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THE USE OF *BACILLUS THURINGIENSIS* SUBSP. *ISRAELENSIS* IN THE ONCHOCERCIASIS CONTROL PROGRAMME: PRESENT STATUS AND PROSPECT

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ABSTRACT

The main strategy of the Onchocerciasis Control Programme in West Africa (OCP) is to interrupt the transmission of the parasite through the control of larval populations of black flies in rivers. To avoid problems of resistance, OCP has adopted, since 1982, a strategy of insecticide rotation application that involves a biological control agent, *Bacillus thuringiensis* subsp. *israelensis (Bti),* in conjunction with six synthetic insecticides. Fourteen years after its introduction in the Programme, the liquid concentrate of *Bti* remains dominant. Between 200,000 and 300,000 litres are used per year, which is more than 50% of the total volume of insecticides applied. Its use is justified because it is harmless to the environment. Furthermore, its complex mechanism of action decreases the risk of any serious resistance developing. However, *Bti* has shown a low cost-efficiency ratio, both in terms of dose and carry, thus limiting its use to the low discharge rivers (below 15 m^3/s), mainly during the dry season period. A rapid calculation shows that if the operational dosage could be decreased by one third, it would allow the use of *Bti* at higher discharges (up to 70 m^3/s) and considerably enhance its usefulness within the actual strategy of rotation of insecticides. That is why the OCP considers the reduction of the operational dose as its main research priority. Research is actually going on, in collaboration with industry and research laboratories, considering the improvement of the fermentation process, the development of oil based formulations and the recombination of *Bti* toxins by genetic engineering.

KEY WORDS: *Bti,* onchocerciasis, black fly control, operational use, West Africa.

INTRODUCTION

The Onchocerciasis Control Programme in West Africa (OCP) uses two methods of control: one is chemotherapy by the administration of a microfilaricide (ivermectin) to the patient; the other is vector control by means of insecticide spraying on watercourses where larvae of the *Simulium damnosum* species complex, the onchocerciasis vector, develop. From 1974 to 1989, vector control was the only method used in treating the disease, thereby freeing numerous regions from this filariasis following the interruption of transmission for a period of time longer than that of the parasite's longevity in man, that is 14–15 years. At present, vector control, associated with ivermectin distribution, remains the preferred method in the areas that have long been subject to black fly reinvasions from non-treated zones, and in the hyperendemic areas and countries which were later included in the Programme (Molyneux, 1995). Six years from the termination of OCP, the search for new larvicides is no longer a priority. The number of treated rivers is decreasing from year to year as the disease recedes and the strategy of rotational use of the seven compounds currently available seems to have eliminated the risk of resistance (Hougard et al., 1993). Six of the compounds are chemical insecticides, among which three are organophosphates (temephos, phoxim and pyraclofos), one pyrethrinoid (permethrin), one pseudo-pyrethrinoid (etofenprox), and one carbamate (carbosulfan). The seventh compound is the biological control agent, *Bacillus thuringiensis* subsp. *israelensis* (*Bti*) introduced in OCP only in the early 1980's. Its role, however, is fundamental in the current vector control system and, unlike the chemical insecticides, the research prospects that it offers for the Programme are important.

THE PLACE OF *BTI* IN THE CURRENT CONTROL SYSTEM

The role and the importance of each of the seven insecticides are determined with regard to two clearly distinct criteria. The first criterion, which is economical, favours the most cost-effective formulations. Indeed, the cost of insecticides and aerial spraying represent more than half of the vector control activities budget (51% in 1995 for a total budget of US $15,000,000). The second criterion is ecological; it favours the insecticides which are the least harmful to human health and to the aquatic environment (river water is used for drinking and is a source of food as well). In the case of *Bti* and with regard to the above-mentioned criteria, a number of characteristics sets it apart and allows for a precise determination of its role within the current vector control system.

The advantages of *Bti*

In terms of environmental safety, *Bti* is no doubt the most "acceptable" of the seven insecticides currently used and therefore the only one that can be used without risk at low discharges, particularly during the dry season. It is totally harmless to man and the other mammals, as well as to aquatic vertebrates, fishes in particular, which are an important source of food for the riverine populations. Its innocuity towards nontarget fauna is also remarkable; after a treatment, only the Chironomidae show a slightly higher faunal drift than the norm (Dejoux et al., 1985). This is confirmed in the longer term as the structures of the entomic fauna remain unchanged after several years of use of the product (Yaméogo et al., 1992). The other advantage of *Bti* over the chemical products is that it has a complex action mechanism which triggers several active proteic toxins at specific sites in the midgut (de Barjac, 1978; Chilcott et al., 1990). These characteristics of the product confer it low resistance prospects, particularly with regard to cross resistance with the chemical insecticides; this was confirmed by the facts that no decrease in black fly susceptibility to *Bti* was observed after fifteen years of intensive use of the product by OCP. The case of a resistance of mosquitoes to *Bacillus sphaericus* noted in Brazil after only two years of operational use (Silva-Filha et al., 1995) does not contradict the present hypothesis insofar as the action mechanism of the bacterium uses only one proteic toxin. Lastly, at equal amounts of formulations, *Bti* has the advantage of being much cheaper than the chemical larvicides, up to six times cheaper in the case of some compounds. This can be partly explained by the very nature of this insecticide, the production of which is based on a fermentation process requiring strict monitoring but, on the other hand, using animal or plant nutrient media which are generally cheap.

The disadvantages of *Bti*

Despite a close and sustained collaboration with the industry to improve the performance of *Bti*, the liquid concentrate used by OCP still poses some application problems. After fifteen years of use, the stability of the formulation under tropical storage conditions has hardly improved (still less than six months) and the only noted progress as compared to the first operational formulation (Guillet et al., 1982) is limited to a slight improvement in spontaneous dispersion in the watercourse (it is no longer necessary to add 20% of water in the tanks of the spraying systems); and a reduction of the operational dose by one quarter (720 mL instead of 960 mL per discharge cubic meter). Under such conditions, and despite its relatively low production cost, the use of *Bti* remains delicate in the context of OCP, which advises against any use of the product at discharges above 15 m^3/s. The operational dose is so high indeed that because of the limited capacity of the spraying system tanks, the helicopters would have to make incessant trips between the river and the insecticide catches. Furthermore the carry of the liquid concentrate (the distance over which the insecticide kills almost all of the larvae) is low by virtue of its low spontaneous dispersion capacity. Consequently, treating a river requires a multiplication of spraying points, and in most cases, a costly treatment of each breeding site.

Utilization results

In spite of these disadvantages, *Bti* is a basic insecticide for the Programme and will undoubtedly remain so until the end of operations scheduled for the year 2002. This can be explained primarily by the fact that when it comes to treating low discharge rivers, the choice of insecticides is very limited. The use of permethrin, carbosulfan, pyraclofos and etofenprox is not authorized for toxicity reasons while an extended use of temephos and phoxim exposes the Programme to a geographic extension of black fly resistance to the organophosphates. That is the reason why *Bti* consumption by the Programme represents more than half of the total insecticide amount (between 200,000 and 300,000 litres of formulation per year), mostly between December and May, the dry season period when most of the rivers have discharges compatible with its intensive use (up to 5,000 km of rivers treated in a single week).

RESEARCH PROSPECTS

The saving of only one third of the operational dose would allow the utilization of *Bti* up to a discharge rate of 70 m^3/s without any logistical difficulties, or even at a higher discharge rate if the formulation has better spontaneous dispersion capacity. That is the reason why research undertaken to this end in collaboration with the industry and various research institutes is part of OCP's priorities. Supposing that the current research activities yield the expected results, OCP would give *Bti* a preponderant role in its vector control strategy on account of its characteristic advantages.

To achieve these objectives, the industry and the research institutes are investing their efforts in three directions. The first is geared toward reaching a complete mastery of the current fermentation process at an industrial scale in order to be able to improve the performance of the current liquid concentrates, thus ensuring a constant quality level of the batches produced. Another is focused on the development of new types of formulations such as the oil-based products which are more efficient and have better dispersion capacities. A third research orientation concerns the development of recombinant strains. This work is being done in collaboration with a molecular biology laboratory specialized in the genetic manipulation of entomopathogenic bacteria. Thus, several strain cultures recombining the different toxins of *Bti* and formulated in aqueous suspensions as required for bio-testing are received in OCP for efficacy testing on *S. damnosum*. Studies are currently in progress and will be published as soon as all the synergy mechanisms between the different toxins have been clearly established. Should a promising recombination be rapidly identified, it would be sent immediately to the industry with a view to obtain a greater quantity of the formulation for a river test.

Concomitantly with this work, efforts are also being made toward improving the stability of the formulations in tropical conditions. The presence of an organic solvent could constitute a stability factor and trials are being conducted currently with *Bti* tanks stored in habitual utilization conditions and to which a solvent in variable quantities has been added. Another way of maintaining the product's effectiveness would be to ship it in its most stable form, i.e. the dehydrated form, then to reconstitute it by directly mixing it with water from the river inside the spraying system's tank. The industry is to send us shortly this new type of dry formulation for experimentation in the coming months.

CONCLUSIONS

Predicting the outcome of the research work conducted under OCP auspices in order to improve the operational formulations of *Bti* would be foolhardy. On one hand our current orientations seem to be promising enough to warrant our hope of rapidly obtaining the expected results before the termination of the Programme. On the other hand, we have to admit that mastering all of the parameters for an industrial scale production of this bacterium is indeed a difficult objective to achieve. Thus, virtually no progress has been recorded in ten years in the operational formulation of the product and many hopes have been disappointed, particularly when it comes to moving from the experimental to the industrial production phase or guaranteeing a stable level in the quality of the operational batches produced. Despite these difficulties and whatever the outcome of the ongoing research, *Bti* has been the only insecticide that proved capable of eliminating *Simulium* species resistant to temephos and chlorphoxim between 1982 and 1985 (Kurtak, 1986). Besides, this insecticide still shows invaluable advantages, which explains why OCP uses *Bti* on such a large scale.

The termination of OCP scheduled for the year 2002 will probably mean the definitive cessation of aerial vector control activities and to a lesser extent, ground activities as well. However, an increase of ground treatments against black fly nuisance, which will be called for on the rivers along which biting densities, will be incompatible with a harmonious socio-economic development of the area (Akpoboua et al., 1994). A training programme for the personnel involved in those treatments is currently under way in the countries where this nuisance exists so that the take over can be achieved in the various cases by either the mobile teams technicians; nurses from the health centres; community health workers; agricultural extension workers; socio-economic development projects workers; or members of the bordering local communities. Among the seven insecticides currently available, *Bti* is the only recommended product for ground treatments, as opposed to temephos which has low toxicity but presents a high risk of resistance induction.

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