Nanotechnology in the Life Sciences

Kamel A. Abd-Elsalam
Ram Prasad *Editors*

Nanobiotechnology Applications in Plant Protection

Volume 2

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Nanotechnology in the Life Sciences

Series Editor

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Nano and biotechnology are two of the 21st century's most promising technologies. Nanotechnology is demarcated as the design, development, and application of materials and devices whose least functional make up is on a nanometer scale (1 to 100 nm). Meanwhile, biotechnology deals with metabolic and other physiological developments of biological subjects including microorganisms. These microbial processes have opened up new opportunities to explore novel applications, for example, the biosynthesis of metal nanomaterials, with the implication that these two technologies (i.e., thus nanobiotechnology) can play a vital role in developing and executing many valuable tools in the study of life. Nanotechnology is very diverse, ranging from extensions of conventional device physics to completely new approaches based upon molecular self-assembly, from developing new materials with dimensions on the nanoscale, to investigating whether we can directly control matters on/in the atomic scale level. This idea entails its application to diverse fields of science such as plant biology, organic chemistry, agriculture, the food industry, and more.

Nanobiotechnology offers a wide range of uses in medicine, agriculture, and the environment. Many diseases that do not have cures today may be cured by nanotechnology in the future. Use of nanotechnology in medical therapeutics needs adequate evaluation of its risk and safety factors. Scientists who are against the use of nanotechnology also agree that advancement in nanotechnology should continue because this field promises great benefits, but testing should be carried out to ensure its safety in people. It is possible that nanomedicine in the future will play a crucial role in the treatment of human and plant diseases, and also in the enhancement of normal human physiology and plant systems, respectively. If everything proceeds as expected, nanobiotechnology will, one day, become an inevitable part of our everyday life and will help save many lives.

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Preface

Plant diseases are caused by bacteria, fungi, insects, nematodes, phytoplasmas, and viruses; the diseases provoked by these pests cause financial losses by reducing attainable yields, product quality, and/or shelf life. Only in the United States, over $600 million is expended annually on fungicides in challenge to control plant pathogens. Traditional plant protection strategies often prove insufficient, considering also that the application of chemical-based pesticides has negative effects on animals and human beings apart from causing decline in soil fertility. Recent industrial advancements have led to the fabrication of nanomaterials of diverse sizes and shapes. These innovations are the base for further engineering to create unique properties targeted toward specific applications. Nanotechnology would deliver green and efficient alternatives for the management of plant diseases without harming the environment, while the most favorable strategies, in recent scenario, are the use of micro- and nanotechnology to promote a more efficient assembly and then release of specific and environmentally sustainable active principles. The wide range of nanotechnology applications in agriculture also includes nanopesticides for the control of plant pathogen interactions and provides new techniques for crop disease control. However, its use in agriculture, especially for plant protection and production, is an under-explored area in the research community. Nanotechnology has many applications in all stages of production, processing, storing, packaging, and transport of agricultural products. Moreover, it will revolutionize the agriculture and food industry by using new and innovative techniques such as precision farming techniques; enhancing the ability of plants to absorb nutrients; improving seed germination and growth, more efficient and targeted use of inputs, plant protection, and pathogen and pesticide/herbicide residue detection; controlling diseases; withstanding environmental pressures; and creating effective systems for processing, storage, and packaging.

This book deals with the application of nanotechnology for quicker, more cost-effective, and precise diagnostic procedures of plant diseases. Additionally, the combination of nanotechnology with microfluidic systems has been effectively applied in molecular plant pathology and can be adapted to detect specific pathogens and toxins. Moreover, the application of nanotechnology in plant disease control, antimicrobial mechanisms, and nanotoxicity on plant ecosystem is discussed in detail.

The second volume of the book focuses on additional information on the applications of nanotechnology in plant protection and plant pathology.

In Chap. 1, Ganguli reviews the intellectual property rights aspects of nanobiopesticides. In Chap. 2, Khan et al. highlight the application of nanomaterials in plant disease diagnosis and management. In Chap. 3, Jayarambabu et al. describe bio-engineered nanomaterials for plant growth promotion and protection. In Chap. 4, Mostafa et al. describe zinc-based nanostructures in plant protection applications. In Chap. 5, Gabal et al. focus on *Botrytis gray mold* nano- or biocontrol: present status and future prospects. In Chap. 6, Biswas and Sinha highlight on the bionanoparticles as antimicrobial agents. In Chap. 7, Priyanka et al. discuss nanopesticides: synthesis, formulation, and application in agriculture. In Chap. 8, Vimala Devi et al. focus on nano-biopesticides for crop protection. In Chap. 9, Lade et al. examine nano-biopesticide: synthesis and applications in plant safety. In Chap. 10, Kalia details on nanoscale fertilizers: harnessing boons for enhanced nutrient use efficiency and crop productivity. In Chap. 11, Shoala et al. give an overview of nanodiagnostic techniques in phytopathogens. In Chap. 12, Hassan Sabry discusses the role of nanotechnology applications in plant parasitic nematode control. In Chap. 13, Haleem Khan explains the cytotoxic potential of plant. Finally, Chap. 14 highlights the applications of engineered nanomaterials against plant pathogenic microorganisms.

We wish to thank the Springer officials, particularly William F. Curtis, Eric Schmitt, Eric Stannard, and Rahul Sharma, for their generous support and efforts in accomplishing this volume. We are highly delighted and thankful to all our contributing authors for their vigorous support and outstanding cooperation to write altruistically these authoritative and valuable chapters. We specially thank our families for their consistent support and encouragement.

With a bouquet of information on the different aspects of plant protections from nanomaterials, the editors hope that this book is a valuable resource for the students of different divisions; the researchers and academicians, working in the field of nanoscience, nanotechnology, plant sciences, agriculture microbiology, and fungal biology; and the scholars interested in strengthening their knowledge in the area of nanobiotechnology.

Giza, Egypt — Kamel A. Abd-Elsalam
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Contents

1 Intellectual Property Rights in Nano-biopesticides 1
Prabuddha Ganguli

2 Application of Nanomaterials in Plant Disease Diagnosis and Management 19
Mujeebur Rahman Khan, Tanveer Fatima Rizvi, and Faheem Ahamad

3 Bio-Engineered Nanomaterials for Plant Growth Promotion and Protection 35
Naradala Jayarambabu and Kalagadda Venkateswara Rao

4 Zinc-Based Nanostructures in Plant Protection Applications 49
Manal Mostafa, Hassan Almoammar, and Kamel A. Abd-Elsalam

5 *Botrytis* Gray Mold Nano- or Biocontrol: Present Status and Future Prospects 85
Esraa Gabal, Amal-Asran, Mohamed A. Mohamed, and Kamel A. Abd-Elsalam

6 Bionanoparticles as Antimicrobial Agents 119
Karabi Biswas and Sankar Narayan Sinha

7 Nanopesticides: Synthesis, Formulation and Application in Agriculture 129
Priyanka Priyanka, Dileep Kumar, Kusum Yadav, and Anurag Yadav

8 Nanobiopesticides for Crop Protection 145
P. S. Vimala Devi, P. Duraimurugan, K. S. V. P. Chandrika, B. Gayatri, and R. D. Prasad

9 Nano-biopesticides: Synthesis and Applications in Plant Safety 169
Bipin D. Lade and Dayanand P. Gogle

10 Nanoscale Fertilizers: Harnessing Boons for Enhanced Nutrient Use Efficiency and Crop Productivity 191
Anu Kalia, Sat Pal Sharma, and Harleen Kaur

11 Nanodiagnostic Techniques in Plant Pathology 209
Tahsin Shoala

12 Role of Nanotechnology Applications in Plant-Parasitic Nematode Control 223
Al-Kazafy Hassan Sabry

13 Cytotoxic Potential of Plant Nanoparticles 241
Ahmed A. Haleem Khan

14 Engineered Nanoparticle-Based Approaches to the Protection of Plants Against Pathogenic Microorganisms 267
Nariman Maroufpoor, Mehrdad Alizadeh, Hamed Hamishehkar, Behnam Asgari Lajayer, and Mehrnaz Hatami

Index 285

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Chapter 1
Intellectual Property Rights in Nano-biopesticides

Prabuddha Ganguli

Contents

1.1 Nano-biopesticides—An Overview 1
1.2 Intellectual Property Rights—Where Does IPR Meet Nano-biopesticides 2
1.3 Introduction to IPR Tools (WIPO and WTO) 4
1.4 Patenting Trends in Nano-biopesticides 6
1.5 Mitigating Potential Risks 15
1.6 Conclusion 16
References 16

1.1 Nano-biopesticides—An Overview

The worldwide biopesticide market, which are biological pesticides derived from natural materials such as plants, animals and bacteria [comprising bioinsecticides, biofungicides, bioherbicides, bionematicides, rodenticides, minerals and plant incorporated protectants (PIP)], is projected to grow at a CAGR of 13.9% till 2025 and reach a value of US$ 9.5bn by the end of 2025 (Transparency Market Research 2017). The key features driving the growth of "Green Agriculture" and "Integrated Pest Management" (IPM) programmes are the sustained need for controlled use of pesticides and fertilizers through environmentally friendly approaches for enhanced efficacy with simultaneous reduction of the amount of active ingredients (AIs) through targeted delivery of the AIs to specific sites, minimised negative environmental impact and preventing infusion of toxic residues in the agro-food value chain (Kumar et al. 2019).

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The global biopesticides market is fragmented in nature, though recent trends in consolidation of positions are led by strategic mergers and acquisitions amongst big players. Start-ups and small innovative companies have sprouted in fairly large numbers in the biopesticides R&D space especially related to their development and application.

Interestingly, the field of nano-biopesticides as "smart delivery systems of biopesticides" is still in its very early days, aggressively exploring commercial feasibilities. Conceptual breakthroughs have been reported with regard to their controlled release kinetics, enhanced permeability, stability, solubility, prevention of premature degradation of active ingredients (AIs) under harsh environment conditions, pesticide loss due to leaching and evaporation, functionality as biosensors for detection of pathogens and pesticide residues, etc.

Scientific published literature in the last two decades is replete with promising results in relatively safer application of biopesticides in pre-harvest and post-harvest agricultural practices as compared to chemical pesticides (Nuruzzaman et al. 2016). Advances in nano-technology leading to the creation of new processes and novel materials with surprising properties opened up wide ranging opportunities in their applications in precision agriculture and food technologies (Duhan et al. 2017; Athanassiou et al. 2018).

The active intervention of "Environmental Regulatory Agencies", "Legislations including the strategic management of Intellectual Property Rights" and "Ethical Overtones" in various jurisdictions needs to be taken into consideration to ensure balanced innovation, commercialisation and fair distribution of value in the marketplace. In recent times, national competition authorities have also begun to play a significant role in regulating the global agro-market dynamics by closely examining IPR licencing deals, collaborations, mergers and acquisitions involving diverse stakeholders.

The interface of nanotechnology [materials measuring between ~1 nm and ~100 nm] as applied in the field of biopesticides and Intellectual Property Rights is to be viewed from these interlaced and/or intercalated perspectives.

1.2 Intellectual Property Rights—Where Does IPR Meet Nano-biopesticides

Intellectual Property Rights (IPR) offers a workable legal framework for ownership in the knowledge space thereby ensuring due recognition and reasonable benefits to the creator/owner of that knowledge and offering him protection and incentive to share his knowledge with the society via fair "knowledge prospecting". Further, traditional knowledge in the public domain that has evolved over generations is recognised as "prior art", and in certain jurisdictions when utilised for development of new commercially exploitable knowledge, must involve fair sharing of benefits between the community liked to the relevant traditional knowledge and the present innovator utilising the traditional knowledge. It is also expected that the innovation process ought to prosper without damage to the environment including plant, animal and human life, and therefore it would be prudent to have such and other ethical & public interest issues incorporated as limitations in the intellectual property laws. It is hoped that a balanced and ethical framework of social governance and knowledge management would encourage development of innovations and advance a sense of respect for owned knowledge, discourage "knowledge piracy", "free riding", "profiteering from counterfeits", and "overuse/misuse" of IPR, thereby founding symbiotic relationships for the positive development of a free and fair society. However, for effective and ethical functioning of a strong and just IPR system, balancing legislations are required to simultaneously encourage innovations and discourage misuse of IPR and unfair/anti-social monopolistic practices. These considerations are most relevant in the context of IPR when applied to knowledge dynamics in the preharvest and post-harvest agricultural practises.

The WTO's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), negotiated during the 1986–94 Uruguay Round, introduced intellectual property rules into the multilateral trading system for the first time [WTO].

The TRIPS Agreement covers five broad areas, namely, (i) how general provisions and basic principles of the multilateral trading system apply to international intellectual property, (ii) what the minimum standards of protection are for intellectual property rights that members should provide, (iii) which procedures members should provide for the enforcement of those rights in their own territories, (iv) how to settle disputes on intellectual property between members of the WTO, and (v) special transitional arrangements for the implementation of TRIPS provisions.

Whilst the WTO agreements entered into force on 1 January 1995, the TRIPS Agreement allowed WTO members certain transition periods before they were obliged to apply all of its provisions. Developed country members were given 1 year to ensure that their laws and practices conform to the TRIPS Agreement. Developing country members and (under certain conditions) transition economies were given 5 years, until 2000. Least-developed countries initially had 11 years, until 2006—now extended to 1 July 2021 in general.

In November 2015, the TRIPS Council agreed to further extend exemptions on pharmaceutical patent and undisclosed information protection for least-developed countries until 1 January 2033 or until such date when they cease to be a least-developed country member, whichever date is earlier. They are also exempted from the otherwise applicable obligations to accept the filing of patent applications and to grant exclusive marketing rights during the transition period.

The areas of intellectual property are covered by Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement under the WTO are Copyright and Related Rights, Trademarks, Geographical Indications, Industrial Designs, Patents, Layout-Designs (Topographies) of Integrated Circuits, Protection of Undisclosed Information and Control of Anti-Competitive Practices in Contractual Licences.

In the context of innovations in the field of nano-biopesticides all the fields of IPR listed in the TRIPs Agreement with the exception of Layout-Designs (Topographies) of Integrated Circuits are relevant.

1.3 Introduction to IPR Tools (WIPO and WTO)

IPR tool	What it protects
Patent	A patent is an exclusive right granted by the government for an invention that satisfies criteria set for patentable subject matter, and further is new, involves an inventive step and is capable of industrial application. It gives its owner the legal right within the territory in which the patent is granted to exclude or stop others from making, using, offering for sale, selling or importing a product or process based on the patented invention.
Utility models (also known as "short-term patents," "petty patents" or "innovation patents")	In many countries, some types of incremental inventions or small adaptations of existing products are protectable as utility models.
Industrial designs	Exclusivity over the ornamental or aesthetic features of a product can be protected through laws on industrial designs, in some countries referred to as "design patents".
Trademarks	Trademark protection provides exclusivity over words, marks and colours used to distinguish the products of one company from those of another.
Copyright and related rights	The form of expression of original literary, artistic and technical works (such as software) may be protected by copyright and related rights.
Geographical indications	A name or indication associated with a place is sometimes used to identify a product. This "geographical indication" does not only say where the product comes from. More importantly, it identifies the product's special characteristics, which are the result of the product's origins. Using the indication when the product was made elsewhere or when it does not have the usual characteristics can mislead consumers, and can lead to unfair competition. The TRIPS Agreement says members have to provide ways to prevent such misuse of geographical indications. For wines and spirits, the TRIPS Agreement provides higher levels of protection, i.e. even where there is no danger of the public being misled. Some exceptions are allowed, for example if the term in question is already protected as a trademark or if it has become a generic term.
Protection of new plant varieties of plants	In many countries, a breeder of a new plant variety may obtain protection in the form of "plant breeder's rights."
Trade secrets	All types of confidential business information, including secret designs, machines and processes, may be protected as trade secrets so long as the information is not generally known, its commercial value derives from its secrecy, and reasonable steps have been taken to keep it secret (for example, restricting access on a "need to know" basis, and entering into confidentiality or non-disclosure agreements.

(continued)

IPR tool	What it protects
Layout-design (or topography) of integrated circuits.	An original layout-design of an integrated circuit may be protected against copying.
Anti-competitive practices in contractual licences	One way for a right holder to commercially exploit his or her intellectual property rights includes issuing a licence to someone else to use the rights. Recognising the possibility that right holders might include conditions that are anti-competitive, the TRIPS Agreement says that under certain conditions, governments have the right to take action to prevent anti-competitive licencing practices. It also says governments must be prepared to consult each other on controlling anti-competitive licencing practices.

As the field of nano-biopesticides is largely invention-led, patent is the most relevant IPR tool that is globally exploited. Hence the a few essential aspects of patents are being elaborated in the next few sections of this chapter. It ought to be noted that trademarks play a significant role in the naming of the products and services. Copyright and design registrations are applicable for the protection of distinctive packaging, instruction booklets, advertising, etc.

A patent is an exclusive right granted by the government for an invention that satisfies criteria set for patentable subject matter, and further is new, involves an inventive step and is capable of industrial application. It gives its owner the legal right to exclude or stop others from making, using, offering for sale, selling or importing a product or process based on the patented invention. A patent is granted by the national patent office of a country or a regional patent office for a group of countries. It is valid for a limited period of time, generally 20 years from the date of filing the application, provided the required maintenance fees are paid on time. A patent is a territorial right, limited to the geographical boundary of the relevant country or region in which it is granted. In return for the exclusive right provided by a patent, the applicant is required to disclose the invention to the public by providing a detailed, accurate and complete written description of the invention in the patent application. The granted patent and, in many countries, the patent application are published in an official journal or gazette.

Further, the International Patent Classification System (IPC) provides hierarchical classification system used to classify and search patent documents. It also serves as an instrument for the orderly arrangement of patent documents, a basis for selective dissemination of information and for investigating the state of the art in given fields of technology. The IPC consists of eight sections, which are divided into 120 classes, 628 subclasses and approximately 70,000 groups. The eight sections are Human Necessities; Performing Operations; Transporting; Chemistry; Metallurgy; Textiles; Paper; Fixed Constructions; Mechanical Engineering; Lighting; Heating; Weapons; Blasting; Physics and Electricity.

Developers of nano-biopesticides are therefore engaged in creating strategic portfolio of patents in countries of their business interests, further monetizing them through their commercialised products in the markets and/or transacting the patents through licencing, assignments, cross-licencing, etc.

Further, patent information is available in the public domain as a rich structured source of technical and legal information on inventions done in various parts of the world. Patent information and its judicious use promote further inventions and the creation/running of sustained businesses.

1.4 Patenting Trends in Nano-biopesticides

A publication in 2015 listing the publications in patent and non-patent literature related to nanomaterials in plant protection and fertilisers (Gogos et al. 2012) reported that most patents in these fields were held by companies like BASF, Dow Agrosciences, Evonik-Degussa, Monsanto, Rhone-Poulec and other relatively smaller companies. This article also reported a list of patents that claimed pesticide products with particles mostly in the nanosize ranges, wherein the function of the nanomaterial varied from being an additive (dispersing agent, UV protection agent, carries, active ingredient, bio-delivery agent, controlled release). Commercially available products reported were Primo MAXX, Banner (as nano emulsions from Syngenta), Karate ZEON (Capsules with λ-cyhalotrin from Sygenta), Demand CS Capsules with pyrethroid (λ-cyhalotrin from Sygenta), ECOFLEX (Aliphatic copolyester, "nanofibre" as a pheromone dispenser from BASF), Aerosil 200 (SiO_2 from Sygenta), Trico TiO_2 23.2% Sheepgrease (pesticide from Omya AG), FEROX Zero-valent iron nanopowder (soil remediation from ARS Technologies, Inc) and SoilSet SiO_2 (soil management from Sequoia Pacific Research Company).

Other commercial products reported are CLARIVA® (from Syngenta International AG, for seed treatment based on natural soil bacteria to protect a plant's root from nematodes, especially for soybeans), SIVANTO® prime (from Bayer AG which is a nature-derived insecticide for efficient control of key adult and immature sucking pests, such as Aphids, whiteflies and psyllids, scales, leaf miners, beetles mirids and selected hoppers, for vegetables, fruits as well as cotton and soybeans), Nimbecidine EC with 0.03% Azadirachtin (from T. Stanes & Company Ltd., India) for multiple modes of action like anti-feedant, repellent, ovi-position deterrent, insect growth regulator for whiteflies, thrips, aphids, caterpillars, mealy bugs, and leafhoppers, and sterilant), Nano-Gro™ (from Agro Nanotechnology Corp. Plant growth regulator and immunity enhancer), NanoMax-NPK (from JU Agri Sciences, India for promoting growth of green leaves, photosynthesis, carbohydrates, oil fats and proteins in crops), Nano-Ag Answer® (from Urth Agriculture, for promoting high yield along with a reduction in watering [~20%] and predatory pests) and Uremic Nano Fertilizer offering plant nutrition with high uptake efficiency and avoiding urea degradation in the presence of sun and heat and lowering damage to soil structure due to the effects of urea (Kumar et al. 2019).

Nano-5® from Uno Fortune Inc is a 3-in-1 Natural Mucilage Organic Fertilizer which promotes cleavage of plant cells, differentiation, proliferation, blooming, fruiting, resistance to cold, drought and ethene, prevention of fruit dropping and splitting, adjusting and shortening the period of production. It further provides prevention and cure of diseases and pests by preventing fusarium, fungi, bacterial wilt, bacteria, virus and pests inhibiting piercing-sucking pests, chewing pests, nematodes, and seasonal diseases and pests (Uno Fortune).

A recent review of covering antimicrobial agents (e.g. silver, titanium dioxide), nano-bio pesticides (hydrophobic silica) and smart delivery systems (polymeric nanoparticles) also listed patents claiming pesticides, anionic herbicides, fertilisers, fungicides, agrochemicals, insect repellants and essential oils in diverse carrier materials such as clays, silicas and polymers (Narayanan et al. 2013). This article further reviewed the development of nano-biosensors for diagnosis of pests and pesticide residues including the use of quantum dots applying the Forster Resonance Energy Transfer (FRET) technology, polymeric particles, clay clays, silica particles, magnetic nanoparticles, nanotitanium dioxides, nanoemulsions, nanocomposites, nanofibers, nanotubes, etc.

Patent Analytics Report covering agricultural nanomaterial released in January 2016 by IP Australia (IP Australia 2016) reviewed the patent status of nanomaterials in agriculture. With specific reference to protection of plants, the technology categories (patent families) covered are bioavailability/activity enhancement, stability enhancement, agent per se, inert carrier, sustained/delayed pesticide release and plant protection. BASF, Shikefeng Chemical Co Ltd., Suzhou Setek Co Ltd., Vive Crop Protection Inc, Dow Agrosciences LLC were reported as the key patent players in these technology categories.

Relecura Technologies Pvt. Ltd, Bangalore, India [Relecura] is a specialised group in patent search and technology mapping. At the request of the author of this chapter, Dr. Murari Venkataraman and Dr. George Koomullil of Relecura conducted a specialised search of patenting activity involving nano-biopesticides. The results of Relecura's search were analysed, and the raw data are reproduced in this chapter with permission of Relecura.

Patenting inventions in nano-biopesticides since 2001 is depicted in Fig. 1.1. Filing of patents in nano-biopesticides is a fairly recent activity which has picked up since 2006 from just 16 filings to about 300 filings in 2017. Clearly, developments in basic science of biopesticides and their allied aspects also accelerated during the same period with patent filings in biopesticides increasing from about 1200 in 2006 to about 11,000 in 2018.

Figure 1.2 presents a snapshot of the geographical spread and intensity of patent filings in nano-biopesticides. China has become a lead country for patent applications followed by US, Europe, India, Canada, Japan, Korea, Australia and others. It is to be noted that WO designates the patent publications of the Patent Cooperation Treaty Application (administered by WIPO).

As patenting transcends beyond academic borders into the commercial world, it is pertinent to explore the origins of the inventing organisations/people in the field of nano-biopesticides. Table 1.1 presents the top patent application holders. DowDupont leads the pack, followed by Vive Crop Protection INC, BASF, ICEUTICA, JIANGSU, BAYER, BIONANOPLUS and others.

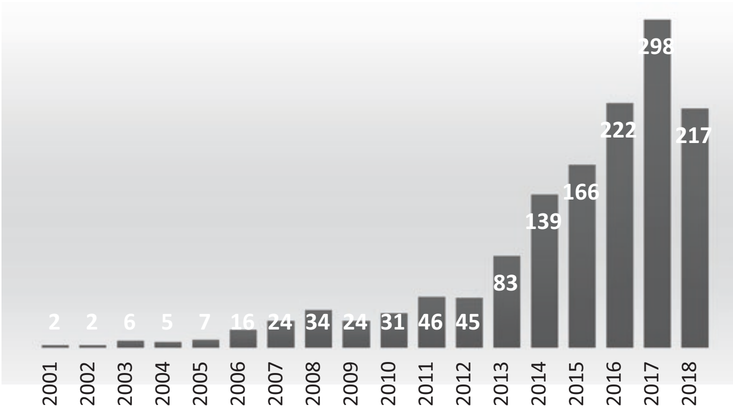

Fig. 1.1 Nano-biopesticide patent applications

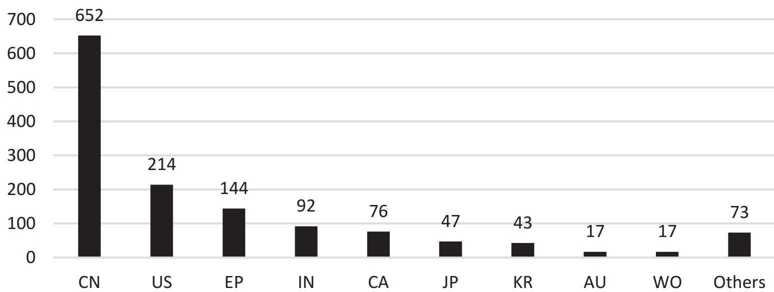

Fig. 1.2 Nano-biopesticide patent applications in various countries

The patent applicants listed in Table 1.1, based on their business interests, have filed their patent applications in various jurisdictions which is reported in Table 1.2. DOWDUPONT, having international operations have filed its patent applications in China, USA, European Patent Office (EP) Canada, India and Japan, Korea, Australia Taiwan and Spain. VIVE CROP PROTECTION INC with VIVE CROP PROT INC have filed patent applications in China, USA, European Patent Office (EP) Canada, India and Japan, Korea, Australia and Spain. BASF has filed its patent applications in China, USA, European Patent Office (EP), Canada, India, Japan, Korea and Spain, whereas ICEUTICA PTY LTD has filed its patent applications in China, USA, European Patent Office (EP), Canada, India, Korea, Australia and Spain.

The Chinese applicants, except for CHEMCHINA, have concentrated only in China. The Japanese companies have concentrated their applications in Japan. Companies such as BIONANOPLUS S L, DENDRITIC NANOTECHNOLOGIES INC, AGFORM LIMITED, INSTILLO GMBH, RAG-STIFTUNG, 3M, A I INNOVATIONS N V have made inroads with specialised technologies, whereas

Table 1.1 Top patent applicants in nano-biopesticides

Top patent applicants	Number of applications
DOWDUPONT	176
VIVE CROP PROTECTION INC	25
BASF	23
ICEUTICA PTY LTD	18
JIANGSU ROTAM CHEMISTRY	17
BAYER	14
BIONANOPLUS S L	13
MAANSHAN KEBANG ECO FERTILIZER	12
NAGAURA YOSHIAKI	11
SHANDONG SUNWAY LANDSCAPE TECHNOLOGY	11
VIVE CROP PROT INC	10
CHINESE ACADEMY OF SCIENCES	9
CHEMCHINA	8
DENDRITIC NANOTECHNOLOGIES INC	8
AGFORM LIMITED	7
INSTILLO GMBH	7
RAG-STIFTUNG	7
UNIVERSITY OF CALIFORNIA	7
3M	6
A I INNOVATIONS N V	6

The *University of California's Center for Environmental Implications of Nanotechnology (UC CEIN)* is working to ensure the responsible use and safe implementation of nanotechnology in the environment through a multi-disciplinary approach to research, knowledge acquisition, education and outreach.

As mentioned earlier in the chapter, the International Patent Classification System (IPC) provides a hierarchical classification system used to classify and search patent documents. The Cooperative Patent Classification (CPC) system, in force from 1 January 2013, is a bilateral system which has been jointly developed by the EPO and the USPTO. Each classification with its subclassification identifies the subject matter that is addressed in the invention. Table 1.3 lists the most frequently occurring CPC Codes whilst searching nano-biopesticide patents/patent applications.

A perusal of Table 1.3 drives home the point that inventions in the field of biopesticides involve the use of heterocyclic compounds of various types; cyclopropane carboxylic acids or derivatives; nitriles, thiocompounds; mixtures of one or more fertilisers with materials not having a specifically fertilising activity but with pesticidal activities; microcapsules; biopesticide dispersions or gels; biopesticides containing material from algae, lichens, bryophyta, multicellular fungi or plants or extracts thereof; biopesticides containing solids as carriers or diluents; macromolecular compounds; biopesticides in shaped forms, e.g. sheets, not provided for in

Table 1.2 Patent filings in various countries by the patent applicants in nano-biopesticides

Patent applicants	CN	US	EP	CA	IN	JP	KR	AU	TW	ES
DOWDUPONT	25	49	29	23	15	2	12	2	4	4
VIVE CROP PROTECTION INC	2	9	3	5	1	1	0	2	0	0
BASF	2	2	7	2	2	3	2	0	0	1
ICEUTICA PTY LTD	4	3	3	3	2	0	1	2	0	0
JIANGSU ROTAM CHEMISTRY	17	0	0	0	0	0	0	0	0	0
BAYER	6	2	1	2	0	0	0	1	1	0
BIONANOPLUS S L	1	2	4	2	2	2	0	0	0	0
MAANSHAN KEBANG ECO FERTILIZER	12	0	0	0	0	0	0	0	0	0
NAGAURA YOSHIAKI	0	0	0	0	0	11	0	0	0	0
SHANDONG SUNWAY LANDSCAPE TECHNOLOGY	11	0	0	0	0	0	0	0	0	0
VIVE CROP PROT INC	1	0	3	4	0	1	0	1	0	0
CHINESE ACADEMY OF SCIENCES	9	0	0	0	0	0	0	0	0	0
CHEMCHINA	0	2	1	1	1	1	0	1	0	0
DENDRITIC NANOTECHNOLOGIES INC	1	1	2	1	1	0	1	0	1	0
AGFORM LIMITED	1	1	1	0	1	1	0	1	0	1
INSTILLO GMBH	1	1	1	1	0	1	1	1	0	0
RAG-STIFTUNG	1	2	1	1	1	1	0	0	0	0
UNIVERSITY OF CALIFORNIA	2	2	1	2	0	0	0	0	0	0
3M	0	2	4	0	0	0	0	0	0	0
A I INNOVATIONS N V	1	2	1	1	1	0	0	0	0	0

any other group of this main group; applications of nanobiotechnology or nano-medicine, e.g. protein engineering or drug delivery.

The inventions in the patents/patent applications claim a range of benefits such as targeted delivery at a predetermined site, controlled delivery, enhanced solubility of the active ingredients (if insoluble or sparingly soluble), increased stability, dispersibility, permeability, wettability, decreased droplet size for better spraying and retention on the substrate, reduced microbial degradation/leaching/evaporation/drainage/runoff/photolysis, choice of appropriate adjuvants for optimal biopesticidal activity, etc.

The nano-materials and phases include polymer and lipid-based nanomaterials, mesoporous inorganic substrates such as silicas, clay-based nanomaterials, layered hydroxides, carbon nano-materials such fullerenes, carbon naoparticles, fullerol and single-walled carbon nanotubes/multiwall carbon nanotubes, nanocapsules, nanospheres, nanogels, micelles, liposomes, nanoemulsions, nanosuspensions, solid lipo-nanoparticles, functionality as biosensors for detection of pathogens and pesticide residues, linking up with communications technologies and in some cases with artificial intelligence.

Claims have also been made on encapsulated biopesticides containing material from algae, lichens, bryophyta, multicellular fungi or plants or extracts thereof. Research centres around the world are undertaking research to improve techniques to enhance their commercial feasibility.

Table 1.3 International Patent Classification of patents/patent applications in nano-biopesticides

PC code	Number of patent applications	Explanation of the CPC codes
A01N 43/40	106	Biopesticides containing six-membered heterocyclic compounds
A01N 43/653	89	Biopesticides containing 1,2,4-triazoles; hydrogenated 1,2,4-triazoles
C05G 3/02	84	Mixtures of one or more fertilisers with materials not having a specifically fertilising activity but with pesticides
A01N 43/78	83	Biopesticides containing 1,3-thiazoles; hydrogenated 1,3-thiazoles
A01N 25/04	82	Biopesticide dispersions or gels
A01N 47/36	82	Biopesticides containing the group N—CO—N directly attached to at least one heterocyclic ring; thio-analogues thereof
A01N 43/50	79	Biopesticides containing 3-diazoles; hydrogenated 1,3-diazoles
A01N 53/00	78	Biopesticides containing cyclopropane carboxylic acids or derivatives thereof
C05G 3/00	78	Mixtures of one or more fertilisers with materials not having a specifically fertilising activity
A01N 43/56	72	Biopesticides with 1,2-diazoles; hydrogenated 1,2-diazoles
A01N 25/28	71	Biopesticide microcapsules
A01N 43/54	71	Biopesticides containing 1,3-diazines; hydrogenated 1,3-diazines
A01N 43/16	67	Biopesticides containing oxygen as the ring hetero atom
A01N 65/00	65	Biopesticides containing material from algae, lichens, bryophyta, multicellular fungi or plants or extracts thereof
A01N 43/90	61	Biopesticides containing two or more relevant hetero rings, condensed amongst themselves or with a common carbocyclic ring system
C05G 3/04	57	Mixtures of one or more fertilisers with materials not having a specifically fertilising activity but with soil conditioners
A01N 43/82	54	Biopesticides containing five-membered rings with three hetero atoms
A01N 25/08	53	Biopesticides containing solids as carriers or diluents
A01N 37/10	53	Biopesticides containing aromatic or araliphatic carboxylic acids, or thio-analogues thereof; derivatives thereof
A01N 43/84	52	Biopesticides containing six-membered rings with one nitrogen atom and either one oxygen atom or one sulfur sulphur atom in positions 1,4
A01N 25/10	50	Biopesticides containing macromolecular compounds

(continued)

Table 1.3 (continued)

PC code	Number of patent applications	Explanation of the CPC codes
A01N 25/34	50	Biopesticides of shaped forms, e.g. sheets, not provided for in any other group of this main group
A01N 43/80	48	Biopesticides containing five-membered rings with one nitrogen atom and either one oxygen atom or one sulfur sulphur atom in positions 1,2
A01N 25/30	47	Biopesticides containing by surfactants
A01N 43/60	47	Biopesticides containing 1,4-diazines; hydrogenated 1,4-diazines
A01N 37/46	45	Biopesticides containing N-acyl derivatives
A01N 43/36	44	Biopesticides with five-membered rings
B82Y 5/00	44	Nanobiotechnology or nanomedicine, e.g. protein engineering or drug delivery
C07D 401/04	44	Biopesticide containing heterocyclic compounds containing two or more hetero rings, having nitrogen atoms as the only ring hetero atoms, at least one ring being a six-membered ring with only one nitrogen atom directly linked by a ring-member-to-ring-member bond
A01N 37/34	43	Biopesticides containing nitriles

Developments in the field of nano-biopesticides embracing the latest techniques have also been patented.

Example of one such latest technique has been exclusively licenced to TechAccel of Shawnee Mission, KS in 2015, for a biopesticide application developed at Kansas State University on a pesticide which is useful for agricultural applications as well as pest management for the home and garden. This pesticide claimed in US Patent No. 8841272, entitled "Double-Stranded RNA-Based Nanoparticles for Insect Gene Silencing", claims a nanoparticle useful for RNA interference of a target insect gene which is composed of a biopolymer matrix and an insect double-stranded RNA ranging from 200 to 1000 base pairs in length; the biopolymer matrix and double-stranded RNA are mixed to self-assemble into the nanoparticle. This nanoparticle achieves a greater effectiveness for delivering RNA inhibitory agents into insects (IPwatchdog 2015).

Another example if the US8575424B2 granted in 2013 to current assignee DOWDUPONT, titled, "Production of functionalized linear DNA cassette and quantum dot/nanoparticle mediated delivery in plants", claims methods for introducing a functionalized linear nucleic acid cassette molecule of interest into a plant cell comprising a cell wall includes use of nanoparticles. In some embodiments, the cell comprising a cell wall is a cultured plant cell. Methods include genetically or otherwise modifying plant cells and for treating or preventing disease in any plant, especially crop plants. Transgenic plants include a nucleic acid molecule of interest produced by regeneration of whole plants from plant cells transformed with functionalized linear nucleic acid cassette molecules.

This field is cross disciplinary bringing together the best minds from all fields of science and technology. Creative collaborations between physicists, biologists, chemists and agricultural scientists are facilitating the development and introduction of new bioformulations for focused delivery and application practices, with near-complete understanding of the impact of plant defence induction kinetics on application timing and placement of formulated products at the desired sites and lead to enhanced field performance, reducing inconsistency of field performance thereby encouraging the farmers to implement the evolving technologies for the betterment of our humankind.

Scientists and academicians from the emerging economies and the developed economies over the last two decades have been intensely engaged in nano-biopesticide-related R&D and voluminous publishing. Surprisingly, the effective commercial output or even patenting from research groups and industries in the emerging economies has been negligible. This is an area of serious concern, and therefore there is an urgent need to integrate IPR as an integral part of the innovation value chain. Most researchers in the field of biopesticides and nano-biopesticides do not refer to patent literature either as a source of structured technical information resource or as a source of live prior art, and hence most academic work in this field lead to “re-inventing the wheel” with little or no commercial value.

Clearly, the global nano-biopesticide market in the future will be in the hands of a few of early-mover the companies listed in Tables 1.1 and 1.2 in this chapter. Strategic consolidation of intellectual property assets through acquisitions, mergers, collaborations and licencing agreements is expected to dominate the business dynamics in the years to come.

Limitations in patenting inventions in nano-biopesticides.

At this stage, it is pertinent to revisit the TRIPS Agreement, especially the Article 27 which states:

1. Subject to the provisions of paragraphs 2 and 3, patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application.

   Subject to paragraph 4 of Article 65, paragraph 8 of Article 70 and paragraph 3 of this Article, patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced.
2. Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect public order or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.

3. Members may also exclude from patentability:
   (a) Diagnostic, therapeutic and surgical methods for the treatment of humans or animals.
   (b) Plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. However, Members shall provide for the protection of plant varieties either by patents or by effective sui generis system or by any combination thereof.

       The provisions of this subparagraph shall be reviewed 4 years after the date of entry into force of the WTO Agreement.

The patent laws in various countries do incorporate exclusion provisions as allowed by Article 27.

In compliance with Article 27.2 and 3, in most national or regional patent laws, patentable subject matter is defined negatively, i.e., by providing a list of what cannot be patented. Whilst there are considerable differences between countries, the following are examples of some of the areas that are excluded from patentability in many jurisdictions:

- Abstractions and scientific theories
- Aesthetic creations
- Schemes, rules and methods for performing mental acts
- Substances as they naturally occur in the world
- Inventions the exploitation of which may affect public order, good morals or public health
- Diagnostic, therapeutic and surgical methods of treatment for humans or animals
- Plants and animals other than microorganisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes
- Computer programs

With specific reference to nano-biopesticides, the following aspects may act as barriers to patentability:

- The possible adverse and/or unforeseen effects on the soil, plants and the environment could invoke provisions in patent laws with regard to exclusions from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect public order or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.
- Plants and animals other than microorganisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes.
- Substances as they naturally occur in the world.
- Abstractions and scientific theories.

Severe doubts have been raised about the phytotoxicity profiles of nano-biopesticides, their possible effects on the bacterial diversity, change in soil pH, effect on root length growth, number of roots, their retention in the soil thereby causing possible long-term damage, the microbes developing resistance to nanoparticles, their effect on other crops, etc are areas of grave concern. Ingestion of the nano-biopesticides by grazing animals, their leaking into the ground water system, their impact on cell biology and possibly influencing the genetic code are areas that need to be looked into with care and caution. These uncertainties may spark negative posturing towards considering inventions in nano-biopesticides as being non-patentable subject matter unless proven otherwise. Using naturally occurring matter (e.g. containing material from algae, lichens, bryophyta, multicellular fungi or plants or extracts thereof) in nano-biopesticides, minerals, clays, etc may be objected from being patentable unless the experiments demonstrate significant intervention from the inventors in their modifications, structuring and incorporations to differentiate them from their naturally occurring state.

Further, a lot is known in traditional agricultural practices where bio-based materials have been used as pesticides for generations by communities and therefore may come on the way of patenting as prior art. In several cases, the mechanisms and modes of action of nanomaterials are not known, and there is a lot of associated hypothecation that may be considered to be abstraction and theorisation.

Constant interactions between the inventors and patent experts will be essential to introduce on-course corrections in the designing of experiments to avoid the general pitfalls of inadequate enablement of the invention by “a person of ordinary skill in the art” and/or inadequate examples by way of experiments to illustrate the range of claims. Extreme care will have to be exercised whilst drafting the patent specifications and structuring the claims to avoid misinterpretation of them being understood to be within the ambit of the exclusions as “non-patentable subject matter”.

1.5 Mitigating Potential Risks

New nanotechnologies including the use of nanoscale materials in the agricultural and food value chain raise pertinent questions about their potential health, safety and environmental impact. This is a subject matter for serious consideration by regulatory agencies including scientific platforms, public and private special interest organizations, industry and industry associations whilst adopting appropriate regulations to ensure responsible development and exploitation of these wonder-material and technologies to their full potential. Major collaborative activities are with active participation of all stakeholders and government, with possible open sharing of data related to health and safety. The challenge is to finally set the standards for testing & monitoring methods, health, safety and environment. Another area that will need due consideration will be the view that competition authorities would take whilst evaluating consolidation of resources in the marketplace by way of IPR transactions between various industry partners, technology transfers, collaborations mergers, acquisitions, creation of joint ventures, pricing of products and services. Business strategies will have to be designed and tailored to balance responsible use of IPR with in the innovation and business value chain.

1.6 Conclusion

Nano-biopesticides is a fast growing commercially attractive proposition in view of a positive shift to green and precision agricultural practices. Being innovation-led, intellectual property rights by way of ownership of inventions, transactions of IP at all stages of the business value chain will play a major role in the market dynamics. Real-time care will have to be taken to ensure that inventions are focused with clear objectives based on patent-based technology landscapes, diligently planned and executed so that at the stage of drafting, filing, prosecuting IP applications, all possible aspects that might come on the way of obtaining the grant of the IPR are taken care of well ahead of time. Further, nano-biopesticides are now becoming fiercely competitive, and therefore one will have to be sensitive to possible infringements of others' IPRs. In addition to inventing, one will also have to ensure that there is freedom to operate in the territories of business interests and hence making IPR an integral part of the innovation-value chain is an imperative.

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