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NEXT-GENERATION BIOPESTICIDES: NANOFORMULATIONS, RNAi-BASED, AND SEAWEED-DERIVED INNOVATIONS

N. R. Thore[1]*, C. S. Mandale[1], P. R. Pagar[1], N. Y. Mhaske[1]
[1]Department of pharmacognosy, K.B.H.S.S. Trust's Institute of Pharmacy Malegaon, India, 423 105.

Corresponding Author - Chetana Sadashiv Mandale
Department of pharmacognosy, K.B.H.S.S. Trust's Institute of Pharmacy Malegaon, Jajuvadi, Malegaon, India, 423 105.
Email I'd – chetanamandale2020@gmail.com

ABSTRACT

The global transition toward sustainable agriculture and reduced chemical pesticide dependency has accelerated research into novel biopesticide technologies. This study comprehensively reviews recent advancements in three innovative categories of biopesticides nanoformulated, RNAi-based, and seaweed-derived products highlighting their mechanisms, efficacy, and potential applications in integrated pest management (IPM). Nanoformulations of botanical biopesticides, particularly those utilizing plant-derived actives such as azadirachtin, eugenol, and curcumin, employ nanocarriers like chitosan, polycaprolactone (PCL), polylactic-co-glycolic acid (PLGA), and silica nanoparticles to enhance bioavailability, stability, and controlled release. RNA interference (RNAi)-based biopesticides represent a new generation of gene-targeted pest control agents that suppress specific pest genes through double-stranded RNA molecules, enabling species-specific and environmentally safe pest management. Similarly, seaweed-based biopesticides derived from macroalgae such as Sargassum, Gracilaria, and Ulva spp. exhibit broad-spectrum antifungal, antibacterial, and insecticidal activity due to their polysaccharide, polyphenol, and terpenoid constituents. Collectively, these novel formulations offer high efficacy, biodegradability, and minimal ecological disruption compared to synthetic pesticides. The integration of nanotechnology, molecular biology, and marine bioresources in pesticide development presents a promising pathway toward eco-friendly and sustainable crop protection strategies.

KEYWORDS: Biopesticides, Nanoformulation, RNA interference (RNAi), Seaweed-derived bioactives, Integrated pest management (IPM), Sustainable crop protection

1. INTRODUCTION

Biopesticides are formulations derived from naturally occurring biological materials that control pest populations through non-toxic and environmentally sustainable mechanisms [1]. Their increasing global adoption is driven by the need for safer alternatives to chemical pesticides, which often cause ecological imbalances, pest resistance, and residue accumulation in food chains. Biopesticides are obtained from diverse sources, including plants such as *Azadirachta indica* (Neem) and *Chrysanthemum cinerariifolium*, microorganisms like *Bacillus thuringiensis*, and beneficial nematodes that parasitize insect pests [2].

Unlike conventional synthetic pesticides, biopesticides act through highly specific mechanisms, such as interference with molting or feeding behavior, inhibition of reproduction, disruption of neuromuscular transmission, or stimulation of systemic acquired resistance in plants. These characteristics contribute to their environmental compatibility, biodegradability, and safety for non-target organisms [3].

The global demand for eco-friendly pest management has accelerated the exploration of novel biopesticide technologies, including nanoformulated, RNAi-based, and seaweed-derived biopesticides. Nanoformulation improves the physicochemical stability, solubility, and targeted delivery of active ingredients, thereby enhancing their field efficacy. Similarly, RNA interference (RNAi)-based biopesticides offer gene-specific pest control through double-stranded RNA (dsRNA)-mediated gene silencing, providing precision and selectivity in pest management. Seaweed-based biopesticides, derived from marine macroalgae, contain biologically active polysaccharides, terpenoids, and phenolic compounds that not only suppress pests and pathogens but also enhance plant defense responses [4].

2. TYPES OF BIOPESTICIDES

Based on their source, makeup, and mode of action, biopesticides can be broadly categorized. The following are the three main categories:

1. Microbiological pesticides
2. Plant-Incorporated Protectants (PIPs)
3. Biopesticides that are biochemical

Bacillus thuringiensis (Bt) is a common example of a microbial biopesticide used against caterpillars, mosquitoes, and black flies. Microbial biopesticides are generated from micro-organisms such as bacteria, fungus, viruses, or algae and target specific pests with minimal influence on non-target species. The Environmental Protection Agency (EPA) regulates both the protein and its genetic material in Plant-Incorporated Protectants (PIPs), which are pesticides made by genetically modified plants with additional genes, such as the Bt gene, that allow the plant to produce its own pest-killing protein.

Synthetic pheromones are frequently employed for insect monitoring and control; biochemical biopesticides, on the other hand, are natural substances that manage pests by interfering with their growth or behavior instead of immediately killing them [5].

3. APPLICATIONS AND USES OF BIOPESTICIDES

Table No. 1 Applications and Uses of Biopesticides

Sr. No.	Name of pesticide	Type of source	Applications	Reference No.
01.	PEOs nt Essential Oils or Polyethylene Oxide)	Plant Source (e.g. leaves , roots , stems , fruits , seeds, etc.)	PEOs have been established as suitable products for biopesticides, but their commercial popularity is dered due to high volatility, faster degradation, and reduced water solubility. Therefore, to overcome these limitations, PEOs are encapsulated inside different matrices for the preservation of their biological properties and increase in durability	[6]
02.	Microbial formulations (e.g., Bacillus thuringiensis, Trichoderma spp., entomopathogenic viruses)	Microbial Source (e.g.bacteria, fungi, viruses)	These act as biocontrol agents targeting insects, pathogens or matodes. They generally have high specificity and lower non-target toxicity than many synthetic pesticides. Challenges include large-scale production, shelf-life, formulation and field stability.	[7]
03.	RNA-based biopesticides (dsRNA, RNAi)	Genetic Source	Delivery of double-stranded RNA to trigger gene silencing in pests (insects, nematodes, pathogens). Offers species-specific control, minimal chemical residues. Costs, delivery stability and regulatory acceptance remain hurdles.	[8]

04.	Nano-formulated biopesticides (nano- encapsulation of botanical extracts, microbial toxins, PEOs etc.)	Nano- technology	psulating actives into nano- or micro-carriers (polymers, nanoparticles) improves stability ainst UV/heat), reduces volatility, enhances delivery and extends persistence. Overcomes many limitations of conventional biopesticides.	[9]
05.	Botanical extracts (non-volatile plant extracts, allelochemicals)	Plant/Weed Source (e.g., ethnobotanical plants)	Extracts from plants contain bioactive metabolites (alkaloids, flavonoids, terpenoids, saponins, tannins) which can act as insecticides/biopesticides. They are eco-friendly alternatives to synthetic pesticides.	[10]
06.	Semiochemicals – Pheromones for pest disruption	Chemical Ecology Source	Use of insect pheromones to disrupt mating, trap pests, monitor populations, or for attract-and-kill ategies. Highly selective, low non-target impact. Reviewed widely.	[11]
07.	Endophyte-based biopesticides (microorganisms living inside plants)	Microbial / Plant Symbiont	Endophytes can produce metabolites or induce plant resistance, thereby acting as biopesticides. This is an emerging area: beneficial microbes are harnessed within plants for pest/pathogen defence.	[12]
08.	Elicitors and plant defence activators (e.g., chitosan, oligosaccharides)	Natural/Polymer Source	These do not directly kill pests but stimulate the plant’s own defence mechanisms (induced resistance) so the plant becomes less susceptible to pests/pathogens.	[13]

09.	Combination/synergistic biopesticides (botanicals + microbes or botanicals + semiochemicals)	Multi-source / Integrated	Combinations of biopesticide types (e.g., botanical extracts + microbial agents) can yield synergistic or sub-lethal effects, improve efficacy, reduce resistance development.	[14]
10.	Semiochemicals – Kairomones / rbivore- induced plant volatiles (HIPVs)	Chemical Ecology Source	Kairomones are volatiles emitted by plants or herbivores which natural enemies exploit to find pests. Used to ract beneficialpredators/parasitoids and improve biological control.	[15]

4. BIOPESTICIDES PRODUCTION

Biopesticides made from renewable resources have recently been acknowledged as a potential solution to resource constraints and environmental contamination. Organic solid waste is regarded as a valuable resource for producing value-added products in a circular economy [16, 17].

4.1 Steps in Biopesticide Production

Table No. 2 General Stages in Microbial Biopesticide Production [18].

Stage	Process	Purpose
Isolation	Collect microbial strains	Identify effective species
Fermentation	Grow microbes	Produce active toxins
Extraction	Separate active compound	Purify product
Formulation	Mix with carrier	Enhance shelf life
Application	Field use	Pest control effectiveness

Table No. 3 Comparative Advantages of Biopesticides Over Chemical Pesticides [18].

Parameter	Biopesticides	Chemical Pesticides
Target specificity	High	Broad-spectrum
Environmental persistence	Biodegradable	Long-lasting residues
Human toxicity	Low	Moderate to high
Resistance development	Slow	Rapid
Impact on beneficial species	Minimal	Adverse

Cost efficiency (long-term)	High	Moderate

5. NANOFORMULATED BIOPESTICIDES

5.1 Concept and Mechanism

Nanobiopesticides are biologically derived chemical complexes that incorporate nanoparticles for pest management applications. The integration of nanotechnology into pesticide formulation significantly enhances their efficiency and effectiveness through the use of polymers, metal oxides, micelles, and other nanostructured carriers [19]. An ideal nanobiopesticide must exhibit key attributes such as increased solubility of poorly soluble active ingredients, targeted and sustained release, and prevention of premature degradation of the active components. Despite being applied in low doses, nanobiopesticides maintain high efficacy due to improved delivery and bioavailability mechanisms.Additionally, their target specificity and biological outcomes can be improved by designing formulations based on an in-depth understanding of the pest or pathogen life cycle and behavioral characteristics. Nanoformulations profoundly influence the physicochemical properties and environmental fate of active ingredients; therefore, parameters such as particle size, morphology, surface characteristics, type of adjuvants, and release kinetics under realistic conditions must be carefully assessed prior to field use [19].

Nanobiopesticides comprise nanoparticles that either serve as active pesticidal ingredients or function as engineered nanostructures possessing pesticidal properties [20]. Their potential has been demonstrated in studies targeting the fourth instar larvae of the filariasis vector *Culex quinquefasciatus* Say and the malaria vector *Anopheles subpictus* Grassi (Diptera: Culicidae), showcasing their effectiveness in vector management and sustainable pest control [21].

5.2 Application Strategy

Table No. 4 Application Strategy

Application Strategy	Strategy	Reference No.
Current Application	Several plants such as *Azadirachta indica* (neem), *Acorus calamus*, *Annona squamosa*, *Vitex negundo*, *Gnidia glauca*, *Toddalia asiatica*, *Argemone mexicana*, and *Calotropis procera* have shown strong pesticidal activity when formulated as stable metallic nanoparticles [22]. These plant-based nanoparticles enhance pest control efficiency while remaining environmentally safe. The use of titanium dioxide nanoparticles (nano-TiO_2) have been reported to	

Strategy	increase chlorophyll content by 45%, photosynthetic rate threefold, and plant dry weight by 73% [23]. Furthermore, smaller nanoparticles improve seed germination efficiency [23]. In *Ocimum sanctum*, bioactive compounds such as phenols, amides, and carboxylic acids reduce silver salts to produce stable silver nanoparticles confirmed through UV–visible spectroscopy [23].	[22,23]
Future Application Strategies	Future strategies for nanobiopesticide development will emphasize the creation of formulations that are highly biodegradable, exhibit minimal phytotoxicity, and have no detrimental effects on seed germination or human health. Such advancements aim to ensure compliance with international nanoregulation and safety standards. Evidence suggests that nanobiopesticide phototoxicity can be significantly minimized through surface modifications and biocompatible coatings. For instance, the phototoxic nature of powdered silver nanoparticles was markedly reduced by applying a nanocoating of polyvinylpyrrole, thereby enhancing their environmental safety and biocompatibility [24].	[24]

5

.3 Development Strategies for Nanoformulated Biopesticides

Pesticides play a crucial role in improving crop productivity; however, more than 90% of conventional pesticides are lost to environmental runoff or remain as residues in agricultural produce. Traditional formulations often contain toxic solvents, exhibit poor dispersion, and suffer from dust drift one of the primary limitations of conventional pesticide delivery systems. To overcome these challenges, nano-based pesticide formulations are being developed to enable the precise and controlled release of active ingredients in response to specific environmental stimuli Key strategic considerations for such nanoformulations include:

(i) development of efficient water-based dispersion systems;

(ii) enhancement of leaf-targeted deposition and dose transfer through nanodelivery;

(iii) improvement of bioavailability mechanisms in nano-based formulations; and

(iv) promotion of natural degradation and biosafety of formulation residues. The effective utilization of nanotechnology in the design and formulation of nano-based pesticides is illustrated in Figure No. 01. Various nanocarriers and structural systems are currently employed to develop these advanced agricultural products [25].

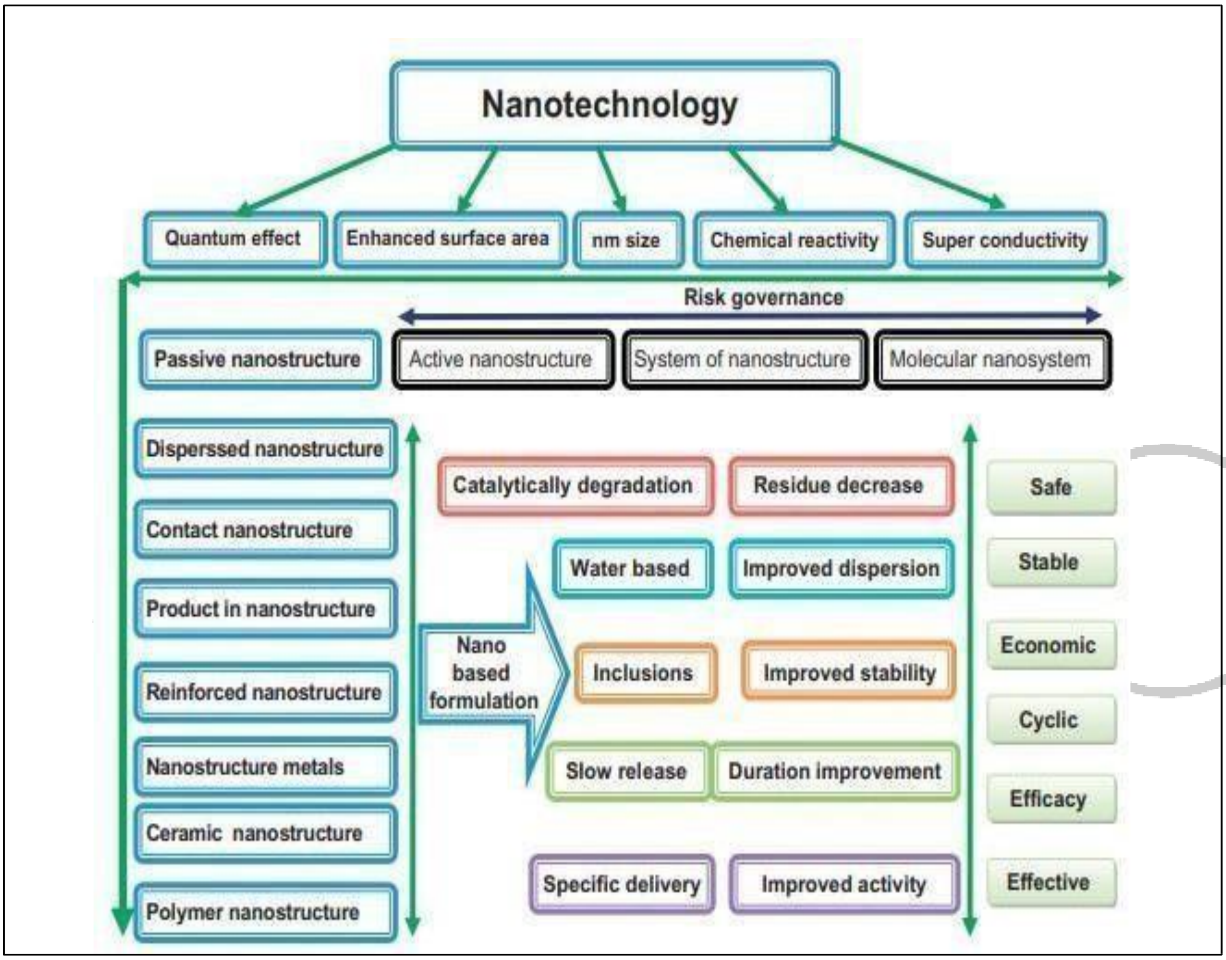

Figure No. 1 The Efficient Use of Nanotechnology for Formulation of Nano-Based Products

5.4 List of Polymers that have Potential for the Formulation of Bionanoparticles for Insecticide Application

No. 5 The List of Polymers that have Potential for the Formulation of Bionanoparticles for Insecticide Application [26].

Polymer	**Active Compound**	**Nanomaterial Form/Structure**
Alginate–bentonite	Imidacloprid	Clay
Carboxymethyl chitosan–ricinoleic	Azadirachtin	Particles

acid		
Carboxymethylcellulose	Carbaryl	Capsule
Chitosan	Etofenprox	Capsule
Chitosan	Piperonyl	Capsule
Glycol–ethylcellulose	Imidacloprid	Capsule
Lignin	Aldicarb	Gel
Lignin	Imidacloprid	Granules
Lignin–polyethylene	Imidacloprid	Capsule
Nanocellulose	Pesticide compound	Fiber
Polyamide	Pheromones	Fiber
Polyethylene glycol	β-Cyfluthrin	Capsule
Polyethylene glycol	Garlic essential oil	Capsule
Polyethylene glycol	Carbofuran	Suspension
Polyethylene glycol–dimethyl ester	Carbofuran	Micelle
Polyvinyl alcohol	Bifenthrin	Capsule
Polyvinylpyrrolidone	Itraconazole	Capsule
Sodium dodecyl sulfate	Novaluron	Powder
Sodium salt	Novaluron	Powder
Starch–polyethylene	Endosulfan	Film

5.5 Release and Delivery of Nanoformulated Biopesticides

The delivery mechanism of nanoformulations is a critical factor in the successful application of nanobiopesticides. These formulations typically consist of organic constituents such as polymers or inorganic components like metal oxides, structured into nanoparticles, nanocapsules, or micelles that enhance the apparent solubility of poorly soluble active ingredients. Such systems enable controlled or targeted release while simultaneously protecting active compounds from premature degradation. Among the various nanoscale architectures, nanocapsules, nanogels, and micelles are the most widely utilized for controlled biopesticide delivery due to their superior encapsulation efficiency and stability. Despite these advantages, the practical implementation of nanobiopesticide delivery systems faces challenges including environmental variability, extensive field coverage requirements, and cost-effectiveness concerns. The development of nanomaterial- based pesticide formulations emphasize low-volume, high-efficiency applications that rely on a targeted delivery strategy informed by the biological characteristics and life cycles of pests and pathogens [27]. Furthermore, before commercialization, nanoparticle-based products must undergo rigorous quality assurance and safety evaluations conducted by national regulatory authorities responsible for food safety and agricultural security. Notably, leading global organic certification organizations such as the Soil Association (United Kingdom) and the Biological Farmers of Australia (BFA) have assessed nanomaterial-based agricultural products and recognized certain nano-enabled agrifoods as compliant with organic standards [28].

5.6 Nanobiopesticide Assays

Laboratory-based assays play a vital role in assessing the efficacy and potential of synthesized silver nanoparticle (AgNP)-based biopesticides. These evaluations are typically conducted through *in vitro* bioassays designed to study pest behavior and susceptibility at various developmental stages, including larvae, pupae, and adults. The assessment strategy often involves using the pest's preferred food source or life stage as a biological target to determine activity levels. Consequently, the antifeedant, larvicidal, and cytotoxic properties of silver nanobiopesticides synthesized from aqueous plant leaf extracts have been systematically evaluated through such controlled laboratory experiments [29].

5.7 Neem-Based Nanoproducts and Their Efficacy Against Various Crop Pests

Table No. 6 Neem-Based Nanoproducts and Their Efficacy against Various Crop Pests

Component	Active Ingredient	Carrier / Nanoparticle	Size (nm / µm)	Pest Controlled	efernce No.
Azadirachtin	Azadirachtin	R–CM–Chitosan	200–500 nm	Lepidopterans	[30]
Neem oil	Azadirachtin	Cyclodextrin and PCL	83.2 nm – 4 µm	ymphs and eggs of *Bemisia tabaci*	[31]
Neem seed kernel	Azadirachtin	PCL	230–245 nm	Larvae of *Plutella xylostella*	[32]
Neem oil	Azadirachtin	Silica nanoparticles	20 nm	*Tuta absoluta*	[33]

5.8 Other Botanical / Plant-Based Nanoproducts and Their Efficacy Against Various Crop Pests

Table No. 7 Other Botanical / Plant-Based Nanoproducts and Their Efficacy against Various Crop Pests

Component	Active Ingredient	Carrier / Nanoparticle	Size (nm / µm)	Pest Controlled	ference No.
Clove oil (*Syzygium aromaticum*)	Eugenol	Chitosan nanoparticles	150–200 nm	*ophilus oryzae* (rice weevil)	[34]
Garlic extract (*Allium sativum*)	Allicin	Lipid nanoparticles	100–180 nm	*Spodoptera litura* (tobacco caterpillar)	[35]
Eucalyptus oil *ucalyptus globulus*)	Eucalyptol	Silica nanoparticles	–120 nm	*Aedes aegypti* (mosquito larvae)	[36]
Lemongrass oil (*Cymbopogon citratus*)		Silver nanoparticles	20–60 nm	*Helicoverpa armigera* (cotton bollworm)	
Peppermint oil (*Mentha piperita*)	Menthol	ZnO nanoparticles	40–80 nm	*Tetranychus urticae* (spider mite)	[38]
Turmeric extract (*Curcuma longa*)	rcumin	PLGA nanoparticles	100–150 nm	*Alternaria alternata* (leaf spot fungus)	
Pyrethrum extract (*Chrysanthemum cinerariifolium*)	Pyrethrins	hitosan–starch nanoparticles	120–180 nm	*Aphis gossypii* (cotton aphid)	[40]
Castor oil (*Ricinus communis*)	icinoleic acid	Silica nanoparticles	80–100 nm	*Tribolium castaneum* (red flour beetle)	
Ginger extract (*Zingiber officinale*)	Gingerol	Silver nanoparticles	30–50 nm	*Callosobruchus maculatus* (pulse beetle)	[42]

5.9 Future of Nanobiopesticides

Recent research indicates that nanobiopesticides possess the potential to mitigate the toxic effects associated with conventional chemical pesticides while enabling precise, target-specific pest control. Their application supports the development of intelligent nanosystems aimed at addressing major agricultural challenges, including environmental imbalance, threats to food security, and reduced crop productivity [43].

6. RNAi-BASED BIOPESTICIDES

The global population has reached approximately 8 billion and is expected to surpass 10 billion by 2080 [44]. With increasing food demand and decreasing arable land due to rapid urbanization, improving agricultural productivity per unit area has become a critical necessity. Among the key factors affecting crop yields, diseases remain a major constraint, and effective disease prevention and control strategies offer a promising means of enhancing production efficiency [45]. The development of chemical pesticides marked the first pesticide revolution, significantly improving pest management and leading to several-fold increases in global crop yields. Later, during the 1990s, the second pesticide revolution emerged with the commercial introduction of genetically modified (GM) crops possessing pest- and disease-resistance genes [46]. However, both chemical pesticides and GM crops present potential safety and ecological risks.

The advent of RNAi-based biopesticides represents a new frontier—often described as the third revolution in pest control by integrating the beneficial aspects of both chemical and transgenic approaches while minimizing their drawbacks [47]. These biopesticides function through RNA interference (RNAi), a mechanism that disrupts the translation of specific mRNAs from target pathogens or pests, effectively inhibiting protein synthesis essential for their growth, development, and reproduction. This selective gene silencing approach allows precise pest control without altering gene expression in crop plants, thereby ensuring food safety and enhancing overall agricultural sustainability [48].

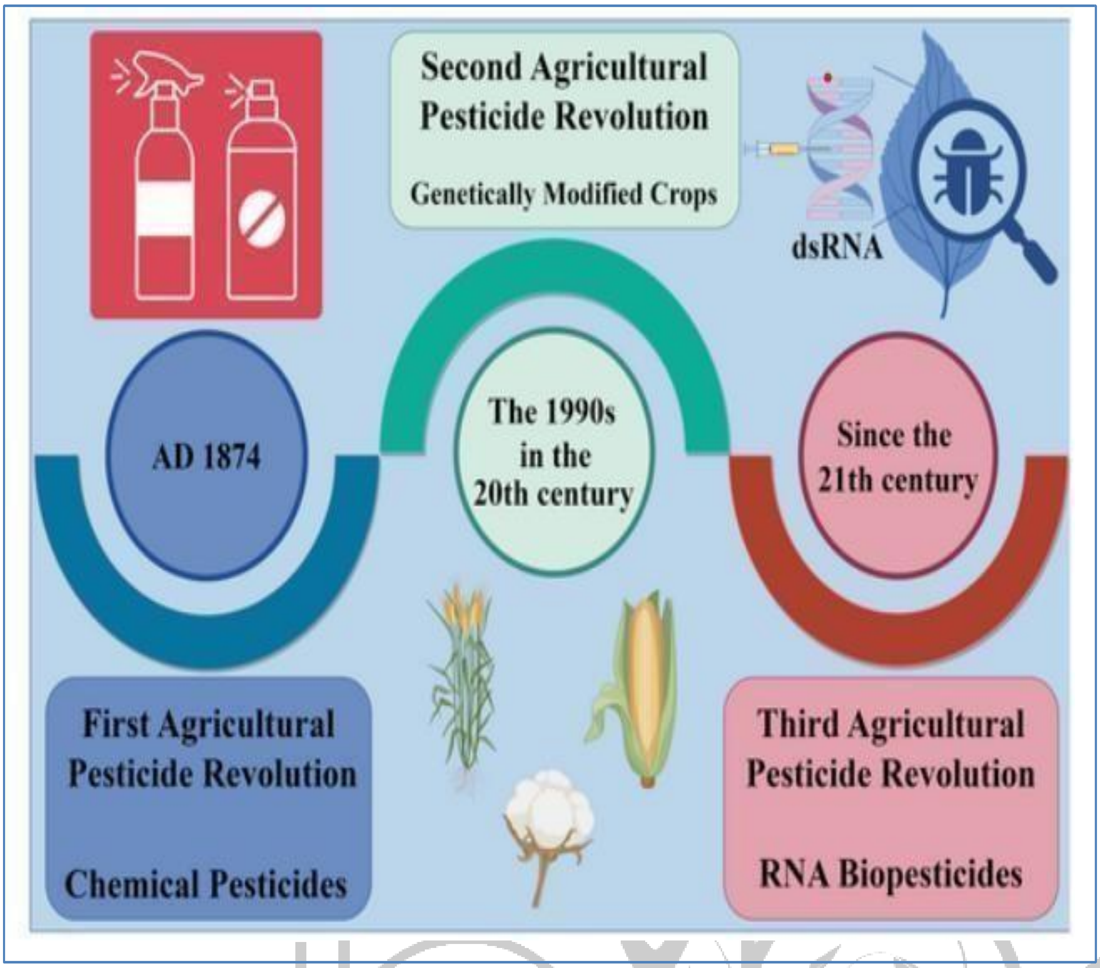

Figure No. 2 Revolutions in the History of Pesticides

6

.1 The Evolution of RNAi Biopesticides

Since their emergence, RNAi-based biopesticides have progressed through multiple developmental phases, encompassing their initial discovery, theoretical investigation, and subsequent practical implementation. These stages can be broadly classified as follows:

6.1.1 Discovery of the RNAi Phenomenon

The foundation of RNA interference (RNAi) research dates back to 1928, when Wingard published the first report describing an immunity-like phenomenon in tobacco leaves, where plants exhibited resistance to secondary infection by the tobacco mosaic virus [49, 50].

Although the underlying mechanism remained unclear at that time, this observation laid the groundwork for future discoveries in gene silencing. In 1992, Romano and Macino identified the phenomenon of exogenous transgene silencing in *Neurospora crassa*, which they termed "quelling", marking a significant step toward understanding post-transcriptional gene regulation. A major breakthrough occurred in 1998, when Fire and colleagues demonstrated that introducing double-stranded RNA (dsRNA) could specifically silence endogenous mRNA sequences in the nematode *Caenorhabditis elegans*, thereby coining the term RNA interference (RNAi) [51]. Following this discovery, RNAi mechanisms became an intensely researched area, leading to an exponential expansion of studies across biological disciplines. In 2004, Baulcombe further refined the conceptual framework of RNA silencing by proposing three distinct RNA-based regulatory pathways: cytoplasmic siRNA-mediated silencing, miRNA-mediated repression of endogenous mRNA, and DNA methylation-driven transcriptional inhibition [52]. These pathways are initiated by the cleavage of dsRNA into short 21–26 nucleotide RNA fragments by the Dicer enzyme, which contains an RNAse III domain. The resulting small RNAs, termed short interfering RNAs (siRNAs) and microRNAs (miRNAs), serve as the core regulators of gene silencing at both transcriptional and post-transcriptional levels [52].

6.1.2 Preliminary Studies on RNAi Biopesticides

The preliminary investigations on RNAi-based biopesticides have primarily concentrated on identifying molecular targets across diverse pest and pathogen species. The nonstructural protein B2 of betanodavirus (β-nodavirus) elevates Bax protein levels and induces mitochondria-mediated apoptosis in grouper liver (GL-av) cells, suggesting that B2 could serve as a potential target for developing RNAi biopesticides against β-nodavirus [53]. Similarly, Dang et al. reported that the application of siRNA targeting the major capsid protein (MCP) gene of the red-spotted grouper nervous necrosis virus (RSIV) significantly reduced MCP expression, leading to decreased viral replication [54]. The citrus red mite, *Panonychus citri*, represents a major pest of citrus crops. Silencing the PcSpo gene, which encodes an enzyme involved in ecdysteroid synthesis, inhibited molting, indicating that the Spook (PcSpo) gene could be an effective RNAi target for the management of mites and other agriculturally significant pests [55].

Furthermore, in the cotton bollworm (*Helicoverpa armigera*), the Cytochrome P450 gene (CYP6AE14) is responsible for metabolizing cotton phenolics such as gossypol. The potential of RNA interference (RNAi) as a universal insect control strategy by feeding larvae with plant material expressing specific dsRNA sequences targeting CYP6AE14. This treatment resulted in a notable decrease in transcript levels within the midgut and subsequently hindered larval development, emphasizing the utility of plant-derived dsRNA for inducing RNAi and developing RNA-based biopesticides targeting *H. armigera* [56]. An *Escherichia coli* strain (HT115) to synthesize dsRNA molecules directed against essential genes, including ribosomal protein *Rpl19*, V-type ATPase subunit D, fatty acid elongase Noa, and small GTPase Rab11, specific to the oriental fruit fly (*Bactrocera dorsalis*). Oral ingestion of this dsRNA by the flies successfully triggered gene silencing, demonstrating the feasibility of achieving RNAi effects through direct ingestion of dsRNA or consumption of dsRNA-producing bacteria. This approach offers promising prospects for the development of cost-effective and target-specific RNA-based biopesticides against *B. dorsalis* [57].

Additionally, Lee et al. conducted a study wherein dsRNA targeting the *Se-Ras* gene, encoding the G-protein Ras, was injected into the beet armyworm (*Spodoptera exigua*). Within 48 hours, a marked reduction in Se-Ras gene expression was detected in hemocytes, leading to inhibited phenoloxidase release. The Se-Ras gene was thereby identified as a crucial molecular target for the design of RNAi-based biopesticides against beet armyworm, representing the first evidence of Ras involvement in the insect's immune defense mechanisms [58].

6.2 Application of RNAi Biopesticides

The first RNA interference (RNAi)-based product, "SmartStax Pro" corn (MON87411), was developed by Monsanto Company (now Bayer) and approved by U.S. regulatory agencies in 2017, followed by China in 2021. This genetically engineered maize combines the *Bacillus thuringiensis* (Bt) Cry3Bb1 toxin with dsRNA targeting the Snf7 gene of the western corn rootworm (*Diabrotica virgifera*). Silencing Snf7, which encodes a transmembrane transport protein, increases larval mortality and reduces corn root damage [59].

In 2020, GreenLight Biosciences submitted an RNA pesticide, GS2, targeting the Colorado potato beetle to the U.S. Environmental Protection Agency (EPA). The company is also developing RNAi-based fungicides for powdery mildew and gray mold, expected to reach the market by 2025.Meanwhile, other agrobiotech firms are pursuing sprayable RNAi technologies. RNAissance Ag LLC is formulating a product against the diamondback moth, and Syngenta is developing RNAi insecticides for Colorado potato beetles, expected to commercialize within 7-10 years. Additionally, Bayer's BioDirect targets the parasitic mite Varroa destructor, a major threat to honeybees. It employs naturally occurring microorganisms that infect and kill mites without harming bees or beneficial insects, providing an eco-friendly pest management approach [60].

7. SEAWEED- DERIVED BIO PESTICIDES

Marine environments encompass more than 70% of Earth's surface, hosting approximately half of the world's biodiversity among its myriad species. Algae live in the upper oceanic layer, which makes up two thirds of the earth [61]. The term "seaweed," sometimes known as "macroalgae" refers to a broad group of organisms with various traits and applications. Natural substances obtained from marine species have been essential for everyday nourishment, act as sustainable source of alternative nutrition and prescribed for prevention of illness throughout history [62]. Currently, the seaweed industry is characterized by a high species concentration, notable regional variations, and rapid expansion. The amount of seaweed that has been grown were increased by an incredible thousandfold since 1950 [63].

Marine seaweed is a type of algae that can perform photosynthesis, which produces oxygen and absorbs carbon dioxide, with the support of a class of green pigments known as chlorophyll. Algae are categorized as macroalgae, which are smaller than microalgae and only visible under a microscope. Macroalgae can reach a maximum depth of 65 m and are more diverse in the oceans.

For this reason, "algae" is often used to refer to "marine macroalgae or seaweeds [64].

7.1 Biorefinery Approaches to Seaweed Biomass

The biorefinery approach for seaweed biomass emphasizes the integrated extraction and utilization of bioactive compounds with potential pesticidal activity, alongside the production of other valuable bioproducts and biofuels. By applying the biorefinery concept, the full potential of seaweed can be harnessed while minimizing waste generation and maximizing overall product yield. Within seaweed-based biorefineries, processes such as fermentation, extraction, and purification are employed to isolate and recover bioactive compounds exhibiting insecticidal, antifungal, or antimicrobial properties [Figure No. 1]. These naturally derived compounds are biodegradable, eco- friendly, and less toxic, distinguishing them from conventional synthetic pesticides. Moreover, the biorefinery paradigm underscores the versatility of seaweed biomass, highlighting its value not only for pest management but also for food, feed, pharmaceutical, and energy applications.

Consequently, seaweed-based biorefineries represent a sustainable and integrated resource management strategy, aligning with the principles of circular bioeconomy and environmental conservation [65].

7.2 Bioactive Compounds and Pest Management

Seaweeds, owing to their vast taxonomic diversity, represent a rich reservoir of bioactive compounds with significant potential in agricultural pest management. Various classes of seaweeds including brown (Phaeophyceae), red (Rhodophyceae), and green (Chlorophyceae) species have demonstrated pest-repellent and antimicrobial properties, making them promising candidates for the development of eco-friendly biopesticides applicable in both agricultural and horticultural systems [66].

Recent studies have identified several bioactive metabolites from seaweeds such as *Ulva ohnoi* and *Derbesia tenuissima*, which exhibit potent pesticidal activity. These species can be cultivated under controlled, land-based systems, enabling the production of high-quality and consistent biomass. Such cultivation uniformity is crucial for ensuring the reproducibility and efficacy of bioactive compound extraction, thereby supporting the commercial-scale production of reliable biopesticides. Furthermore, the biodegradable and environmentally benign nature of these compounds positions seaweed-derived bioactives as sustainable alternatives to conventional synthetic pesticides, contributing to safer and more sustainable crop protection strategies [67].

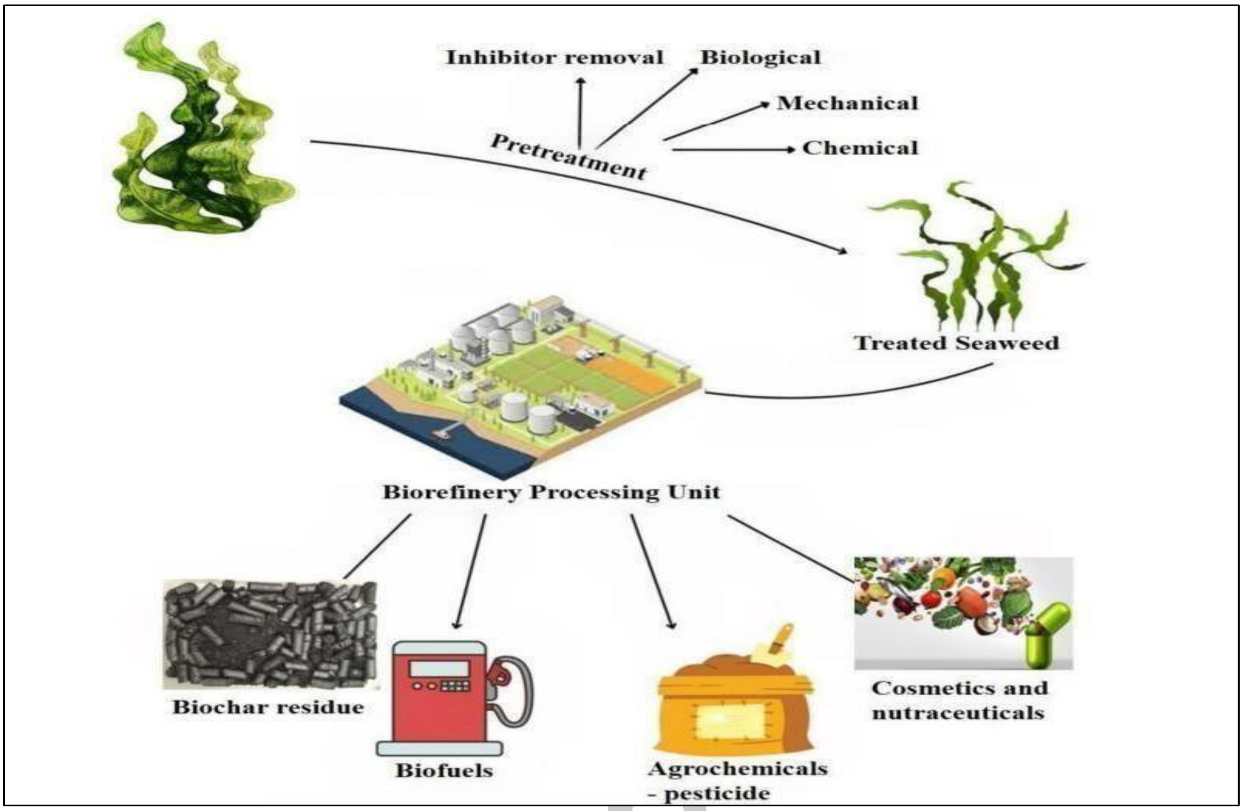

Figure No. 3 Biorefinery Process of Pesticide Production from Marine Seaweeds

7.3 Importance of Seaweeds in Biopesticides Production

In the context of sustainable agriculture, seaweeds have gained considerable attention due to their remarkable potential in the production of biopesticides [Figure No. 04]. Their growing importance is attributed to a combination of unique biochemical properties and environmental benefits, which make them an appealing and eco-compatible alternative to conventional synthetic pesticides. Seaweeds not only provide a renewable and abundant biomass source, but also contain a wide array of bioactive secondary metabolites with insecticidal, antifungal, and antiviral activities. The following section provides a detailed overview of the role and significance of seaweeds in biopesticide synthesis and their relevance in promoting environmentally sustainable pest management practices [68].

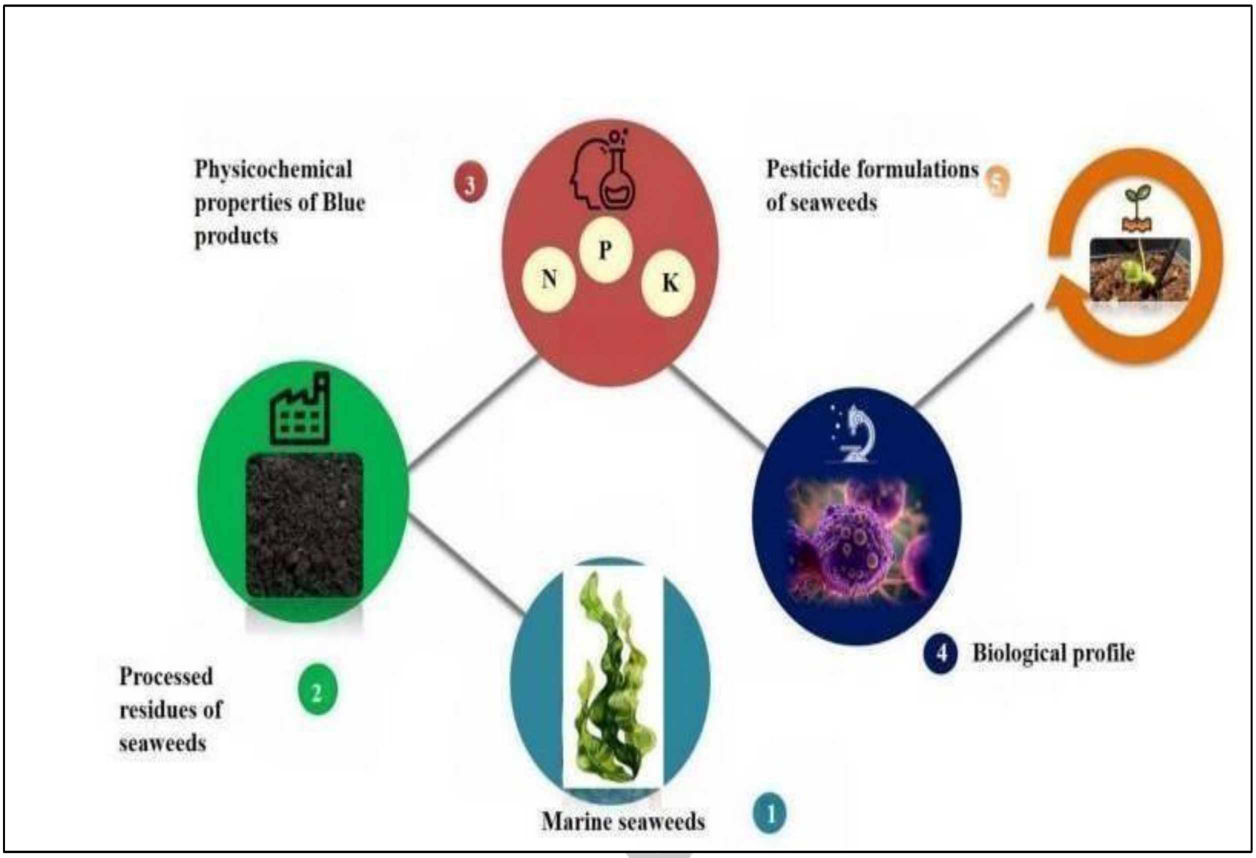

Figure No. 4 Biopesticides Derived from Seaweeds through Different Processes

7.4 Future Perspectives of Seaweeds Biopesticides

7.4.1 Potential for Seaweeds in Biopesticides Market

Extensive research in recent years has highlighted seaweeds as promising eco-friendly alternatives to conventional chemical pesticides. These marine macroalgae are abundant sources of bioactive metabolites with notable pesticidal properties, including polysaccharides, polyphenols, and halogenated compounds. Such constituents exhibit diverse modes of action functioning as natural repellents, growth inhibitors, or antimicrobial agents against a wide range of pests and pathogens. The emerging understanding of these biochemical interactions has positioned seaweeds as valuable resources in the biopesticide industry, offering dual benefits of effective pest suppression and environmental sustainability. Consequently, the exploitation of seaweed-derived compounds presents a viable strategy for developing next-generation biopesticides that are both efficient and ecologically responsible [69].

7.4.1 Innovation in Biopesticide Technology

Nanoformulation technology enhances the targeted delivery, stability, and bioavailability of active pesticidal components, thereby improving their overall efficiency and persistence under field conditions. Through the application of nanotechnology, biologically synthesized pesticides have been developed using cost-effective natural resources, such as seaweeds particularly green algae. These nano-based biopesticides offer a safe and sustainable approach to controlling a wide range of agricultural pests, including fungal and bacterial pathogens, while minimizing adverse environmental impacts [70].

8. CONCLUSION

Innovative biopesticides, including nanoformulated, RNAi-based, and seaweed-derived products, are transforming sustainable pest management. Nanoformulations enhance delivery, stability, and controlled release, while RNAi allows precise, gene-targeted pest suppression, and seaweed extracts act as both pest deterrents and plant biostimulants. These technologies provide environmentally friendly, target-specific, and effective alternatives to conventional pesticides, addressing resistance, pollution, and food safety concerns. Integrating them into IPM strategies promotes sustainable agriculture and reduces chemical dependence. Maximizing their potential requires interdisciplinary research, regulatory harmonization, public awareness, and cost-effective production. With strategic development, these biopesticides can revolutionize pest management, protect ecosystems, and support global food security responsibly.

9. REFERENCES

1. Copping LG, Menn JJ. Biopesticides: a review of their action, applications and efficacy. Pest Management Science: Formerly Pesticide Science. 2000 Aug; 56(8):651-76.
2. Srivastava N, Kumari U, Kumar J. Microbial Biopesticides: An Eco-Friendly Approach for a Sustainable Agro-ecosystem. InMicrobial Products 2022 Nov 16;1:189-203.
3. Thakore Y. The biopesticide market for global agricultural use. Industrial Biotechnology. 2006 Sep 1;2(3):194-208.
4. Qiao H, Chen J, Dong M, Shen J, Yan S. Nanocarrier-based eco-friendly RNA pesticides for sustainable management of plant pathogens and pests. Nanomaterials. 2024 Nov 22;14(23):1874.
5. Kalra A and Khanuja SPS. Research and Development priorities for biopesticide and biofertiliser products for sustainable agriculture in India, In. Business Potential for Agricultural Biotechnology (Teng, P. S. ed.), Asian Productivity Organisation. 2007;96-102.
6. Gupta I, Singh R, Muthusamy S, Sharma M, Grewal K, Singh HP, Batish DR. Plant essential oils as biopesticides: Applications, mechanisms, innovations, and constraints. Plants. 2023 Aug 10;12(16):2916.
7. Ayilara MS, Adeleke BS, Akinola SA, Fayose CA, Adeyemi UT, Gbadegesin LA, Omole RK, Johnson RM, Uthman QO, Babalola OO. Biopesticides as a promising alternative to synthetic pesticides: A case for microbial pesticides, phytopesticides, and nanobiopesticides. Frontiers in microbiology. 2023 Feb 16; 14:1040901.
8. Prakash NR, Ahuja A, Kumar S, Saini V, Anokhe A, Jayaswal D, Kumar K. RNA interference in agricultural insect pest management: Status and perspectives. Indian Journal of Experimental Biology. 2024 Nov 1;62(11).
9. Vivekanandhan P, Panikar S, Sethuraman V, Usha-Raja-Nanthini A, Shivakumar MS. Toxic and synergetic effect of plant essential oils along with nano-emulsion for control of three mosquito species. Journal

of Natural Pesticide Research. 2023 Sep 1; 5:100045.

10. Gakuya DW, Itonga SM, Mbaria JM, Muthee JK, Musau JK. Ethnobotanical survey of biopesticides and other medicinal plants traditionally used in Meru central district of Kenya. Journal of ethnopharmacology. 2013 Jan 30;145(2):547-53.
11. Alam A, Abbas S, Abbas A, Abbas M, Hafeez F, Shakeel M, Xiao F, Zhao CR. Emerging trends in insect sex pheromones and traps for sustainable management of key agricultural pests in Asia: beyond insecticides—a comprehensive review. International Journal of Tropical Insect Science. 2023 Dec;43(6):1867-82.
12. Ayelo PM, Pirk CW, Yusuf AA, Chailleux A, Mohamed SA, Deletre E. Exploring the kairomone-based foraging behaviour of natural enemies to enhance biological control: a review. Frontiers in Ecology and Evolution. 2021 Apr 22; 9:641974.
13. Verma VC, Gond SK, Kumar A, Kharwar RN, Boulanger LA, Strobel GA. Endophytic fungal flora from roots and fruits of an Indian neem plant Azadirachta indica A. Juss., and impact of culture media on their isolation. Indian journal of microbiology. 2011 Oct;51(4):469-76.
14. Thakur M, Sohal BS. Role of elicitors in inducing resistance in plants against pathogen infection: a review. International Scholarly Research Notices. 2013;2013(1):762412.
15. Reddy DS, Chowdary NM. Botanical biopesticide combination concept—a viable option for pest management in organic farming. Egyptian Journal of Biological Pest Control. 2021 Dec;31(1):1-0.
16. Nicholson GM. Fighting the global pest problem: Preface to the special Toxicon issue on insecticidal toxins and their potential for insect pest control. Toxicon. 2007; 49:413–422.
17. Galanakis, C.M. Recovery of high added-value components from food wastes: Conventional, emerging technologies and commercialized applications. Trends Food Sci. Technol. 2012, 26, 68–87.
18. Galanakis, C.M.; Markouli, E.; Gekas, V. Recovery and fractionation of different phenolic classes from winery sludge using ultrafiltration. Sep. Purif. Technol. 2013, 107, 245–251.
19. Ragaei M, Sabry AK. Nanotechnology for insect pest control. International journal of science, environment and technology. 2014;3(2):528-45.
20. Bergeson LL. Nanosilver pesticide products: what does the future hold?. Environmental Quality Management. 2010 Jun 1;19(4).
21. Lade SJ, Donges JF, Fetzer I, Anderies JM, Beer C, Cornell SE, Gasser T, Norberg J, Richardson K, Rockström J, Steffen W. Analytically tractable climate–carbon cycle feedbacks under 21st century anthropogenic forcing. Earth System Dynamics. 2018 May 17;9(2):507-23.
22. Benelli G, Canale A, Toniolo C, Higuchi A, Murugan K, Pavela R, Nicoletti M. Neem (Azadirachta indica): towards the ideal insecticide. Natural product research. 2017 Feb 16;31(4):369-86.
23. Mishra V, Mishra RK, Dikshit A, Pandey AC. Interactions of nanoparticles with plants: an emerging prospective in the agriculture industry. InEmerging technologies and management of crop stress tolerance 2014 Jan 1;3(8):159-180.
24. Lu W, Senapati D, Wang S, Tovmachenko O, Singh AK, Yu H, Ray PC. Effect of surface coating on the toxicity of silver nanomaterials on human skin

keratinocytes. Chemical physics letters. 2010 Feb 25;487(1-3):92-6.

25. Zhao X, Cui H, Wang Y, Sun C, Cui B, Zeng Z. Development strategies and prospects of nano- based smart pesticide formulation. Journal of agricultural and food chemistry. 2017 Jun 27;66(26):6504-12.
26. Huang B, Chen F, Shen Y, Qian K, Wang Y, Sun C, Zhao X, Cui B, Gao F, Zeng Z, Cui H. Advances in targeted pesticides with environmentally responsive controlled release by nanotechnology. Nanomaterials. 2018 Feb 11;8(2):102.
27. Manjunatha BA, Gogoi P. Anomaly based intrusion detection in mixed attribute dataset using data mining methods. Journal of Artificial Intelligence. 2016;9(1-3):1-1.
28. Scrinis G, Lyons K. 252 Nanotechnology and the Techno-Corporate Agri-food Paradigm.
InFood Security, Nutrition and Sustainability.2010;1(1): 252-270.
29. Kamaraj C, Rajakumar G, Rahuman AA, Velayutham K, Bagavan A, Zahir AA, Elango G. Feeding deterrent activity of synthesized silver nanoparticles using Manilkara zapota leaf extract against the house fly, Musca domestica (Diptera: Muscidae). Parasitology research. 2012 Dec;111(6):2439-48.
30. Feng BH, Peng LF. Synthesis and characterization of carboxymethyl chitosan carrying ricinoleic functions as an emulsifier for azadirachtin. Carbohydrate polymers. 2012 Apr 2;88(2):576-82.
31. Salles Carvalho S, Djair Vendramim J, Major Pitta R, Rossi Forim M. Eficiência de nanoformulações a base de óleo de nim sobre Bemisia tabaci (GENN.) Biótipo B (Hemiptera: Aleyrodidae). Semina ciÃªnc. agrar. 2012:193-202.
32. Forim MR, Costa ES, Da Silva MF, Fernandes JB, Mondego JM, Boiça Junior AL. Development of a new method to prepare nano-/microparticles loaded with extracts of Azadirachta indica, their characterization and use in controlling Plutella xylostella. Journal of Agricultural and Food Chemistry. 2013 Sep 25;61(38):9131-9.
33. El-Samahy M, El-Ghobary AM, Khafagy IF. Using silica nanoparticles and neemoil extract as new approaches to control Tuta absoluta (meyrick) in tomato under field conditions. Int. J. Plant Soil Sci. 2014;3(10):1355-65.
34. Hasheminejad N, Khodaiyan F, Safari M. Improving the antifungal activity of clove essential oil encapsulated by chitosan nanoparticles. Food chemistry. 2019 Mar 1; 275:113-22.
35. Ibrahim SS, Salem NY, Abd ElNaby SS, Adel MM. Characterization of Nanoparticles Loaded with Garlic Essential Oil and Their Insecticidal Activity Against Phthorimaea
Operculella (Zeller) (PTM) (Lepidoptera: Gelechiidae). International Journal of Nanoscience and Nanotechnology. 2021 Aug 1;17(3):147-60.
36. Silvério MR, Espindola LS, Lopes NP, Vieira PC. Plant natural products for the control of Aedes aegypti: The main vector of important arboviruses. Molecules. 2020 Jul 31;25(15):3484.
37. Mukarram M, Choudhary S, Khan MA, Poltronieri P, Khan MM, Ali J, Kurjak D, Shahid M. Lemongrass essential oil components with antimicrobial and anticancer activities.
Antioxidants. 2021 Dec 22;11(1):20.

38. Gostin IN, Popescu IE. Evaluation of the essential oils used in the production of biopesticides:
assessing their toxicity toward both arthropod target species and beneficial pollinators.
Agriculture. 2023 Dec 30;14(1):81.
39. Chavana J, Joshi NK. Toxicity and risk of biopesticides to insect pollinators in urban and agricultural landscapes. Agrochemicals. 2024 Feb 29;3(1):70-93.
40. Albuquerque PM, Azevedo SG, de Andrade CP, D'Ambros NC, Pérez MT, Manzato L. Biotechnological applications of nanoencapsulated essential oils: A review. Polymers. 2022 Dec 15;14(24):5495.
41. Rajkumar V, Gunasekaran C, Dharmaraj J, Chinnaraj P, Paul CA, Kanithachristy I. Structural characterization of chitosan nanoparticle loaded with Piper nigrum essential oil for biological efficacy against the stored grain pest control. Pesticide biochemistry and physiology. 2020 Jun 1; 166:104566.
42. Plaeyao K, Kampangta R, Korkokklang Y, Talodthaisong C, Saenchoopa A, Thammawithan S, Latpala K, Patramanon R, Kayunkid N, Kulchat S. Gingerol extract-stabilized silver nanoparticles and their applications: Colorimetric and machine learning-based sensing of Hg (ii) and antibacterial properties. RSC advances. 2023;13(29):19789-802.
43. Nuruzzaman MD, Rahman MM, Liu Y, Naidu R. Nanoencapsulation, nano-guard for pesticides: a new window for safe application. Journal of agricultural and food chemistry. 2016 Feb 24;64(7):1447-83.
44. Venugopal NV, Sainadh NV. Novel polymeric nanoformulation of Mancozeb–An eco- friendly nanomaterial. International Journal of Nanoscience. 2016 Aug 16;15(04):1650016.
45. B. K. Singh, M. Delgado-Baquerizo, E. Egidi, et al., "Climate Change Impacts on Plant Pathogens, Food Security and Paths Forward," Nature Reviews Microbiology 21, no. 10 (2023): 640–656.
46. Huang Y, Dai Y, Huang Z, Zhang M, Xiu L, Zhang X, Zhang Y, Huang L. RNA-Based Biopesticides: Pioneering Precision Solutions for Sustainable Aquaculture in China. Animal Research and One Health. 2025 May;3(2):165-76.
47. M. Guan, C. H. A. O. Zijian, Y. A. N. Shuo, et al., "Research Status and Development Prospect of RNA Pestcide," Modern Agrochemicals 22, no. 02 (2023): 11–18.
48. R. Kaur, A. Choudhury, S. Chauhan, A. Ghosh, R. Tiwari, and M. V. Rajam, "RNA Interference and Crop Protection Against Biotic Stresses," Physiology and Molecular Biology of Plants 27, no. 10 (2021): 1–2.
49. M. Rao and S. Sockanathan, "Molecular Mechanisms of RNAi: Implications for Development and Disease," Birth Defects Research Part C: Embryo Today—Reviews 75, no. 1 (2005): 28–
42.
50. B. Ghoshal and H. Sanfaçon, "Symptom Recovery in Virus-Infected Plants: Revisiting the Role of RNA Silencing Mechanisms," Virology 479 (2015): 167–179.
51. Leonetti P, Stuttmann J, Pantaleo V. Regulation of plant antiviral defense genes via host RNA- silencing mechanisms. Virology Journal. 2021 Sep 26;18(1):194.
52. D. Baulcombe, "RNA Silencing in Plants," Nature 431, no. 7006 (2004): 356–363.

53. Y. C. Su, J. L. Wu, and J. R. Hong, "Betanodavirus Non-Structural Protein B2: A Novel Necrotic Death Factor That Induces Mitochondria-Mediated Cell Death in Fish Cells," Virology 385, no. 1 (2009): 143–154.
54. L. T. Dang, H. Kondo, I. Hirono, and T. Aoki, "Inhibition of Red Seabream Iridovirus (RSIV) Replication by Small Interfering RNA (siRNA) in a Cell Culture System," Antiviral Research 77, no. 2 (2008): 142–149.
55. G. Li, J. Z. Niu, M. Zotti, et al., "Characterization and Expression Patterns of Key Ecdysteroid Biosynthesis and Signaling Genes in a Spider Mite (Panonychus Citri)," Insect Biochemistry and Molecular Biology 87 (2017): 136–146.
56. Y. B. Mao, W. J. Cai, J. W. Wang, et al., "Silencing a Cotton Bollworm P450 Monooxygenase Gene by Plant-Mediated RNAi Impairs Larval Tolerance of Gossypol," Nature Biotechnology 25, no. 11 (2007): 1307–1313.
57. X. Li, M. Zhang, and H. Zhang, "RNA Interference of Four Genes in Adult Bactrocera Dorsalis by Feeding Their dsRNAs," PLoS One 6, no. 3 (2011): e17788.
58. S. Lee, S. Shrestha, S. V. Prasad, and Y. Kim, "Role of a Small G Protein Ras in Cellular Immune Response of the Beet Armyworm, Spodoptera Exigua," Journal of Insect Physiology 57, no. 3 (2011): 356–362.
59. De Schutter K, Taning CN, Van Daele L, Van Damme EJ, Dubruel P, Smagghe G. RNAi- based biocontrol products: Market status, regulatory aspects, and risk assessment. Frontiers in insect Science. 2022 Jan 5;1:818037.
60. A. Inberg, "BioDirect™ to Control Varroa Destructor-New Biologicals for Effective Protection from the Devastating Honey Bee Parasitic Mite," in 2016 International Congress of Entomology (ESA, 2016).
61. Gomez-Zavaglia A, Prieto Lage MA, Jimenez-Lopez C, Mejuto JC, Simal-Gandara J. The potential of seaweeds as a source of functional ingredients of prebiotic and antioxidant value. Antioxidants. 2019 Sep 17;8(9):406.
62. Azmi R, Ugur E, Seitkhan A, Aljamaan F, Subbiah AS, Liu J, Harrison GT, Nugraha MI, Eswaran MK, Babics M, Chen Y. Damp heat–stable perovskite solar cells with tailored- dimensionality 2D/3D heterojunctions. Science. 2022 Apr 1;376(6588):73-7.
63. Cai W, Zhang C, Zhang S, Ai S, Bai Y, Bao J, Chen B, Chang N, Chen H, Cheng L, Cui X. The 2021 China report of the Lancet Countdown on health and climate change: seizing the window of opportunity. The Lancet Public Health. 2021 Dec 1;6(12):e932-47.
64. Medeiros-Ribeiro AC, Aikawa NE, Saad CG, Yuki EF, Pedrosa T, Fusco SR, Rojo PT, Pereira RM, Shinjo SK, Andrade DC, Sampaio-Barros PD. Immunogenicity and safety of the CoronaVac inactivated vaccine in patients with autoimmune rheumatic diseases: a phase 4 trial. Nature medicine. 2021 Oct;27(10):1744-51.
65. Siller-Sánchez A, Ruiz HA, Aguilar CN, Rodríguez-Jasso RM. Biorefinery approach for red seaweeds biomass as source for enzymes production: food and biofuels industry. InGreen Bio- processes: enzymes in industrial food processing 2018 Nov 4 ;1(2):413-446
66. Lomartire S, Gonçalves AM. An overview of potential seaweed-derived bioactive

compounds for pharmaceutical applications. Marine Drugs. 2022 Feb 15;20(2):141.

67. Mata R, Josef AK, Hertwig R. Propensity for risk taking across the life span and around the globe. Psychological science. 2016 Feb;27(2):231-43.
68. Tervo-Clemmens B, Karim ZA, Khan SZ, Ravindranath O, Somerville LH, Schuster RM, Gilman JM, Evins AE. The developmental timing but not magnitude of adolescent risk-taking propensity is consistent across social, environmental, and psychological factors. Journal of Adolescent Health. 2024 Mar 1;74(3):613-6.
69. Duarte CM, Chapuis L, Collin SP, Costa DP, Devassy RP, Eguiluz VM, Erbe C, Gordon TA, Halpern BS, Harding HR, Havlik MN. The soundscape of the Anthropocene ocean. Science. 2021 Feb 5;371(6529): eaba4658.
70. Khalid M, Iffat Naqvi S, Hussain N, Rahman M, Fawad, Mirjavadi SS, Khan MJ, Amin Y. 4-Port MIMO antenna with defected ground structure for 5G millimeter wave applications. 2020 Jan 1;9(1):71.