Barriers to the Use of Entomopathogenic Nematodes as Biocontrol Agents: South Africa as a Case Study

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Pesticides are synonymous with conventional agriculture, however in recent years, synthetic pesticides have been scrutinised for environmental and human health-related toxicity. Biopesticides are a sustainable alternative, with biopesticide technology promising to meet the market halfway by means of maintaining the current agricultural economic structure, using input technologies, but sustainably, to promote biodiversity and healthy ecosystem functioning. Biopesticides, which have the potential to mitigate the impact of ecosystem collapse from intense agriculture and climate change, have received heavy investment for product development. However, multiple barriers to biopesticide commercialisation are preventing their widespread use in viticulture and other South African agricultural industries. A literature review has established that the barriers can be simplified into three main categories: regulatory, commercial, and educational. This review seeks to understand the barriers and why, after many years of research and development and considerable investment, the South African biopesticide market is still only a fraction of the size of the synthetic product market. Global research is considered, as the issue is not a solely South African one, and multiple countries are facing similar barriers to achieving biopesticide commercial success. Moreover, this review provides the context as to why, after almost 20 years of research and product development, a locally produced entomopathogenic nematode biopesticide product is still unavailable to South African growers, despite the high demand for such a product.

INTRODUCTION

Synthetic pesticide use is synonymous with conventional agriculture and has been so since the Green Revolution (Gaud, 1968; Tilman, 1998). The Green Revolution and its associated agricultural practices reduced hunger and malnutrition in many parts of the world, but what was not accounted for, was the need to feed an ever-increasing number of people. To continue producing food at such high volumes, the growers and producers needed to transition to a new kind of food production, resulting in heavy synthetic inputs and neglect of soil health and ecosystem services, which is now the dominant method of crop production across the globe (Tilman *et al*., 2011; Romero, 2016).

Primarily, these methods assisted in preventing yield loss from pest and pathogen using pesticides, creating a vicious cycle, known as the pesticide treadmill (Van den Bosch, 1977), whereby the more input growers used, the more input they would require in the following year, as ancient natural pest control systems floundered under a tide of poison (Warrior, 2000). The overuse of synthetic pesticides is now the fastest growing agent of global warming and climate change (Tilman, 1998; Shattuck, 2021). Since the year 2000, global pesticide imports (used as a proxy for the overall use of synthetic pesticides) has increased by 292% (Shattuck, 2021), whereas total land acreage has increased by only 12% (Widmar, 2018). According to Tilman (1998), “It is not clear which is greater - the success of modern high-intensity agriculture, or its shortcomings”.

The most obvious solution to this was simply to stop relying on the use of so many pesticides, or to use eco-friendly products. However, with the extent of damage already caused, the situation is much more complex, and rebuilding soil health and natural pest defence systems, as well as adopting new alternative products, is likely to be difficult. The current system relies heavily on monocropping which is a system that is highly susceptible to pestilence, and which relies on intense synthetic inputs (Machado, 2009). While there has been a shift in growing practices that use natural systems to combat pest invasion, the damage to the environment, and the subsequent loss of the natural enemies of pests, is extensive (Warrior, 2000), resulting in further need for chemical use.

The United Nations (UN) Sustainable Development Goals (SDGs) sought to address the issue of the overuse and damage of synthetic pesticides, encouraging nations to review their currently registered synthetic products. The result has been the banning of multiple classes of synthetic pesticide products. However, without such products, the crops involved would be more susceptible to pests with no

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natural or artificial defences (Warrior, 2000). Therefore, agriculture has turned to alternative products with a negligible environmental and human health impact, but which are, nevertheless, effective pest control agents. The use of the natural enemies of many pests, in the place of synthetics, has received a considerable amount of attention, with it having led to an increase in development of pesticide products containing formulations of microorganisms or eco-friendly biochemicals (Mishra *et al*., 2014). Such products have come to be known as biopesticides.

The concept of using biological organisms for pest control is an ancient one, with it having been used for at least the last two millennia (Van Lenteren, 2012), and the presence of natural enemies is critical to a healthy and functioning agricultural ecosystem. Thus, the fact that extensive monocropping will be a reality for the near future, and, with it, the susceptibility to pest infestation, biopesticides promise to meet the market halfway, by means of maintaining the current economic structure, but in a sustainable manner, by way of promoting biodiversity and natural enemies (Lacey *et al*., 2015).

However, if biopesticides show so much promise at such a crucial stage in the fight against climate change, the question is: where are they and what is preventing their growth? Barriers to biopesticide growth and market capture are significant in almost every country. In recent years, due to the threat of climate change, a resurgence has occurred in the effort to integrate biopesticides successfully into our agricultural systems. Yet, reoccurring problems have arisen, which have prevented significant growth of the market, predominantly in the developing world, resulting in synthetic pesticides continuing to dominate the landscape (Glare *et al*., 2012).

South Africa, which fares better than most of its other developing African comrades in terms of agriculture and novel technology uptake and development, is recognised as an international leader in agriculture. However, in recent years, South Africa has been heavily scrutinised for its outdated pesticide policies and practices, and for its lack of investment in alternative products (Dalvie *et al*., 2009; South Africa DAFF, 2010), which has placed enormous strain on its export relationships. This has spurred on the development of alternative products, and a considerable amount of capital has been invested by the state in the biological control industry. However, South Africa is still subject to the hurdles facing biopesticides, with the country having also seen slow development of the biopesticide industry.

The present review seeks to break down the nature of the causes surrounding the slow biopesticide industry growth. The legislative environment, market barriers and education are the three primary factors that are involved in the biopesticide market failure. Discerning the problems facing such failure requires research into various disciplines, and the solution to these problems requires an understanding of the cyclical nature of the inter-relationship of each problem within each field. The current review seeks to address and discuss these issues and is written within the South African context.

However, as the problem involved extends beyond South Africa in its ambit, the relevant global reports will be reviewed, to gain an enhanced understanding of how some countries have created strong biopesticide markets. Moreover, the review will also serve as a case study, conducted from the perspective of a single potential entomopathogenic nematode (EPN) South African biopesticide product with great commercial potential. Conducting the review from such an angle should provide insight into the process leading from the discovery to the commercialisation of a new product and to an understanding of why, after 20 years and significant investment, a locally produced EPN biopesticide product is still unavailable to South African producers.

Global barriers to biopesticide success

The barriers to biopesticide success can be simplified into three main categories: legislation that is primarily concerned with the registration process of new products prior to market access; market barriers that concern competition, market access, access to capital and distribution channels; and, finally, education that concerns such aspects as the growers' perception of the usefulness of biopesticides, the correct methods of application and the higher education requirements for further research and development. Each factor is briefly discussed separately below, keeping in mind that a considerable amount of overlap exists between the factors, manifesting in multiple seemingly repetitive points.

The registration and policy environment of biopesticides

According to Godfrey (2013), "in the right policy environment, this next generation of agricultural products could make a world of difference, not only for impoverished farmers, but also, critically, for Africa's malnourished and vitamin-deficient populations". The main policy concern is biopesticide product registration, which is often the core reason for biopesticides failing to reach the market (Chandler *et al*., 2011). Many different reasons exist as to why the registration policy fails to assist the production of new bioproducts, with the main one being that biopesticides are distinct from synthetic products (Cherry & Gwynn, 2009). Many countries have failed to update their pesticide registration policies, procedures, and guidelines in tune with the rapid growth of the biological market. This has resulted in the registration review process of new biopesticide products using an inappropriate synthetic pesticide model, which has resulted in extended and expensive registration process and delayed market access (Plimmer, 1993; Lahlali *et al*., 2022). The above means that data requirements and evaluation methods are often inappropriate and counterproductive for biologicals, resulting in an extended registration process, delayed market access and an increased cost of registration (ACP, 2004; Arora *et al*., 2016).

Many countries, early on, took cognisance of the problems, reforming their policies to establish a constructive business sphere for biopesticides that sought to exploit their market potential (Hokkanen & Menzker-Hokkanen, 2008; Ravensberg, 2011) while maintaining the current agribusiness model (Waage, 1997). The United States of America (USA) led the way with developing a biopesticide market, by means of implementing such forward-thinking policies as the almost complete removal of registration for native entomopathogens. The data required for the approval

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of such entomopathogens is the efficacy data showing that the product works as per label claims. In addition, registration guidelines that considered new data requirements unique to and strictly for biologicals, and such organisations that promote biopesticide value as the Biopesticide Industry Alliance (BPIA) were established (Miller & Aplet, 1993; FAO/IPPC, 1996; Hajek *et al*., 2007). The subtle changes reduced the length of time from registration application to approval (24 and 28 months), compared to the length of registration time (75 months) that it did in the European Union (EU) (Arora *et al.*, 2016). However, the EU also sort to address this issue in 2022 with the Farm to Fork Strategy under the EU Green Deal. This strategy looked at increasing the introduction of biological pesticides into the market by simplifying and loosening the data requirements for biologicals.

The EU situation is far more complicated than is the prevailing situation in South Africa, as their parliament must try to navigate the demands of multiple member countries, each with their own requirements and considerations for local business, their own citizens and the environment. The EU Registration of Biological Control Agents (REBECA) and the Farm to Fork Strategy have been established to accelerate the process and to have an enhanced understanding of the difficulties experienced by all the stakeholders concerned. Key to the proposal has been the comparing and aligning of the registration requirements of the EU with those of the progressive USA (Ravensberg, 2011). In relation to such comparison and alignment, a separate issue is the creation of a universal and harmonious registration system for biologicals. However, as of 2016, the EU still trailed the USA in developing its biopesticide industry, and, in fact, when comparing the number of registered biopesticide-active ingredients (RBAIs) with that of other major pesticide-use countries, the EU lagged again, with only 68 RBAIs, with Brazil and China having 100 and 111 RBAIs, respectively. In contrast, the USA has a staggering 400 RBAIs (Balog *et al*., 2016).

Balog *et al*. (2016) found a trend among countries with a slow-growing biopesticide industry. Their finding concerns those countries that have implemented strict environmental policies and regulatory acts have, inadvertently, prevented the growth of an industry that is poised to have a major impact on the fight against rapid climate change. For example, from the year 2000 to 2015, the EU adopted 14 regulatory acts regarding biopesticide registration, compared to its 181 environmental regulatory acts relating to pesticide use. In contrast, the USA has implemented only 20 environmental regulatory acts relating to pesticides. The limited number of such acts in the USA is because the country considers biopesticides to have no harmful ecological impact and requires only a show of no risk to human health. The USA shares such a sentiment of negligible environmental eco-toxicity with India, Brazil and China (Balog *et al.,* 2016).

The EU situation is troubling for such countries as South Africa, which rely on the EU as an important export partner. With the EU pesticide regulatory environment being difficult to navigate, it also becomes difficult for those exporting products to implement the correct growing practices. The disparity of the laws on pesticide use among the different countries has resulted in a strained relationship with the EU, particularly in South Africa’s fruit export industry. South African growers continue to use chemicals that are unacceptable to EU countries, mainly because there are few alternative products to synthetics available to them (Hatting & Malan, 2017).

South African pesticides are governed by the Fertilisers, Farm Feeds, Agriculture Remedies, and Stock Remedies Act 36 of 1947. In striving to improve the situation, since the 1970s, the South African government has slowly phased out certain synthetic pesticide products and classes like monocrotophos (2005), chlorpyrifos (2010), endosulfan (2012) and aldicarb (2012) (Hatting & Malan, 2017). However, multiple pesticides that have already been banned in the EU are still being sold in the Global South. The year 2010 saw the introduction of the Pesticide Management Policy for South Africa, with, in 2013, the government introducing its Bioeconomy Strategy (South Africa DST, 2013). The Strategy supports the National Environmental Management: Biodiversity Act 10 of 2004 (NEMBA), in relation to the National Environmental Management Act 107 of 1998 (NEMA) (South Africa DAFF, 2010) which aligns with the Convention on Biological Diversity (CBD) (2010). At the tenth conference of the parties of the CBD in Nagoya, Japan, guidelines were proposed to encourage biodiversity research and to ensure that local communities benefited from the biodiversity resources, as well as that the existing biodiversity was protected and maintained by means of bioprospecting. The laws implemented by different governments, thus, took into consideration the enormous potential that the environment holds.

Following the CBD, the regulatory acts implemented sought to establish South Africa as a leading biotechnological country, and an enormous amount of capital investment was provided to multiple projects, through such organisations as the Technology Innovation Agency (TIA). The provision of investment was aimed at developing such biological products as biopesticides, using safe biochemical and native microorganisms. Furthermore, in 2010, specific guidelines were implemented specifically for the registration of such biological remedies as biopesticides (South Africa DAFF, 2010), with the documents again being updated in 2015 (South Africa DAFF, 2015 a, b, c). In 2013, the South African Bioproducts Organisation (SABO) was established to aid discussion between those selling bioproducts and the industry. Such progress was positive for South Africa, with the associated guidelines being continually updated.

Though the existence of such guidelines has served to streamline the biopesticide registration process, locally produced biopesticide products are still scarce in South Africa. The NEMBA, in trying to protect the environment and to ensure that the local communities shared in the rewards of bioprospecting, has inadvertently problematised the registration process (Alexander *et al*., 2021). The laws involved have deterred investment, due to the difficult bioprospecting permit laws concerned, and they have prolonged an already expensive registration process. Alexander *et al*. (2021) state that the legislation surrounding biodiversity and bioprospecting research is having a knock-on effect that is impacting on such areas as undergraduate research and training, postgraduate enrolment in biodiversity science programs, biodiversity science career prospects, decreasing local professional capacity.

Many of the policies implemented concerned the import and export of foreign organisms. However, such need not be a concern in terms of biological products using strictly native organisms, especially in South Africa. The importing and mass release of foreign organisms is a contentious issue, and much debate surrounds their introduction. Imported foreign organisms should undergo a risk analysis, as it can pose significant risk or biological pollution to an ecosystem, additionally, local species are often better adapted to their native environment (Abate *et al.*, 2017). However, the importation of high-volume, low-cost exotic microorganisms into developing countries for field application, disrupts the identification of locally isolated species as either indigenous or foreign, weakening local biodiversity assessment studies. In terms of biological control, hundreds of thousands of new natural enemies still await discovery (Van Lenteren, 2012).

Although South Africa has implemented the recommended policies and despite it having actively tried to grow the biological industry, some unnecessary regulations are still in place that hinder growth. Seven different government agencies and departments administer biopesticide registration in South Africa (Rother *et al*., 2008; South Africa DAFF, 2015 a, b, c), with there being a lack of collaboration between the groups concerned. For example, although both the Department of Agriculture and the Department of Environmental Affairs are concerned with issues relating to biopesticides, a weak bridge exists between the two departments in South Africa, and the responsibilities of the pesticide registration process are diverse. Thus, without appropriate collaboration and communication, the delays that are present in the registration process are costly for any registering business.

Another challenge to the development of a viable biopesticide industry is the responsibility of the Department of Health (DoH) in terms of the biopesticide registration process. According to the South African Department of Agriculture, Forestry and Fisheries (2015a), the development of biopesticides requires the production of "reports and summary on the pharmacology, toxicology and environmental impact studies of the active ingredient and its metabolites and/or degradation products according to OECD guidelines", as well as reports on formulation toxicity. However, the studies concerned are expensive and timely for the registering companies involved. Moreover, in South Africa, no laboratory yet exists that can conduct the necessary tests, as there is a lack of knowledge concerning biological skills on how to test for the toxicology of the organisms, because their use as a pesticide is so new. Companies are, therefore, often forced to outsource to be able to gather such data, which increases the expense of the process, and companies simply cannot afford such outsourcing without seriously jeopardising the commercialisation effort. Without the local capacity to compile such reports, the products tend to sit in "registration limbo", with approximately 500 products not currently being able to be processed and registered (S. Storey, personal communication).

An idea that is gaining traction in terms of overcoming the reoccurring problems is the development of a universal and uniform registration system for biological products. Currently, the registration requirements differ greatly between the different countries concerned, but such groups as the Organisation for Economic and Co-operative Development (OECD), the International Organisation for Biocontrol (IOCB), the Codex Alimentarius Commission (Codex), the North American Free Trade Agreement (NAFTA) and the International Code of Conduct for the Distribution and Use of Pesticides (CoC) have attempted to harmonise and standardise the global pesticide registration policy (Arora *et al*., 2016; Handford *et al*., 2015). Not only will a universal system assist registration, but it will also encourage trade and ensure that new research and policy are better aligned than they were in the past, as well as it helping to protect the planet from excessive climate change. In embracing the concept, Canada and the USA have developed a joint review system through the US Environmental Protection Agency (EPA) and through Health Canada's Pest Management Regulatory Agency (PMRA) (Leahy *et al*., 2014). The system has yielded positive results, with products reaching the market quicker, and within a shortened and less expensive registration period, which has been achieved by means of removing unnecessary impact and toxicity assessment trials when crossing borders (Arora *et al*., 2016).

The summation of the registration issues above has provided South African growers with three choices: to continue using synthetic products, whether or not they are banned; to use unregistered and, thus, illegal biologicals that have no efficacy data in terms of their South African performance and which usually contain foreign organisms; or to change their entire growing structure and to divert to something that is akin to regenerative agriculture, with zero input. With no alternatives currently being available, such is now the reality for South African crop growers. As the situation is critical, the South African government must address the issues concerned as soon as possible. Significant investment has already taken place in terms of the research into, and the development of, biopesticides. However, few of the projects have yielded products, due to the registration hurdles concerned.

Commercial, economic and market barriers

In developing countries, pesticide use has increased, as they become mired in the global pesticide complex (Koul, 2011; Schreinemachers & Tipraqsa, 2012; Shattuck, 2021; Shattuck, et al. 2023). The multifaceted nature of synthetic pesticide growth is mainly attributed to the increase in the number of off-patent product formulations (with 79% of the available synthetic pesticides being off-patent derivatives in 2014), In addition, the emerging low-cost manufacture of pesticides, particularly in China, has driven down costs and scaled up production capacity (Haggblade *et al*., 2017; Shattuck, 2021). Also, the long-existing policies and laws that govern pesticide use have resulted in both European and American, red-listed products being used in the developing countries, particularly in Africa (Bega, 2021). The developing countries have tended readily to adopt synthetic pesticide technology, due to the price reduction involved, regardless of the impact that this might have on their health, as well as

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on the health of the greater environment, with their practice having created a significant market for agrochemicals.

Fortunately, the biopesticide market is growing rapidly (Marrone, 2014, 2023; Olson, 2015; Samada & Tambunan, 2020; Wilson *et al*., 2020). Such rapid growth is largely due to the demand for eco-friendly products and to the banning of multiple classes of synthetics, since the early 2000s. Biopesticides have captured a large part of the market in both Europe and North America, with South America and Asia, and particularly India, also having significant biopesticide markets (Gryzwacz *et al*., 2009). In Africa, few locally produced biopesticides products exist, with the African countries coming to rely almost exclusively on synthetic pesticides, as they cannot afford imported registered biopesticides.

The large multinationals were expected to play a large part in biopesticide development, as the synthetic market came under strain, and they did so for a time. However, the multinationals were initially deterred from developing biopesticides for the following reasons: their research and development budgets were usually directed towards potential biological solutions that possess chemicals, and that are basically risk-free (Bailey *et al*., 2010); they were deterred from doing so due to the limited success of biopesticide ventures in the past (Gaugler, 1997; Warrior, 2000; Benuzzi, 2004; Gelernter, 2005) they reduced their amount of investment in biopesticides, as a result of the low profits (Droby *et al*., 2009; Stewart, 2001; Hallett, 2005; Mishra *et al*., 2014); the return on investment (ROI) was less secure with biopesticides than it was with synthetic pesticides (Evans, 2004; Stewart, 2001), due to the difficulty of establishing intellectual property for such complex organisms as fungi and nematodes; and, finally, because the mass consolidation of the large corporations stifled investment (and still does), competition and innovation, and, thus, novel product development (Diez *et al*., 2018).

Many of these factors are still major deterrents to multinational investment into the biopesticide market, and only multinational corporations, that control a large portion of the market, possess the financial capacity to research and develop novel products. Small start-up companies often cannot afford the cost of product development, optimisation, registration, and highly qualified scientific personnel. This is especially true in the developing world and developing biopesticides using local microorganisms, as an example, is an extremely difficult endeavour without significant financial support. However, blaming large multinationals and focusing on such matters as corporate maleficence (which is exacerbated by the popular media) minimises the importance of the global pesticide complex that is now "deeply embedded in agrarian life" (Shattuck, 2021). Substituting synthetics for biopesticides, or, at least, integrating biopesticides into a synthetic spray programme is difficult, as the whole system involved is inherently, resistant to change, including the end-user.

Although the biopesticide industry is poised to disrupt the pesticide market, the structure of the biopesticide market, and how biopesticides function, needs to be better understood by all the stakeholders concerned than they are at present. Also, a crucial aspect to understand within the biopesticide market is the difference between the discovery, the screening and the research and development phase of biopesticides versus that of synthetics (Lahlali *et al*., 2022). The high cost of expenditure often does not lie in the actual product development, but in the registration (ACP, 2004; Arora *et al*., 2016). If the registration problem is rectified, developing a biopesticide will prove to be far cheaper than developing a synthetic product.

From 1995 to 2014, the cost of developing a synthetic pesticide increased by 188%, with it now requiring between $250 and $300 million to bring such a product to market. The escalation in costs has come about because the length of the product development phase has increased from 8.3 years in 1995 to 11.3 years in 2014. Of even greater financial consideration, the expensive ecotoxicity, the product efficacy and the non-target trials can currently cost up to $20 million dollars, and take between three and four years (Panetta, 1999; Sparks, 2013; Phillips McDougell, 2016). Moreover, the discovery process and the screening of potential compounds now requires more time than it did in the past. In 1956, the number of compounds that were screened for product potential was 1800, with it being 10 000 by 1972, 20 000 by 1977, and 50 000 by 1994. In recent years, approximately 140 000 compounds are screened before a potential candidate is chosen. Noteworthy is that the screening process is much more efficient with the modern computing programmes that can screen thousands of compounds in a relatively short space of time (Sparks, 2013), and with the advent if artificial intelligence, this process is now even more rapid (Djoumbou-Feunang *et al*., 2023).

The issue of decreased pesticide discovery success is further exacerbated by the reduced number of companies that are actively involved in the research and development of both synthetics and biopesticides. Sparks (2013) showed that in 1950, 1960, 1970 and 1980, there were 34, 49, 44 and 38 companies researching new products, respectively. The number was slashed to only six companies in 2010, which was mostly due to the numerous mass mergers that occurred in the industry at the time. With the merger of Dow and Dupont in 2017 and with ChemChina's acquisition of Syngenta in 2017 (with ChemChina notably spending most of its research budget on the improved production and formulation of off-patent products, rather than on the development of new products), with the result being that the number of companies researching new products declined even further.

The case for biopesticides is that it takes $3 to $5 million dollars from discovery to market for biopesticides, with the time to market ranging from 3 to 5 years, depending on the active ingredient organism and the size of the investment concerned (Marrone, 2011). In the right policy environment, such as that in the USA, the registration process tends to cost less than a few million dollars (Marrone, 2023). Accordingly, it is far cheaper to develop a biopesticide than it is to develop a synthetic. The reduced cost of development would seem to serve as an attractive trait for potential investors, yet, coupled with the difficulty of navigating the registration system, a large knowledge gap also exists regarding how the biopesticide market functions.

Conventional agricultural practice uses a so-called pesticide calendar, whereby, depending upon the crop concerned, the producers are told that certain products must be sprayed at certain times of the year. The spraying of biopesticides, in contrast, often does not fit into the calendar, and, moreover, should not be arbitrarily sprayed, regardless of whether a pest is present. Biopesticides, instead, tend to conform to the cyclical nature of agriculture within the ambit of an integrated pest management (IPM) programme (Cherry & Gwynn, 2009). For example, a pest might only manifest itself once a year, as is usually the case with insect pests. The biopesticide should then be applied to control the pest for the period concerned. Once the pest threat is under control, the application of the biopesticide should cease, with reapplication occurring if the pest returns the following season. Investors often fail to understand the cyclical nature of biopesticides, with them questioning why a product should not be applied monthly for maximum and rapid return on their investment. Investors tend to be reluctant to invest in a product that is applied only once a year. The result has been low investment from venture capitalists, like those in South Africa (Sheila Storey, personal communication).

Additionally, when those with access to capital for rapid biopesticide product development are unwilling to invest in research and development, the responsibility for the difficult and expensive research and development phase falls to industry, academic institutions and the state. Only once a product is registered and there is proof of concept for its mass production and formulation is the investment attractive to large companies and to venture capitalists. Without the support of the wealthy private sector, which has the capacity for scaling up, and for the implementation and maintenance of quality control systems and marketing (Cherry & Gywnn, 2009), the biopesticide industry will be slow to reach its potential.

The lack of investment from wealthy corporations tends to perpetuate the biopesticide market access problem even further. For example, the infrastructure for establishing a synthetic pesticide is well-entrenched, including the necessary trained personnel. Biopesticide technology, which is a multidisciplinary science, requires the input of highly trained scientists and engineers for purposes of product development, mass production, and field trials assessing efficacy and ecology. Training such people is expensive and takes years. Thus, the input of suitably trained personnel, the physical infrastructure and the institutional capacity of the biopesticide industry, including the necessary bioprocessing plants and research facilities, are necessary for development (Dalvie *et al*., 2009).

Another crucial part of the biopesticide industry infrastructure is the logistics concerning the distribution of biopesticides. In the early 2000's, Benuzzi (2004) argued that, on almost every occasion where a large synthetic-producing company tried to develop a biopesticide, the project failed. The cause of such failure tended to be because of the adoption of an incorrect approach to biopesticides, because of the lack of technical knowledge, because the market is too small, or because the use of the existing distribution channels had been unsuccessful. Benuzzi (2004) emphasises that the distribution of a biopesticide product must be carefully planned.

In many countries, it has been similarly highlighted that a major issue in the development of a biopesticide market is an unestablished distribution network (Blum, 2002). As synthetic producers have strong distribution channels, new biopesticide companies are likely to try and set up their own sales team and distribution channels, to avoid competing with synthetic producers, which adds to the expenses and requires an in-depth knowledge of agricultural logistics (Marrone, 2007). This seems like the logical solution to avoid competing with large corporations, but it is far too expensive for small biopesticide producers to undertake. In contrast, using the existing distribution channels requires training dealers and technicians in the product basics. In addition, due to the absence of a distribution network, the producer of a biopesticide must bear the full cost of marketing the product themselves (Blum, 2002).

In South Africa, the policy environment, the low amount of investment and the lack of suitably qualified personnel has created the perfect setting for the establishment of a pseudo- black market. Crop growers with fears relating to exports urgently desire sustainable products, but, according to legislation, cannot use unregistered biopesticides containing foreign organisms or synthetic products. The synthetic product is an export risk and, thus, the only option for a producer is to use unregistered biopesticides, with foreign organisms as active ingredients. Commercial growers producing high-value crops demand to be able to use biopesticides, and, if the demand exists, it is likely to be met, despite the current legislation. South Africa has access to few locally produced biopesticides, with unregistered biopesticides, which are sold in large quantities, posing a significant risk to the environment. The safe use of an imported biopesticide product containing foreign organisms is dubious in the absence of sound safety trial data. The issue is compounded by the existence of untrained field scientists and pesticide dealers who fail to understand the dangers of unregistered biopesticide use, or who fail to understand the correct methods of application for such products, resulting in inferior product performance and, thus, a decrease in biopesticide product confidence. Moreover, a huge demand still exists for synthetic pesticide products in South Africa, where a large rural farming sector exists, whose produce is mostly used for home consumption (Lehiff & Cousins, 2005), and which cannot afford expensive new agricultural technology.

The demand for expensive biopesticides, in contrast, usually comes from niche market, high- value crops that are not farmed by rural farmers, so that a significant portion of the market is unavailable to biopesticide producers (Grzywacz *et al*., 2014), while a large rural market still exists for synthetic producers to exploit. This additional market barrier is almost non-existent in the developed countries.

Education barriers

Beyond the policy environment and the market barriers preventing biopesticide-related success, multiple education and training barriers exist. What is quite clear when considering all the previously discussed points is that a massive knowledge gap exists between those who research, govern, invest in, sell and use bioproducts.

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A realistic estimate and understanding of what to expect and what not to expect is critically important. A cultural transition and change in mindset from chemical to biological pesticide use cannot be successful without proper education and training at all levels in the distribution chain from the manufacturer to the distributors to the retailer, and finally at the grower level.
(Warrior, 2000)

Currently, considerable lack of faith exists in the use and performance of biopesticides, as well as there being a lack of awareness of biopesticide benefits, of knowledge about biopesticides, and of grower confidence in biopesticide products. Growers also tend to receive advice regarding biopesticide use from synthetic suppliers who lack the appropriate knowledge (Arora *et al*., 2010; Sachdev & Singh, 2016). The existence of such knowledge gaps has resulted in inappropriate bioproduct legislation, a low degree of investment, incorrect incorporation into the existing pesticide application programmes, and the end-users' uncertainty about, and mistrust of, the efficacy of new bioproducts (Lahlali *et al*., 2022).

The legislation regarding bioproducts is susceptible to unsuitable policy and to inappropriate practices and guidelines when those governing bioproduct use lack the necessary expertise (Chandler *et al*., 2011). Consider the following: the decision to register a biopesticide is the responsibility of a government official or of a registrar, who is advised by a registration committee. When the officials concerned lack the appropriate knowledge, and usually when the development of new technologies progresses rapidly, the decisions that tend to be made regarding data requirements can be inappropriate. The data requested is often subject to inappropriate requirements, due to the limited knowledge of micro and macro-organisms, of the complexity of the existing microbial systems, and there is usually a misunderstanding of how to evaluate biopesticides correctly (Mensink & Scheepmaker, 2007; Laengle & Strasser, 2010), which delays the entry of the product onto the market.

Government officials also need to understand what biopesticides are, as well as, more importantly, what they are not (Cherry & Gwynn, 2009; Grzywacz *et al*., 2009). The registration committee of any country, at the very least, requires a 'biopesticide champion' (Cherry & Gwynn, 2009), with possession of excellent biopesticide knowledge, who can vouch for their safety and who can point out irregularities in the system. Only if the legislation of biopesticides complies with the appropriate registration requirements and allows for rapid commercialisation, with those that govern the management of biopesticides being well-equipped with the right knowledge, will the biopesticide market flourish.

Considering the end-consumer and their perception of biopesticides is also important. Having a new product available does not necessarily mean that it will be purchased, due to the different farming strategies and product preferences involved. New products are a risk for growers, who will, ultimately, base their decision to purchase on the yields, profitability, asset endowment and level of risk involved (Bowman & Zilberman, 2013). Growers, who are often risk-averse, tend to be reluctant to alter their current practices, with them often having conservative attitudes towards change (Bowman & Zilberman, 2013), and with them being unlikely to adopt new products, even if they are forced to change (Bateman, 1998). However, when the growers have managed to attain high yields using synthetic products, their faith in such products tends to be unwavering. The situation is problematic, in terms of the products based on novel technologies being advertised to the growers. Growers are often unwilling to purchase new products, regardless of their merit, due to their limited understanding of the new technology.

The willingness to purchase is directly related to education. Several recent studies have shown that growers are unwilling to purchase biopesticides in the absence of knowledge transfer on biopesticide science, on IPM, and in terms of the ability to access such educational resources as scientific publications and university resources (Coulibaly *et al*., 2007; Goldberger & Lehrer 2016; Constantine *et al*., 2020; Nyangau *et al*. 2020; Guo *et al*. 2021). The willingness to purchase and the grower's decision-making abilities are also influenced by social factors. Guo *et al*. (2021) found that the product preference and the choices of neighbouring growers, or of growers in the same community, can radically influence product choice. The influence of one's peers is a serious consideration in terms of adopting new products. Guo *et al*. (2021) found that, even if a grower was willing to purchase a biopesticide, with their behaviour reflecting such willingness, they might, later, abandon their use of the biopesticide if their neighbouring peers continued to use synthetics.

Furthermore, without sufficient appropriate training and education, growers might remain unaware of the correct method of application for biopesticide products. Biopesticides often require specific environmental conditions, cannot be used in conjunction with certain chemicals, and might require a complete shift in the overall pest strategy that a grower implements. If a biopesticide is applied incorrectly, it will be relatively ineffective, with it seeming not to work as per the label claims. When the grower deems a product to be ineffective, and they are unaware of their incorrect use of the product, the grower might refrain from using the same product in the following season. A grower who adopts a new product is likely to test it on a few hectares during the first season and slowly increase its use over the next season, leading to its full adoption during the third season, and will often abandon the product if it proves ineffectual after the first season (Marrone, 2007).

Often, the only access to biopesticide information and to the correct application of biopesticides is provided to growers by the pesticide dealers themselves, especially in the case of rural farmers and those in poor, undeveloped countries lacking in internet access (Rother *et al*., 2008). When growers use the existing distribution channels, the dealers, usually being synthetic pesticide representatives, tend to be insufficiently qualified to market biopesticides (Blum, 2002). In describing the pesticide sales environment in the past, Benuzzi (2004) and Gaugler (1997) state how dealers and technicians would attempt to convince a grower of the ineffectiveness and the slow action of biopesticides, to try and peddle their own synthetic product, and so earn as much commission as possible. Moreover, should a dealer recommend a new product, and it falls short of the client's expectation, the dealer would risk losing the client concerned. So, a pesticide dealer would tend to promote products with which they are familiar and which they can confidently claim to work, to maintain their own job security, which is an understandable position. A psychological battle exists where "when a BCA [Biological Control Agent] fails, biocontrol does not work 'forever' and when a chemical does not work, there is always another, better one" (Benuzzi, 2004). Growers have tended to rely on synthetics for so long, that they are often reluctant to switch to new eco-friendly products, especially when the synthetic solution appears to work well (Chandler *et al*., 2011).

Such sociological and psychological research is crucial to understanding the more human- centred issues that tend to hinder biopesticide success. Moreover, studies of this nature are especially applicable to South Africa, which shares the greater African problem of having only limited access to both non-formal and formal education and training. It is crucial that socio-economic research be conducted, to reach an understanding of the underlying factors that influence why end-consumers do not adopt biopesticides. In the absence of such knowledge, both the public and the private sectors risk making wrong decisions in relation to the promotion of biopesticides (Guo *et al*., 2021).

As a developing nation, South Africa has a large rural farming sector, which is largely uneducated, and which tends to have only limited access to new products using novel technologies. In the rural sectors, the demand for easy-to-use pesticides is high, with the pesticide industry often targeting the growers through aggressive marketing campaigns (Rother *et al*., 2008). The following statement from Aga, 2019, illustrates how the notion of the pesticide complex is deeply embedded in rural agriculture in India, which is strikingly like the current situation in South Africa. As farmers adopt new, expensive commercial crops, which are often ecologically unsuitable, and in which their accumulated experience is thin, they encounter a "thick fog of uncertainty" – about weather, rainfall, pests, fungi, diseases, and prices. They are unsure of themselves and the market, and there is virtually no state-led support system. This provides fertile ground for the corporate marketing of agrichemicals, as medicine for crops and the changing agrarian relations and conditions of cultivation.

It is imperative that South African growers, particularly in the rural communities, are trained in pesticide use and are encouraged to adopt eco-friendly affordable products and growing methods. In the interviews conducted with government officials by Rother *et al*. (2008), the situation in South Africa was described by an agricultural official in Gauteng as

I personally think that we are sitting on an environmental and human health time bomb. It is only by God's grace that in general most rural farmers are not sufficiently wealthy yet to be able to afford to use large volumes of pesticides. But it is coming. The greatest moral responsibility we have is to train the rural communities as quickly as possible. This will of course take time, people, money…

Anon

The South African government has taken cognisance of the issues and has begun various initiatives and implemented key policies to help rural or emerging growers to commercialise in such a way as to provide access to new technologies. Of particular importance was the creation of the Integrated Sustainable Rural Development Programme, 2001, and a Strategic Plan was created for the South African Department of Agriculture in 2007 (Rother *et al*., 2008). However, though such programmes may be available, the organisations concerned, including the Agricultural Research Council (ARC), which is responsible for providing extensive training, have few programmes and limited funding for such endeavours. It is imperative that the South African government ramp up investment into pesticide education systems to protect our agricultural industry.

Entomopathogenic nematode biopesticide commercialisation

Entomopathogenic nematodes (EPNs) of the families Steinernematidae and Heterorhabditidae have received wide-ranging attention as safe and successful biocontrol agents for soilborne insect pests. EPNs utilisation as a biocontrol agent commenced in 1931 in the USA, to control the Japanese beetle, *Popillia japonica* Newman (Coleoptera: Scarabaeidae). Currently, EPN-based biopesticide products are sold by numerous companies around the world, for the control of a variety of economically important pest insects (Ravensberg, 2011; Abate *et al*., 2017). For the past 15 to 20 years, the number of EPN- producing companies was relatively stable (Ehlers & Shapiro-Ilan, 2005), but in recent years it has begun to accelerate.

The commercial potential of EPNs was realised in the 1980s (Miller & Bedding 1982; Bedding, 1984; Pace *et al*., 1986), when a method of *in vitro* mass production on the commercial scale was established, which could, in time, match the scale of production for some chemical-based insecticide competitors. While the production technology has been refined and optimised, the EPNs occupy, niche markets and in time, have the potential to expand to larger markets (Bateman, 1998; Ehlers, 2001).

Progress during the 1990s was substantial, as EPNs rose in popularity because of the development of large-scale bioreactor production and easy-to use formulations (Ehlers, 2001; Ehlers & Shapiro-Ilan, 2005; Georgis *et al*., 2006), the number of EPN producers began to increase. The sales of nematode biopesticides were worth US$ 18.1 million in 2010 (Lacey *et al*., 2015), making up only 4.5% of total biopesticide sales. The interest in, and the growth of EPNs, came about largely because they were one of the earliest microorganisms to gain registration exemption in the developed countries, due to their negligible impact on human health and the environment (Rizvi *et al.*, 1996 Gaugler, 1997; Ehlers, 2011).

Despite there being significant interest and demand for an EPN biopesticide, the commercialisation of EPNs has seen multiple successes and failures (Shapiro-Ilan *et al.,* 2002). EPNs have never fully captured a significant share of the market, because numerous factors besides product efficacy affect their adoption by growers, such as improper labelling, refrigeration requirements, incorrect handling and

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application, and increased costs compared to those incurred with synthetic products (Georgis *et al*., 2006). Unfortunately, early in the commercialisation of EPNs, their perception was often impacted on by the improper targeting of the insects concerned. The commercial companies tended to target insects that were found on commercial crops, because such insects had a significant impact on market share (Georgis, 2004; Georgis *et al*., 2006). What should be pursued is predictable control, which is notoriously difficult to achieve, due to the complex interplay of abiotic and biotic factors, with it being the "greatest intellectual challenge facing biological control today" (Georgis & Gaugler, 1991). Though this was a comment from three decades ago, the point remains today.

In the developed world, multiple EPN-producing companies exist, such as the previous Becker Underwood (acquired by BASF) in the USA, e-nema in Germany and Koppert Biological Systems in the Netherlands (Ravensberg, 2011; Abate *et al*. 2017). However, EPN biopesticide-producing companies are scarce in the developing world, especially in Asia and Africa.

Entomopathogenic nematodes have been identified as a potential new biopesticide candidate for agricultural pest control in South Africa, on a variety of crops and against a wide range of pests. Much of the research that has been conducted so far in South Africa has focused on obtaining local EPN isolates to screen for pathogenicity and efficacy against such pests as *Cydia pomonella* L. (Lepidoptera: Tortricidae), *Thaumatotibia leucotreta* (Meyrick) (Lepidoptera: Tortricidae) and *Eldana saccharina* Walker (Lepidoptera: Pyralidae) (Malan & Hatting, 2015; Malan & Ferreira, 2017; Hatting & Malan, 2017; Hatting *et al*., 2019), and on using native EPNs species to target important pests Malan and Hatting (2015).

However, little to no work has yet been done either on mass culturing (Ferreira *et al*., 2014, 2016; Ramakuwela *et al*., 2016; Dunn et al., 2019) formulations (Kagimu *et al*., 2017, 2021, Kagimu & Malan, 2019; Nxitywa & Malan, 2021 a, b), or on nematode ecology after application, of the local EPN species. Currently, only one EPN-based product is available in South Africa, being the imported Cryptonem®, with the active ingredient *H. bacteriophora*. Its use extends across the African continent and although large investments have been provided to increase nematology research to such areas as sub-Saharan Africa (Cordata *et al*., 2019), the capacity for EPN mass production is low in Africa.

The reason for a locally produced EPN product not yet having been developed in South Africa is the poor legislation that has been enacted regarding biopesticides, particularly in the case of such entomopathogens as fungi, nematodes and parasitoids. As was previously described, the inadequate regulation of such production has affected research, investment, education and end-consumer perception. Even though the registration guidelines have recently been updated (DAFF 2015, SA, a, b, c), the data requirement guidelines are still inappropriate, especially regarding the requirements set by the South African Department of Health.

Currently, the requirements for the mass culturing of EPNs for commercialisation require a permit, bioprospecting permits, and a declaration of safety conforming to the requirements relating to the Non-Proliferation of Weapons of Mass Destruction Act 87 of 1993, of which all are counterproductive to the commercial success of such a safe biopesticide. Such requirements do not apply to EPNs in the developed countries. Although strict laws have been implemented to protect the grower and to ensure that the local communities benefit from the local biodiversity, the laws and policies concerned are preventing new, eco-friendly bioproducts from entering the market in South Africa.

Due to the high rate of capital investment and the restrictive legislative environment, there is reluctance to invest in EPN biopesticide research. At a virtual conference that was held by the South African Society for Enology and Viticulture (SASEV) (2020), Allsopp and Malan (2020) state that, although 20 years of research has been undertaken, the necessary efficacy field trials for an EPN product have not yet been conducted, and a suitable product has not yet been commercialised. Moreover, the authors say that most of the research on EPNs is undertaken at universities, and the that the study period of a postgraduate student is too short for the appropriate trials to be undertaken, and no contingency plan is in place for taking the next step towards the commercialisation of a potential usable product. Although multiple trials showing the efficacy of EPNs have been conducted in South Africa (Hatting & Malan, 2017; Malan & Ferreira 2017; Dlamini *et al*., 2019; Steyn *et al*., 2019; Moore *et al*., 2021; Malan & Knoetze, 2024), the information made available from such trials is often not accepted, due to the strict formalities, rules and regulations involved.

Unfortunately, in South Africa, because growers are becoming increasingly desperate for pesticide products that facilitate their export relationships, and as there are few locally produced products available, growers are still currently willing to purchase unregistered imported products. Claiming that an imported foreign EPN is safe for the environment without the necessary data to substantiate the claim must be claimed with caution. Despite multiple foreign EPN biopesticide products with refined mass production protocols, long-distance distribution channels and easy-to-use formulations being available for South African producers, only poor excuses have, so far, been offered for not yet developing local products (Abate *et al*., 2011).

CONCLUSION

The predicted boom of the biopesticide market has not yet fully materialised, but it is still growing at a reasonable rate (Glare *et al*., 2012; Arora, 2015;). Biopesticides currently occupy a small percentage of the pesticide market, with most of the market being in the developed world. In Asia and Africa, local biopesticide production is small, with the regions concerned still relying heavily on synthetic inputs. Biopesticides will struggle to grow and compete with the synthetic industry if the developing nations are absent from the biopesticide production scene.

Much of the growth of biopesticides in the developed world is due to the appropriate legislation that has supported and accelerated commercialisation. A positive legislative environment is the key to unlocking the biopesticide market in any given country, as it encourages investment, education and training. Under the right legislation environment, such commercial barriers as low investment and market access diminish. Only when legislation supports rapid commercialisation and when it uses a streamlined and inexpensive registration system, does biopesticide capital investment become more attractive, and establishing new products will become easier for investors than it has been in the past.

The situation, in turn, is likely to result in a much greater variety of locally produced, cheaper products than are available now. Furthermore, new products will lead to increased investment in the research and training of all stakeholders, thus growing the base of personnel with biopesticide science knowledge.

The potential of biopesticides to help decrease further environmental damage from unchecked synthetic pesticide use is significant. Biopesticides could very well have majority control of the market in the very near future, but the possession of such control will only be possible with the right strategy, to ensure that the process of discovery, development, registration and commercialisation goes smoothly and is well-supported by appropriately qualified stakeholders. The requirements for the development of a successful biopesticide market are clear and doable, and it is imperative that countries begin to support the rapid development of local biopesticide markets.

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