Phytoprotection

Research Challenges and Needs for Safe Use of Microbial Organisms (*Bacillus thuringiensis*)

Jacques Boisvert

Volume 79, numéro 4, 1998

OECD Workshop - Sustainable Pest Management, Safe Utilization of New Organisms in Biological Control. Montréal, Québec, Canada. September 27-30, 1998.
Atelier de l'OCDE - Gestion durable des ennemis des cultures, Utilisation sécuritaire de nouveaux organismes de lutte biologique. Montréal, Québec, Canada. 27-30 Septembre 1998.

URI : https://id.erudit.org/iderudit/706156ar
DOI : https://doi.org/10.7202/706156ar

Aller au sommaire du numéro

Éditeur(s)

Société de protection des plantes du Québec (SPPQ)l

ISSN

0031-9511 (imprimé)
1710-1603 (numérique)

Découvrir la revue

Citer cet article

Boisvert, J. (1998). Research Challenges and Needs for Safe Use of Microbial Organisms (*Bacillus thuringiensis*). *Phytoprotection*, *79*(4), 44–49. https://doi.org/10.7202/706156ar

Research Challenges and Needs for the Safe Use of Microbial Organisms (*Bacillus thuringiensis*)

Jacques Boisvert

Département de Chimie-Biologie, Université du Québec à Trois-Rivières, 3351, Blvd des Forges. CP. 500, Trois-Rivières (Québec) Canada G9A 5H7.

To talk about the next challenges and the safe utilisation of Bt based products, it is to my thinking extremely important to look at what has been done in the past and use " the good, the bad and the ugly " that happened, to improve the future.

In the early 1960's, the concept of biological control of insect pests was not fairly only new, but it involved " unusual researchers " claiming that it was possible to fight nature with nature. At that time, there were many concerns being thrown at the scientific community and the public about the safety hazards, problems, long term effects created by the extensive use of chemical pesticides. Still many pesticides were still considered as magic bullets, because everytime something would be published on the " bad chemicals " another one (better !) would be created and rapidly put on the market.

But thanks to the " persistence " of some researchers, the idea of using microbes to fight effectively certain insect pests that were creating lots of damages to forestry and agricultural industries, the name *Bacillus thuringiensis* (Bt) became almost a trade mark. Not only to other researchers but also to funding agencies !!

Although known to many people working in laboratories, the potential of Bt as a microbial insecticide really started to develop when experimental field trials were made and showed promising results. Using better strains, with better efficacies, formulated material, improved techniques of application, all these were possible. Some people were again dreaming about another " magic bullet " even if cautions were thrown all over the place.

In the 1970's, formulations were getting registered by regulatory agencies, thus providing researchers with the possibility of doing large scale experiments. At the same time, basic research was being made on the mode of action of Bt, strain specificity, dosage of the toxic inclusions, discovery of new strains, establishment of standards and protocols to assay newly discovered material. During that period, Bt was presented as an ideal microbial agent since it did not have the drawbacks of the " bad chemicals ":. Contrary to the chemicals it had a narrow spectrum of activity, a short persistence , thus no accumulation in the environment and could be produced cheaply using standard fermentation procedures.

Up to the 1980's, successes were numerous according to the published literature. But there were also many failures on the field, most of which were never published for many reasons. Then, there were some doubts as to the real effective potential of Bt. Nevertheless, progress was being made in many areas. Improved formulations or at least a whole lot of different formulations, improved delivery techniques, other strains with new specificity were discovered. *Bacillus thuringiensis israelensis* was found to be highly active against mosquitoes. Malaria, onchocerciasis, yellow fever , dengue hemorragic fever etc. would eventually become diseases

of the past !!! The " magic bullets " were increasingly numerous and there seemed no limits.

Later during that period, laboratories researchers learned a lot about Bt and its toxic constituents, their mode of action, species sensitivity etc.. But some failures and the fact that the market for Bt based products was still waiting to reach the expected exponential growth that was claimed at that time, produced a strange shift in the mind of many people involved in the field of biological control using Bt based products. What were advantages compared to the " bad chemicals " suddenly became disadvantages. Now the spectrum of activity of Bt was too narrow, it persistence in the field was to short, the timing of the application of the formulation was too difficult, to time consuming to users, the costs of the formulation were too high, shelf-life was too short.

But it is amazingly interesting to note that during the same period, although Bt was having a relatively good success (potentially speaking) with the scientific community, the regulatory agencies and the industrial producers, many concerns were also raised.

The scientific community was becoming inquisitive about many things: what is really Bt, a pathogen or not ? what are the impacts on other populations ? can large scale applications to destroy a pest affect other species especially beneficial species ? have people made long term ecological impact studies ? what is present informulations that could cause « colateral « damage?

After having realised the effects of " chemicals pesticides " on the environment, well publicised I might add, now it was the turn of the public to ask questions. The syndrome of "not in my back yard" was not a fad but something real and it extended to more then the backyards.

Regulatory agencies were also getting some questions, although I must admit that because of confidentiality agreement involved in homologation processes, they were in a rather difficult position. But still their lack of answers to some questions, promoted more awareness and more questions, on the part of ecological groups. In turn it created another phenomena; these groups gathered in their ranks, biochemists, microbiologists, mathematical modeling experts, economists, and to top it all, lawyers !!! And the media were having a good time with this !!! Many questions were asked, and some people realised that there were no answers because in parts, the necessary research had not been done, or had been partially done or had been so badly done that now the chicken had to go back to the barn !!!

Early 1980's, was the time to step in with the " Age of Aquarius ": molecular biology. Combined with the biochemical researches done earlier, it was the occasion to improve things so that users would be happy. They (!!) demanded larger spectrum of activity, longer persistence, ease of utilisation, low cost of application etc. Molecular biology combined with integrated pest management: an assortment of magic bullets with a better riffle !!!

During that period, Bt genes were shuffled all over the place, a tremendous amount of money, time and also acquisition of important data were made. The genes went from one species to other Bt species, to other bacteria, to plants, to viruses, to " you name it we can do it ". Great achievements were done with Bt and molecular biology. New (!!) organisms were developed so that indeed larger and multispectrum of activity were achieved, but the short persistence remained a constant problem. Now there were Bt strains with activity against lepidopteran, diptera and coleoptera either singly or in combinations, giving rise to new markets, fresh research money and possibly new developments. But always there were limitations with the toxicity and also the delivery systems. But when we look at the literature, one of the many concerns of the molecular biologists involved in Bt research, was the lack of knowledge on the target species !!! Equally important, many new serotypes of Bt with different specificity and efficacy were discovered and today there is at least 51 of them.

We can produce good bullets, but we do not know enough about the target and its highly sophisticated techniques of camouflage and we know little on how it interacts with its habitat !!! But also at the same time, many people realised that the enemies (insects pests) were formidable ones. New formulations, improved delivery systems were developed and tested with some success as some informations were found on behavior and the life cycle of the targets.

During that period, there were a lot of pressure put on regulatory agencies. From regulating on the use and the environmental effects of chemical pesticides to the emergence of biological control using wild-type organisms with various formulations, then the appearance of new (!!) organisms created by molecular biologists, formulated by industries, combined with the persistent market pressure and lobbying from the promoters and the users.

The agencies were during that period, and my feeling is that, they are still not prepared to deal adequately, with such rapid activity. I think that even today they are lacking the necessary personnel in number and in qualification to investigate and evaluate new and improved formulations. What do we do ? do we stop everything until we get our breath back ? you may have to recommend to increase the efficacy (personal, competence) of regulatory agencies, but will government accept that ? are industries willing to help ?

The type of pressures put on regulatory agencies can be understood, when we look at some published literature. I would like to resume a paragraph written ten years ago, by researchers representing an industry involved in biological control. It is said that : to avoid regulatory restrictions associated with the testing and use of organisms produced using recombinant DNA technology, some people have utilised an intermediate strategy (conjugation). Because these organisms (produced by conjugation) are considered by regulatory agencies to be genetically manipulated rather than genetically engineered, some were approved for use.

Does that mean that whenever a set of regulations is proposed by the agencies, researchers should try to find a way around it ?

In Canada, the period from 1980 to 1990 saw many groups of people objecting to large scale treatment against the use of Bt for the control of spruce bud worm and other insect pests of agricultural importance; and also *Bt israelensis* treatment of marshes and rivers against mosquitoes and black flies At the beginning, these groups of concerned citizens were composed of environmentalists and ordinary people who were simply afraid of getting sprayed with a bacteria (and it did happened !!), closely related to a known pathogen (Bacillus cereus) and also afraid of what would happen to their ecosystem. Some researchers worried about the rapid progression of experimental field testings and I guess remembering what happened with chemical pesticides, started asking questions about the possibility of resistance of the targets and ecological impacts. But the prospect of resistance was not highly considered at the time because it involved the development of resistance to 3-4 toxic molecules acting together on the target.

These groups were usually confronted against experts representing the industries and also people from government agencies sometimes involved in research with the producers and the promoters !!! It is not surprising today, to see independent researchers involved with these groups and even some are well implicated in the field of biological control if not directly involved with Bt research .

It is interesting to note that these groups were actually using the same questions raised by researchers admitting (in books and review of literature) that although a lot of things were known about Bt, there was little information on the target species and its ecology, on the possible long term effects on the ecosystem, possible effects on beneficial organisms, persistence in various environments, the safety of the bacteria and even the safety of other constituents of the formulations used. Just imagine the concerns raised when

promoters started talking about genetically modified or genetically manipulated organisms.

One important discovery (in 1987-89) was the acetate technique developed to detect Bt organisms in many types of habitat and the fact that indeed Bt strains were found to be distributed all over the world. Now suddenly Bt was not a freak of nature but a species distributed all over and that the species had enormous proprieties as far as specificity was concerned, but also the fact that this technique provided a mean and an incentive to find other Bt species with different specificities and efficacies.

In 1991, the first international conference on Bt was organised in Oxford (England) and grouped researchers from microbial ecology, molecular biology to protein crystallographers coming from universities, government research agencies to industries. Some extremely important progress were presented and discussed as well as future challenges for the many people involved in biological control using Bt. The expectations for the next decade were very high especially for the industries. But it was the contrary for those involved with regulatory agencies who thought that research was moving faster that they could make regulations !!!

During this meeting some important statements were made while some issues were not or barely addressed by invited researchers. Maybe we could use that as a base to discuss about future challenges.

One invited speaker said and I quote: " Thus the stage appears to be set for the realisation of Bt's true potential as a bioinsecticide and for substantial market expansion. **However**, current technological advances are outstripping **the ecological knowledge that is required** for their deployment as environmentally acceptable insect control strategies. **Ecological risks** need to be assessed, new **regulatory requirements** have to be met, and **public acceptance** has to be gained before transgenic plants and living recombinant organisms can be put to use ".

In actual fact, during this important meeting, there was little or nothing on " the ecological knowledge ", on " regulatory needs " and on " the public acceptance ". When ecology and risk assessment was debated, it was admitted that there had been few published quantitative studies on the environmental impacts of Bt insecticides, but in the same paper, it is reported that no adverse environmental impact has been reported (published) !!! not to say the least of the fact that wild strains of Bt had never been " conclusively " implicated in any human or mammalian health incidents.

How many long term studies on ecological impacts using independent researchers, were funded by industries or government agencies ? Who is willing to start and fund a five year research program involving independent ecologists, microbiologists, physiologists, biochemists etc.

How can you gain public acceptance when one reads that " Bt does not persist or spread in the land environment and that recombinant genes expressed in Bt strains will remain within or close to the area of release ". How do we explain their presence and distribution in nature ? Especially when the author makes in the same paper a most likely hypothesis, " that soil acts as a reservoir or sink for Bt spores which may then spread long distances by wind dissemination ".

I would like to end this long but necessary introduction by looking at one of the concluding remark made during this Oxford meeting: " We now have the opportunity to demonstrate the lessons of past use of chemical insecticides by developing sound strategies for using Bt based biotechnology products in pest management systems in advance of their actual commercialisation and marketing ". In 1980, basically the same remark was made except for the " biotechnology products " part !!!!

Have we really learned lessons from the past or are we in the process of repeating the same mistakes ? Although the problems of resistance are increasing, have we developed sound strate-

gies for pest management to avoid this problem ? Have we since that meeting in Oxford, met the challenges that were put forward to the scientific community ? Have we fill up the scientific gaps that were required to meet the concerns of many of the participants ? Are we going too fast, taking too many risks ? is the use of DNA technology the only way to improve biological control ?

It is almost impossible during this meeting to discuss of all the next research challenges especially when I see the term " new organisms ". Furthermore, to me research does not only means laboratory or field work. Research also involves new ideas, new involvements, new agreements, new partnerships etc.

All sorts of challenges can be made to the various groups attending this current meeting. Taken as a whole one of the biggest challenge would be as was said repeatedly over the last 10-20 years: to get people from various field of research to actually work together. In fact very seldom do you see in the published literature, the necessary assortment of researchers needed to tackle some of the questions and concerns raised earlier. How many times have we seen industries, regulating agencies, funding agencies and university researchers get together, work together and publish together.

For regulatory agencies, a big and most crucial challenge would be to stay ahead of the rapid progress in the field of biotechnology and research in biological control so that regulations for homologation, experimental field testing would be sound and adapted to the actual reality of the time and costs involved in biological control research. Furthermore, somebody, somehow will have to find ways to increase the number competent personal in regulatory agencies, so that they can at least follow research progresses and activities. In many respect, most agencies are behind all that creating major difficulties for researchers, industries and users.

One of the challenge of the regulatory agencies should be to convince funding agencies to put high priority on projects designed to investigate ecological impacts, persistence, resistance detection and management strategies etc. implicating multidisciplinary approaches.

Another challenge of these agencies should be to propose to researchers, complete, scientifically acceptable and standardised protocols for testing new strains, new formulations, new delivery technologies for environmental impacts.

There are many challenges facing industries involved in biological control using Bt whether as wild strains or as modified organisms. Very few if none of the industries can carry alone all the research needed to answer the multitude of questions raised by other researchers, by the regulatory agencies and by the public.

Industries will need to do more research using independent university researchers. Especially in areas sensitive to the public. They are aware of research between industries and government agencies and since it does involve confidentiality agreements, it is difficult to stay neutral when debating the pro and cons of biological control.

Industries will have to do research or get the research done, for better understanding of the targets . When a presumed target is not responding, is it because of the target itself or the strain or the delivery system. Since according to many authors many basic knowledge of the targets are not investigated sufficiently it may be that failures are not the fault of the strain but could be on the delivery system.

Industries will need to investigate means of reaching the public and the users. Informations on the products, the formulations, on the purpose of field experiments should be better explained. How many times have we seen misinterpretations, miscalculations and absences of information on the publicity distributed during scientific meeting attended by groups opposing biological treatments, especially those involv-

ing genetically modified or manipulated microorganisms.

There is an urgent need for research on resistance, its occurence, its mecanism and how to manage or avoid it. Does resistance occurs during experimental field trials ? If so, research should provide ways to monitor resistance and detect it at a very early stage. If users are responsible, extensive investigations should be made to see what went wrong. Was it a wrong dosage by the user or was it the dosage proposed by the industry.

Finally, are wild type and transformed strains of Bt safe to utilise ? Safe for environment ? I guess this would be quite debatable. As proponents would argue: nothing of importance has been published. As opponents would answer: have you looked for it and if you find something will you publish it ?

There has been a fair amount of research done on the innocuity of some serotypes of Bt, and the results are good. Indeed, there is no conclusive evidence implicating Bt and human casualty.

But some of the research or surveillance program conducted during large scale treatments were so badly constructed and executed, that in fact " no conclusive evidence " could have implicated Bt. It is important to know that using standard medical microbiology laboratory techniques, *Bacillus thuringiensis* will show up as *Bacillus cereus* a small pathogen rarely implicated in food poisoning and in mild intestinal problems.

To put forward three questions as a base for discussion is a difficult task, but here we go:

- Are we moving too fast, should we slow down and really look at the failures and the gaps before going to molecular biology.
- How do we explain the fact that although great expectations were put forward over the last 15 years, the use of Bt based products is still very restricted.
- What can be done in order for industries, regulating agencies, funding agencies, government research centers and universities to work together toward the same goal and with the same satisfaction.