PREPARATIVE FORMS OF THE PLANT GROWTH REGULATOR FLOROXAN

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Abstract

The plant growth regulator floroxan, 3,3,3-trifluoro-2-hydroxy-2-[4-(methylamino)phenyl]propionic acid ethyl ester hydrochloride, is the development of the Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Sciences (INEOS RAS) and has been studied for many years. To improve the physicochemical properties of floroxan, many research efforts have been aimed at developing its application forms. Having high efficiency at a dose of 100 mg/L, floroxan has great prospects for the use as a component in compositions with the known preparations for pre-sowing treatment of seeds of cultivated plants. The recent joint studies of researchers from Russia and Uzbekistan allowed for developing and offering for agriculture the promising preparations such as protectants for cereal crops, herbicide antidotes, and compositions for cotton and a number of vegetable crops.

Key words: floroxan, preparative forms, fungicides, protectants, biological efficacy.

Abbreviations

– chemical plant protection preparations (pesticides, CPPPs)
– All-Russian Research Institute of Phytopathology (VNIIF)
– plant growth regulator (PGR)
– solid dispersion (SD)
– glycyrrhizic acid (GA)
– SD of the floroxan/glycyrrhizic acid composition (FGA)
– active ingredient (AI)
– suspension concentrate (SC)
– suspoemulsion (SE)
– sodium carboxymethyl cellulose (NaCMC)
– complex preparation with floroxan (CPFl)
– tetramethylthiuram disulfide (TMTD)
– biologically active compound (BAC)

Introduction

A hydrochloride salt of 3,3,3-trifluoro-2-hydroxy-2-[4-(methylamino)phenyl]propionic acid ethyl ester known as floroxan is the development of researchers from the INEOS RAS. The joint studies with specialists of the All-Russian Research Institute of Phytopathology (VNIIF, Golitsino, Moscow Oblast) revealed its unique properties as a plant growth regulator (PGR) for a number of agricultural crops, such as rapeseed, corn, and sunflower [1]. The preparation was found to exhibit biological activity at doses up to 100 mg/ha, which hindered its application as a separate agent in agricultural practice on an industrial scale. The importance of further studies aimed at the rational incorporation of floroxan in the preparations for effective plant protection was obvious and required an integrated approach involving chemists, technologists, agronomists, and biologists.

As is known, the use of pesticides is currently an objective necessity and an integral part of the technology of crop cultivation around the world [2]. For many decades, the chemical methods of plant protection have been developing in two directions. The first one is connected with the search for the most effective chemical agents and the technologies for their application, while the second one is aimed at improving the safety and environmental friendliness of the chemical methods [3]. One of the effective and readily available methods for limiting the pesticide load on agrocenosis is to reduce the consumption rates of pesticides, in particular, by creating their nanostructured forms [4].

The development of agriculture and the transfer of crop production to an industrial basis led to more frequent massive outbreaks of diseases on various crops. In this regard, balanced and rational chemicalization is one of the most important prerequisites for increasing the overall level of crop yields [5]. Therefore, the consumption of chemical plant protection preparations (CPPPs) is growing every year and the range of pesticides is constantly updated and extended to provide an increase in their efficiency and a decrease in the consumption rates [6].

Among the numerous methods for improving the productivity of crops, of particular importance is the combination of fungicides with PGRs. The latter have a triple effect on plants: stimulation of physiological processes, an increase in the plant's own resistance to the action of unfavorable factors, and an increase in nonspecific immunity [7]. Such protective and stimulating compositions increase the yield of wheat by reducing stress loads on plants, developing disease resistance, and exhibiting growth-regulating activity, which leads to an increase in the yield and improvement in the grain quality [8].

The advantages of PGRs are their complete environmental safety, versatility of action, including the ability to reduce various stressful effects of the environment on plants, which determines the high prospects for their widespread use in modern agricultural technologies. Thus, Ryabchinskaya and Zimina [9] presented the classification of PGRs according to the nature of their origin (chemical, biological, natural, *etc.*) and showed their diversity and versatility. The review provides the analysis of 143 publications, covering the period from 2001 to 2017. The authors noted that PGRs are used for treating from 50 to 80% of the area of agricultural crops. At the same time, the use of PGRs results in an increase in the plant productivity, which is comparable to or exceeds the efficiency of microelements and organo-mineral fertilizers. Furthermore, their versatility allows for increasing the resistance of plants to a complex of adverse environmental factors, including harmful organisms and the stressful effects of pesticides on plants.

After the above-mentioned review, the researchers from the INEOS RAS and VNIIF demonstrated the potential of production of new PGRs based on sydnonimine derivatives [10]. The stimulating effect of the compounds explored on the growth of corn seedlings reached 46%, whereas that for the root system reached 71% in doses (1–10 g/t of seeds). Subsequently, the sydnonimine derivatives were shown to stimulate the growth of an extended panel of plant objects, including corn, sunflower, and winter wheat upon pre-sawing treatment at doses of 0.5–5 g/t of seeds [11].

Vasilyeva *et al.* [12] described the results of investigations on the effect of PGRs Albite, Ribav-Extra, Mival-agro, Energy-M, Cresacin, and Gibbersib on the growth and development of potatoes, yield, distribution, and degree of development of the main crop diseases. The analysis of the resulting data showed that the preparations explored had a positive effect on the germination of potatoes, increasing it by 17–77% relative to the control, and reduced the spread and degree of development of Alternaria leaf blight at the initial stage of its development compared to the control.

The research groups of L. V. Dyadyuchenko and V. V. Taranenko studied new pyridine derivatives as PGRs on winter wheat [13, 14] and rapeseed [15]. These compounds were found to possess high growth-stimulating activity, which was confirmed by the results of three-year field trials. The PGRs had a positive effect on the formation of the crop structure, provided a significant increase in the yield, and improved the quality of winter wheat grains. In the case of soybean, these PGRs provided a reliable and stable increase in the yield by 12.1–20.9% and improvement of the grain quality: the protein content increased by 0.5–0.6%, while the oil content increased by 0.5–1.5%.

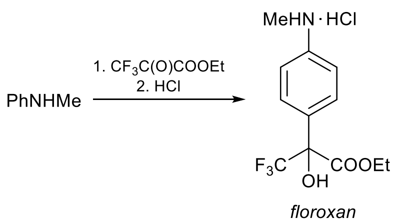
Lukatkin [16] studied the effect of the synthetic analogs of cytokinins, namely, cytodef and thidiazuron on the growth, development and productivity of cucumber grown in protected ground. It was revealed that the treatment of young plants with various concentrations of the preparations had a positive effect on the growth of cucumber; the best results were achieved at the thidiazuron concentrations of 10^{-8} M/L and the cytodef doses ranging from 10^{-8} to 10^{-6} M/L. The treatment of cucumber with cytodef and thidiazuron increased the productivity of plants and the marketability of the resulting fruits. Under stressful temperature conditions, these preparations contributed to a better condition of the plants.

In the past decade, our research group has shown the prospects of mechanochemical modification of poorly soluble substances of biologically active compounds (BACs) with hydrophilic polymers [17]. The products of the mechanical treatment are solid dispersions (SDs) of the BAC/polymer composition, which feature improved solubility and high activity with a decrease in the dosage of substances. This approach was also utilized to modify the properties of floroxan using various polymers.

The goal of this review is to analyze and summarize the results of investigations devoted to the improvement of biological properties of floroxan by developing alternative formulations, SDs with polymers, and incorporating it in the compositions of the known fungicides and antidote agents for the development of promising CPPPs.

Floroxan as an effective component of the fungicidal protectants of cereal crops

A systematic study of the reactivity of trifluoropyruvic acid esters led to the development of methods for the *C*-oxyalkylation of various types of aromatic and heteroaromatic compounds [18]. In particular, the ability of such fluorine-containing ketoesters to quantitatively *C*-oxyalkylate π-donor aromatic systems under mild conditions was established. The appropriate substrates are, for example, *N*-alkylanilines. The extensive screening of the *C*-oxyalkylation products allowed for selecting a PGR which received the commercial name floroxan [1]. The developed technological method for obtaining floroxan includes the *C*-oxyalkylation of *N*-methylaniline with ethyl trifluoropyruvate followed by the precipitation of the target product from dichloromethane upon treatment with hydrogen chloride (Scheme 1). The isolation of the product as a hydrochloride salt ensures an efficient method for purifying floroxan and provides it in a stable water-soluble form.



Scheme 1. Synthesis of floroxan.

At the same time, these characteristics of floroxan are not ideal. Therefore, it was necessary to develop optimal preparative forms (formulations) that would facilitate its chemical stability and would enable the application of floroxan in the composition of complex preparations, which would reduce the agrochemical processing. It should be noted that the development of preparative forms is very important for BACs and defines their further prospects. An improperly prepared form of application can "ruin the life" of even active molecules. Thus, Tropin [19] showed that the effectiveness of pesticides depends not only on their active compounds but also in a great measure on their formulations, which largely determine the composition content, the stability of working suspensions and solutions, the level of spray drift, and the quality of application to the treated surface. Moreover, in current conditions, when the preparations in Russia are developed mainly from the active ingredients (AIs) of foreign companies, it is important to optimize the composition of formulations and to create new preparative forms that would provide the maximum effect of AIs [20]. There are all prerequisites for the promotion of floroxan in the market of plant protection products, in particular, by developing its advanced formulations. The modification of floroxan with polysaccharides allows one to significantly improve its technological characteristics (chemical stability, easy handling, *etc.*) and to achieve high biological efficacy. This is particularly important if take into account that in 1991, based on the results of three-year state tests, floroxan was recommended for the temporary registration on cotton. The collapse of the USSR prevented the completion of its registration. During these tests, floroxan was used as an aqueous solution both for pre-sowing seed incrustation at a dose of 100 mg/t of seeds and for spraying vegetative plants in the phase of 4–5 true leaves at a dose of 20 g/ha. Therewith, an increase in the yield of raw cotton was 15–20%. This floroxan form was not optimal due to instability of an aqueous solution and inconvenience of its use for the treatment of seeds and green plants, which required the development of alternative formulations with high adhesive properties.

When looking for options to incorporate floroxan in CPPP formulations, we took into account that one of the most environmentally safe and economically justified methods of their use is seed dressing [21]. This is explained by the fact that this method does not require additional processing of plants, and the preparations have time to completely decompose before the crop ripening period. In all developed countries, seed dressing is a legally compulsory phytosanitary measure. Considering that the use of PGRs is an important element of modern agricultural technologies, floroxan was used both in the form of SDs with polysaccharides and as a part of compositions with the known fungicides during germination of spring wheat seeds [22]. The laboratory assessment of the fungicidal and growth-stimulating activity of the resulting formulations showed that the compositions of floroxan (with a content of 10^{-6}%) both in the form of SDs obtained by mechanical processing and in the composition with the known fungicides are promising protectants for cereal crops with high biological activity.

Our investigations were concerned with the following two methods for obtaining multicomponent compositions based on the known fungicides and floroxan using mechanochemical modification.

– A solid-phase method was used in the case of utilization of high-melting active substances of fungicides for the creation of compositions. This method afforded the SDs with the enhanced solubility of these substances.

– The liquid-phase method was used in the case of low-melting substances and liquid polymeric substances. This method provided stable suspension concentrates (SCs). The resulting multicomponent compositions (one or more fungicides, floroxan) showed a broader spectrum of biological activity, which was manifested in increased fungicidal activity, removal of the retardant effect of triazoles, and stimulation of growth processes. The most promising complex formulations were the emulsion forms with the addition of floroxan (at a concentration of 10^{-6}%), which was confirmed by the results of a comprehensive evaluation of the morphometric parameters of wheat and barley seedlings (length of a coleoptile, cotyledon leaf, roots, and their number), germination energy and seed germination, as well as the degree of suppression of seminal infection.

The complex protection of plants from diseases, pests, and weeds is the most important element of agricultural technology. The use of fungicides is important not only to protect plants from diseases and thus to increase the plant yields, but also to obtain high quality crops. A significant spread of the diseases such as wheat fusarium, wheat and rye rust, rye ergot, and others not only reduces the crop yields, but also prevents the use of crops for human and animal nutrition, which determines the urgency of the creation of new preparations for plant protection through the development of effective formulations.

One of the latest advances in the field of plant protection is the development of new nanoscale forms of plant protection preparations that offer convenient and technological application forms, the improved penetration of an active substance into plant tissues, and the reduced consumption of application rates [23]. The suspension methods were used to obtain multicomponent concentrates of the protectants based on fungicides such as imazalil, metalaxyl, and tebuconazole, involving floroxan (0.3%) and the bioregulator cresacin (5.9%) in their compositions. The formulations represented the SCs with high quality (stability of the working solution, wettability of biological objects, and safety of the active substance), which showed synergy of biological properties (acceleration of the plant growth and lengthening of their root system, reduction in the development of seed diseases), which confirmed the prospects of incorporation of PGRs in the composition of fungicidal protectants [24].

Taking into account that the creation of new formulations, development of methods for their application, improvement of their properties that affect the grain quality, as well as elucidation of their effect on the crop productivity are urgent tasks [25], the continuous efforts have been focused on the selection of a spectrum of fungicides that are widely used in practice, in combination with floroxan as a promising PGR [26]. Thus, upon development of the formulations based on prochloraz, imazalil, and tebuconazole [27], special attention was paid to the physicochemical properties of the AIs of these fungicides. Taking into account the low melting points of the selected AI fungicides, the liquid-phase suspension technology was used that allows one to obviate local temperature changes [28]. The preparative forms of these fungicides and floroxan were obtained in the form of the SC and suspoemulsion (SE) with the optimal technological parameters. The evaluation of the biological efficacy of disinfection of spring wheat seeds with fungicidal protectants with the addition of floroxan (0.8% content in the composition) confirmed their high activity associated with the stimulation of growth processes. At the same time, the stimulation of the growth of the root system in the field led to a decrease in the infestation of plants with root rot. A more balanced development of plants in combination with fungicidal protection increased its resistance to stress, which is a positive moment when growing spring wheat in modern cultivation technologies [27].

The investigations of multicomponent suspension agents based on imazalil, metalaxyl, and tebuconazole with floroxan under conditions of laboratory experiments and greenhouse trials on spring wheat revealed their growth-stimulating and protective effect [28]. Under laboratory conditions, the fungicidal compositions with floroxan were shown to suppress seed infection by 2 times and had a pronounced growth-stimulating effect on the leaves and roots of 7-day-old seedlings of spring wheat, increasing laboratory seed germination. The compositions were effective against common root rot, improved the field germination of seeds, increased the aboveground and root mass of plants, and affected the wheat productivity, which ensured an increase in the grain yield up to 0.62 t/ha [29].

Use of floroxan and its derivatives in the composition of antidote protectants to reduce the phytotoxicity of sulfonylurea herbicides

One of the major challenges of modern agriculture is the search for new antidotes to eliminate the phytotoxicity of sulfonylureas, which, having high herbicidal activity for a long time (several years), lead to negative environmental consequences. Thus, the systematic use of sulfonylureas led to the contamination of up to 22% of soils in the Russian Federation with their residues, which is more than 17 million hectares of agricultural land [30]. The residues of these herbicides do not have high selectivity and can exert a toxic effect also on cultivated plants. To relieve the negative effects of sulfonylurea residues, the use of antidotes is recommended, which reduce the phytotoxic effect of herbicides on a cultivated plant [31, 32].

In pursuit of the antidotes to sulfonylurea herbicides, researchers of the INEOS RAS and VNIIF explored the potential of floroxan derivatives, in particular, the diarylurea derivatives bearing a floroxan moiety. According to the results of biological screening, ethyl 2-{4-[3-(4-chlorophenyl)-1-methyl-ureido]-phenyl}-2-hydroxy-3,3,3-trifluoropropionate was identified as the most promising antidote. A preparative form of the latter represented the SD containing polypropylene glycol, surfactants, and an aqueous solution of NaCMC [33]. The pre-sowing treatment of rape seeds with this preparation at a rate of 1 g/t of seeds effectively diminished the toxic effect of the herbicide and led to an increase in the aboveground mass of plants by 41% compared to the control. It should be noted that the activity of the well-known antidotes such as furilazole and 1,8-naphthalic anhydride, when used at a dose of 1 g/t of seeds, was not high: they only slightly suppressed the effect of the herbicide, while an increase in the aboveground mass of plants was only 5–14% relative to the control [34].

To develop a complex multifunctional protectant that would exhibit both fungicidal activity and antidote effect towards soil residues of sulfonylureas, a preparation was developed in the form of the SC, which included the fungicide substances tebuconazole and TMTD, naphthalic anhydride (antidote), and floroxan [28]. The performed biological assays confirmed that this composition has a complex action: fungicidal, antidote, and growth-regulating. At the same time, the antidote effect of the composition in soils with metsulfuron-methyl residues exceeded the effect of the known preparations bearing the same antidote owing to a synergistic effect of the composition components [35], which is manifested in a significant increase in the germination of seeds of the explored crops (spring rapeseed, spring wheat, and corn) (up to 30%), while the biomass of some of the crops also significantly increased (up to 27%). Nowadays, research on the development of such multicomponent and multifunctional protectants continues [36].

Effect of floroxan on the biological activity of the composite preparations when applied to cotton and vegetable crops

As is known, the modern crop cultivation technologies ensure the control of plant development using PGRs [26]. The latter can increase the plant immunity and resistance to mold, fungi, and other parasites, alleviate the negative impact of pesticides, promote the proper formation of shoot structure, accelerate plant growth, foster the processes of flowering and ripening, improve the quality of fruits and increase their number. The promising PGRs with a mediator response to stresses include floroxan which has proven itself in the pre-sowing treatment of rapeseed, corn, sunflower [1], wheat, and barley seeds [2].

Both from the theoretical and practical points of view, it seemed reasonable to study the described compositions based on floroxan on other agricultural crops, in particular, cotton and a number of vegetable crops in order to develop the convenient application forms and the technology for plant treatment.

In some countries including the Republic of Uzbekistan, cotton is an important agricultural and industrial crop. Due to the peculiarities of soil and climatic conditions, a stable harvest of raw cotton requires not only the adherence to the rules of agricultural technology and balanced mineral nutrition, but also the rational use of PGRs [37]. Cotton, being a warm-weather crop with a long growing season, late and prolonged ripening, especially needs to reduce the juvenile period of plant life in order to accelerate the onset of flowering and ripening and hence to increase the fraction of the crop harvested before the first frost [38]. Another problem in the cultivation of cotton is the abscission of fruit elements [39, 40]. According to Prokofiev and Rasulov [41], this process can be regulated using PGRs.

In view of the above, it seemed interesting to use floroxan in cotton sowing to obtain friendly and healthy seedlings as well as to accelerate the crop ripening, which is also of high practical importance. In this respect, the previous findings were attempted to revise by creating a new formulation of floroxan in the form of an SC [42]. In order to study the effect of the pre-sowing treatment of cotton seeds with the SC of floroxan (content 10^{-5}%) on the development and yield of cotton, the microplot tests were carried out. According to the results obtained, the pre-sowing treatment of cotton seeds had the following effects:

– facilitated seed germination and accelerated the main phases of plants;

– affected the content of chlorophyll in cotton leaves (in particular, these parameters exceeded the control ones by 48–92%);

– accelerated the growth dynamics of the main stem and fruit-forming branches, activated the formation of fruit elements, and increased the set of cotton bolls. As a result, by the end of the growing season, there were an increase in the number of bolls on a plant compared to the control and an increase in the cotton yield up to 38.4 c/ha, which exceeded the control by 20% [42].

The tomato leaf miner *Tuta absoluta Meyrick* is known to be a dangerous pest of nightshade crops. At present, the mining moth is also registered in the Republic of Uzbekistan. It damages and destroys plants and fruits of the nightshade family both on the field and under cover; therewith, the plants are damaged from the moment of planting seedlings until the fruiting state [43]. Zakirova *et al.* [44] revealed the high activity of the extract of *Haplophyllum perforatum* against a number of insect pests, including the tomato miner moth *Tuta absoluta Meyrick*. To increase the activity of the extract, the research efforts were aimed at obtaining a complex preparation with the addition of floroxan (at a rate of 0.2 kg/ha) (CPFl) and studying its effect on the physiological parameters of tomato plants when they were infected with the tomato miner moth. The evaluation of the biological efficacy of the CPFl composition against larvae of *Tuta absoluta* during the growing season of tomatoes revealed its high activity, which was reflected in an increase in the content of photosynthetic pigments and an increase in the leaf surface area with a simultaneous reduction in the pest population.

To improve the stability and water solubility of floroxan, a method for treating floroxan with PVP and polysaccharides (arabinogalactan, glycyrrhizic acid (GA) and its derivatives) using mechanochemical processing was suggested. The resulting floroxan/polymer (1:9) SDs formed in water the corresponding supramolecular complexes with increased efficiency [45]. The SDs represented free-flowing powders, convenient for use and stable upon storage. They form stable working solutions that are convenient to use for seed and plant treatment and facilitate higher adhesion to seeds and leaves.

The complex studies on cotton and eggplant revealed a promising preparation based on the floroxan/GA (1:9) (FGA) composition which exhibits plant growth-stimulating activity that exceeds the activity of floroxan. In addition, it is environmentally benign, stable upon prolonged storage, highly soluble in water, and easy to use [46]. The pre-sowing soaking of cotton seeds with FGA demonstrated its higher efficiency in terms of the germination, growth and development of cotton, as well as the formation of fruit elements compared to floroxan. Spraying eggplant with FGA during the growing season afforded better plant growth stimulation in terms of the leaf surface area, the chlorophyll pigment content, the plant height, as well as the number of leaves and buds compared to floroxan. This result can be explained by the fact that FGA, due to the incorporation of GA in its composition, forms a supramolecular complex in water, which provides increased solubility of floroxan, its bioavailability and penetration through plant membranes, and, consequently, a general increase in its biological activity, as was shown with the examples of a range of biologically active molecules [47, 48].

Conclusions

This review illustrates the efficiency of our approach to the development of complex preparations using floroxan. Due to the low application rate of floroxan—100 mg/t of seeds, the recommendations were provided on the methods for incorporating floroxan in the compositions of complex multifunctional preparations that addressed the issues associated with its chemical stability, solubility, and the development of convenient PGRs.

The performed investigations provided the following advances for agricultural practice:

– innovative multicomponent and multifunctional protectants for cereal crops (wheat, barley);

– antidote protectants to alleviate the phytotoxicity of metsulfuron-methyl residues in soil;

– composite preparations for the application on cotton, eggplant, and other vegetable crops.

To promote floroxan in the market of plant protection agents, the advanced formulations were proposed. Thus, the modification of floroxan with polysaccharides can significantly improve its technological characteristics (adhesion to biological objects, ease of use, *etc.*) and ensure high efficiency.

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References

1. RU Patent 2369094, **2009**.
2. L. D. Grishechkina, V. I. Dolzhenko, O. V. Kungurtseva, T. I. Ishkova, S. D. Zdrozhevskaya, *Agrokhimiya*, **2020**, *9*, 32–47. DOI: 10.31857/S0002188120090070
3. A. I. Illarionov, *Ecotoxicology of Pesticides*: *Textbook*. Voronezh, VOVGAY, **2016** (in Russian).
4. O. I. Teplyakova, N. G. Vlasenko, A. V. Dushkin, *Agrokhimiya*, **2020**, *5*, 31–37. DOI: 10.31857/S0002188120050142
5. N. G. Vlasenko, *Vestn. Zashch. Rast*., **2008**, *2*, 3–10.
6. V. A. Zakharenko, *Agrokhimiya*, **2020**, *3*, 43–48. DOI: 10.31857/S000218812003014X
7. O. A. Shapoval, I. P. Mozharova, A. A. Korshunov, *Zashch. Karantin Rast.*, **2014**, *6*, 16–20. EDN: SDVVVF
8. A. A. Savchenko, *Vestn. KrasGAU*, **2007**, *2*, 324–326.
9. T. A. Ryabchinskaya, T. V. Zimina, *Agrokhimiya*, **2017**, *12*, 62–92. DOI: 10.7868/S0002188117120092
10. I. A. Cherepanov, Yu. Ya. Spiridonov, O. A. Chichvarina, A. S. Samarskaya, A. B. Ponomarev, S. K. Moiseev, *Agrokhimiya*, **2018**, *9*, 50–55. DOI: 10.1134/S0002188118090053
11. Yu. Ya. Spiridonov, I. A. Cherepanov, V. A. Abubikerov, I. Yu. Spiridonova, N. V. Kalganova, N. G. Frolova, S. K. Moiseev, *Agrokhimiya*, **2022**, *3*, 41–46. EDN: XNUOVR
12. S. V. Vasilyeva, V. N. Zeyruk, M. K. Derevyagina, G. L. Belov, V. A. Barkov, *Agrokhimiya*, **2019**, *7*, 45–51. DOI: 10.1134/S0002188119070135

13. L. V. Dyadyuchenko, V. V. Taranenko, V. D. Strelkov, M. S. Sokolov, *Agrokhimiya*, **2019**, *6*, 14–17. DOI: 10.1134/S0002188119060036
14. L. V. Dyadyuchenko, V. V. Taranenko, V. S. Muravyov, *Agrokhimiya*, **2021**, *12*, 64–68. DOI: 10.31857/S0002188121100070
15. L. V. Dyadyuchenko, V. V. Taranenko, I. G. Dmitrieva, *Agrokhimiya*, **2020**, *5*, 12–16. DOI: 10.31857/S0002188120050075
16. A. S. Lukatkin, *Agrokhimiya*, **2023**, *2*, 41–47. EDN: MSYTLK
17. S. S. Khalikov, A. V. Dushkin, *Pharm. Chem. J.*, **2020**, *54,* 504–508. DOI: 10.1007/s11094-020-02229-4
18. N. D. Chkanikov, A. S. Golubev, *INEOS OPEN*, **2021**, *1*, 1–19. DOI: 10.32931/io2105r
19. V. P. Tropin, *Zashch. Karantin Rast.*, **2007**, *6.* 32. EDN: LETVOP
20. S. D. Karakotov, P. V. Saraev, *Adaptively Integrated Plant Protection*, Moscow, Pechatnyi Gorod, **2019**, pp. 65–76 (in Russian).
21. V. I. Dolzhenko, G. Sh. Kotikova, S. D. Zdrozhevskaya, L. D. Grishechkina, L. A. Burkova, A. V. Gerasimova, A. I. Silaev, T. I. Milyutenkova, E. B. Belykh, *Dressing of Seed Material*, Moscow, St. Petersburg, Agrorus, **2003** (in Russian).
22. N. G. Vlasenko, S. V. Burlakova, S. S. Khalikov, O. Yu. Fedorovskii, N. D. Chkanikov, *Agrokhimiya*, **2017**, *7*, 49–54. DOI: 10.7868/S0002188117070079
23. S. S. Khalikov, O. I. Teplyakova, N. G. Vlasenko, *Agrokhimiya*, **2022**, *2*, 45–55. DOI: 10.31857/S0002188122020065
24. N. G. Vlasenko, S. V. Burlakova, O. Yu Fedorovskii, N. D. Chkanikov, S. S. Khalikov, *Agrokhimiya*, **2018**, *10*, 40–45. DOI: 10.1134/S0002188118100149
25. S. F. Buga, A. G. Zhukovski, A. G. Ilyuk, *Zashch. Karantin Rast.*, **2009**, *8,* 22–25. EDN: KXXILT
26. L. D. Prusakova, N. N. Malevannaya, S. L. Belopukhov, V. V. Vakulenko, *Agrokhimiya*, **2005**, *11*, 76–86. EDN: HSGKRL
27. N. G. Vlasenko, S. V. Burlakova, N. D. Chkanikov, S. S. Khalikov, *Agrokhimiya*, **2019**, *6*, 44–49. DOI: 10.1134/S0002188119020145
28. S. S. Khalikov, N. D. Chkanikov, Yu. Ya. Spiridonov, A. P. Glinushkin, *Agrokhimiya*, **2016**. *6*, 39–45. EDN: WHGKHR
29. S. V. Burlakova, N. G. Vlasenko, N. D. Chkanikov, S. S. Khalikov, *Agrokhimiya*, **2020**, *5*, 72–79. DOI: 10.31857/S000218812005004X
30. Yu. Ya. Spiridonov, P. S. Khokhlov, V. G. Shestakov, *Agrokhimiya*, **2009**, *5*, 81–91. EDN: KAVJKT
31. M. R. Pitina, N. L. Poznanskaya, *Agrokhimiya*, **1994**, *4*, 114–120.
32. H. K. Yablonskay, V. V. Kotlyarov, Yu. P. Fedulov, *Sci. J. KubSAU*, **2013**, *94*, 603–621. EDN: RUYCQZ
33. O. Yu. Fedorovsky, S. S. Khalikov, Yu. Ya Spiridonov, N. D. Chkanikov, *Agrokhimiya*, **2019**, *5*, 29–34. EDN: NVFBQW
34. RU Patent 2666732, **2017**.
35. RU Patent 2585858, **2015**.
36. N. D. Chkanikov, Yu. Ya Spiridonov, S. S. Khalikov, A. M. Muzafarov, *INEOS OPEN*, **2019**, *5*, 145–152. DOI: 10.32931/io1921r
37. Sh. Kh. Abdullaev, F. A. Abdullaev, *Proc. Conf. "Modern Trends in the Development of the Agrarian Complex"*, Salty Zaimishche, **2016**, pp. 829–833.
38. N. N. Nazirov, *Science and Cotton*, Tashkent, Uzbekistan, **1977** (in Russian).
39. A. Sh. Bakasov, L. G. Vodogreeva, G. Geldiev, *Izv. AN Turkmen. SSR*, *Ser. Biol. Nauk*, **1987**, *3*, 56–58.
40. A. A. Borodulina, *Falling Ovaries in Cotton*, Tashkent, Izd. Akad. Nauk Uzbekskoi SSR, **1960** (in Russian).
41. A. A. Prokofiev, S. Rasulov, *Russ. J. Plant Physiol.*, **1976**, *3*, 525–530.
42. E. R. Kurbanova, R. P. Zakirova, Yu. Ya. Spiridonov, S. S. Khalikov, N. D. Chkanikov, *Agrokhimiya*, **2019**, *6*, 27–33. DOI: 10.1134/S0002188119060085
43. G. A. Zharmukhamedova, V. A. Shlyakhtich, *Zashch. Karantin Rast.*, **2017**, *4*, 36–37. EDN: YPWHSX
44. S. M. Turaeva, U. B. Mamarozikov, N. K. Khidirova, R. P. Zakirova, *Zashch. Karantin Rast.*, **2019**, *7*, 47–48. EDN: UOFLNU
45. R. P. Zakirova, S. M. Turaeva, E. R. Kurbanova, N. D. Chkanikov, S. S. Khalikov, *Agrokhimiya*, **2022**, *1*, 46–49. DOI: 10.31857/S0002188122010124
46. R. P. Zakirova, S. S. Khalikov, E. R. Kurbanova, S. M. Turaeva, N. D. Chkanikov, *Agrokhimiya*, **2023**, *5*, 34–40. EDN: USROJJ
47. O. Yu. Selyutina, I. E. Apanasenko, A. G. Shilov, S. S. Khalikov, N. E. Polyakov, *Russ. Chem. Bull*., **2017**, *66*, 129–135. DOI: 10.1007/s11172-017-1710-2
48. O. Yu. Selyutina, E. A. Shelepova, E. D. Paramonova, L. A. Kichigina, S. S. Khalikov, N. E. Polyakov, *Arch. Biochem. Biophys.*, **2020**, *686*, 108368. DOI: 10.1016/j.abb.2020.108368