DsRNA-Biopesticides as Sustainable Alternatives to Chemical Pesticides in India: Prospects, Challenges and Regulatory Landscape

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ABSTRACT

Indian agriculture faces challenges to increase productivity to support a rapidly growing population while reducing the ecological and health costs associated with intensive crop protection practices. Although chemical pesticides remain dominant, their excessive application has led to biodiversity loss, environmental contamination, pest resistance, and chronic human health concerns. In this context, exogenous double-stranded RNA (dsRNA)-based biopesticides have emerged as a promising, next-generation pest management strategy. RNA interference (RNAi)-based products offer high species specificity, minimal non-target effects, rapid environmental degradation, and compatibility with integrated pest management (IPM) and green chemistry principles. The paper reviews the prospects, challenges, and regulatory landscape of dsRNA biopesticides in India. The growing biopesticide market, supportive national sustainability goals, and alignment with the UN Sustainable Development Goals underscore its potential to reduce dependence on conventional chemicals. However, key challenges remain, including large-scale production costs, formulation stability, efficient delivery systems under field conditions, variable RNAi efficacy across insect taxa, and limited public awareness. Regulatory uncertainty further constrains adoption, as India currently lacks a dedicated framework tailored to RNA-based pesticides, with approvals falling under existing biopesticide or chemical pesticide regulations. Establishing science-based, transparent regulatory guidelines, investing in indigenous R&D, and strengthening public-private partnerships will be critical for the successful deployment of dsRNA biopesticides in India. Overall, exogenous dsRNA biopesticides represent a sustainable and innovative alternative for Indian agriculture, provided technical and regulatory barriers are systematically addressed.

Keywords : Green chemistry pesticides, RNAi, exogenous dsRNA, Novel technique, Plant protection, Environmentally sustainable

Introduction

India's agricultural sector supports nearly 58% of the population, that surpasses 1.38 billion in 2025 (FAO, 2020). It is projected to reach 1.5 billion by 2030 (United Nations, 2017), requiring a significant increase in agricultural productivity. Pest and disease-induced

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losses account for ~15.7% of total farm output, translating to over ~USD 36 billion annually. Chemical pesticides have long played a central role in securing food production, especially since the Green Revolution. However, excessive and often unregulated use has created severe ecological and public health challenges. Globally, 3.39 million tons (mt) of pesticides were applied in 2020, with India consuming 61,702 t (FAO, 2022), while the highest amount was observed in 2021-22 at 51,900 t (MoA&FW, India, 2023). Pesticide usage in India was averaged around 0.24 kg/ha in 2023 (FAOSTAT, 2023; Subash *et al.*, 2017). Despite their effectiveness, conventional pesticides contribute to biodiversity loss, soil degradation, water contamination, and chronic health problems, including endocrine disruption and cancer. Widespread resistance has emerged in numerous pest species, further compromising their long-term efficacy. Persistent residues accumulate in soil and water bodies, disrupting ecological balance and harming non-target organisms such as pollinators, natural enemies, and beneficial soil microbes. Continuous use of similar chemical classes accelerates resistance development, leading to higher application rates, pest resurgence, and secondary pest outbreaks.

Chemical pesticides constitute nearly 92% of total use, while biopesticides account for only 8% (Kumar and Pathak, 2024; MoA&FW, India, 2023). However, the adoption of biopesticides is gradually increasing as integrated pest management (IPM) programs expand. Between 2018-19 and 2022-23, chemical pesticide consumption remained relatively stable at 40-48 thousand tons, whereas biopesticide usage rose from 3.8 to 5.0 thousand tons (MoA&FW, India, 2023). State-level trends reveal pockets of reduction, particularly in Maharashtra and Jammu & Kashmir, driven by policy incentives for biopesticides (Singh and Narayanan, 2015). The biopesticides market size in 2026 is estimated at USD 7.43 billion, up from USD 6.72 billion in 2025, with projections reaching USD 12.28 billion by 2031 (Biopesticides Market Report, 2026). India's agricultural biologicals market is projected to grow from USD 573 million in 2024 to USD 1646 million by 2032 (Anon., 2026a). The need to transition toward sustainable, low-risk pest management technologies is increasingly evident. Goal 2 of the United Nations Sustainable Development Goals (SDGs) calls for sustainable agricultural practices that inherently involve reducing reliance on harmful chemicals. The reduction of chemical pesticides is also directly addressed in SDG Goal 12 on responsible consumption and production and SDG Goal 3 on good health and well-being. Green chemistry principles advocate designing pest control solutions that minimize hazardous inputs and reduce environmental persistence. It includes using biodegradable molecules, renewable resources, and formulations that limit off-target effects. RNA-based biopesticides exemplify these principles. They offer species specificity, degrade into harmless nucleotides, and avoid bioaccumulation. Integrating RNA-based biopesticides and similar biological tools within green chemistry frameworks aligns with India's national priorities of sustainable agriculture, reduced chemical load, and One Health approaches.

DsRNA-Based Pesticides

Double-stranded RNA (DsRNA)-based pesticides constitute an emerging class of biopesticides that exploit the RNA interference (RNAi) pathway, an evolutionarily conserved, sequence-specific gene-silencing mechanism naturally present in most eukaryotes. During RNAi, dsRNA is processed into small interfering RNAs (siRNAs), which guide the degradation of complementary messenger RNA (mRNA), thereby suppressing expression of essential genes. In pest management, exogenously applied dsRNA molecules are designed to target key genes in insects, pathogens, or weeds. Upon ingestion or absorption, they trigger temporary or reversible gene silencing, leading to mortality, reduced fecundity, or impaired development. Because dsRNA sequences can be precisely tailored to individual species, these pesticides offer unparalleled specificity compared to conventional chemicals (Figure 1). Importantly for India, dsRNA-based pesticides do not involve transgenic modification, making them more acceptable under biosafety regulations and public perception. Naturally occurring mechanisms in organisms are used to temporarily alter gene function, inducing desired changes in their life cycles or biology, thereby enabling management of the target species. It does not change the genome organisation; the alteration in the gene is temporary and resumes within a short time. The rapid environmental degradation of dsRNA limits persistence and minimizes risks to non-target organisms. However, its high instability under natural environmental conditions hinders its field adaptability and commercial deployment. Emerging formulation technologies, including nanoparticle encapsulation, liposomal delivery, and biodegradable polymer matrices, enhance dsRNA stability under field conditions. Topical dsRNA products are emerging, with Calantha from GreenLight Biosciences undergoing extensive field testing and now registered in several US states. Additional herbicide and mite-targeting products are in development, and Renaissance BioScience Corp has announced an innovative yeast-based platform technology for the low-cost production and effective delivery of RNA (Anon., 2026b; GreenLight Biosciences, 2026a; Renaissance BioScience, 2026). The commercial introduction of 'Calantha' has boosted dsRNA-pesticide research worldwide. To date, several dsRNA biopesticide products are in the pipeline in different countries, including India. However, regulatory divergence across countries continues to slow widespread commercialization. As India seeks to reduce chemical pesticide dependency and promote biological innovations under initiatives such as *Atmanirbhar Krishi* and One Health, dsRNA-based pesticides offer a promising, scalable, and environmentally aligned solution for sustainable pest management. A dsRNA bioformulation, 'RiboThrips', developed by ICAR-Indian Agricultural Research Institute (IARI), and licensed to ATGC Biotech Pvt. Ltd., is probably the first of its kind in the country. Lack of regulatory guidelines for exogenous dsRNA-based products slows their widespread field deployment for pest and disease management in India.

Mechanism and Advantages : RNAi is a conserved post-transcriptional gene-silencing mechanism in which small non-coding RNAs direct the degradation of complementary messenger mRNA, thereby suppressing gene expression. It has been established that dsRNA is a far more potent trigger of gene silencing than single-stranded RNA (ssRNA), while subsequent work showed that environmental dsRNA, for example, from *Escherichia coli* fed to *Caenorhabditis elegans* could also induce silencing (Fire *et al.*, 1998; Timmons and Fire, 1998). Earlier observations of post-transcriptional gene silencing were recognized as RNA-mediated only in 1989 (Fire *et al.*, 1998), and RNAi is now understood as part of a complex network governing cellular defence, RNA surveillance, and development.

The application of exogenous dsRNA for pest control became feasible after studies in 2006 demonstrated orally administered dsRNAs induced RNAi responses in insects (Araujo *et al.*, 2006; Turner *et al.*, 2006), followed by the first report of topically applied dsRNA to kill *Aedes aegypti* (Pridgeon *et al.*, 2008). RNAi also functions as a natural immune mechanism against viruses, bacteria, and fungi in plants and invertebrates (Katiyar-Agarwal *et al.*, 2006; Obbard *et al.*, 2009; Stram and Kuzntzova, 2006; Zhao *et al.*, 2018). The discoveries have driven rapid application of dsRNA in therapeutics (Hirschi *et al.*, 2015; Lares *et al.*, 2010; Witwer and Hirschi, 2014) and in plant protection (Baum *et al.*, 2007; Burand and Hunter, 2013; Koch and Kogel, 2014; Mao *et al.*, 2007). Exogenous dsRNA-based crop protection can be achieved by microinjecting dsRNA into plants or by applying synthetic dsRNA as a topical spray. Although microinjection-based dsRNA delivery has provided a powerful reverse genetic tool for investigating gene function, it is obviously not a practical means of delivering dsRNA for pest control. Topically applied dsRNA has emerged as a powerful tool in crop protection. While externally applied dsRNA can be directly ingested by pests, leaf cuticle barriers limit its uptake into plant cells, necessitating formulation strategies to enhance penetration.

Specificity to Target Organisms and Minimal Off-target Effects : A defining advantage of dsRNA pesticides is their exceptional sequence specificity. RNAi requires precise or near-precise base pairing between siRNAs and target mRNAs, allowing dsRNA constructs to silence only the intended genes in target organisms. Advanced bioinformatic screening of dsRNA sequences against genomes or transcriptomes of beneficial insects, vertebrates, and plants minimizes off-target homology. The precision of the dsRNA mechanism sharply contrasts with the broad-spectrum effects of chemical pesticides, enabling dsRNA sprays or host-induced gene silencing (HIGS) plants to protect pollinators, predators, parasitoids, and soil microbiota. Off-target risks are further reduced because RNA molecules degrade rapidly under UV radiation, microbial activity, and RNases, thereby limiting their environmental persistence.

Environmental Benefits and Compatibility with IPM : DsRNA pesticides offer multiple ecological and agronomic benefits. As biodegradable molecules, they break down into harmless ribonucleotides without contaminating soil, water, or food chains. Their highly

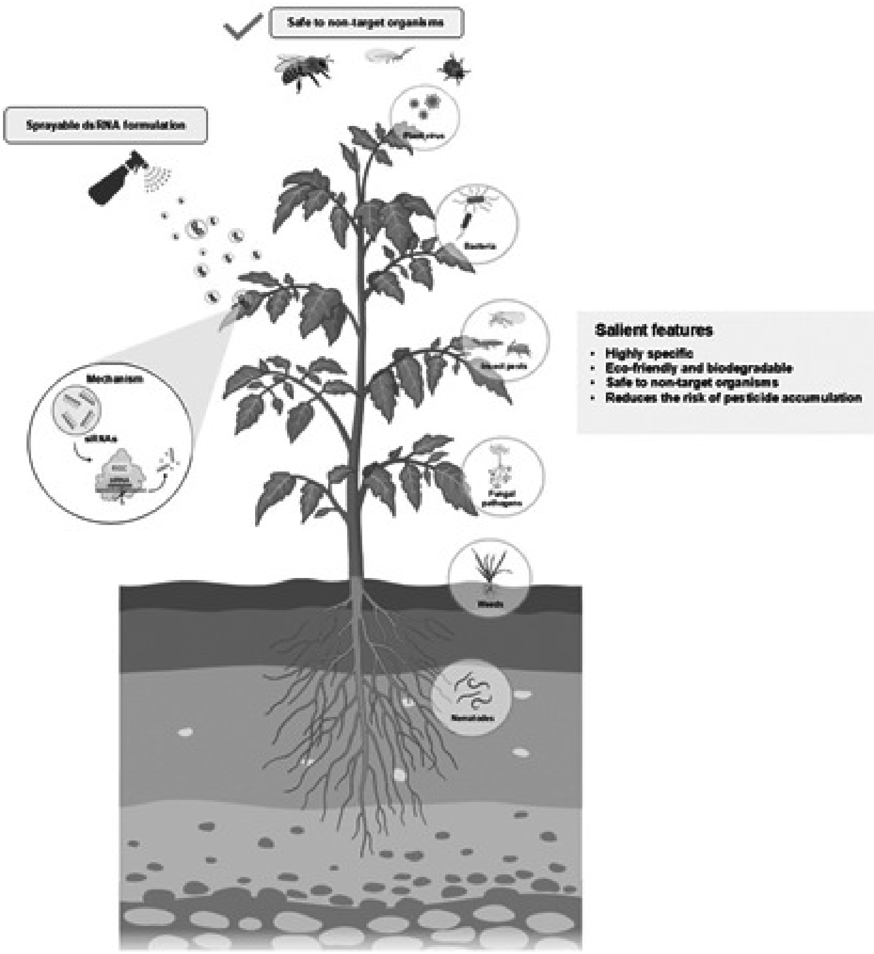

Figure 1. DsRNA pesticides for management of pests and diseases

selective mode of action results in minimal toxicity to non-target organisms, including beneficial arthropods, fish, birds, and mammals. Exogenous dsRNA approaches also support resistance management by simultaneously targeting multiple essential genes or pathways, thereby slowing the evolution of resistance compared with single-site chemical pesticides. Furthermore, dsRNA tools are compatible with biological control agents and can be integrated seamlessly into IPM programs without disrupting parasitoids, predators, or microbial biocontrol organisms.

Current Status in India

***Research and Application of dsRNA Pesticides* :** India is in a formative phase of adopting exogenous dsRNA-based pest management, with ICAR institutes and universities advancing dsRNA research across major crops and pest systems. Over the past five years, several studies have explored dsRNA targeting fungal pathogens such as *Magnaporthe oryzae* and *Phytophthora infestans* (Sarkar and Roy-Barman, 2021; Sundaresha *et al.*, 2022) and plant viruses such as chilli leaf curl virus (ChiLCV) (Chakraborty and Ghosh, 2022; Singh *et al.*, 2022), groundnut bud necrosis virus (GBNV) (Gupta *et al.*, 2021; Manik *et al.*, 2025), tomato leaf curl Palampur virus (ToLCPalV), papaya leaf curl virus (PaLCuV) (Priyanka *et al.*, 2025), papaya ringspot virus (PRSV) (Vadlamudi *et al.*, 2020), mungbean yellow mosaic virus (MYMV) (Kamesh Krishnamoorthy *et al.*, 2023) and pigeonpea sterility mosaic emaravirus (PPSMV) (Patil *et al.*, 2021). Application of exogenous dsRNA has been successfully evaluated in altering behaviour and fitness of insect pests such as *Thrips palmi* (Rakesh *et al.*, 2024), and *Bemisia tabaci* (Chakraborty and Ghosh, 2022), *Helicoverpa armigera* (Chikate *et al.*, 2016), *Plutella xylostella* (Sharath Chandra *et al.*, 2019), *Tuta absoluta* (Ramkumar *et al.*, 2021). However, their efficacy as pesticides under real field conditions, extensive field trials and safety data generation are required for commercial-level adoption and field deployment. A key milestone is the development of RiboThrips by ICAR-IARI, India's first dsRNA bioformulation (IP application: 202511073344), which has been licensed to ATGC Biotech Pvt. Ltd. for large-scale production. RiboThrips offers >12-month shelf life, enhanced plant and insect uptake, and field-tested efficacy against thrips and other sucking pests, while using biodegradable materials to ensure environmental safety. Similar customizable dsRNA formulations for additional pests and viruses are under development at ICAR-IARI. Although India has yet to have any registered dsRNA products or regulatory guidelines, the current products provide a strong foundation for future dsRNA-based crop protection.

Fungal Pathogens: In India, exogenous dsRNA has been evaluated in managing fungal pathogens, such as *Magnaporthe oryzae* and *Phytophthora infestans*. A significant advancement in potato was achieved by ICAR-Central Potato Research Institute (CPRI), which demonstrated that exogenous dsRNA targeting *Phytophthora infestans*, combined with nanoclay carriers, effectively reduced late blight severity (Sundaresha *et al.*, 2022).

Although efforts in India to deploy dsRNA for the management of fungal pathogens remain limited, exogenous dsRNA has been successfully applied globally against a wide range of phytopathogenic fungi. Effective control has been demonstrated for more than a dozen species, including *Botrytis cinerea* (McLoughlin *et al.*, 2018; Niño-Sánchez *et al.*, 2022; Patel *et al.*, 2008), *Sclerotinia sclerotiorum* (Mukherjee *et al.*, 2024), *Rhizoctonia solani* (Wang *et al.*, 2016, 2024; Zhao *et al.*, 2021), *Aspergillus niger*, *Verticillium dahliae* (Qiao *et al.*, 2021), *Aspergillus fumigatus* (Kanhayuwa *et al.*, 2015), *Puccinia striiformis* f. sp. *tritici* (Zhu *et al.*, 2017), and *Fusarium oxysporum* and *F. asiaticum* (Mosa and Youssef, 2021; Song *et al.*, 2018). A significant technical advancement in dsRNA-based pest and pathogen management is the use of layered double hydroxide (LDH) clay particles as carriers for delivering biologically active dsRNA. The formulation, known as 'BioClay', enhances the stability and persistence of dsRNA on plant surfaces, thereby extending its protective efficacy against target pathogens. When applied as BioClay, dsRNA significantly prolonged protection against *B. cinerea*, extending the effective window from 1 to 3 week(s) on tomato leaves and from 5 to 10 days on tomato fruits compared with naked dsRNA (Niño-Sánchez *et al.*, 2022). The upcoming product from GreenLight Biosciences to control *Erysiphe necator* (powdery mildew) in grapevines would be a groundbreaking first dsRNA fungicide in the market (GreenLight Biosciences, 2026b).

***Viral and Bacterial Diseases* :** In India, several studies on dsRNA-based management of viral diseases have been reported, including up to 100% PRSV protection via dsRNA targeting CP and HC-Pro (Vadlamudi *et al.*, 2020). Though DNA viruses are less responsive, cocktail dsRNAs reduced ChiLCV incidence by ~66% (Singh *et al.*, 2022), and conserved-region dsRNAs reduced the infection of PaLCuV and ToLCPaLV (Priyanka *et al.*, 2025). Foliar application of dsRNA targeting *B. tabaci hsp70* significantly reduced ChiLCV copies in whiteflies and ceased ChiLCV spread to healthy plants (Chakraborty and Ghosh, 2022). Foliar application of dsRNA targeting the NSs gene of GBNV resulted in strong symptom suppression and 20-fold (cowpea) and 12.5-fold (*N. benthamiana*) reductions in viral RNA (Gupta *et al.*, 2021). Additionally, dsRNA targeting both NSs and NP genes confers superior resistance to GBNV (Manik *et al.*, 2025). Foliar application of dsRNA targeting key viral genes of MYMV significantly reduced symptom severity and viral accumulation in mungbean (Kamesh Krishnamoorthy *et al.*, 2023).

In case of bacterial pathogens, exogenous application of cationic poly-aspartic acid-derived polymer (CPP6)-*encapsulated dsRNA showed enhanced stability and conferred resistance against* Xanthomonas oryzae pv. oryzae (Pal *et al.*, 2024). CPP6 stabilizes dsRNAs during prolonged exposure at varied temperatures and pH, and protects against RNase A degradation. CPP6 enhances dsRNA uptake via roots or foliar spray and facilitates systemic movement, thereby inducing endogenous gene silencing.

Global studies support viral suppression ranging from 14 to 99% for tobamoviruses, potyviruses, and alfamoviruses (Tenllado and Díaz-Ruíz, 2001), including zucchini yellow mosaic virus (ZYMV) (Kaldis *et al.*, 2018). BioClay-formulated dsRNA against aphid-mediated transmission of a bean common mosaic virus (BCMV) conferred antiviral protection, reducing virus accumulation for ~20-30 days after a single spray (Worrall *et al.*, 2019). Exogenous application of virus-specific dsRNAs from DNA-A ORFs significantly reduced tomato leaf curl New Delhi (ToLCNDV) virus accumulation and symptom severity (Frascati *et al.*, 2024). dsRNA targeting cucumber green mottle mosaic virus (CGMMV) also reduced viral accumulation and symptom severity (Delgado-Martín *et al.*, 2022).

***Insect and Mite Pests* :** RNAi has been most effective in insects, especially Coleopterans, with improved results in Hemipterans and Lepidopterans due to better formulations. Topical application of dsRNAs targeting *B. tabaci* genes (*hsp70*, *fas2*) caused up to ~82 % and ~72 % adult mortality in whitefly, respectively (Chakraborty and Ghosh, 2022). Topical application of dsRNA targeting several other genes *(TLR3, TOB1*) in *B. tabaci* was also successful in suppressing the *B. tabaci* population by influencing fitness (Thesnim *et al.*, 2023). Sprayable dsRNA was found to be effective in suppressing *T. palmi* population (Rakesh *et al.*, 2024). Several other dsRNA constructs targeting essential genes in *B. tabaci* (Chakraborty and Ghosh, 2022; Kaur *et al.*, 2020; Srivastava *et al.*, 2025; Upadhyay *et al.*, 2011), *H. armigera* (Chikate *et al.*, 2016), and *T. absoluta* (Ramkumar *et al.*, 2021) have been reported to cause strong gene knockdown, increased mortality, and reduced fecundity, highlighting their potential as targets for dsRNA-based pesticides. ICAR–IARI has achieved a notable technological milestone with the development of a biopolymer-conjugated dsRNA bioformulation, RiboThrips. The formulation has demonstrated effective field-level control of thrips across multiple crops, supported by enhanced stability, systemic uptake, and shelf life. RiboThrips is the first dsRNA-based biopesticide licensed in India, and similar dsRNA bioformulations targeting other insect pests are currently under development. Globally, dsRNA products such as GreenLight's 'Calantha' for Colorado potato beetle (Rodrigues *et al.*, 2021; Welsh, 2024) and mite-control product 'Norroa' (Bortolin *et al.*, 2025; McGruddy *et al.*, 2024; GreenLight Biosciences, 2026c) highlight commercial viability.

***Nematodes* :** Delivery remains the primary barrier in targeting nematodes with dsRNA. Nevertheless, approaches such as root dipping, soil drenching with nanoclay-dsRNA complexes, and foliar-mediated uptake have shown promise against *Meloidogyne graminicola* and *Globodera pallida* (Bairwa *et al.*, 2024; Kumari *et al.*, 2017). The early findings indicate feasibility but require improved stabilization and targeted delivery strategies.

***Weeds* :** Globally, targeting photosynthesis genes (gene0004558, gene0004560, gene0026534, gene0025307, gene0029128) in *Mikania micrantha* caused plant death (Mai *et al.*, 2021), and in 2025, GreenLight Biosciences announced the first dsRNA herbicide for horseweed (GreenLight Biosciences, 2026d). In India, dsRNA-based weed control research remains conceptual, focusing on computational design of dsRNAs against parasitic and herbicide-resistant weeds, with experimental validation yet to begin.

***Key Indian Institutions and Ongoing Projects* :** India's RNAi research is led by ICAR-IARI, ICAR-CPRI, ICAR-Indian Institute of Horticultural Research (IIHR), alongside agricultural universities, with additional contributions from emerging biotechnology start-ups. Notable progress includes nanoclay-dsRNA trials for late blight in potato (Sundaresha *et al.*, 2022) at ICAR-CPRI, management of whitefly and ChiLCV by topical dsRNA (Chakraborty and Ghosh, 2022) and of thrips and tospoviruses by sprayable dsRNA (Rakesh *et al.*, 2024) at ICAR-IARI, and management of PPSMV by dsRNA application under field conditions at ICAR-IIHR (Patil *et al.*, 2021). Although most of the works remain at the pilot, greenhouse, or semi-field levels, some of them have demonstrated strong efficacy under real-field conditions. A major translational breakthrough is the proven field-scale performance of RiboThrips, developed by ICAR-IARI, which delivers reliable, broad-spectrum control of thrips across multiple crops under real agricultural conditions. The next critical phase will require multi-location field trials, biosafety evaluations, toxicity data generation and environmental persistence studies aligned with Organisation for Economic Co-operation and Development (OECD) RNAi risk assessment guidelines (OECD 2019, 2020, 2023), enabling eventual regulatory approval and field deployment in India.

Challenges and Bottlenecks

India faces a substantial gap between laboratory success and the field-level performance of dsRNA pesticides. Rapid degradation of naked dsRNA under UV radiation and RNase activity limits its persistence, underscoring the need for advanced carriers for practical use. Although nanomaterial and polymer-based formulations show promise, they require toxicological and non-target assessments before deployment. Regulatory ambiguity under the Insecticides Act (1968) and the Pesticide Management Bill (2020) further complicates field-level deployment. Despite these constraints, India is well-positioned to scale exogenous dsRNA pesticides through standardized guidelines aligned with OECD/EPA frameworks, national manufacturing capacity, and public-private partnerships.

Technical Challenges

***Stability, Environmental Persistence, and Shelf Life* :** Field instability remains one of the biggest technical hurdles for dsRNA. Naked dsRNA degrades rapidly, often within 24-48 h, due to UV, temperature, and RNase activity. However, formulation options such as nanoclay, liposomes, carbon dots, and biodegradable polymers improve stability and uptake. The shelf life of dsRNA products is another challenge that needs to be enhanced to facilitate commercial adoption and transportation.

***Delivery Systems and Uptake Efficiency* :** Uptake efficiency varies significantly across pest groups. Lepidopterans possess strong digestive nucleases, and sap-feeding insects (whiteflies, aphids, thrips) have cuticular and systemic barriers that limit dsRNA entry. Tailored delivery strategies that enhance gut stability, plant penetration, and systemic movement are essential.

***Field Efficacy and Standard Protocol* :** Although dsRNA performs well under laboratory and greenhouse conditions, field efficacy remains inconsistent. There is no standardized evaluation protocol for dsRNA pesticides. Multi-location trials in diverse agroclimatic regions and in different crops are needed to generate robust datasets on efficacy, persistence, dosage, and compatibility with IPM.

Economic and Scalability Constraints : The production cost to produce 1 g of dsRNA (100 to 800 bp) has declined markedly from 12,500 USD in 2008 to 100 USD in 2016, and to less than 60 USD by July 2018 (Guan *et al.,* 2021). More recently, the cost of *in vitro* production of dsRNA has been quoted as low as 0.50 USD/g (INR 45.08/g), with the application rate of 2-10 g/ha (Tardin-Coelho *et al.*, 2025). Global groups such as GreenLight Biosciences and RNAissance Ag have reduced the cost of dsRNA to approximately EUR 1/g (INR 105/g) through microbial fermentation and cell-free systems (GreenLight Biosciences, 2026a). India lacks comparable, industrially scalable platforms. Establishing domestic dsRNA biomanufacturing through plant protection products (PPPs) and BIRACsupported facilities will be essential for affordability.

Regulatory Challenges

India lacks a dedicated regulatory pathway for dsRNA-based pesticides. Current laws categorize pest control agents broadly, leaving the data requirements and safety assessment criteria for RNA-based products undefined. Emerging frameworks from the US EPA and the OECD emphasize exposure characterization, species specificity, and environmental fate rather than classical toxicology. Adoption of similar science-led guidelines in India would enable investment and adoption; until then, regulatory uncertainty remains a major bottleneck.

Public Acceptance and Risk Perception : Public understanding of exogenous dsRNA-based pesticides is limited, and the term "RNA" is often conflated with Genetically Modified Organisms (GMOs), which contributes to scepticism among farmers and policymakers. Clear communication, farmer field demonstrations, and capacity-building through *Krishi Vigyan Kendras* (KVKs) and state extension systems are crucial to building trust. Importantly, exogenously applied dsRNA does not alter the genetic composition of the target organism; its effects are transient and operate through a naturally occurring RNAi mechanism for pest management. Positioning dsRNA within familiar categories such as biopesticides or green chemistry solutions can further support social and regulatory acceptance.

Recent Advancements

Global progress in dsRNA biopesticides has accelerated, with sprayable or microbially produced platforms entering early field trials. Companies such as RNAissance Ag, GreenLight Biosciences, Bayer Crop Sciences and RNAgri have advanced industrial fermentation and microbial encapsulation systems for dsRNA synthesis and formulation. Delivery mechanisms, including microbial expression, nanoparticle or clay encapsulation, liposomes, and plastid-based production, are being refined. However, market entry is slowed by production costs, stability issues, and a lack of regulations. Approved products such as 'Calantha' and 'Norroa' of GreenLight Biosciences (GreenLight Biosciences, 2026e) indicate that regulatory pathways are maturing internationally, and recent patent activity signals a competitive innovation space relevant for India.

Novel Formulations and Delivery Technologies : Recent advances emphasize protecting dsRNA from UV/RNase degradation and improving uptake in insects and plants. A wide array of nanocarriers, including LDH clays, chitosan nanoparticles, carbon dots, MOFs, liposomes, and biodegradable polymers, shows improved persistence, controlled release, leaf adhesion, and intracellular uptake (Das *et al.*, 2015). Smart or responsive carriers capable of releasing dsRNA upon pathogen/pest cues, and co-delivery systems combining dsRNA with adjuvants or low-dose chemicals, are emerging to overcome species-specific RNAi barriers. MOF-based carriers in particular show enhanced delivery and potential synergy with existing actives (Gao *et al.*, 2025). Practical improvements in spray techniques and UV-shielding matrices, such as nanoclay films and polymers, have led to more consistent greenhouse and small-field performance, as supported by recent synthesis reviews (Chen *et al.*, 2025; Fletcher *et al.*, 2020).

***Patents and Intellectual Property Landscape* :** The IP environment for dsRNA-based pest management has become increasingly active, with major companies such as GreenLight Biosciences securing broad claims on dsRNA compositions, formulations, and delivery systems (GreenLight Biosciences, 2026f). Patent databases show multiple families focusing on arthropod control, stability enhancement, and scalable production (Bortolin *et al.*, 2025; Stokstad, 2024). For start-ups and academic groups, freedom-to-operate assessments are now essential due to potentially broad formulation and process claims. Key concern areas include sequence-specific patents (typically narrow), delivery/formulation technologies (often broad), and production-platform patents such as microbial expression or cell-free enzymatic systems (Puralewski *et al.*, 2024). There are approximately 65 patents on topical RNAi, of which the top 10 players own 47%. Additionally, 1321 patents refer to dsRNA nanoformulations for agriculture, of which 26% are owned by the top 10 players (Basso *et al.* 2025). Indian institutions aiming for commercialization will need careful IP mapping or strategic licensing. The first IP filed in India (202511073344) for the management of thrips using biopolymer-conjugated dsRNA pesticides by ICAR-IARI. Several other dsRNA synthesis and formulation platforms are in the pipeline for IP and strategic licensing.

***Recent Scientific Publications and International Progress* :** Recent reviews (Chen *et al.*, 2025) highlight that the principal bottleneck in SIGS is no longer the RNAi mechanism but formulation and delivery, with well-formulated dsRNA achieving reliable control across several pest-crop systems. Field trials report strong control of major pests such as Colorado potato beetle and corn rootworm, demonstrating that dsRNA products can perform comparably to conventional pesticides when supported by robust carriers (Bortolin *et al.*, 2025; Head *et al.*, 2017; Khajuria *et al.*, 2018). New mechanistic research confirms improved environmental stability and enhanced knockdown using LDH and other nanocarriers, while MOF-based delivery shows promise for overcoming species-specific RNAi resistance (Gao *et al.*, 2025). Commercial advancements of other dsRNA-based products (Lee, 2025; Mai *et al.*, 2021; OECD, 2019; Sponsler *et al.*, 2019), such as dsRNA herbicides, are expected to shape global standards for cost, formulation, and regulatory requirements.

Policy and Regulatory Landscape for India

***Overview of dsRNA Regulation in Other Countries* :** Globally, regulatory treatment of exogenous dsRNA-based biopesticides is rapidly evolving but remains anchored within existing pesticide frameworks rather than GMO legislation. The United States regulates externally applied dsRNA under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), classifying them as biochemical pesticides because they act through a naturally occurring, non-toxic mechanism and do not alter genomes. US EPA reviews for products such as Calantha have established practical requirements for molecular characterization, environmental fate, non-target safety, and bioinformatics-based off-target analysis (Dietz-Pfeilstetter *et al.*, 2021; Rodrigues *et al.*, 2021; Stokstad, 2024). Australia's APVMA similarly regulates dsRNA within the Agricultural and Veterinary Chemicals Code Act 1994 (APVMA, 2020, 2022), treating them as agricultural chemical products, while the OGTR (OGTR, 2020) excludes spray-induced gene silencing products from GMO regulation, provided they contain no genetically modified organisms.

In the European Union, purified externally applied dsRNA is regulated under Regulation (EC) No. 1107/2009 for PPPs, not under GMO directives, unless the dsRNA originates from or contains living genetically modified organisms (EPA, 2013, 2023). European Food Safety Authority (EFSA) continues to refine dsRNA-specific guidance, emphasizing exposure characterization and environmental fate (Dietz-Pfeilstetter *et al.*, 2021; EFSA, 2023a; Fletcher *et al.*, 2020). Canada's Pest Management Regulatory Agency (PMRA, 2021) evaluates dsRNA on a case-by-case basis under the Pest Control Products Act (2002), with attention to bioinformatics, persistence, and non-target effects. China's Institute for the Control of Agrochemicals (ICAMA) under the Ministry of Agriculture and Rural Affairs treats dsRNA under the conventional pesticide rules in the Pesticide Management Regulations as per the Amendment in 2017. This approach allows ICAMA to manage novel RNAi-based pesticides within the established framework. Brazil regulates dsRNA through its multi-agency agrochemical framework under Law No. 7802/1989 and Decree No. 4074/2002 (Tardin-Coelho *et al.*, 2025). New Zealand remains the most permissive, as its Environmental Protection Authority ruled in 2018 that externally applied dsRNA is not a new organism under the Hazardous Substances and New Organisms Act (1996) and therefore does not trigger GMO controls (New Zealand EPA, 2018).

The current regulation of dsRNA reflects its broad regulation under pesticide regulations across different countries, rather than under a GMO perspective. Nevertheless, OECD (2019) and EFSA (2023a,b) have proposed internationally harmonized principles for dsRNA risk assessment, including problem formulation, tiered testing, species-specificity evaluation, and environmental safety considerations.

***Lessons From Global Practices and Implications for India* :** Global regulatory experience demonstrates three core principles relevant to India. First, clear classification is essential for the use of exogenous dsRNA in agriculture. Most countries define externally applied dsRNA as a biochemical or agricultural chemical pesticide rather than a GMO, aligning oversight with pesticide authorities rather than with genetic engineering regulators. The exogenous dsRNA is non-living, transient, non-heritable, and environmentally degradable, and therefore fundamentally different from transgenic RNAi crops. Second, comprehensive risk assessment frameworks are necessary that focus on environmental fate, non-target effects, and off-target gene homology. International status emphasize that exogenous dsRNA-based products require tailored evaluation rather than relying solely on chemical pesticide toxicology (De Schutter *et al.*, 2022; Tardin-Coelho *et al.*, 2025). Third, public perception matters; countries with transparent communication strategies and early stakeholder engagement have experienced smoother regulatory acceptance. For India, the lessons underscore the importance of public clarity on biosafety, transparent communication, and alignment with OECD principles to foster confidence among regulators, farmers, and industry stakeholders.

***Proposed Regulatory Pipeline for India Under the Biopesticide Framework*:** India currently lacks a dedicated regulatory pathway for dsRNA-based pesticides. The exogenous dsRNA-based products can be most appropriately classified as biological biopesticides under the Insecticides Act, 1968, and regulated by the Central Insecticides Board and Registration Committee (CIBRC). External dsRNA-based products act through a naturally occurring, non-transgenic mechanism and do not alter genomes. Their classification as non-GMO aligns with international regulatory practice and India's own legal framework, which states that externally applied dsRNA is not covered under the "Rules, 1989" for genetically engineered organisms, since it is a non-transformative, non-living molecule that does not alter genomes (MoEFCC, 1989). Regulatory control should remain with CIBRC rather than the RCGM/DBT system, as in the US EPA biochemical pesticide pathway.

The regulatory pipeline for India should include pre-screening of dsRNA target specificity, characterization of formulation components, environmental fate testing, and tiered non-target assessments. These steps align with the OECD guidelines for RNAi risk assessment. India is a key partner of the OECD, collaborating on various initiatives, including chemical safety, where Indian labs conduct pesticide testing in accordance with OECD guidelines, enabling global regulatory acceptance through the OECD Mutual Acceptance of Data (MAD) system. India's National Good Laboratory Practice (GLP) programme aligns with OECD principles, supporting data quality for pesticide registration in other countries. Establishing a regulatory pipeline for dsRNA pesticides that explicitly follows OECD standards would significantly accelerate global market access, reduce duplicative testing, and strengthen regulatory confidence. Such alignment would position India as a global leader in dsRNA-based pesticide development, testing, and commercialization, supporting both domestic innovation and international deployment of next-generation, sustainable crop protection technologies.

However, any nano-based dsRNA product should incorporate India's 2020 DBT Guidelines for Nano-Based Agri-Input Products. The nano-carrier-based products should undergo detailed physico-chemical characterization, stability analysis, excipient disclosure, toxicology testing, and environmental impact assessment, ensuring that nano-enabled dsRNA formulations meet internationally accepted safety criteria for nanomaterials. Establishing such a unified, dsRNA-compatible biopesticide pipeline will provide predictable regulatory expectations for innovators while protecting ecological and human health.

Proposed Registration Procedures and Suggested Standard Data Requirements in India: Standard registration of exogenous dsRNA-based biopesticides in India should follow a tiered, risk-based approach modelled on US EPA biochemical pesticide guidelines and EFSA and OECD RNAi frameworks. Applicants should submit data on molecular identity, dsRNA sequence specificity, bioinformatics analysis for potential off-target effects, and stability in soil, water, and sunlight. Environmental fate studies should evaluate degradation kinetics, movement through soil and water systems, and interactions with microbial communities. Non-target risk assessments must include pollinators, aquatic organisms, natural enemies, beneficial arthropods, and soil organisms, reflecting the ecological significance of these taxa in Indian agroecosystems. Acute and chronic toxicity testing should be reduced relative to chemical pesticides due to the faster biodegradability of dsRNA. However, formulation components containing nanocarriers must meet the country's nano-safety requirements and OECD test guidelines.

Multilocational field performance data, including dose-response studies, persistence under Indian agro-climatic conditions, and compatibility with IPM programs, should be mandatory. India can adapt EPA and EFSA criteria to define data expectations for product chemistry, mode of action, target gene validation, and resistance management. A streamlined dossier structure is likely to accelerate approvals while ensuring biosafety. Public-private partnerships, particularly involving ICAR institutes, can support multi-location field trials that generate the necessary registration data.

Future Research Directions

***Target Identification and Validation*:** Future research must prioritize systematic identification and functional validation of essential genes in India-specific pests and pathogens. The future research includes high-throughput screening, RNAi sensitivity assays, and confirmation of off-target safety to ensure that selected dsRNA sequences deliver robust, species-specific knockdown. Strengthening genomic resources for major Indian insects, fungal pathogens, nematodes, and weeds will be crucial for building a reliable pipeline of validated RNAi targets.

***Developing Crop-Specific Formulations*:** Developing crop-tailored formulations that withstand India's diverse agro-climatic conditions, especially monsoonal rainfall, high UV exposure, and variable soil chemistry, would be a critical research priority. The formulation should be suited to different crop canopies, leaf surfaces, and pest feeding behaviours covering horticultural, pulse, fibre, and vegetable crops.

Long-term Ecological Impact Studies : A comprehensive environmental assessment is needed to reassure regulators, farmers, and the public. Long-term field studies should examine dsRNA persistence in soil and water, degradation pathways, impacts on beneficial insects, soil microbiomes, and biodiversity.

Applying OECD-aligned risk assessment frameworks will help demonstrate environmental safety and support regulatory approval of dsRNA-based biopesticides in India.

Optimization of Cost-effective Production and Delivery Systems **:** A major future direction is the development of low-cost, scalable dsRNA production platforms such as microbial fermentation, cell-free enzymatic systems, and bioreactor-based processes. Parallel efforts must refine delivery systems to improve stability and reduce application costs.

Conclusion

Topical dsRNA-based biopesticides represent a promising new class of precise, eco-friendly crop protection tools that act through the natural RNAi pathway without modifying plant or pest genomes. Their transient, non-heritable mode of action, high target specificity, and rapid biodegradability position them as suitable candidates for regulation under India's biopesticide category of the Insecticides Act, 1968. The proposed framework would be consistent with international guidelines from OECD (2019), EFSA (2023), the US EPA, and the Australian OGTR (OGTR, 2013, 2018, 2020), all of which treat topically applied dsRNA as non-GMO, low-risk technologies. Global progress, including GreenLight Biosciences' Calantha, validated through extensive field trials across North America and Europe and now registered in more than 30 US states and pipeline products, underscores that commercialization is feasible when supported by clear regulatory pathways and coherent science-policy frameworks.

In India, the first patent for an exogenous dsRNA-based bioformulation has been filed by ICAR-IARI and licensed to ATGC Biotech Pvt. Ltd. Several other products are in the pipeline in Indian research labs. The challenge lies not in scientific capacity but in establishing regulatory clarity, enhancing field validation, and ensuring cost-effective production. Regulatory guidelines for exogenous dsRNA-based products should be issued to classify them as biological biopesticides under the Insecticides Act, 1968, and to regulate them by the CIBRC, aligned with OECD and EPA standards. Equally important are scalable, low-cost dsRNA manufacturing platforms and microbial or cell-free production systems, which will be pivotal to making the technology accessible to smallholder farmers.

The next few years are critical. Accelerated pilot trials, early regulator engagement, targeted IP strategies, and public-private partnerships will determine how quickly India can move from research to deployment. With sustained policy support, transparent communication, and strategic investment, India is well-positioned to become a global leader in dsRNA biopesticide innovation, reducing dependence on chemical pesticides, strengthening environmental stewardship, and advancing a resilient, sustainable agricultural future.

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