BIOLOGICAL SCIENCES

APPLICATION OF THIENOPYRIMIDINE DERIVATIVES AS NEW ECO-FRIENDLY WHEAT GROWTH REGULATORS

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ABSTRACT

Our work is devoted to the development of new effective and environmentally friendly wheat growth regulators based on chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives. A comparative analysis of the regulatory effect of thienopyrimidine derivatives and the plant hormone auxin IAA, as well as plant growth regulators Methyur and Kamethur on the growth and photosynthesis of wheat (*Triticum aestivum* L.) variety Tyra was carried out. Growth parameters such as average shoot and root length (mm) and photosynthesis parameters such as content of photosynthetic pigment (µg/ml) of wheat grown from seeds soaked in water 10^{-7}M solution of thienopyrimidine derivative were significantly increased after 3 weeks compared to those of control wheat plants grown from seeds soaked in distilled water. The regulatory effect of thienopyrimidine derivatives on the growth and photosynthesis of wheat was similar to the effect of the plant hormone auxin IAA and growth regulators Methyur and Kamethur used in a similar concentration of 10^{-7}M in water solution for seed treatment. The most physiologically active thienopyrimidine derivatives were selected and the relationship between their chemical structure and regulatory effect on the growth and photosynthesis of wheat plants was analyzed. The proposed mechanisms of regulatory effect at the physiological and molecular levels of chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives on plant growth are discussed.

Keywords: *Triticum aestivum* L., eco-friendly plant growth regulators, auxins, cytokinins, thienopyrimidine derivatives.

INTRODUCTION.

Modern agriculture uses breeding methods along with intensive technologies to grow the strategically important cereal crop wheat (*Triticum spp.*) in the context of global climate change and environmental pollution to provide food supply for the world's population [1-10]. Eco-friendly plant growth regulators created on the basis of plant hormones or their synthetic analogues with phytohormone-like effects, as well as natural biostimulants, help improve the growth and development of wheat during the vegetation phase, increase yields and improve the adaptation of wheat crop to stress factors of abiotic and biotic nature [11-20].

Currently, considerable attention has been paid to the development of new eco-friendly plant growth regulators based on chemical nitrogen-containing heterocyclic compounds, which, when used in low concentrations from 10^{-4}M to 10^{-9}M, are non-toxic to humans, animals and the environment, and demonstrate a phytohormone-like effect on the growth and development, as well as on the yield of the main grain, legume, vegetable and industrial crops [21, 22]. Among chemical nitrogen-containing heterocyclic compounds, the most promising for agriculture are pyrimidine derivatives, which can find practical application in agriculture as new eco-friendly plant growth regulators that promote the plant growth and development during ontogenesis, as well as herbicides, pesticides and insecticides that inhibit various enzymes of weeds and insects [23-29].

These include the most well-known plant growth regulators developed on the basis of 6-methyl-2-mercapto-4-hydroxypyrimidine (Methyur) and potassium salt of 6-methyl-2-mercapto-4-hydroxypyrimidine (Kamethur), as well as new chemical nitrogen-containing heterocyclic compounds [21, 22, 30, 31]. Our numerous studies have shown that plant growth regulators Methyur and Kamethur, and new chemical nitrogen-containing heterocyclic compounds, pyrimidine derivatives can exert phytohormone-like effects on cell elongation, division, and differentiation, enhancing seed germination, formation and growth of shoots, adventitious and lateral roots of plants in the vegetative stage, and enhancing the synthesis of photosynthetic pigments in plant leaves, which ensures plant productivity [21, 22, 30-41]. This can explain the fact that today it is pyrimidine derivatives that are of significant interest for the development of new eco-friendly wheat plant growth regulators for use in sustainable agriculture [42-47]. The use of plant growth regulators Methyur and Kamethur, and new chemical nitrogen-containing heterocyclic compounds, pyrimidine derivatives as synthetic analogues of natural phytohormones alone or in combination with mineral fertilizers allows to improve the growth and development of the root system and shoots of wheat plants, the formation of reproductive organs in plants and the improvement of metabolism in plant cells due to the intake of additional mineral nutrition [42-47].

The advantage of the practical use of chemical nitrogen-containing heterocyclic compounds, in particular pyrimidine derivatives is their wide spectrum of physiological activity on different plant species and varieties; in addition, they can be used only at the stage of pre-sowing treatment of seeds without additional treatment of plants at the stage of vegetation, which has a significant economic effect and environmental safety, preventing them from developing grains, beans and fruits and accumulating in the soil and groundwater [21, 22, 30-41, 42-47]. The application of chemical nitrogen-containing heterocyclic compounds, in particular pyrimidine derivatives, will increase the yield of wheat crop, its adaptation to abiotic and biotic stresses, while reducing the amount of toxic pesticides and fungicides entering the soil and plants consumed by humans and animals [48-51].

The aim of this work is to study the regulatory effect of new chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives on the growth and photosynthesis of an important cereal crop – winter wheat (*Triticum aestivum* L.) variety Tyra.

MATERIALS AND METHODS.

Plant hormone auxin IAA (1*H*-indol-3-yl)acetic acid) was produced by Sigma-Aldrich, USA (Figure 1); plant growth regulators, derivatives of sodium and potassium salts of 6-methyl-2-mercapto-4-hydroxypyrimidine (Methyur, Kamethur) and new thienopyrimidine derivatives were synthesized at the Department for Chemistry of Bioactive Nitrogen-Containing Heterocyclic Compounds, V.P. Kukhar Institute of Bioorganic Chemistry and Petrochemistry of the National Academy of Sciences of Ukraine (Figure 1, Table 1).

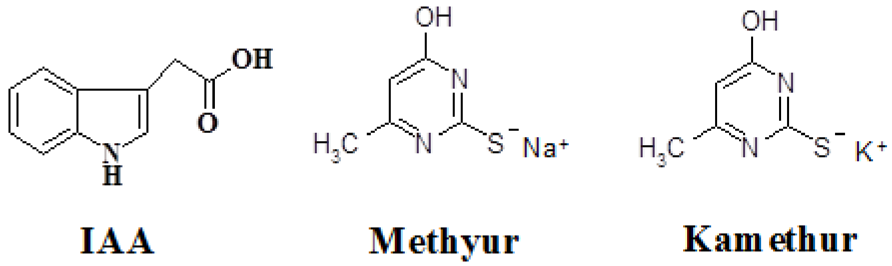
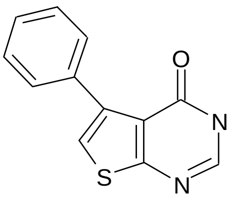
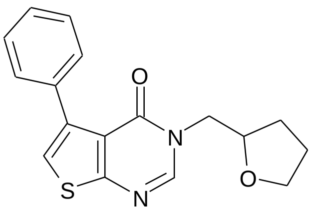
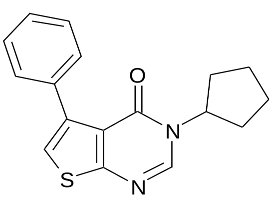
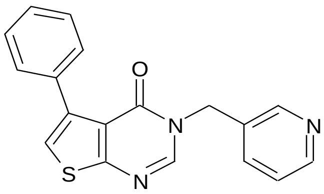
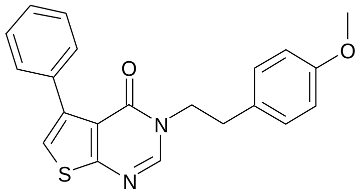
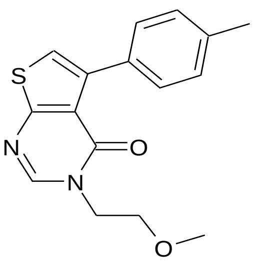
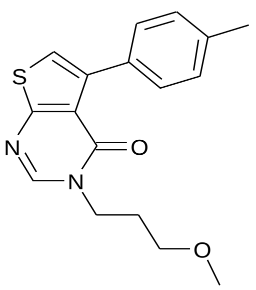
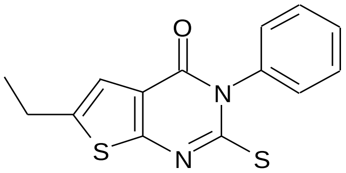
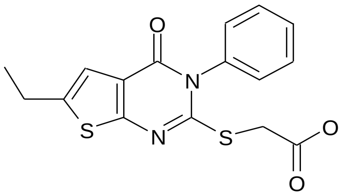
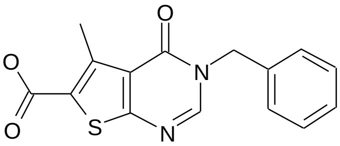
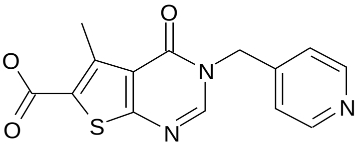
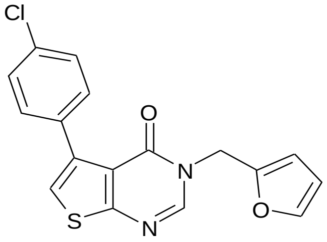
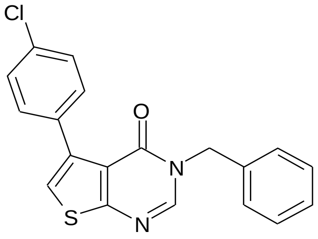


Figure 1. Chemical structures of the plant hormone auxin IAA (1H-indol-3-yl)acetic acid), MW=175,19, plant growth regulators, derivatives of sodium salt of 6-methyl-2-mercapto-4-hydroxypyrimidine (Methyur), MW=165,17, potassium salt of 6-methyl-2-mercapto-4-hydroxypyrimidine (Kamethur), MW=181,28

Table 1.
Chemical structures of chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives (compounds № 1 – 13)

Chemical compound	Chemical structure	Chemical name and relative molecular weight (g/mol)
1		5-Phenyl-3*H*-thieno[2,3-*d*]pyrimidin-4-one MW=228,274
2		5-Phenyl-3-(tetrahydrofuran-2-ylmethyl)-3*H*-thieno[2,3-*d*]pyrimidin-4-one MW=312,393
3		3-Cyclopentyl-5-phenyl-3*H*-thieno[2,3-*d*]pyrimidin-4-one MW=296,394

4		5-Phenyl-3-pyridin-3-ylmethyl-3*H*-thieno[2,3-*d*]pyrimidin-4-one MW=319,388
5		3-[2-(4-Methoxyphenyl)-ethyl]-5-phenyl-3*H*-thieno[2,3-*d*]pyrimidin-4-one MW=362,454
6		3-(2-Methoxyethyl)-5-*p*-tolyl-3*H*-thieno[2,3-*d*]pyrimidin-4-one MW=300,382
7		3-(3-Methoxypropyl)-5-*p*-tolyl-3*H*-thieno[2,3-*d*]pyrimidin-4-one MW=314,409
8		6-Ethyl-2-mercapto-3-phenyl-3*H*-thieno[2,3-*d*]pyrimidin-4-one MW=288,393
9		(6-Ethyl-4-oxo-3-phenyl-3,4-dihydrothieno[2,3-*d*]pyrimidin-2-ylsulfanyl)acetic acid MW=346,43
10		3-Benzyl-5-methyl-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidine-6-carboxylic acid MW=300,339
11		5-Methyl-4-oxo-3-pyridin-4-ylmethyl-3,4-dihydrothieno[2,3-d]pyrimidine-6-carboxylic acid MW=301,326

12		5-(4-Chlorophenyl)-3-furan-2-ylmethyl-3*H*-thieno[2,3-*d*]pyrimidin-4-one MW=342,806
13		3-Benzyl-5-(4-chlorophenyl)-3*H*-thieno[2,3-*d*]pyrimidin-4-one MW=352,845

To study the effect of chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives on plant growth, the seeds of winter wheat (*Triticum aestivum* L.) variety Tyra were sterilized with 1 % $KMnO_4$ solution for 15 min, then treated with 96 % ethanol solution for 1 min, after which they were washed three times with sterile distilled water. After this procedure, wheat seeds were placed in the plastic cuvettes (each containing 25 - 30 seeds) on the perlite moistened with distilled water (control sample) or water solutions of auxin IAA, or plant growth regulators Methyur and Kamethur, or thienopyrimidine derivatives used in a concentration of 10^{-7}M (experimental samples). Then the wheat seeds were placed in a thermostat for germination in the dark at a temperature of 20-22 °C for 48 hours. After the appearance of wheat seedlings, they were placed in a climate chamber, where they were grown for 3 weeks at the 16/8 h light/dark conditions, at the temperature 22-24 °C, light intensity of 3000 lux, and air humidity 60-80 %. Comparative analysis of morphometric parameters of wheat plants (average length of shoots and roots (mm)) was carried out at the end of the three-week period according to the method [52]. The morphometric parameters determined on the experimental wheat plants were compared with similar parameters of control plants and expressed in (%).

To perform the extraction of photosynthetic pigments, we homogenized a sample (500 mg) of wheat leaves in the porcelain mortar in a cooled at the temperature 10 °C 96 % ethanol at the ratio of 1: 10 (weight: volume) with addition of 0,1-0,2 g $CaCO_3$ (to neutralize the plant acids). The 1 ml of obtained homogenate was centrifuged at 8000 g in a refrigerated centrifuge K24D (MLW, Engelsdorf, Germany) during 5 min at the temperature 4 °C. The obtained precipitate was washed three times, with 1 ml 96 % ethanol and centrifuged at above mentioned conditions. After this procedure, the optical density of chlorophyll a, chlorophyll b and carotenoid in the obtained extract was measured using spectrophotometer Specord M-40 (Carl Zeiss, Germany).

The content of chlorophyll a, chlorophyll b, and carotenoids in wheat leaves was calculated in accordance with formula [53, 54]:

Cchl a = 13.36×A664.2 – 5.19×A648.6,
Cchl b = 27.43×A648.6 – 8.12A×664.2,
Cchl (a + b) = 5.24×A664.2 + 22.24×A648.6,
Ccar = (1000×A470 – 2.13×Cchl a – 97.64×Cchlb)/209,

Where,
Cchl – concentration of chlorophylls (μg/ml), Cchl a – concentration of chlorophyll a (μg/ml), Cchl b – concentration of chlorophyll b (μg/ml), Ccar – concentration of carotenoids (μg/ml), A – absorbance value at a proper wavelength in nm.

The chlorophyll and carotenoids content per 1 g of fresh weight (FW) of extracted from wheat leaves was calculated by the following formula (separately for chlorophyll a, chlorophyll b and carotenoids):

$A_1=(C\times V)/(1000\times a_1)$,
Where, A_1 – content of chlorophyll a, chlorophyll b, or carotenoids (mg/g FW),
C - concentration of pigments (μg/ml),
V - volume of extract (ml),
a_1 - sample of wheat leaves (g).

The content of chlorophyll a, chlorophyll b, and carotenoids (%) determined in the experimental wheat plants, compared with similar parameters determined in control plants, were expressed in %.

Each experiment was performed three times. Statistical processing of the experimental data was carried out using Student's t-test with a significance level of $P\leq0.05$; mean values ± standard deviation (± SD) [55].

RESULTS AND DISCUSSION.

Currently, the development of new synthetic analogues of auxins and cytokinins that exhibit physiological effects similar to these plant hormones on the germination of plant seeds, the growth of shoots and roots of plants in the vegetative stage and an increase in photosynthesis and crop yields is a very urgent task for agriculture [56-61].

In this work, the regulatory effect of chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives on the morphometric parameters (average length of shoots and roots (mm)) and the content of photosynthetic pigments (chlorophyll a, chlorophyll b, chlorophylls a+b, and carotenoids (µg/ml)) of winter wheat (*Triticum aestivum* L.) variety Tyra was studied in comparison with the regulatory effect of the plant hormone auxin IAA or plant growth regulators Methyur and Kamethur, capable of exhibiting phytohormone-like effect on various plant species [21, 22, 30, 31, 32, 38-47].

It has been shown that thienopyrimidine derivatives (compounds № 1–13) promote the growth and development of shoots and roots in the vegetative phase of wheat. Their regulatory effect was similar to the effect of auxin IAA or plant growth regulators Methyur and Kamethur.

Auxin IAA and plant growth regulators Methyur and Kamethur showed a high regulatory effect on the average length of shoots (mm), which increased: by 16,05% - under the effect of IAA, by 14,01% - under the effect of Methyur, by 12,99 % - under the effect of Kamethur, respectively, compared to similar indicators of control wheat plants grown on distilled water (Figure 2).

Among all studied chemical nitrogen-containing heterocyclic compounds, derivatives of thienopyrimidine № 2, 7–10 and 13 showed a high regulatory effect similar to IAA, Methyur and Kamethur on the average length of shoots (mm), which increased by 10,63–24,74%, respectively, compared to similar indicators of control wheat plants grown on distilled water (Figure 2).

Chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives № 1, 3, 4, 6 and 12 showed the least regulatory effect on the average length of shoots (mm), which increased by 5,15–8,47%, respectively, compared to similar indicators of control wheat plants grown on distilled water (Figure 2). The regulatory effect of chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives № 5 and 11 did not statistically significantly differ from the control, or was lower than the control wheat plants grown on distilled water (Figure 2).

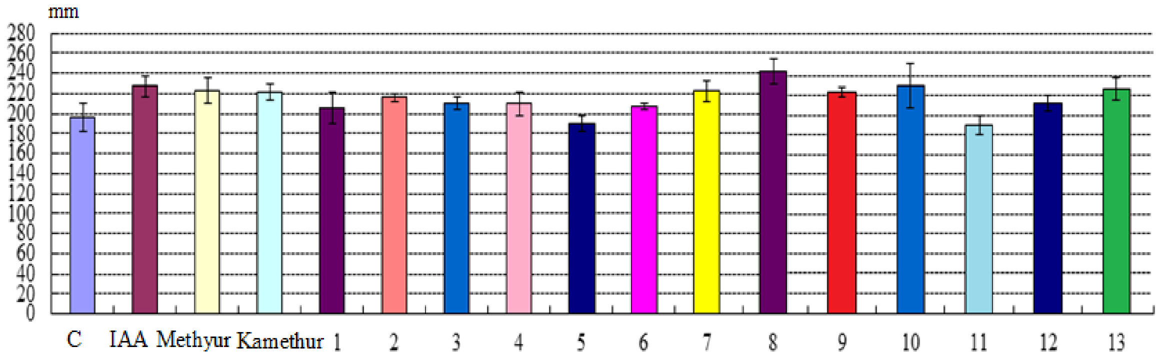


Figure 2. The regulatory effect of auxin IAA, plant growth regulators Methyur and Kamethur and thienopyrimidine derivatives (compounds № 1-13) in a concentration of 10^{-7}M on the average length of shoots (mm) of 3-week-old winter wheat (Triticum aestivum L.) variety Tyra compared to control plants.

Auxin IAA, plant growth regulators Methyur and Kamethur also showed a high regulatory effect on the average length of roots (mm), which increased: by 31,5% - under the effect of IAA, by 38,84% - under the effect of Methyur, by 51,58% - under the effect of Kamethur, respectively, compared to similar indicators of control wheat plants grown on distilled water (Figure 3).

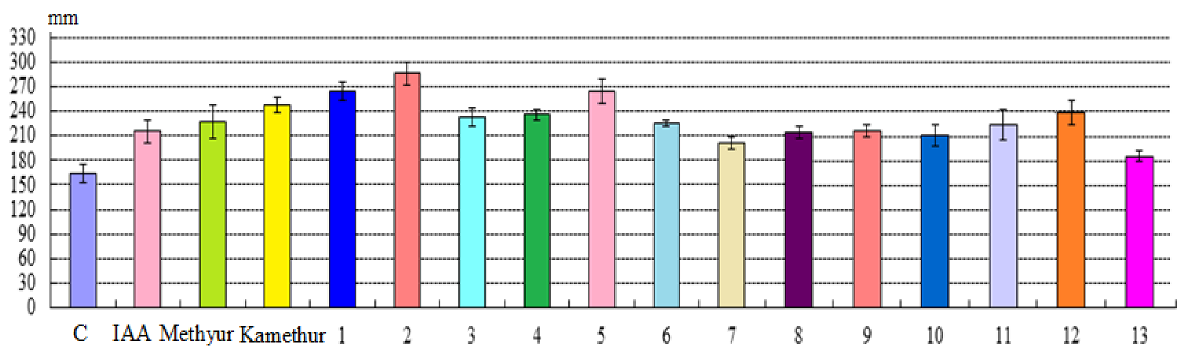


Figure 3. The regulatory effect of auxin IAA, plant growth regulators Methyur and Kamethur and thienopyrimidine derivatives (compounds № 1-13) in a concentration of 10^{-7}M on the average length of roots (mm) of 3-week-old winter wheat (Triticum aestivum L.) variety Tyra compared to control plants.

Among all studied chemical nitrogen-containing heterocyclic compounds, derivatives of thienopyrimidine № 1–6 and 8–12 showed a high regulatory effect similar to IAA, Methyur and Kamethur on the average length of roots (mm), which increased by 29,66–74,72%, respectively, compared to similar indicators of control wheat plants grown on distilled water (Figure 3).

Chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives № 7 and 13 showed the least regulatory effect on the average length of roots (mm), which increased by 4,07–22,57%, respectively, compared to similar indicators of control wheat plants grown on distilled water (Figure 3).

The obtained results indicate that the use of the most physiologically active compounds, thienopyrimidine derivatives № 2–10 and 12 improves the vegetative growth of winter wheat (*Triticum aestivum* L.) variety Tyra. This fact can be explained by the auxin-like effect of chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives, on the elongation, division and differentiation of plant cells, which are the main processes of *de novo* shoot and root organogenesis [62-64].

A comparative study of the regulatory effect of chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives and the plant hormone auxin IAA or plant growth regulators Methyur and Kamethur on the content of photosynthetic pigments (chlorophyll a, chlorophyll b, chlorophylls a+b, and carotenoids (µg/ml)) in the leaves of winter wheat (*Triticum aestivum* L.) variety Tyra was also carried out.

Auxin IAA, plant growth regulators Methyur and Kamethur showed a high regulatory effect on the content of photosynthetic pigments (µg/ml), chlorophyll a increased: by 35,31% - under the effect of IAA, by 57,96% - under the effect of Methyur, by 51,41% - under the effect of Kamethur; chlorophyll b increased: by 27,33% - under the effect of IAA, by 51,2% - under the effect of Methyur, by 53,33% - under the effect of Kamethur; chlorophylls a+b increased: by 33,36% - under the effect of IAA, by 56,32% - under the effect of Methyur, by 51,87% - under the effect of Kamethur; carotenoids increased: by 31,22% - under the effect of IAA, by 50,81% - under the effect of Methyur, by 45,58% - under the effect of Kamethur, respectively, compared to similar indicators of control wheat plants grown on distilled water (Figure 4).

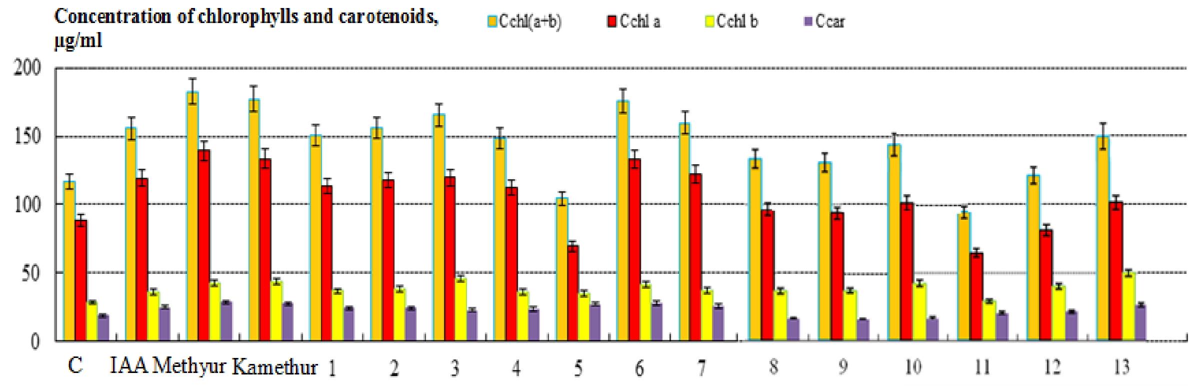


Figure 4. The regulatory effect of auxin IAA, plant growth regulators Methyur and Kamethur and thienopyrimidine derivatives (compounds № 1-13) in a concentration of 10^{-7}M on the content of chlorophyll a, chlorophyll b, chlorophylls a+b, and carotenoids (µg/ml) in the leaves of 3-week-old winter wheat (Triticum aestivum L.) variety Tyra compared to control plants.

Chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives № 1–4, 6–10 and 13 showed a high regulatory effect similar to IAA, Methyur and Kamethur on the content of photosynthetic pigments (µg/ml), which increased: chlorophyll a - by 6,14–51,27%, chlorophyll b - by 27,67–76,3%, chlorophylls a+b - by 27,15–50,17%, respectively, compared to similar indicators of control wheat plants grown on distilled water (Figure 4).

Chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives № 5, 11 and 12 had a regulatory effect only on the content of chlorophyll b (µg/ml), which increased by 4,46–42,91%, respectively, compared to similar indicators of control wheat plants grown on distilled water (Figure 4).

According to the content of carotenoids (µg/ml), chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives № 1–7, 11 and 13 showed the highest regulatory effect, the content of carotenoids increased by 11,79–46,16%, respectively, compared to similar indicators of control wheat plants grown on distilled water (Figure 4).

Thus, the conducted studies show that chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives show selectivity in the regulation of the biosynthesis of photosynthetic pigments in the leaves of wheat plants. Among all studied thienopyrimidine derivatives, compounds № 1–4, 6–10, and 13 showed the highest regulatory effect on increasing the content of photosynthetic pigments (chlorophylls a and b, as well as carotenoids) in the leaves of 3-week-old wheat plants, while compounds № 5, 11, and 12 showed a slightly lower regulatory effect.

It can be concluded that the regulatory action of chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives, is similar to the plant hormones cytokinins, which are known to delay leaf senescence, activate photosynthetic processes, and prevent the degradation of photosynthetic pigments such as chlorophylls and carotenoids in plant leaves [65-68].

Analyzing the obtained results, it can be assumed that the highest regulatory effect of chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives № 1–4, 6–10, 12 and 13 on the growth and photosynthesis of wheat is related to the presence of substituents in their chemical structure (Table 1): compound № 1 contains phenyl group - in position 5 of the 3*H*-thieno[2,3-*d*]pyrimidin-4-one ring; compound № 2 contains phenyl group in position 5, tetrahydrofuran-2-ylmethyl group in position 3 of the 3*H*-thieno[2,3-*d*]pyrimidin-4-one ring; compound № 3 contains a phenyl group in position 5, a cyclopentyl group in position 3 of the 3*H*-thieno[2,3-*d*]pyrimidin-4-one ring; compound № 4 contains phenyl group in position 5, pyridin-3-ylmethyl group in position 3 of the 3*H*-thieno[2,3-*d*]pyrimidin-4-one ring; compound № 6 contains *p*-tolyl group in position 5, 2-methoxyethyl group in position 3 of the 3*H*-thieno[2,3-*d*]pyrimidin-4-one ring; compound № 7 contains a *p*-tolyl group in position 5, a 3-methoxypropyl group in position 3 of the 3*H*-thieno[2,3-*d*]pyrimidin-4-one ring; compound № 8 contains ethyl group in position 6, phenyl group in position 3, mercapto group in position 2 of the 3*H*-thieno[2,3-*d*]pyrimidin-4-one ring; compound № 9 contains an ethyl group in position 6, a phenyl group in position 3, a sulfonylacetic acid residue in position 2 of the 4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidine ring; compound № 10 contains methyl group in position 5, benzyl group in position 3, carboxyl group in position 6 of the 4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidine ring; compound № 12 contains 4-chlorophenyl group in position 5, furan-2-ylmethyl group in position 3 of the 3*H*-thieno[2,3-*d*]pyrimidin-4-one ring; compound № 13 contains benzyl group in position 3, 4-chlorophenyl group in position 4 of the 3*H*-thieno[2,3-*d*]pyrimidin-4-one ring.

The decrease of the regulatory effect of chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives № 5 and 11 on the growth and photosynthesis of wheat can be explained by the presence of substituents in their chemical structures (Table 1): compound № 5 contains phenyl group in position 5, 2-(4-methoxyphenyl)ethyl group in position 3 of the 3*H*-thieno[2,3-*d*]pyrimidin-4-one ring; compound № 11 contains methyl group in position 5, pyridin-4-ylmethyl group in position 3, carboxyl group in position 6 of the 4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidine ring.

It is evident that chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives are capable of regulating auxin and cytokinin signaling in plant cells, as well as modulate the activity of key enzymes of biosynthesis, transport, metabolism, conjugation and oxidation of endogenous auxins and cytokinins [69-83].

Conclusion. Based on the obtained results, it is possible to propose the practical application of Methyur and Kamethur and most active chemical nitrogen-containing heterocyclic compounds, thienopyrimidine derivatives № 1–4, 6–10, 12 and 13 in a concentration of 10^{-7}M as new eco-friendly plant growth regulators to improve the growth of roots and shoots and increase the content of photosynthetic pigments of winter wheat (*Triticum aestivum* L.) variety Tyra during the vegetative stage.

Statement of conflict of interest.

The authors are declared that they have no conflict with this research article.

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