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Review

Applications and development trends in biopesticides

Pengfei Leng[1], Zhiming Zhang[1], Guangtang Pan[1] and Maojun Zhao[2]*

[1]Key Laboratory of Biology and Genetic Improvement of Maize for Southwest China, Ministry of Agriculture; Maize Research Institute, Sichuan Agricultural University, Ya'an 625014, China.
[2]College of Biology and Science, Sichuan Agricultural University, Sichuan Yaan 625014, PR China.

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Biopesticides are very effective in the agricultural pest control without causing serious harm to ecological chain or worsening environmental pollution. The research and development of practical applications in the field of biopesticides greatly mitigate environmental pollution caused by chemical pesticide residues and promotes sustainable development of agriculture. Since the advent of biopesticides, a large number of products have been released, several of which have already played dominant roles in the market. The development of biopesticides stimulates modernization of agriculture and will, without doubt, gradually replace chemical pesticides. Many biopesticides are ideal substitutes for their traditional chemical counterparts in pollution-free agricultural production, but some of them display certain toxicity; this should be taken into consideration by the researchers in the field. In this paper, we discuss the current development and application of biopesticides from various categories, the problems occurring in the process of their development and proposing the introduction of various constraints. We review various studies and analyze the development trends in biopesticides in agriculture, demand, market and other fields.

Key words: Biopesticides, application status, constraint, development trends.

INTRODUCTION

Over years, chemical pesticides had made a great contribution to the fight against pests and diseases. However, their widespread and long-term use resulted in insecticide resistance and biomagnifications of insecticides, which in turn resulted in restrictions on their export. Problems, like soil and water contamination and dramatic increase of the harmful residues in many primary and derived agricultural products arose, which endangered both the general environment and human health. It is estimated that the financial cost of the damage to the environment and social economy is about $ 8.1 billion a year (Shen and Zhang, 2000). The use of synthetic organic insecticides in crop pest control programs around the world had caused tremendous damage to the environment, pest resurgence, pest resistance to insecticides, and lethal effects on non-target organisms (Abudulai et al., 2001).

As early as 7th to 5th century BC, Chinese farmers had made use of plants, such as *Illiciumlasnceolatum* A.C.Smith to prevent pests, and China was one of the earliest countries that used biopesticides. "Biopesticides are certain types of pesticides derived from such natural materials as bacteria, plants, animals, and certain minerals" (US Environmental Protection Agency Pesticides, 2008). Based on the natural resources from which they are isolated, biopesticides are classified as microbial pesticides, botanical pesticides, zooid pesticides and genetically modified plants. The number of areas in which they were used increased year by year; they were fast becoming the preferred choice for pest control. Biopesticides were usually applied to control rather than to eradicate pests, often incorporating a delay factor; they were also more selective than chemical pesticides. In fact, most biopesticides had the advantage of higher selectivity and non-target biological safety. According to the research of Cheng (2000), the KT50 of toosendanin (an insecticidal component isolated from the fruits of *Melia azedarach* L.) in ladybug was over 1080 min while that of methyl 1605 (also named parathion methyl, developed by I.G. Farben AG) was only 78.1min. The biopesticides characteristics also included low-residue and high-performance, fewer poisonous side effects and

*Corresponding author. E-mail: pfleng@163.com.

good compatibility with the environment. The resistance to biopesticides in target organisms was not easily generated, unlike in many cases of their chemical counterparts. They are fast becoming a new trend in the global pesticide industry.

RESEARCH AND DEVELOPMENT OF BIOPESTICIDES

Over the past 10 years, with the rapid development of new techniques, such as molecular biology, genetic engineering, protein engineering and others, all gradually improving the biopesticides production, the field had developed excellent application prospects, with extensive social and economical benefits. The superior characteristics of biopesticides attracted more attention than ever before and made them a hot spot of research in biotechnology institutions and companies. The research and application of biopesticides had been well developed and biopesticides gradually replaced the highly toxic pesticides in the market. In recent years, chemical pesticides' production declined by 2% per year (Cheng et al., 2010), while biopesticides' output increased at the annual rate of 20%. In 2005, the total demand for all kinds of biopesticides in China reached 145,000 tons, while the total sales were valued at about 0.8 to 1 billion yuan. There were almost 122 biochemical pesticide active ingredients registered with the Environmental Protection Agency (EPA), which include 18 floral attractants, 20 plant growth regulators, six insect growth regulators, 19 repellents, and 36 pheromones (Steinwand, 2008).

In China, the research and application of biopesticides began in early 1950s. In 2006, Sichuan Academy of Agricultural Science succeeded in developing nano-pesticides (<100 nm) from a plant source, with advantages of environmental protection, high efficiency and low toxicity, which had a direct effect on pest control practices (Gao, 2006). In China, *Bacillus thuringiensis* (*B.t*) insecticides account only for 2% of the market, cotton bollworm viral insecticides for 0.2%, and botanical pesticides' market share is about 0.5%. Zhu (2009) predicts that "biopesticides could replace more than 20% of chemical pesticides during the next 10 years". There were more than 30 research institutions and 200 biopesticide enterprises (about 2000 pesticide manufacturing enterprises) in China, with annual production of approximately 100,000 tons (Cheng et al., 2010). In Canada, between 1972 and 2008, the Pest Management Regulatory Agency approved registration of 24 microbial active substances with 83 formulations. The majority of the registrations (55/83) occurred since 2000 and at the beginning of 2008 there were 10 new products (a combination of new active substances, strains, formulations, and uses) under regulatory evaluation (Bailey et al., 2010). The main varieties are *B.t.* pesticides, botanical pesticides (rotenone, saponin, etc.), viral pesticides (Heliothis Armigera Nuclear Polyhedrosis Viruses, etc.), fungal pesticides (Trichoderma, etc.) and plant growth regulation pesticides (gibberellin, etc.).

There had been about 30 kinds of commercialized biopesticides in the world (Xu, 2008) up to 2009. In 1997, the sales of *B.t.* products reached $ 984 million and went up to $ 3.6 billion in 2005. In 2006, the global leading species of biopesticides were as follows: *B.t. CryF1*, *NRRL21882* (*Aspergillus flavus*), *Bacillus licheniformis* strain *SB3086*, etc (Wang, 2006). Developed countries pay great attention to the projected rapid pace of the development of biopesticides. In the early stage, few kinds of biopesticides were registered in developed countries; only 16 were registered in America in 1996, while 1090 products had been registered by the end of 2003, with product sales of nearly $ 2.2 billion. As of October 2008, there were 327 biopesticides registered in China, accounting for 1.6% of total registered pesticide products (Institute for the Control of Agrochemicals, Ministry of Agriculture (ICAMA), 2008). In India, by 2006 only 12 biopesticides (such as *B.t.*, *Trichoderma*, *Pseudomonas*, and *Beauveria* species) had been registered, but 194 substances were listed as chemical pesticides (Gupta, 2006). And in Japan, there were over $ 9 million in sales of biopesticides each year, as described by Kunimi (2007). In 2008, from January to November, biochemical pesticides and microbial pesticides manufacturing industry in China achieved a total industrial output value of 9.6 billion yuan, the increase of 45.20% over the same period of the preceding year. The total profit reached 624 million yuan, showing an increase of 29.98%. The new developed and registered biopesticides are increasing at a rate of 4% each year and the market share of biopesticides will rise to 30% (Cheng et al., 2010).

CATEGORIES OF BIOPESTICIDES

Microbial pesticides

Microbial pesticides are some of the earliest developed and widely used biopesticides. Russia, Australia, the United States, Canada, Japan and other countries have done a lot of research on microbial pesticides. EPA indicates that more than 200 products are sold in the United States, compared to only 60 similar products available in the European Union. In Japan, 231 host-virus associations, 63 fungi, 38 protozoa, 15 bacteria and five nematodes had been reported (Table 1) (Kunimi, 2007). Until 2003, 168 viruses (1663 host-virus associations), 411 fungi, 1504 protozoa, 51 bacteria and 146 nematodes had been registered in the global insect pathogen database (Braxton et al., 2003), and 270 bacterial products, 22 fungal products, and 35 viral products were registered in China until 2008 (ICAMA, 2008). In total, at least 410 biopesticide production units had been

Table 1. Microbial insecticides registered in Japan.

Pathogen	Target pest	Trade name	Dealer/Company	Year of the first registration
Viral insecticides				
Adoxophyes orana granulovirus (GV)+Homona magnanima GV	*Adoxophyes honmai and Homona magnanima*	Hamaki-Tenteki	Arysta Life Science Co.	2003
		Kayaku Hamaki-Tenteki	Nippon Kayaku Co. Ltd.	2004
Bacterial insecticides				
Bacillus thuringiensis kurstaki	Lepidopteran larvae	Toarowa[a]	Otsuka Chemical Co. Ltd.	1981
	Lepidopteran larvae	Esmark	Sumitomo Chemical Co. Ltd.	1998
	Lepidopteran larvae	Guardjet	Kubota Co.; Syngenta Japan Co. Ltd.	2001
	Lepidopteran larvae	Dipol	Sumitomo Chemical Co. Ltd.	1982
	Lepidopteran larvae	Tuneup	SDS Biotech Co. Ltd.	2000
	Lepidopteran larvae	Fivestar	Agro-Kanesho Co. Ltd.	1996
	Lepidopteran larvae	BioMax DF	Nihon Green & Garden Co.	2002
	Lepidopteran larvae	Esmark	Sumitomo Chemical Co. Ltd.	1998
Bacillus thuringiensis aizawai	Lepidopteran larvae	Quark	Arysta Life Science Co.	1999
	Lepidopteran larvae	XenTari	Arysta Life Science Co.	1997
	Lepidopteran larvae	Florbac	Sumitomo Chemical Co. Ltd.	2001
	Lepidopteran larvae	Sabrina	Meiji Seika Kaisha, Ltd.	2006
	Lepidopteran larvae	Sabrina	Sankei Chemical Co. Ltd.	
Bacillus thuringiensis aizawai +kurstaki	Lepidopteran larvae	Bacilex	SDS Biotech Co. Ltd.	1982
Bacillus thuringiensis japonensis	Cockchafers and white grubs	BuiHunter	Sumitomo Chemical Co. Ltd.	2001
Fungal insecticides				
Beauveria bassiana	Thrips, whiteflies, diamondback moth	BotaniGard	Arysta Life Science Co.	2002
Paecilomyces fumosoroseus	Whitefly, aphids	Preferd	Tokai Bussan Co. Ltd.	2001
Lecanicillium longisporum	Aphids	Vertalec	Arysta Life Science Co.	2000
Parasitic nematodes				
Steinernema carpocapsae	Weevils, black cutworm, common cutworm, peach fruit moth	Bio Safe	SDS Biotech Co. Ltd.	1993
Steinernema glaseri	White grubs, weevils, blackcutworm, blue grass webworm, lawn grass cutworm	Bio Topia	SDS Biotech Co. Ltd.	2000

[a]Spore-killed formulation.

established in India, while 130 in the private sector. Approximately 40 commercial mycoinsecticides available on Brazilian market were registered by 19 companies (Kabaluk et al., 2010). As of 2010, Canada had registered 32, 12 of which were bacterial species, 11 fungi, six nematodes, two viruses, and one protozoan based microbial pesticide. Microbial biopesticides represent less than 1% of the global market in agrochemical crop production (Hajek, 2004).

For all crop types, bacterial biopesticides claim about 74% of the market; fungal biopesticides, about 10%; viral biopesticides, 5%; predator biopesticides, 8%; and

Table 2. List of different *Trichoderma* sp. and respective BCA facts.

Active agent	Antagonist against	Responsible metabolites/factor	Disease/epidemic control
T. harzianum 1051, T. harzianum 39.1	*Crinipellis perniciosa*	Chitinase, *N*-acetylglucosaminidase, β-1,3-glucanase,total cellulase, endoglucanase, aryl-β-glucosidase, β-glucosidase, protease and amylase	Witches' broom disease (*Crinipellis perniciosus*) of Cocoa
T. lignorum, T. virens, T. hamatum, T.harzianum and T. pseudokoningii (Rifai)	*Rhizoctonia solani*	Unknown inhibitory substances; extracellular,metabolites or antibiotics, or lytic enzyme action	Damping-off of bean
T. viride, T. harzianum	*Aspergillus flavus and Fusarium moniliforme*	Lipolytic, proteolytic, pectinolytic and cellulolytic enzymes. Unknown (mycotoxins) antibiotic compounds (e.g., peptides, cyclic polypeptides)	Fungal-seed-associated
T. harzianum, BAFC 742	*Sclerotinia sclerotiorum, BAFC 2232*	β-1,3-Glucanase and chitinase	Fungal-soybean plant
T. harzianum 25, T. viride	*Serpula lacrymans*	Antibiotic; anthraquinones	Fungal wood decay
T. virens "Q" strain	*Rhizopus oryzae/Pythium sp.*	Plant phytoalexin induction by antibiotic compound,gliovirin	Cotton seedling disease
T. virens isolates GL3 and GL21; T.harzianum T-203	*Rhizoctonia solani, Pythium ultimum, and Meloidogyne incognita*	Antibiotics gliovirin and gliotoxin, and other inhibitory metabolites	Damping-off of cucumber

"other" biopesticides, 3% (Thakore, 2006). However, only a few entomopathogens have been developed as bio-control agents. *Trichoderma*, as a safety and promising microbial pesticides, has a better potential biocontrol and has been extensively studied. In general, the current literature indicated that *Trichoderma* sp. has been used mostly as biopesticide agent (Table 2) (Mausam et al., 2007). China, Russia, Belarus and to a lesser extent India and Thailand, had also become significant producers of *B.t.* products which are used extensively. Dror et al. (2009) reviewed the accumulating data in *B.t.* delta-endotoxin Cry1C research as a potential biopesticide in plants.

Botanical pesticides

Botanical pesticides derived from some parts or active ingredients of plants were of insect killing, sterilization, weed control, and plant growth regulating activities. China was the first country to engage in the research and development using insecticidal plants. The development of botanical pesticides made use of mainly secondary metabolites of plants, such as flavonoids, alkaloids, etc. During the last 30 years, Chinese researchers have examined 10 kinds of pesticidally active ingredients in plants, such as tobacco, derris, bloodvine and celastraceae, and developed a number of botanical pesticides. 792 kinds of botanical products had been registered in the United States by 2003: 283 plant growth regulators and pesticides, 231 pheromones and 104 repellents (Table 3) (Pesticides registration [EB/OL], 2002). A plant extract from the giant knotweed *Reynoutria sachalinensis* (F. Schmidt) Nakai (Milsana) had shown high efficiency to control powdery mildews on various crops including the tomato powdery mildew species *Oidium neolycopersici* (Trottin et al., 2003) and *Leveillula taurica* (Konstantinidou et al., 2006). Another product that will be commercialized soon by Marrone Organic Innovations is based on an enzyme extracted from giant knotweed, an abundant invasive plant species in the US and native to Asia. Another botanical insecticide Azadirachtin, extracted from the leaves of *Azadirachta indica,* blocks the synthesis and release of moulting hormones from the prothoracic glands, leading to incomplete ecdysis in immature insects (Isman, 2006). Azadirachtin did not directly kill pests, but altered the life-processing behavior in such a manner that the insect can no longer feed,

Table 3. Biochemical and botanical pesticides registered in the United States (2003).

Series	Active ingredient	Content	Product	Note
1	Flower and plant volatile substance	16	88	Most were vegetable oil
2	Plant growth regulator and pesticides	26	283	
3	Pheromone	43	231	
4	Repellent	16	104	
5	Other biopreparates	23	86	Including harpin
6	Virus	8	12	
Total		124	792	

breed or undergo metamorphosis (Elahi, 2008).

Zooid pesticides

Zooid pesticides were derived from animals including animal toxin (bee venom, spider venom, scorpion venom, etc.), insect hormone (juvenile hormone analogue, ecdysone, etc.), pheromone (sex pheromones, repellants, etc.) and natural enemy (predators, parasites, etc.). They affect the survival of pests while do less or even no harm to the organisms. Some classes of low molecular mass toxins had been reported in spider venoms, these compounds act as reversible inhibitors of monoamine oxidase and are very toxic to insects and are neurotoxic, convulsivant and lethal to rats (Saidemberg et al., 2009). Laura and Francesca (2010) suggested that the use of sex pheromones for the control of invasive populations of the crayfish *Procambarus clarkia* and the results showed that males were attracted by the females' sex pheromones. In India and Thailand natural enemies (parasites and predators) had been successfully developed into plant protection tools for farmers. The 22 North American insectaries produced 38 natural enemy species. Commercial natural enemies constituted less than 10% of the biologically based pest control market, with an estimated gross annual value of $ 25 to 30 million at the wholesale level (Keith and Christy, 2008). As long-term solutions against invasive insect and mite pests, arthropod-pathogenic microbes and nematodes had been used much less frequently than introductions of parasitoids and predators (Hajek, 2004). However, some pathogens and nematodes introduced for classical biological control had succeeded in providing substantial and long-term control of pests (Goettel and Hajek, 2001). Commodities produced by Koppert Company in Netherlands occupy most of the European market and were widely used in orchards, greenhouses and on horticultural crops. In the United States, 10% of greenhouses, 8% of nurseries and 19% of orchards use natural enemies of insects.

Genetically modified plants

Genetically modified plants are plants which have pesticidal traits and they are genetically modified by some special genes so that these plants produce some materials in plants that can be used as pesticides. Although genetically modified crops have been banned by many countries, scientists are still trying to enhance disease and pest resistance in some plants by introducing new genes. These genes are always homologous so they would do no harm to other lives. Zhang et al. (2011) transformed hpRNA expression vectors containing inverted-repeat sequences of targeting coat protein gene of maize dwarf mosaic virus to the susceptible maize inbred line, which overcame the low efficiency of agronomic protection from maize dwarf mosaic disease. Research is still underway and further development is needed, therefore, genetically modified plants can be regarded as a subset of biopesticides that we have discussed briefly in this paper.

One of the main purposes of research in this field is to find a gene or genes which, when transferred into a plant, would produce toxins with the effect of poisoning insect pests. Such a gene should be also reliably inherited in the plant host. Two kinds of crops are relevant to plant protection schemes: insect resistant transgenic crops and the plants with herbicide resistance. The already launched mature product varieties were: the anti-glyphosate series of Monsanto, such as corn, soybean, cotton, rape and sugar beet, and anti-glufosinate-ammonium series of AgrEvo, for instance soybeans and cotton. All the plants are strictly regulated by pesticide regulation department of each country, such as EPA which regulates these products in the US. Up to date, many new varieties of crops with a wide range of resistance to pests and diseases have been produced in America, Japan, United Kingdom, Australia, Russia and other countries. The global area of genetically modified crops increased approximately 60-fold during the 11-year period from 1996 to 2006: from 1.7 million to 102 million ha (James, 2006). Some insect-resistant plants with transferred *B.t.* toxoprotein genes had been used to prevent the spread of specific pests (Table 4) (Huang, 2001). A successful exogenous gene transmission into crops, creating plants such as transgenic *B.t.* insect-resistant cotton and maize, was equivalent to biosynthesis of active ingredients using the crop's own molecular machinery and had effects similar to bio-synthetic pesticides (Isik and Guenther,

Table 4. Insect-resistant plants transferred *B.t.* toxoprotein genes.

Plant	Gene	Type	Target pest	Source
Baccy	*cry* Ⅰ *A(a)*	WT	*Manduca sexta(L)*	Barton etc.
	cry Ⅰ *A(b)*	WT	*Manduca sexta(L)*	Vaeck etc.
	cry Ⅰ *A(b)* & *(c)*	PW	*Manduca sexta(L)*	Perlak etc.
	cry Ⅰ *A(b)*	WT	*Manduca sexta(L)*	Williams etc.
Chloroplast	*cry* Ⅰ *A(c)*	WT	Cigarette beetle *Helicoverpa zea, Susumia exigua Butler (L)*	McBride etc.
	cry Ⅰ *C*	S	*Spodoptera littoralis (L)*	Strizhov etc.
Tomato	*cry* Ⅰ *A(b)*	WT	*Heliothis virescens (L)*	Fichoff etc.
Cotton	*cry* Ⅰ *A(b)* & *(c)*	S	*H. zea,* cigarette beetle *(L)*	Perlak etc.
Potato	*cry* Ⅰ *A(B)*	WT	*Phthorimaea operculella Zeller (L)*	Peferoen etc.
	cry Ⅲ *A*	S	Potato bug *(C)*	Adang etc.
	cry Ⅲ *A*	S	Potato bug *(C)*	Perlak etc.
Lucerne	*cry* Ⅰ *C*	S	*Spodoptera littoralis (L)*	Strizhov etc.
Canola	*cry* Ⅰ *A(c)*	S	Diamondback moth *H. zea, (L)* Cabbage looper, *Susumia exigua Butler (L)*	Stewart etc.
Soybean	*cry* Ⅰ *A(c)*	S	*H. zea,* cigarette beetle *(L) Pseudoplusia includens (L)*	Stewart etc.
Maize	*cry* Ⅰ *A(b)*	S	Corn borer*(L)*	Kozel etc.
Rice	*cry* Ⅰ *A(b)*	S	*Chilo suppressalis (L)*	Fujimoto etc.
			Cnaphalocrocis medinalis Guenee (L)	Wunn etc.
Alamo	*cry* Ⅰ *A(a)*	PM	*Lymantria dispar Linnaeus (L)*	McCown etc.
	cry Ⅲ *A*	WT	*Chrysomela tremulae (C)*	Cornu

L, Lepidoptera; C, coleoptera; WT, natural genes; PM, partly modified genes; S, synthetic gene.

2008). A 3-year field study with *B.t.* corn confirmed that the release of Cry protein in root exudates continued throughout growth, and levels of the protein in soil did not correlate with a specific period of plant growth (Nguyen, 2004; Baumgarte and Tebbe, 2005). Genetically engineered herbicide-tolerant crops do not belong to the pesticide group, but are associated with the concept of pesticide accessory factors. There is no doubt that transgenic crops with insect resistance, disease resistance and tolerance to herbicides have the most potential for research and development in agricultural biotechnology.

CONSTRAINT FACTORS IN THE DEVELOPMENT OF BIOPESTICIDES

Classical biological control has achieved successful pest control in a number of cases, although in general there was lack of long term, quantitative and objective monitoring of such programs, which makes evaluation of the overall costs and benefits difficult (Thomas and Reid, 2007) and there were many reasons for the slow development of biopesticides. According to the research by Samuel and Graham (2003), the reasons not to use biopesticides were as follows: too expensive (41%), do not think it works (30%), need more information about how to garden organically (25%), never considered/ thought about these methods (24%), and cannot find the right products to buy (24%). The indisputable fact was that it had lagged far behind the demands of social development and environmental protection; therefore biopesticides industry needed to be further encouraged (Zhu et al., 2004).

Biopesticides are inferior to chemical pesticides in some respects, such as quantities required, more slow-acting and might be very specific to the life cycle of the pest (Clemson HGIC, 2007). Biopesticides cannot offer a significant contribution in cases of sudden, widespread and devastating diseases and catastrophic plagues of insect pests. Although the biopesticides are slow to act, they supply environmental protection and do not harm the natural environment. Biopesticides are high-technology products; we need a smooth transition to the new technology, including a wider acceptance of the concept and a well defined process to adapt the production to the new technology.

The registration of biopesticides often poses a particular challenge to regulatory authorities and the special biological properties of these natural control agents should be taken into account. For small biopesticides companies aiming to development a range of niche products, the cost, such as a simple Tier 1 toxicity tests cost is at least $ 150,000, and could represent a serious constraint to registering new biopesticide products. The most important thing for new products appearing on the market is a well organized promotion; the agriculture-related constitutions should intensify propaganda and promote the use of biopesticides, and make it easier for the farmers to master the skills of using such new products. The prescribed storage conditions for biopesticides have to be followed rigorously as the time frame for their use is limited and the shelf life of most biological live agents is less than three months. In accordance with the provisions of existing Chinese pesticides standards, pesticides' storage limit should be at least two years and the effective ingredient decomposition rate should not exceed 5%. This is one of the most important technical problems facing the biopesticides industry. Biopesticides work mainly through destroying insect intestinal cells and their killing speed is low, in spite of their high efficiency. Farmers generally lack the basic skills required for their use and they do not understand the mode of action of biopesticides; inevitably, this will affect their use and promotion. There is still a large need for end-user education on biopesticides, what they are, how they work and when to spray.

It is generally believed that biopesticides are ideal 'green' pesticides with characteristics of high safety, no pollution, and non-toxic to human and non-target animals; however, there are different levels of potential safety issues, depending on the products' sources. Some of the most important examples of biopesticides are toxins from microbial pesticides group. *Metarhizium anisopliae's* streptozotocin was toxic to the shrimp (*Palaemonetes pugio*) and frog (*Xenopus laevis*); the LC_{50} is 52 and 32 mg/L, respectively. It can also cause a certain degree of damage in head cartilage, as well as facial and intestinal abnormalities in the frog embryo (Genthner, 1998). In addition, alien species could also threaten the resident species. Shi (2001) discussed that the introduction of *Coccinella se*ptempunctata Linnaeus might have been the reason for some local populations' decline in the Midwest of America. The existence of transgenic crops might have many potential adverse effects on the environment; anti-viral gene might recombine with viruses to generate a super virus, with devastating consequences for cultivated plants.

The development of a more balanced regulatory system for biopesticides production would be beneficial for natural enemies and other biopesticides for agricultural development without risk to people or environment, and the process of registration could be speeded up and the cost might be cut down. There are a great number of important flaws in the current regulatory system though, such as requirements and permitting process for the natural enemy industry, lack of balance, transparency, and efficiency. The regulatory system should be more flexible and it must have the full and justified trust of the public. Pheromones and microbial pesticides have received high marks through the regulated industry and registrations need to retain some balance in the long run, especially regarding granting of waivers for environmental testing. Some analysts had identified an important problem which was the lack of consistency among some institutions, such as animal and plant health inspection service (APHIS), EPA, and Food and Drug Agency (FDA), in the agencies' regulatory oversight of natural enemies and microbial pesticides (Miller and Aplet, 1993; Kough, 1995; Lake, 1995; Hommel, 1995). It is important, for example, that EPA continue toxicity studies on certain microbial products; the other agencies are unequipped to take over that function. Certainly regulatory gaps exist, but these can be addressed within the current institutional framework.

DEVELOPMENT TRENDS

The general development trend

According to Biopesticides Industry Coalition of American (BPIA) and the European Association for International Producers of Biological Control Products' (IBMA) released data, in 2006 global sales of biopesticides were worth about $ 1.04 billion, accounting for 2.9% of total pesticide sales (5.2% increase in 2005); the market for biopesticides is growing at approximately 10% per year. By 2010, global sales hit $1 billion mark and accounts for 4.2% percent of the overall pesticides market and the share is expected to increase tremendously in the next five years (Sarah, 2011). Much of this rapid growth is due to the fact that, perhaps surprisingly, more than 80% of biopesticides are used, not by organic farmers, but by producers employing conventional farming practices. Report from Frost and Sullivan (2009) said that increasing demand for chemical-free crops and more organic farming had led to augmented usage of biopesticides in North America and Western Europe. This puts the value of biopesticides in those combined markets at $ 594.2 million in 2008, and forecast that market will nearly double by 2015 to a market value of $1.02 billion.

Demand for biopesticides

Restrictions in the development of chemical pesticides

Although the use of chemical pesticides is still larger and many newly developed pesticides are safer to use and have safer LD_{50}s, the development is still restricted by their inner shortcomings. With the growing awareness of natural environment protection problems and rapid growth of biopesticides the development of chemical pesticides has become more difficult and stringent. International demand for chemical pesticides tends to be saturated, with the exception of a small number of fungicides and herbicides which have been given a larger development space. Pesticide production enterprises are forced to put more emphasis on increasing the product variety and, in general, reduce the output. There are several inherent problems associated with the chemical pesticides, such as product development and drug resistance. Biopesticides are environment-friendly and support sustainable development of agriculture; they will replace chemical pesticides probably in a gradual manner.

Increasing demand for environmental protection

Along with the enhanced awareness of environmental protection, limitations in agricultural products export are increasing; in 2003, the sale of 320 kinds of pesticides was officially banned by the European Union. Therefore, the development of biopesticides industry is very important for sustainable development of agriculture, to protect people's lives and health, preserve the natural environment and create favorable conditions for export of global agricultural products. Increasingly, the sustained development of biopesticides is becoming imperative to increase the quality and safety of agricultural production, enhance agricultural products' economic value and promote the development of 'green' agriculture industry.

Sustained government policy

In view of the highlighted difficulties and problems in the current development of biopesticides, many countries take active measures to promote such development. On one hand, the access restrictions to certain agricultural and derived products are being continuously multiplied; many countries have explicitly prohibited the use of highly toxic and residual chemical pesticides. On the other hand, the research and development funding is being increased; enterprises' taxation is often relaxed to promote the advantages of resource integration, encourage innovation and large-scale production of bio-pesticides. At the same time, enterprises and agricultural departments should work together to strengthen the promotion of biopesticide technologies, to help farmers master the necessary skills and encourage them to use pollution-free biological substances.

Strengthening cooperation

As more developing countries join the World Trade Organization (WTO), new companies enter the pesticides market and look for cooperation opportunities to reduce production costs and enhance the competitiveness. From the perspective of global, the six large companies Bayer, Syngenta, BASF, DuPont, Dow AgroSciences, and Monsanto account for 70% of the world pesticide sales market. Merging, reorganization and association of strong enterprises are one of the trends in the development of the world's safe and efficient pesticides. Cooperation with foreign enterprises will help to introduce more new product varieties, make use of novel technologies and equipment, optimize and upgrade the structure and improve the management and general efficiency. This is conducive to the creation of scale benefit, saves resources, reduces costs and enhances the market competitiveness. This should result in product quality enhancement and increase competitiveness, helping to expand exports. Strengthening cooperation with external companies is one way to encourage and support the development of biopesticides.

Biopesticides market

Development of biopesticides industry has to be treated as a strategic, comprehensive and forward-looking task. Obviously, the development of such industry strongly relates to research in biopesticides, but at the same time it is necessary to take into account the industry's two distinct aspects. A number of institutions have done some preliminary research in the field of the biopesticides industrialization; however, no systematic reports have appeared so far. There is no doubt that it is necessary to strengthen the collaboration of enterprises and research institutes. Biopesticides cannot completely replace chemical pesticides as yet; agricultural production can benefit while biopesticides and chemical pesticides co-exist. Therefore, we should accelerate the practical application of research results and promote the large-scale industrial development. Currently, North America consumes about 40% of global biopesticides production, the total US biopesticides market is valued at around $ 205 million and expected to increase to approximately $ 300 million by the end of the decade. With European and Oceanic Countries accounting for 20% respectively, the European market are estimated at around $ 135 million and achieved approximately $ 270 million by 2010, making the European biopesticides market the fastest-growing. Within South and Latin America, which together represent 10% of the global biopesticide market, chemical pesticides sales are expected to decline and biopesticide sales to increase moderately. Although relatively small, the Asian market presents a large opportunity for biopesticides, as the mega-economies of China and India adopt more biopesticide use. According to India's agricultural ministry, biopesticides represent only 2.89% of the overall pesticides market of 100,000 metric tons, but should increase by an estimated 2.3% per year (Source: BBC research).

There is no doubt that biopesticides will come into being; a variety of novel techniques will be used to improve or modify existing biopesticides, which will further accelerate their development. Biopesticides have attracted extensive attention as integrated pest management agents in which they are often applied as augmentative agents and augmentative biological control has been advanced as an alternative to chemical pesticides by scientists for many years (Obrycki et al., 1997; Ridgway and Inscoe, 1998; Van Lenteren, 2000). They are natural parts of the crop ecosystem but artificial propagation and application are required if they are to perform effectively as crop protection agents. Van Lenteren (2003) had asserted that the practice of augmentative biological control was expanding. Collier and Van Steenwyk (2004) concluded that augmentative releases were usually less effective than chemical pesticides, and that if most of the releases in these studies were practiced at a commercial scale, the purchased natural enemies would often cost more than production costs plus pesticide costs. The applications of biopesticides have a bright future and the use of them would be argumentative while it is different from unquestioned inundative use. It is necessary to control the use of biopesticides, because some kinds of biopesticide products might result in environment pollution or be harmful to the natural enemies while others might be toxic to other live beings. For instance, in India, inundative releases of natural enemies have been restricted to only egg parasitoids, particularly *Taraxacum japonicum* and *Trichogramma chilonis* mainly because of their amenability. It can be foreseen that biopesticides will make more contribution for humans to fight against diseases, insects and other agricultural pests and they will be the focus of pesticide industry in future.

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