



P-ISSN2349-8528  
 E-ISSN 2321-4902  
 IJCS 2016; 4(5): 106-120  
 © 2016 JEZS  
 Received: 16-07-2016  
 Accepted: 17-08-2016

**Victoria Tsygankova**  
 Department for Chemistry of Bioactive  
 Nitrogen-Containing Heterocyclic  
 Compounds, Institute of Bioorganic  
 Chemistry and Petrochemistry, National  
 Academy of Sciences of Ukraine,  
 Murmanskaya Str, Kyiv, Ukraine

**Yaroslav Andrusevich**  
 Department for Chemistry of Bioactive  
 Nitrogen-Containing Heterocyclic  
 Compounds, Institute of Bioorganic  
 Chemistry and Petrochemistry, National  
 Academy of Sciences of Ukraine,  
 Murmanskaya Str, Kyiv, Ukraine

**Olexandra Shtompel**  
 Department for Chemistry of Bioactive  
 Nitrogen-Containing Heterocyclic  
 Compounds, Institute of Bioorganic  
 Chemistry and Petrochemistry, National  
 Academy of Sciences of Ukraine,  
 Murmanskaya Str, Kyiv, Ukraine

**Stepan Pilyo**  
 Department for Chemistry of Bioactive  
 Nitrogen-Containing Heterocyclic  
 Compounds, Institute of Bioorganic  
 Chemistry and Petrochemistry, National  
 Academy of Sciences of Ukraine,  
 Murmanskaya Str, Kyiv, Ukraine

**Volodymyr Prokopenko**  
 Department for Chemistry of Bioactive  
 Nitrogen-Containing Heterocyclic  
 Compounds, Institute of Bioorganic  
 Chemistry and Petrochemistry, National  
 Academy of Sciences of Ukraine,  
 Murmanskaya Str, Kyiv, Ukraine

**Andrii Kornienko**  
 Department for Chemistry of Bioactive  
 Nitrogen-Containing Heterocyclic  
 Compounds, Institute of Bioorganic  
 Chemistry and Petrochemistry, National  
 Academy of Sciences of Ukraine,  
 Murmanskaya Str, Kyiv, Ukraine

**Volodymyr Brovarets**  
 Department for Chemistry of Bioactive  
 Nitrogen-Containing Heterocyclic  
 Compounds, Institute of Bioorganic  
 Chemistry and Petrochemistry, National  
 Academy of Sciences of Ukraine,  
 Murmanskaya Str, Kyiv, Ukraine

**Correspondence**  
**Victoria Tsygankova**  
 Department for Chemistry of Bioactive  
 Nitrogen-Containing Heterocyclic  
 Compounds, Institute of Bioorganic  
 Chemistry and Petrochemistry, National  
 Academy of Sciences of Ukraine,  
 Murmanskaya Str, Kyiv, Ukraine

## Study of growth regulating activity derivatives of [1,3]Oxazolo[5,4-*d*]pyrimidine and N-Sulfonyl substituted of 1,3-Oxazole on soybean, wheat, flax and pumpkin plants

**Victoria Tsygankova, Yaroslav Andrusevich, Olexandra Shtompel, Stepan Pilyo, Volodymyr Prokopenko, Andrii Kornienko and Volodymyr Brovarets**

### Abstract

In our work the low molecular weight heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole were synthesized. Comparative analysis of plant growth stimulating activity of these heterocyclic compounds and plant hormones auxins IAA and NAA, and cytokinin Kinetin was conducted. It was found that all tested heterocyclic compounds used in concentration  $10^{-9}$ M/l of distilled water revealed high auxin-like growth stimulating activity on the soybean (*Glycine max* L.) of cultivar Valuta, wheat (*Triticum aestivum* L.) of cultivar Zimoyarka, and flax (*Linum usitatissimum* L.) of cultivar Svitanok. The growth parameters of 20<sup>th</sup>-day-old seedlings of soybean, wheat, and flax grown on the  $10^{-9}$ M water solutions of heterocyclic compounds were as generally similar or higher than the growth parameters of seedlings grown on the water solution of auxins IAA and NAA used in the same concentration as compared to lower growth parameters of control untreated seedlings grown on the distilled water. Specific bioassay on cytokinin-like activity, conducted on the isolated cotyledons of muscat pumpkin (*Cucurbita moschata* Duch. et Poir.) of cultivar Gilea, showed that all testing heterocyclic compounds used in concentration  $10^{-9}$ M/l of distilled water demonstrated expressive cytokinin-like stimulating effect on the growth of the isolated cotyledons of pumpkin. Obtained data confirm perceptiveness of application derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole in the agricultural practice for intensification of growth and development of soybean, wheat, flax and pumpkin plants.

**Keywords:** [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole, IAA, NAA, Kinetin, *Glycine max* L., *Triticum aestivum* L., *Linum usitatissimum* L., *Cucurbita moschata* Duch. et Poir

### 1. Introduction

The main task for successful development of high-intensive world agriculture is an improving of crop growth and increase their productivity under unfavorable of abiotic and biotic stress-factors of environment (i.e. drought, cold, salinity, soil pollution and various plant pathogenic organisms) [1-5]. Today the different classes of plant growth regulatory compounds of natural origin such as phytohormones or their synthetic analogs, biostimulants, herbicides, organic fertilizers and micronutrients are widely used in the agricultural practice to accelerate plant growth and increase their productivity, and to protect against environmental stress-factors [6-15]. Together with traditional plant growth regulators the new classes of biologically active compounds created on the base of synthetic or natural low-molecular weight heterocyclic compounds derivatives of pyridine, pyrimidine, pyrazole, triazine, oxazole, and isoflavones are widely applied in the agricultural industry as plant growth regulators, herbicides, fungicides and antibacterial agents [16-25]. Advantage of application of these heterocyclic compounds in the agricultural practice is their high effectiveness at very small concentrations and environmental safety due to lack of toxic effect on the human, animal and plant cells; moreover they are widely used in the medical practice as therapeutic agents for treatment of nervous, allergic, gastroesophageal, cancer, bacterial, viral, fungal, infectious, and inflammatory diseases [26-32].

Soybean, wheat, flax and pumpkin are the most economically valuable crops cultivated over the world [33-36]. Soybean (*Glycine max* L.) belongs to important grain legumes and oilseed crop, which is source of more than 40% of proteins and 50% of oil used in the world food industry [37, 38]. Rhizobium-legume symbiosis enhances fixation of atmospheric nitrogen and increases soil fertility [39, 40]. Biodegradable soy protein isolate is an important basic material for food industry, agriculture and biotechnology [41]. Soybean contains biologically active compounds used in medical practice such as isoflavones, lectins, saponins, peptid lunazin and protease inhibitors such as Bowman-Birk protease inhibitor (BBI) and Kunitz trypsin inhibitor (KTI) that revealed cytotoxic activity against cancer [42-45].

Wheat (*Triticum aestivum* L.) is the major strategic cereal crop which is cultivated over the world [46-50]. Wheat provides by 30% of the food calories consumed by world population (4.5 billion people) [48, 49]. Wheat is also used as a raw material for the production of malt and beer [50]. Wheat contains various bioactive compounds such as alkaloids, saponins, glycosides, terpenoids, steroids, flavonoids and tannins that may be used for purposes of pharmaceutical industry [51]. However, despite the rapidly increasing of wheat sowing, there are significant problems with the increasing of the productivity of this crop because world population is expected to reach 9.7 billion people by 2050 [52].

Flax (*Linum usitatissimum* L.) is the oldest crop which is cultivated in more than 20 world countries [53-55]. Flax is widely used to produce cellulosic fiber for textile and paper industry and seed oil for food, cosmetic and pharmaceutical industry [55-57]. Flax seed lignan secoisolariciresinol diglucoside (SDG) and seed oil which contains more than 50% of omega-3 fatty acid -  $\alpha$ -linolenic acid (ALA), sterols and tocopherols are used as supplements to dietary food and as pharmaceutical drugs for treatment of different diseases: weight gain, heart disease, hypertension, atherosclerosis, diabetes, arthritis, memory problems, depression, cancer, inflammatory diseases, kidney disorders etc. [56-58]. Moreover flax oil has polymer-forming properties due to high content of linolenic acid; therefore it is an ideal raw material for manufacture of paints, varnishes and ink [36, 56, 59].

Pumpkin (*Cucurbita pepo* L.) is the wide cultivated crop which is used as an important source for human dietary food, pharmaceutical products and animal forage [60-62]. Pumpkin seed oil contains biologically active compounds such as sterols, omega-3 and omega-6 essential fatty acids, tocopherols and carotenoids that have antidiabetic, antifungal, antibacterial, antioxidant and antiinflammatory properties due to which it is used in medical practice for protection and therapy of many diseases, such as hypertension, diabetes, cancer etc. [63-67].

Unfortunately the adverse environmental factors negatively impact on growing and productivity of these crops [68-70]. Today the various phytohormones, plant growth regulators, biostimulants, herbicides as well as fertilizers, micronutrients and vitamins are widely used for improvement of growth and development of soybean [71-74], wheat [75-81], flax [82-86] and pumpkin plants [87, 88].

The elaboration of new effective ecologically safe plant growth regulators created on the base of low molecular weight heterocyclic compounds for improving of growth and increase of productivity of these crops is alternative strategic approach. At the Institute of Bioorganic Chemistry and Petrochemistry of National Academy of Sciences of Ukraine the new effective plant growth substances elaborated on the

base of low molecular weight five and six-membered heterocyclic compounds are synthesized. Our previous researches showed that some low molecular weight heterocyclic compounds created on the base of derivatives of pyridine, pyrimidine, pyrazole and isoflavones revealed high stimulating shoot organogenesis activity in the isolated tissue cultures of *Linum usitatissimum* L. cultivar heavenly *in vitro* conditions and high stimulating effect on germination of seeds and vegetative growth of maize (*Zea mays* L.) cultivar Odesskaya 10 [58, 89]. Therefore the great theoretical and practical interest is possibility of application of new classes of low molecular weight heterocyclic compounds for intensification of growth and development of the important for agriculture crops such as soybean, wheat, flax and pumpkin.

The objective of this work was study of growth stimulating activity of low molecular weight heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole according to their impact on the acceleration of growth and development of the soybean, wheat and flax plants and on the growth of biomass of the isolated cotyledons of pumpkin.

## 2. Materials and Methods

### 2.1 Synthesis of heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole

Low molecular weight heterocyclic compounds were synthesized at the Department for Chemistry of Bioactive Nitrogen-Containing Heterocyclic Compounds of Institute of Bioorganic Chemistry and Petrochemistry of NAS of Ukraine.

#### 2.1.1 General

IR spectra (KBr) were recorded with the Vertex 70 instrument. <sup>1</sup>H NMR spectra were obtained with the Varian Mercury spectrometer (400 MHz) in DMSO-*d*<sub>6</sub>, with TMS as internal standard. GC-MS spectra were registered with the Agilent 1100 Series HPLC device equipped with a mass selective UV diode array detector. Conditions of the GC-MS analysis were as follows: Zorbax SB-C18 column (1.18  $\mu$ m, 4.6  $\times$  15 mm, PN 821975-932); acetonitrile-water (95 : 5), 0.1% aqueous trifluoroacetic acid; eluent flow rate 3 mL/min; injection volume 1  $\mu$ L; UV detector (215, 254, 285 nm); chemical ionization at atmospheric pressure (APCI), scanning range *m/z* 80–1000. Elemental analysis was performed at the analytical laboratory of the Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Sciences of Ukraine. Melting points were measured using the Fisher-Johns apparatus. The reaction progress was monitored by TLC on Silufol UV-254 plates eluting with the 9:1 chloroform-methanol mixture and developing with UV irradiation.

#### 2.1.2 General procedure for synthesis of 7-amino-5-aryl-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidines (compounds №1 and №4, Table 1)

Mixture of 4-cyano-1,3-oxazole-5-sulfonyl chloride (0.01 mol), appropriate amidine hydrochloride (0.01 mol) and triethylamine (0.02 mol) in 50 ml of anhydrous tetrahydrofuran was stirred at 20–25 °C for 48 h. The precipitate was filtered off; the solvent was removed in a vacuum. The residue was treated with water, filtered off, dried, and purified by recrystallization from acetonitrile [90].

### 2.1.3 General procedure for synthesis of 5-aryl-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine-7(6*H*)-ones (compounds №2 and №3, Table 1)

Mixture of methyl 5-chlorosulfonyl-2-phenyl-1,3-oxazole-4-carboxylate (0.001 mol), corresponding amidine hydrochloride (0.001 mol), and triethylamine (0.002 mol) in 10 mL of anhydrous tetrahydrofuran was stirred at 20–25°C during 24 h and then at 65°C during 1 h. After cooling, 20 mL of water was added. The precipitate was filtered off, dried, and purified by recrystallized from solvent system (MeCN-DMF, 3:1) [91].

### 2.1.4 General procedure for synthesis of 2-aryl-5-(piperidine-1-ylsulfonyl)-1,3-oxazole-4-carbonitriles (compounds №5 and №6, Table 1)

To a solution of 2-aryl-4-cyano-1,3-oxazole-5-sulfonyl chloride (0.001 mol) was added piperidine (0.0008 mol) and triethylamine (0.0008 mol). The mixture was heated for 2 h

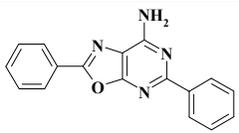
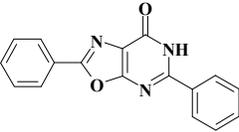
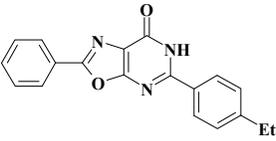
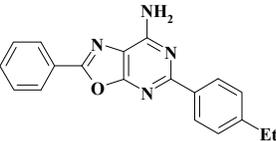
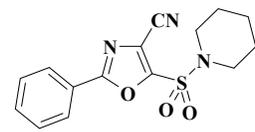
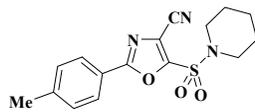
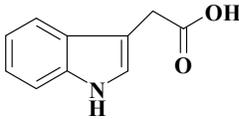
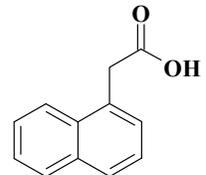
and kept at 20–25°C for 12 h. The precipitate was filtered off; the solvent was removed in a vacuum. The residue was treated with water, filtered off, dried and purified by recrystallized from ethanol [92].

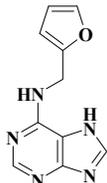
### 2.2 Chemical structures of heterocyclic compounds and phytohormones used for bioassays

In our experiments we conducted comparative analysis of plant growth regulating activity of low molecular weight five and six-membered heterocyclic compounds: derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine (compounds № 1–4) and *N*-sulfonyl substituted of 1,3-oxazole (compounds № 5 and № 6), as well as phytohormones auxins IAA (compounds № 7) and NAA (compound № 8) and cytokinin Kinetin (compound № 9).

Chemical structures of phytohormones and heterocyclic compounds used for bioassays are shown on the Table 1.

**Table 1:** Chemical structures of synthetic compounds used for bioassays

Compound No	Structural formula	Name	Molar mass
1		7-Amino-2,5-diphenyl[1,3]oxazolo[5,4- <i>d</i> ]pyrimidine	288.31
2		2,5-Diphenyl[1,3]oxazolo[5,4- <i>d</i> ]pyrimidin-7(6 <i>H</i> )-one	289.30
3		5-(4-Ethylphenyl)-2-phenyl[1,3]oxazolo[5,4- <i>d</i> ]pyrimidin-7(6 <i>H</i> )-one	317.35
4		7-Amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4- <i>d</i> ]pyrimidine	316.37
5		2-Phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile	317.37
6		2-Tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile	331.40
7		IAA (1 <i>H</i> -Indol-3-ylacetic acid)	175.19
8		NAA (1-Naphthylacetic acid)	186.21

9		Kinetin ( <i>N</i> -(2-Furylmethyl)-7 <i>H</i> -purin-6-amine)	215.22
---	---	--	--------

### 2.3 Impact of synthetic heterocyclic compounds on growth and development of soybean, wheat and flax plants

In the laboratory conditions we studied impact of synthetic heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and *N*-sulfonyl substituted of 1,3-oxazole on germination of seeds and growth of seedlings of crops: the soybean (*Glycine max* L.) of cultivar Valuta, wheat (*Triticum aestivum* L.) of cultivar Zimoyarka and flax (*Linum usitatissimum* L.) of cultivar Svitanok. With this aim seeds of soybean, wheat and flax plants were surface sterilized successively in 1% KMnO<sub>4</sub> solution for 3 min and 96% ethanol solution for 1 min and then washed three times in the sterilized distilled water. After this procedure seeds were placed in the cuvettes (each containing 50 seeds) on the perlite moistened with distilled water (control) or with water solution of each heterocyclic compound used in concentration 10<sup>-9</sup>M/l of distilled water or water solution of auxins IAA or NAA used in the same concentration (experiment). Control and experimental seeds were placed in the thermostat for their germination in darkness at the temperature 25 °C during the 48 hours. Sprouted seedlings were placed in the plant growth chamber in which seedlings were grown for 20 days at the 16/8 h light/dark conditions, at the temperature 24 °C, light intensity 3000 lux and air humidity 60-80%. Comparative analysis of biometric indexes of seedlings (i.e. number of germinated seeds (%), seedlings height (cm), roots number (pcs), roots length (mm)) was carried out at the 20<sup>th</sup> day after their sprouting according to the guideline [93].

### 2.4 Impact of synthetic heterocyclic compounds on the growth of biomass of the isolated cotyledons of pumpkin

To determine stimulating activity of tested heterocyclic compounds on the growth of muscat pumpkin (*Cucurbita moschata* Duch. et Poir.) of cultivar Gilea, we used specific bioassay on cytokinin-like activity, which was conducted on the isolated cotyledons of this plant [94]. With this aim seeds were surface sterilized in 1% KMnO<sub>4</sub> solution for 3 min and 96% ethanol solution for 1 min and then washed with distilled water. After this procedure seeds were placed in the cuvettes (each containing 20-25 seeds) on the filter paper moistened with distilled water. After this procedure seeds were placed in the thermostat for their germination in darkness at the temperature 25 °C during the 96 hours. The 4<sup>th</sup>-day-old pumpkin seedlings were separated from cotyledons using sterile scalpel. The isolated cotyledons were weighted and placed in the cuvettes (each containing 20 seeds) on the filter paper moistened with distilled water (control) or with water solution of each heterocyclic compound used in concentration 10<sup>-9</sup>M/l of distilled water or with water solution of phytohormone cytokinin - Kinetin used in the same concentration (experiment). Control and experimental isolated cotyledons were placed in the plant growth chamber in which they were grown during 16 days at the above mentioned conditions. To determine the index of growth of biomass (g) of the isolated cotyledons of pumpkin, they were washed with sterilized distilled water and weighted with the interval of each 4 day.

### 2.5 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 [95].

## 3. Results

### 3.1 Stimulating effect of chemical heterocyclic compounds and auxin NAA on the growth and development of soybean seedlings

In the laboratory conditions we studied impact of chemical heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and *N*-sulfonyl substituted of 1,3-oxazole as well as phytohormone auxin NAA on the germination of seeds and growth of soybean (*Glycine max* L.) of cultivar Valuta. It was shown that all tested heterocyclic compounds and phytohormone auxin NAA used in concentration 10<sup>-9</sup>M/l of distilled water revealed high stimulating effect on the growth of the 20<sup>th</sup>-day-old soybean seedlings and considerably improved growth and development of their root system (Fig. 1).



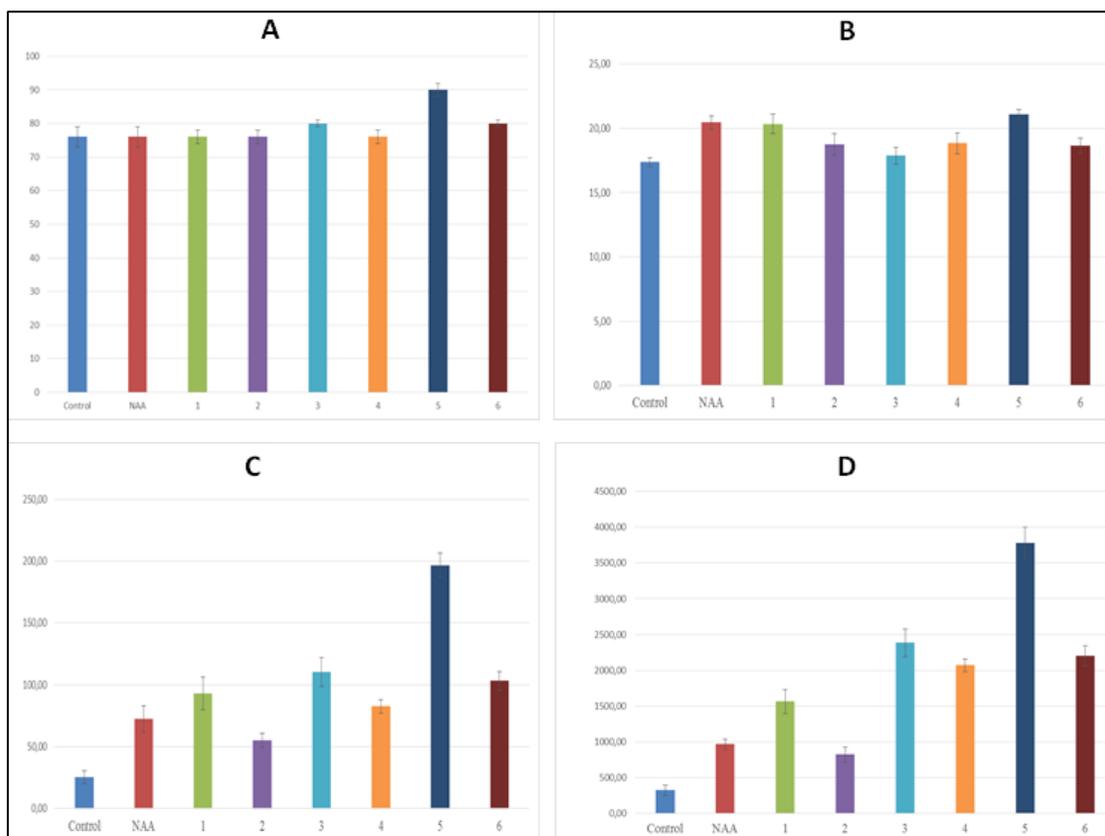
**Fig 1:** Impact of chemical heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine (№1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine, №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine), compounds derivatives of *N*-sulfonyl substituted of 1,3-oxazole (№5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile and №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile), and phytohormone auxin NAA on the root formation of the 20<sup>th</sup>-day-old soybean seedlings as compared to control (C) soybean seedlings

The comparative analysis of biometric indexes of 20<sup>th</sup>-day-old soybean seedlings (i.e. number of germinated seeds (%), length of seedlings (cm), total number of roots (pcs), total length of roots (mm)) showed that the biometric indexes of seedlings grown on the 10<sup>-9</sup>M water solution of chemical heterocyclic compounds were similar or higher than the biometric indexes seedlings grown on the 10<sup>-9</sup>M water solution of phytohormone auxin NAA used at the same concentration as compared to lower biometric indexes seedlings grown on the distilled water (control). The results of stimulating effect of the heterocyclic compounds on the biometric indexes of 20<sup>th</sup>-day-old soybean seedlings are shown on the Fig 2.

Particularly it was found that the biometric indexes of soybean seedlings grown on the 10<sup>-9</sup>M water solution of compound №1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-

*d*]pyrimidine were as generally higher than the biometric indexes of soybean seedlings grown either on the distilled water (control) or on the  $10^{-9}$ M water solution of auxin NAA as follows: according with length of seedlings – at the 17% as compared with control; according with total length of roots –

at the 4.85 times as compared with control and at the 62% as compared with NAA; according with total number of roots – at the 3.72 times as compared with control, and at the 28% as compared with NAA, respectively (Fig. 2).



**Fig 2:** Impact of chemical heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine (№1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine, №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine), compounds derivatives of *N*-sulfonyl substituted of 1,3-oxazole (№5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile and №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile), and phytohormone auxin NAA on the biometric indexes of 20<sup>th</sup>-day-old soybean seedlings

A – number of germinated seeds (%), B – length of seedlings (cm), C – total number of roots (pcs), D – total length of roots (mm)

The biometric indexes of 20<sup>th</sup>-day-old soybean seedlings grown on the  $10^{-9}$ M water solution of the compound №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one were as generally higher than the biometric indexes of soybean seedlings grown on the distilled water (control) as follows: according with length of seedlings – at the 8% as compared with control; according with total length of roots – at the 2.5 times as compared with control; according with total number of roots – at the 2.2 times as compared with control (Fig. 2).

The biometric indexes of soybean seedlings grown on the  $10^{-9}$ M water solution of compound №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one were as generally higher than the biometric indexes of soybean seedlings grown either on the distilled water (control) or on the  $10^{-9}$ M water solution of auxin NAA as follows: according with total length of roots – at the 7.4 times as compared with control and at the 2.47 times as compared with NAA; according with total number of roots – at the 4.4 times as compared with control, and at the 52% as compared with NAA, respectively (Fig. 2).

The biometric indexes of soybean seedlings grown on the  $10^{-9}$ M water solution of compound №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine were as

generally higher than the biometric indexes of soybean seedlings grown either on the distilled water (control) or on the  $10^{-9}$ M water solution of auxin NAA as follows: according with length of seedlings – at the 8% as compared with control; according with total length of roots – at the 6.4 times as compared with control and at the 2.15 times as compared with NAA; according with total number of roots – at the 2.59 times as compared with control, and at the 55% as compared with NAA, respectively (Fig. 2).

The biometric indexes of soybean seedlings grown on the  $10^{-9}$ M water solution of compound №5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile were as generally higher than the biometric indexes of soybean seedlings grown either on the distilled water (control) or on the  $10^{-9}$ M water solution of auxin NAA as follows: according with length of seedlings – at the 21% as compared with control; according with total length of roots – at the 11.7 times as compared with control and at the 3.9 times as compared with NAA; according with total number of roots – at the 7.7 times as compared with control, and at the 2.7 times as compared with NAA, respectively (Fig. 2).

The biometric indexes of soybean seedlings grown on the  $10^{-9}$ M water solution of compound №6 - 2-tolyl-5-(piperidin-1-

ylsulfonyl)-1,3-oxazole-4-carbonitrile were as generally higher than the biometric indexes of soybean seedlings grown either on the distilled water (control) or on the  $10^{-9}$ M water solution of auxin NAA as follows: according with length of seedlings – at the 7% as compared with control; according with total length of roots – at the 6.8 times as compared with control and at the 2.3 times as compared with NAA; according with total number of roots – at the 4.1 times as compared with control, and at the 73% as compared with NAA, respectively (Fig. 2).

Thus, the comparative analysis of biometric indexes of 20<sup>th</sup>-day-old soybean seedlings grown on the  $10^{-9}$ M water solution of heterocyclic compounds showed that the highest growth stimulating activity from tested compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine revealed compounds: №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one and №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine. At the same time the compounds №1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine and №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one demonstrated lower growth stimulating activity. The obtained results of different growth stimulating activity of compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine obviously may be explained by the presence of phenyl substituents at the 5<sup>th</sup> and 7<sup>th</sup> positions of pyrimidine fragment in these heterocyclic compounds.

The highest growth stimulating activity from tested compounds derivatives of N-sulfonyl substituted of 1,3-oxazole revealed compound №5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile. It is possible to suppose that the high growth stimulating activity of compound №5 obviously can be explained by the presence of phenyl substituent at the 2<sup>nd</sup> position of oxazole. While the compound №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile, which has a similar to compound №5 structure, but differs by the presence of tolyl substituent at the 2<sup>nd</sup> position of oxazole, showed lower activity than the compound №5 and at the same time higher than the activity of auxin NAA. The obtained data witness that the various substituents at the 2<sup>nd</sup> position of oxazole impact on the activity of N-sulfonyl substituted of 1,3-oxazole.

### 3.2 Stimulating effect of chemical heterocyclic compounds and auxins IAA and NAA on the growth and development of wheat seedlings

In our experiments we also studied impact of chemical heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole as well as phytohormones auxins IAA and NAA on the germination of seeds and growth of wheat (*Triticum aestivum* L.) of cultivar Zimoyarka. The high stimulating effect of all tested heterocyclic compounds and phytohormones auxins IAA and NAA on the growth of 20<sup>th</sup>-day-old wheat seedlings and development of their root system was observed at their using in concentration  $10^{-9}$ M/l of distilled water (Fig. 3).

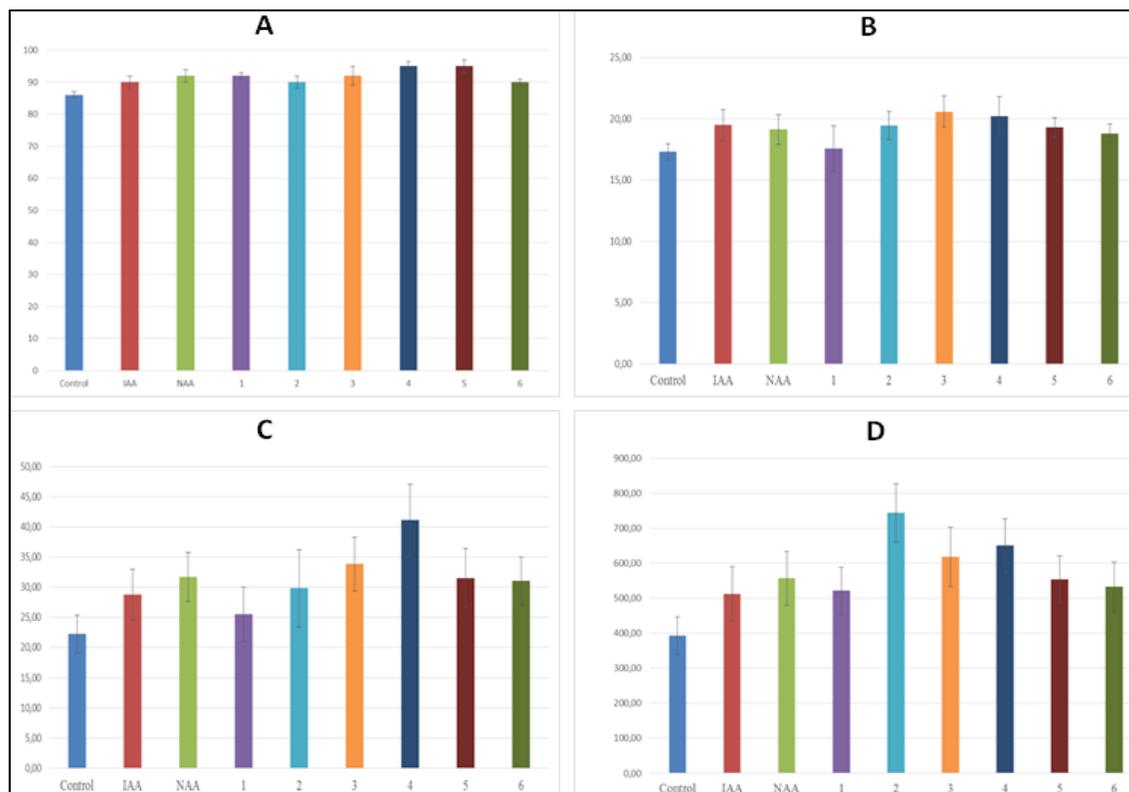


**Fig 3:** Impact of chemical heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine (№1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine, №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine), compounds derivatives of N-sulfonyl substituted of 1,3-oxazole (№5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile and №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile), and phytohormones auxins IAA and NAA on the root formation of the 20<sup>th</sup>-day-old wheat seedlings as compared to control (C) wheat seedlings

The comparative analysis of biometric indexes of 20<sup>th</sup>-day-old wheat seedlings (i.e. number of germinated seeds (%), length of seedlings (cm), total number of roots (pcs), total length of roots (mm)) showed that the biometric indexes of seedlings grown on the  $10^{-9}$ M water solution of chemical heterocyclic compounds were similar or higher than the biometric indexes seedlings grown on the  $10^{-9}$ M water solution of phytohormones auxins IAA and NAA used at the same concentration as compared to lower biometric indexes seedlings grown on the distilled water (control). The results of stimulating effect of the heterocyclic compounds on the biometric indexes of 20<sup>th</sup>-day-old wheat seedlings are shown on the Fig 4.

Particularly it was found that the biometric indexes of wheat seedlings grown on the  $10^{-9}$ M water solution of compound №1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine were as generally higher than the biometric indexes of wheat seedlings grown either on the distilled water (control) or on the  $10^{-9}$ M water solution of auxins IAA and NAA as follows: according with length of seedlings – at the 17% as compared with control; according with total length of roots – at the 32% as compared with control; according with total number of roots – at the 85%, 51% and 20% as compared with control, IAA and NAA, respectively (Fig. 4).

The biometric indexes of 20<sup>th</sup>-day-old wheat seedlings grown on the  $10^{-9}$ M water solution of the compound №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one were as generally higher than the biometric indexes of wheat seedlings grown either on the distilled water (control) or on the  $10^{-9}$ M water solution of auxins IAA and NAA as follows: according with length of seedlings – at the 13% as compared with control; according with total length of roots – at the 89%, 45% and 34% as compared with control, IAA and NAA, respectively; according with total number of roots – at the 30% as compared with control (Fig. 4).



**Fig 4:** Impact of chemical heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine (№1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine, №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine), compounds derivatives of N-sulfonyl substituted of 1,3-oxazole (№5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile and №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile), and phytohormones auxins IAA and NAA on the biometric indexes of 20<sup>th</sup>-day-old wheat seedlings  
A – number of germinated seeds (%), B – length of seedlings (cm), C – total number of roots (pcs), D – total length of roots (mm)

The biometric indexes of wheat seedlings grown on the 10<sup>-9</sup>M water solution of compound №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one were as generally higher than the biometric indexes of wheat seedlings grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of auxins IAA and NAA as follows: according with length of seedlings – at the 20%, 6% and 8% as compared with control, IAA and NAA, respectively; according with total length of roots – at the 57%, 21% and 11% as compared with control, IAA and NAA, respectively; according with total number of roots – at the 57%, 24% and 16% as compared with control, IAA and NAA, respectively (Fig. 4).

The biometric indexes of wheat seedlings grown on the 10<sup>-9</sup>M water solution of compound №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine were as generally higher than the biometric indexes of wheat seedlings grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of auxins IAA and NAA as follows: according with length of seedlings – at the 16% as compared with control; according with total length of roots – at the 66%, 27% and 17% as compared with control, IAA and NAA; according with total number of roots – at the 65%, 31% and 23% as compared with control, IAA and NAA, respectively (Fig. 4). The biometric indexes of wheat seedlings grown on the 10<sup>-9</sup>M water solution of compound №5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile were as generally higher than the biometric indexes of wheat seedlings grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of auxin IAA as follows: according with length of

seedlings – at the 13% as compared with control; according with total length of roots – at the 41% and 8% as compared with control and IAA, respectively; according with total number of roots – at the 53% as compared with control (Fig. 4).

The biometric indexes of wheat seedlings grown on the 10<sup>-9</sup>M water solution of compound №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile were as generally higher than the biometric indexes of wheat seedlings grown on the distilled water (control) as follows: according with length of seedlings – at the 10% as compared with control; according with total length of roots – at the 36% as compared with control; according with total number of roots – at the 10% as compared with control (Fig. 4).

Thus, the comparative analysis of biometric indexes of 20<sup>th</sup>-day-old wheat seedlings grown on the 10<sup>-9</sup>M water solution of heterocyclic compounds showed that the highest growth stimulating activity from tested compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine revealed compounds: №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one and №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine. The obtained results obviously may be explained by the presence of different substituents at the 7<sup>th</sup> position of pyrimidine fragment: of oxygen - at the compound №3 or amino group - at the compound №4, respectively.

At the same time the compounds №1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine and №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one revealed lower growth stimulating activity on the wheat seedlings.

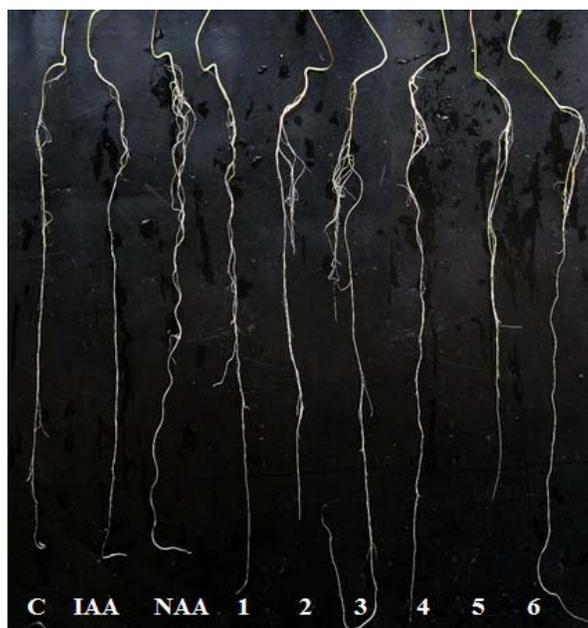
These compounds that are derivatives of the compounds №3 and №4 contain also phenyl substituent at the 5<sup>th</sup> position and amino group at the 7<sup>th</sup> position of pyrimidine fragment.

Obviously that growth stimulating activity of compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine may be depended from substituents at the 5<sup>th</sup> and 7<sup>th</sup> positions of pyrimidine fragment.

The results of our experiments showed that the minor growth stimulating activity on the wheat seedlings demonstrated compounds derivatives of N-sulfonyl substituted of 1,3-oxazole: compound №5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile and compound №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile, which was not significantly differed between these compounds, therefore correlation between chemical structure and biological activity has not been found in these compounds.

### 3.3 Stimulating effect of chemical heterocyclic compounds and auxins IAA and NAA on the growth and development of flax seedlings

In our laboratory experiments we also studied stimulating effect of chemical heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole as well as phytohormones auxins IAA and NAA on the growth and development of flax (*Linum usitatissimum* L.) of cultivar Svitanok. Our results demonstrated that all tested heterocyclic compounds and phytohormones auxins IAA and NAA used in concentration  $10^{-9}$ M/l of distilled water revealed high stimulating effect on the germination of seeds and growth of 20<sup>th</sup>-day-old flax seedlings, and on the formation of their root system (Fig. 5).

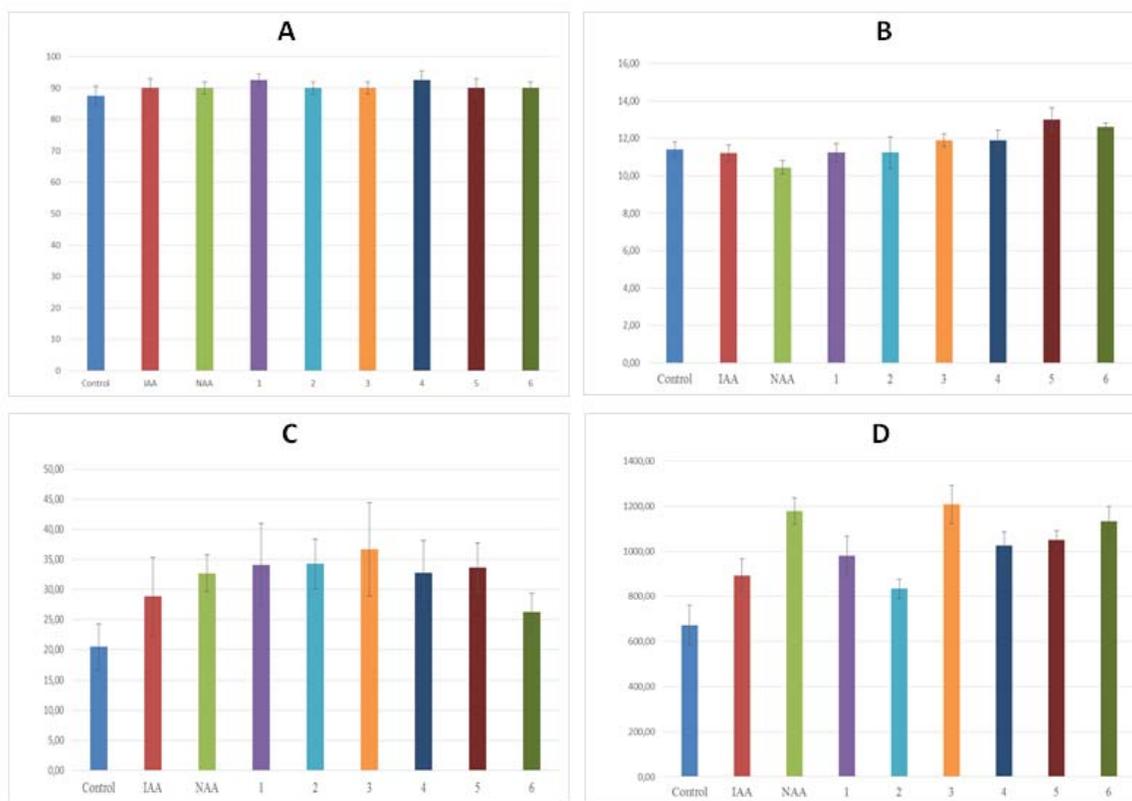


**Fig 5:** Impact of chemical heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine (№1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine, №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine), compounds derivatives of N-sulfonyl substituted of 1,3-oxazole (№5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile and №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile), and phytohormones auxins IAA and NAA on the root formation of the 20<sup>th</sup>-day-old flax seedlings as compared to control (C) flax seedlings

The comparative analysis of biometric indexes of 20<sup>th</sup>-day-old flax seedlings (i.e. number of germinated seeds (%), length of seedlings (cm), total number of roots (pcs), total length of roots (mm)) showed that the biometric indexes of seedlings grown on the  $10^{-9}$ M water solution of chemical heterocyclic compounds were similar or higher than the biometric indexes of seedlings grown on the  $10^{-9}$ M water solution of phytohormones auxins IAA and NAA used at the same concentration as compared to lower biometric indexes of seedlings grown on the distilled water (control). The results of impact of the heterocyclic compounds on the biometric indexes of 20<sup>th</sup>-day-old flax seedlings are shown on the Fig. 6. Particularly it was found that the biometric indexes of flax seedlings grown on the  $10^{-9}$ M water solution of compound №1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine were as generally higher than the biometric indexes of flax

seedlings grown either on the distilled water (control) or on the  $10^{-9}$ M water solution of auxins IAA and NAA as follows: according with total length of roots – at the 46%, 10% as compared with control and IAA, respectively; according with total number of roots – at the 66%, 18% and 4% as compared with control, IAA and NAA, respectively (Fig. 6).

The biometric indexes of flax seedlings grown on the  $10^{-9}$ M water solution of compound №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one were as generally higher than the biometric indexes of flax seedlings grown either on the distilled water (control) or on the  $10^{-9}$ M water solution of auxins IAA and NAA as follows: according with total length of roots – at the 24% as compared with control; according with total number of roots – at the 66%, 18% and 4% as compared with control, IAA and NAA, respectively (Fig. 6).



**Fig 6:** Impact of chemical heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine (№1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine, №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine), compounds derivatives of N-sulfonyl substituted of 1,3-oxazole (№5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile and №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile), and phytohormones auxins IAA and NAA on the biometric indexes of 20<sup>th</sup>-day-old flax seedlings  
A – number of germinated seeds (%), B – length of seedlings (cm), C – total number of roots (pcs), D – total length of roots (mm)

The biometric indexes of flax seedlings grown on the 10<sup>-9</sup>M water solution of compound №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one were as generally higher than the biometric indexes of flax seedlings grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of auxins IAA and NAA as follows: according with total length of roots – at the 80% vs 35% and 3% as compared with control, IAA and NAA, respectively; according with total number of roots – at the 79%, 27% and 12% as compared with control, IAA and NAA, respectively (Fig. 6).

The biometric indexes of flax seedlings grown on the 10<sup>-9</sup>M water solution of compound №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine were as generally higher than the biometric indexes of flax seedlings grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of auxins IAA and NAA as follows: according with total length of roots – at the 53% and 15% as compared with control and IAA, respectively; according with total number of roots – at the 60% vs 14% as compared with control and IAA, respectively (Fig. 6).

The biometric indexes of flax seedlings grown on the 10<sup>-9</sup>M water solution of compound №5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile were as generally higher than the biometric indexes of flax seedlings grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of auxins IAA and NAA as follows: according with length of seedlings – at the 14%, 16% and 24% as compared with control, IAA and NAA, respectively; according with total length of roots – at the 56% and 18% as compared with

control and IAA, respectively; according with total number of roots – at the 64% and 17% as compared with control and IAA, respectively (Fig. 6).

The biometric indexes of flax seedlings grown on the 10<sup>-9</sup>M water solution of compound №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile were as generally higher than the biometric indexes of flax seedlings grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of auxins IAA and NAA as follows: according with length of seedlings – at the 11%, 13% and 21% as compared with control, IAA and NAA, respectively; according with total length of roots – at the 68% and 27% as compared with control and IAA, respectively; according with total number of roots – at the 28% as compared with control (Fig. 6).

The obtained results of biometric indexes of 20<sup>th</sup>-day-old flax seedlings witness that the highest growth stimulating activity showed compound derivative of [1,3]oxazolo[5,4-*d*]pyrimidine: №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one. Possibly, the high stimulating effect of this compound on the growth of flax seedlings may be explained by the presence 4-ethylphenyl substituent at the 5<sup>th</sup> position and oxygen at the 7<sup>th</sup> position of pyrimidine fragment of this compound.

At the same time the compound №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine, which contains amino group at the 7<sup>th</sup> position of pyrimidine fragment, and compound №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, which contains phenyl substituent at the 5<sup>th</sup> position of pyrimidine fragment, revealed lower activity than the compound №3.

Obviously that growth stimulating activity of compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine may be depended from substituents at the 5<sup>th</sup> and 7<sup>th</sup> positions of pyrimidine fragment.

Among the compounds derivatives of and N-sulfonyl substituted of 1,3-oxazole the highest growth stimulating activity revealed compound №5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile, which contains phenyl substituent at the 2<sup>th</sup> position of oxazole.

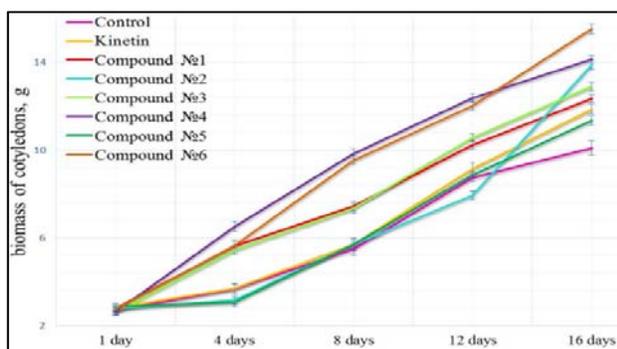
At the same time, the compound №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile, which contains tolyl substituent at the 2<sup>th</sup> position of oxazole, showed lower activity. Thus, the growth stimulating activity of these compounds may be depended from the presence of different substituents at the 2<sup>th</sup> position of oxazole.

### 3.4 Stimulating effect of synthetic heterocyclic compounds on the growth of biomass of the isolated cotyledons of pumpkin

In our researches we also studied stimulating effect of heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole on the growth of muscat pumpkin (*Cucurbita moschata* Duch. et Poir.) of cultivar Gilea using specific bioassay on cytokinin-like activity conducted on the isolated cotyledons of this plant.

It was found that according to indexes of growth of biomass of the isolated cotyledons of pumpkin during the 16 days all tested compounds used in concentration 10<sup>-9</sup>M/l of distilled water showed expressive cytokinin-like activity, which was similar or higher than the activity of phytohormone cytokinin Kinetin used in the same concentration.

The comparative analysis of biomass of the isolated cotyledons of pumpkin showed that the highest growth stimulating activity revealed compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine: №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one and №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine, and compound derivative of N-sulfonyl substituted of 1,3-oxazole: №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile (Fig. 7).



**Fig 7:** Impact of chemical heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine (№1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine, №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine), compounds derivatives of N-sulfonyl substituted of 1,3-oxazole (№5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile and №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile), and phytohormone cytokinin Kinetin on the growth of biomass of the isolated cotyledons of pumpkin during the 16 days with the interval of each 4 day

Among the compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine the compound №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine, which contains amino group at the 7<sup>th</sup> position of pyrimidine fragment, showed the highest activity; the indexes of growth of biomass of the isolated cotyledons of pumpkin grown on the 10<sup>-9</sup>M water solution of compound №4 were higher at the 40% and 19% than the indexes of growth of biomass of the isolated cotyledons of pumpkin grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of cytokinin Kinetin, respectively (Fig. 7).

The high activity demonstrated also compound №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, which contains phenyl substituent at the 5<sup>th</sup> position of pyrimidine fragment; the indexes of growth of biomass of the isolated cotyledons of pumpkin grown on the 10<sup>-9</sup>M water solution of compound №2 were higher at the 38% and 17% than the indexes of growth of biomass of the isolated cotyledons of pumpkin grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of cytokinin Kinetin, respectively (Fig. 7).

The lower activity showed compound №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, which contains 4-ethylphenyl substituent at the 5<sup>th</sup> position and oxygen at the 7<sup>th</sup> position of pyrimidine fragment; the indexes of growth of biomass of the isolated cotyledons of pumpkin grown on the 10<sup>-9</sup>M water solution of compound №3 were higher at the 28% and 9% than the indexes of growth of biomass of the isolated cotyledons of pumpkin grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of cytokinin Kinetin, respectively (Fig. 7).

The lower activity showed also compound №1 - 7-amino-2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidine, which contains phenyl substituent at the 5<sup>th</sup> position and amino group at the 7<sup>th</sup> position of pyrimidine fragment; the indexes of growth of biomass of the isolated cotyledons of pumpkin grown on the 10<sup>-9</sup>M water solution of compound №1 were higher at the 22% and 4% than the indexes of growth of biomass of the isolated cotyledons of pumpkin grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of cytokinin Kinetin, respectively (Fig. 7).

Among the compounds derivatives of N-sulfonyl substituted of 1,3-oxazole the compound №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile that contains tolyl substituent at the 2<sup>th</sup> position of oxazole, showed highest activity; the indexes of growth of biomass of the isolated cotyledons of pumpkin grown on the 10<sup>-9</sup>M water solution of compound №6 were higher at the 54% and 31% than the indexes of growth of biomass of the isolated cotyledons of pumpkin grown either on the distilled water (control) or on the 10<sup>-9</sup>M water solution of cytokinin Kinetin, respectively (Fig. 7).

At the same time the compound №5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile that contains phenyl substituent at the 2<sup>th</sup> position of oxazole revealed lower activity; the indexes of growth of biomass of the isolated cotyledons of pumpkin grown on the 10<sup>-9</sup>M water solution of compound №5 were higher at the 23% than the indexes of growth of biomass of the isolated cotyledons of pumpkin grown on the distilled water (control) (Fig. 7).

Obviously that the growth stimulating cytokinin-like activity of compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine may be depended from substituents at the 5<sup>th</sup> and 7<sup>th</sup> positions of pyrimidine fragment, while as activity of compounds

derivatives of N-sulfonyl substituted of 1,3-oxazole may be depended from substituents at the 2<sup>th</sup> position of oxazole.

#### 4. Discussion

Today the numerous studies are devoted to impact of different classes of regulatory compounds of synthetic or natural origin as well as organic and mineral fertilizers for improving of growth and increase of productivity of important for agriculture crops such as soybean [71-74], wheat [75-81], flax [82-86] and pumpkin [87, 88]. The new promising approach is the elaboration of new classes of regulatory substances created on the base of low molecular weight heterocyclic compounds as effective environmentally safe substitutes of phytohormones and traditional plant growth regulators for acceleration of growth of these crops and improving quality of production.

Our previous researches confirmed high stimulating effect of heterocyclic compounds derivatives of pyridine, pyrimidine, pyrazole and isoflavones on shoot organogenesis of flax *in vitro* and on vegetative growth of maize [58, 89]. At the same time numerous literature data witness about widespread application in the agricultural practice of different classes of low molecular weight heterocyclic compounds derivatives of pyridine, pyrimidine, pyrazole, triazine, oxazole, oxazolo-pyrimidine and isoflavones as new effective plant growth regulators, herbicides, fungicides and antibacterial agents [15-25, 96-107]. Taking into account the results of our previous researches and literature data the great theoretical and practical interest is study the possibility of using of low molecular weight heterocyclic compounds for intensification of growth and development of soybean, wheat, flax and pumpkin plants.

The results of this work indicate that low molecular weight five and six-membered heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole used at very low concentration 10<sup>-9</sup>M/l of distilled water demonstrated high auxin-like and cytokinin-like stimulating effect on the growth of the important for agriculture crops such as soybean, wheat, flax and pumpkin. It was found that growth stimulating activity of these compounds was various depending on plant species and different substituents in the chemical structure of heterocyclic compounds.

Study of stimulating activity of heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole on the growth of 20<sup>th</sup>-day-old seedlings of soybean (*Glycine max* L.) of cultivar Valuta showed that highest activity revealed compounds №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine and №5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile.

Obviously, high growth stimulating activity of these compounds may be explained by the presence of phenyl substituents at the 5<sup>th</sup> and 7<sup>th</sup> positions of pyrimidine fragment in the compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and presence of phenyl substituent at the 2<sup>nd</sup> position of oxazole in the compounds derivatives of N-sulfonyl substituted of 1,3-oxazole.

Comparative analysis of stimulating activity of heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole on the growth of wheat (*Triticum aestivum* L.) of cultivar Zimoyarka indicated that highest activity revealed compounds: №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, which contains oxygen at the 7<sup>th</sup> position of pyrimidine fragment and

№4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine, which contains amino group at the 7<sup>th</sup> position of pyrimidine fragment of oxazole. Obviously, growth stimulating activity of compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine may be depended from substituents at the 5<sup>th</sup> and 7<sup>th</sup> positions of pyrimidine fragment.

Investigation of stimulating activity of heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole on the growth of flax (*Linum usitatissimum* L.) of cultivar Svitank showed that highest activity revealed compounds: №3 - 5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, which contains 4-ethylphenyl substituent at the 5<sup>th</sup> position and oxygen at the 7<sup>th</sup> position of pyrimidine fragment and №5 - 2-phenyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile, which contains phenyl substituent at the 2<sup>th</sup> position of oxazole. Possibly, the high stimulating effect of these compounds may be depended from substituents at the 5<sup>th</sup> and 7<sup>th</sup> positions of pyrimidine fragment in the compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and substituents at the 2<sup>th</sup> position of oxazole in the compounds derivatives N-sulfonyl substituted of 1,3-oxazole.

Specific bioassay on cytokinin-like activity showed that among heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole the highest stimulating effect on the growth of biomass of isolated cotyledons of muscat pumpkin (*Cucurbita moschata* Duch. et Poir.) of cultivar Gilea demonstrated compounds: №2 - 2,5-diphenyl[1,3]oxazolo[5,4-*d*]pyrimidin-7(6*H*)-one, which contains phenyl substituent at the 5<sup>th</sup> position of pyrimidine fragment, №4 - 7-amino-5-(4-ethylphenyl)-2-phenyl[1,3]oxazolo[5,4-*d*]pyrimidine, which contains amino group at the 7<sup>th</sup> position of pyrimidine fragment, and №6 - 2-tolyl-5-(piperidin-1-ylsulfonyl)-1,3-oxazole-4-carbonitrile, which contains tolyl substituent at the 2<sup>th</sup> position of oxazole.

Obviously, the growth stimulating cytokinin-like activity of these compounds may be depended from substituents at the 5<sup>th</sup> and 7<sup>th</sup> positions of pyrimidine fragment in the compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine, while as activity of compounds derivatives of N-sulfonyl substituted of 1,3-oxazole may be depended from substituents at the 2<sup>th</sup> position of oxazole.

#### 5. Conclusion

The stimulating activity of low molecular weight five and six-membered heterocyclic compounds derivatives of [1,3]oxazolo[5,4-*d*]pyrimidine and N-sulfonyl substituted of 1,3-oxazole on the growth of soybean (*Glycine max* L.) of cultivar Valuta, wheat (*Triticum aestivum* L.) of cultivar Zimoyarka, flax (*Linum usitatissimum* L.) of cultivar Svitank plants and growth of biomass of isolated cotyledons of muscat pumpkin (*Cucurbita moschata* Duch. et Poir.) of cultivar Gilea was studied. According to obtained biometric indexes of plant growth and growth of biomass of isolated cotyledons it was shown that heterocyclic compounds used in concentration 10<sup>-9</sup>M/l of distilled water demonstrated auxin- and cytokinin-like activity, which was similar or higher than the activity of phytohormones auxins IAA and NAA, and cytokinin Kinetin. The growth stimulating activity of these compounds was various depending on plant species and different substituents in the chemical structure of heterocyclic compounds. Obtained data confirmed the possibility of practical application in the agricultural industry of

heterocyclic compounds derivatives of [1,3]oxazolo[5,4-d]pyrimidine and N-sulfonyl substituted of 1,3-oxazole as new effective stimulators of growth and development of soybean, wheat, flax and pumpkin plants.

## 6. References

- Lipiec J, Doussan C, Nosalewicz A, Kondracka K. Effect of Drought and Heat Stresses on Plant Growth and Yield: A Review. *Int. Agrophys.* 2013; 27:463-477. doi: 10.2478/intag-2013-0017
- Sanghera GS, Wani SH, Hussain W, Singh NB. Engineering Cold Stress Tolerance in Crop Plants. *Curr Genomics.* 2011; 12(1):30-43. doi: 10.2174/138920211794520178
- de Oliveira AB, Alencar NLM, Gomes-Filho E. Comparison Between the Water and Salt Stress Effects on Plant Growth and Development. In: *Responses of Organisms to Water Stress.* In Tech. 2013, 67-94. <http://dx.doi.org/10.5772/54223>
- Ahmad P, Azooz MM, Prasad MNV. (Eds.) *Ecophysiology and Responses of Plants under Salt Stress.* Springer-Verlag New York, 2013; 16:512. DOI 10.1007/978-1-4614-4747-4\_2
- Fritz RS, Simms EL. (Eds.). *Plant Resistance to Herbivores and Pathogens: Ecology, Evolution, and Genetics.* The University of Chicago Press, Ltd., London. 1992, 590.
- Wania SH, Kumarb V, Shriramc V, Sah SK. Phytohormones and their metabolic engineering for abiotic stress tolerance in crop plants. *The Crop Journal.* 2016; 4:162-176. <http://dx.doi.org/10.1016/j.cj.2016.01.010> 2214-5141/
- Basra AS. (Ed). *Plant Growth Regulators in Agriculture and Horticulture: Their Role and Commercial Uses.* Haworth Press, Inc., New York, London, Oxford. 2000, 264.
- Rademacher W. *Plant Growth Regulators: Backgrounds and Uses in Plant Production.* *J Plant Growth Regul.* 2015; 34(4):845-872.
- Siddiqui MW, Zavalá A, Hwang JF, Andy CA. (Eds.). *Postharvest Management Approaches for Maintaining Quality of Fresh Produce.* Springer International Publishing, Switzerland. 2016, 222. <http://www.springer.com/it/book/9783319235813>
- Jardin P. Plant biostimulants: Definition, concept, main categories and regulation. *Sci. Hort.* 2015; 196(30):3-14. <http://www.sciencedirect.com/science/article/pii/S0304423815301850>
- Bradáčová K, Weber NF, Morad-Talab N, Asim M, Imran M, Weinmann M *et al.* Micronutrients (Zn/Mn), seaweed extracts, and plant growth-promoting bacteria as cold-stress protectants in maize. *Chem. Biol. Technol. Agric.* 2016; 3:19. DOI 10.1186/s40538-016-0069-1
- Ponomarenko SP, Hrytsaenko ZM, Tsygankova VA. Increase of plant resistance to diseases, pests and stresses with new biostimulants. *Acta Horticulturae: I World Congress on the Use of Biostimulants in Agriculture.* Strasburg (France). 2012; 1009:225-233. <http://agris.fao.org/agris-search/search.do?recordID=US201400150177>
- Victoria Tsygankova, Elena Shysha, Yaroslav Andrushevich, Anatoly Galkin, Galina Iutynska, Alla Yemets *et al.* Using of new microbial biostimulants for obtaining in vitro new lines of *Triticum aestivum* L. cells resistant to nematode *H. avenae*. *European Journal of Biotechnology and Bioscience.* 2016; 4(4):39-53. <http://www.biosciencejournals.com/archives/2016/vol4issue4/4-4-26.1.pdf>
- Mostafa GG. Improving the Growth of Fennel Plant Grown under Salinity Stress using some Biostimulants. *American Journal of Plant Physiology.* 2015; 10(2):77-83. DOI: 10.3923/ajpp.2015.77.83
- Bhardwaj D, Ansari MW, Sahoo RK, Tuteja N. Biofertilizers function as key player in sustainable agriculture by improving soil fertility, plant tolerance and crop productivity. *Microbial Cell Factories.* 2014; 13(66): 1-10. DOI: 10.1186/1475-2859-13-66
- Taylor EC, Wipf P. (Eds.). *Chemistry of Heterocyclic Compounds: A Series Of Monographs.* Series Online ISSN: 1935-4665. Series DOI: 10.1002/SERIES1079. <http://onlinelibrary.wiley.com/bookseries/10.1002/SERIES1079>
- Majumdar DK. *Pulse Crop Production: Principles and Technologies.* Amazon Digital Services LLC. 2011, 572. <https://www.amazon.com/Pulse-Crop-Production-Principles-Technologies-ebook/dp/B00K7YG0EA>
- Scriven EFV, Murugan R. *Pyridine and Pyridine Derivatives.* Kirk-Othmer Encyclopedia of Chemical Technology. John Wiley & Sons, Inc. 2005; 20:1-53. <http://onlinelibrary.wiley.com/doi/10.1002/0471238961>
- Dai H, Li YQ, Du D, Qin X, Zhang X, Yu HB *et al.* Synthesis and biological activities of novel pyrazole oxime derivatives containing a 2-chloro-5-thiazolyl moiety. *J Agric Food Chem.* 2008; 56(22):10805-10810. <http://www.ncbi.nlm.nih.gov/pubmed/18959421>
- Corsi C, Wendeborn SV, Bobbio C, Kessabi J, Schneiter P, Grasso V *et al.* pyrazole derivatives for use as plant growth regulators. EP Patent 2358699A1. 2011. <http://www.google.com/patents/EP2358699A1?cl=deFl>
- Nimbalkar S, Hote SV. Pyrazole Derivatives and their Synthesis - A review. *International Journal on Recent and Innovation Trends in Computing and Communication.* 2015; 3(2):61-65. <http://www.ijritcc.org/download/ICAET15TR061499.pdf>
- 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(11):496-505.
- Basedia DK, Dubey BK, Shrivastava B. A Review on Synthesis and Biological activity of Heterocyclic Compounds bearing 1, 3, 5-Triazine Lead Moiety. *American Journal of Pharm Tech Research.* 2011; 1(4):174-193. <http://www.ajptr.com/archive/volume-1/december-2011-issue-4/article-49.html>
- Acton QA. (Ed.). *Pesticides-Advances in Research and Application: 2013 Edition.* Scholarly Editions, Georgia. 2013, 862.
- Preedy VR. (Ed). *Isoflavones: Chemistry, Analysis, Function and Effects.* CPI Group (UK). Ltd, Croydon, CR0 4YY, UK. 2013, 683.
- Joule JA, Mills K. (Eds). *Heterocyclic Chemistry at a Glance.* 2nd ed. John Wiley & Sons, Ltd. 2012, 230.
- Saini MS, Kumar A, Dwivedi J, Singh R. A review: biological significances of heterocyclic compounds. *International Journal of Pharma Sciences and Research (IJPSR).* 2013; 4(3):66-77.
- Quin LD, Tyrell JA. (Eds). *Fundamentals of heterocyclic chemistry: Importance in Nature and in the Synthesis of*

- Pharmaceuticals. John Wiley & Sons, Inc., Hoboken, New Jersey. 2010, 344.
29. Armenise D, Carocci A, Catalano A, Muraglia M, Defrenza I, De Laurentis N *et al.* Synthesis and Antimicrobial Evaluation of a New Series of N-1,3-Benzothiazol-2-ylbenzamides. *Journal of Chemistry*. 2013. Article ID 181758: 7  
<https://www.hindawi.com/journals/jchem/2013/181758/ref/>
  30. Arshad M, Khan TA, Khan MA. 1,2,4-triazine derivatives: Synthesis and biological applications. *International Journal of Pharma Sciences and Research (IJPSR)*. 2014; 5(4):149-162.
  31. Griffioen G, COUPET LME, DUHAMEL HR, Wera S, GOMME E *et al.* Thiadiazole derivatives for the treatment of neurodegenerative diseases. Patent US 20090054410 A1. 2009.  
<http://www.google.com/patents/US20090054410>
  32. Jin Z. Muscarine, imidazole, oxazole, and thiazole alkaloids. *Nat. Prod. Rep.* 2011; 28:1143-1191.
  33. Encyclopedia of Food Grains. Wrigley C.W., Corke H., Seetharaman K., Faubion J. (Eds.). Elsevier Ltd. Academic Press. 2016, 1976.
  34. Bajaj YPS. (Ed.). *Legumes and Oilseed Crops I. Biotechnology in Agriculture and Forestry 10*. Springer-Verlag, Berlin Heidelberg. 1990, 175.
  35. Ondigi AN, Toili WW, Ijani ASM, Omuterema SO. Comparative analysis of production practices and utilization of pumpkins (*Cucurbita pepo* and *Cucurbita maxima*) by smallholder farmers in the Lake Victoria Basin, East Africa. *African Journal of Environmental Science and Technology*. 2008; 2(9):296-304.
  36. Jhala AJ, Hall LM. Flax (*Linum usitatissimum* L.): Current Uses and Future Applications. *Australian Journal of basic and Applied Sciences*. 2010; 4(9):4304-4312. ISSN 1991-8178  
<http://agronomy.unl.edu/documents/jhala-2010-30.pdf>
  37. Hildebrand DF, Phillips GC, Collins GB. Chapter Crops I. Volume 2 of the series *Biotechnology in Agriculture and Forestry. Soybean [Glycine max (L.) Merr.]*. Textbook of field crops. 2015, 283-308.  
[http://link.springer.com/chapter/10.1007/978-3-642-61625-9\\_15](http://link.springer.com/chapter/10.1007/978-3-642-61625-9_15)
  38. Ahmad P. (Ed.). *Legumes under Environmental Stress: Yield, Improvement and Adaptations*. Wiley Blackwell. 2015, 328.  
<http://eu.wiley.com/WileyCDA/WileyTitle/productCd-1118917081,subjectCd-LS98.html>
  39. Zahran HH. *Rhizobium-Legume Symbiosis and Nitrogen Fixation under Severe Conditions and in an Arid Climate*. *Microbiol Mol Biol Rev.* 1999; 63(4):968-989.
  40. Khan MS, Almas Z, Javed M. (Eds.). *Microbes for Legume Improvement*. Springer-Verlag/Wien. 2010, 536.  
<http://www.springer.com/us/book/9783211997529>
  41. Song F, Tang DL, Wang XL, Wang YZ. Biodegradable soy protein isolate-based materials: a review. *Biomacromol.* 2011; 12:3369-3380.
  42. Kennedy AR. The Bowman-Birk inhibitor from soybeans as an anticarcinogenic agent. *Am J Clin Nutr.* 1998; 68(6 Suppl):1406S-1412S.
  43. Hernández-Ledesma B, Hsieh CC, de Lumen BO. Lunasin and Bowman-Birk protease inhibitor (BBI) in US commercial soy foods. *Food Chemistry*. 2009; 115(2):574-580.
  44. Kobayashi H, Suzuki M, Kanayama N, Terao T. A soybean Kunitz trypsin inhibitor suppresses ovarian cancer cell invasion by blocking urokinase upregulation. *Clin Exp Metastasis*. 2004; 21(2):159-66.
  45. González-Montoya M, Ramón-Gallegos E, Robles-Ramírez M, Mora-Escobedo R. Evaluation of the Antioxidant and Antiproliferative Effects of Three Peptide Fractions of Germinated Soybeans on Breast and Cervical Cancer Cell Lines. *Plant Food Hum Nutr.* 2016; 71:1-7.
  46. Shewry PR. DARWIN REVIEW. *Wheat. J Exp Bot.* 2009; 60(6):1537-1553.  
doi:10.1093/jxb/erp058.  
<https://jxb.oxfordjournals.org/content/60/6/1537.full.pdf+html>
  47. Snape JW, Pánková K. *Triticum Aestivum* L (Wheat). eLS. Wiley Online Library. 2013.  
DOI: 10.1002/9780470015902.a0003691.pub2
  48. Shiferaw B, Smale M, Braun HJ, Duveiller E, Reynolds M, Muricho G. Crops that feed the world. 10. Past successes and future challenges to the role played by wheat in global food security. *Food Sec.* 2013; 5(3):291-317.  
doi:10.1007/s12571-013-0263-y.  
<http://link.springer.com/article/10.1007/s12571-013-0263-y>
  49. Reynolds M, Bonnett D, Chapman S, Furbank R, Mane' Ya, Mather D *et al.* Raising yield potential of wheat. I. Overview of a consortium approach and breeding strategies. *J Exp Bot.* 2011; 62:439-452.
  50. Faltermaier A, Waters D, Becker T, Arendt E, Gastl M. Common wheat (*Triticum aestivum* L.) and its use as a brewing cereal – a review. *J. Inst. Brew.* 2014; 120:1-15.
  51. Pathak V, Shrivastav S. Biochemical studies on wheat (*Triticum aestivum* L.). *Journal of Pharmacognosy and Phytochemistry*. 2015; 4(3):171-175.
  52. *World Population Prospects, the 2015 Revision*. United Nations New York, 2015.  
[https://esa.un.org/unpd/wpp/publications/files/key\\_findings\\_wpp\\_2015.pdf](https://esa.un.org/unpd/wpp/publications/files/key_findings_wpp_2015.pdf)
  53. Oomah BD. Flax seed as a functional food source. *J Sci Food Agric.* 2001; 81:889-894.
  54. Wang Zh, Hobson N. The genome of flax (*Linum usitatissimum*) assembled de novo from short shotgun sequence reads. *Plant J.* 2012; 72:461-473.
  55. Shim YY, Gui B, Arnison PG, Wang Y, Reaney MJT. Flaxseed (*Linum usitatissimum* L.) bioactive compounds and peptide nomenclature: A review. *Trends in Food Science & Technology*. 2014; 38(1):5-20.  
<http://www.sciencedirect.com/science/article/pii/S0924224414000697>
  56. Hall LM, Booker H, Siloto RMP, Jhala AJ, Weselake RJ. Chapter 6. Flax (*Linum usitatissimum* L.). In: *Industrial Oil Crops, First Edition*. 2016, 157-194.  
[http://agronomy.unl.edu/Jhala/publications/Book%20Chapter-Flax-Hall\\_2016.pdf](http://agronomy.unl.edu/Jhala/publications/Book%20Chapter-Flax-Hall_2016.pdf)
  57. Czemplik M, Boba A, Kostyn K, Kulma A, Miłucha A, Sztajnert M *et al.* Flax Engineering for Biomedical Application. In: *Biomedical Engineering, Trends, Research and Technologies / S. Olsztynska (Ed.)*. In Tech Publisher. 2011, 644.  
[http://cdn.intechopen.com/pdfs/12834/InTech-Flax\\_engineering\\_for\\_biomedical\\_application.pdf](http://cdn.intechopen.com/pdfs/12834/InTech-Flax_engineering_for_biomedical_application.pdf)
  58. Tsygankova VA, Bayer OO, Andrushevich Ya V, Galkin AP, Brovarets VS, Yemets AI, Blume Ya B. Screening of

- five and six-membered nitrogen-containing heterocyclic compounds as new effective stimulants of *Linum usitatissimum* L. organogenesis *in vitro*. Int J Med Biotechnol Genetics. 2016; S2(001):1-9.  
<http://scidoc.org/specialissues/IJMBG/S2/IJMBG-2379-1020-S2-001.pdf>
59. Oil and Colour Chemists' Association. Surface Coatings. Raw Materials and Their Usage. 1993; 1:610.  
DOI 10.1007/978-94-011-1220-8.
  60. Habib A, Biswas S, Siddique AH, Manirujjaman M, Uddin B, *et al.* Nutritional and Lipid Composition Analysis of Pumpkin Seed (*Cucurbita maxima* Linn.). J Nutr Food Sci. 2015; 5:374.  
doi:10.4172/2155-9600.1000374
  61. Jacobsen SE, Sørensen M, Pedersen SM, Weiner J. Using our agrobiodiversity: plant-based solutions to feed the world. Agron. Sustain. Dev. 2015; 35:1217-1235.  
DOI 10.1007/s13593-015-0325-y.
  62. Elhardallou SB, Elawad AM, Khairi NA, Gobouri AB, Dhahawi HO. A Review on Omega-3 and Omega-6 Essential Fatty Acids: Uses, Benefits and their Availability in Pumpkins (*Cucurbita maxima*) Seed and Desert Dates (*Balanites aegyptiaca*) Seed Kernel Oils. Pakistan Journal of Biological Sciences. 2014; 17:1195-1208. DOI: 10.3923/pjbs.2014.1195.1208
  63. Hayek SA, Gyawali R, Ibrahim SA. Antimicrobial Natural Products. In: Microbial pathogens and strategies for combating them: science, technology and education. Méndez-Vilas A. (Ed.). © FORMATEX. 2013, 910-921.  
<http://www.formatex.info/microbiology4/vol2/910-921.pdf>.
  64. Muruganantham N, Solomon S, Senthamilselvi MM. Antimicrobial activity of *Cucurbita maxima* flowers (Pumpkin). Journal of Pharmacognosy and Phytochemistry. 2016; 5(1):15-18.
  65. Stevenson D, Eller F, Wang L, Jane J, Wang T, Inglett G. Oil and tocopherol content and composition of pumpkin seed oil in 12 cultivars. J Agric Food Chem. 2007; 55(10):4005-13. DOI: 10.1021/jf0706979
  66. Procida G, Stancher B, Cateni F, Zacchigna M. Chemical composition and functional characterisation of commercial pumpkin seed oil. J Sci Food Agric. 2013; 93(5):1035-41. doi: 10.1002/jsfa.5843.
  67. Bardaa S, Halima N, Aloui F, Mansour R, Jabeur H, Bouaziz M, Sahnoun Z. Oil from pumpkin (*Cucurbita pepo* L.) seeds: evaluation of its functional properties on wound healing in rats. Lipids Health Dis. 2016; 15:73. doi: 10.1186/s12944-016-0237-0.
  68. Lipiec J, Doussan C, Nosalewicz A, Kondracka K. Effect Of Drought And Heat Stresses On Plant Growth And Yield: A Review. Int. Agrophys. 2013; 27:463-477. doi: 10.2478/intag-2013-0017
  69. Thuzar M, Puteh AB, Abdullah NAP, Lassim MBM, Jusoff K. The Effects of Temperature Stress on the Quality and Yield of Soya Bean [(*Glycine max* L.) Merrill.]. Journal of Agricultural Science. 2010; 2(1):172-179.
  70. Haggag WM, Abouziena HF, Abd-El-Kreem F, El Habbasha S. Agriculture biotechnology for management of multiple biotic and abiotic environmental stress in crops. J Chem Pharm Res. 2015; 7(10):882-889.
  71. Mouhib NM. Plant growth modification of soybeans [*Glycine max* (L.) Merr] treated with selected chemicals. 1981. Retrospective Theses and Dissertations. Iowa State University. Paper 7454.  
<http://lib.dr.iastate.edu/cgi/viewcontent.cgi?article=8453&context=rtd>
  72. Khatun S, Roy TS, Haque MN, Alamgir B. Effect of Plant Growth Regulators and Their Time of Application on Yield Attributes and Quality of Soybean. International Journal of Plant & Soil Science. 2016; 11(1):1-9. ISSN: 2320-7035.
  73. Egamberdieva D, Wirth S, Behrendt U, Allah EFA, Berg G. Biochar Treatment Resulted in a Combined Effect on Soybean Growth Promotion and a Shift in Plant Growth Promoting Rhizobacteria. Frontiers in Microbiology. 2016; 7:1-11.  
doi:  
10.3389/fmicb.2016.00209  
<http://journal.frontiersin.org/article/10.3389/fmicb.2016.00209/abstract>
  74. Khaswa SL, Dubey RK, Singh S, Tiwari RC. Growth, productivity and quality of soybean [*Glycine max* (I) Merrill) under different levels and sources of phosphorus and plant growth regulators in sub humid Rajasthan. African Journal of Agricultural Research. 2014; 9(12):1045-1051. DOI: 10.5897/AJAR2013.8328
  75. Barányiová I, Klem K. Effect of application of growth regulators on the physiological and yield parameters of winter wheat under water deficit. Plant Soil Environ. 2016; 62(3):114-120. doi: 10.17221/778/2015-PSE
  76. Laghari GM, Oad FC, Tunio S, Gandahi AW, Siddiqui MH, Jagirani AW, Oad SM. Growth, Yield And Nutrient Uptake Of Various Wheat Cultivars Under Different Fertilizer Regimes. Sarhad J Agric. 2010; 26(4):489-497.
  77. McKee IF, Long SP. Plant growth regulators control ozone damage to wheat yield. New Phytologist. 2001; 152:41-51.
  78. Baranyiova I, Klem K, Kren J. Effect of exogenous application of growth regulators on the physiological parameters and the yield of winter wheat under drought stress. MENDELNET. 2014, 442-446.
  79. Shekoofa A, Emam Y. Effects of Nitrogen Fertilization and Plant Growth Regulators (PGRs) on Yield of Wheat (*Triticum aestivum* L.) cv. Shiraz. J Agric Sci Technol. 2008; 10:101-108.
  80. Sagar RK, Kumar CS, Singh A, Maurya JN. Variation in physical and biochemical characteristics of wheat plants treated with sewage water & plant growth regulators. Nat Sci. 2013; 11(6):129-135.
  81. Kumar CS, Singh A, Sagar RK, Negi MPS, Maurya JN. Study of indole acetic acid and antioxidant defense system of wheat grown under sewage water. International Journal of Environmental Sciences. 2012; 3(2):821-832.
  82. Tomas AS, Akin D, Foulk J, Dodd RB. Effect of two growth regulators on yield and fiber quality and quantity in flax (*Linum usitatissimum* L.). Quarterly (Plant Growth Regulator Society of America). 2005; 33(3):90-100.
  83. Rastogi A, Siddiqui A, Mishra BK, Srivastava M, Pandey R, Misra P *et al.* Effect of auxin and gibberellic acid on growth and yield components of linseed (*Linum usitatissimum* L.). Crop Breeding and Applied Biotechnology. 2013; 13:136-143.
  84. Rehman H, Nawaz Q, Basra SMA, Afzal I, Yasmeen A, Hassan F. Seed Priming Influence on Early Crop Growth, Physiological Development and Yield Performance of Linola (*Linum usitatissimum* L.). Journal of Integrative Agriculture Advanced. Online Publication: 2013. Doi: 10.1016/S2095-3119(13)60521-3.

85. Bakry BA, Tawfik MM, Mekki BB, Zeidan MS. Yield and Yield Components of Three Flax Cultivars (*Linum usitatissimum* L.) In Response to Foliar Application with Zn, Mn and Fe under Newly Reclaimed Sandy Soil Conditions. *Am-Euras. J Agric & Environ Sci.* 2012; 12(8):1075-1080.
86. Emam MM, El-Sweify AH, Helal NM. Efficiencies of some vitamins in improving yield and quality of flax plant. *African Journal of Agricultural Research.* 2011; 6(18):4362-4369, DOI: 10.5897/AJAR11.1104.
87. Sedghi M, GHOLIPOURI A, SHARIFI RS. Gama-Tocopherol Accumulation and Floral Differentiation of Medicinal Pumpkin (*Cucurbita pepo* L.) in Response to Plant Growth Regulators. *Not. Bot. Hort. Agrobot. Cluj.* 2008; 36(1):80-84.  
<http://www.notulaeobotanicae.ro/index.php/nbha/article/view/101>
88. El Shora HM, Ali AS. Plant growth regulators induced urease activity in *Cucurbita pepo* L. cotyledons. *Acta Biol Hung.* 2016; 67(1):53-63.  
doi: 10.1556/018.67.2016.1.4.
89. Victoria Tsygankova, Yaroslav Andrusevich, Olexandra Shtompel, Artem Hurenko, Roman Solomyannyj, Galyna Mrug, Mikhaylo Frasinuk, Volodymyr Brovarets. Stimulating effect of five and six-membered heterocyclic compounds on seed germination and vegetative growth of maize (*Zea mays* L.). *International Journal of Biology Research.* 2016; 1(4):1-14.  
[https://www.academia.edu/29094174/Stimulating\\_effect\\_of\\_five\\_and\\_six-membered\\_heterocyclic\\_compounds\\_on\\_seed\\_germination\\_and\\_vegetative\\_growth\\_of\\_maize\\_Zea\\_mays\\_L\\_](https://www.academia.edu/29094174/Stimulating_effect_of_five_and_six-membered_heterocyclic_compounds_on_seed_germination_and_vegetative_growth_of_maize_Zea_mays_L_)
90. Kornienko AN, Pil'ov SG, Prokopenko VM, Rusanov EB, Brovarets VS. Interaction of 2-aryl-4-cyano-1,3-oxazole-5-sulfonyl chlorides with amidines. *Russian Journal of General Chemistry.* 2013; 83(7):1402-1405.
91. Kornienko AN, Pil'ov SG, Prokopenko VM, Brovarets VS. Synthesis of methyl 2-aryl-5-chlorosulfonyl-1,3-oxazole-4-carboxylates and their reactions with amines and amidines. *Russian Journal of General Chemistry.* 2014; 84(8):1555-1560.
92. Kornienko AN, Pil'ov SG, Prokopenko VM, Brovarets VS. Synthesis of 2-aryl-4-cyano-1,3-oxazole-5-sulfonyl chlorides and N-substituted sulfonamides. *Russian Journal of General Chemistry.* 2012; 82(11):1855-1858.
93. Voytshovska OV, Kapustyan AV, Kosik OI, Musienko MM, Olkhovich OP, Panyuta OO *et al.* *Plant Physiology: Praktykum.* Parshikova T.V. (Ed.). Lutsk: Teren. 2010, 420. (In Ukr.).  
<http://biol.univ.kiev.ua/metod/fbr/PRAKTYKUM.pdf>
94. Kursanov AL, Kulaeva ON, Mikulovich TP. The interaction of hormones in their influence on the growth of isolated cotyledons of pumpkin. *Russ J Plant Physiol.* 1969; 16(4):680-686. (In Russ.).  
<http://www.disserscat.com/content/vliyanie-uslovii-mineralnogo-pitaniya-na-soderzhanie-i-effektivnost-fitogormonov>
95. Bang H, Zhou XK, van Epps HL, Mazumdar M. (Eds.). *Statistical Methods in Molecular Biology.* Series: *Methods in molecular biology*, New York: Humana Press. 2010; 13(620):636.  
<http://www.springer.com/gp/book/9781607615781>
96. Minn K, Dietrich H, Dittgen J, Feucht D, Häuser-Hahn I, Rosinger CH. Pyrimidine derivatives and their use for controlling undesired plant growth. Patent US 8329717 B2. 2008. <http://www.google.com/patents/US8329717>
97. Zhao Q, Sh. Liu, Yo Li Q. Wang, Design, Synthesis, and Biological Activities of Novel 2-Cyanoacrylates Containing Oxazole, Oxadiazole, or Quinoline Moieties *J Agric Food Chem.* 2009; 57:2849-2855.
98. Newton T, Waldeck I. Oxazole carboxamide herbicides. Patent US6096688 A. 2000.  
<https://www.google.ch/patents/US6096688>
99. Mukai T, Fukai Yu, Matsumoto J, Ishikawa Ya, Hoshino K, Yazawa K *et al.* a new antimicrobial compound with salicylic acid residue from *Nocardia transvalensis* IFM 10065. *J. Antibiot.* 2016; 59:366-369.
100. Shinji Nihon Nohyaku Co. Ltd. KAWAGUCHI, Shuji Nihon Nohyaku Co. Ltd. KUMATA, Chikako Nihon Nohyaku Co. Ltd. OTA. Novel herbicides, usage thereof, novel thienopyrimidine derivatives, intermediates of the same, and process for production thereof. Patent EP1544202A1. 2005.  
<https://www.google.com/patents/EP1544202A1?cl=en29>
101. Miller MJ, Moraski GC, Markley LD, Davis GE. Imidazo [1,2-a]Pyridine Compounds, Synthesis Thereof, And Methods of Using Same. Patent US. 20120220457 A1. 2012. <http://www.google.ch/patents/US20120220457>
102. Sergiev I, Alexieva V, Ivanov S, Bankova V, Mapelli S. Plant Growth Regulating Activity of Some Flavonoids. *Comptes Rendus de l'Academie Bulgare des Sciences.* 2004, 57(4): 63-68.  
<http://articles.adsabs.harvard.edu/full/2004CRABS..57d..63S/D000063.000.html>
103. Zhao Q, Liu Sh, Li Yo, Wang Q. Efficient and Flexible Synthesis of Highly Functionalised 4-Aminooxazoles by a Gold-Catalysed Intermolecular Formal [3+2] Dipolar Cycloaddition. *J Agric Food Chem.* 2009; 57:2849-2855.
104. Xiao Sh, Guo D, Zhang M, Peng Sh, Chen F, Zhou Ya, Ding L. Two novel 2,5-diphenyl oxazole derivatives from *Gymnotheca chinensis* *Chin. Chem. Lett.* 2016; 27:1064-1066.
105. Baum JS, Chen TM. Plant growth and development modification using benzoxazole derivatives. Patent US 4659360 A. 1987.  
<http://www.google.ch/patents/US4659360>
106. Chang JH, Baum JS. Phenylmethyl-4,4-dimethyl-3-isoxazolidinone plant regulators. Patent US 4892578 A. 1990. <https://www.google.ch/patents/US4892578>
107. Müller KH, Feucht D, Gesing RFE, Hacker E, Hills M, Huff HP *et al.* Application of 2-Iodo-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)carbonyl] benzol sulphonamide and/or its salts for inhibiting unwanted plant growth in selected agricultural crop cultures or non-cultivated land. Patent EP2052603A1. 2009.  
<https://www.google.co.in/patents/EP2052603A1?cl=fr>