

## LEAD-LIKE PROPERTIES OF A NOVEL PYRIDINE AMINOPHOSPHONATE: SYNTHESIS, PREDICTIVE EVALUATION AND BIOLOGICAL TESTING

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**Abstract.** *Introduction.* Aminophosphonate derivatives attract considerable interest as a class of low-molecular-weight compounds capable of exerting regulatory effects in biological systems of different origin. Early-stage characterization of biological potential can be achieved by combining predictive approaches with experimental investigation. *The aim* of this study is to synthesize a new aminophosphonate, obtain its water-soluble form and evaluate its biological activity in a “prediction-experiment” format. Dimethyl((3-phenoxyphenyl)((pyridin-2-ylmethyl)amino)methyl)phosphonate (**PMAAPh**) has been synthesized by the Kabachnik-Fields reaction, and then its succinate salt (**PMAAPh-Suc**) has been obtained to improve the solubility in water. The structure of the compound has been confirmed by the methods of a physicochemical analysis (NMR and IR spectroscopy). The predicted biological activity, pharmacokinetic properties, and toxicity have been assessed, using *in silico* tools. *Experimental studies* have been performed, using plant models *in vitro*, and a model of experimental pancytopenia *in vivo*. The computer screening has shown that aminophosphonate **PMAAPh** meets the main criteria for pharmacological similarity and belongs to toxicity class III. The experiment has demonstrated that **PMAAPh-Suc** stimulates the germination and vigor of wheat seeds, and also stimulates hematopoiesis. Taken together, these findings provide a basis for the further investigation of the biological activity of this aminophosphonate.

**Key words:** pyridin-2-ylmethanamine, aminophosphonate, *in silico* analysis, myelostimulating activity, plant growth-stimulating activity

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## 1. Introduction

In recent years, a clear trend has emerged towards the use of integrated approaches that combine the computational prediction methods with the experimental studies [1,2]. The application of *in silico* tools makes it possible to assess drug-likeness, potential biological activity, and toxicological risks of new molecules at the early stages of the research, whereas subsequent *in vitro* and *in vivo* investigations allow for the characterization of their effects on the growth-related and regenerative processes in biological systems of different origins.

Such an integrative strategy is regarded as an effective means of identifying promising low-molecular-weight compounds with a regulatory activity and a balanced safety profile, thereby underscoring the relevance of the further research in this field.

## 2. Experimental part

The IR spectra were recorded on a Nicolet 5700 FT-IR spectrometer, using thin-films. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were obtained on a JEOL JNM-ECA 400 spectrometer in  $\text{CDCl}_3$ .

*Dimethyl* *((3-phenoxyphenyl)((pyridin-2-ylmethyl)amino)methyl)phosphonate (PMAAPh)*. A round-bottom flask equipped with a mechanical stirrer, a Dean–Stark apparatus, and a reflux condenser was charged with pyridin-2-ylmethanamine (0.02 mol), 3-phenoxybenzaldehyde (0.02 mol), and dimethyl phosphite (0.03 mol) in 150 mL of absolute benzene. The reaction mixture was refluxed for 48 h. After the completion of the reaction, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography on  $\text{Al}_2\text{O}_3$  using chloroform/acetone (20:1, v/v) as the eluent. The second fraction was collected to afford **PMAAPh** as a yellow oil.  $R_f=0.43$  (chloroform/acetone (20:1, v/v))

Molecular formula:  $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_4\text{P}$ . Yield: 6.23 g (80%).  $n_D^{20}=1,382$ . IR (film),  $\nu$ ,  $\text{cm}^{-1}$ : 3459 (N–H); 1252 (P=O); 1056 (P–O–C); 1040 (C–O–C); 3020, 1585, 1491, 756, 683 (Ph).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 8.48 (d,  $J = 5.3$  Hz, 1H, pyridine–H), 7.55 (m,  $J = 7.0$  Hz, 1H, pyridine–H), 7.27 (q,  $J = 7.3$  Hz, 3H, Ar–H), 7.16 (d,  $J = 7.0$  Hz, 2H, Ar–H), 7.09 (d,  $J = 5.4$  Hz, 2H, Ar–H), 7.04 (q,  $J = 6.8$  Hz, 1H, pyridine–H), 6.93 (dt,  $J = 24.3, 6.8$  Hz, 3H, Ar–H, pyridine–H), 3.85 (dd,  $J = 14.3, 5.6$  Hz, 1H, CH–P), 3.73–3.62 (m, 4H,  $\text{CH}_3$ , N–H), 3.58 (dd,  $J = 10.6, 5.7$  Hz, 3H,  $\text{CH}_3$ ), 3.14 (s, 2H,  $\text{CH}_2$ ).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$ : 158.83 (Cq, pyridine), 157.54 (Cq, Ar–O), 157.11 (Cq, Ar–O), 149.39 (CH–N, pyridine), 137.48 (CH, pyridine), 136.54 (Cq, Ar), 129.97 (CH, pyridine), 129.83 (2CH, Ar), 123.62 (CH, Ar), 123.56 (CH, Ar), 123.42 (CH, Ar), 123.21 (CH, Ar), 122.44 (CH, Ar), 119.09 (2CH, Ar), 118.52 (CH, Ar), 60.57 (CH–P), 53.70 ( $\text{CH}_3$ ), 53.62 ( $\text{CH}_3$ ), 52.72 ( $\text{CH}_2$ ).

**PMAAPh Succinate (PMAAPh-Suc)**. **PMAAPh** (0.01 mol) and succinic acid (0.01 mol) were thoroughly ground in a mortar with a small amount of ethanol until a homogeneous mixture was obtained. The ethanol was evaporated at 50–

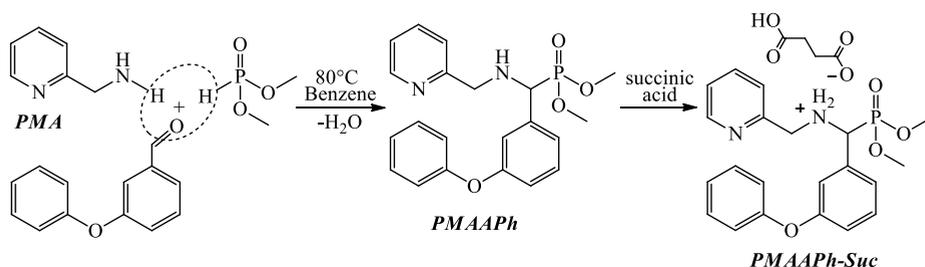
55°C in a drying oven. **PMAA $Ph$ -Suc** was obtained as a yellow powder. M.p.=176–177°C.

**Biological Assays.** The procedures for determining the seed germination energy, laboratory germination, and germination intensity of wheat seeds, as well as the methodology for evaluating myelostimulating activity, were carried out according to the previously described protocols [3].

*In silico* tools [4-6].

### 3. Results and Discussion

At the initial stage of the study, the target aminophosphonate derivative dimethyl ((3-phenoxyphenyl)((pyridin-2-ylmethyl)amino)methyl)phosphonate (**PMAA $Ph$** ) has been synthesized, using the three-component Kabachnik–Fields reaction, which is one of the most common and efficient approaches for the preparation of  $\alpha$ -aminophosphonates. The obtained compound has been isolated in an individual form. To improve the aqueous solubility of **PMAA $Ph$** , its succinate salt (**PMAA $Ph$ -Suc**) has been subsequently prepared by treating the free base with a succinic acid.



The IR spectrum of **PMAA $Ph$**  exhibits an absorption band corresponding to the N–H stretching vibrations at  $3459\text{ cm}^{-1}$ , as well as the characteristic bands of the dimethoxyphosphoryl fragment, namely the P=O and P–O–CH<sub>3</sub> stretching vibrations at  $1252$  and  $1056\text{ cm}^{-1}$ , respectively. The presence of the phenoxyphenyl substituent is confirmed by the aromatic ring bands at  $3020$ ,  $1585$ ,  $1491$ , and  $756\text{ cm}^{-1}$ , along with the C–O–C stretching band of the ether linkage at  $1040\text{ cm}^{-1}$ .

A key diagnostic feature of **PMAA $Ph$**  formation in the NMR spectra is the signal of the methine group at the phosphorus-containing center (CH–P). In the <sup>13</sup>C NMR spectrum, this signal is observed at  $\delta\ 60.57$ , while in the <sup>1</sup>H NMR spectrum the corresponding CH–P proton resonates at  $\delta\ 3.85$ . Its chemical shift and splitting pattern (dd,  $J = 14.3, 5.6\text{ Hz}$ , 1H) reflect the influence of the adjacent heteroatoms (P and N), which is typical for  $\alpha$ -aminophosphonates. The N–H proton falls within the signal region of the OCH<sub>3</sub> groups of the phosphonate moiety ( $\delta\ 3.73\text{--}3.62$ , m, 4H), so it is not considered as a separate resonance.

The *in silico* methods are an effective modern tool for the early-stage biologically active substance evaluation. They enable simultaneous assessment of

the drug-like properties, predicted biological activity, pharmacokinetic profile, and potential toxicity of the new compounds, enabling a rational selection of the most promising structures even before the experimental work.

In our initial study, an *in silico* analysis has been used for a comprehensive evaluation of the aminophosphonate (**PMAAPh**). The first step has been to evaluate the biological potential (predict the spectrum of the biological activity) of **PMAAPh**, using the PASS program (Table 1). The analysis indicates a notable cardiometabolic and regulatory potential of the compound. The types of activity with the highest probability of manifestation ( $P_a > 0.5$ ) are: cholesterol antagonism ( $P_a = 0.605$ ), treatment of restenosis ( $P_a = 0.539$ ), antianginal activity ( $P_a = 0.504$ ), and potential effectiveness in the treatment of Alzheimer's disease ( $P_a = 0.505$ ). The predicted inhibitory activity against glutamate-5-semialdehyde dehydrogenase also reaches high values ( $P_a = 0.531$ ), which demonstrates the possible effect of the compound on amino acid metabolism and energy metabolism. The moderate  $P_a$  values for the regulation of calcium metabolism ( $P_a = 0.479$ ), hypolipidemic effect ( $P_a = 0.356$ ) and treatment of atherosclerosis ( $P_a = 0.410$ ) also demonstrate the potential of the studied aminophosphonate in terms of cardiovascular and metabolic disorders.

**Table 1** – PASS-predictive analysis of the biological activity of **PMAAPh**

<b>Pa</b>	<b>Pi</b>	<b>Activity</b>	<b>Pa</b>	<b>Pi</b>	<b>Activity</b>
0.605	0.019	Cholesterol antagonist	0.410	0.035	Atherosclerosis treatment
0.539	0.005	Restenosis treatment	0.351	0.030	Stroke treatment
0.505	0.012	Alzheimer's disease treatment	0.346	0.025	HIV attachment inhibitor
0.531	0.054	Glutamate-5-semialdehyde dehydrogenase inhibitor	0.340	0.106	Neurodegenerative diseases treatment
0.473	0.004	Antischistosomal	0.332	0.015	Bone formation stimulant
0.504	0.041	Antianginal	0.299	0.003	Factor VIIa inhibitor
0.479	0.018	Calcium regulator	0.356	0.071	Hypolipemic

The activities predicted at lower  $P_a$  values, such as inhibition of HIV attachment, stimulation of bone formation, and inhibition of factor VIIa (Table 1), have not been a priority in this study. These areas require the further experimental verification. Based on the PASS profile, **PMAAPh** can be classified as a promising structure, primarily in the context of cardiometabolic regulation and enzyme inhibition. This justifies the further *in vitro* and *in vivo* studies.

Since the PASS algorithms are primarily focused on predicting the biological activity without considering the pharmacokinetic characteristics of the compound, an additional computational evaluation has been performed in the next step, using the SwissADME platform (Table 2). The data in Table 2 indicate that **PMAAPh** has a balanced physicochemical profile that meets the generally accepted requirements for orally active compounds. The compound is characterized by moderate lipophilicity (Consensus LogP = 3.03) and a high predicted gastrointestinal absorption rate. Furthermore, the bioavailability index has an

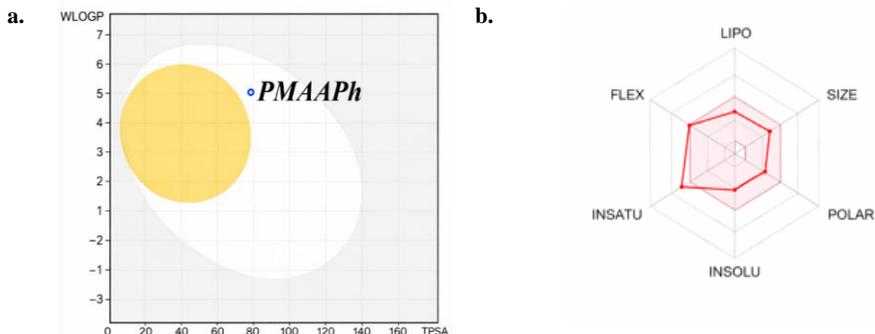
acceptable value (0.55). The topological polar surface area (TPSA = 79.49 Å<sup>2</sup>) indicates a predominantly peripheral pharmacological action. This is consistent with the lack of penetration across the blood-brain barrier predicted by the BOILED-EGG model (Figure 1a). Within this model, the white-colored region corresponds to a high probability of an intestinal absorption. The yellow zone indicates a potential permeability across the blood-brain barrier. Thus, the localization of *PMAAph* within the white region and outside the yellow zone indicates a favorable absorption profile. This also indicates a predominantly peripheral pharmacological action.

**Table 2** – The key calculated ADME and drug-likeness parameters of *PMAAph*

Parameter	Value	Extended comment
Molecular weight (MW)	<b>398.39 g/mol</b>	MW complies with Lipinski's rule (below 500 g/mol). MW places the compound within the classical lead-like range (300–450 g/mol).
Consensus LogP (Po/w)	<b>3.03</b>	This value falls within the range of moderate lipophilicity, indicating a good balance between membrane permeability and water compatibility. This means absorption in the gastrointestinal tract without an excessive hydrophobicity, which could lead to nonspecific binding or increased toxicity.
TPSA	<b>79.49 Å<sup>2</sup></b>	The TPSA assay shows that the standard threshold for blood-brain barrier penetration is exceeded. This indicates a primarily peripheral pharmacological profile and also explains the lack of a predictable CNS penetration.
Rotatable bonds	<b>9</b>	A relatively high number of rotatable bonds reflects an increased conformational flexibility, which may reduce an oral exposure consistency and contributes to the lead-likeness violations, but can enhance an adaptability to diverse biological targets.
Water solubility	<b>Low–moderate</b>	The differences between the ESOL/AlI and SILICOS-IT models indicate the marginal solubility of <i>PMAAph</i> in water, which significantly limits the ADME profile. Therefore, the formation of <i>PMAAph-Suc</i> is necessary.
GI absorption	<b>High</b>	Despite the limited intrinsic solubility, a high predicted gastrointestinal absorption suggests that <i>PMAAph</i> retains sufficient permeability, consistent with its moderate lipophilicity and BOILED-Egg analysis.
BBB permeation	<b>No</b>	The lack of the BBB permeation reduces the risk of the side effects upon the central nervous system, and supports the development of <i>PMAAph</i> for peripheral therapeutic applications.
P-gp substrate	<b>Yes</b>	The predicted interaction with P-glycoprotein suggests that efflux mechanisms may partially limit a systemic exposure, potentially contributing to the interindividual variability in pharmacokinetics.
Lipinski / Egan / Muegge	<b>Passed</b>	The compliance with multiple drug-likeness filters confirms a generally well-balanced physicochemical profile suitable for the further pharmacological development.
Bioavailability score	<b>0.55</b>	A moderate bioavailability score indicates a reasonable oral exposure potential, while leaving room for the improvement through the chemical or formulation optimization.

The radar diagram (Figure 1b) shows how the compound meets the key drug-likeness criteria, such as lipophilicity (LIPO), molecular size (SIZE), polarity (POLAR), solubility (INSOLU), saturation (INSATU), and molecular flexibility

(FLEX). As the diagram shows, most parameters are within the optimal ranges, with only flexibility and solubility showing slight deviations. Based thereupon, it seems justified to obtain succinate salt (PMAA $\text{Ph}$ -Suc) to improve solubility.



**Figure 1** – An illustration of the predicted ADME properties and pharmacokinetic profile of PMAA $\text{Ph}$  (**a** – BOILED-EGG diagram, **b** – radar plot).

To obtain a more comprehensive safety profile, the ADMET analysis has been supplemented with the computational toxicity prediction, using the ProTox-3.0 platform (Table 3). Overall, the compound exhibits a generally favorable predicted toxicology profile.

Specifically, hepatotoxic effects are not predicted (DILI: inactive, probability 0.74), and cardiotoxicity is also not expected (inactive, 0.71). The model also does not predict neurotoxicity or nephrotoxicity, with the corresponding inactive probabilities of 0.53 and 0.59. These results support the rationale for considering this compound early in the evaluation of the drug candidates. ProTox-3.0 does not predict the carcinogenic, mutagenic, immunotoxic, or general cytotoxic effects (inactive, probability range 0.57–0.86). Taken together, these results suggest the absence of the structural features typically associated with a significant toxicity.

However, there are several predicted endpoints: potential respiratory toxicity (activity, 0.69), ecotoxicity (activity, 0.66), food-related toxicity (activity, 0.60), and blood-brain barrier-related toxicity (activity, 0.70).

According to ProTox-3.0, the predicted  $\text{LD}_{50}$  value for PMAA $\text{Ph}$  is 200 mg/kg. This places the compound in toxicity class III (out of six), corresponding to a moderate acute toxicity.

Overall, the obtained data allow the compound to be considered an acceptable lead-like candidate in terms of its toxicological profile, with certain parameters requiring the further experimental validation and optimization. Thus, the results of the *in silico* evaluation provided a well-founded basis for the transition from the computational prediction to the experimental verification of the biological activity of the compound *in vitro* and *in vivo*.

**Table 3** – Toxicological profile of *PMAAPH* according to ProTox-3.0

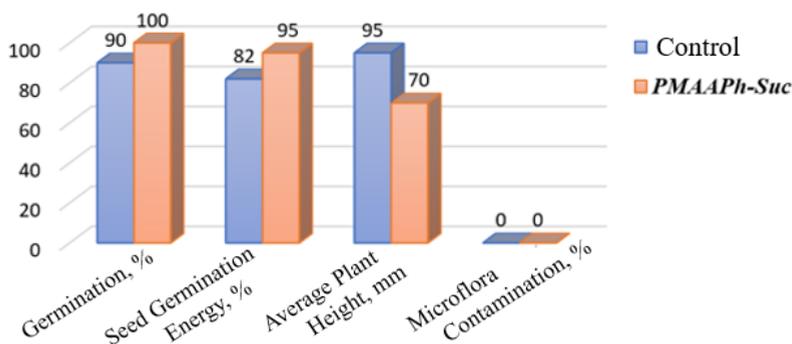
LD <sub>50</sub> (mg/kg)	Toxicity class		Toxicity endpoints		
200	III		Endpoint	Prediction	Probability
			Carcinogenicity	Inactive	0.57
<b>Organ toxicity</b>			Immunotoxicity	Inactive	0.86
Endpoint	Prediction	Probability	Mutagenicity	Inactive	0.66
Hepatotoxicity	Inactive	0.74	Cytotoxicity	Inactive	0.70
Neurotoxicity	Inactive	0.53	BBB-related toxicity	Active	0.70
Nephrotoxicity	Inactive	0.59	Ecotoxicity	Active	0.66
Cardiotoxicity	Inactive	0.71	Clinical toxicity	Inactive	0.52
Respiratory toxicity	Active	0.69	Nutritional toxicity	Active	0.60

Although PASS primarily predicted cardiometabolic and enzymatic activity, the study sought to expand the scope of the study and evaluate the compound's effects on plant growth and hematopoiesis as a manifestation of the broader metabolic potential of aminophosphonates. It should be noted that PASS algorithms are primarily focused on pharmacological and biomedical effects and are not intended to predict phytostimulating activity.

Given the previously reported ability of aminophosphonates to influence the growth-related processes in the biological systems of various origins [7], the next stage of this study has focused on investigating the plant growth–stimulating activity of *PMAAPH-Suc*. Under the laboratory conditions, the effect of the novel aminophosphonate, tested at a standard screening concentration of  $10^{-3}$  M, on the germination energy, laboratory germination, and germination intensity of wheat seeds (cultivar Kazakhstan 10) has been evaluated (Figure 2).

The seed treatment with *PMAAPH-Suc* has resulted in an increase in germination up to 100% and an enhancement of the germination energy up to 95.0% compared with the control group. At the same time, the average height of seedlings has slightly decreased, which may indicate a redistribution of the growth processes at the early stages of ontogenesis.

Previously, aminophosphonates of this structural series have been shown to exhibit myelostimulating activity, providing the rationale for further investigation of the obtained compound [8]. *PMAAPH-Suc* has been evaluated for the myelostimulatory activity (a stimulatory effect influencing the proliferative activity of erythro-, thrombocyto-, and leukopoiesis) (Table 4).



**Figure 2** – The diagram illustrating the effect of *PMAAPh-Suc* on the germination, growth, and development of wheat seedlings under the laboratory conditions.

**Table 4** – The key hematological parameters

Blood parameters	<i>PMAAPh-Suc</i>	Control group	Placebo group	Intact group
WBC, $\cdot 10^9/L$	$7.58 \pm 3.47$	$6.25 \pm 0.85$	$3.65 \pm 0.7$	$7.74 \pm 1.11$
RBC, $10^{12}/L$	$7.85 \pm 1.07$	$7.42 \pm 1.12$	$5.23 \pm 1.75$	$7.14 \pm 2.17$
HGB, g/L	$145 \pm 16.7$	$126.5 \pm 2.06$	$101 \pm 10.9$	$124.5 \pm 1.31$
PLT, $\cdot 10^9/L$	$797 \pm 29$	$698 \pm 17.2$	$617 \pm 14.6$	$745.0 \pm 15.71$
NEU, $\cdot 10^9/L$	$4.12 \pm 1.82$	$3.18 \pm 0.44$	$1.86 \pm 3.26$	$3.16 \pm 0.44$

Against the background of pancytopenia induced by the cytostatic agent cyclophosphamide, an administration of the studied *PMAAPh-Suc* has been accompanied by the pronounced leukopoiesis-stimulating activity, exceeding the effect of the reference drug methyluracil (control group (CG)). The compound moderately and in a balanced manner has stimulated proliferation in the erythrocytic, leukocytic, and thrombocytic lineages of hematopoiesis. The erythrocyte count (RBC) has recovered to  $(7.85 \pm 1.07) \cdot 10^{12}/L$ , exceeding the placebo group (PG) and corresponding to the control group (CG). Hemoglobin concentration (HGB) has been  $(145 \pm 16.7) \cdot g/L$ , exceeding the CG level  $(126.5 \pm 2.06) \cdot 10^9/L$ . The total leukocyte count (WBC) has reached  $(7.58 \pm 3.47) \cdot 10^9/L$ , which is slightly higher than in the CG  $(6.25 \pm 0.85) \cdot 10^9/L$  and 2.07 times higher than in the PG  $(3.65 \pm 0.7) \cdot 10^9/L$ . The Garkavi index has indicated a rapid recovery of hematopoiesis without disturbance of the lymphocyte-to-granulocyte ratio. The platelet count (PLT) has increased to  $(797 \pm 29) \cdot 10^9/L$ , exceeding the PG  $(617 \pm 14.6) \cdot 10^9/L$  and CG  $(698 \pm 17.2) \cdot 10^9/L$ . Effective restoration of the granulocyte–agranulocyte balance has been observed: the absolute neutrophil count (NEU) has been  $(4.12 \pm 1.82) \cdot 10^9/L$ , which is 1.29 times higher than in the CG, while the absolute lymphocyte count has reached  $(2.98 \pm 1.40) \cdot 10^9/L$ , exceeding the PG. Thus, *PMAAPh-Suc* has exhibited moderate leukopoiesis-, erythropoiesis-, and thrombocytopoiesis-stimulating activity, reaching the levels comparable to those of the intact animals. The

observed stimulation of hematopoiesis, a peripheral biological process, is also consistent with the proposed lack of BBB permeability (SwissADME). Further research is needed to clarify the underlying mechanisms.

#### 4. Conclusion

A new aminophosphonate, dimethyl ((3-phenoxyphenyl)((pyridin-2-ylmethyl)amino)methyl)phosphonate (**PMAA $Ph$** ), has been synthesized via the Kabachnik–Fields reaction, and its structure has been characterized by the IR and NMR spectroscopy. To improve an aqueous solubility, the succinate form of the compound (**PMAA $Ph$ -Suc**), has been obtained.

Based on the *in silico* analysis (PASS, SwissADME, ProTox-3.0), **PMAA $Ph$**  has been shown to possess a balanced physicochemical profile, meet the main criteria of drug-likeness, and exhibit the moderate predicted bioavailability with a predominantly peripheral activity. The toxicity prediction has indicated a moderate acute toxicity ( $LD_{50} = 200$  mg/kg, toxicity class III) in the absence of the pronounced organ-specific or genotoxic risks. The obtained *in silico* predictions, indicating the potential cardiometabolic activity of the compound, create a reasonable basis for further targeted research in this direction.

The results of the *in vitro* studies have demonstrated that **PMAA $Ph$ -Suc** affects the early plant growth processes, manifested by changes in the seed germination energy and laboratory germination of wheat seeds, indicating its potential as a regulator of growth processes.

Under the *in vivo* conditions in an experimental pancytopenia model, **PMAA $Ph$ -Suc** has exhibited a moderate and balanced effect on the main hematopoietic lineages, promoting restoration of the erythro-, leuko-, and thrombocytopoiesis parameters without a significant disturbance of their ratios.

Overall, the obtained data allow **PMAA $Ph$**  and its succinate form to be considered as promising lead-like compounds of interest for the further in-depth studies in the biomedical and agrobiological fields.

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#### LEAD-LIKE СВОЙСТВА НОВОГО ПИРИДИНАМИНОФOSFONATA: СИНТЕЗ, ПРЕДИКТИВНАЯ ОЦЕНКА И БИОЛОГИЧЕСКИЕ ИССЛЕДОВАНИЯ

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**Резюме.** Введение. Аминофосфонатные производные представляют интерес как класс низкомолекулярных соединений, способных оказывать регулирующее действие в биологических системах различной природы. Сочетание предиктивных и экспериментальных подходов позволяет

получить комплексную характеристику их биологического потенциала на ранних этапах исследования. Целью настоящей работы являлся синтез нового аминокислотного производного, получение его водорастворимой формы и проведение комплексной предиктивно-экспериментальной оценки биологической активности. Синтез dimethyl ((3-phenoxyphenyl)((pyridin-2-ylmethyl)amino)methyl)phosphonate (**PMAA $\Phi$** ) осуществляли по реакции Кабачника–Филдса; для повышения растворимости получена его сукцинатная форма (**PMAA $\Phi$ -Suc**). Структуру соединений подтверждали методами ЯМР- и ИК-спектроскопии. *In silico*-анализ включал оценку биологической активности, фармакокинетических и токсикологических параметров. *Экспериментальные исследования* проводили на растительных моделях и в условиях экспериментальной панцитопении *in vivo*. Установлено, что **PMAA $\Phi$**  соответствует критериям лекарственноподобия и относится к III классу токсичности. **PMAA $\Phi$ -Suc** проявляет регулирующее влияние на рост растений и показатели кровотока. Полученные данные позволяют рассматривать соединение как перспективный объект для дальнейших исследований биологически активных соединений.

**Ключевые слова:** 2-(аминометил)пиридин, аминокислотный фосфонат, *in silico* анализ, миелостимулирующая активность, стимулирующая рост растений активность.

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## ЖАҢА ПИРИДИНАМИНОФОСФОНАТТЫҢ LEAD-LIKE ҚАСИЕТТЕРІ: СИНТЕЗ, ПРЕДИКТИВТІК БАҒАЛАУ ЖӘНЕ БИОЛОГИЯЛЫҚ ЗЕРТТЕУЛЕР

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**Түйіндеме.** *Кіріспе.* Аминокислотный фосфонат туындылары әртүрлі табиғаттағы биологиялық жүйелерде реттеуші әсер көрсетуге қабілетті төмен молекулалы қосылыстар класы ретінде үлкен қызығушылық тудырады. Предиктивтік және эксперименттік тәсілдерді ұштастыра қолдану зерттеудің бастапқы кезеңдерінде олардың биологиялық әлеуетіне кешенді сипаттама беруге мүмкіндік береді. Осы жұмыстың мақсаты жаңа аминокислотный фосфонат туындысын синтездеу, оның суда жақсы еритін түрін алу және биологиялық белсенділігін кешенді предиктивтік-эксперименттік бағалау болды. Dimethyl ((3-phenoxyphenyl)((pyridin-2-ylmethyl)amino)methyl)phosphonate (**PMAA $\Phi$** ) Кабачник–Филдс реакциясы бойынша синтезделді; ерігіштігін арттыру мақсатында оның сукцинаттық түрі (**PMAA $\Phi$ -Suc**) алынды. Қосылыстардың құрылымы ЯМР және ИК-спектроскопия әдістерімен дәлелденді. *In silico* талдау биологиялық белсенділікті, фармакокинетикалық және токсикологиялық параметрлерді бағалауды қамтыды. *Эксперименттік зерттеулер* өсімдік модельдерінде және *in vivo* жағдайында эксперименттік панцитопения моделінде жүргізілді. Зерттеу нәтижесінде **PMAA $\Phi$**  дәріге ұқсастық критерийлеріне сәйкес келетіні және уыттылықтың III класына жататыны анықталды. **PMAA $\Phi$ -Suc** өсімдіктердің өсу процестеріне және қан түзу көрсеткіштеріне реттеуші әсер көрсететіні байқалды. Алынған деректер бұл қосылысты биологиялық белсенді заттарды әрі қарай зерттеу үшін перспективалы нысан ретінде қарастыруға мүмкіндік береді.

**Түйін сөздер:** 2-(аминометил)пиридин, аминокислотный фосфонат, *in silico* анализі, миелоциталандыргыш белсенділік, өсімдіктердің өсуін ынталандырушы белсенділік

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## References

1. Al-Mohaya M., Mesut B., Kurt A., Çelik Y. S. In silico approaches which are used in pharmacy. *Journal of Applied Pharmaceutical Science*, **2024**, *14*, No.4, 225–239. DOI:10.7324/JAPS.2024.154854
2. Chang Y., Hawkins B. A., Du J. J., Groundwater P. W., Hibbs D. E., Lai F. A guide to in silico drug design. *Pharmaceutics*, **2023**, *15*, No.1, 49. DOI:10.3390/pharmaceutics15010049
3. Ten A. Yu., Dauletbakov A. A., Gubenko M. A., Belyankova Ye. O., Bayazit S., Assylbekova S. Ye., Zolotareva D. S., Yu V. K. Biopharmaceutical potential of aminophosphonates based on morpholinoethylamine. *Chemical Journal of Kazakhstan*, **2025**, No.1 (89), 48–58. (In Russ.). DOI:10.51580/2025-1.2710-1185.05
4. PASS at <https://way2drug.com/PassOnline/> (Accessed January 14, 2026).
5. SwissADME at <https://www.swissadme.ch/> (Accessed January 15, 2026).
6. ProTox III at <https://tox.charite.de/protox3/> (Accessed January 15, 2026).
7. Patent RK 36847. Soedinenie dimetil((3,4-dimetoksifenil)(4-(pirimidin-2-il)piperazin-1-il)metil)fosfonata v komplekse s  $\beta$ -tsiklodekstrinom, obladayushchee roststimuliruyushchei aktivnost'yu [Dimethyl((3,4-dimethoxyphenyl)(4-(pyrimidin-2-yl)piperazin-1-yl)methyl)phosphonate in complex with  $\beta$ -cyclodextrin exhibiting growth-stimulating activity]. **2024**. A.Yu. Ten, V.K. Yu, T.Ye. Zharkynbek, N.S. Mukhamadiyev, G.Zh. Mendibayeva, Ye. Dauletkeldi, U.S. Kemelbekov. (accessed on 12 July 2024). <https://gosreestr.kazpatent.kz/Invention/Details?docNumber=375005>
8. Balabekova M. K., Kairanbayeva G. K., Yu V. K., Ten A. Yu., Tokusheva A. N., Musayev A. T., Koks S. The effect of MXF-19 on T regulatory lymphocytes of rats under conditions of aseptic inflammation caused by metal-induced immunodepression. *Journal of Medicinal Chemistry Sciences*, **2025**, *8*, No.5, 469–478. DOI:10.3390/molecules30132741