Commercial Development and Future Prospects for Entomogenous Nematodes[1]

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Abstract: Although entomogenous nematodes generally have many of the attributes of the ideal biocontrol agent, many of these attributes make the nematodes less than desirable for commercial production. Environmental limitations, lack of patent protection, "shelf life," shipping problems, and the need for users to receive specialized training are factors that have discouraged the involvement of larger companies. The future of these nematodes as commercially available biocontrol products appears to lie with the smaller "cottage industries" or with government-subsidized production. Problems encountered with attempts to produce commercially the mosquito parasite *Romanomermis culicivorax* are discussed. *Key words:* mermithid nematodes, mass production, commercial developmment of mermithids, *Romanomermis culicivorax*.

Only in recent years have nematodes gained more than a passing interest as potential biological control agents of insects. The earlier neglect is evident in the many volumes written on the subject of biological control before 1970.

Although a number of nematode species show promise as biocontrol agents, interest has been slow to develop because sufficient material has not been available in most cases to permit significant testing of these agents outside the laboratory. The two noticeable exceptions are *Neoaplectana carpocapsae* Weiser, a parasite of terrestrial insects, and *Romanomermis culicivorax* Ross and Smith, a parasite of larval mosquitoes. Both species can be readily mass produced and have been extensively field tested (8). Webster (9) recently discussed the potential of entomophilic nematodes as they relate to insect management; therefore, that subject will not be covered here. The following discussion concerns the status of *R. culicivorax* and problems encountered with recent attempts to produce commercially this agent for the control of mosquitoes.

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DISCUSSION

Romanomermis culicivorax has drawn much attention since its isolation and development (3) because this species possesses the following characteristics of an ideal biological control agent: (a) it is host specific (for mosquitoes) and has not been found to parasitize nontarget organisms in nature; (b) parasitism by this species is always lethal to the host unless there is host resistance as is seen in a few species; (c) it is easily manipulated in the laboratory; (d) it can be mass produced in vivo using mosquito larvae as hosts; (e) it can be easily disseminated in the environment with standard pesticide application techniques; (f) it has demonstrable potential for establishment and recycling in the environment and gives control for extended periods; and (g) it presents no threat to the environment.

However, *R. culicivorax*, has biological limitations. Physical factors such as humidity, temperature, salinity, pollution, and other water quality factors can seriously limit the usefulness of this agent (7). In addition, host susceptibility to parasitism varies with the species of host as well as with the age of the host at the time of exposure. The nematode is subject to predation and infection, and users should have specific knowledge of handling, storage, shipping, and application procedures.

Perhaps the most important limiting factor in the development of biological control agents is the difficulty of producing sufficiently large quantities of the parasite for field testing. *Romanomermis culicivorax* can be readily mass produced using the mosquito *Culex pipiens* L. as the host. The general procedures call for the rearing of 16,000–20,000 infested mosquitoes per rearing tray, which results in the production of 10–15 g of postparasites and eventually 10–15 $\times$ 10^6 infective-stage parasites (4). This amount of material is sufficient to treat 1/2–2 acres of breeding area, depending on dosage desired and other factors.

Because of successful mass production, *R. culicivorax* has been extensively field tested in recent years (7). To date, the most extensive attempt to control mosquitoes with a biological control agent was conducted on Lake Apostepeque, El Salvador, with *R. culicivorax*. For the study, 6,392 g (>14,000,000) of nematodes were produced over a 6-wk period. This operation required ca. 100 work-hours per week and was conducted using an established system without the benefit of modifications and technology that would normally be employed in ongoing commercial mass-production systems (6). Treatment of 13.2 ha of surface area during 11 treatments over a 7-wk period resulted in a 17-fold reduction in *Anopheles* spp. breeding in the lake (2).

One of the important advantages of an ideal biocontrol agent (over chemical pesticides) is its ability to become established and give continuous control. *Romanomermis culicivorax* has become established and has continued to produce varying levels of parasitism in many of the habitats in which it has been introduced (1,5). For example, a fresh water swamp in Louisiana treated in 1973 on two occassions has since continued to produce high levels of parasitism (up to 100% in 1980) despite drying of the area for prolonged periods and extensive flushing action as the result of periodic rains (as high as 60 cm during a 24-h period).

With the kinds of benefits and results just mentioned, why are we so slow to develop biological control agents as commercially available products? Let us look at *Bacillus thuringiensis* Berliner, perhaps the most successful of the biological control agents for insects to date. Only a handful of companies produce *B. thuringiensis* for commercial sale, and none of these firms owes its beginning, or current existence, to its biological control products. A number of other "biologicals" such as mosquito fish, parasitic wasps, ladybugs, praying mantis eggs and adults, and at least one insect virus are sold on a limited basis, but the sales volume of these products is quite small in comparison to that of *B. thuringiensis*. In a real sense, this bacterium represents the only biological that has been successfully marketed on a nationwide basis over a relatively long period by private industry.

It is possible that many of the current producers entered the *B. thuringiensis* market in an attempt to profit from their excess fermentation capacity. It would also seem logical for manufacturers to reduce or eliminate *B. thuringiensis* production if a more profitable fermentation process became available. Biological control products are no different from any other product; they are produced in response to a consumer need, with the express intent of creating a profit for the manufacturer. Without the profit incentive, production will cease.

In a real sense, biological control finds itself in a "Catch-22" situation. Biological agents are desirable for many reasons, but perhaps the most significant one is their host specificity. This ability to selectively kill only harmful pests is their unique advantage over chemical pesticides. But in being highly specific, their use is limited to, at most, only a few target insects. This means that the total product volume sold per year will be considerably less than would be sold if the product were applicable to a range of pests. A small sales volume takes production economics out of the reach of the larger manufacturer. The net result is a higher priced product, and most producers today are not interested in developing expensive products with limited sales potential. The potential for in situ recycling of the agent only serves to further threaten the already limited market.

Another serious hurdle to the introduction of new biologicals is the necessary approval required from the Environmental Protection Agency (EPA). It is estimated that the testing requirements of various regulatory agencies can cost manufacturers from $3 to $10 million for a single chemical. In the case of mosquito control, the entire pesticide budget for the 490 + mosquito control agencies in the United States rarely exceeds $10 million per year. One cannot expect a company to develop a new pest control agent that costs more to register than can be recouped in a few years through sales of the product. Unfortunately, many of the biological agents would seem to fall into this expensive no-man's land. The attributes that make them so desirable limit the totality of their use to a point where their development does not make good economic sense.

As a result, few, if any, companies can be enticed to produce biological agents for sale when their total sales volume will be extremely small, primarily as a result of the high cost of their product. If EPA registration is required, it is doubtful whether a net profit will ever be realized on a biological agent. If biologicals exempt from EPA registration could be identified, firms could probably produce such products and make a reasonable return on their investment. However, *total dollar profit* will be relatively small, even though the *percentage return on investment* is average or better. This means that large corporations will not be interested in such a venture. Major U.S. corporations prefer to invest their vast resources in large enterprises, as opposed to diversifying them into smaller, more numerous ventures. This leaves the development of new biologicals to small corporations and partnerships.

Two other factors make production of biologicals a risky business. First, biologicals, by definition, are living organisms (in this sense, sex pheromones and insect growth regulator compounds are not true biologicals). To keep biologicals alive, one must keep them in favorable environmental conditions. Shipping and storing biological agents are major problems for any producer. Second, the people who will use biologicals must be trained and develop some degree of skill in application. If you treat a biological agent as you would a chemical, it does not stand a chance. Biologicals cannot be frozen, cooked, ground to pieces, or stored on a shelf for 3 yr.

It is difficult to convince even career-oriented, conscientious pest control personnel to learn a whole new set of procedures for applying an expensive product with limited shelf-life characteristics; it is much easier to spray relatively inexpensive chemicals with tried-and-true methods and equipment.

We find ourselves in a serious dilemma. We are being constantly challenged by far-sighted academicians and environmentalists to embrace biological control and to restrain the "irresponsible" activities of industry. At the same time, however, laws and regulations are passed that delay or prevent development of the very biologicals that might provide alternatives to the use of chemical pesticides.

Of course, industry, always mindful of the bottom line, continues to produce whatever will sell to whomever will buy, provided a profit can be shown.

The outlook for biological control is bleak.

In 1977 a company, which will remain nameless, began looking for new biological agents worthy of commercial development. One of the self-imposed limitations in its selection of new agents for consideration was that they be exempt from costly EPA registration. It became evident quite early in this search that many biologicals were being studied in laboratories throughout the world, but that most of them were years away from mass-production attempts and their exemption from U.S. registration was questionable.

However, one potential biological agent, *R. culicivorax*, met the criterion of exemption from EPA pesticide registration, and the methods for mass production had been developed and widely publicized.

The company decided to allocate two years of effort (six person years), commencing in September 1977, to attempt the development of this parasite into a commercial product. First the staff became familiar with the rearing system and set up its own. During the subsequent 6–12 months, efforts were focused on becoming proficient at the mass-rearing procedures and acquiring the finesse to operate such a system efficiently. There were many hard lessons to be learned because the mass rearing of any living organism is, in many respects, an art form. A number of proprietary devices were designed and constructed to increase the efficiency (and lower the costs) of production because successful development of mass-rearing procedures in government laboratories and academic institutions does not guarantee successful industrial commercialization. The next major hurdle was to design a shipping container that would keep the nematode eggs viable during shipment and storage prior to use. That task occupied 12 months of development efforts. Numerous concepts and experimental designs followed by extensive shipping studies resulted in an effective container which permitted quality-control guarantees for the new product.

This brings the discussion to the one central issue that ultimately must be faced. Will the consumer (in this case mosquito-abatement district personnel) pay a price premium for biological agents when less expensive chemical pesticides are available? For *R. culicivorax,* some preliminary market research said no. Most mosquito-abatement district personnel operate on limited budgets and use the most cost-effective mosquito control methods available. However, a small percentage (10%) of these personnel said they were searching for more ecologically sound control methods consistent with an integrated pest management philosophy. The latter group appeared sufficient to provide adequate capital to pursue the marketing venture with *R. culicivorax.*

As pointed out earlier, private industry is profit oriented and will change direction whenever it is deemed appropriate. Thus, just two months prior to test marketing of this biological product, the company changed its program and divested itself of all biological control research and development and, in doing so, terminated research on *R. culicivorax.* And today we still do not know if entomogenous nematodes can be developed into a profit-making venture.

CONCLUSION

Those characteristics that make true biocontrol agents attractive (host specificity, recycling, etc.) can also make them unattractive as commercial products. Problems of environmental limitations, lack of patent protection, storing, and shipping problems, and special training needed by users tend to discourage the involvement of the larger companies with this kind of product. It appears that the future of many of these biocontrol agents lies with so-called cottage industries (small corporations or partnerships) or with government-subsidized production. Much work is presently underway with viruses, bacteria, fungi, protozoans, and nematodes in the hope of developing them to the same stage as that reached with *R. culicivorax.* When and if the researchers reach this point, will they find the same economic road blocks in their path as were found with the development of *R. culicivorax?*

As things now stand, we still await the success of that first truly effective commercially available product which will demonstrate the feasibility of nematodes as biocontrol agents for insect control. Although attempts to produce *R. culicivorax* commercially are not underway at this time, the successes and failures with this agent will serve as a model for other biocontrol agents as they approach the same stage of development.

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