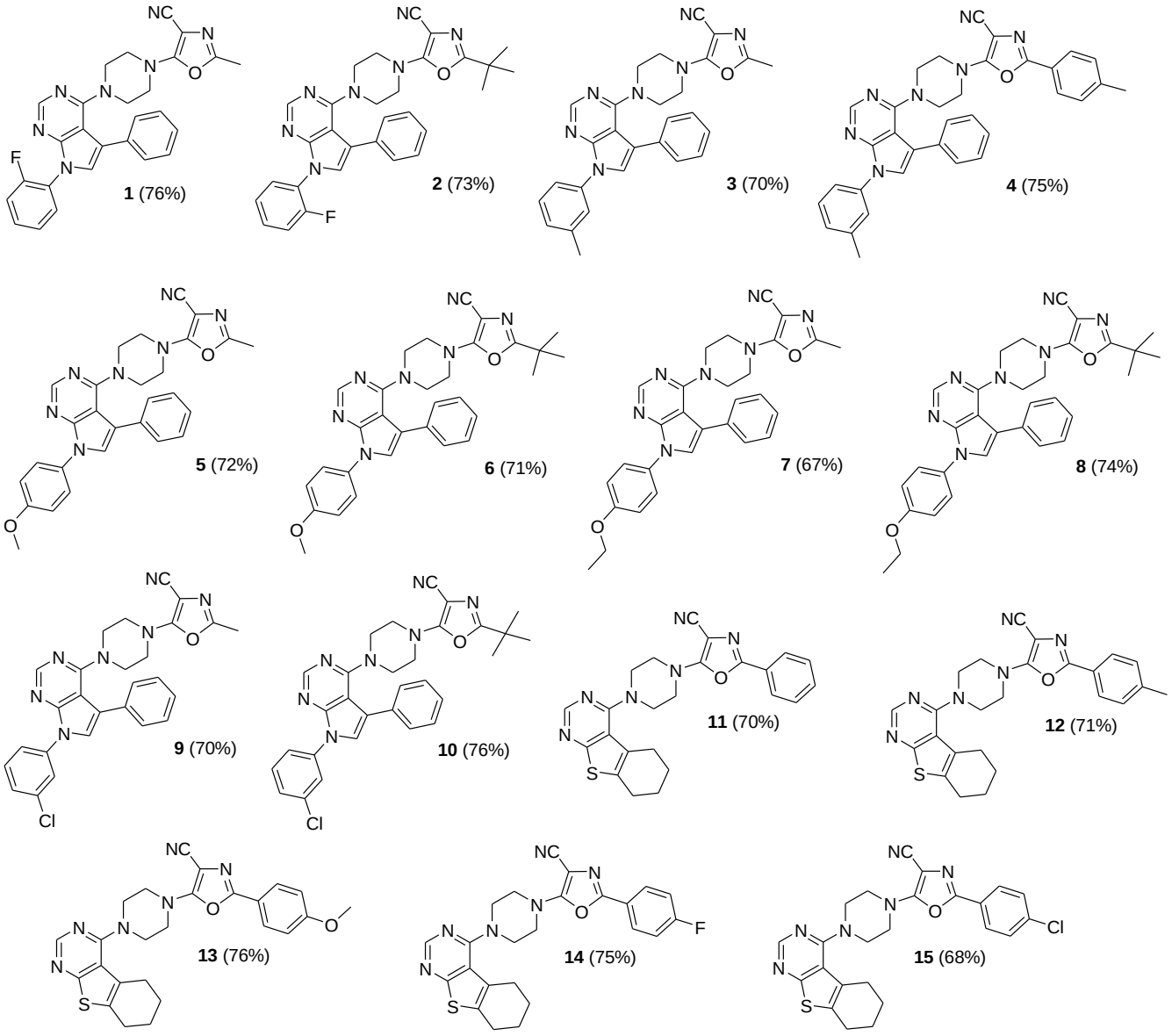


R = CH_3, $C(CH_3)_3$, C_6H_5, 4-$CH_3C_6H_4$, 4-$CH_3OC_6H_4$, 4-FC_6H_4, 4-ClC_6H_4;
Ar = 2-FC_6H_4, 3-$CH_3C_6H_4$, 4-$CH_3OC_6H_4$, 4-$C_2H_5OC_6H_4$, 3-ClC_6H_4



Scheme 1. Synthesis of target 5-amino-4-cyano-1,3-oxazoles (**1-15**).

Table 1. Calculated druglikness parameters of compounds **1-15**[*].

№	Physico-chemical indicators						Lipophilicity	Solubility in water
	MW	nA	n-RB	n-HBA	n-HBD	TPSA	Log $P_{o/w}$ (cons)	Log S (ESOL)
1	479.51	36	4	6	0	87.01	4.13	-6.39
2	521.59	39	5	6	0	87.01	4.98	-7.37
3	475.54	36	4	5	0	87.01	4.16	-6.53
4	551.64	42	5	5	0	87.01	5.46	-7.99
5	491.54	37	5	6	0	96.24	3.83	-6.30
6	533.62	40	6	6	0	96.24	4.68	-7.28
7	505.57	38	6	6	0	96.24	4.17	-6.54
8	547.65	41	7	6	0	96.24	4.99	-7.52
9	495.96	36	4	5	0	87.01	4.35	-6.83
10	538.04	39	5	5	0	87.01	5.21	-7.80
11	442.54	32	3	5	0	110.3	3.95	-6.19
12	456.56	33	3	5	0	110.3	4.35	-6.49
13	472.56	34	4	6	0	119.6	4.04	-6.26
14	460.53	33	3	6	0	110.3	4.34	-6.35
15	476.98	33	3	5	0	110.3	4.58	-6.78

[*]MW – molecular weight;
nA – number of atoms in a molecule;
n-RB – number of rotational bonds;
n-HBA – number of O and N atoms as H-bond acceptors;
n-HBD – number of OH and NH groups as H-bond donors;
TPSA – topological polar surface area;
Log $P_{o/w}$ (cons) – coefficient between *n*-octanol and water. The consensus log $P_{o/w}$ is the arithmetic mean of the values predicted by the five methods (XLOGP3, WLOGP, MLOGP, SILICOS-IT, iLOGP);
Log S (ESOL) – index water solubility [28].

Table 2. Druglikeness parameter filters.

	Filter	Lipinski	Ghose	Veber	Egan	Muegge
Descriptors	MW	< 500 Da	180-480			200-600
	nHBD	< 5				<=5
	nHBA	< 10				<=10
	LogP	< 5	-0.4 to +5.6		<=5.88	-2 to 5
	nA		20 to 70			
	TPSA			<=140	<=131.6	<150
	nRB			<=10		<=15

A series of 4-(piperazin-1-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine derivatives **I** were found to be potential anticancer agents and Akt inhibitors with IC_{50} values of 18.0 and 21.3 nM [9, 10]. Pyrrolopyrimidines described in [11] have been regarded as a novel class of LIM-kinase 2 inhibitors. Compounds **II** demonstrated potent enzyme inhibition of targets Akt1/2/3, *p*-PRAS40 in tumor xenografts, combined with high solubility and good ADME properties for development therapeutic agents [12]. Substance **III** is selective highly potent p70S6K inhibitor, has a reasonable ADME profile, and is efficacious in the PC3 xenograft model [13].

The development of the chemistry of functional derivatives of 1,3-oxazole is due to the successful search for bioactive drugs through these derivatives. In particular, in recent years, a number of works have been published on the biological activity of derivatives of 5-amino-1,3-oxazole-4-carbonitriles, which have proven to be effective inhibitors of pyruvate kinase [14], protein kinase SK2 [15], aminoglycoside-modifying enzymes [16], monoamine oxidase [17], lipoxygenase [18, 19], PHIP(2) [20], and have also shown antitumor [21, 22] and antimicrobial [23] activity. This allows us to consider such derivatives as 5-piperasine-substituted 1,3-oxazole-4-carbonitriles with pyrrolo[2,3-*d*]pyrimidine and thieno[2,3-*d*]pyrimidine fragments as promising compounds for further functionalization to increase their biological activity and to search for new potent drugs.

Results and Discussion

Based on the previous developments in the field of bioactive 5-amino-4-cyano-1,3-oxazoles [14-23] and also pyrrolo[2,3-*d*]pyrimidines and thieno[2,3-*d*]pyrimidines, we chose the following synthesis path for the obtaining of target structures **1-15**.

Compounds **II** and **III** were obtained by the synthetic route described in [24, 25]. Reaction of *N*-(2,2-dichloro-1-cyanovinyl)amides **I** with piperazine-substituted pyrrolo[2,3-*d*]pyrimidine **II** and thieno[2,3-*d*]pyrimidine **III** derivatives was carried out according to the known procedure [26, 27]. This reaction occurs at a temperature of 20-25 °C in anhydrous tetrahydrofuran in the presence of triethylamine. The reaction proceeds regioselectively with the formation of 5-amino-1,3-oxazoles **1-15** in yields of 67-76% (Scheme 1).

The composition and structure of substituted 2-amino-1,3-oxazole-4-carbonitriles **1-15** are confirmed by the results of elemental analysis, IR spectra, ^{1}H NMR and chromatographic-mass spectra (*Experimental section*). Their IR spectra are characterized by absorption bands of CN groups (2202-2216 cm^{-1}). In the ^{1}H NMR spectra, along with the signals of the aryl substituents, characteristic signals of pyrrolo[2,3-*d*]pyrimidine and thieno[2,3-*d*]pyrimidine rings are presented as singlets in the ranges of 8.57-8.40 and 7.94-7.58 ppm, piperazine group appear in the spectrum at δ 3.39-3.26 ppm. The molecular ion peaks in the chromatographic-mass spectra correspond to the calculated ones.

Molecular properties and Drugglikes evaluation

Predictions of the physicochemical properties of a molecule are essential for ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) and drug similarity analysis. These predictions are based on several factors, including the area of the polar Van der Waals surface, which plays a crucial role in molecular recognition. Additionally, the number of atoms that act as donors or acceptors of bonds influences the molecule's ability to form stable complexes with its target. Other important properties include the molecule's solubility in water, which is a key characteristic of bioavailability, and lipophilicity, which refers to the ability of molecules to permeate membranes. The prediction of these physicochemical parameters was conducted using the SwissADME online platform, and the results are presented in Table 1.

To assess druglikeness, several filters can be applied to evaluate compounds based on specific indicators, helping to identify the most promising candidates. Table 2 provides five distinct perspectives on the evaluation of druglikeness parameters, along with the ranges for each individual indicator.

Analyzing the obtained results, the following observations can be noted:

• **Molecular Weight**: All compounds fall within the acceptable ranges of the Lipinski and Muegge filters, with only seven compounds passing the Ghose rule.

• **Number of Hydrogen Bond Donors**: All compounds meet the criteria of the presented filters.

• **Number of Hydrogen Bond Acceptors**: All compounds also pass the criteria of the presented filters.

• **Number of Atoms**: All compounds comply with the Ghose rule filter.

• **Number of Rotatable Bonds (nRot or nRB)**: All compounds adhere to the Veber and Muegge rules.

• **Topological Surface Polarization Area (TPSA)**: All compounds satisfy the requirements of the Veber, Egan, and Muegge rule filters.

• **Lipophilicity Index**: Compounds **4** and **10** do not meet the Lipinski and Muegge rule filters but are included in the analysis per the Ghose and Egan rules.

To estimate the water solubility index (Log S), we will use the following ranking: insoluble <−10 <poorly <−6 <moderately <−4 <soluble <−2 <very <0 <highly [29].

Accordingly, the predicted values indicate poor solubility for all products.

Pharmacocinetics

Pharmacokinetic parameters can help characterize a molecule as a potential drug candidate. Predicting these parameters is crucial for making informed decisions about selecting compounds for *in vitro* evaluation, as well as during the synthesis and optimization phases of molecular design. This process can influence the structure of a molecule to achieve high permeability, an optimal balance of efficacy and safety, and improved metabolic stability. Studying pharmacokinetic parameters in silico at the early stages of drug candidate development can significantly enhance the likelihood of overall success throughout the process [30]. For predicting pharmacokinetic parameters, we selected several tools, including the SwissADME and pkCSM online resources, which are backed by substantial theoretical evidence and are widely used in the scientific community [31-35].

Absorption parameters predicted in pkCSM are presented in Table 3, including Intestinal absorption, Caco2 permeability, Skin Permeability, P-glycoprotein substrate, P-glycoprotein inhibitor **I** and **II**.

The pkCSM platform provides various metrics to evaluate the absorptive properties of compounds, including:

• **Caco-2 Permeability**: This model predicts the permeability coefficient of compounds through a monolayer of human colorectal adenocarcinoma epithelial cells, based on data from 574 molecules.

• **Intestinal Absorption**: Compounds with an absorption rate of less than 30% are classified as poorly absorbed.

Table 3. Predicted absorption indices.

№	Absorption indices					
	Intestinal absorption (GI absorption)	Caco2 permeability	Skin Permeability (Log K_p), cm/s	P-glycoprotein substrate (P-gp)	P-glycoprotein inhibitor I	P-glycoprotein inhibitor II
1	100%	1.25	-2.74	No	Yes	Yes
2	99.16%	1.29	-2.74	No	Yes	Yes
3	100%	1.10	-2.74	No	Yes	Yes
4	99.30	1.05	-2.735	No	Yes	Yes
5	100	0.44	-2.73	No	Yes	Yes
6	100	0.59	-2.73	No	Yes	Yes
7	100	0.43	-2.73	No	Yes	Yes
8	100	0.58	-2.73	No	Yes	Yes
9	98.63	1.09	-2.74	No	Yes	Yes
10	97.24	1.14	-2.74	No	Yes	Yes
11	94.58	1.37	-2.73	No	Yes	Yes
12	95.00	1.36	-2.72	No	Yes	Yes
13	95.48	1.06	-2.74	No	Yes	Yes
14	94.45	1.37	-2.73	No	Yes	Yes
15	93.55	1.35	-2.73	No	Yes	Yes

Table 4. Predicted distribution indices*.

№	VDss (human)	Fraction unbound (human)	BBB permeability	CNS permeability
1	0.057	0.341	-1.184	-2.103
2	0.032	0.339	-1.165	-1.823
3	0.28	0.322	-0.984	-1.94
4	0.122	0.327	-1.044	-1.537
5	0.705	0.27	-1.205	-2.132
6	0.507	0.27	-1.165	-1.817
7	0.791	0.267	-1.229	-2.14
8	0.583	0.268	-1.189	-1.825
9	0.29	0.318	-1.159	-1.899
10	0.306	0.307	-1.14	-1.619
11	0.003	0.209	-0.858	-1.787
12	0.293	0.099	-0.847	-1.721
13	0.068	0.12	-1.082	-2.037
14	0.14	0.101	-1.055	-1.834
15	0.281	0.093	-1.022	-1.681

*VDss (human) – steady-state volume of distribution, the theoretical volume into which the total dose of a drug must be evenly distributed to obtain the same concentration as in blood plasma.
Fraction unbound (human) – the fraction of the free form of the drug in the blood serum.
BBB permeability – an indicator characterizing the ability of the drug to penetrate the blood-brain barrier.
CNS permeability – permeability of the CNS.

Table 5. Predicted metabolism indices.

№	CYP-450						
	CYP2D6 (S)	CYP3A4 (S)	CYP1A2 (I)	CYP2C19 (I)	CYP2C9 (I)	CYP2D6 (I)	CYP3A4 (I)
1	-	+	-	+	+	-	-
2	-	+	-	+	+	-	-
3	-	+	-	+	+	-	-
4	-	+	-	+	-	-	-
5	-	+	-	+	+	-	+
6	-	+	-	+	+	-	-
7	-	+	-	+	+	-	+
8	-	+	-	+	+	-	+
9	-	+	-	+	+	-	-
10	-	+	-	+	+	-	-
11	-	+	+	+	+	-	+
12	-	+	+	+	+	-	+
13	-	+	-	+	+	-	+
14	-	+	+	+	+	-	+
15	-	+	+	+	+	-	+

.

• **Skin Permeability**: A compound is considered to have relatively low skin permeability if its log Kp is greater than -2.5.

• **P-glycoprotein Substrate**: P-glycoprotein is an ATP-binding cassette transporter (ABC) that serves as a biological barrier, removing toxins and xenobiotics from cells. Screening for P-glycoprotein transport is conducted using MDR-knockout transgenic mice and cell systems. The predictive model for this property is built using 332 compounds to determine whether a given compound is a P-glycoprotein substrate.

• **P-glycoprotein I Inhibitor and P-glycoprotein II Inhibitor**: Modulating P-glycoprotein-mediated transport can have significant pharmacokinetic implications for P-glycoprotein substrates. This can be leveraged for therapeutic benefits or may lead to contraindications. Predictive models were developed using compounds characterized as inhibitors of P-glycoprotein **I** and **II**, specifically compounds 1273 and 1275, respectively.

Compounds **1-15** exhibit a high degree of absorption (over 95%) when administered orally. Most of these compounds demonstrate significant permeability (greater than 0.09) through a monolayer of human colorectal adenocarcinoma epithelial cells, which serves as a model for predicting absorption through the human intestinal mucosa. However, compounds **5, 6, 7**, and **8** show moderately absorbent permeability values (below 0.6), likely due to the presence of *p*-methoxy and *p*-ethoxy functional groups.

Analyzing the LogKp index reveals that all compounds are not expected to be absorbed through the skin (with a value greater than -2.5), suggesting they should be safe for skin contact, except in cases of specific allergic reactions that this index does not account for.

To evaluate the stability of intracellular drug concentrations, which is essential for maintaining a consistent therapeutic effect, we assessed the compounds' potential to act as substrates or inhibitors of P-glycoprotein I and II. The prediction indicates that all compounds are possible inhibitors of P-glycoprotein **I** and **II** while not showing a tendency to be substrates for it.

Compounds **1-15** can achieve high concentrations in the body, which may enhance treatment efficacy. However, this also poses a risk of potentially toxic accumulation within the body.

The distribution of compounds in the body is characterized by several indicators: the steady-state volume of distribution (VDss), the free form fraction, permeability through the blood-brain barrier (BBB permeability), and permeability into the central nervous system (CNS permeability). The calculation of these distribution indicators was performed using the online platform pkCSM (Table 4).

A higher VDss indicates that the drug is more widely distributed throughout the body rather than remaining in blood plasma. An indicator is considered low if it is below –0.15 and high if it is above 0.45.

When developing a new biologically active compound, it's important to consider the potential for the molecule to bind to serum proteins, as only the unbound (free) form is biologically active. The bound form of the drug cannot perform its pharmacological function.

The ability of a molecule to cross the blood-brain barrier is crucial for drug biotargets in the brain, as this can help

reduce side effects and overall toxicity. A compound is regarded as having good permeability across the blood-brain barrier if its parameter value is greater than 0.3, while a value above -1 indicates that the compound is poorly distributed in the brain.

The CNS permeability index assesses the ability of a compound to penetrate the central nervous system from the bloodstream. Compounds with a value greater than -2 are considered capable of penetrating the CNS, while those with a value less than -3 are unable to do so.

The prediction results indicate that most compounds, with the exception of compounds **5, 6, 7**, and **8**, are poorly distributed throughout the body and tend to remain in the blood plasma. Compounds **12, 13, 14**, and **15** showed the highest levels of binding to blood proteins, with only about 10% of the drug remaining in a free state. For the other compounds, this figure ranges from 20-30%, which is typical for most drugs. This allows them to circulate in the blood and reduces the rate of excretion. A high fraction of free drug can increase the risk of toxic effects; however, compounds **1-15** did not exceed this threshold and exhibited a moderate level of binding to blood proteins.

Cytochrome P450 inhibitors play a crucial role in drug metabolism. Cytochrome P450 is an important detoxification enzyme primarily found in the liver, where it oxidizes xenobiotics to facilitate their excretion. This enzyme can deactivate many medications, while some drugs may be activated by it. Inhibitors, such as grapefruit juice, can significantly impact drug metabolism and are therefore contraindicated. The calculation of these metabolism indicators was performed using the online platform pkCSM (Table 5).

It is essential to assess the ability of compounds to inhibit cytochrome P450, including models for different isoforms. A compound is classified as an inhibitor if the concentration required for 50% inhibition is less than 10 μM.

Compounds **1-15** are not substrates of CYP2D6 and act as inhibitors of CYP1A2, with the exception of compounds **11, 12, 14** and **15**. This indicates a low likelihood of these compounds interacting with other drugs or being affected by genetic variations in metabolic activity. All compounds are substrates of CYP3A4, allowing us to predict their metabolism in the body. However, this also increases the risk of interactions with other drugs. Specifically, compounds **5, 7, 8** and **11-15** are also inhibitors of CYP3A4, which can elevate the concentration of drugs metabolized by this enzyme, raising the risk of toxicity.

Additionally, all compounds except for compound **4** inhibit CYP2C9, potentially enhancing the effectiveness of other drugs metabolized by this enzyme. This can be particularly beneficial for medications with a narrow therapeutic index. However, it may also increase the concentration of drugs such as ibuprofen, diclofenac, and warfarin, heightening the risk of toxicity and adverse interactions. Lastly, all compounds have the potential to inhibit CYP2C19, which can pose additional risks when taken concurrently with certain medications, including sertraline, citalopram, phenobarbital, carbamazepine, omeprazole, and clopidogrel.

To evaluate excretion, the pkCSM platform analyzed total clearance and the potential of compounds to act as substrates for the renal organic cation transporter OCT2 (Table 6).

Table 6. Predicted excretion indices.

№	Total Clearance	Renal OCT2 substrate
1	0.709	-
2	0.521	-
3	0.905	-
4	0.797	-
5	0.822	-
6	0.635	-
7	0.858	-
8	0.671	-
9	0.286	-
10	0.259	-
11	0.04	-
12	0.02	-
13	0.067	-
14	0.113	-
15	0.094	-

The total clearance for most compounds ranges from 0.259 to 0.905, which can be classified as normal, moderate, or high clearance. In contrast, for compounds **11-15**, the total clearance was between 0.02 and 0.113, indicating a low level of clearance and slow elimination from the body. Based on the results obtained, compounds **1-15** are not substrates of renal OCT2. To evaluate toxicity, the pkCSM platform analyzed AMES toxicity, T. pyriformis toxicity, maximum tolerated dose, minnow toxicity, oral rat acute toxicity (LD_{50}), oral rat chronic toxicity (LOAEL), and specific toxicity: hERG I and II inhibitors, hepatotoxicity, and skin sensitization (Table 7).

The results indicate that the compounds are not mutagenic based on the AMES test. The calculated LD_{50} values suggest a very low toxicity for these compounds, which corresponds to the 4th toxicity class as per the toxicity classification set by the Organization for Economic Cooperation and Development (OECD Test No. 425). Substances in this category are generally not dangerous, even at high doses. Oral rat chronic toxicity ranges from 0.010 to 0.574 mg/kg_bw/day. For compounds **1-15**, the chronic toxicity for rats can be estimated as low, since the value is less than 1 mg/kg_bw/day.

The maximum tolerated dose for compounds **1, 4, 6** and **8** to **11** is over 0.477 mg/kg/day, while for the other

Table 7. Predicted toxicity indices*.

№	Toxicity indices									
	AMES	MTD	hERG I inhibitor	hERG II inhibitor	LD_{50}	LOAEL	Hepatotoxicity	Skin Semsitisation	TP	MT
1	-	0.698	-	+	2.76	0.09	+	-	0.285	-2.422
2	-	0.686	-	+	2.826	0.161	+	-	0.285	-3.033
3	-	0.659	-	+	2.805	0.146	-	-	0.285	-3.043
4	-	0.573	-	+	2.636	-0.222	-	-	0.285	-4.000
5	-	0.422	-	+	2.977	0.517	-	-	0.285	-2.279
6	-	0.625	-	+	2.898	0.229	-	-	0.285	-4.473
7	-	0.454	-	+	2.979	0.524	-	-	0.285	-2.444
8	-	0.644	-	+	2.893	0.236	-	-	0.285	-4.638
9	-	0.663	-	+	2.784	-0.081	-	-	0.285	-3.261
10	-	0.645	-	+	2.871	-0.010	-	-	0.285	-3.872
11	-	0.577	-	+	2.564	0.233	+	-	0.288	-2.462
12	-	0.145	-	+	2.800	0.574	+	-	0.295	-2.115
13	-	0.382	-	+	2.903	0.433	+	-	0.289	-2.110
14	-	0.141	-	+	2.815	0.402	+	-	0.293	-1.999
15	-	0.167	-	+	2.836	0.347	+	-	0.294	-2.333

*AMES – is an evaluation method used to determine the mutagenic potential of substances on bacteria (ehe Ames test).
MTD – max. tolerated dose
LD_{50} – oral rat acute toxicity, mol/kg
LOAEL – Oral Rat Chronic Toxicity
TP – T.Pyriformis toxicity
MT – Minnow toxicity

compounds, it is lower than 0.477 mg/kg/day. In terms of minnow toxicity, the lethal concentration (LC_{50}) results show that for compounds **1, 5, 7**, and **11** to **15**, this concentration is low; however, for compounds **2** to **4** and **6** to **10**, the LC_{50} values are high.

Specific toxicity assessments reveal concerns regarding cardiotoxicity, hepatotoxicity, and skin sensitization. Predictions regarding the compounds' potential to act as hERG I and II inhibitors show that compounds **1** to **15** may inhibit hERG II, which implies they could impact potassium efflux in cardiac cells and potentially cause cardiac arrhythmias. However, they do not inhibit hERG I, suggesting that while these compounds may have undesirable effects, they are not definitively cardiotoxic, as the functions of hERG II have yet to be thoroughly studied.

Additionally, compounds **1, 2**, and **11** to **15** are predicted to be hepatotoxic, but none of the compounds show sensitizing properties.

Conclusions

Fifteen new derivatives of pyrrolo[2,3-*d*]pyrimidine and thieno[2,3-*d*]pyrimidine, specifically piperazin-1-yl-1,3-oxazole-4-carbonitriles, were synthesized, and their ADMET indices were predicted. The predictions included an analysis of molecular properties, drug-likeness, and pharmacokinetic parameters such as absorption, distribution, metabolic stability, and excretion, as well as toxicity profiles. Among the fifteen compounds, compounds **1-4** and **9, 10** stood out as they passed most drug-likeness filters and exhibited acceptable predicted pharmacokinetic parameters along with a moderate toxicity profile.

Notes

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The authors declare no conflict of interest.

Author contributions. **N.M.S.**: synthesis of compounds. **O.O.S.**: prediction ADMET, writing most of the manuscript. **M.V.K.**: writing experimental section, writing of the manuscript. **O.P.K.**: investigation, synthesis of compound. **S.G.P.**: synthesis of the compound, conceptualization, supervision. **Ye.S.V.**: writing of the manuscript, synthesis of the compounds. **V.S.B.**: supervision, review & editing.

Experimental section

The solvents were purified according to the standard procedures. All materials were purchased from commercial sources and used without further purification. ^{1}H NMR spectra were recorded on a Bruker Avance DRX-500 (500 MHz) or Varian VXR-400 spectrometer (400 MHz) and ^{13}C

NMR spectra were recorded at Bruker 170 spectrometer (101, 126 MHz) spectra in DMSO-d_6 solution. Chemical shifts are reported in ppm downfield from TMS as internal standards. Mass spectra were recorded on an LC-MS instrument with chemical ionization (CI). LC-MS data were acquired on an Agilent 1100 HPLC system equipped with DAD/ELSD/LCMS-6120 diode matrix and mass-selective detector. Melting points were measured on a MPA100 OptiMelt automated melting point system. Combustion elemental analysis was performed by hand in the V.P. Kukhar Institute of Bioorganic Chemistry and Petrochemistry analytical laboratory. The carbon and hydrogen contents were determined using the Pregl gravimetric method, nitrogen – using the Duma's gasometrical micromethod, sulfur – by the Scheininger titrimetric method, chlore – by the Scheininger titrimetric method.

*General methodology of synthesis of 5-amino-4-cyano-1,3-oxazoles (**1-15**).*

A mixture of 0.0020 mol of dichloroacrylonitrile **I** and 0.0040 mol of triethylamine in 20 ml of anhydrous tetrahydrofuran, 0.0025 mol of the corresponding amine (**II**, **III**) was added. The mixture was stirred on a magnetic stirrer at 20-25 °C for 48 h. The precipitate was filtered of, the solvent was removed *in vacuo*, the residue was treated with water, filtered of, dried and purifed by recrystallization.

*5-(4-(7-(2-Fluorophenyl)-5-phenyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)piperazin-1-yl)-2-methyloxazole-4-carbonitrile (**1**).*

Yield: 0,73 g (76%); white crystals, solid, mp 203-205 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.45 (s, 1H), 7.93-7.88 (m, 3H), 7.60 (d, J = 7.7 Hz, 2H), 7.49 (t, J = 7.7 Hz, 2H), 7.41-7.34 (m, 3H) or 7.37 (dt, J = 15.5, 8.1 Hz, 3H), 3.35-3.34 (m, 4H), 3.27-3.26 (m, 4H), 2.23 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.5, 161.3, 153.2, 151.7, 151.1, 139.1, 137.6, 134.3, 129.2, 129.1, 128.5, 127.6, 126.4, 125.2, 124.8, 121.5, 117.3, 116.4, 106.3, 82.2, 48.3, 45.7, 21.3; IR (KBr) v 2360, 2335, 2211 (CN), 1637, 1596, 1558, 1511, 1441, 1420, 1386, 1369, 1233, 829, 757, 692, 510; Found, %: C, 67.74; H, 4.66; N, 20.47. $C_{27}H_{22}FN_7O$. Calculated, %: C, 67.63; H, 4.62; N, 20.45. LC-MS (CI) m/z $(M+H)^+$ 480.

*2-(tert-Butyl)-5-(4-(7-(2-fluorophenyl)-5-phenyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)piperazin-1-yl)oxazole-4-carbonitrile (**2**).*

Yield: 0,76 g (73%); white crystals, solid, mp 204-206 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.46 (s, 1H), 7.95 (s, 1H), 7.92-7.89 (m, 2H), 7.61 (d, J = 7.2 Hz, 2H), 7.51 (t, J = 7.6 Hz, 2H), 7,42-7,35 (m, 3H) or 7.35-7.21 (m, 3H), 3.39-3.36 (m, 4H), 3.31-3.29 (m, 4H), 1.22 (s, 9H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.6, 162.5, 161.2, 159.8, 158.2, 154.0, 151.3, 150.7, 134.4, 133.3, 130.4, 128.9, 128.2, 126.4, 125.6, 125.3, 125.1, 116.9, 116.2, 114.2, 103.6, 96.4, 47.6, 45.2, 33.3, 27.2, 18.4; IR (KBr) v 2986, 2908, 2204 (CN), 1643, 1595, 1553, 1511, 1441, 1383, 1366, 1266, 1231, 1157, 1113, 1078, 1016, 965, 833, 764, 701, 654; Found, %: C, 69.15; H, 5.48; N, 18.83. $C_{30}H_{28}FN_7O$. Calculated, %: C, 69.08; H, 5.41; N, 18.80. LC-MS (CI) m/z $(M+H)^+$ 522.

*2-Methyl-5-(4-(5-phenyl-7-(m-tolyl)-7H-pyrrolo[2,3-d]-pyrimidin-4-yl)piperazin-1-yl)oxazole-4-carbonitrile (**3**).*

Yield: 0,67 g (70%); white crystals, solid, mp 186-188 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (s, 1H), 7.92 (s, 1H), 7.69-7.65 (m, 2H), 7.61 (d, J = 7.2 Hz, 2H), 7.50 (t, J = 7.6 Hz, 2H), 7.44-7.35 (m, 2H), 7.21 (d, J = 7.0 Hz, 1H), 3.35-3.34 (m, 4H), 3.28-3.26 (m, 4H+H_2O), 2.39 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 160.64, 160.43, 152.07, 151.61, 151.21, 139.19, 137.46, 134.83, 129.45, 129.15, 128.83, 127.76, 127.29, 125.49, 124.93, 121.60, 117.52, 116.64, 104.39, 85.12, 48.31, 45.82, 21.47, 13.52; IR (KBr) v 2845, 2216 (CN), 2199, 1595, 1555, 1442, 1424, 1387, 1263, 778, 693; Found, %: C, 70.76; H, 5.32; N, 20.64. $C_{28}H_{25}N_7O$. Calculated, %: C, 70.72; H, 5.30; N, 20.62. LC-MS (CI) m/z $(M+H)^+$ 476.

*5-(4-(5-Phenyl-7-(m-tolyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl)piperazin-1-yl)-2-(p-tolyl)oxazole-4-carbonitrile (**4**).*

Yield: 0,83 g (75%); white crystals, solid, mp 146-148 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.46 (s, 1H), 7.90 (s, 1H), 7.61-7.65 (m, 6H), 7.48-7.53 (m, 2H), 7.34-7.39 (m, 2H), 7.21-7.25 (m, 3H), 3.31 (s, 8H), 2.39 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 160.3, 160.2, 152.2, 151.2, 151.1, 140.8, 139.2, 137.6, 134.8, 130.0, 129.4, 129.2, 128.8, 127.8, 127.3, 125.8, 125.4, 124.9, 123.3, 121.5, 117.4, 116.4, 104.3, 86.4, 48.3, 45.7, 39.3, 21.5; IR (KBr) v 2972, 2214 (CN), 1610, 1553, 1443, 1423, 1382, 1248, 1263, 970. Found, %: C, 74.13; H, 5.34; N, 17.82. $C_{34}H_{29}N_7O$. Calculated, %: C, 74.03; H, 5.30; N, 17.77. LC-MS (CI) m/z $(M+H)^+$ 552.

*5-(4-(7-(4-Methoxyphenyl)-5-phenyl-7H-pyrrolo[2,3-d]-pyrimidin-4-yl)piperazin-1-yl)-2-methyloxazole-4-carbonitrile (**5**).*

Yield: 0,71 g (72%); beige crystals, solid, mp 170-172 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.43 (s, 1H), 7.85 (s, 1H), 7.73 (d, J = 7.4 Hz, 2H), 7.59 (d, J = 7.6 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.3 Hz, 1H), 7.09 (d, J = 9.0 Hz, 2H), 3.82 (s, 3H), 3.38-3.23 (m, 8H), 2.23 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.5, 160.4, 160.1, 159.7, 159.0, 154.3, 152.5, 150.6, 134.4, 133.8, 130.2, 128.6, 128.3, 126.7, 125.5, 125.5, 125.3, 117.0, 116.0, 114.3, 103.6, 96.7, 55.5, 47.8, 45.3, 26.5; IR (KBr) v 2861, 2210 (CN), 1635, 1591, 1553, 1513, 1439, 1186, 1158, 934, 835, 761, 697; Found, %: C, 68.46; H, 5.15; N, 19.98. $C_{28}H_{25}N_7O_2$. Calculated, %: C, 68.42; H, 5.13; N, 19.95. LC-MS (CI) m/z $(M+H)^+$ 492.

*2-(tert-Butyl)-5-(4-(7-(4-methoxyphenyl)-5-phenyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)piperazin-1-yl)oxazole-4-carbonitrile (**6**).*

Yield: 0,76 g (71%); white crystals, solid, mp 212-214 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.40 (s, 1H), 7.76

(s, 1H), 7.70 (d, *J* = 9.2 Hz, 2H), 7.57 (d, *J* = 7.7 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.06 (d, *J* = 9.2 Hz, 2H), 3.80 (d, *J* = 2.0 Hz, 3H), 3.36 (d, *J* = 5.2 Hz, 4H), 1.21 (s, 9H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.5, 160.4, 160.0, 159.6, 158.0, 154.1, 151.5, 150.5, 134.4, 133.7, 130.2, 128.6, 128.3, 126.7, 125.5, 125.5, 125.2, 116.9, 116.0, 114.3, 103.5, 96.7, 55.4, 47.8, 45.3, 33.1, 27.6, 18.4; IR (KBr) *v* 2972, 2908, 2862, 2206 (CN), 1644, 1594, 1554, 1514, 1493, 1441, 1379, 1342, 1302, 1250, 1271, 1177, 1147, 1112, 1080, 1032, 968, 935, 909, 833. Found, %: C, 69.79; H, 5.88; N, 18.39. $C_{31}H_{31}N_7O_2$. Calculated, %: C, 69.77; H, 5.86; N, 18.37. LC-MS (CI) m/z $(M+H)^+$ 534.

*5-(4-(7-(4-Ethoxyphenyl)-5-phenyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)piperazin-1-yl)-2-methyloxazole-4-carbonitrile (**7**).*

Yield: 0,68 g (67%); white crystals, solid, mp 201-203 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.53 (s, 1H), 7.58 (d, *J* = 3.0 Hz, 1H), 7.69-7.62 (m, 2H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.10-7.04 (m, 2H), 4.15-4.02 (m, 2H), 3.36-3.28 (m, 4H), 3.25-3.22 (m, 4H), 1.35 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.5, 160.5, 160.1, 159.7, 159.2, 154.3, 152.6, 150.9, 134.3, 133.3, 130.2, 128.6, 128.1, 126.7, 125.3, 125.2, 125.1, 116.9, 116.0, 114.3, 103.7, 96.8, 59.2, 56., 47.9, 45., 26.8; IR (KBr) *v* 2861, 2210 (CN), 1641, 1595, 1553, 1512, 1436, 1380, 1280, 1246, 1189, 1174, 1156, 1118, 1045, 927, 963, 826, 761, 692. Found, %: C, 68.91; H, 5.39; N, 19.42. $C_{29}H_{27}N_7O_2$. Calculated, %: C, 68.89; H, 5.38; N, 19.39. LC-MS (CI) m/z $(M+H)^+$ 506.

*2-(tert-Butyl)-5-(4-(7-(4-ethoxyphenyl)-5-phenyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)piperazin-1-yl)oxazole-4-carbonitrile (**8**).*

Yield: 0,81 g (74%); white crystals, solid, mp 164-166 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.40 (s, 1H), 7.78 (d, *J* = 3.0 Hz, 1H), 7.71-7.64 (m, 2H), 7.57 (d, *J* = 7.7 Hz, 2H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.08-7.00 (m, 2H), 4.13-4.00 (m, 2H), 3.38-3.31 (m, 4H), 3.31-3.24 (m, 4H), 1.33 (s, 3H), 1.20 (s, 9H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.9, 161.3, 160.3, 160.0, 158.6, 154.2, 151.7, 150.6, 134.4, 133.7, 130.4, 128.5, 128.2, 126.2, 125.2, 125.8, 125.3, 116.7, 116.7, 114.4, 103.7, 94.1, 82.3, 55.5, 47.4, 45.3, 33.0, 27.4, 21.3; IR (KBr) *v* 2972, 2909, 2864, 2206 (CN), 1644, 1593, 1551, 1514, 1442, 1247, 1177, 1192, 1115. Found, %: C, 70.23; H, 6.11; N, 17.92. $C_{32}H_{33}N_7O_2$. Calculated, %: C, 70.18; H, 6.07; N, 17.90. LC-MS (CI) m/z $(M+H)^+$ 548.

*5-(4-(7-(3-Chlorophenyl)-5-phenyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)piperazin-1-yl)-2-methyloxazole-4-carbonitrile (**9**).*

Yield: 0,69 g (70%); white crystals, solid, mp 190-192 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (s, 1H), 8.10 (d, *J* = 2.5 Hz, 1H), 8.03 (d, *J* = 2.2 Hz, 1H), 7.93 (dd, *J* = 8.0, 2.5 Hz, 1H), 7.64-7.54 (m, 3H), 7.54-7.47 (m, 2H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 3.38-3.33 (m, 8H), 2.24 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 197.3, 183.6, 176.5, 173.6, 160.6, 160.3, 152.2, 151.8, 151.4, 140.1, 138.9, 134.5, 133.9, 131.3, 129.2, 128.8, 127.4, 126.9, 125.1, 123.8, 122.6, 118.0, 116.3, 104.5, 85.1, 48.3, 45.8, 13.5; IR (KBr) *v* 2920, 2860, 2203 (CN), 1637, 1594, 1558, 1483, 1443, 1382, 1243, 694, 690; Found, % C, 65.41; H, 4.49; Cl, 7.14; N, 19.79. $C_{27}H_{22}ClN_7O$. Calculated, %: C, 65.39; H, 4.47; Cl, 7.15; N, 19.77. LC-MS (CI) m/z $(M+H)^+$ 496.

*2-(tert-Butyl)-5-(4-(7-(3-chlorophenyl)-5-phenyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)piperazin-1-yl)oxazole-4-carbonitrile (**10**).*

Yield: 0,82 g (76%); white crystals, solid, mp 213-215 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.52 (s, 1H), 8.11-7.91 (m, 3H), 7.65-7.36 (m, 7H), 3.39-3.28 (m, 8H), 1.25-1.22 (m, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 160.5, 160.2, 154.5, 152.3, 151.4, 141.8, 138.9, 134.6, 133.9, 131.3, 129.2, 128.8, 127.4, 126.9, 125.1, 123.8, 122.6, 118.1, 116.4, 104.5, 97.7, 85.0, 48.3, 45.7, 33.6, 28.1; IR (KBr) *v* 2855, 2202 (CN), 1626, 1582, 1554, 1484, 1438, 1246, 1016, 772, 697. Found, %: C, 67.02; H, 5.28; Cl, 6.55; N, 18.26. $C_{30}H_{28}ClN_7O$. Calculated, %: C, 66.97; H, 5.25; Cl, 6.59; N, 18.22. LC-MS (CI) m/z $(M+H)^+$ 538.

*2-Phenyl-5-(4-(5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4-yl)piperazin-1-yl)oxazole-4-carbonitrile (**11**).*

Yield: 0,62 g (70%); yellowish crystals, solid, mp 210-212 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.54 (s, 1H), 7.88 (d, *J* = 5.3 Hz, 2H), 7.52-7.48 (m, 3H), 3.82-3.77 (m, 4H), 3.53-3.51 (m, 4H), 2.97-2.86 (m, 4H), 1.90-1.74 (m, 4H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 193.2, 188.9, 181.4, 174.0, 167.4, 161.3, 160.2, 158.5, 151.4, 142.2, 131.9, 130.5, 129.1, 125.3, 116.1, 86.3, 49.1, 45.7, 26.0, 25.3, 22.2, 15.6; IR (KBr) *v* 2945, 2866, 2834, 2211 (CN), 1607, 1583, 1533, 1504, 1437, 1372, 1245, 974, 694. Found, %: C, 65.19; H, 5.08; N, 19.03; S, 7.24. $C_{24}H_{22}N_6OS$. Calculated, %: C, 65.14; H, 5.01; N, 18.99; S, 7.24. LC-MS (CI) m/z $(M+H)^+$ 443.

*5-(4-(5,6,7,8-Tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4-yl)piperazin-1-yl)-2-(p-tolyl)oxazole-4-carbonitrile (**12**).*

Yield: 0,65 g (71%); yellowish crystals, solid, mp 228-230 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.56 (s, 1H), 7.78-7.76 (m, 2H), 7.32 (d, *J* = 7.9 Hz, 2H), 3.80-3.77 (m, 4H), 3.53-3.51 (m, 4H), 2.96-2.87 (m, 4H), 2.35 (s, 3H), 1.95-1.70 (m, 4H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 185.2, 171.1, 162.2, 158.5, 153.2, 150.3, 142.9, 138.1, 133.9, 130.5, 104.1, 97.1, 58.0, 47.4, 26.0, 15.1, 8.5; IR (KBr) *v* 2923, 2864, 2208 (CN), 1609, 1583, 1532, 1503, 1437, 1373, 975. Found, %: C, 65.81; H, 5.33; N, 18.45; S, 7.01. $C_{25}H_{24}N_6OS$. Calculated, %: C, 65.77; H, 5.30; N, 18.41; S, 7.02. LC-MS (CI) m/z $(M+H)^+$ 457.

*2-(4-Methoxyphenyl)-5-(4-(5,6,7,8-tetrahydrobenzo-[4,5]thieno[2,3-d]pyrimidin-4-yl)piperazin-1-yl)oxazole-4-carbonitrile (**13**).*

Yield: 0,72 g (76%); white crystals, solid, mp 205-207 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.57 (s, 1H), 7.81 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 8.5 Hz, 2H), 3.84-3.74 (m, 8H), 3.35 (s, 3H), 2.97-2.86 (m, 4H), 1.90-1.75 (m, 4H); ^{13}C NMR (126 MHz, DMSO-d$_6$) δ 187.4, 171.1, 162.2, 158.5, 153.2, 150.3, 142.9, 138.1, 133.9, 130.5, 104.1, 97.1, 58.0, 47.4, 26.0, 15.1, 8.5; IR (KBr) ν 2940, 2860, 2837, 2215 (CN), 1610, 1533, 1502, 1363, 1252, 982. Found, %: C, 63.59; H, 5.15; N, 17.79; S, 6.76. $C_{25}H_{24}N_6O_2S$. Calculated, %: C, 63.54; H, 5.12; N, 17.78; S, 6.78. LC-MS (CI) m/z (M+H)$^+$ 473.

*2-(4-Fluorophenyl)-5-(4-(5,6,7,8-tetrahydrobenzo[4,5]-thieno[2,3-d]pyrimidin-4-yl)piperazin-1-yl)oxazole-4-carbonitrile (**14**).*

Yield: 0,69 g (75%); beige crystals, solid, mp 238-240 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.54 (s, 1H), 7.94-7.92 (m, 2H), 7.37-7.34 (m, J = 8.7 Hz, 2H), 3.79 (t, J = 4.9 Hz, 4H), 3.52 (t, J = 5.1 Hz, 4H), 2.97-2.86 (m, 4H), 1.91-1.74 (m, 4H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 188.9, 181.4, 174.0, 167.4, 161.3, 160.2, 158.5, 151.4, 142.2, 131.9, 130.5, 129.1, 125.3, 116.1, 86.3, 49.1, 45.7, 26.0, 25.3, 22.2, 15.6; IR (KBr) ν 2942, 2868, 2209 (CN), 1620, 1599, 1534, 1503, 1436, 1224, 1151, 974. Found, %: C, 62.64; H, 4.62; N, 18.29; S, 6.95. $C_{24}H_{21}FN_6OS$. Calculated, %: C, 62.59; H, 4.60; N, 18.25; S, 6.96. LC-MS (CI) m/z (M+H)$^+$ 461.

*2-(4-Chlorophenyl)-5-(4-(5,6,7,8-tetrahydrobenzo[4,5]-thieno[2,3-d]pyrimidin-4-yl)piperazin-1-yl)oxazole-4-carbonitrile (**15**).*

Yield: 0,65 g (68%); yellowish crystals, solid, mp 218-220 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.53 (s, 1H), 7.87 (d, J = 8.3 Hz, 2H), 7.56 (d, J = 8.5 Hz, 2H), 3.81-3.74 (m, 4H), 3.52-3.50 (m, 4H), 2.96-2.85 (m, 4H), 1.91-1.73 (m, 4H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 195.4, 188.9, 181.4, 167.4, 161.3, 160.2, 158.5, 151.4, 142.2, 131.9, 130.5, 129.1, 125.3, 116.1, 86.3, 49.1, 45.7, 26.0, 25.3, 22.2, 15.6; IR (KBr) ν 2939, 2866, 2210 (CN), 1617, 1598, 1534, 1435, 1371, 1246, 1088, 973. Found, %: C, 60.46; H, 4.48; Cl, 7.45; N, 17.66; S, 6.71. $C_{24}H_{21}ClN_6OS$. Calculated, %: C, 60.43; H, 4.44; Cl, 7.43; N, 17.62; S, 6.72. LC-MS (CI) m/z (M+H)$^+$ 477.

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Синтез нових піроло[2,3-*d*]піримідинових та тієно[2,3-*d*]піримідинових похідних піперазин-1-іл-1,3-оксазол-4-карбонітрилів, прогноз та оцінка їх властивостей ADMET

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Резюме: Відкриття нуклеозидних антибіотиків дало поштовх для розвитку хімії піроло[2,3-*d*]піримідинів і тієно[2,3-*d*]піримідинів як біологічно активних сполук. У цій роботі описано універсальний та ефективний підхід до синтезу нових піроло[2,3-*d*]піримідинових та тієно[2,3-*d*]піримідинових похідних піперазин-1-іл-1,3-оксазол-4-карбонітрилів. Розглянуто їх потенціал як біологічно активних сполук і прогнозовано ADMET-показники для оцінки їх подальшого застосування як фармацевтичних субстанцій.

Ключові слова: піроло[2,3-*d*]піримідин; тієно[2,3-*d*]піримідин; 1,3-оксазол; прогнозування ADMET.