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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(1*H*-Indol-3-ylaceticacid) and NAA(1-Naphthylaceticacid) 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 8^{th}-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 8^{th}-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}Mup to 10^{-9}M on various agricultural crops [50 - 57].

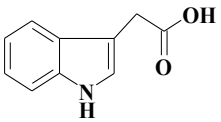
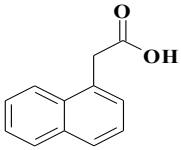
The goal of the present work is to explore the possibility of application of new synthetic LMWHC, derivatives of pyrimidine to improve growth and development of tomato (*Solanum lycopersicum* L.) cultivar Fakel during the vegetative stage.

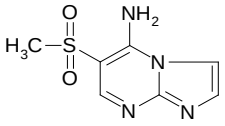
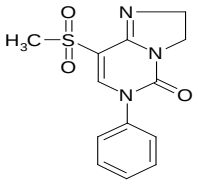
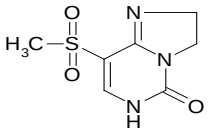
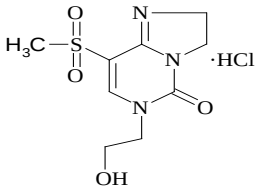
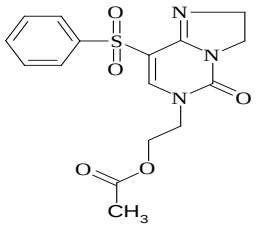
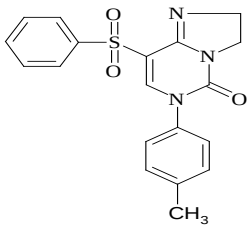
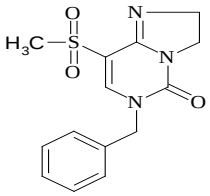
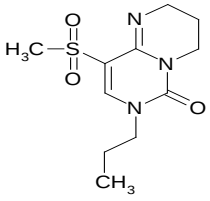
1. Materials and Methods

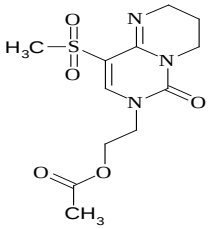
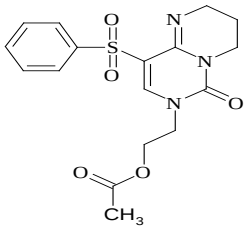
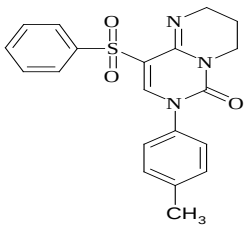
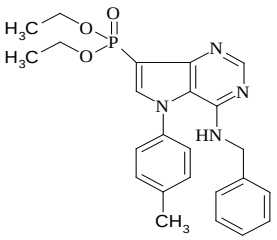
1.1. Chemical structure of synthetic LMWHC and plant hormones used for bioassays

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(1*H*-Indol-3-ylaceticacid) and NAA(1-Naphthylaceticacid)(Table 1).

Table 1.The chemical name, structure and relative molecular mass of plant hormones auxins IAA and NAA, and synthetic LMWHC

Compound	Chemical structure of compounds	Chemical name and relative molecular mass of compounds
IAA		1*H*-Indol-3-ylaceticacid MM=175.19
NAA		1-Naphthylaceticacid MM=186.21

1		6-(Methanesulfonyl)imidazo[1,2-*a*]pyrimidin-5-ylamine; MM=212.23
2		8-(Methanesulfonyl)-6-phenyl-2,6-dihydroimidazo[1,2- *c*]pyrimidin-5(3*H*)-one; MM=291.33
3		8-(Methanesulfonyl)-2,6-dihydroimidazo[1,2-*c*]pyrimidin-5(3*H*)-one; MM=215.23
4		6-(2-Hydroxyethyl)-8-(methanesulfonyl)-2,6-dihydroimidazo[1,2-*c*]pyrimidin-5(3*H*)-one hydrochloride; MM=295.75
5		2-[8-(Benzenesulfonyl)-5-oxo-2,3-dihydroimidazo[1,2-*c*]pyrimidin-6(5*H*)-yl]ethyl acetate; MM=363.39
6		8-(Benzenesulfonyl)-6-(4-methylphenyl)-2,6-dihydroimidazo[1,2-*c*]pyrimidin-5(3*H*)-one; MM=367.43
7		6-Benzyl-8-(methanesulfonyl)-2,6-dihydroimidazo[1,2-c]pyrimidin-5(3H)-one; MM=305.36
8		9-(Methanesulfonyl)-7-propyl-2,3,4,7-tetrahydro-6*H*-pyrimido[1,6-*a*]pyrimidin-6-one; MM=271.34

9		2-[9-(Methanesulfonyl)-6-oxo-3,4-dihydro-2*H*-pyrimido[1,6-*a*]pyrimidin-7(6*H*)-yl]ethyl acetate; MM=315.35
10		2-[9-(benzenesulfonyl)-6-oxo-3,4-dihydro-2*H*-pyrimido[1,6-*a*]pyrimidin-7(6*H*)-yl]ethyl acetate; MM=377.42
11		9-(Benzenesulfonyl)-7-(4-methylphenyl)-2,3,4,7-tetrahydro-6*H*-pyrimido[1,6-*a*]pyrimidin-6-one; MM=381.46
12		Diethyl [4-(benzylamino)-5-(4-methylphenyl)-5*H*-pyrrolo[3,2-*d*]pyrimidin-7-yl]phosphonate; MM=450.48

2.2. Plant treatment and growing conditions

Seeds of tomato(*Solanum lycopersicum* L.)cultivar Fakel were surface sterilized by 1 % $KMnO_4$ 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 o f pyrimidine used at the concentration 10^{-9}M, or plant hormones auxins IAA(1*H*-Indol-3-ylaceticacid) and NAA(1-Naphthylaceticacid)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 8weeks 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 8thweek 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 $P \leq 0.05$, 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(1*H*-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(1*H*-Indol-3-ylaceticacid) and NAA(1-Naphthylaceticacid) used at the concentration 10^{-9}M on shoots and roots growth ofthe 8th-week-old tomato seedlings (*Solanum lycopersicum* L.)cultivarFakelas compared with shoots and roots growth of the 8th-week-old tomato seedlings grown in perlite moistened with distilled water(control (C))

The conducted statistical analysis showed that the shoots and roots morphometric parameters of the 8th-week-old tomato seedlings(i.e. length of shoots (cm), average shoot mass (g), length of the main root (cm), and average root mass (g)) grown in perlite moistened with solutions of some synthetic LMWHC, derivatives of pyrimidine used at the concentration 10^{-9}M were similar or higher to the shoots and roots morphometric parameters of 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 (Fig. 2 - Fig.5).

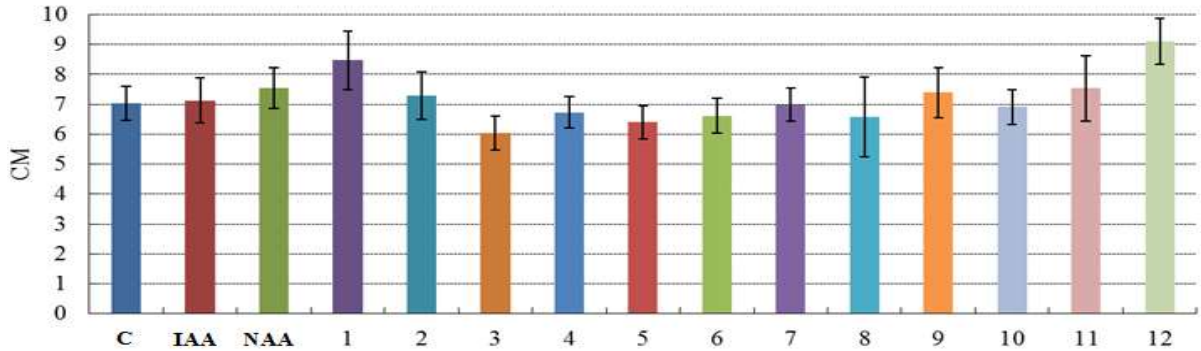


Fig 2. Effect of synthetic LMWHC, derivatives of pyrimidine (compounds № 1-12) and plant hormones auxins IAA(1*H*-Indol-3-ylaceticacid) and NAA(1-Naphthylaceticacid)used at the concentration 10^{-9}M on length of shoots (cm) on the 8th-week-old tomato seedlings (*Solanum lycopersicum*L.)cultivar Fakel as compared with length of shoots (cm) on 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 N AA 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 % and80 %, respectively, as compared with similar parameters on the 8th-week-old tomato seedlings grown in perlite moistened with distilled water (control), and 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 N AA used at the same concentration 10^{-9}M (Fig. 3).

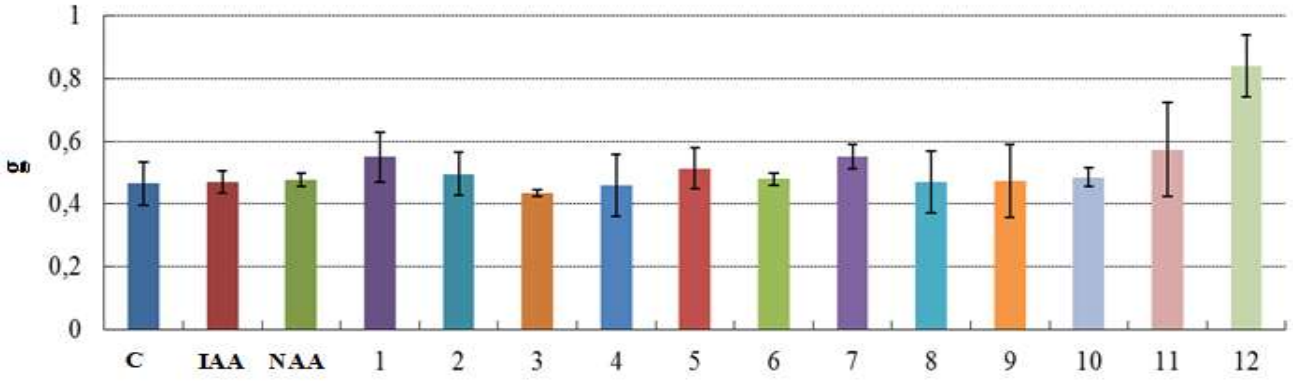


Fig. 3. Effect of synthetic LMWHC, derivatives of pyrimidine (compounds № 1-12) and plant hormones auxins IAA and NAA used at the concentration 10^{-9}M on average shoot mass (g) on the 8th-week-old tomato seedlings(*Solanum lycopersicum* L.)cultivar Fakel as compared with average mass of shoots (g)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

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 I AA 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 N AA 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).

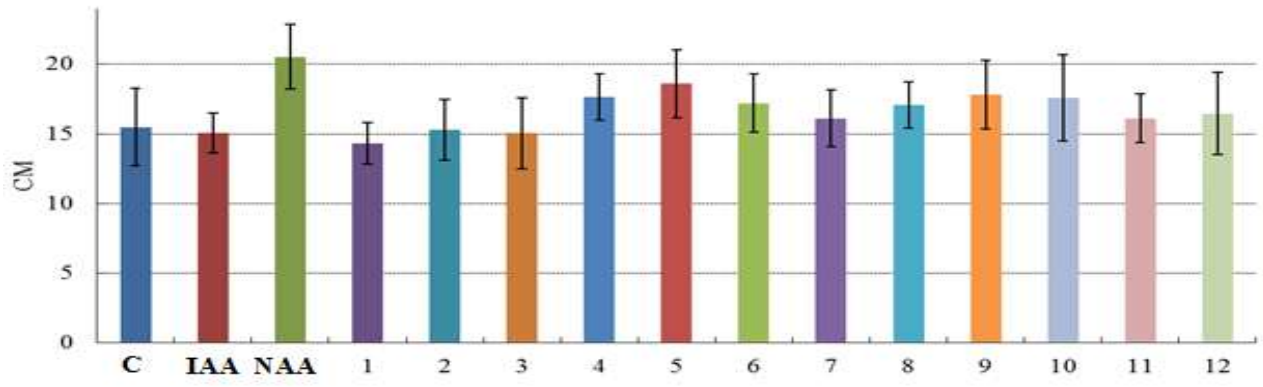


Fig 4. Effect of synthetic LMWHC, derivatives of pyrimidine (compounds № 1-12) and plant hormones auxins IAA and NAA used at the concentration 10^{-9}M on length of main root (cm) on the 8th-week-old tomato seedlings(*Solanum lycopersicum* L.)cultivar Fakel as compared to length of main root (cm) on 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 I AA 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 N AA used at the same concentration 10^{-9}M (Fig. 5).

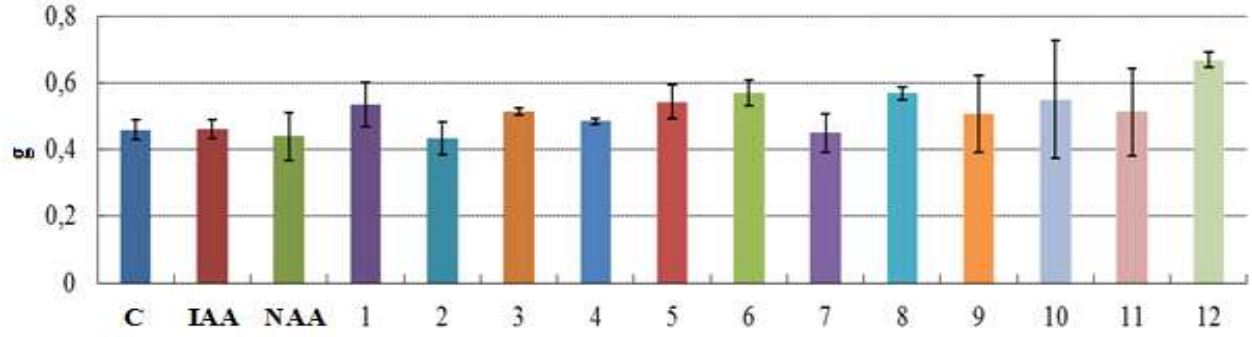


Fig. 5. Effect of synthetic LMWHC, derivatives of pyrimidine (compounds № 1-12) and plant hormones auxins IAA and NAA used at the concentration 10^{-9}M on average root mass (g) on the 8th-week-old tomato seedlings(*Solanum lycopersicum* L.)cultivarFakel as compared with average mass of roots (g) on 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 I AA 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 N AA 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)-5*H*-pyrrolo[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-(methanesulfonyl)-2,6-dihydroimidazo[1,2-*c*]pyrimidin-5(3*H*)-one hydrochloride contains hydroxyethyl group in the 6 position, the compound № 5 – 2-[8-(Benzenesulfonyl)-5-oxo-2,3-dihydroimidazo[1,2-*c*]pyrimidin-6(5*H*)-yl]ethyl acetatecontains 2-acetoxyethylgroup in the 2 position, the compound № 6 - 8-(Benzenesulfonyl)-6-(4-methylphenyl)-2,6-dihydroimidazo[1,2-*c*]pyrimidin-5(3*H*)-one contains 4-methylphenyl group in the 6 position, the compound № 7 – 6-Benzyl-8-(methanesulfonyl)-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-(Methanesulfonyl)-7-propyl-2,3,4,7-tetrahydro-6*H*-pyrimido[1,6-*a*]pyrimidin-6-one does not contain any substituent in the 6 position, the compound № 9 - 2-[9-(Methanesulfonyl)-6-oxo-3,4-dihydro-2*H*-pyrimido[1,6-*a*]pyrimidin-7(6*H*)-yl]ethyl acetate contains 2-acetoxyethyl group in the 2 position and methanesulfonyl group in 9 position, the compound № 10 - 2-[9-(benzenesulfonyl)-6-oxo-3,4-dihydro-2*H*-pyrimido[1,6-*a*]pyrimidin-7(6*H*)-yl]ethyl acetate contains 2-acetoxyethyl group in the 2 position and benzenesulfonyl group in the 9 position, the compound № 11 - 9-(Benzenesulfonyl)-7-(4-methylphenyl)-2,3,4,7-tetrahydro-6*H*-pyrimido[1,6-*a*]pyrimidin-6-one contains 4-methylphenyl group in the 7 position and benzenesulfonyl 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 (ABPs) 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, andnetwork of transcription factors that bind to promoter elements in genes encodingprotein-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 cells, and auxin transport, perception and signalling are restored leading to improved plant cell division and extension that are the main processes ofplant 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 ofsynthetic 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 theindirect, mediated through endogenous phytohormonesaction of synthetic LMWHC, derivatives of pyridine – lutidine N-oxide (Ivin) and pyrimidine –6-methylthiouracil(Methyur)on plant cell extension, and published works of other authors [87 - 92]thatshowed 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 8^{th}-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 8^{th}-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.

5. References

1. Gerszberg A., Hnatuszko-Konka K., Kowalczyk T., Kononowicz A.K. Tomato (*Solanum lycopersicum* L.) in the service of biotechnology, Plant Cell Tiss Organ Cult, 2015; 120: 881–902.
2. Composition of Foods Raw, Processed, Prepared, *USDA National Nutrient Database for Standard Reference, Release 27*. United States Department of Agriculture, 2015.
3. Agarwal S., Rao A.V. 2000. Tomato lycopene and its role in human health and chronic diseases. CMAJ: Canadian Medical Association Journal. 163(6): 739-744.
4. Bramley P.M. Is lycopene beneficial to human health?, Phytochemistry, 2000; 54(3): 233-236.
5. Basu A., Imrhan V. Tomatoes versus lycopene in oxidative stress and carcinogenesis: conclusions from clinical trials, European journal of clinical nutrition, 2007; 61(3): 295-303.
6. Hwang E.S., Bowen P.E. Can the consumption of tomatoes or lycopene reduce cancer risk?, Integrative cancer therapies, 2002; 1(2): 121-132.
7. Oboh G., Bakare O.O., Ademosun A.O., Akinyemi A.J., Olasehinde T.A.Inhibition of Cholinesterases and Some Pro-Oxidant induced Oxidative Stress in Rats Brain by Two Tomato (*Lycopersicon Esculentum*) Varieties, IJBS, 2015; 11(1): 48-53.
8. Ellinger S, Ellinger J, Stehle P. Tomatoes, tomato products and lycopene in the prevention and treatment of prostate cancer: do we have the evidence from intervention studies?, Curr Opin Clin Nutr Metab Care, 2006; 9(6): 722-727.
9. Gitenay D., Lyan L., Rambeau M., Mazur A., Rock E. Comparison of lycopene and tomato effects on biomarkers of oxidative stress in vitamin E deficient rats, Eur J Nutr., 2007; 46(8): 468-475.
10. Sayre R.M., Toyama T.K. The effect of root knot nematodes on the yield of processing tomatoes, Can J Plant Sci, 1964; 44: 265–267.
11. Panthee D.R. and Chen F. Genomics of Fungal Disease Resistance in Tomato, Curr Genomics, 2010; 11(1): 30–39.
12. EL-Saka Z.I. and Zaki K.I. Tomato Breeding For Early Blight Disease Resistance, JAVS, 2015; 8(3): 88-94.

13. Lee J.M., Oh Ch.-S., Yeam I. Molecular Markers for Selecting Diverse Disease Resistances in Tomato Breeding Programs, Plant Breed Biotech, 2015; 3(4): 308-322.
14. ItakoA.T., Júnior J.B.T., Júnior T.A.F.S., Soman J.M., Maringoni A.C. Chemical products induce resistance to *Xanthomonas perforans* in tomato, Brazilian Journal of Microbiology, 2015; 46(3): 701-706.
15. Castro P.R.C. Plant growth regulators in tomato crop production, Acta Hortic, 1980; 100: 99-104.
16. Cato S.C., Macedo W.R., Peres L.E.P., Castro P.R.C. Sinergism among auxins, gibberellins and cytokinins in tomato cv. Micro-Tom, Horticultura Brasileira, 2013; 31: 549-553.
17. Al-Amri S.M. Improved growth, productivity and quality of tomato (*Solanum lycopersicum* L.) plants through application of shikimic acid, Saudi J Biol Sci, 2013;20(4): 339–345.
18. Abebie B., Desalegn L. Effects of Gibberellic acid and 2,4-dichloro-phenoxyacetic acid spray on fruit yield and quality of tomato (*Lycopersicon esculentum* Mill.), Journal of Plant Breeding and Crop Science, 2010; 2(10): 316-324.
19. Bakrim A., Lamhamdi M., Sayah F., Chibi F. Effects of plant hormones and 20-hydroxyecdysone on tomato (*Lycopersicum esculentum*) seed germination and seedlings growth, AFR J BIOTECHNOL, 2007; 6(24): 2792-2802.
20. Baliyan S.P., Rao K.S.M., Baliyan P.S., Mahabile M. The effects of 4-chlorophenoxyacetic acid plant growth regulator on the fruit set, yield, and economic benefit of growing tomatoes in high temperatures, International Journal of Agricultural Science and Research (IJASR), 2013; 3(2): 29-36.
21. Choudhury S., Islam N., Sarkar M.D., Ali M.A. Growth and Yield of Summer Tomato as Influenced by Plant Growth Regulators, International Journal of Sustainable Agriculture, 2013; 5(1): 25-28.
22. de Jong M., Mariani C., Vriezen W.H. The role of auxin and gibberellin in tomato fruit set, J Exp Bot, 2009; 60(5): 1523-1532.
23. Gelmesa D., Abebie B., and Desalegn L. Effects of Gibberellic acid and 2,4-Dichlorophenoxy Acetic Acid Spray on Vegetative Growth, Fruit Anatomy and Seed Setting of Tomato (*Lycopersicon esculentum* Mill.), Science, Technology and Arts Research Journal, 2013; 2(3): 25-34.
24. AlbaceteA., Cantero-NavarroE., BalibreaM.E., Groß kinskyD.K., GonzálezM.C., Martínez-AndújarC., SmigockiA.C., RoitschT., andPérez-AlfoceaF. Hormonal and metabolic regulation of tomato fruit sink activity and yield under salinity, J Exp Bot, 2014; 65(20): 6081–6095.
25. Khaled A.M., Sikder S., Islam M.R., Hasan M.A., Bahadur M.M. Growth Yield and Yield Attributes of Tomato (*Lycopersicon esculentum* Mill.) as Influenced by Indole Acetic Acid, J Environ Sci & Natural Resources, 2015; 8(1): 139-145.
26. Kumar A., Biswas T.K., Singh N., Lal E.P. Effect of Gibberellic Acid on Growth, Quality and Yield of Tomato (*Lycopersicon esculentum* Mill.), IOSR Journal of Agriculture and Veterinary Science, IOSR-JAVS, 2014; 7(7): 28-30.
27. Matsuo S., Kikuchi K., Fukuda M.,Honda I., Imanishi S. Roles and regulation of cytokinins in tomato fruit development, J Exp Bot, 2012; 63(15): 5569–5579.
28. Nowaczyk P., Nowaczyk L. The effect of growth regulators on tomato (*Lycopersicon esculentum*) fertility, Acta Physiol Plan, 2000; 22(3): 309-311.
29. Rahman M., Nahar M.A., Sahariar M.S., Karim M.R. Plant growth regulators promote growth and yield of summer tomato (*Lycopersicon esculentum* Mill.), Progressive Agriculture, 2015; 26: 32-37.
30. Schwabe W.W. Possible application of growth regulators in tomato production, Acta Hort (ISHS), 1986; 190: 309-314.
31. van Tonder C.S.M., Combrink N.J.J. The effect of plant-growth regulators on the production of out-of-season greenhouse tomatoes (*Lycopersicum esculentum*), South African Journal of Plant and Soil, 2003; 20(4): 165-168.
32. Uddain J., Hossain K.M.A., Mostafa M.G., and Rahman M.J. Effect of Different Plant Growth Regulators on Growth and Yield of Tomato, International Journal of Sustainable Agriculture, 2009; 1(3): 58-63.
33. Baliyan S.P., Rao K.S.M., Baliyan P.S., Mahabile M. The effects of 4-chlorophenoxyacetic acid plant growth regulator on the fruit set, yield, and economic benefit of growing tomatoes in high temperatures, International Journal of Agricultural Science and Research (IJASR), 2013; 3(2): 29-36.
34. Bukowska B. Toxicity of 2,4-Dichlorophenoxyacetic Acid – Molecular Mechanisms, Polish J Environ Stud, 2006; 15(3): 365-374.

35. Celik I., Tuluce Y. Determination of toxicity of subacute treatment of some plant growth regulators on rats, Environ Toxicol, 2007; 22(6): 613–619.
36. Hąc-Wydro K., Flasiński M. The studies on the toxicity mechanism of environmentally hazardous natural (IAA) and synthetic (NAA) auxin- the experiments on model Arabidopsis thaliana and rat liver plasma membranes,Colloids Surf B Biointerfaces, 2015; 130: 53-60.
37. Cansev A., Gulen H., Zengin M.K., Ergin S., Cansev M., Kumral N.A. Use of pyrimidines in stimulation of plant growth and development and enhancement of stress tolerance, 2016, Patent 20160000075.
38. Whittingham W.G., Winn C.L., Glithro H., Boussemghoune M.A., Aspinall M.B. Pyrimidine derivatives and their use as herbicides, 2010, Patent WO2010092339 A1.
39. Minn K., Dietrich H., Dittgen J., Feucht D., Häuser-Hahn I., Rosinger C.H. Pyrimidine derivatives and their use for controlling undesired plant growth, 2008, Patent US 8329717 B2.
40. Kuragano T., Tanaka Y. Dérivés de la pyrimidine et herbicides les contenant, 2002, Patent WO 2002038550 A1.
41. Takahashi A., Yamada S., Yamada H., Kawana T. Mitotic disruption by a novel pyrimidine herbicide, NS-245852, in oat (*Avena sativa* L.) roots, Weed Biology and Management, 2001; 1(3): 1.
42. Jain K.S., Chitre T.S., Miniyar P.B., Kathiravan M.K., Bendre V.S., Veer V.S., Shahane S.R., Shishoo C.J. Biological and medicinal significance of pyrimidines, Curr Sci,2006; 90(6): 793-803.
43. Jain K.S., Arya N., Inamdar N.N., Auti P.B., Unawane S.A., Puranik H.H., Sanap M.S., Inamke A.D., Mahale V.J., Prajapati C.S., Shishoo C.J. The Chemistry and Bio-Medicinal Significance of Pyrimidines & Amp; Condensed Pyrimidines, Curr Top Med Chem, 2016; 16(28): 3133-3174.
44. Galmarini C.M., Jordheim L., Dumontet C.Pyrimidine nucleoside analogs in cancer treatment, Expert Rev Anticancer Ther, 2003; 3(5): 717-728.
45. Parker W.B. Enzymology of purine and pyrimidine antimetabolites used in the treatment of cancer, Chemical reviews, 2009; 109(7): 2880.
46. Kumar R., Arora J., Prasad A.K., Islam N., Verma A.K. Synthesis and antimicrobial activity of pyrimidine chalcones, MCRE, 2013; 22(11): 5624-5631.
47. Kumar R., Arora J., Ruhil S., Phougat N., Chhillar A.K., Prasad A.K. Synthesis and Antimicrobial Studies of Pyrimidine Pyrazole Heterocycles, Advances in Chemistry, 2014; Article ID 329681, 1-12.
48. Raghunat, S.A., Manjunatha Y., and Rayappa K. Synthesis, antimicrobial, and antioxidant activities of some new indole analogues containing pyrimidine and fused pyrimidine systems, Med Chem Res, 2012; 21(11): 3809-3817.
49. Stuart A.L., Ayisi N.K., Tourigny G., Gupta V.S. Antiviral activity, antimetabolic activity and cytotoxicity of 3′-substituted deoxypyrimidine nucleosides, Journal of Pharmaceutical Sciences, 1985; 74(3): 246–249.
50. Tsygankova V., Andrusevich Ya., Shtompel O., Hurenko A., Solomyannyj R., Mrug G., Frasinyuk M., Brovarets V. Stimulating effect of five and six-memberedheterocyclic compounds on seed germination and vegetative growth of maize(*Zea mays*L.), International Journal of BiologyResearch, 2016; 1(4):1-14.
51. Tsygankova V., Andrusevich Ya., Shtompel O., Romaniuk O., Yaikova M., Hurenko A., Solomyanny R., Abdurakhmanova E., Klyuchko S., Holovchenko O., Bondarenko O., Brovarets V. Application of Synthetic Low Molecular Weight Heterocyclic Compounds Derivatives of Pyrimidine, Pyrazole and Oxazole in Agricultural Biotechnology as a New Plant Growth Regulating Substances, Int J Med Biotechnol Genetics, 2017; S2:002: 10-32.
52. Tsygankova V.A., Andrusevich Ya.V., Shtompel O.I., Kopich V.M., Pilyo S.G., Prokopenko V.M, Kornienko A.M, BrovaretsV.S. Intensification of Vegetative Growth of Cucumber by Derivatives of [1,3]oxazolo[5,4-d]pyrimidine and N-sulfonyl substituted of 1,3-oxazole, Research Journal of Life Sciences, Bioinformatics, Pharmaceutical, and Chemical Sciences (RJLBPCS), 2017;3(4): 107–122.
53. Tsygankova V., Andrusevich Ya., Kopich V., Shtompel O., Pilyo S., Kornienko A.M, BrovaretsV. Use of Oxazole and Oxazolopyrimidine to Improve Oilseed Rape Growth, Scholars Bulletin, 2018; 4(3): 301–312.
54. Tsygankova V.A., Andrusevich Ya.V., Shtompel O.I., Pilyo S.G., Kornienko A.M., Brovarets V.S. Using of [1,3]oxazolo[5,4-d]pyrimidine and N-sulfonyl substituted of 1,3-oxazole to improve the growth of soybean seedlings, Chemistry Research Journal, 2018**,** 3(2): 165-173.
55. Tsygankova V.A., Andrusevich Ya.V., Shtompel O.I., Pilyo S.G., Kornienko A.M., Brovarets V.S. Acceleration of vegetative growth of wheat (*Triticum aestivum* L.) using [1,3]oxazolo[5,4-*d*]pyrimidine

and N-sulfonyl substituted 1,3-oxazole, The Pharmaceutical and Chemical Journal, 2018; 5(2): 167-175.

56. Tsygankova V.A., Andrusevich Ya.V., Shtompel O.I., Shablykin O.V., Hurenko A.O., Solomyanny R.M., Mrug G.P., Frasinyuk M.S., Pilyo S.G., Kornienko A.M., Brovarets V.S. Auxin-like effect of derivatives of pyrimidine, pyrazole, isoflavones, pyridine, oxazolopyrimidine and oxazole on acceleration of vegetative growth of flax, International Journal of PharmTech Research, 2018, 11(3): 274-286.
57. Tsygankova V.A., Andrusevich Ya.V., Shtompel O.I., Solomyanny R.M., Hurenko A.O., Frasinyuk M.S., Mrug G.P., Shablykin O.V., Pilyo S.G., Kornienko A.M., Brovarets V.S. Study of auxin-like and cytokinin-like activities of derivatives of pyrimidine, pyrazole, isoflavones, pyridine, oxazolopyrimidine and oxazole on haricot bean and pumpkin plants, International Journal of ChemTech Research, 2018, 11(10): 174-190.
58. Voytsehovska O.V., Kapustyan A.V., Kosik O.I., Musienko M.M., Olkhovich O.P., Panyuta O.O., Parshikova T.V., Glorious P.S. Plant Physiology: Praktykum, Lutsk: Teren, 2010.
59. BangH.,ZhouX.K,vanEppsH.L.,Mazumdar M. Statistical Methodsin Molecular Biology,Series:Methods inmolecular biology, NewYork: Humana press, 2010.
60. Woodward AW, Bartel B. Auxin: regulation, action, and interaction, Ann Bot, 2005; 95(5): 707–735. doi:10.1093/aob/mci083.
61. Zhao Yu. Auxin biosynthesis and its role in plant development, Annu Rev Plant Biol, 2010; 61: 49-64.
62. Sauer M., Robert S., Kleine-Vehn J. Auxin: simply complicated, J Exp Bot, 2013; 64(9): 2565-2577.
63. Enders T.A., Strader L.C. Auxin activity: Past, present, and future, Am J Bot, 2015; 102(2): 180–196. doi:10.3732/ajb.1400285
64. Woodward A.W., Bartel B. A receptor for auxin, Plant Cell, 2005; 17(9): 2425–2429. doi:10.1105/tpc.105.036236
65. Tsygankova V.A., Galkina L.A., Musatenko L.I., Sytnik K.M. Genetic and epigenetic control of plant growth and development. Molecular-genetic control of transmission and realization of auxin signals, Biopolym Cell, 2005; 21(3): 187-219.
66. Teale W.D., Paponov I., Palme K. Auxin in action: Signalling, transport and the control of plant growth and development, Nat Rev Mol Cell Biol, 2006; 7(11): 847-859. DOI: 10.1038/nrm2020.
67. Effendi Y., Scherer G.F. Auxin binding-protein1 (ABP1), a receptor to regulate auxin transport and early auxin genes in an interlocking system with PIN proteins and the receptor TIR1, Plant Signal Behav, 2011; 6(8): 1101–1103. doi:10.4161/psb.6.8.16403
68. Hayashi K. The Interaction and Integration of Auxin Signaling Components, Plant and Cell Physiol, 2012; 53(6): 965–975. https://doi.org/10.1093/pcp/pcs035
69. Lavy M., Estelle M. Mechanisms of auxin signaling, Development, 2016; 143(18): 3226–3229. doi:10.1242/dev.131870
70. Leyser O. Auxin Signaling, Plant Physiol, 2017; 176(1): 465–479. doi:10.1104/pp.17.00765
71. Hagen G. and Guilfoyle T. Auxin-responsive gene expression: Genes, promoters and regulatory factors, Plant Molecular Biology, 2002; 49(3-4): 373-85. DOI: 10.1023/A:1015207114117
72. Chapman E.J. and Estelle M. Mechanism of Auxin-Regulated Gene Expression in Plants, Annu Rev Genet, 2009; 43: 265–285.
73. Bouzroud S., Gouiaa S., Hu N., Bernadac A., Mila I., Bendaou N., Smouni A., Bouzayen M., Zouine M. Auxin Response Factors (ARFs) are potential mediators of auxin action in tomato response to biotic and abiotic stress (*Solanum lycopersicum*), PLoS ONE, 2018; 13(2): e0193517.
74. Tsygankova V.A. Genetic Control and Phytohormonal Regulation of Plant Embryogenesis, Int J Med Biotechnol Genetics (IJMBG), 2015; 3(1): 9-20.
75. Cherenkov P., Novikova D., Omelyanchuk N., Levitsky V., Grosse I., Weijers D., Mironova V. Diversity of cis-regulatory elements associated with auxin response in Arabidopsis thaliana, J Exp Bot, 2018; 69(2): 329-339. doi: 10.1093/jxb/erx254.
76. Majda M., Robert S. The Role of Auxin in Cell Wall Expansion, Int J Mol Sci, 2018; 19(4): 951.
77. Catalá C, Rose JK, Bennett AB. Auxin-regulated genes encoding cell wall-modifying proteins are expressed during early tomato fruit growth, Plant Physiol, 2000; 122(2): 527–534.
78. Tsygankova V.A., Galkina L.A., Musatenko L.I., Sytnik K.M. Genetic and epigenetic control of plant growth and development. Genes of auxin biosynthesis and auxin-regulated genes controlling plant cell division and extension, Biopolym Cell, 2005; 21(2): 107-133.

79. Shaul O., Van Montagu M., and Inze D. Cell Cycle Control in Arabidopsis, Annals of Botany, 1996; 78: 283–288.
80. Komaki S. and Sugimoto K. Control of the Plant Cell Cycle by Developmental and Environmental Cues, Plant Cell Physiol, 2012; 53(6): 953–964.
81. Robert C. Hare. Indoleacetic Acid Oxidase, Botanical Review, 1964; 30(1): 129-165.
82. Tandon P., Arya H.C. Association of Auxin Protectors, Peroxidase, Indoleacetic Acid Oxidase and Polyphenol Oxidase in Zizyphus Gall and Normal Stem Tissues Grown in Culture Biochemie und Physiologie der Pflanzen, 1982; 177(2): 114-124.
83. Liu Z.H., Hsiao I.C., and Pan Ya.W. Effect of naphthaleneacetic acid on endogenous indole-3-acetic acid, peroxidase and auxin oxidase in hypocotyl cuttings of soybean during root formation,Bot Bull Acad Sin, 1996; 37(4): 247-253.
84. Gaspar T., Kevers C., Penel C., Greppin H., Reid D.M., Thorpe T.A. Plant hormones and plant growth regulators in plant tissue culture, In Vitro Cell Dev Biol Plant, 1996; 32(4): 272-289.
85. Šimonová E., Henselová M., Zahradník P. Benzothiazole derivatives substituted in position 2 as biologically active substances with plant growth regulation activity, Plant Soil Environ, 2005; 51: 496-505.
86. Tsygankova V.A., ZayetsV.N., Galkina L.A., Blume Ya.B. The phytohormone-mediated action of the synthetic regulators on cell extension growth in higher plants,Biopolym Cell, 1999; 15(5): 432–441.
87. Yip W.K., Yang S.F. Effect of thidiazuron, a cytokinin–active ureaderivative, in cytokinin-dependent ethylene production system, Plant Physiol, 1986; 80: 515-519.
88. Murthy B.N.S., Murch S.J., Saxena P.K. Thidiazuron-induced somatic embryogenesis in intact seedlings of peanut (Arachis hypogea): Endogenous growth regulator levels and significance of cotyledons, Physiol Plantarum, 1995; 94: 268-276.
89. Hutchinson M.J., Saxena P.K. Role of purine metabolism in thidiazuron-induced somatic embryogenesis of geranium (Pelargonium hortorum Bailey) hypocotyl cultures,Physiol Plantarum, 1996, 98: 517–522.
90. Murthy B.N.S., Murch S.J., Saxena P.K. Thidiazuron: A potent regulator of in vitro plant morphogenesis, In Vitro Cell Dev Biol Plant, 1998; 34: 267-275.
91. Guo B., Abbasi B.H., Zeb A., Xu L.L. and Wei Y.H. Thidiazuron: A multi-dimensional plant growth regulator, Afr J Biotechno, 2011; 10(45): 8984-9000.
92. Thidiazuron: From Urea Derivative to Plant Growth Regulator, Naseem A., Mohammad F. (Eds.), Springer Singapore, 2018, 491 p.

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