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Prospects for using pesticides in agriculture

Perspektywy stosowania pestycydów w rolnictwie

Summary. Concerns about food safety issues have put considerable pressure on pesticide producers in Europe and worldwide to reduce the levels of pesticide residues in food. The aim of this work is to assess the use of traditional pesticides and their effects, to present perspectives in this field and to identify regulatory needs for their use and implementation. The work is based on a systematic review in which the research problem was defined, primary sources were selected and critically appraised, data were collected, analysed and evaluated, and conclusions were formulated. The state of the pesticide market and the current legal requirements for risk assessment in relation to exposure to chemical substances were reviewed. Food safety issues are presented through the prism of pesticide residues in food. Their widespread use and considerable persistence have made them ubiquitous in the natural environment and their residues pose a threat to the environment and to human and animal health. It has been shown that the most important factor influencing the search for new tools to control diseases and pests of crops is the progressive development of resistance of these populations to currently used pesticides. Various alternatives to the phasing out of synthetic pesticides in the form of natural products are therefore being developed to support the development of the natural products market.

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Natural phytotoxins can be used as herbicides, but it is more effective to use bioherbicides as templates for synthetic herbicides. They can also be used to discover new modes of action and molecular targets for future herbicides.

Key words: bioherbicides, bioinsecticides, natural phytotoxins, pheromones, pesticide toxicity

INTRODUCTION

Due to the considerable durability of pesticides and their potential threat to the environment, water and soil pollution by products of their decomposition has increased. In recent years, consumers have been paying more and more attention to the potential health effects of synthetic chemicals in food. Concern over food safety issues has resulted in considerable pressure on pesticide producers in Europe and worldwide, not only from consumers but also from various committees and social organizations around the world, to reduce the level of pesticide residues in food from farms were synthetic plant protection products. Currently, there is a great demand for new, innovative and safe crop protection products that increase the ability to control weeds, diseases and pests in crops. This can be ensured by natural phytotoxins, bioherbicides, biofungicides, bioinsecticides or pheromones [Grotowska et al. 2018, Duke et al. 2022]. These tools are not fully used to control weeds, diseases and pests. For example, natural phytotoxins can be used directly as herbicides, but are not as effective as using them as templates for synthetic herbicides. They can also be used to discover new modes of action and for molecular targets for future herbicides. The development and institutional approval of microbial bioherbicides for use in e.g., floodplain crops are relatively inexpensive and effective [He et al. 2022]. Attention has been drawn to the existence of very strong correlations between exposure to pesticides and the occurrence of leukemia, skin cancer, prostate cancer, lung cancer and neurodegenerative diseases [Graña et al. 2020]. In addition, attention was also focused on the ban on the use of pesticides that are carcinogenic, mutagenic, toxic substances, and especially those that disrupt the hormonal balance in the reproduction process, and on the possibility of using biopesticides that decompose quite quickly and constitute a special group of active substances in plant protection. Their use in plant protection can lead to many positive changes, such as: reducing pesticide residues in food and in the environment, and thus reducing the risk for consumers. The aim of the work is to assess the use of traditional pesticides and their effects, and to identify perspectives in this field and regulatory needs regarding their use and approach to risk assessment, as well as challenges related to the implementation of harmonized guidelines at the European and international level.

MATERIAL AND METHODS

In the literature review, renowned internet search engines, including Scopus, PubMed, Google Scholar and others, were used, with the use of keywords and phrases such as: bioherbicides, bioinsecticides, biopesticides, pesticide toxicity, natural pesticides, essential oils. A systematic review was carried out, the research problem was defined, primary sources were selected and critically assessed, data was collected, analysed and conclusions were formulated. In total, 73 papers closely related to the research objective were selected. The analysis takes into account publications on the consequences of the use of chemical plant protection products in agriculture and draws attention to new research on the use of biopesticides that are safe for health and the environment.

PESTICIDES

One of the most important challenges and priorities of EU policy is environmental protection. Environmental protection requirements are defined by applicable legal regulations. Farmers applying for direct payments should maintain agricultural land in an appropriate condition. In order to protect nature on arable land, the following actions are taken: introducing a multi-species crop rotation, using catch crops: undersown crops, stubble and winter catch crops, establishing afforest strips and mid-field plantings, maintaining fallow and fallow land in a proper condition, implementing the principles of good agricultural practice, prohibiting burning vegetation in meadows, pastures, wastelands, ditches, stubble fields, and implementing agri-environmental programs [Góral and Rembisz 2017]. The development of plant production is associated with the selection of varieties, rational use of fertilizers and modern plant protection products. A sustainable farming system in agriculture, in addition to the economic aspect, should also take into account the environmental aspect, assuming the reduction of the use of chemical plant protection products [Mrówczyński and Roth 2009, Petit et al. 2015]. A long period of degradation and high toxicity of pesticides pose a threat not only to the natural environment, but also to human and animal health. Therefore, the European Union has taken action to achieve sustainable use of pesticides. The Directive of the European Parliament and of the Council No. 2009/128/EC of 21 October 2009 established a framework for Community action for the sustainable use of pesticides.

Pesticides – definition and classification

Pesticides (Latin: *pestis* – plague, *occido* – kill), i.e., plant protection products, belong to a group of chemical compounds with a high toxic effect. The introduction of these compounds into the environment takes place in a conscious and controlled manner. According to the American Environmental Protection Agency (EPA), pesticides are substances or mixtures of substances that have the ability to destroy, repel or inhibit the development of pests [Grotowska et al. 2018]. These are substances of synthetic and natural origin. Inorganic pesticides, based on arsenic and fluorine, are used all over the world. Plant pesticides, based on nicotine, constitute a separate group. Synthetic pesticides contain halogen compounds, e.g., HCH (hexachlorocyclohesane), and organophosphorus compounds [Żelechowska et al. 2001, Duke et al. 2019, 2022]. Pesticides are widely used in agriculture, forestry and orchards. They are also used in residential buildings to control insects and rodents. The classification of pesticides is based on the type of active ingredients, as well as their mode of action, toxicity, chemical structure and durability [Żelechowska et al. 2001, Grotowska et al. 2018, He et al. 2022]. Pesticides are divided into:

– organic compounds containing a carbon skeleton, which may occur as natural components in nature (some secondary metabolites) or substances obtained by organic synthesis from various organic substrates [Hassaan and El Nemr 2020],

– inorganic of natural origin or formed by chemical reactions, which are compounds of: antimony, copper, fluorine, boron, selenium, mercury, thallium, phosphorus, zinc and sulfur. A group of organometallic pesticides can also be distinguished due to the presence of a metallic element [Tudi et al. 2021, Duke et al. 2022].

It is practically impossible to estimate an environmentally acceptable level of pesticide consumption, because the long-term environmental and health effects are unknown, therefore the goal is to reduce pesticide consumption as much as possible. The effectiveness of active substances is selective in relation to a specific species of harmful organisms; therefore, the utility classification of pesticides is based mainly on their species effectiveness. The above criterion divides pesticides into the following groups: herbicides, fungicides, bactericides, attractants, growth regulators, repellents and zoocides [Wrzosek et al. 2009, Kaur et al. 2019]. Traditional, chemical herbicides can also be divided into groups according to the following criteria:

− – product name; however, products with different names may contain the same active substances, with the same or different concentrations of the active substance and a different formulation (different formulations, different manufacturers),

– active substance,

– chemical group, herbicides contain different active substances with a similar chemical structure,

– HRAC category – mechanism of action; different chemical groups may have a similar mechanism of action on weeds [Kaur et al. 2019, Duke et al. 2022].

Due to the high contamination of soils, waters and food with pesticide residues, efforts should be made to abandon or reduce the use of herbicides. The main reasons why reducing the use of herbicides is necessary are:

– protecting consumers and field workers from the health risks and harmful effects of pesticide use and ingestion through food and drinking water.

– protection of the environment against harmful effects related to the use of pesticides, both direct and indirect, in agricultural areas, near watercourses and sensitive natural habitats [Wrzosek et al. 2009, He et al. 2022, Duke et al. 2022].

The growing problem of resistance of weeds to herbicides is very important not only for the farmer, but also for the consumer. WRP [163/2020] presented what types of weed resistance and what symptoms observed in arable fields after application of herbicides may be of concern to the farmer in terms of the emergence of weed resistance [Kaur et al. 2019]. The problem of weed control is exacerbated by herbicide resistance, which some weed species have developed over time due to overuse of herbicides or their evolution (natural selection process) towards favorable conditions [Owen and Zelaya 2005]. Weeds can be resistant to specific herbicides (selective) or to a broad spectrum of herbicides (non-selective) [Owen and Zelaya 2005, Busi et al. 2013]. These weed traits have evolved gradually based on mechanisms such as: absorption, metabolism, translocation, detoxification and site of action that confer resistance to weeds [Ma et al. 2013, Sammons and Gaines 2014].

Currently, plant protection products, including herbicides, which have obtained appropriate authorizations/certificates issued by the Ministry of Agriculture and in the form of a register, can be used in the EU. Currently, there are over 1,000 herbicide trade names registered in Poland, which does not mean that they are available for sale. One of the most popular active substances is tribenuron methyl, which is present in as many as 32 products that differ mainly in the trade name, and to a lesser extent in the content and form. Typically, the license holder registers 2–4 names for one product. Herbicides registered for use by professional users – with appropriate training – contain from one to three active substances. Depending on the product, they may have the same or a different mechanism of action. The division of herbicides into HRAC groups is most important from the point of view of resistance prevention (fig. 1).

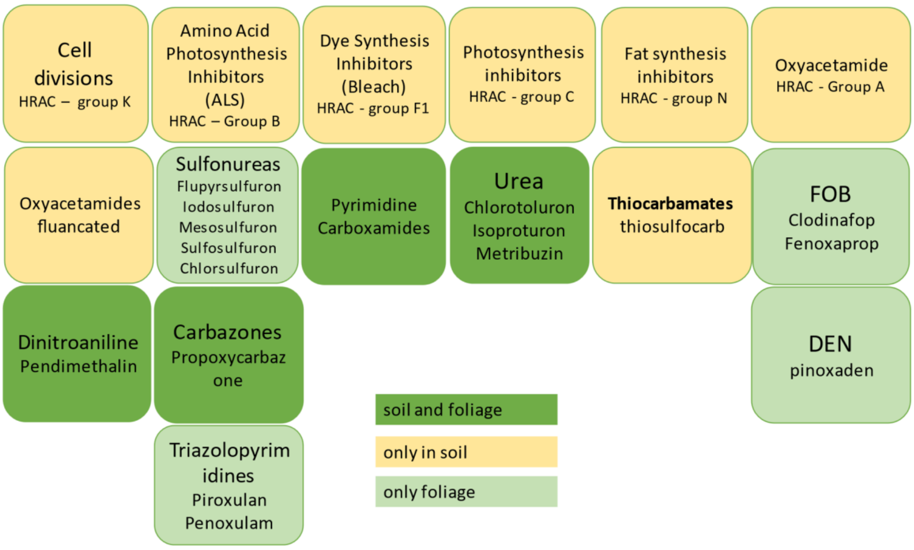

Fig. 1. Division of herbicides into HRAC groups

The Global Herbicide Resistance Action Committee (HRAC) has produced information on the 2020 review of the MoA herbicide classification. To support the adoption of responsible resistance management practices, CropLife International members have committed to including icons and mode groups on all crop protection product labels by 2023. In the meantime, the classification of herbicides in the innovative MoA technology has been updated [He et al. 2022, *Bioherbicides Market* 2022]. To ensure a global consensus between Herbicide Resistance Action Committee (global and regional organizations), CropLife (international and Australian organizations) and other herbicide associations (e.g. WSSA), this classification has been harmonized around the world and a transition has been made from alphabetic codes to numerical codes which are more global and sustainable [FAOSTAT 2022].

The division of herbicides into individual mechanisms of action and groups is not simple, but it is worth knowing it so that when selecting herbicide solutions, the preparations should be properly selected, so that their effectiveness is as high as possible in all conditions of use. One way of avoiding or minimizing the already existing problem of resistance is the so-called rotation of herbicides, i.e., alternating use of agents with different mechanisms of action. If there is a reduced effectiveness of the treatment with an agent that has been used for years. The reason is most often progressive resistance, and then it is not enough to use an agent with a different name, then a preparation containing a different active substance with a different mechanism of action should be used [Duke et al. 2022]. Currently, it often happens that the same active substance is present in many products from different manufacturers and differs in name, concentration of the active substance and other components indirectly affecting the effectiveness of the treatment [Duke et al. 2019, 2022]. Another way to counteract the spread of resistance to weeds is to use mixtures of active substances with different mechanisms of action. This solution gives higher efficiency due to the fact that the weed is in at least two places at the cellular level [Duke et al. 2022, He et al. 2022].

Pesticide toxicity

The most important feature of pesticides used in agriculture is their selectivity. A group of these compounds should be characterized by high toxicity in relation to pests, but low in relation to other organisms. In addition to the above features, they should be sufficiently durable. Therefore, herbicides should be biodegradable, which should be reflected in the environment. The durability of pesticides varies in a wide range, e.g., the disintegration time of fosdrin is short and amounts to 35 days, DDT is degraded in 4 to 30 years, and the pesticide shradan decomposes for 100 years [Wójtowicz and Szychowski 2014, Mołoń and Durak 2018]. It turns out, however, that a major disadvantage of pesticides is their lack of selectivity. In addition, some of them are unstable and under the influence of elevated temperature, humidity or photochemical transformations they transform into compounds of even greater toxicity [Kowalska and Kowalski 2019].

The mode of action of pesticides varies, and therefore, in many situations, they cannot be unambiguously classified. It is well known that organophosphate pesticides are extremely neurotoxic because they irreversibly inhibit acetylcholinesterase, an enzyme that hydrolyzes acetylcholine at the neuromuscular junctions and cholinergic synapses of the brain [Barr et al. 2004]. Highly water-soluble pesticides such as 2,4-D are less persistent in the environment and are likely to biodegrade quickly. Therefore, they are not exposed to accumulation in the soil, volatilization and bioconcentration in organisms [Katagi 2010]. Glyphosate has also been considered a relatively safe compound in the environment due to its rapid deactivation in soil through absorption and degeneration [Motharasan et al. 2018], research by Kowalska and Kowalski [2019] showed that the presence of glyphosate in the soil can even increase the activity of microorganisms, but it has recently been withdrawn. He et al. [2022] summarized the positive and negative sides of herbicides that have been observed in recent years, such as the use of solanyl diphosphate synthase (SPS), fatty acid thioesterase (FAT), plastid peptide deformylase (PDEF) and dihydroxy acid dehydratase (DHAD) in the production of.

For many years, there have been discussions among scientists and practitioners about the anticipated and perceived threats posed by pesticides to human health and the environment. Pesticides can enter the body through skin contact or inhalation [Nicolopoulou-Stamati et al. 2016]. After entering the body, organochlorine pesticides can cause adverse health effects, such as: endocrine disorders [Mnif et al. 2011], hematological and hepatic changes [Freire et al. 2015], and embryonic disorders [Kezios et al. 2013]. Studies by medical professionals have shown possible associations between exposure to organophosphate pesticides and serious health outcomes, including cardiovascular disease [Lim et al. 2015], reproductive system [Mehropour et al. 2014] and nervous [Steenland et al. 1994, He et al. 2022]. All these signals indicate the need to abandon traditional, chemical herbicides or other plant protection products in favor of safe, natural products (biopesticides).

Biopesticides

An alternative to chemical plant protection products used in agriculture are more and more often biopesticides of natural origin [Martyniuk 2012, Mfarrej and Rara 2018]. Biopesticides are preparations that contain substances of plant origin, e.g., secondary metabolites, plant growth regulators, as well as compounds of animal origin, such as pheromones [Orlikowski and Skrzypczak 2003, Mołoń and Durak 2018]. After the detection of dangerous chemical residues of pesticides in food and the increase in consumer awareness of food safety, social consumer organizations led to the banning of certain pesticides. As a result, interest in pesticides of plant origin has increased, which are increasingly used in organic farming. Currently, it is fashionable in the world to eat food produced with the use of harmless, preferably natural plant protection products. Plants that are a source of commercially available natural pesticides include, among others: pyrethrum (*Tanacetum cinerariifolium*) [Dolinsek et al. 2007, Sun et al. 2020], neem (*Azadirachta indica*) [Nisbet 2000, Boeke et al. 2004], sabadilla (*Schoenocaulon officinale*) [Nayak and Dibyarani 2020], and ryania (*Ryania speciosa*) [Arnason et al. 2012].

Few naturally occurring compounds are used in practice to control weeds. These are simple organic acids such as: acetic acid, an organic weed control agent [Dayan and Duke 2010, Duke et al. 2019]. Various plant essential oils are suitable for weed control, such as: lemongrass, clove, cinnamon, citrus and pine oil [Duke et al. 2019]. Some of the ingredients in these oils are interesting because of their unique or novel mode of action [Graña et. al. 2020]. However, all of these products are not as effective as commercial, synthetic herbicides, requiring much more weed control product at much higher cost. Commercial farmers use very little of these products due to cost and lack of effectiveness. For organic farmers, the cost of non-chemical weed control agents is lower than most commercial products. For example, Boyd et al. [2006] found that the total cost of a number of seedbed treatments, including labor, for weed control is significantly lower than for weed control with a clove oil product. The literature on the use of exotic essential oils as herbicides is extensive (e.g. Hazrati et al. 2017), however, the cost of these essential oils can be even higher than those already on the market as herbicides. The cost of weed control with these products can sometimes be higher than the value of the yield. There are still no all-natural commercial products that can compete with synthetic herbicides. These natural, commercial products are mainly used by small backyard farms that want greener pest control without the side effects and are not concerned about the cost.

There is also a group of compounds whose operation is based on the use of living organisms in them [Martyniuk 2012]. The microorganisms that are the active ingredients of these biopreparations include bacteria belonging to the genus Bacillus and Pseudomonas as well as fungi of the genus *Trichoderma*, *Pythium* and *Matharhizium*. A large group also includes biopreparations based on viruses, microscopic nematodes and mites [Kachhawa 2017]. Organic substances present in biopreparations, sources of carbon, energy and electrons are used by microorganisms, thanks to which they can reproduce, and organic substances are gradually biodegraded to harmless end products [Grzyb et al. 2019]. In the opinion of these authors, a necessary condition for the effective use of microbiological technology is the appropriate selection of a biopreparation containing such microorganisms that will find optimal conditions for operation in a given environment, i.e., have features that enable their adaptation and development. Probiotechnology is used in plant cultivation to fertilize the soil and improve the decomposition of post-harvest residues, in animal husbandry to improve the quality of bedding and reduce odors in farm rooms, in municipal management to dispose of sewage and waste, and in revitalization of the environment for water purification and soil phytoremediation [Nowak et al. 2013, Upadhayay et al. 2018, Horodyska et al. 2021, Książek-Trela et al. 2022].

In agriculture, essential oils obtained from plants, which are natural complex secondary metabolites characterized by a strong odor, volatility and lower density than water, are of increasing importance [Said-Al Ahl et al. 2017]. Grudzińska and Czerko [2016] evaluated the effect of peppermint and caraway oils on the germination of potato tubers during storage and the organoleptic properties of potatoes after cooking. These authors showed that the inhibition of germination after application of the oils depended on the cultivar grown. The peppermint preparation most effectively inhibited the germination of tubers of the Bursztyn cultivar (59.3% effectiveness), and the cumin preparation of tubers of the Stasia cultivar (60% effectiveness). Flesh structure and mealiness of potato tubers did not change after application of natural sprout growth inhibitors. The use of peppermint worsened the taste and odor of cooked tubers of all varieties. Similar studies were conducted by Zheljazkov et al. [2022] who investigated 18 essential oils and several pure compounds as sprout inhibitors. They showed that lemon balm oil (*Melissa officinalis* L.) inhibited germination, while oil from the seeds of *Coriandrum sativum* L. and a mixture of essential oils from *Lavandula angustifolia* Mill. and *Salvia sclarea* L. suppressed germination. Zheljazkov et al. [2022] further tested pure, isolated compounds on cultivars (Ranger Russet, Terra Rosa, and Dakota TrailBlazer), along with the main compound in *Melissa officinalis* (citral), where they proved that β-citronellol reduced sprout length and sprout count in all strains tested while citral and (+)-α-terpineol reduced sprout length and sprout count in 'Ranger Russet' compared to two potato cultivars controls.

Bioherbicydy

There is a great need for new weed control options in crops that can be provided by both natural phytotoxins and microbial bioherbicides. In recent times, farmers have been using biological weed control agents, made from microbes and certain types of insects. They are environmentally friendly and keep costs lower than conventional herbicides. Bioherbicides do not harm crops or human health. With the development of organic farming, these substances are gaining great popularity around the world. Compared to insect and crop pathogen control products, these tools are not yet fully utilized for weed control [Duke et al. 2022]. Natural phytotoxins can be used directly as herbicides, but this approach has not been as successful as using them as templates for synthetic herbicides. They can also be used to discover new modes of action and molecular targets for future herbicides. The development and approval by EU regulators of microbial bioherbicides for use in, for example, floodplain rice crops are relatively inexpensive. In addition, bioherbicides have a low environmental impact and have good social acceptance. Despite these advantages, however, their success is limited by narrow host specificity, quality control, short shelf life, microenvironmental requirements, and variable efficacy [Kaur et al. 2010, Ibáñez and Blázquez 2019, Frabboni et al. 2019]. New technologies can overcome these problems. In the US, microbial bioherbicides can be preparations of killed microorganisms containing phytotoxins, produced before killing them. This approach overcomes some of the disadvantages of using living organisms [Duke et al. 2022]. Natural products and weed control based on or inspired by microorganisms should play a greater role in the future.

Microbes associated with plants and plant growth traits have great potential to solve environmental problems and play a fundamental role in increasing plant biomass and yields in both greenhouse and field conditions [Duke and Pawles 2008]. Figure 2 illustrates the mechanism of action of bioherbicides.

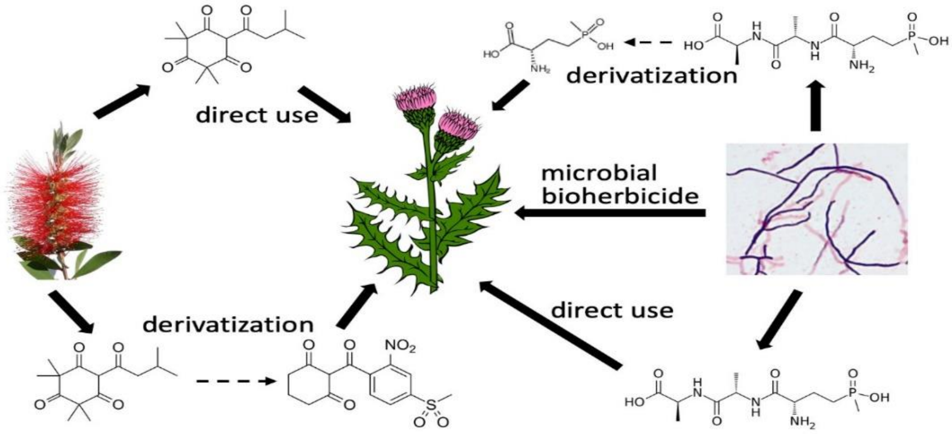

Fig. 2. Mechanism of bioherbicides [source: own adapted on Duke et al. 2022]

Examples of microbial bioherbicides for use in agriculture that have been commercialized at one time or gotten to the trade name stage. Some of the products were reintroduced with new trade names (tab. 1).

Table 1. Examples of microbial bioherbicides

Microbe and reference	Weed target(s) and status	Trade name	Year of introduction or registration
Alternaria cassia Bannon1988	*Cassia obtusifolia* *C. coccidentalis* *Crotalaria spectabilis* Never commercialized	Casst™	never
Alternaria destruens Bewick et al. 2000	*Cusucta* spp. Discontinued	Smolder™	2005
Chondrostereum pupureum Hintz 2007	*Populus* and *Alnus* spp. Unknown	Chontrol™	2004
Colletotrichum acutatum Morris 1989	*Hakea sericea* Discontinued	Hakatak™	1990
Colletotrichum gloeosporio-dides f. sp. *aeschynomene* Cartwright et al. 2010	*Aeshynomene vigrinica* Available on demand	Collego®	1982
Colletotrichum gloeosporiodides f. sp. *Malvae* Boyetchko et al. 2007	*Acacia earnsii* and *A. pycnantha* Discontinued	Stumpout™	1997
Cylindrobasidium leave Morris et al. 1999	*Acacia mearnsii* and *A. pycnantha* Discontinued	Stumpout™	1997
Phoma macrostoma Bailey et al. 2011	many broadleaf weed species Available	Bio-Phoma™	2016
Phytophthora palmivora Ridings 1986	*Morrentia odera-ta* Discontinued	DeVine®	1982
Pseudomonas fluorescens Kennedy et al. 2001	*Bromus tecto-rum* Discontinued	D7®	2014
Puccinia canaliculata Phatak et al. 1983	*Cyperus esculentus* Discontinued	Dr. Biosed-ge™	1987
Puccinia thlaspeos Knopp et al. 2002	*Isatis tinctorial* Discontinued	Woad War-rior®	2002
Sclerotina minor Watson 2018	*Taraxacum officinale* Discontinued	Sarritor®	2009
Several fungi Gale and Goutler 2013	*Parkinsonia aculea-te* Available	Di-Bak®	2019
Streptomyces scabies O'Sullivan et al. 2015	several grass and broadleaf weeds Never commercialized	Opportune™	2012
Tobacco mild green mosaic vírus Charudattan and Hiebert 2007	*Solanum viarum* Available	SolviNix™	2014
Xanthomonas campestris pv. *poae* Imaizaumi et al. 1999	*Poa annua* Discontinued	Camperico™	1997

Source: own adapted on Duke 2022.

Allelochemicals and allelopathic compounds as bioherbicides

Weeds, starting from the first application of synthetic herbicides in plant protection systems, constantly develop resistance due to the long-term exploitation of single-target herbicides in plants. For example, this was the case with triazine herbicides, photosynthesis inhibitors, which effectively eliminated many species of weeds. However, inappropriate use of herbicides against weeds inhabiting fields, application at an incorrect development stage and in unsuitable weather conditions contributed to the accumulation of active compounds in the soil, the accumulation of seeds of many weed species there and the acceleration of the evolution of the resistant of biotypes weeds [Duke 2005, Busi et al. 2013]. So far, over 300 species and over 400 herbicide-resistant weed biotypes have been identified [Owen and Zelaya 2005, Gaines et al. 2020]. Most of them are resistant to group B, C1 and A herbicides on the HRC scale, which are inhibitors of acetolactate synthase (ALS), as well as photosystem II and acetyl-CoA carboxylase. Of the known weed species, ten pose the greatest threat to crops that cause serious yield losses, including ryegrass (*Lolium rigid* Gaud.), wild oats (*Avena fatua* L.) and red amaranth (*Amaranthus retroflexus* L.). The fairly rapid evolution of weed species resistant to herbicides requires rapid, new, innovative solutions to limit the economic losses generated by weeds may be greater than those caused by other pathogens. Since it is unlikely to move away from chemical herbicides with current agricultural practices, it is necessary to develop new classes of herbicides with new mechanisms of action and previously unexploited target sites. Currently used synthetic herbicides are not approved for use in organic farming. In addition, the application of plant protection products also requires social acceptance [Sammons and Gaines 2014, Yan et al. 2018]. The number of synthetic chemicals with new destinations is dropping drastically. Ecological trends in weed control force scientists to reach for new, innovative sources and tools. Natural compounds are a huge field for research and for discovering new, environmentally safe herbicides, the so-called "bioherbicides", which are based on compounds produced by living organisms. According to the CAS (Chemical Abstracts Service) registry, a large group of plant secondary metabolites is represented among 24 million organic compounds. Some of these compounds are involved in allelopathic interactions.

Recently, there has been much information about the allelopathic potential of essential oils from various plant species on weed germination. Batish et al. [2004] evaluated the effect of volatile eucalyptus oil from the leaves of *Eucalyptus citriodora* on some plant species such as: *Triticum aestivum*, *Raphanus sativus*, *Cassia occidentalis*, *Amaranthus viridis* and *Echinochloa crus-galli*. A complete inhibition of germination was observed in the case of *Amaranthus viridis*, and the smallest effect was noted on *Raphanus sativus* plants. The bioherbal activity of the hydrodistilled volatile oil from *Artemisia scoparia* against the following weeds: *Achyranthes aspera*, *Cassia occidentalis*, *Parthenium hysterophorus*, *Echinochloa crus-galli*, and *Ageratum conyzoides* was studied by Indian scientists [Kaur et al. 2010]. The authors obtained the highest effectiveness of the oil on *Echinochloa crus-galli* and *Parthenium hysterophorus* plants. Ibáñez and Blázquez [2019], in the cultivation of cucumber and tomato and the invasive plant *Nicotiana glauca*, tested the effectiveness of *Eucalyptus citriodora*, *Lavandula*, *angustifolia* and *Pinus sylvestris* oils on weeds (*Portulaca oleracea*, *Lolium multiflorum* and *Echinochloa crus-galli*). The most sensitive weed in tomato cultivation was the species *Lolium multiflorum*, especially in terms of the use of lavender essential oil, and in the case of cucumber, no significant reduction in weed germination was found when *Lavandula angustifolia* and *Pinus sylvestris* were applied. The evaluation of the effectiveness of weed control in organic cultivation of chamomile (*Matricaria chamomilla* L.) was carried out by scientists from a university in Italy [Frabboni et al. 2019]. They evaluated the allelopathic effects as natural herbicides of two essential oils extracted from oregano (*Origanum vulgare* L.) and rosemary (*Rosmarimum officinalis* L.). Their effectiveness depended on the concentration of substances and weed species. The reduction of *Amaranthus retroflexus* L., *Portulaca oleracea* L., *Convolvulus arvensis* L., *Eruca sativa* L. and *Papaver rhoeas* L. after application of the oils was 50–86%, while *Solanum nigrum* L., *Fumaria officinalis* L., *Beta vulgaris* L., *Lamium maculatum* L., *Avena* spp. L., *Veronica persica* L. – 29–39%.

Allelopathins are products of secondary metabolism and are non-nutritive primary metabolites [Busi et al. 2013] and are representatives of many chemical groups, which include: triketones, terpenes, benzoquinones, coumarins, flavonoids, terpenoids, strigolactones, phenolic acids, tannins, lignins, fatty acids and non-protein amino acids. These biochemicals are synthesized during the shikimate pathway or, in the case of essential oils, the soprenoid pathway. They can be divided into 10 categories [Gaines et al. 2020] according to their different structures and properties as: water-soluble organic acids, straight-chain alcohols, aliphatic aldehydes and ketones; simple lactones; long chain fatty acids and polyacetylenes; quinines (benzoquinone, anthraquinone and complex quinines); phenols; cinnamic acid and its derivatives; coumarins; flavonoids; tannins; steroids and terpenoids (sesquiterpene lactones, diterpenes and triterpenoids) [Gaines et al. 2020, Duke et al. 2022]. Allelochemicals are released into the environment by various plant organs, such as roots, rhizomes, leaves, stems, bark, flowers, fruits and seeds (fig. 3a) [Sołtys et al. 2013].

The number of allelopathic interactions is negative and positive interactions are rare. Allelopathic compounds affect mainly the germination and growth of neighboring plants by interfering with their physiological processes, including photosynthesis, water and hormonal balance or respiration. At the basis of their action is primarily the inhibition of enzyme activity. The ability of an allelochemical to inhibit or retard plant growth and/or seed germination is defined as “allelopathic potential” or “phytotoxic potential”. An example is soil depletion due to the accumulation of allelopathy’s, which can be prevented by fertilizers and crop rotation. Plants producing allelopathy’s are considered “donors”, and plants to which allelopathy’s are directed are called “targets” or “acceptors”. The strength of the allelopathic effect is modified in the soil (Fig. 3b). Most allelochemicals penetrate into the soil as active compounds, e.g., cyanamides, heliannuols, phenolic acids or momilactones, etc. Some of them are modified to a form activated by microorganisms or habitat conditions (pH, temperature, light, oxygen, humidity, etc.) [Sołtys et al. 2013, Duke et al. 2022].

3a 3b

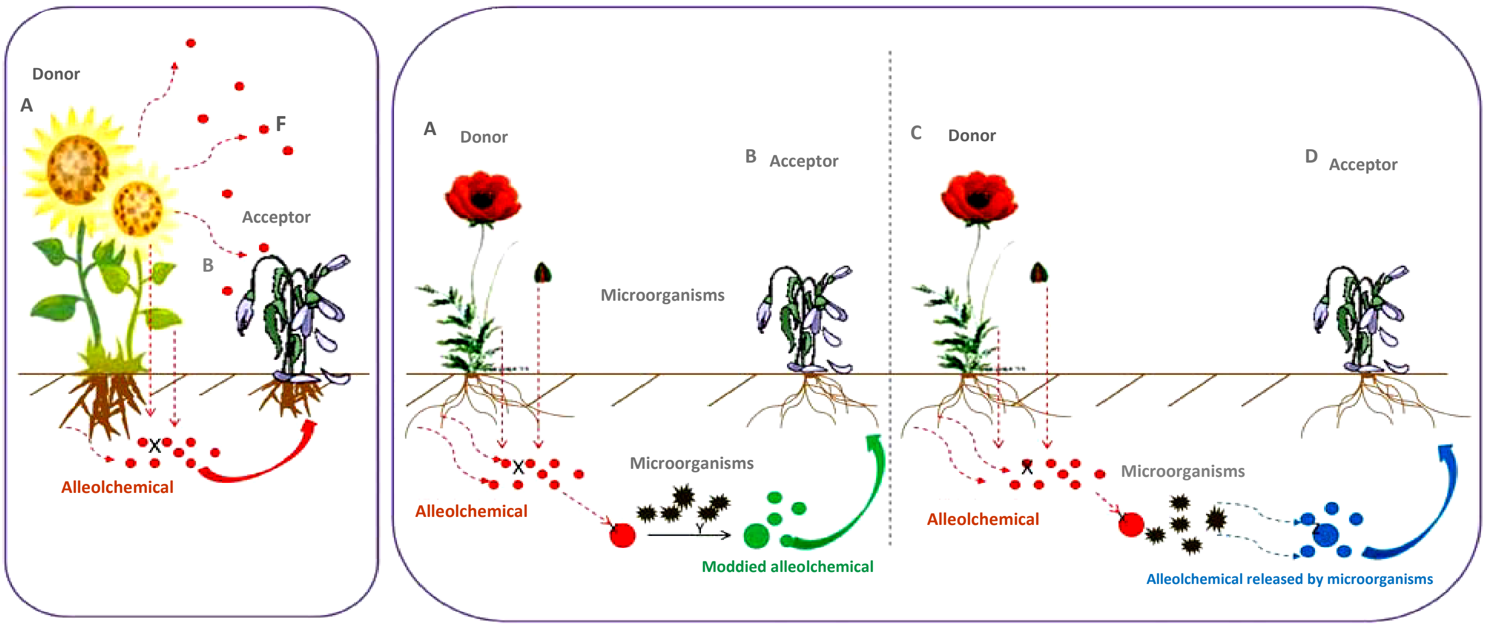

Fig. 3. Nature of allelopathic interactions. (3a) Plant A releases X and F allelochemicals that directly affect the growth of plant B. (3b) Left side: plant A releases the X allelochemical, modified or activated by microorganisms, into the Y allelochemical, affecting the growth of plant B; right side: plant A releases the X allelochemical, which in turn stimulates the microorganisms to produce the Z allelochemical, which affects the growth of plant B

Source: own adopted on Sołtys et al. [2013]

Using bioherbicides as templates for better herbicides

Simplifying the structure of natural compounds to reduce costs or change their structure has been a major success, both in the production of commercial pesticides and pharmaceuticals. There are relatively few commercial herbicides whose origin can be compared to natural products [Sparks et al. 2017, Duke et al. 2022, He et al. 2022]. Similarities between commercial herbicides and natural compounds may be coincidental as there is no public documentation of their derivatization from a natural molecule. Two examples of such similarities are the very strong similarity of the herbicide endothall to the natural compound cantharidine, which is obtained from insects, which is very phytotoxic, and the herbicide cinmethylin, which is similar to the monoterpene 1,4-cineol [Yan et al. 2018]. Both have similar modes of action unique to herbicides. Cimetiline inhibits acyl-ACP thioesterase and endothall inhibits serine-threonine protein phosphatase [Campe et al. 2018]. These modes of action have not been clearly defined and recognized by the Herbicide Resistance Action Committee. There are cases of potent natural phytotoxins with new target molecular proteins that can be modified to improve their physicochemical properties or to reduce the production costs of this compound. For example, the microbial tetrapeptide tentoxin inhibits the chloroplast CF1 ATPase and is very active against key weed species at low concentrations and is harmless to corn and soybeans [Duke 2005, Duke et al. 2019]. Efforts have been made to produce analogs to reduce costs and improve the herbicidal activity of this molecule [Yan et al. 2018]. Similarly, the potent bacterial phytotoxin hydantocidin, which damages plants by inhibiting adenyl succinate synthetase, has been the subject of attempts to create more effective herbicides. Hydantocidin is a pro-herbicide that must be phosphorylated to inhibit its target enzyme [He et al. 2022]. This target enzyme is not used by any commercial herbicide. These are examples of potential herbicides with novel modes of action that would be very useful in managing the evolution of herbicide resistance, even though novel modes of action alone are not a solution to this problem [Gaines et al. 2020]. There are also examples of natural phytotoxins that share the mode of action of commercial herbicides but bind to the molecular target differently than commercial herbicides, rendering target-resistant weeds susceptible to them. For example, the fungal metabolite tenuazoic acid is a PSII inhibitor that binds D1 differently than triazine herbicides. Derivatives of this compound have been patented as herbicides [Jumper et al. 2021]. Tenuazonic acid itself is a good herbicide for cotton, which is naturally tolerant to it. This acid, a hypothetical non-host selective mycotoxin isolated from *Alternaria alternata*, is a key factor in brown spot disease on Crofton weeds (*Ageratina adenophora*) and other crops. Previous studies have shown it to be a natural photosystem II inhibitor that binds to the D1 protein to block electron transfer. Although the crude extract of the *A. alternata* metabolite containing TeA has been bioassayed, the herbicidal activity of the synthesized TeA has not yet been evaluated and awaits testing [He et al. 2022].

Bioherbicides used to identify new targets

Herbicides with new modes of action are in high demand due to the evolution of weed resistance to herbicides from almost all classes of modes of action [Duke et al. 2019, Gaines et al. 2020] and the lack of commercial herbicides with new modes of actions in the last 30 years [Duke 2005, 2008, Duke et al. 2019, 2022]. Therefore, herbicides with novel molecular targets are needed for herbicide resistance management strategies. One way to achieve this is to determine that inhibiting the new molecular target will kill the plants. For several possible reasons, not all potential molecular targets are suitable as herbicide targets [Dayan and Duke 2010]. However, there are many natural compounds that kill plants by inhibiting of enzymes to molecular targets that are not among those available in commercial herbicides, indicating that these are potentially good targets to guide the discovery of new herbicides [He et al. 2022, *Bioherbicides Market* 2022]. Since then, several new molecular targets of microbial metabolite phytotoxins have been promoted.

Prospects for the bioherbicides market

With the development of organic farming, bioherbicides are gaining immense popularity around the world. Management of insect and plant pathogens with microbial biopesticides is much more effective. Killed microbe preparations containing potent phytotoxins avoid some of the problems associated with live microbes, and such products are under development. This type of product may also offer more than one new mode of action in a single formulation. Accurate and intelligent spraying systems can improve the economics of both natural product-based herbicides and microbial bioherbicides [He et al. 2022]. Killed microbe preparations containing potent phytotoxins avoid some of the problems associated with live microbes, and such products are under development. This type of product may also offer more than one new mode of action in a single formulation. Accurate and intelligent spraying systems can improve the economics of both natural product-based herbicides and microbial bioherbicides [Duke et al. 2022].

The analysis of the bioherbicides market segment carried out for 2021 shows that, according to application, fruit and vegetables are considered the main application segment on the bioherbicides market, due to their widespread use in the cultivation and protection of agricultural products. It is expected that the demand for fruit and vegetables, with the current trend of organic farming, will be the main factor responsible for the growth of this market segment. Turf grass and ornamental grass turned out to be the fastest growing segment of these applications, which is expected to increase even three times in the future. Commercially, bioherbicides are most commonly used around railroad tracks to remove weeds. The North American market has the largest share in the global market of bioherbicides, in regional terms, compared to the market in other regions of the world. The support of governments around the world for environmental and health protection and the high demand for organic food are expected to drive market growth in the region. Today and in the future, Europe will account for the largest share of the global market, followed by markets in the Asia-Pacific region. The Asia-Pacific market is expected to see moderately faster revenue growth over the coming year. It is also expected that the demand for organic products in countries such as China, India and Australia will drive market growth in the region [FAO 2022, FAOSTAT 2022].

Scope of the bioherbicides market

The global market of bioherbicides in 2021 is estimated at approx. USD 1.6 billion. It is expected that by 2030 this value will increase threefold. The sources of bioherbicides are mainly microbiological, biochemical and other materials. Bioherbicides are produced in liquid, granular or other forms. Their use is most often carried out by treating seeds, in soil applications, foliar applications during vegetation on the leaves and after harvest. Bioherbicides are used in agricultural production, in the cultivation of cereals, oilseeds and legumes, in the production of fruit and vegetables, as well as in non-agricultural crops, in the cultivation of lawns and ornamental plants and in plantation crops (tab. 2) [FAO 2022, FAOSTAT 2022]

Table 2. Global bioherbicides market in 2021 and forecast for 2022–2030

Specification	Details		
The base year	2021	forecast period	2022–2030
Historical date	2017 to 2021	market size in 2021	1,6 billions of US dollars
Prognosis period 2022–2030	14.6%	market size in 2029	4.7 billions of US dollars
Segments	source	microbiological, biochemical, other	
	via the recepture	granules, liquid	
	via the application	seed treatment: soil application, leaves, after harvest, agricultural products, cereal grains, oilseeds and pulses, fruits vegetables, non-agricultural crops, turf and ornamentals, plantation crops	

Source: FAO 2022, FAOSTAT 2022.

The ranking of the bioherbicides market by region is as follows: North America > Europe > Asia Pacific > Middle East and Africa > South America [FAO 2022, FAOSTAT 2022].

Bioinsecticides

Insecticidal pyrethrins are obtained from achenes found in flower heads and are a component of a natural pesticide that is neurotoxic and very effective in combating many insect species [Hitmi et al. 2000]. Neem-based products are extracted from the neem tree *Azadirachta indica*, which belongs to the *Meliaceae* family [Schmutterer 1990]. Sabadilla is used as a selective natural insecticide, it is present in the ground seeds of *Schoenocaulon officinale* (*Liliaceae*) growing in Central and South America [Nayak and Dibyarani 2020]. It is effective against thrips, bed bugs, caterpillar larvae and snails. Ryania is an extract from the South American shrub *Ryania* sp. containing the diterpene alkaloid ryanodine, which is a contact insecticide intended for the control of pests of horticultural and ornamental crops. Its toxic effect consists in blocking Ca^{+2} ion channels [Arnason et al. 2012]. Researchers in Tunisia and Algeria have demonstrated effective insecticidal effects of essential oils from *Pinus brutia*, *Laurus nobilis*, *Liquidambar orientalis*, *Juniperus communis* subsp. *nana* Willd, *Cupressem pervirens*, *Lavandula stoechas*, *Lavandula angustifolia*, *Eucalyptus camaldulensis* and *Thymus vulgaris* against pine wandering moth larvae [Jemba et al. 2012]. *Mentha piperita* oil repels ants, flies, moths and is also effective against *Callosobruchus stepmother* and

Tribolium castanum [Kordali et al. 2005]. *Zingiber officinale* and *Piper cubebaberry* rhizome oils show insecticidal and anti-nutritional activity against *Tribolium castaneum* and *Sitophilus oryzae* [Chaubey 2012]. Various parts of plants (bark, flowers, leaves, roots, seeds and stems) are used to protect field crops and in warehouses in Uganda, which are obtained from plants such as: *Azadirachta indica*, *Cannabis sativa*, *Capsicum annuum* L. (syn. *Capsicum frutescens* L.), *Cupressus lusitanica* Mill., *Moringa oleifera* Lam., *Musa* spp., *Nicotiana tabacum, Tagetes erecta* L., *Tagetes minuta* L. and *Tephrosia vogelii* [Mugisha-Kamatenesi et al. 2008]. Plants are burned to obtain plant ash, which is then used to control pests such as the corn borer (*Busseola fusca*), the banana beetle (*Cosmopolites sordidus*), the bean fly (*Ophiomyia phaseoli*), the grain moth (*Sitotroga cerealella*), the corn borer (*Maruca vitrata* and *Nezara viridula*) and aphids (*Aphis craccivora*, *Aphis fabae* and *Rhopalosiphum maidis*). Eugenol (main ingredient, e.g., clove and cinnamon), carvacrol (found in thyme, thyme, marjoram, cumin, oregano), citronellal (in lemongrass), thymol (in thyme and oregano), terpineol (in nutmeg and orange oil), anethole (in anise oil). This author proved that the following substances have the greatest toxic effect on the tobacco caterpillar (*Spodoptera litura*): eugenol, terpineol, citrolellal.

LEGAL ASPECTS IN THE FIELD OF BIOPESTICIDES

EU chemicals and pesticides legislation aims to protect human health and the environment and prevent trade barriers. These include rules on the marketing and use of certain categories of chemical products, a set of harmonized restrictions on the marketing and use of certain dangerous substances and preparations, and rules for dealing with major accidents, as well as procedures for the export of dangerous substances. EU chemicals policy changed dramatically with the adoption in 2006 of regulation 1907/2006/ec [Regulation (EC) No 1907/2006]. The regulation entered into force on 1 june 2007 and thus established a new legal framework for the development, testing, manufacturing, marketing and use of chemicals. Increasing the level of protection of human health and the environment throughout the union and worldwide should be based on and implemented by the same identification and labeling criteria to describe hazardous chemicals. Therefore, in 2008, regulation no. 1272/2008/EC on the classification, labeling and packaging of substances and mixtures (CLP) [Regulation (EC) No 1272/2008] was issued in order to adapt the EU system to the global harmonized classification system agreed at the un and labeling of chemicals (GHS). In 2009, the pesticides package was adopted, which includes: directive 2009/128/EC on the sustainable use of pesticides, aimed at reducing environmental and health risks while maintaining crop productivity and improving the control of pesticide use and distribution. On 14 October 2020, the commission published a new chemicals strategy for sustainable development [European Commission 2020]. It is part of the EU’s zero pollution target, which is a key commitment under the European green deal. Under the European green deal, and in particular the farm to fork and biodiversity strategy, the commission will take action to reduce the use and risks of chemical pesticides by 50% by 2030, including the use of more hazardous pesticides. To this end, the commission will review the sustainable use of pesticides directive and promote wider use of alternative ways to protect crops from pests and diseases. The new green deal is therefore a response to the great challenges facing the world, including Europe. It is also an ambitious plan to transform the economy of the eu area, which aims to ensure a sustainable future for current and future generations.

SUMMARY

The use of pesticides in agriculture is largely responsible for obtaining higher yields of plants of high quality and suitability for food processing. Obtaining a raw material with such characteristics may, however, be associated with a negative impact of pesticides on health and the natural environment. Therefore, it is justified to search for and market non-toxic, rapidly biodegradable preparations, which can also be used in ecological farming systems. Such products can be biopesticides. They have a low environmental impact and are widely accepted by society. Despite their advantages, their use is limited by, for example, narrow host specificity, multiple quality checks, short shelf life, microenvironmental requirements and variable efficacy. New technologies in plant protection can overcome these problems. Over the last 20 years, many effective herbicides with new modes of action (MoAs) have come onto the market. The positive and negative sides of herbicides are summarized. Some commercial herbicides have been developed based on new targets, such as solanesyl homogentisate transferase (HST) or dihydroorotate dehydrogenase (DHODH) [He et al. 2022, *Bioherbicides Market* 2022], which will provide a new reference and idea for the molecular design of herbicides in the future.

Microbial bioherbicides may be killed micro-organism preparations containing phytotoxins that are prepared before the micro-organisms are killed. This approach overcomes some of the disadvantages of using living organisms. Natural products and weed control based on or inspired by microorganisms should play a greater role in the future. Allelopathy phenomena and phytotoxic interactions between plants can support weed control. Allelochemicals, called biocommunicators, seem to be a good challenge for combining traditional agricultural practices and new approaches in weed and pest control strategies. Although they have already been used to defend crops against pathogens, insects and nematodes, in parallel with some attempts to use them to control weeds. In sustainable and organic agriculture, crop rotation, cover crops, dead and living mulch are used for this purpose. In natural ecosystems as well as in agricultural systems, allelopathic interactions are involved in every aspect of plant growth, as they can act as both stimulants and suppressors. The multi-faceted approach and 'plant-plant' and 'plant-microbial' interactions in ecosystems, as well as current research at the molecular, cytological or physiological level, allow us to better understand and understand the processes taking place in the environment. Knowledge about the toxic properties of water extracts of various allelopathic plants provides the basis for creating an innovative approach to weed control.

Strict legislative regulations in the EU made large companies interested in this issue out of concern for the environment and started research and development activities. For example, the British start-up MoA dealing with agricultural biotechnology raised huge funds to solve problems related to herbicide resistance by discovering new, alternative and sustainable technologies [*Bioherbicides Market* 2022].

CONCLUSIONS

1. Pesticides whose active substances are dangerous to human health and the environment and should be systematically removed from the Register of plant protection products and withdrawn from trade, and the chemical compounds replacing them should be subject to appropriate comparative assessment procedures.

2. The most important factor influencing the search for new tools to combat diseases and pests of crop plants is the progressive evolution of the resistance of these populations to currently used pesticides.

3. In order to ensure a huge demand for new possibilities of weed control in agricultural crops and to ensure food security for humans and animals, new, innovative plant protection products must be introduced. These can be natural phytotoxins or microbial bioherbicides. These tools are currently not fully used for weed control. Natural phytotoxins can be used directly as herbicides, but it is more effective to use bioherbicides as templates for synthetic herbicides. They can also be used in molecular targets for future herbicides.

4. High use of bioherbicides, instead of tillage and chemical weed control, will preserve natural resources and is one of the key factors for market development. This will make it possible to increase food production and improve its quality, as well as to improve the sustainability of the natural environment.

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