# Novel Insecticide Molecules: Understanding the Structure and Mode of Action

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## ABSTRACT

In the realm of agriculture, the management of pest populations presents an ongoing challenge critical to ensuring global food security. While cultural, biological and mechanical methods offer alternative approaches to pest control, the immediate effectiveness of insecticides makes them indispensable to farmers facing the relentless onslaught of crop-damaging pests. This reliance on insecticides, particularly traditional ones like organophosphates, has led to widespread issues such as the development of insect resistance. However, recent years have witnessed a paradigm shift towards the adoption of novel insecticides with distinct modes of action, addressing both resistance and environmental concerns. By leveraging the unique properties of these compounds, agricultural stakeholders can pave the way for sustainable global food production while mitigating the detrimental impacts of insecticide resistance. This article aims to explore the potential of novel insecticides in enhancing pest control strategies and ensuring the long-term sustainability of agriculture.

## INTRODUCTION

Throughout the annals of agricultural history, humanity has grappled with the relentless challenge of pests and diseases threatening the sustainability of our food supply. Dating back over millennia, the earliest recorded attempts at pest control can be traced to the Sumerians approximately 4,500 to 5,000 years ago, who ingeniously utilized sulphur compounds to combat insects and mites. This pioneering endeavour marked the inception of humankind's enduring quest to protect crops from destructive pests, laying the groundwork for the evolution of pest management practices. Following World War II, the introduction of organic chemistry to the field of pesticide science opened new frontiers in agricultural pest management. This pivotal moment heralded the advent of industrial pesticide science, paving the way for significant advancements in combating agricultural pests.

Throughout the history of insecticide development, trends have shifted from the widespread use of organophosphates, carbamates and synthetic pyrethroids to the emergence of nicotinic
and diamide insecticides. However, in recent years, attention has turned towards compounds with novel modes of action, diverging from traditional classifications. These novel insecticides hold promise in addressing the challenge of insecticide resistance and reducing environmental impact.

The emergence of insecticide-resistant pests poses a formidable challenge to agriculture worldwide. Consequently, the continual development of insecticides with unique modes of action remains crucial for maintaining effective pest control strategies. By understanding the structure (Fig.1) and mode of action of these novel insecticides, we can unlock their potential to revolutionize pest management practices and ensure the sustainability of global food production.

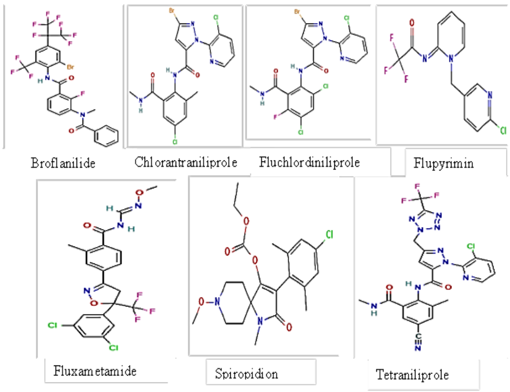


**Fig. 1: Molecular structures of different novel insecticides (PubChem)**

### Insecticides and their mode of action

#### 1. Broflanilide

Broflanilide is available as Cimegra® insecticide, Davantor® insecticide and Exponus® insecticide. Mitsui Chemicals Agro Industries, features a distinctive chemical composition identified as a meta-diamide, demonstrating significant efficacy against a wide range of pests, develop it. Due to its novel mechanism of action, the Insecticide Resistance Action Committee (IRAC) has classified broflanilide into a new group known as Group 30. Available in India under formulations, broflanilide 20 % SC, broflanilide 300 % SC (CIB&RC, 2023).

Due to its novel mode of action, broflanilide is anticipated to demonstrate significant effectiveness against caterpillars, beetles and thrips, including those that have developed resistance to diamide and other types of insecticides. In home, it controls pests such as ants, flies, termites and cockroaches. Broflanilide once applied on insects, prevents Gamma-aminobutyric acid (GABA) from transmitting inhibitor signals, which causes over excitations of the nervous system and leads to incapacitation of the insect. It does this binding to a novel insecticide site in GABA receptor site and locks it close. Its powerful mode of action protects most important crops and homes worldwide. Application methods include seed treatment and foliar spray.

**2. Chlorantraniliprole**

Chlorantraniliprole, marketed as Coragen® by DuPont company worldwide. It is a novel insecticide categorized under the anthranilic diamide class of compounds, is designed to manage Lepidopteran, Coleopteran and certain Dipteran pests in commercial agriculture, targeting both perennial and annual crops. In India it is available in different formulations such as chlorantraniliprole 18.50 % SC, chlorantraniliprole 00.40 % GR, chlorantraniliprole 35 % WG, chlorantraniliprole 50% W/w FS.

This product is applicable for both field, protected crops and approved for use in certain non-agricultural contexts, particularly in turf and ornamental plants in select regions. It functions as a residual insecticide, targeting larvae and certain adult insects through ingestion and contact. Among these entry routes, ingestion proves to be the most efficient, often necessitating a lower dosage for effective response. These insecticides stimulate ryanodine receptors, which are calcium-activated channels within muscle cell sarcoplasmic reticulum. These receptors enhance a minor calcium signal, triggering a significant release of calcium from cellular reserves necessary for muscle contraction. Direct activation of these receptors by the insecticides induces persistent muscle contractions, resulting in swift cessation of feeding, regurgitation, lethargy and muscle tetany. It has been categorized by IRAC as a group 28 insecticide.

**3. Fluchlordiniliprole**

Fluchlordiniliprole, a proprietary amide/pyridylpyrazole compound developed autonomously by Hailir Pesticides and Chemicals, features an anthranilic diamide structure. In June 2021, it was assigned an ISO generic name – fluchlordiniliprole, with the CAS number 2129147-03-9 and the molecular formula $C_{17}H_{10}BrCl_3FN_5O_2$. This compound operates through a unique mechanism of action, displaying heightened insecticidal efficacy while avoiding resistance from conventional insecticides. Notably environmentally friendly and low in toxicity to mammals, it holds promising prospects in the market. It marks the Hailir Group's inaugural independently developed insecticide, with its formulation series slated for release in 2022. This introduction presents a fresh solution for managing resistant Lepidoptera pests.

**4. Flupyrimin**

Meiji Seika Pharma has unveiled a ground-breaking insecticide known as flupyrimin. Flupyrimin 10 % SC is available as Viola. This discovery boasts essential biological attributes, displaying remarkable insecticidal effectiveness against resistant rice pests while also demonstrating enhanced safety towards beneficial organisms, including pollinators. The mode of action for flupyrimin involves acting as a competitive modulator of nicotinic acetylcholine receptors. It competes with acetylcholine for binding sites on insect nicotinic acetylcholine receptors, disrupting nerve signalling and causing paralysis, ultimately leading to the insect's death. It has been categorized by IRAC as a group 4 insecticide.

**5. Fluxametamide**

Fluxametamide, marketed as Gracia® by Nissan Chemical, is an isoxazoline compound registered in Japan since January 2019. Its mode of action targets the GABA (γ-aminobutyric acid) chloride channels, acting as an inhibitor. This mechanism effectively controls a wide range of pests including Lepidoptera, Thysanoptera, Diptera, Acari, Coleoptera and some Hemiptera, while showing minimal impact on bee-visiting insects.

The systemic absorption of isoxazolines enhances their effectiveness, leading to the selective inhibition of GABA- and glutamate-gated chloride channels in targeted pests. This inhibition results in hyperexcitation and eventual death of the pests. Importantly, the low sensitivity of GABA channels in mammals to isoxazolines, combined with the absence of anion-inhibitory glutamate channels in mammals, contributes to its low toxicity potential in mammals. Shinwa, a technical formulation containing 10% w/w of fluxametamide in an emulsifiable concentrate (EC) form, demonstrates effective control over lepidopteran pests and thrips across a wide range of crops. It is classified under IRAC group 30.

### 6. Spiropidion

Spiropidion (SYN546330) marketed as ELESTAL® Neo is an insecticide developed by Syngenta, belonging to the tetramic acid chemical class. While Bayer leads in the Keto-enol class with products like spirotetramat and spiromesifen, spiropidion stands out for its unique mode of action. Targeting a wide range of pests including aphids, whiteflies, psyllids, scales, and various mites, spiropidion offers effective control across crops such as apples, grapes, oranges, tomatoes, beans, cotton and potatoes.

Its mode of action involves, disrupting fatty acid biosynthesis and biomembrane formation, affecting both immature stages and adult fecundity. Featuring contact and two-way translaminar activity, spiropidion protects new growth against re-infestation and roots against pest damage. One notable aspect is its pro-insecticidal nature, remaining inactive until within the host organism. This characteristic enhances efficacy while minimizing environmental impact. Overall, spiropidion presents a promising solution for pest management in diverse agricultural settings. It has been categorized by IRAC as a group 23 insecticide.

### 7. Tetraniliprole

Tetraniliprole will be the first registered diamide insecticide offering control corn rootworm larvae in corn through soil application and control of flea beetles in corn and potatoes. It would also be the first diamide offering control of wireworms in potatoes and similar crops and control of cutworms in tobacco via soil application. The purified active ingredient is a solid powder with an acetous odour, while the technical material is light yellow powder with no specific odour. Tetraniliprole is neither flammable, explosive, nor oxidising.

Tetraniliprole belongs to the anthranilamide class of insecticides and is classified as a diamide chemical. Its mode of action primarily involves ingestion, as it disrupts ryanodine-sensitive calcium release channels in insects. This interference results in the loss of muscle control and subsequent immobility of the insects. Tetraniliprole has been categorized by IRAC as a group 28 insecticide.

## CONCLUSION

The diversity of insecticides discussed herein showcases a spectrum of innovative solutions aimed at addressing the challenges posed by pest management in agriculture. From broflanilide with its novel meta-diamide composition to chlorantraniliprole anthranilic diamide structure, each compound offers unique mechanisms of action targeting a wide range of pests. Similarly, the introduction of fluchlordiniliprole, flupyrimin, fluxametamide, spiropidion and tetraniliprole presents promising advancements in pest control, reflecting a concerted effort towards sustainability and efficacy. These insecticides not only combat resistance but also demonstrate improved safety profiles and environmental compatibility, aligning with the goals of modern agricultural practices. Overall, the development and utilization of these novel insecticides signify a crucial step forward in ensuring the long-term sustainability and productivity of global agriculture. However, continued research and vigilance are essential to monitor their effectiveness, environmental impact and any potential emergence of resistance, thereby maintaining the efficacy and integrity of pest management strategies in the face of evolving challenges.

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