Opportunities and prospects for the development of complex biocompatible plant protection products based on some natural nitrogen compounds for solving agricultural problems

Z Khaptsev¹, A Bogdanov², M Kadomtseva³, P Smutnev¹ and L Isaicheva¹

¹Saratov State Vavilov Agrarian University, Saratov, 410005, Russia
²Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center, Russian Academy of Sciences, Kazan, 420088, Russia
³Institute of Agrarian Problems, Russian Academy of Sciences, Saratov, 410012 Russia

E-mail: dfst@list.ru

Abstract. The work summarizes the literature data on the use of pesticides in agriculture, as well as the damage they cause to the environment and human health. The possibilities and prospects for the development of complex biocompatible plant protection products based on some natural nitrogen compounds to solve agricultural problems and reduce damage from the use of pesticides are analyzed.

1. Introduction
Currently, various chemical compounds are widely used in crop production and their use is steadily growing [1]. According to the World Health Organization, more than 1000 types of pesticides are used all over the world to protect food from damage or destruction by pests. The United Nations Population Division estimates that the world's population will reach 9.7 billion by 2050, up 30% from 2017. And almost all of this demographic growth will occur in developing countries. In developing countries, the Food and Agriculture Organization (FAO) predicts that 80% of the increase in food production required by this population growth will come from increased yields and re-planting of crops per field. And only 20% of this growth in food production will be provided through the expansion of cultivated areas. In this regard, agricultural chemistry will continue to play an important role in the development of the economy, and the use of new generation pesticides will prevent large-scale crop losses [2]. According to various estimates, in 2020 the world consumption of agrochemicals will grow by 3.5 million tons [3].

2. Materials and methods
At the same time, the volumetric use of organic additives (pesticides, growth stimulants, herbicides, defoliants) is one of the main causes of death in humans and animals as a result of poisoning, which is especially acute in low and middle income countries [4-8]. The adverse effects of pesticide residues on human health are a global threat, as their adverse effects on human health can occur through ingestion, inhalation and direct contact with human skin [9].

Studies have shown that only 0.1% of the chemicals used in agriculture reach the goal, while the rest enter the environment practically unchanged through leaching or evaporation [10]. One of the
consequences of the accumulation of pesticides in the environment is the development of genetic resistance in pests to the drugs used [11]. In addition, currently used pesticides can have an adverse effect on the microbial communities of the soil and plant symbiont microbes [12]. In this case, there is a continuous transfer of these substances along the food chains and their accumulation in the final links, to which man belongs.

3. Results and Discussion
This problem is also relevant in the Russian Federation. So, for example, the mass death of bees in the regions of the Russian Federation has recently been associated with the uncontrolled use of pesticides in the processing of fields. In addition, according to the results of a survey conducted in 2019 by the network divisions of Roshydromet, the share of soils contaminated with pesticides above the established hygiene standards increased compared to 2018 and amounted to 3.3% in spring and 5.9% in autumn (in 2018 - 1.6% in spring and 1.0% in autumn, in 2017 - 7.1% in spring and 2.2% in autumn). In 2019, areas whose soil is contaminated with pesticides above the permissible level were found on the territory of 13 constituent entities of the Russian Federation (in 2018 - on the territory of 8 constituent entities). Despite the fact that drugs with DDT have not been used on the territory of Russia for a long time, the soils of agricultural lands are contaminated with this pesticide to a greater extent than others, the content of which in the soil is monitored by the Roshydromet network. This is due, first of all, to the high resistance of this chemical to degradation in various environmental conditions. Areas contaminated with dalapone, simazine, THAN herbicides and 2.4-D are also detected [13]. All this leads to a constant search for new, safer compounds for use in agriculture. In this regard, indole derivatives are a promising platform for creating highly effective and rapidly decomposing pesticides, among which isatin is the most attractive in terms of biological and synthetic availability (figure 1).

Isatin itself (1H-indole-2,3-dione) was first obtained by Erdman and Laurent in 1841 as a product of the oxidation of the natural blue dye indigo with nitric and chromic acids [14-15]. It is isolated from some plants, tissues of mammals and amphibians, coal tar [16]. Considering the fact that isatin and its compounds possess antibacterial [17-19], antiviral [20], and antifungal properties, they can be used to protect plants from phytopathogens.

One of the key factors determining the breadth of the search and development of new organic substances for the needs of agriculture and limiting the scale of biological tests are their easy synthetic availability, cheap starting reagents, water solubility, biocompatibility, and low toxicity. Within the framework of compliance with these conditions, the direction associated with the production, primary biological screening and study of the toxicity of a new class of water-soluble indole derivatives, isatin-3-hydrazones, is currently actively developing (figure 2).
For the entire series obtained, the possession of high antibacterial activity against Staphylococcus aureus and Pseudomonas aeruginosa was established. Leading compounds are 2-4 times more active than the reference drug, the widely used antibiotic norfloxacin, against S. aureus 209p, and 2 times against B. cereus 8035 (table 1). This fact suggests that these compounds will be active against bacterial phytopathogens. In this case, it should be especially noted the complete absence of toxicity of these compounds in relation to normal cells of humans and cattle - erythrocytes, hepatocytes, as well as lung cells of cattle.

Table 1. Some data on the antimicrobial activity of isatin derivatives.

| Compound   | Staphylococcus aureus | Bacillus cereus | Escherichia coli | Pseudomonas aeruginosa |
|------------|-----------------------|-----------------|------------------|------------------------|
| (5-Me)     | 7.8                   | 15.6            | >500             | >500                   |
| (5-Et)     | 7.8                   | >500            | >500             | >500                   |
| (5-OMe)    | 15.6                  | >500            | >500             | >500                   |
| (5-Br)     | 31.3                  | 125             | >500             | >500                   |
| (5.7-di-Br)| 31.3                  | 125             | -                | -                      |

It is also promising to develop the direction of obtaining and studying phosphorus-containing substances for the treatment of plant diseases. Thus, it was shown that phosphate derivatives of hydrazones (figure 3) of isatin have a higher activity against phytopathogenic sugarcane fungi Colletotrichum falcatum, Fusarium oxysporum, and Curvularia pallescence than some currently used synthetic fungicides [20].

The importance of the development of the “phosphorus” direction is confirmed by the data described in [19]. Evaluation of the fungicidal activity of dialkylphosphoryl hydrazones against Rhizoctonia solani and Fusarium oxysporum showed that some derivatives (figure 4) are able to effectively inhibit their growth. In addition, these biologically active compounds did not interfere with
the germination of lettuce seeds, which indicates the absence of phytotoxicity, making them potential leaders in the search for new fungicides.

At the same time, substances containing an isatin fragment may have a stimulating effect on the plant itself due to the conversion of isatin into isatate, which has auxin activity [10-14]. In addition, the potential possibility of using secondary metabolites of some plants containing isatin for weed control has been found [9].

The growth-regulating activity of isatin was also demonstrated in [8]. Thin-layer explants taken from pedicels and pedicels of tomatoes gave calli with high organogenetic potential. Of the 15 cultivars tested, 7 regenerated roots, shoots, and ultimately whole fruit plants. Calli grown on a modified Murashige-Skoog medium reacted to various auxins and cytokinins with different morphogenetic patterns. Thus, naphthalene acetic acid produced root-producing calli, while the auxin precursor isatin (indole-2, 3-dione) caused the formation of calli with vegetative and flower shoots, rarely giving roots. This may be due to the slow and steady conversion of isatin to active auxin [17-16], in contrast to naphthalene acetic acid, which immediately exhibits a high level of active auxin. The highest frequency of formation of vegetative shoots (100%) and flowers (50%) was obtained using 10 μM isatin and 3 μM zeatin. Some flowers have turned into ripe fruits. The high frequency of induction of vegetative shoots and flowers in front of the roots using isatin suggests its usefulness in micropropagation from plant tissue cultures.

The analysis showed that isatin and its derivatives have a high potential for the creation of non-toxic pesticides and plant growth stimulants on their basis. The cheapness of the initial reagents for the synthesis, the availability of natural raw materials and the ease of modification of this nitrogenous heterocycle determine the relevance and prospects for the search for new biocompatible preparations based on it. At the same time, in our opinion, it seems certain that compounds of this class will be in demand in agricultural production, especially in the system of organic farming.

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Figure 4. Phosphoryl-hydrazones with antigungal activity.
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