Study of regulating activity of synthetic low molecular weight heterocyclic compounds, derivatives of pyrimidine on growth of tomato *(Solanum lycopersicum L.)* seedlings

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**Abstract**: The comparative analysis of growth regulating activity of new synthetic low molecular weight heterocyclic compounds (LMWHC), derivatives of pyrimidine, and plant hormones auxins IAA (1H-Indol-3-ylacetic acid) and NAA (1-Naphthylacetic acid) on vegetative growth of tomato *(Solanum lycopersicum L.)* cultivar Fakel was conducted in the laboratory conditions. Our study showed that synthetic LMWHC, derivatives of pyrimidine used at the concentration 10^(-9) M demonstrated high auxin-like regulating activity on growth of tomato seedlings during the 8 weeks. The morphometric parameters of shoots and roots on the 8th-week-old tomato seedlings grown in perlite moistened with solutions of synthetic LMWHC, derivatives of pyrimidine used at the concentration 10^(-9) M were similar or higher to the morphometric parameters of shoots and roots on the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control) or solutions of plant hormones auxins IAA and NAA used at the same concentration 10^(-9) M on average: to 21 - 30 % - for length of shoots, to 8 - 80 % - for average shoot mass, to 10 - 20 % - for length of main root, to 10 - 46 % - for average root mass, respectively. It was found that the plant growth regulating activity of these compounds depended on different substituents in the chemical structure of heterocyclic compounds. The obtained results proved the possibility of practical application of synthetic LMWHC, derivatives of pyrimidine as new effective regulators for vegetative growth of tomato *(Solanum lycopersicum L.)* cultivar Fakel.

**Key words**: tomato *(Solanum lycopersicum L.)*, plant growth regulators, synthetic low molecular weight heterocyclic compounds, derivatives of pyrimidine, auxins IAA and NAA.

**Introduction**

An actual problem for the modern agriculture is the development of new plant growth regulators to improve growth during the growing season and increase the yield of tomato *(Solanum lycopersicum L.)*, which

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is one of the main food crops cultivated in different countries [1]. According to the National Nutrient Database of the US Department of Agriculture, tomato fruit contains important for human health dietary nutrients, biologically active compounds and phytochemicals [2]. The use of fresh tomato fruit and tomato food products in human diet food reduces the risk of chronic diseases, such as cancer, cardiovascular and some age-related diseases[3 – 9].

The low resistance of tomato plants to unfavorable abiotic and biotic stress-factors and diseases caused by pathogens and parasites can lead to crop losses and reduced product quality [10 - 14]. Nowadays, plant hormones and natural biostimulants are widely used to improve tomato growth and productivity, and increase plant resistance to unfavorable abiotic and biotic stress-factors [15 - 33]. To the main disadvantages of practical application of traditional plant growth regulators belong low growth regulating activity when used at high concentrations, their storage instability and toxicity to humans, animals and environment[34- 36].

Currently, new synthetic low molecular weight heterocyclic compounds (LMWHC), derivatives of pyrimidine are proposed to be used as new effective substitutes of traditional plant growth regulators due to the wide specifics of their growth regulating effect on the major crops when their using at low non-toxic for human, animal and environment concentrations [37 - 41]. Along with the use of synthetic LMWHC, derivatives of pyrimidine in agriculture, they are widely used in medical practice as therapeutic agents for treatment of cancer, bacterial, viral, fungal, infectious and inflammatory diseases [42 - 49].

Taking into account this fact, the promising approach is the development of new effective and environmentally safe plant growth regulators on the base of synthetic LMWHC, derivatives of pyrimidine to improve the growth and productivity of tomato.

Our previously conducted researchers have shown that new synthetic LMWHC, derivatives of pyrimidine, synthesized in V.P. Kukhar Institute of Bioorganic Chemistry and Petrochemistry of NAS of Ukraine, demonstrated high growth regulating activity at very low concentrations ranging from \(10^{-8}\)M up to \(10^{-9}\) M on various agricultural crops [50 - 57].

The goal of the present work is to explore the possibility of application of new synthetic LMWHC, derivatives of pyrimidine to improve growth and development of tomato (Solanum lycopersicum L.) cultivar Fakel during the vegetative stage.

1. Materials and Methods

1.1. Chemical structure of synthetic LMWHC and plant hormones used for bioassays

We conducted comparative analysis of the plant growth regulating activity of new synthetic LMWHC, derivatives of pyrimidine (compounds №1-12) and plant hormones auxins IAA(1H-Indol-3-ylacetic acid) and NAA(1-Naphthylacetic acid)(Table 1).

| Compound | Chemical name and relative molecular mass of compounds |
|----------|------------------------------------------------------|
| IAA      | 1H-Indol-3-ylacetic acid MM=175.19                     |
| NAA      | 1-Naphthylacetic acid MM=186.21                        |

Table 1. The chemical name, structure and relative molecular mass of plant hormones auxins IAA and NAA, and synthetic LMWHC
|   | Structure | Description | Molar Mass (MM) |
|---|-----------|-------------|----------------|
| 1 | ![Structure](image1.png) | 6-(Methanesulfonyl)imidazo[1,2-a]pyrimidin-5-ylamine; | MM=212.23 |
| 2 | ![Structure](image2.png) | 8-(Methanesulfonyl)-6-phenyl-2,6-dihydroimidazo[1,2-c]pyrimidin-5(3H)-one; | MM=291.33 |
| 3 | ![Structure](image3.png) | 8-(Methanesulfonyl)-2,6-dihydroimidazo[1,2-c]pyrimidin-5(3H)-one; | MM=215.23 |
| 4 | ![Structure](image4.png) | 6-(2-Hydroxyethyl)-8-(methanesulfonyl)-2,6-dihydroimidazo[1,2-c]pyrimidin-5(3H)-one hydrochloride; | MM=295.75 |
| 5 | ![Structure](image5.png) | 2-[8-(Benzenesulfonyl)-5-oxo-2,3-dihydroimidazo[1,2-c]pyrimidin-6(5H)-yl]ethyl acetate; | MM=363.39 |
| 6 | ![Structure](image6.png) | 8-(Benzenesulfonyl)-6-(4-methylphenyl)-2,6-dihydroimidazo[1,2-c]pyrimidin-5(3H)-one; | MM=367.43 |
| 7 | ![Structure](image7.png) | 6-Benzyl-8-(methanesulfonyl)-2,6-dihydroimidazo[1,2-c]pyrimidin-5(3H)-one; | MM=305.36 |
| 8 | ![Structure](image8.png) | 9-(Methanesulfonyl)-7-propyl-2,3,4,7-tetrahydro-6H-pyrimido[1,6-a]pyrimidin-6-one; | MM=271.34 |
2.2. Plant treatment and growing conditions

Seeds of tomato (*Solanum lycopersicum* L.) cultivar Fakel were surface sterilized by 1% KMnO₄ solution for 3 min followed by treatment with 96% ethanol solution for 1 min, and then washed three times with sterile distilled water. After this procedure seeds were placed in the cuvettes (each containing 25-30 seeds) in perlite moistened with distilled water (control), or with the solutions of synthetic LMWHC, derivatives of pyrimidine used at the concentration 10⁻⁹ M, or plant hormones auxins IAA (1H-Indol-3-ylacetic acid) and NAA (1-Benzylacyclic acid) used at the same concentrations 10⁻⁹ M. Afterward, tomato seeds were placed in the thermostat for their germination in the darkness at the temperature 23 °C during 48 hours. Sprouted tomato seedlings were placed in the growth chamber where seedlings were grown for 8 weeks at the 16/8 h light/dark conditions, at the temperature 24 °C, light intensity 3000 lux and air humidity 60-80%. The comparative analysis of the growth parameters of tomato seedlings (i.e. length of shoots (cm), average shoot mass (g), length of the main root (cm), and average root mass (g)) was carried out at the end of the 8th week after seed germination according to the guideline [58].

2.3. Statistical Analysis

All experiments were performed in three replicates. Statistical analysis of the data was performed using dispersive Student’s-t test with the level of significance at P≤0.05, the values are mean ± SD [59].
3. Results and discussion

3.1. Regulating activity of synthetic LMWHC and auxins IAA and NAA on morphometric parameters of tomato seedlings

In the laboratory conditions we studied growth regulating activity of new synthetic LMWHC, derivatives of pyrimidine used at the concentration $10^{-9}$ M and plant hormones auxins IAA(1H-Indol-3-ylaceticacid) and NAA(1-Naphthylaceticacid) used at the same concentration $10^{-9}$ M on shoots and roots growth of the 8th-week-old tomato seedlings(*Solanum lycopersicum* L.) cultivar Fakel.

It was found that synthetic LMWHC, derivatives of pyrimidine showed auxin-like regulating effect on growth and development of shoot and root system of tomato seedlings during the 8 weeks (Fig. 1).

![Fig. 1. Effect of synthetic LMWHC, derivatives of pyrimidine (compounds № 1-12) and plant hormones auxins IAA(1H-Indol-3-ylaceticacid) and NAA(1-Naphthylaceticacid) used at the concentration $10^{-9}$ M on shoots and roots growth of the 8th-week-old tomato seedlings (*Solanum lycopersicum* L.) cultivar Fakel as compared with shoots and roots growth of the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control (C))]
Among synthetic LMWHC, derivatives of pyrimidine the highest regulating activity on growth of tomato shoots revealed the compounds № 1 and № 2. The morphometric parameters of length of shoots on the 8th-week-old tomato seedlings grown in perlite moistened with solutions of the compounds № 1 and № 2 used at the concentration 10^{-9}M were increased on average: to 21 % and 30 %, respectively, as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control), to 17 % and 79 %, respectively, as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with solution of auxin IAA used at the same concentration 10^{-9}M, and to 12 % and 21 %, respectively, as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with solution of auxin NAA used at the same concentration 10^{-9}M (Fig. 2).

The morphometric parameters of average shoot mass (g) on the 8th-week-old tomato seedlings grown in perlite moistened with solutions of the compounds № 1 and № 2 used at the concentration 10^{-9}M were increased on average: to 18 % and 80 %, respectively, as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control), to 8 % and 25 %, respectively, as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with solution of auxin NAA used at the same concentration 10^{-9}M (Fig. 3).

![Fig. 3. Effect of synthetic LMWHC, derivatives of pyrimidine (compounds № 1-12) and plant hormones auxins IAA and NAA used at the concentration 10^{-9}M on average shoot mass (g) on the 8th-week-old tomato seedlings (Solanum lycopersicum L.) cultivar Fakel as compared with average mass of shoots (g) on the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control (C))](image)

The lower regulating activity on growth of tomato shoots revealed the compounds № 5, 7, and 11. The morphometric parameters of average shoot mass (g) on the 8th-week-old tomato seedlings grown in perlite moistened with solutions of the compounds № 5, 7, and 11 used at the concentration 10^{-9}M were increased on average: to 10 - 23 % as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control), to 9 - 22 % as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with solution of auxin IAA used at the same concentration 10^{-9}M, and to 7 - 20 % as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with solution of auxin NAA used at the same concentration 10^{-9}M (Fig. 3).

It was found that all synthetic LMWHC, derivatives of pyrimidine demonstrated auxin-like stimulating effect on growth of tomato root. The highest regulating activity on growth of tomato main root revealed the compounds № 4, 5, 6, 8, 9 and № 10. The morphometric parameters of length of main root on the 8th-week-old tomato seedlings grown in perlite moistened with solutions of the compounds № 4, 5, 6, 8, 9 and № 10 used at the concentration 10^{-9}M were increased on average: to 10 - 20 %, respectively, as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control), to 14- 24 %, respectively, as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with solution of auxin IAA used at the same concentration 10^{-9}M (Fig. 4).
Fig 4. Effect of synthetic LMWHC, derivatives of pyrimidine (compounds № 1-12) and plant hormones auxins IAA and NAA used at the concentration $10^{-9}$M on length of main root (cm) on the 8th-week-old tomato seedlings (*Solanum lycopersicum* L.) cultivar Fakel as compared to length of main root (cm) on the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control (C)).

The highest regulating activity to increase the mass of the root on the 8th-week-old tomato seedlings revealed the compounds № 1 and 12; the morphometric parameters of average root mass (g) on the 8th-week-old tomato seedlings grown in perlite moistened with solutions of the compounds № 1 and 12 used at the concentration $10^{-9}$M were increased on average: to 16 % and 46 % as compared to similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control) or with solution of auxin IAA used at the same concentration $10^{-9}$M, to 22 % and 52 % as compared to similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with solution of auxin NAA used at the same concentration $10^{-9}$M (Fig. 5).

Fig 5. Effect of synthetic LMWHC, derivatives of pyrimidine (compounds № 1-12) and plant hormones auxins IAA and NAA used at the concentration $10^{-9}$M on average root mass (g) on the 8th-week-old tomato seedlings (*Solanum lycopersicum* L.) cultivar Fakel as compared with average mass of roots (g) on the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control (C)).

The lower regulating activity on growth of tomato shoots revealed the compounds № 4, 5, 6, 8, 9, 10 and 11. The morphometric parameters of average root mass (g) on the 8th-week-old tomato seedlings grown in perlite moistened with solutions of the compounds № 4, 5, 6, 8, 9, 10 and 11 used at the concentration $10^{-9}$M were increased on average: to 10 - 23 % as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control) or with solution of auxin IAA used at the same concentration $10^{-9}$M, to 15 - 30 % as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with solution of auxin NAA used at the same concentration $10^{-9}$M (Fig. 5).

It was found that the plant growth regulating activity of synthetic LMWHC, derivatives of pyrimidine was varied depending on different substituents in their chemical structure. Among tested compounds the highest growth regulating activity showed the compound №1 – 6-(Methanesulfonyl)imidazo[1,2-a]pyrimidin-5-ylamine,
which belongs to derivatives of dihydroimidazo[1,2-c]pyrimidine containing methylsulfonyl group in the 6 position of dihydroimidazo[1,2-c]pyrimidine, and the compound № 12 - Diethyl [4-(benzylamino)-5-(4-methylphenyl)-5H-pyrolo[3,2-d]pyrimidin-7-yl]phosphonate, which belongs to derivatives of pyrrolo[3,2-d]pyrimidine containing benzylamino substituent in the 4 position and 4-methylphenyl substituent in the 5 position of pyrimidine fragment.

The high regulating activity showed the compounds №4, 5, 6, 7, 8, 9, 10 and 11, which belong to derivatives of dihydroimidazo[1,2-c]pyrimidine and pyrimido[1,6-a]pyrimidine. This fact is explained by the presence of various substituents in their chemical structure: the compound № 4 - 6-(2-Hydroxyethyl)-8-(methylene)sulfonfyl)-2,6-dihydroimidazo[1,2-c]pyrimidin-5(3H)-one hydrochloride contains hydroxyethyl group in the 6 position, the compound № 5 - 2-[8-(Benzensulfonfyl)-5-oxo-2,3-dihydroimidazo[1,2-c]pyrimidin-6(5H)-yl]ethyl acetate contains 2-acetoxyethyl group in the 2 position, the compound № 6 - 8-(Benzenesulfonfyl)-6-(4-methylphenyl)-2,6-dihydroimidazo[1,2-c]pyrimidin-5(3H)-one contains 4-methylphenyl group in the 6 position, the compound № 7 - 6-Benzyl-8-(methylene)sulfonfyl)-2,6-dihydroimidazo[1,2-c]pyrimidin-5(3H)-one contains 6-Benzyl group in 6 position of dihydroimidazo[1,2-c]pyrimidine, the compound № 8 - 9-(Methanesulfonfyl)-7-propyl-2,3,4,7-tetrahydro-6H-pyrimido[1,6-a]pyrimidin-6-one does not contain any substituent in the 6 position, the compound № 9 - 2-[9-(Methanesulfonfyl)-6-oxo-3,4-dihydro-2H-pyrimido[1,6-a]pyrimidin-7(6H)-yl]ethyl acetate contains 2-acetoxyethyl group in the 2 position and methanesulfonfyl group in 9 position, the compound № 10 - 2-[9-(Benzenesulfonfyl)-6-oxo-3,4-dihydro-2H-pyrimido[1,6-a]pyrimidin-7(6H)-yl]ethyl acetate contains 2-acetoxyethyl group in the 2 position and benzenesulfonfyl group in the 9 position, the compound № 11 - 9-(Benzenesulfonfyl)-7-(4-methylphenyl)-2,3,4,7-tetrahydro-6H-pyrimido[1,6-a]pyrimidin-6-one contains 4-methylphenyl group in the 7 position and benzenesulfonfyl group in the 9 position of the pyrimidine fragment.

Probably, the high plant growth regulating activity of synthetic LMWHC, derivatives of pyrimidine or synthetic analogs of auxin could be explained by their auxin-like inducing effect on plant growth and development, and plant cell metabolism [60 - 63]. It is possible to assume that the molecular mechanisms of action of these synthetic LMWHC, derivatives of pyrimidine might be associated with their regulatory action (by analogy with plant hormone auxin) on the network of key auxin-binding proteins (ARFs) that may be the auxin receptors involved in auxin signalling and transport, network of auxin response transcription factors (ARFs) that are DNA-binding proteins, which recognize and bind to auxin responsive cis-acting promoter elements (AuxREs) in early/primary auxin response genes, and network of transcription factors that bind to promoter elements in genes encoding protein-enzymes responsible for plant cell division and extension [64 - 80].

Otherwise, there could be an alternative mode of action related to the inhibitory effect of synthetic LMWHC, derivatives of pyrimidine or synthetic analogs of auxin on activity of a key enzyme IAA-oxidase, which is involved in the enzymatic destruction (degradation) of auxin [81]. As a result, the level of endogenously synthesized auxin IAA is increased in the plant cell, and auxin transport, perception and signalling are restored leading to improved plant cell division and extension that are the main processes of plant growth and development [64 – 80].

In support of the bottom concept indicate published works [82, 83], which showed the effect of exogenously applied synthetic analogs of auxin on decrease in activity of IAA-oxidase and vice versa on increase in level of synthesis of endogenous auxin IAA in plant cells.

The authors of the work [84] also suggested that synthetic auxins might affect the level of synthesis of endogenous auxin modifying directly synthesis of enzyme IAA-oxidase and indirectly through effectors of IAA-oxidase.

Similar studies were conducted in a work [85] that showed that synthetic 2-R substitutedbenzothiazole derivatives demonstrated dominant auxine-like plant growth promoting activity. Based on obtained results, showing that the plant growth promoting activity of synthetic benzothiazole compounds can be correlated with the activity of IAA synthetase, the authors have proposed that the mode of action of synthetic 2-R substitutedbenzothiazole derivatives as auxine-like substances is due to their possible regulation of synthesis or degradation of endogenous auxin indole-3-acetic acid (IAA) in plants.
The assumptions discussed in the works [82-85] are consonant with our early published work [86], which testified in favor of the indirect, mediated through endogenous phytohormones action of synthetic LMWHC, derivatives of pyrimidine – 1-utidine N-oxide (Ivin) and pyrimidine – 6-methylthiouracil (Methyur) on plant cell extension, and published works of other authors [87 - 92] that showed the effect of exogenously applied synthetic multi-dimensional plant growth regulator Thidiazuron (TDZ; N-phenyl-1,2,3-thidiazole-5ylurea) on increase in concentrations of endogenous cytokinins, auxin, ethylene and ABA in plant cells.

Authors of work[91] also suggested that the powerful cytokinin-like regulatory effect of TDZ on plant grow this associated with its influence on metabolism of endogenous plant hormones, either directly or indirectly through prevention the breakdown of endogenous purines by inhibiting cytokinin oxidase, due to which plant cell division and regeneration occur.

4. Conclusion

The regulating activity of synthetic LMWHC, derivatives of pyrimidine on growth of tomato (Solanum lycopersicum L.) cultivar Fakel during the 8 weeks was studied. It was found that the derivatives of pyrimidine used at the concentration 10^{-9} M demonstrated the auxin-like plant growth regulating activity, which was similar or higher of the activity of plant hormones auxins IAA and NAA. The obtained morphometric parameters of 8th-week-old tomato seedlings grown in perlite moistened with solutions of synthetic LMWHC, derivatives of pyrimidine used at the concentration 10^{-9} M were similar or higher than similar parameters of 8th-week-old tomato seedlings grown either in perlite moistened with distilled water (control) or solutions of plant hormones auxins IAA and NAA used at the same concentration 10^{-9} M. The plant growth regulating activity of synthetic LMWHC, derivatives of pyrimidine was varied depending on different substituents in their chemical structure. The obtained results proved the possibility of practical application of synthetic LMWHC, derivatives of pyrimidine as new effective regulators to improve growth of tomato (Solanum lycopersicum L.) cultivar Fakel during the vegetative stage.

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