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MICROBIOLOGICAL CONTROL IN PHYTOSANITARY OPTIMIZATION TECHNOLOGIES FOR AGROECOSYSTEMS: RESEARCH AND PRACTICE
(review)

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A b s t r a c t

Phytosanitary optimization of agroecosystems targeted to control harmful arthropods and plant pathogens should use a complex of multifunctional biologics based on microbial antagonists of pathogens, producers of bioactive substances and entomopathogens (V.D. Nadykta et al., 2010; Rohini et al.; 2016, M. Ghorbanpour et al., 2017). The most promising microbial strains for plant protection are those possessing not only a direct target effect but also the ability to increase plant disease resistance due to phytoregulatory activity (I.I. Novikova, 2016). The holistic concept of microbiological protection involves the development and use of biological products based on living cultures of entomopathogenic microorganisms and antagonistic microbes with preventive and prolonged action, as well as formulations based on metabolite complexes to quickly reduce the density of phytopathogen populations (I.I. Novikova et al., 2016). Developing multifunctional biological products for plant protection is based on technological strains with high biological activity that are safe for humans and warm-blooded animals. It has been shown that the role of entomopathogenic viruses, microsporidia, bacteria and fungi in the dynamics of the number of phytophagous insects is determined by the type of pathogenesis (obligate or facultative). In case of intracellular obligate parasitism of baculoviruses and microsporidia, mass epizootics were observed in unpaired silkworms (*Lymantria dispar* Linnaeus), leafworms (family *Tortricidae* Latreille), cabbage whitewash (*Pieris brassicae* Linnaeus), meadow and corn moths (*Loxostege sticticalis* Linnaeus, *Ostrinia nubilalis* Hübner), ginger pine (*Neodiprion sertifer* Geoffroy) and black bread (*Cephus pygmeus* Linnaeus) sawflies, Siberian silkworm (*Dendrolimus sibiricus* Tschetverikov), cotton (*Helicoverpa armigera* Hübner) and gray grain scoops (*Apamea anceps* Denis & Schiffermüller) (I.V. Issy, 1986; A. Vey et al., 1989; A.N. Frolov et al., 2008; V.A. Pavlyushin et al., 2013). The regulatory role of *Entomophthora* infection is most pronounced in various species of aphids and some species of locusts (G.R. Lednev et al., 2013). For facultative parasitism which is characteristic of entomopathogenic fungi of genera *Beauveria*, *Metarhizium*, *Lecanicillium*, etc. (E. Quessada-Moraga et al., 2004), as well as bacteria of *Bacillus thuringiensis* group (N.V. Kandybin, 1989) and genus *Xenorhabdus* members, the most important factor of virulence is toxigenicity against host insects (M. Faria et al., 2007). Hydrolytic enzymes (chitinases, lipases, proteases), toxins, and antiphagocytic defense are factors of entomopathogenic fungi virulence. Microbiological protection of plants from diseases is based on the use of highly competitive strains that synthesize complexes of hydrolases and biologically active compounds and efficiently colonize suitable ecological niches (I.V. Maksimov et al., 2015; I.I. Novikova, 2016; I.I. Novikova et al., 2016). A number of active compounds produced by rhizosphere microorganisms possess elicitor activity and trigger induced resistance (J.W. Kloepper et al., 2009; N. Ohkama-Ohtsu et al., 2010). The effectiveness of biologicals developed at the All-Russian Research Institute of Plant Protection against the main harmful diseases of crops reaches 60-90%, which provides a 20-25 % increase in productivity and improves the quality of crop production (I.I. Novikova, 2017). The plant microbiological protection concept relies on the search for promising producers of novel biologicals among wider range of microbial species and strains, on the design of new formulations optimal in specific environmental conditions, and on biological plant protection and integrated plant protection management which combines biological products for various purposes depending on the specific complex of plant pathogens and the local phytosanitary situation in general (N.A. Belyakova et al., 2013).

Keywords: biologicals, bio-effectiveness, entomopathogenic microorganisms, antagonist microbes, harmful arthropods, plant pathogenic fungi, plant pathogenic bacteria, usable pesticides, bioactive complexes, elicitors

Phytosanitary optimization of agroecosystems via use of ecologically low-hazard products for plant protection can effectively improve crop production and quality to solve the pressing problems worldwide. The environmental effects, resource and energy efficiency of agro-technologies which provide optimized conditions for useful organisms and increase the stability of agrobiocenoses are the main indicators of the adaptability and efficiency of agriculture [1-3]. In the last decade, the strategy and tactics of phytosanitary optimization with environmentally low-hazard plant protection products and innovative technologies for their application have been significantly rethought. The general concept of plant protection as a scientific discipline is the construction of intensive and ecologically sustainable agroecosystems based on the optimization of trophic connections and other mechanisms of biocenotic regulation.

Here, we aimed to characterize the state and current trends in the development of microbiological plant protection in the Russian Federation and abroad based on fundamental and applied research data.

At present, anthropogenic impact results in a deep transformation of the structure and functional patterns of various types of agroecosystems [4, 5]. In agrobiocenoses, as monodominant systems, there is an increase in the population density and harmfulness of a number of plant pathogens, harmful arthropods and weeds with intensive formation of groups of dominant and superdominant species. Cases of their mass reproduction occur more and more frequently, zones of severity expand, and microevolution within populations is activated. Along with a general decrease in the diversity of biological communities, these factors worsen the phytosanitary state of crops, leading to a global problem.

The higher human impact inevitably leads to significant changes in the pedosphere which ensures transformation of photosynthetically assimilated atmospheric carbon during the carbon cycle in the biosphere. In particular, the main soil functions (matter and energy transformation, the role of a protective and buffer biogeocenotic barrier, sanitary function) become wane [6, 7]. Low amount of organic fertilizers, crop rotation neglect and monoculture practice speed up soil dehumification, depletion of soil microbiocenoses, a decrease in natural soil suppressivity, and the accumulation of soil infectious agents. These weaken the sustainability of agroecosystems self-regulation and cause phytosanitary destabilization.

Plants are the core of complex biogeocenotic consortia which comprise various groups of heterotrophs, including plant pathogens and pests, as well as their antagonists and hyperparasites. The biocenotic process which involves organisms of each trophic level determines stability and phytosanitary well-being of agroecosystems. Biocenotic principles of microbiological plant protection are the essence of a bioprotection approach, and biodiversity of multifunctional microbial entomopathogens, antagonists and hyperparasites is, in turn, a cornerstone of the microbe-based protection methods. Phytophagous insects significantly affect phytosanitary state of agroecosystems. Among 80 insect species that reduce crop yield and quality, there are super dominants in a state of ecological explosion with a significant spatial expansion and rising harmfulness, e.g. locust beetles (family *Acridoidea* MacLeay), pest bug (*Eurygaster integriceps* Puton), Colorado potato beetle (*Leptinotarsa decemlineata* Say), meadow moth (*Loxostege sticticalis* Linnaeus), cotton moth (*Helicoverpa armigera* Hübner), cereal ground

(*Zabrus tenebrioides* Goeze) etc. Plant protection against harmful insects requires more chemical treatments, which led to the appearance in Russia of about 40 resistant populations of phytophagous insects. Entomopathogenic microorganisms (viruses, microsporidia, bacteria, fungi, nematodes) play a significant role in the dynamics of insect populations, causing massive epizootics of insect hosts or a decrease in the number of pests (mostly during overwintering) by 15-30%. For example, entomophthora of the Italian locust (*Calliptamus italicus* Linnaeus), migratory locust (*Locusta migratoria* Linnaeus) and pea aphid (*Acyrthosiphon pisum* Harris) affects up to 100% of the population. The regularly occurring microsporidiosis of cabbage butterfly (*Pieris brassicae* Linnaeus) has practically led to its elimination in the northwestern region of the Russian Federation, and no harmfulness has yet been observed [8, 9]. However, low incidence of epizooties and the limited number of species of the obligate entomopathogens do not allow us to rely on their constant and stable sanitary effect while biologicals based on selected highly virulent and technologically advanced producer strains can provide effective protection against phytophagous insects in agrocenoses [10, 11].

Fundamental research (All-Russian Research Institute of Plant Protection — VIZR, Institute of Systematics and Ecology of Animals SB RAS, All-Russian Research Institute of Agricultural Microbiology, All-Russian Research Institute of Biological Plant Protection) made it possible to advance in understanding the mechanisms of pathogenesis when insects are infected by entomopathogenic viruses, microsporidia, and micromycetes. The investigations have established the role of hydrolytic enzymes (chitinases, lipases, proteases), toxins, and antiphagocytic defense factors in the virulence of entomopathogenic fungi (*Beauveria bassiana*, *Metharrizium anisopliae*, *Verticillium lecanii*) upon insect infestation [10, 11]. Virulence in fungi is of a polydeterminant nature, including the ability of spores to germinate on the cuticle of the host insect, the activity of the formation of enzymes that ensure the penetration of the pathogen through the cuticle, the rate of accumulation of fungal biomass in the body cavity, and the synthesis of toxins. Genetic improvement of strains in virulence is based on the specified set of traits.

The role of entomopathogens in the dynamics of phytophagous insect populations is determined by the host-parasite relationships. Ultimately, the type of pathogenesis (obligate or facultative) determines whether the abundance of insect pests is regulated, or the usual decrease in the population density of phytophages occurs. In case of intracellular obligate parasitism of baculoviruses and microsporidia, which are well adapted for survival in the external environment with subsequent constant persistence in natural populations of insects, there is a high incidence of epizootics in the gypsy moth (*Lymantria dispar* Linnaeus), leafworms (*Tortricidae* Latreille), cabbage white (*P. brassicae*), meadow moth (*Loxostege sticticalis* Linnaeus), and corn moth (*Ostrinia nubilalis* Hübner) [12-14]. Mass viral epizootics were noted in red pine and black-yellow sawflies, Siberian silkworms, cotton and gray grain moths [11].

Entomophthora fungi which are obligate pathogens of insects penetrate into the host's body through the cuticle and parasitize in organs and tissues without penetration into cells with pathogenesis duration up to 14 days. The regulating role of entomophtoras is mostly manifested against various aphids (pea aphid *A. pisum*) and some species of locusts: the Italian locust (*C. italicus*), Moroccan locust (*Dociostaurus maroccanus* Thunberg), and migratory locust (*L. migratoria*). A distinctive feature of the relationship between the host and the parasite in obligate parasitism is the absence of pronounced symptoms of toxicosis in insects, which indicates a low synthesis of toxins in upon viral, microsporidia, and entomophthora infections [12-14].

Under facultative parasitism, which is characteristic of entomopathogenic fungi from the genera *Beauveria*, *Metarhizium*, *Lecanicillium*, *Conidiobolus* and *Isaria*, *Bacillus thuringiensis* bacteria and the genus *Xenorhabdus* representatives, the most important factor of virulence is toxigenicity towards insect hosts. Most of the entomopathogenic fungi (*B. bassiana*, *M. anisopliae*, *L. muscarium*, and *Conidiobolus obscurus*) enter the body of host insects through the cuticle or spiracles, with germ hyphae secreting proteases, lipases, and chitinases to accelerate degradation of the integument. In the body of diseased insects, hyphae bodies and the embryonic mycelium appear, and the produced toxins accelerate pathogenesis and death of the host. The toxins of these fungi are low molecular weight cyclic peptides [15], organic acids, glycoproteins, and other metabolites. The causative agents of muscardinosis produce bovericin, boverolid, warfarin and piridoverin. It was shown that bassiacridin the *B. bassiana* toxin, is highly active against larvae of the migratory locust (*L. migratoria*). Noted that the pathogenesis in larvae is accompanied by intense tissue melanization, and phagocytic defense is not effective, since when granulomas appear, fungal elements produce growing hyphae from cell aggregations [16].

The pathogenic effect of the gram-positive spore-forming soil bacterium *B. thuringiensis* (Bt), whose host insect range reaches hundreds of species, has been studied in detail. During oral infection, under the influence of proteases in the insect intestine, the lysis of the protein crystal and the activation of protoxin occur, which leads to the death of the host [17]. It is characteristic that in bacteriosis, the biotrophic phase is practically not observed, and the main accumulation of bacterial cells in the host's body occurs postmortem. Protein δ-endotoxins, which are encoded by *cry* and *cyt* genes located on the Bt plasmids, play the main role in the toxigenicity of the Bt group. More than 100 genes of Bt β-endotoxins are known [18]. Other entomotoxins, namely α-, β- and γ-exotoxins, are also involved in the Bt virulence [18].

Bt-based commercial biologics provide the bulk of microbiological plant protection against phytophagous insects. At present, a total of 171 mycoinsecticidal biologicals based on *B. bassiana*, *M. anisopliae*, *Isaria fumosorosea*, and *L. muscarium* strains have been developed, of which 75% are worldwide marketable [19, 20]. The formulations based on selected strains of entomopathogenic fungi of genus *Lecanicillium*, affecting sucking insects (greenhouse whitefly *Trialeurodes vaporariorum* Westwood), aphids (*Aphidoidea* Latreille), etc., are suggested (a totola of 20 biological products). Experimental batches of Verticillin M (FGBNU VIZR, Russia) based on a toxigenic strain of *Lecanicillium muscarium* were effective in protecting greenhouse crops against whiteflies (*Aleyrodidae* Westwood), aphids (*Aphidoidea* Latreille), thrips (*Thripuidae* Stevens), and tetranium ticks [20].

In modern plant protection technologies, special attention is paid to bioinsecticides based on microbial metabolites [21, 22]. Russian actinomycete-based preparations Fitoverm®, EC (LLC NBTs Farmbiomed, Russia) and Agrovertin (new name Akarin; CJSC Agrovetservice, Russia) contain avermectins, a natural macrolide compounds, insecticidal preparation SpinTor™ (Dow AgroSciences Vertriebsgesellschaft mbH, Austria) is based on spinosad which contains macrocyclic lactones of the spinosyn group in the active complex [23, 24]. Streptozonin, ossamycin, and deoxyossamycin are the actinomycetes-based preparations with spiroketal macrolides as an active ingredient, which are highly effective against insect and mite pests [25]. Among the widely known microbial insectoacaricides, it is worth noting a group of milbemycins [25], similar in properties to avermectins, and niccomycin, a specific inhibitor of chitin synthesis [26]. For a success of the antiresistant plant protection program, and given the characteristics of entomophages, the main biocontrol agents, the means for plant protection should include a wide range of biologicals with active ingredients of different nature, which are effective, environmentally friendly and entomophages compatible. Therefore, the search continues for new microbial strains that produce metabolites with a wide spectrum of insectoacaricidal action.

The search for insecticidal streptomycetes in soils of different climatic zones allows for a more targeted identification and selection of strains to develop more specialized biologicals [27]. Particularly, the soils from India, China, Egypt, Vietnam, Ukraine and Western Siberia have been surveyed. Our long-term studies have shown the maximum biodiversity of insectoacaricide producers in chernozem and sod-podzolic uncultivated soils of Western Siberia [28]. In the State Collection of Microorganisms Pathogenic for Plants and Their Pests (GCM VIZR, Russia) (WFCC WDCM No. 760, http://www.ckp-rf.ru/usu/200616/), there are over 1000 actinomycetes strains as potential producers of bioactive substances (BAS) of various chemical nature.

The VIZR model of microbial stepwise screening on a wide range of test insects and ticks has been used to develop a number of biological products not affecting warm-blooded animals and humans and compatible with entomophages. In the conditions of the Leningrad region, in Tajikistan, Belarus and Georgia, experimental batches of *Streptomyces aurantiacus* 0775-based biological Aleucid [28], with 9-dimethyl-piericidin as an active ingredient, showed high efficiency against harmful sucking arthropods, in particular in all life stages of the greenhouse whitefly (*T. vaporariorum*). Test batches of the Indocid based on *Streptomyces loidensis* P-56 strain from the India soils are active against various aphids (*Aphididae* Latreille), thrips (*Thripidae* Stevens), and common spider mite (*Tetranychus urticae* C.L. Koch). The insecticidal products of the strain are depsipeptides of the ostreogricin type. For test batches of Gerben, a *S. herbaricolor* S-100 strain-based biological developed at VIZR, the death rates of melon aphids (*Aphis gossypii* Glover), *peach aphids* (*Myzodes persicae* Sulz.), spotted greenhouse aphids (*Neomyzus circumflexus* Buckton), legume aphids (*Aphis fabae* Scopoli), pea aphids (*A. pisum*) aphids, and common spider mite (*T. urticae*) reached 60-100% [28, 29].

The beneficial microorganisms of the rhizo- and phyllosphere are in constant and dynamic associative relationships with plants [30]. Bacteria from the genera *Pseudomonas*, *Bacillus*, *Streptomyces*, and *Serratia* are of the greatest importance for the biocontrol of plant pathogenic species [31-33]. The mechanisms of microbial-plant interactions resulting in the suppression of plant pathogen populations are complex and diverse [34-36]. Plant protection involves the use of highly competitive microbial strains that can synthesize complexes of hydrolases and bioactive compounds and effectively colonize appropriate ecological niches [37-39]. Many compounds produced by rhizosphere microorganisms possess elicitor activity and can trigger mechanisms of induced resistance [40-42].

The synthesis of various antibiotics classes (peptides, macrolides, polyene compounds, aminoglycosides, etc.) is of paramount importance for bioactivity of microbial antagonists of plant pathogens [43]. Antibiotics can disrupt the synthesis of proteins and cell wall components, leading to membrane dysfunction, and inhibit oxidase activity. E.g., phenazine produced by *Pseudomonas* strains inhibits growth of *Fusarium oxysporum* and *Gaeumannomyces graminis*, affecting the redox potential in fungal cells, and 2,4-diacetylphloroglucinol inhibits germination of *Pythium* spp. zoospores due to membrane lysis [43]. Metabolites of *Bacillus* strains (proteins, peptide and polyene antibiotics, cyclic lipopeptides, phenolic compounds, and cyanide) are active against gram-negative and gram-positive bacteria, as well as various plant pathogenic fungi (*Fusarium*, *Alternaria*, *Drechlera*, *Colletotrichum*, *Verticillium*, *Phoma*, *Phomopsis*, *Sclerotinia*, *Puccinia*, etc.)

[43, 44]. Chitinases, glucanases, proteases, and lipases, which lyse cell walls of plant pathogenic micromycetes and cause degradation of their effector molecules, mainly peptides, are essential for the antagonistic mechanisms [45]. Micromycetes *Trichoderma* spp. synthesizing rich hydrolase complexes occupy a special position as producers of polyfunctional biofungicides. Together with high hyperparasitic, antagonistic activity and suppression of plant pathogenic soil micromycetes (due to produced antibiotics and enzymes), they increase plant disease resistance, have a phytoregulatory effect, improve nitrogen utilization via stimulation of *Azotobacter* and nodule bacteria. It should be noted that *Trichoderma* strains are involved in the decomposition of complex organic polymers, enriching the soil with nutrients available to plants [45].

The ability of beneficial microorganisms of the rhizo- and phyllosphere to synthesize metabolites with hormonal and signaling functions that affect plant growth and resistance is essential for ensuring a comprehensive protective effect. Among the discovered natural growth regulators are abscisic (ABA), jasmonic and salicylic acids, cytokinins, gibberellins, and auxins [46-48]. It has been shown that many bacterial strains of *Azospirillium*, *Pseudomonas*, *Bacillus*, etc. can synthesize auxins that activate plant root growth, which allows plants to acceleratly pass through the phases sensitive to infection [49-51]. *Bacillus* strains are capable of producing gibberellins [52]. Members of *Bacillus*, *Rhizobium*, *Arthtrobacter*, *Azotobacter*, *Azospirilium*, and *Pseudomonas* genera produce cytokinins. Inoculation of plants with cytokinin-producing *B. subtilis* strains leads to a significant increase in the content of chlorophyll and cytokinins, as a result of which the root biomass and the aerial part increase [53]. Representatives of *Bacillus*, *Pseudomonas*, *Azospirillum*, *Brevibacterium*, and *Lysinibacillus* genera show the ability to produce ABA. In other words, beneficial microbiota can optimize the endogenous hormonal balance of plants [54-56].

Proper mineral nutrition is essential to increase plant disease resistance and provide diseases control. Many rhizosphere microorganisms can solubilize phosphates due to certain metabolites, e.g. organic acids and phosphatases [56-59]. The role of plants in plant-microbial interactions is also active [60, 61]. It should be especially noted that bioactive substances synthesized by microorganisms have elicitor properties and activate the mechanisms of systemic induced resistance in plants [62, 63].

Many bacterial determinants (MAMPs, microbe-associated molecular patterns), in particular antibiotics, siderophores, hormone metabolites, biosurfactants, lipopolysaccharides, flagellin, and volatile organic compounds, induce defense reactions in plants [59, 60].

The biosurfactants produced by *Pseudomonas* and *Bacillus* bacteria are cyclic lipopeptides of three families, iturins, surfactins, and fengicins. By decreasing the surface tension coefficient of water and forming gels, they increase the availability of hardly soluble hydrophobic compounds for roots [64, 65]. Microbial lipopeptides, due to biofilms formed on the surface of rhizoplane, protect plants against pathogen invasions and bacterial cells from unfavorable environmental factors. As biofilms can change the permeability or destroy the structure of the cytoplasmic membrane by binding to the lipid bilayer, fengicins and iturins possess antifungal activity, and surfactins exhibit antiviral, antimycoplasmic, and antibacterial properties [66, 67]. Fengicin and iturin form pores in the membrane, while surfactin dissolves it [68, 69]. Surfactin and fengicin stimulate synthesis of secondary metabolites with an increase in the activity of enzymes of lipoxygenase pathway that results in elicitor activity [70]. It has been shown that the *Pseudomonas* strains are capable of forming lipopeptides of four families, amphysines, syringomycins, tolaazines, and viscosines.

Massitolide A from the viscosine group produced by *P. fluorescens* SS101 exhibits direct antagonism towards *Phytophthora infestans* and induces disease resistance in tomato plants [71].

The main mechanism of action of siderophores is the competition for Fe^{3+} between beneficial rhizosphere microorganisms and plant pathogens. However, it has been also shown that siderophores can induce resistance in plants [72]. Pseudobacins produced by *Bacillus* sp. SLS18 can suppress *F. oxysporum* in iron-poor soils, by *P. putida* WCS 358 can inhibit *Ralstonia solanacearum* on eucalyptus plants, by *B. cinerea* on tomato plants, and by *Erwinia carotovora* on tobacco plants [73]. In contrast, strains that did not produce pseudobacin failed to induce plant resistance to systemic diseases. Pseudobacin of *P. fluorescens* WCS 374 induced systemic resistance against rice blast caused by ascomycete *Magnaporthe oryzae* due to activating synthesis of phenolic compounds and H_2O_2 in the epidermis and strengthening the plant cell wall in the infected zone [74].

Thus, to date, a diverse set of information has been accumulated on the physiological, biochemical and ecological characteristics of microorganisms inhabiting the rhizo- and phyllosphere, as well as the mechanisms of their antagonistic activity [75, 76].

Fundamental research determines strategy to select beneficial microorganisms, and to develop technologies for manufacturing formulations of biologicals that provide a protective effect, increase yields and improve product quality. The researchers of the All-Russian Research Institute of Plant Protection have proposed an original paradigm of crop protection given multifactorial nature and diversity of the target objects upon a long-term phytosanitary destabilization. The paradigm is based on the on the harmful species dynamics control, crop immunity, and selective and multifunctional biologicals, given the regularities of the parasitocenoses functioning and plant-microbial communities [77]. It is applicable for intensive crop production, greenhouses and organic farming conditions. This is a continuation of the research on microbiological plant protection, entomology, phytopathology and mycology conducted in the VIZR since the 1930s and initiated by the researchers of leading Leningrad and Moscow scientific schools (E.N. Pavlovsky, G. Ya. Bei-Bienko, A.V. Znamensky, I.V. Vasilev, N.F. Meyer, L.S. Zimin, A.A. Yachevsky, N.A. Naumov, K.M. Stepanov, M.S. Dunin, V.P. Pospelov). Long-term studies have substantiated the prospects of using antagonistic microbes and entomopathogenic species to control populations of plant pathogens and harmful arthropods in agroecosystems [78]. As a result, conceptual approaches to the creation and use of two types of multifunctional biological products have been developed. The first group of the preparations provides direct suppression of the reproduction of plant pathogens, while the second group increases plants resistance and improve plant physiological state. Biologicals derived from living microorganism have preventive and prolonged effect and are the strategic mainstay of microbiocontrol, while those based on active metabolite complexes can be used tactically to quickly suppress actively propagating species, for example, powdery mildew and rust fungi. The development of such multifunctional products involved the use of strains that are technologically advanced and safe for warm-blooded animals and humans, with high and complex activity, i.e. bactericidal, fungicidal, antiviral properties, plant growth regulation, virulence, and toxicity [78]. Promising strains should have high ecological plasticity, competitiveness, and the ability to synthesize a set of substances with high target effects. The adaptability should also be regarded, namely the ability of the strain to utilize available and cheap substrates, resistance to drying and concentration methods, prolonged targeted activity and viability in different formulations.

Ecological plasticity and high adaptability allow strains to effectively restrain an increase in the density of plant pathogen populations for a long time. Golovlev [79] introduced the concept of “ecological tactics” of microorganisms, that is, ways of responding to changes in environmental conditions and types of behavior in the same environment, the number of which can be very large. A microorganism’s strategy is environmental tactics combination. Ecologically plastic species of the genera *Streptomyces* and *Bacillus* which dominate in various soil ecosystems (chernozems, gray forest soils, salt marshes, etc.) play a significant role in ensuring the dynamic stability of soil microbiocenoses [79]. *Bacillus* strains in an optimal habitat show growth parameters characteristic of r-strategists. On the contrary, under unfavorable conditions they form endogenous spores, like L-strategists. In addition, in microbial saturated rhizo- and phylloplanes communities, bacilli exhibit the K strategy. Actinomycetes can also show a mixture of K and L strategies. In our opinion, it is bacilli and actinomycetes of some genera that are most promising for introduction into agroecosystems for a long-term control of plant pathogens.

Polyfunctionality of microbial producers is due to substances with various target bioactivities produced as a result of strict natural selection during evolution of soil-living microorganisms under the habitat saturation. The concept of “phenotype metastability” by Golovlev [80] implies phenotypic variability within the framework of a constant genotype, which can be considered as a way of adaptation to a changing environment and the result of a specific form of natural selection under these conditions. Phenotype metastability emerged evolutionarily as a way of species stabilization rather than the generation of diversity and further divergence [80]. The species capable of forming a wide range of secondary metabolites are the most competitive during adaptogenesis. For the development of multifunctional biological products, it is these species and strains that are of greatest interest.

Bacillus and *Streptomyces* strains are widely used in biotechnologies due to diversity of metabolic processes and low pathogenicity. Bacilli and streptomycetes are well suited for biotechnologies of manufacturing biologicals and to the greatest extent meet the requirements for strains to be introduced into agrobiocenosis for biocontrol of plant pathogens. *Bacillus* strains are one of the most diverse and widespread groups of microorganisms [33, 35, 37]. They synthesize a variety of bioactive substances, mainly of a protein nature, which are important in the induction of plant disease resistance [36, 38]. Actinomycetes are also valuable in industrial biotechnology as producers of antibiotics and bioactive substances. The efficiency of spore dispersal, resistance to drying and temporary lack of nutrients determines the wide distribution of actinomycetes in nature and their high technological effectiveness [81]. Strains of the genus *Streptomyces* is one of the most numerous groups among actinomycetes [82]. Peptide, macrolide, and polyene antibiotics produced by streptomycetes in addition to hydrolases are of great importance for soil suppressivity [83]. Although actinomycetes have long been widely used in medicine and veterinary medicine, they have little use in agriculture is limited. It should be noted that, among almost 14000 known active microbial secondary metabolites, about 9000 are produced by actinomycetes, 80% of which belong to the genus *Streptomyces* [81]. In this regard, it is obvious that the physiological and biochemical characteristics of actinomycetes determine the expediency of their use as producers of specific biologically active compounds for plant protection.

At present, biological products in the world pesticide market still make about 2%, but their use has been increasing by 20% per year in recent years, while the production of chemical pesticides has been increasing annually by only 3%. The USA and the EU produce over 75% of the world's biopesticides. Annual sales of biocontrol products by the largest companies Valent Bioscience (USA), Certis (USA), Koppert Biological Systems (Netherlands), Pasteuria Bioscience (USA), Isagro (Italy), Terra Nostra Technology (Canada) overcome USD 100 million. In the world market, 90% of commercial biopesticides are *B. thuringiensis*-based, followed by, according to the degree of commercialization, entomopathogenic nematodes, micromycetes, and, finally, antagonist microbes. The largest pesticide manufacturer, Bayer AG (Germany), produces commercial biofungicides Sonata® (*Bacillus pumilus* QST 2808), Rhapsody® and three formulations of Serenade® (*Bacillus subtilis* QST 713) (https://www.agroxxi.ru). In Russia, biologicals Fitosporin (LLC Bashinkom), Baktofit (LLC PJSC Sibbiopharm), Rizoplan (LLC Biopesticides), etc., are widely used to protect plants against diseases.

In the State Collection of Microorganisms Pathogenic to Plants and Their Pests (SCM VIZR), the total number of accessions reaches 8120. Among them, over 200 strains of various taxonomic affiliations are biocontrol microbial agents that perspective for plant protection against pests and diseases. Particularly, these strains have been used to develop formulations of six multifunctional biological products, Gamair, Alirin-B, Vitaplan, Trichotsin, Sternifag, and Glyocladin (registered jointly by the FGBNU VIZR and ZAO ABT-group), which protect crops against diseases and increase yields as plant growth stimulators.

Alirin-B (*B. subtilis* B-10) is intended for plant protection against fungal diseases. The strain synthesizes polypeptide and polyene antibiotics, and the main active substance alirin B_1 is assigned to bacteriocins [84]. *B. subtilis* M-22-based Gamair is effective against mycoses and bacterioses; the Gamair A strain synthetizes the polypeptide which is close to bacillin and belongs to mediocidin subgroup 1A, as well as gamair B, C, and D strains — the hexaene antibiotics of different structure [85].

Lab samples and pilot batches of several new biopreparations based on the most active strains show high efficiency for different crops. A promising strain *Streptomyces felleus* S-8 synthesizes alirinomycin C, the original antibiotic which belongs to the subgroup of basic macrolides of the carbomycin-cirramycin type and is highly active against plant pathogenic micromycetes [86]. Strains *S. chrysomallus* P-21 and *S. globisporus* L-242 produce a variety of compounds with high fungicidal, antiviral activity and phytoregulatory action. The *S. chrysomallus* P-21 strain produces chrysomal A, the original polypeptide antibiotic classified as a threonine-type peptidolactone. Both strains also produce heptaene aromatic antibiotics of the polyester group. Globerin and chrysomal C are assigned to the subgroup of aromatic heptaene polyenes [87]. Polyene antibiotics bind to certain components of fungal surface and have a selective membranotropic effect. According to the classification, the original antibiotics chrysomal C and globerin are assigned to the subgroup levorin-partricin-trichomycin. It was found that chrysomal C is closest to levorin, while globerin is closest to partricin [88].

The use of multifunctional formulations based on several strains producing bioactive substance is an innovative approach which can significantly increase the effectiveness of biologicals and expand the range of their action. An example is *B. subtilis* BKM B-2604D- and *B. subtilis* BKM B-2605D-based biopreparation Vitaplan, SP. *B. subtilis* BKM B-2605D produces a polypeptide close to bacillin, as well as hexaenic antibiotics one of which is attributed to the mediocidin subgroup. *B. subtilis* BKM B-2604D synthesizes antibiotics of various structures (polypeptide antibiotic which belongs to bacteriocins and polyene antibiotic) [84, 85].

The analysis of experimental data shows the prospects for the use of microbial producers of antibiotics as the basis of multifunctional biologicals for protecting plants from pathogens and clarifies the role of secondary microbial metabolites of various chemical structures in the mechanism of complex activity of producer strains. Nevertheless, the selection of a stable, highly active strain is a necessary, but not sufficient condition for effective microbiological protection. The key problem is development of formulations which are suitable for manufacturing, fully correspond to the producer strain biological characteristics, and thus ensure long-term microbial cell viability and biological activity during storage and application [89].

Effectiveness of *Bacillus subtilis*-based biologicals for integrated and biological crop protection systems in the regions of the Russian Federation [90-92]

Biologials (developer)	Crop, variety of hybrid, location	Disease	Effectiveness, %	Increase in yield
Alirin-B, DP (VIZR)	Winter wheat variety Bezenchukskaya 380, SKhPK Grachevskii, Lipetsk Province	Root rot Septoria Brown rust Fusarium head blight	60-80 85-90 75-80 60-70	8-10%
	Sugar beet, hybrid XM-5455, OOO Zarech'e, Voronezh Province	Complex of diseases (cercosporosis, phomosis, bacteriosis)	60-65	93.3 c/ha
	Appli tree variety Idared, OPKh Tsentral'noe, Krsnodar	Scab, powdery mildew	96-99	10-20 c/ha
	Strawberry variety Zenga Zengana, CT Sad, Voronezh Province	Gray rot	87	28.8-38.6%
Gamair, DP (VIZR)	Sunflower variety Rodnik, SKhPK Grachevskii, Lipetsk Province	White rot, phomosis	80-98	22%
Vitaplan, DP (VIZR)	Spring wheat variety Pobeda, GNU NV NIISKh test field, Volgograd Province	Root rot Septoria Powdery mildew	61-67 55-59 52-62	12.8-14.1%
	Winter wheat variety Rufa, Experimental Farm of Kuban Agrarian University, Krasnodar Territory	Root rot Septoria Powdery mildew	64-77 61-71 66-73	8.3-16.6%
	Spring barley variety Mamlyuk, Luk'yanenko KNIISKh, Krasnodar Territory	Net blotch	48-62	23.1-26.2%
	Winter barley variety Dobrynya, Experimental and Training Farm of Kuban Agrarian University, Krasnodar Territory	Root rot Net blotch	64-80 63-64	21.5-26.7%
	Potato variety Svetlyachok 1, Moldova. PMR GU Republican toxicological laboratory	Late blight, Rhizoctoniae, Alternaria	60-80	42.0-45.0%
	Carrot variety Nantskaya, OOO Nadezhda-2, Volgograd Province	Alternaria	58-70	11.8-12.4%
	Watermelon variety Sakharnyi malysh, OOO Nadezhda-2, Volgograd Province	Root rot and wilt Anthracnose	69-73 72-77	14.5-17.4%
	Melon variety Lada, OOO Nadezhda-2, Volgograd Province	Peronosporosis Root rot and wilt	56-67 49-69	8.4-12.8%
	Apple tree varieties Sinap Orlovskii and Pamyat' voinu, OOO Maslovskie sady, Orel Province	Scab, moniliosis, powdery mildew	93-100	10-25 c/ha
	Grape variety Bianka, SKNIISiV, Karsnodar, OOO AF Yuzhnaua, Temryuk region (the Anapa-Taman' agro-eco zone)	Mildew Oidium	64-74 86-100	29-39% for yield, 13-19% for sugar content
	Bulb onion variety Khaltsedon, GNU NV NIISKh, Volgograd Province	Peronosporosis	62-77	8.9%
	White cabbage variety Stakhanovka 1513, AF Moskovskii, Moscow Province	Blackleg, slimy bacteriosis	58-68	15.7-34.2%
	Sugar beet variety L'govskaya 52, beetroot variety Bordo 237, OOO RusAgro-Druzhba, Belgorod Province	Root rots (Fusarium, Phoma, Pythium) Cercosporosis	58-82 64-75	10.5%

Long-term on-farm tests showed the effectiveness of the biologicals suggested by us against diseases of cereals, vegetables, fruits and berries, potatoes and sugar beets showed by three biologicals [90-92] (data are summarized in the table).

Thus, 40 biological products have been developed in Russia to protect plants. Together with foreign producers, microbiological protection of agricultural crops against pests, diseases and weeds is provided by 300 biological products, which, of course, is a significant resource for phytosanitary optimization and achieving environmental safety in crop production [93]. Biologicals are effectively integrated into zonal protection systems for grain, potatoes and vegetable crops in the Russian Federation. Technologies for bioprotection of vegetable and ornamental crops in greenhouses have also been created which effectively combine biological products and entomophages [94].

So, the stable protective effect of biologicals is based on i) constant monitoring of harmful and useful populations in the agrobiocenosis; ii) obligatory preventive treatments using products with both protective and phytoregulatory properties; iii) coincidence of the conditions optimal for entomophages' reproduction and high virulence of microbial producers; iv) the complex action which ensures effectiveness towards diseases, harmful arthropods and depression of rapidly reproducing species; v) compatibility of entomophages, biologicals and other elements of bioprotection system. The range of biological products should expand both by involving new genera, species and producer strains, and by improving the formulations for different environmental conditions. In biological and integrated crop protection, multifunctional targeted biological products adjusted to the composition of harmful species and the phytosanitary situation in general are the most prospective.

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