The Pharma Innovation Journal 2022; 11(4): 558-570

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2022; 11(4): 558-570
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www.thepharmajournal.com
Received: 20-01-2022
Accepted: 31-03-2022

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Novel insecticides and their prospects in integrated pest management

Naveen Rao and khushkaran Singh

Abstract
At present, the main tool for controlling insect pests are broad-spectrum neurotoxic insecticides. These chemicals have a number of serious drawbacks including their toxicity to mammals including humans and non-target organisms as well as their persistence in the environment. Another major problem associated with their utilization is the possible development by the insects of genetically-based resistance to insecticides which may lead to unexpected control failures. Therefore, the development of novel biorational, specific and non-toxic approaches to pest control is highly desirable. The term biorational is derived from two words, biological and rational, referring to pesticides of natural origin that have limited or no adverse effects on the environment or beneficial organisms. Biorationals also called as selective pesticides or reduced risk pesticides or green chemistry pesticides.

Keywords: Insect Pests, IPM, Biorational, Insecticides, Non target effects and IGRs

Introduction
Pesticide is any substance or mixture of substances intended for preventing, destroying, controlling, attracting or repelling any pest, including unwanted species of plants or animals, causing harm during or otherwise interfering with the production, processing, storage, transport or marketing of food, agricultural commodities or substances that may be administered to animals for the control of ectoparasites or endoparasites. Pesticides have become an integral part of our modern agriculture and play an essential role in increasing crop production by reducing the incidence of pest attacks. However, this term excludes the use of plant and animal nutrients, animal drugs, food additives, and fertilizers [1].

Insecticides and pest management
To protect our crops from losses due to insect pests and increase farmers' benefits, insecticides are being used. Insecticides have been in use since the early period. Chinese people use wood ash, powder of chalk to control insect pests. Even in India, neem leaves were used. Evidence of insecticides was in use as early as 200 B. C. During this period, the compound used was Bitumen/Coal tar or asphalt. These compounds were used to control pests of the grapevine. In 1000 BC sulphur was used for fumigation purposes. Then in 40-90 A.D. toxic nature of arsenic compound was known. In 900 A.D., arsenic compound came into use to control garden pests. Arsenic sulphide was used for this purpose. In 1669, arsenic compounds were used for controlling pests of honey hives. Then in 1800, natural insecticides or compounds were discovered. Pyrethrum was early found, extracted from roots of chrysanthemum. In 1867, the Parris Green compound was used to control the Colorado potato beetle in U.S. In 1874, DDT was discovered, and in 1939, its insecticidal properties were discovered by Paul H. Muller. Then came the era of synthetic organic pesticides. Then, organophosphates, carbamates, and synthetic pyrethroids were discovered and were used on a large scale for insect pest management.

Need for new chemistry
During the twentieth century, significant progress in synthesizing synthetic organic chemicals has resulted in the synthesis of effective insecticides such as organochlorines, organophosphates, carbamates, and pyrethroids. Unfortunately, many of these chemicals are harmful to man and beneficial organisms and have led to the problems of resistance, resurgence, and secondary pest outbreak in insect pests [2]. The usage of endosulfan, acephate, chlorpyriphos, profenophos, quinalphos, and synthetic pyrethroids such as deltamethrin, fenvalerate, cypermethrin etc. will continue for the management of insect pests.

However, monocrotophos may be limited because of the resurgence of whitefly and less degree of bollworm control (Table 1). New molecules such as acetamiprid, imidacloprid, indoxacarb, spinosad etc., are likely to be the future crop protection chemicals in the country [3]. The introduction of new chemistry played a significant role in managing key insect pests.

Table 1: Limitations of Conventional insecticides

Insecticide Group	Limitations
Organochlorines	Highly persistent, residual problem, toxicity to humans
Organophosphates	Resistance, resurgence and toxic to N.E.
Carbamates	Toxicity to N.E.
Synthetic Pyrethroids	Resistance, resurgence and secondary pest outbreak

New Chemistries

A number of newer insecticides with a unique mode of action have been registered during the late 1990s and early 2000s [2]. These insecticides play an essential role in the IPM of many insect pests with good bio-efficacy, high selectivity, and low mammalian toxicity, making them attractive replacements for organochlorines and organophosphates carbamates and pyrethroid insecticides [4].

1) Neonicotinoids

Neonicotinoids are synthetic analogs of nicotine. These are the most widely used insecticides worldwide. These act on the central nervous system of insects and have low mammalian toxicity. Neonicotinoids have been classified into three classes based on their structure as:

a) Chloronicotinyls
b) Thianicotinyls
c) Furanicotinyls

a) Chloronicotinyls: These are first generation neonicotinoids and belong to insecticidal class II. These insecticides are:

Imidacloprid: IUPAC: [1-(6-chloro-3-pyridylmethyl)-2-nitroimidazolidin] -1- [(6-chloro-3-pyridinyl)methyl]-N-nitro-2-imidazolidinimine Imidacloprid was the first insecticide of this class introduced by Bayer Crop Sciences in 1991. It is possibly the most widely used insecticide in the worldwide market. It is now applied against soil, seed, timber, animal pests, and foliar treatments for crops, including cereals, cotton, grain, legumes, potatoes, pome fruits, rice, turf, and vegetables. It is systemic and effective against sucking insects and has prolonged residual activity. The application rates for neonicotinoid insecticides are much lower than older, traditionally used insecticides. It is a systemic, polar molecule and transports well through the xylem. It is used for seed treatment also. Imidacloprid is registered in approximately 120 countries and is used on over 140 different crops [5].

Formulations: 17.8% SL (Confidor®), 70% WS (Gaucho®)

Acetamiprid: IUPAC: ((E)-N1-[(6-chloro-3-pyridyl) methyl]-N2-cyano-N1-methylacetamidine) Acetamiprid was introduced by M/s Nippon Soda Co. Ltd. in 1995 for soil and foliar applications. In particular, acetamiprid shows excellent activity against aphids, whitefly, and thrips. Due to its unique acting mechanism, high efficacy, relatively low toxicity, no evidence of carcinogenicity, neurotoxicity, mutagenicity, or endocrine disruption, acetamiprid is being more competitive and has been considered as a favorable alternative to the organophosphate insecticides, which have caused severe environmental pollution and been banned in many countries. Acetamiprid degrades rapidly and poses low environmental risks [6].

The persistence of acetamiprid in alluvial soil was studied at two concentration levels, 1 and 10 ppm, and under three moisture regimes, i.e., dry, field capacity, and submerged. Among the field capacity and submerged moisture regimes, acetamiprid persisted longer under the submerged conditions. The half-life values varied from 15.7-17.4 days under field capacity and 19.2-29.8 days under submerged conditions. Under air-dry conditions, the longer persistence and slower dissipation could be attributed to the low microbial activity in dry soil [7].

Formulations: 20% S.P. (Pride®)

Thiacloprid: IUPAC: [(Z)-3-(6-chloro-3-pyridylmethyl)-1,3-thiazolidin-2-ylidene cyanamide] Thiacloprid is a neonicotinoid insecticide with systemic properties. It was introduced by Bayer Crop Sciences in 2000 and was recently introduced into India for foliar application and broad-spectrum efficacy against sucking and biting insects [8]. It has activity against sucking insects such as aphids, whiteflies, and some jassids. It is also active against weevils, leafminers, and *Cydia pomonella* in apple and various species of beetles good plant compatibility in all the relevant crops [9]. Based on its high insecticidal activity with a favorable ecological profile and safety to bees, it is particularly useful in horticulture and modern crop protection systems. This compound is safe for the egg parasitoid *Trichogramma cocoeciae* Marchal [10] bees and important beneficial organisms and showed no phytotoxicity to any of the crops tested even at high concentrations [9].

Formulations: 480 SC (Calypso®)

Nitenpyram: IUPAC: (E)-N-(6-chloro-3-pyridylmethyl)-N-ethyl-N'-methyl-2-nitrovinylidenediamine. Nitenpyram is a neonicotinoid insecticide introduced by Takeda Chemical Industries Ltd. in 1995. Nitenpyram is an insecticide used in agriculture and veterinary medicine to kill external parasites of livestock and pets. It is a neonicotinoid, a neurotoxin that blocks neural messages in the central nervous system of insects, causing rapid death. Nitenpyram does not kill insect eggs and has no long-term activity. Thus, it is not effective as a long-term flea preventative. It is usually used to quickly kill nymph and adult fleas on an infested animal, combined with a longer-term flea preventative like fipronil or lufenuron to prevent reinfestation.

Formulations: 95% TC (Bestguard®)

b) Thianicotinyls: These are second generation neonicotinoids. These are N-nitroguanidines.this group includes-

Thiamethoxam: IUPAC: [(EZ)-3-(2-chloro-1,3-thiazol-5-ylmethyl)-5-methyl-1,3,5-oxadizine-4-ylidene (nitro) amine]

Thiamethoxam is a novel neonicotinoid belonging to the sub-class of thianicotinyl compounds, and it has a unique structure and outstanding insecticidal activity introduced by Novartis in 1998. The 4-nitroimino-1,3,5-oxadiazinan attached to the halogenated thianicotinyl moiety in thiamethoxam exhibits high insecticidal activity. It is a systemic insecticide for soil and foliar applications and controls various pests. It has high water solubility (4.1 g L^{-1} at 25 ^{0}C), low octanol-water partitioning coefficient (0.74), and low vapor pressure (4.95 X 10^{-11} mmHg at 25 ^{0}C).

Thiamethoxam is presently one of the most effective chemicals to control sucking pests such as aphids, whiteflies, thrips, some micro Lepidoptera, and many coleopteran species. It was also reported to have termiticidal properties [10] and antifeedant action [11]. The compound shows contact and systemic activity and is recommended for soil, foliar, and seed treatments in most agricultural crops worldwide. It has slightly acute toxicity (LD_{50} value is 1530 mg kg^{-1} to rats) and is classified by the EPA as toxicity category III in acute oral and dermal studies. Low use rates, flexible application methods, excellent efficacy, long-lasting residual activity, and favorable safety profile make this new insecticide well-suited program in many cropping systems [12].

Formulations: 25%WG (Actara®), 30% FS (Cruiser®), 70% WS (Slayer®)

Clothianidin: IUPAC: [(E)-1-(2-chloro-1,3-thiazol-5-ymethyl)-3-methyl-2-nitroguanidine] Clothianidin is a novel, highly effective systemic and contact insecticide exhibiting low mammalian toxicity [13]. Clothianidin was introduced by Takeda Chemical Industries and Bayer Crop Science jointly in 2002. It is active on hemipteran pest species, such as aphids, leafhoppers, planthoppers, many coleopterans, and some lepidopteran pest species with a low application rate and has been commercialized to control these pests [14]. Clothianidin can be used for various application techniques, including foliar, seed treatment, soil drench, and soil application due to its physicochemical and excellent root systemic properties.

Formulations: 50% W.G. (Dantop®), 600 FS (Poncho®)

(c) Furanicotinyls: It is a third-generation neonicotinoid and includes a single insecticide belonging to insecticidal class U.

Dinotefuran: IUPAC: [(EZ)-(RS)-1-methyl-2-nitro-3-(tetrahydro-3-furylmethyl) Guanidine] Dinotefuran is a new neonicotinoid developed by Mitsui chemicals and first registered in Japan in 2002 under the trade name of Starkle® and Albarin®. It has a distinct tetrahydro-3-furyl methyl group instead of the aromatic heterocyclic ring previously considered indispensable for insecticidal activity of neonicotinoids. Dinotefuran was discovered by research using acetylcholine as the lead compound through a 3-methoxy propyl compound and its cyclization. It has excellent insecticidal properties and offers excellent control of various pests in many kinds of crops [15]. It is used to control sucking and chewing insects infesting leafy vegetables.

Furthermore, it has very low phytotoxicity to be utilized for many kinds of crops. Its oral LD_{50} in rats is 2000-2804 mg kg^{-1}. Dinotefuran is water-soluble and has excellent systemic and translaminar action in many plants. This property enables dinotefuran to be applied using various methods and various formulations.

Formulations: 20% SG - Starkle®, Safari®

Mode of action: The mode of action of neonicotinoids is similar to the natural insecticide nicotine, which acts on the central nervous system. Neonicotinoids interact with post synaptic nicotinic acetylcholine receptors at the central and peripheral nervous system, resulting in excitation and paralysis, followed by death. These compounds interact with nAChR in a structure-activity relationship resulting in excitation and paralysis followed by death. Their selectivity results from a higher affinity to the insect nAChR than vertebrates compared to the original nicotine [16, 17]. Hence, it has been suggested that these new compound ds are called neonicotinoids [18, 19].

The binding assay using insect nAChRs and the electrophysiological study showed that dinotefuran acted on nAChRs ass an agonist. However, in the binding study, the affinity of dinotefuran against the binding site of other neonicotinoids was very low, suggesting that this compound acts on a different site than other neonicotinoids.

Status of Neonicotinoid Insecticides - Market Environment

The remarkable success of neonicotinoids is reflected in their turnover figures in 1990 compared with 2005. In 1990, before the launch of the first neonicotinoid insecticide imidacloprid, the agrochemical market was dominated by organophosphates (O.P.s) (43%), pyrethroids (18%), and carbamates (16%). In 2005, neonicotinoids had gained a market share of 16%, mainly at the expense of O.P.s (25%) and carbamates (10%) [20].

Environmental impact of neonicotinoids

The neonicotinoid insecticides imidacloprid, acetamiprid, dinotefuran, thiamethoxam, and clothianidin are commonly used in green houses and interiors capes (plant interiors capes and conservatories) to manage a wide range of plant-feeding insects such as aphids, mealybugs, and whiteflies. However, these systemic insecticides may also be harmful to natural enemies, including predators and parasitoids. Predatory insects and mites may be adversely affected by neonicotinoid systemic insecticides when they: (1) feed on pollen, nectar, or plant tissue contaminated with the active ingredient; (2) consume the active ingredient of neonicotinoid insecticides while ingesting plant fluids; (3) feed on hosts (prey) that have consumed leaves contaminated with the active ingredient. Parasitoids may be affected negatively by neonicotinoid insecticides because foliar, drench, or granular applications may decrease host population levels so that there are not enough hosts to attack and thus sustain parasitoid populations. Furthermore, host quality may be unacceptable for egg lying by parasitoid females [21].

Long-term use of imidacloprid in a wide range of rice-growing areas might be associated with high resistance levels in *N. lugens*. Field populations had developed variable resistance levels to neonicotinoids, with a high resistance level to imidacloprid (R.R.: 135.3–301.3-fold), a medium resistance level to imidacloprid (R.R.: 35–41.2-fold), a low resistance level to thiamethoxam (up to 9.9-fold) [22].

There is controversy over the role of neonicotinoids

concerning pesticide toxicity to bees and imidacloprid effects on the bees population. Neonicotinoid use has been strictly limited in France since the 1990s when they were implicated in a mass die-off of the bee population. It is believed by some to account for worker bees neglecting to provide food for eggs and larvae and for a breakdown of bees' navigational abilities and possibly leading to what has become generally known as Colony Collapse Disorder, which is usually associated with the mite *Varroa destructor*. Also, in May 2008, Germany banned the seed treatment with neonicotinoids due to adverse effects upon bee colonies.

2) Bacterial fermentation products

These include spinosyns (spinosad and spinetoram), avermectins (abamectin and emamectin benzoate) and milbemycins. Out of these, spinosad and emamectin benzoate is commonly used on different crops.

1) Spinosyns: The spinosyns, a novel family of insecticidal macrocyclic lactones, are active on many insect pests, especially lepidopterans and dipterans. More than 20 spinosyns and more than 800 spinosoids (semi-synthetic analogs) have been isolated or synthesized [23].

a) Spinosad: During the late 1950s, companies including the Dow AgroSciences and Eli Lilly, began to look for naturally occurring pest control products actively. As a result of these efforts, a scientist from the Natural Products division of Eli Lilly, while vacationing in the Caribbean in 1982, visited an abandoned distillery and collected several soil samples. These samples were returned to the laboratory to determine the presence of biological activity. Three years later, the fermentation products from these samples were shown to have insecticidal activity [2]. By 1986, Eli Lilly's scientists identified the organism producing the biologically active substances. They determined that this was a new species of actinomycete bacteria and named it *Saccharopolyspora spinosa* Mertz and Yao [24]. Spinosad is a mixture of two active metabolites, Spinosyn A (85%) and Spinosyn D (15%). In 1995, because of its favorable environmental and toxicological profile, spinosad was classified by USEPA as a reduced risk product. It belongs to insecticidal class III.

Formulations: 45% SC (Tracer®)

Mode of action: Spinosad has a novel excitatory action on the central nervous system of insects. The mode of action is similar to that of neonicotinoids but affects the different binding sites. It alters the function of nicotinic acetylcholine receptors and GABA-gated ion channels [25]. It results in hyperexcitation, muscle contractions, paralysis, and death of insects.

Environmental impact

Spinosad exhibits wide margins of safety to many beneficial insects and related organisms. It has relatively low activity against predaceous beetles, sucking insects, lacewings, mites, and shows lower spinosad activity against some important beneficial insects than technical cypermethrin. However, spinosad seems to have few lethal effects on predators and harms parasitoids [26, 27]. In the last decade, several laboratory studies have focused on the lethal and sublethal impacts of spinosad towards predators (spiders, mites, and insects) and parasitoids, while only one study has dealt with the side effects of spinetoram.

b) Spinetoram: Is a semi-synthetic spinosyn composed of the new spinosyns J and L (semi-synthetic). It was introduced by Dow AgroSciences in 2005 and registered by EPA in September 2007 as a reduced risk insecticide. It belongs to insecticidal class U.

Formulations: Delegate® (W.G.), Radiant® (SC)

2) Avermectins: Avermectins were discovered in a culture of *Streptomyces avermitilis* in 1976 by scientists working at Merck and Co. These are among the most potent anthelminthic, acaricidal and insecticidal compounds known. Chemically these are a family of 16-membered macrocyclic lactones. Among the eight analogs identified, avermectin B1 (commercialized as Abamectin) is insecticidally most active. Abamectin is a mixture of avermectin B1a (80%) and Avermectin B1b (20%) belonging to insecticidal class Ib. Another commercial avermectin is Ivermectin, successfully used to control animal parasites. Abamectin shows selectivity in practice because it is rapidly absorbed by plant tissues and does not persist as a contact poison. It has proven effective in controlling leafminer and *Liriomyza trifolii* in celery without damaging the parasitoid complex.

The search for new avermectins resulted in the development of new derivatives which exhibit essentially the same mode of action but differ in their biological activity. Among the new avermectins is the emamectin benzoate; it exhibits excellent activity against lepidopterous pests and a wide range of insect species and belongs to insecticidal class II.

Formulations:

Abamectin: Agri-Mek® 15% EC

Emamectin benzoate: Proclaim® 5% WSG

Ivermectin: Ivomec® 1% S

Mode of action: They bind with high affinity to sites in various insect species' heads and neuronal muscle membranes, acting as agonists for GABA-gated chloride channels [28]. They affect the nervous system of arthropods by increasing chloride ion flux at the neuromuscular junction, resulting in cessation of feeding and irreversible paralysis.

Environmental impact: Abamectin is considered as a selective pesticide with relatively low toxicity to many non-target arthropods. It is used at meager rates and degrades rapidly when exposed to light, mainly when applied as a thin film on either an inert surface or leaves. However, abamectin is toxic to soil invertebrates, while emamectin benzoate is biodegradable in soil [29].

3) Milbemycins: Milbemycin (Milbemectin) is an insecticide and acaricide, a fermentation product from a soil-dwelling actinomycete, *Streptomyces hygroscopicus* subsp. *aureolacrimosus*. It is a mixture of milbemycin A3 and milbemycin A4 ratio 3:7. It is used to control citrus red mite, pink citrus red mite, Kanazawa spider mite and is also recommended to control leafminers in citrus, tea, and protected ornamentals. These compounds' structure and biological activities are similar to those of avermectins. It belongs to insecticidal class II.

Formulations: Milbeknock® (1% EC)

Environmental impact: It does not persist in the environment and is considered to be relatively non-toxic to non-target organisms, although some beneficial insects are susceptible [30].

3) Phenyl pyrazoles
These are the chemicals principally with herbicidal effects.

Fipronil: IUPAC: {5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(trifluoromethyl) sulfinyl] – 1H-pyrazole-3-carbonitrile}.
It was developed by Rhône-Poulenc Ag Company (now Bayer Crop Science) between 1985 and 1987 and placed on the market in 1993. Fipronil contains a trifluoromethyl sulfinyl substituent which is essential in its outstanding performance against a number of insects. It exhibits both herbicidal and insecticidal activities. It is an insecticide with contact, stomach, and systemic action. It is highly effective against lepidopterous larvae and agricultural pests such as Orthopterous pests and coleopterous larvae in the soil, termites, and onion maggots [31]. It also has a broad application range and can be applied as a foliar spray, seed treatment, and *via* the soil application. Fipronil is considered an important addition to IPM programs.

Mode of action: It acts on γ-aminobutyric acid (GABA), blocking chloride channels. Competitive binding has demonstrated that this compound has a greater affinity to the target site in insects than in mammals, resulting in a high selectivity toward insects [32].

Formulations: 5% SC (Regent®)

Environmental impact: Fipronil is a moderately hazardous pesticide belonging to insecticidal class II and is moderately persistent in soil and water. Fipronil residues tend to remain in the upper 15 cm soil layer and have a low potential to leach to the groundwater. In aquatic environments, fipronil residues rapidly move from water to the sediment, with over 95% of residues being found in or on the sediments within one week. It is highly to bees and parasitoid *Bracon hebetor* also, a 300 fold increase in resistance to fipronil in DBM has been found [33].

4) Oxadiazines
Indoxacarb: IUPAC: Methyl 7-chloro-2,5-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy) phenyl] amino] carbonyl] indeno [1,2-e] [1,3,4] oxadiazine - 4a (3*H*) - carboxylate Indoxacarb is a new insecticide produced by DuPont and registered in 2000 belonging to insecticidal class II. The EPA has designated it as a "Reduced-risk" pesticide and considered organophosphate replacement. Indoxacarb possesses excellent rain fastness, excellent photostability and is effective at high temperatures. It has been recommended to control lepidopteran pests of vegetables at a relatively low use rate and favorable toxicological profile. Field studies in the cotton belt in the USA found that indoxacarb was effective in controlling the *Heliothus* complex (*Helicoverpa zea* and *Heliothus virescens*), fall armyworm, beet armyworm, cabbage looper, soybean looper, and tarnished plant bug [34].

Formulations: 15.8% EC (Avaunt®), 14.5% SC (Indica®)

Mode of action: This pro-insecticide is bioactivated in the insect by enzymatic (insect esterase) N-decarbomethoxylation changing it to a more active, highly insecticidal metabolite that acts by inhibiting sodium ion entry into nerve cells, resulting in the paralysis and death of target insect pests [35].
Indoxacarb can play a vital role in resistance management programs as there is no cross-resistance with the current insecticides such as pyrethroids, organophosphates, and carbamates has been reported [35]. It has no appreciable effect on some essential natural enemies, such as *Orius* and *Phytoseiulus* species [36]. Hence, it can be considered an important addition to insect pest management programs.

Environmental Impact: Indoxacarb is considered a reduced-risk pesticide with low mammalian toxicity and a favorable environmental /ecological profile. This pesticide is toxic to mammals, birds, fish, and aquatic invertebrates. Runoff from treated areas may be hazardous to aquatic organisms in neighboring areas.

5) Anthranilic Diamide
Rynaxypyr: IUPAC: 3-bromo-4'-chloro-1-(3-chloro-2-pyridyl)-2'-methyl 6'-(methylcarbamoyl) pyrazole -5-carboxanilide.
Rynaxypyr is the first insecticide from a new chemistry class, the anthranilic diamides, controlling almost all the economically important insect pests. Due to its unique chemical structure and novel mode of action, rynaxypyr effectively controls pest populations resistant to other insecticidal products. Rynaxypyr moves into the leaf tissue where it is protected from wash-off while remaining available to chewing insects feeding on either surface of the leaf. This translaminar activity, rain fastness, insecticidal potency, and resistance to photo-degradation are the bases for long-lasting crop protection under a wide range of conditions. It belongs to insecticidal class U.

Mode of action: Rynaxypyr controls the insect pests through a new mode of action, activating insect ryanodine receptors which play a critical role in muscle functioning. Cells require a regulated calcium release from internal stores into the cytoplasm for muscle contraction, and ryanodine receptors act as selective ion channels, modulating calcium release. Rynaxypyr binds to the receptors, causing uncontrolled release and depletion of internal calcium, preventing further muscle contraction. Insects treated with rynaxypyr exhibit rapid cessation of feeding, lethargy, regurgitation, and muscle paralysis, ultimately leading to death [37].

Formulations: 20% SC (Coragen®)

Field application: Rynaxypyr is highly potent and efficacious against many economically important lepidopterous species. Rynaxypyr also effectively controls selected species from other orders such as Coleoptera, Diptera, Hemiptera and Isoptera. Rynaxypyr is particularly potent against neonates as they hatch from eggs (ovi-larvicidal activity).

Environmental impact: Rynaxypyr has a low impact on the environment when applied according to recommendations.

High temperature, alkaline p.H. and U.V. light enhance degradation, producing non-toxic degradation products. The sequestration of rynaxypyr in the soil matrix, low water solubility, and non-volatility indicate a low potential for movement towards surface and ground water. Rynaxypyr has a low impact on non-target organisms such as birds, fish, mammals. Earthworms, microorganisms, algae, other plants, and many non-target arthropods.Some aquatic invertebrates, such as *Daphnia* sp. are sensitive to rynaxypyr.

6) Pyridine Azomethines

Pymetrozine: IUPAC: [(E)-4,5-dihydro-6-methyl-4(3-pyridylmethyleneamino)-1,2,4-triazin-3(2H)-one].

Pymetrozine is a novel pyridine azomethine insecticide and is highly specific against sucking insect pests [38]. It belongs to insecticidal class U.

Mode of action: The mode of action of pymetrozine in insects has not been precisely determined. However, it may involve effects on neuroregulation or nerve-muscle interaction. Physiologically, it appears to prevent these insects from inserting their stylet into the plant tissue and interferes with feeding behavior, resulting in the complete cessation of feeding within hours of contact [39]. Aphids remain alive for 2 to 4 days before they die of starvation.

Formulations: 50% W.G. (Fulfill®)

Field application: It controls aphids and whitefly in vegetables, potatoes, ornamentals, cotton and citrus fruit, tobacco, and both juvenile and adult stages are susceptible. Pymetrozine also reduces direct damage and virus transmission by aphids [40].

Environmental impact: Because of its specificity for sucking insects, it is relatively non-toxic to most natural enemies. The compound appears to have great promise in IPM programs due to its high degree of selectivity, low mammalian toxicity, safer for birds, fish, and non-target arthropods.

7) Pyridine carboxamid

Flonicamid: IUPAC: *N*-cyanomethyl-4-(trifluoromethyl) nicotinamide. Flonicamid is the only molecule of this class effective against sucking pests developed by Ishihara Sangyo Kaisha in 2000. It belongs to Insecticidal class II and possesses excellent activity against all aphid species, thrips, whitefly, plant hopper, and plant bugs.

Mode of action: It is a feeding depressant (antifeedant, selective feeding blocker. It results in modifying the feeding behavior of sucking insect pests leading to starvation and death of insects [41]. It has systemic and translaminar activity and gives long-term control. It exhibits excellent aphicidal activity and moderate toxicity to other sucking insect pests such as thrips, whiteflies etc.

Formulations: 50% WG (Ulala®)

Environmental impact: Flonicamid has an excellent toxicological, environmental and ecotoxicological profile. It has no negative impact on beneficial insects and natural enemies, and thus, Flonicamid can provide new options to integrated pest management programs.

8) Benzoyl Phenyl Ureas

Novaluron: IUPAC: [1-(3-chloro-4-(1,1,1-trifluoro-2-trifluoromethyoxyethoxy) phenyl)-3-(2,6-difluorobenzoyl)urea].

Novaluron is an insecticide of the benzoylphenyl urea class of insect-growth regulators. Novaluron acts as an insecticide mainly by ingestion but has some contact activity. It belongs to insecticidal class U.

Mode of action: It is a relatively new CSI (Chitin Synthesis Inhibitor) that inhibits the chitin formation on larvae of various insects (Lepidoptera, Coleoptera, Homoptera, and Diptera). BPUs are selective compounds that affect the larval stage by inhibiting the molting process. The reduced level of chitin in the cuticle seems to result from inhibition of biochemical processes leading to chitin formation. By inhibiting chitin synthesis, larval insect stages are targeted with death from abnormal endocuticular deposition and abortive molting [42].

Novaluron kills the insects over a few days by disrupting the normal growth. It has potent insecticidal activity against several important foliage-feeding insect pests. It is a potent suppressor of lepidopteran larvae such as *Spodoptera littoralis, Helicoverpa armigera* (by ingestion), and cotton whitefly larvae *B. tabaci* (by contact).

Formulations: 10% EC (Rimon®), (Diamond®)

Environmental impact: Novaluron has low toxicity to birds and mammals tested. Novaluron was of low toxicity to earthworms and had no adverse effects on soil microflora [43]. Technical Novaluron was of low toxicity to honey bees. The very low vapor pressure of novaluron indicates little potential for volatilization from soil or plant surfaces. Due to its very low water solubility, novaluron does accumulate in fish.

Other insecticides of this group are diflubenzuron, fufenoxuron, lufenuron and chlorfluazuron.

9) Triazapentadiene

Amitraz: IUPAC: 1,5-di-(2,4-dimethylphenyl)-3-methyl-1,3,5-triazapenta-1,4-diene. Amitraz is a member of the formamidine pesticide family. It is an acaricide and insecticide indicated to control ticks, mites, lice, and other infestations on sheep, cattle, and swine with good therapeutic results. However, amitraz poisoning is often encountered in animals and can also find its way into the human body through the food chain [2]. Increased concerns in recent years on possible health risks due to amitraz residues have greatly influenced the need to set up monitoring programs to determine amitraz at low levels. It should be pointed out that amitraz is a very labile pesticide whose degradation products include 2,4-dimethylaniline (2,4-DMA). Thus, analysis of amitraz should also include analysis of 2,4-DMA. In China, amitraz is approved for use in animal husbandry, and the maximum residue limits in swine and sheep livers are set at 0.2 and 0.1 ppm.

Mode of action: The mechanism of action is similar to other α 2-adenoreceptors agonists and the inhibition of the enzyme monoamine oxidase. Sedation, analgesic effects, and cardiovascular depression similar to the 2- adenoreceptors

agonists have been described in several species after amitraz injection. It has been thought that amitraz's mode of action also involves the interaction with the neuromodulator octopamine. This interaction is probably the reason for the increased nervous activity of ticks as a response to amitraz.
It is used to control bollworms, whitefly, and leafworms on cotton and worldwide to control acarine such as *Varroa jacobsoni*. The USEPA classified amitraz as class III i.e., slightly toxic insecticide.

Formulations: 20% EC (Mitac®), (Blatex®).

Environmental impact: It is highly toxic to fresh water fish but slightly toxic to mammals, and non-toxic to honey bees.

10) Thiadiazines
Buprofezin: IUPAC: (2-tert-butylimino-3-isopropyl-5-phenyl-1,3,5-thiadiazinan-4-one).
Buprofezin was introduced by Nihon Nohyaku Co., Ltd in 1984. It is an insect growth regulator belonging to the insecticidal class U. It acts specifically on hemipteran pests such as the greenhouse whitefly *Trialeurodes vaporariorum* (Westwood), sweet potato whitefly *Bemisia tabaci*, brown planthopper *Nilaparvata lugens* Stal, and citrus scale insects *Aonidiella aurantii* (Maskell). This insect growth regulator is effective against the nymphal stages of whitefly, scales, and mealybugs.

Mode of action: Buprofezin acts by inhibiting chitin biosynthesis, suppressing adults' oviposition, and reducing eggs' viability. It inhibits chitin biosynthesis and the subsequent cuticle deposition in the integument [44]. As a result of chitin deficiency, the pro-cuticle of the nymphs loses its elasticity, and the insect is unable to complete the moulting process.

Formulations: 44% S.C. (Applaud®)

Environmental impact: The compound has a mild effect on natural enemies [45] and is considered an essential component in IPM programs for controlling whiteflies in various agricultural systems.

11) Thio Urea Derivatives
Diafenthiuron: IUPAC: 1-*tert*-butyl-3-(2,6-diisopropyl-4-phenoxyphenyl) thiourea. Diafenthiuron is a new type of thiourea developed by Syngenta that acts specifically on sucking pests such as mites, whiteflies, and aphids [43]. It belongs to insecticidal class III.

Mode of action: It is a pro-insecticide photochemically converted in sunlight to its carbodiimide derivative, a more powerful toxicant than diafenthiuron [46]. The carbodiimide acts as an adenosine triphosphatase (ATPase) inhibitor following metabolic activation to the corresponding carbodiimide [47]. The carbodiimide metabolite inhibits mitochondrial respiration by selective and covalent binding to the proteolipid ATPase.
Diafenthiuron inhibits ATPase activities in assays carried out with bulb mites *Rhizoglyphus echinopus*, the two-spotted spider mite *Tetranychus urticae*, and the blue gill *Lepomis macrochirus.* Biological tests revealed a decreased toxicity of diafenthiuron in the presence of piperonyl butoxide, indicating the importance of cytochrome P450 in metabolizing difenthiuron [48].

Formulations: 50% WP (Polo®)
Environmental impact: Diafenthiuron has lower mammalian toxicity and relatively low toxicity to beneficial insects and predatory mites [49]. It is considered an essential addition in pest management programs in various agricultural systems for controlling the diversity of sucking pests.

12) Quinazolines
Fenazaquin: IUPAC: 4-*tert*-butylphenethyl quinazolin-4-yl ether
Dow Agro Sciences introduced this insecticide in 1993. It is a broad-spectrum acaricide and highly effective against the egg stage of mites. It is a contact poison belonging to the insecticidal class II.

Mode of action: It inhibits mitochondrial electron transport chain by binding complex I at co- enzyme Q. The mitochondrial electron transport coupled with oxidative phosphorylation is an essential process in many organisms. The electrons of reduced cofactors such as NADH (nicotineamide adenine dinucleotide) are transferred *via* several different enzyme complexes (sites) to finally reduce oxygen to water, producing ATP, the all-important energy source of all cells. Thus, this insecticide inhibits ATP synthesis, resulting in the death of insects [50].

Formulations: 10% EC (Magister®)

Target insects: This insecticide is effective against mites in tea and chilli.

Environmental impact: This insecticide is relatively safer to beneficial/predatory mites such as *Phystoseiulus* spp, A*mplyeius spp.* and *Agistemus spp*, which help in the reduction of mite population, but toxic effects on *Neoseiulus californicus* and *C. montrouzieri* has been reported [51]. Fenazaquin has the highest impact on *N. californicus.*

13) Pyridazinones
Pyridaben: IUPAC: 2-tert-butyl-5-(4-tert-butylbenzylthio)-4-chloropyridazin-3(2H)-one
Pyridaben was discovered and introduced by Nissan Chemical Industries Ltd. and first marketed in Belgium in 1990. It is a non-systemic insecticide and an acaricide active against all the stages of insect pests, especially against larvae and nymphs. It results in rapid knockdown of insect pests and has prolonged residual activity. It is used to control insect pests of Acari, Aleyrodidae, Aphididae, Cicadellidae, and Thysanoptera families on field crops, fruit trees, ornamentals, and vegetables.

Mode of action: It acts as the inhibitor of mitochondrial electron transport at complex I.

Formulations: 95% TC, 20% WP (Sanmite®, Nexter®), 10% EC.

Mammalian toxicology: Acute oral LD_{50} value for male rats

is 1350 ppm, female rats is 820 ppm, male mice is 424 ppm, and female mice is 383 ppm. It belongs to toxicity class III.

Environmental impact: An orally administered dose is excreted mainly in the feces in animals like rats, goats, and hens. After application to citrus and apple, pyridaben degrades gradually photochemically and is not translocated into the pulp. It readily degrades microbiologically in aerobic soils.

14) Pyrazoles

Fenpyroximate: IUPAC: *tert*-butyl (*E*)-α-(1,3-dimethyl-5-phenoxypyrazol-4- ylmethyleneamino-oxy)-*p*-toluate.
This insecticide was introduced in 1991 by Nihon Nohyaku Co., Ltd. It belongs to insecticidal class II. It is effective against red spider mites, and two-spotted mites on ornamental herbaceous plants, shrubs, trees, including greenhouse and interior treatments against spider mites. This insecticide was designed primarily as non-systemic contact and stomach miticides but did limited control of psylla, aphids, whitefly, and thrips. It controls all stages of mites, gives fast knockdown, inhibits molting of immature stages of mites, and has prolonged residual activity.

Mode of action: Mitochondrial complex- I electron transport inhibitor.

Formulations: 5% S.C. (Mitigate®)
Other insecticides of this class are tolfenpyrad 15 E.C. (Torac®) and tebufenpyrad 95% T.C., 20% W.P. (Pyranica®), (Masai®).

Environmental impact: Its oral LD_{50} value for male rats is 480 and 245 mg/kg for female rats. It is not carcinogenic, teratogenic, or mutagenic in long-term studies. It has no adverse effect on honeybees at 250 ppm and is relatively non-toxic to predacious mites. However, it has a little adverse effect at 25-50 ppm *on Chrysopa nipponensis*, *Harmonia axyridis*, *Ephedrus japonicus*, *Misumenops tricuspidatus*, *Lycosa pseudoannulata*, *Orius sp.*and *Scolothrips sp.*

15) Pyridalyl

Pyridalyl is an insecticide of a novel chemical class (unclassified insecticides).

IUPAC: 2,6-dichloro-4-(3,3-dichloroallyloxy)phenyl 3-[5-(trifluoromethyl)-2-pyridyloxy]propyl ether**.**
Pyridalyl (common name) is a novel insecticide invented and developed by Sumitomo Chemical Co., Ltd. Pyridalyl was first registered in 2004 as an agricultural chemical in Japan and Korea and is sold under the name "Pleo®flowable." Sumitomo chemical is subsequently developing this compound in many other countries also. It is a novel insecticide that exerts excellent control against lepidopterous and thysanopterous pests on cotton, vegetables, and fruits. It is also effective on pests that have developed resistance to existing insecticides, indicating a different mode of action than conventional insecticide. Furthermore, pyridalyl is highly safe for various important beneficial arthropods, which makes it compliant with IPM. It belongs to insecticidal class U.

Mode of action: As a result of comparisons between the action mechanisms of pyridalyl and those of existing insecticides, we have confirmed that pyridalyl, does not act upon the nervous system, as do organo-phosphoric pesticides and synthetic pyrethroids; it does not inhibit insect growth, as do IGR agents; and does not inhibit the respiratory system. Pyridalyl possesses a specific type of toxicity for insect cells. It inhibits the cell growth caused by the artificial inhibition of proteins [52].
After 100 ppm of pyridalyl was locally applied to the surface of a tobacco cutworm (*Spodoptera litura*) larva, it died a few hours later. However, after application, the larva did not vomit up body fluids or go into convulsions, typical of lethality. Instead, the entire body of the larva merely appeared to go flaccid. Furthermore, when pyridalyl is applied topically at sub-lethal doses, the treated skin becomes blackened, indicating necrosis.

Cross Resistance

Many lepidopterous pests have developed resistance to insecticides that have been in use for relatively long periods, such as organo-phosphates and pyrethroids. This phenomenon is undeniable in insects that have relatively short generation periods. More specifically, throughout Japan *Plutella xylostella* has developed a high resistance to organo-phosphates, synthetic pyrethroids, benzoylphenyl urea and chlorfenapyr. Pyridalyl shows strong insecticidal activity against *Plutella* strains, both those having resistance to the abovementioned existing insecticides and those that are susceptible.

Formulations: 10% E.C. (Pleo®)

Environmental impact: Its oral LD_{50} value for male rats is 480 and 245 mg/kg for female rats. It is not carcinogenic, teratogenic, or mutagenic in long-term studies. It poses no adverse effect on honeybees at 250 ppm. It is relatively non-toxic to predacious mites. Nevertheless, it has a little adverse effect at 25-50 ppm *on Chrysopa nipponensis*, *Harmonia axyridis*, *Ephedrus japonicus*, *Misumenops tricuspidatus*, *Lycosa pseudoannulata*, *Orius sp.*and *Scolothrips sp.*

16) Thiazolidines

Hexythiazox: IUPAC: (4*RS*,5*RS*)-5-(4-chlorophenyl)-*N*-cyclohexyl-4-methyl-2-oxo- 1,3-thiazolidine-3-carboxamide. Hexythiazox was introduced by Nippon Soda Co. Ltd. and first registered in 1989. It belongs to insecticidal class U. Hexythiazox is a new acaricide with ovicidal, larvicidal, and nymphicidal activities with long-lasting effects against many mites and can be applied at any stage of plant growth from budding to fruiting. There are several application timings to protect the crops. It is commonly used on okra, brinjal, citrus, tea, apples, and chilli. It is effective against eggs and larvae of mites.

Mode of action: Its mode of action is unknown or non-specific mode of action, but it is potent a mite growth inhibitor.

Formulations: 50% WP (Hexygon®), 5.45% EC (Maiden®)

Environmental impact: It shows low toxicity to mammals and aquatic organisms and has no adverse effects on beneficial insects and natural enemies. It is non-toxic to birds and bees.

17) Diacylhydrazines

Methoxyfenozide: IUPAC: (N-*tert*-butyl-N'-(3-methoxy-*o*-toluoyl)-3,5-xylohydrazide). Methoxyfenozide is a diacylhydrazine insecticide that acts as an insect growth regulator. It belongs to insecticidal class U.

Mode of action: Diacylhydrazines are MACs (molt accelerating compounds), disrupts or mimics the insect moulting hormone i.e., ecdysone, which induces moulting and metamorphosis. Insects affected by this insecticide begin to moult (shed their skin) but cannot complete this cycle. They cannot get free of their old skin, stop feeding within 1 to several days, and eventually starve to death. This insecticide must be eaten to be effective. Since it can take some time to stop feeding, this compound should be applied before larvae hatch. It is probably most effective against young larvae. This compound is not systemic within apple foliage and expanding foliage and terminals must be resprayed to ensure adequate coverage of a tree [53].

Formulations: 2F (Intrepid®)

Other insecticides of this group are tebufenozide (Confirm®, Mimic®) and halofenozide (Mach 2®). Tebufenozide is effective in controlling a variety of lepidopterous insect pests [54], as is methoxyfenozide.

Field application: It can be used on crops like apple, pear, berries, cole crops, leafy and fruiting vegetables, ornamental herbaceous plants, shrubs. It is effective against leafrollers, webworms, armyworms, cabbage worms, diamondback moths, etc.

Environmental impact: Diacylhydrazines are safer for pollinators, mites, and other beneficial insects. Due to their novel mode of action, the diacylhydrazines display a very favorable mammalian and environmental toxicity profile and good selectivity towards beneficial insects. These are stable to heat, light, water, and safe to beneficial fauna [55].

18) Triazines

Cyromazine: IUPAC: N-Cyclopropyl-1, 3, 5-triazine-2, 4, 6-triamine.

Cyromazine is a triazine insect growth regulator used as an insecticide and an acaricide. It is a cyclopropyl derivative of melamine. It is mainly used to control dipteran insect pests. It is an effective larvicide against many dipteran and lepidopteran species [56]. Cyromazine has good activity against many dipteran species, especially when it is orally administered to larvae which usually exhibit a wide range of morphological abnormalities. It belongs to insecticidal class U. In veterinary medicine, cyromazine is used as an ectoparasiticide.

Mode of action: Cyromazine works by affecting the nervous system of the immature larval stages of certain insects. Cyromazine is characterized by a rapid stiffening of the cuticle, affecting mainly larvae of Diptera. Cyromazine-induced reduction in cuticle extensibility may be responsible for the other symptoms of poisoning and hence may be the primary effect of the insecticide. Moreover, cyromazine induces gross deformities in larvae and pupae of dipteran insects [57] and reduces egg laying and egg hatch when fed to *Lucilia cuprina* adult. It has a translaminar activity that quickly penetrates leaves. It is active against a narrow range of insect-pests, notably the larval stages of dipterans and leafminers. The current uses of cyromazine are for *Liriomyza* leafminers in cole crops, lettuce, peppers, spinach, celery, tomatoes, and cucurbits.

Formulations: 75% WP (Trigard®)

Environmental impact: Cyromazine is non-toxic to crustaceans, bees, and birds. Because of its high level of specificity, cyromazine is much less toxic to natural enemies than IGRs such as diflubenzuron, making it highly compatible with integrated pest management (IPM) programs.

19) Tetronic acid and Derivatives

Spiromesifen: IUPAC: 2-oxo-3-(2,4,6-trimethylphenyl)-1-oxaspiro [4,4] non-3-en-4-yl 3,3-dimethylbutanoate Spiromesifen is a novel insecticide and acaricide belonging to the new chemical class of spirocyclic phenyl-substituted tetronic acids, recently introduced by Bayer Crop Science. Spiromesifen is especially active against whiteflies (*Bemisia* spp. and *Trialeurodes* spp.) and tetranychid spider mite species as *Tetranychus* spp. after foliar application [41]. It belongs to insecticidal class U.

Mode of action: Spiromesifen is a lipid biosynthesis inhibitor and works by preventing the treated mite or whitefly from maintaining proper water balance, causing desiccation, i.e., the treated mite or whitefly dries up and dies [41]. Depending upon the temperature, this occurs within 3 to 10 days after treatment. Speed of activity typically is faster on outdoor crops than greenhouse crops. All developmental stages of mites and whitefly are affected. As with many products, the activity against whitefly immatures is more rapid than against adults.

Formulations: 24% SC (Oberon®)

Field application: It provides outstanding control of whiteflies. It is one of the few products that will provide dependable control of all known Q biotype whiteflies. The Q biotype is tolerant to or resistant to numerous insecticides and insect growth regulators.

Environmental impact: Side effects of spiromesifen on *Eretmocerus mundus* were evaluated by laboratory studies and field trials in commercial green-houses under IPM programs. The analysis of the data on mortality revealed that cypermethrin significantly increased the mortality of *E. mundus* adults 3 hours after application, while spiromesifen was not significantly different from the control [58]. Therefore, spiromesifen has to be considered as harm-less to *E. mundus* adults.

20) Carbazate Miticides

Bifenazate: IUPAC: Isopropyl 2-(4-methoxybiphenyl-3-yl) hydrazinoformate.

Bifenazate was launched in 1999. It belongs to insecticidal class U.

Mode of action: It is neuroactive, but the exact mode of action is unknown.

Field application: Bifenazate is registered to control mite pests in the greenhouse, shade house, nursery, field, landscape, and interiorscape grown ornamentals.

Formulations: 24% SC (Floramite®)

Environmental impact: Bifenazate is considered to be neither mobile nor persistent in the aquatic and soil environment. Bifenazate would be expected to exhibit a low potential to contaminate ground and surface water [3]. The available data indicate that bifenazate is categorized as highly toxic to freshwater fish (LC_{50} = 0.58-76 ppm) and aquatic invertebrates (LC_{50}/EC_{50} = 0.50 ppm) on an acute basis. Bifenazate is categorized as slightly toxic to avian species on an acute oral basis (LD_{50} = 1032 mg/kg) and as moderately toxic to avian species on a subacute dietary basis (LC_{50} = 656-1862 ppm). Bifenazate is practically non-toxic to small mammals on an acute oral basis (LD_{50}>5000 mg/kg). An analysis of the results indicates that bifenazate is moderately toxic to bees on an acute contact basis (LD_{50}=7.5 ug/bee).

21) Pyrroles

Chlorfenapyr: IUPAC: 4-Bromo-2-(4-chlorophenyl)-1-ethoxymethyl-5-trifluoromethyl- *1H*-pyrrole-3-carbonitrile. Chlorfenapyr is an effective insecticide and acaricide, acting as stomach and contact poison. It has good translaminar but limited systemic activity in plants and belongs to insecticidal class II.

Mode of action: This compound is a pro-insecticide. The biological activity depends upon its activation to another chemical. Oxidative removal of the N-ethoxymethyl group of chlorfenapyr with mixed-function oxidases forms the compound CL-303268. CL-303268 uncouples oxidative phosphorylation at the mitochondria, disrupting the production of ATP, cellular death, and ultimately insect mortality [41].

Field application: It controls many species of insects and mites, including those resistant to carbamate, organophosphate, and pyrethroid insecticides and also chitin synthesis inhibitors in cotton, vegetables, citrus, vines, and soybean. Among the pests resistant to conventional products controlled by chlorfenapyr are *Leptinotarsa decemlineata*, *Helicoverpa* sp., *Heliothus* sp., *Plutella xylostella*, *Spodoptera litura*, and *Tetranychus* sp.

Formulations: 10% SC (Lepido®)

Environmental impact: No wildlife exposure and other significant environmental exposure risk.

22) Phathalic acid Diamides

Flubendiamide: IUPAC: N1-[4-(heptafluoropropan-2-yl)-2-methylphenyl]-3-iodo-N2-(1- methanesulfonyl-2-methylpropan-2-yl)benzene-1,2-dicarboxamide.

It is a new lepidopteran insecticide promoted by Bayer Crop Science. It is the next generation in Lepidoptera pest management. It was initially discovered by researchers from Nihon Nohyaku and is the first commercial member of a new, promising class of insecticide called 1,2- benzenedi carboxamides or phthalic acid diamides, with exceptional activity against a broad spectrum of lepidopterous insects. It belongs to insecticidal class III.

Mode of action: It exhibits excellent larvicidal activity as an orally ingested toxicant by targeting and disrupting calcium balance resulting in rapid cessation of feeding and death of the insect.

Formulations: 20% WG (Takumi®), 39.35% SC (Fame®).

Environmental impact: It is much safer for natural enemies as indicated by the high EC_{30} values of this insecticide against various natural enemies [59], and these properties of flubendiamide seem very suitable for controlling lepidopterous pests under resistance management and integrated pest management programs.

23) Pyridines

Pyriproxyfen: IUPAC:4-phenoxyphenyl (*RS*)-2-(2-pyridyloxy) propyl ether 2-[1-(4-phenoxyphenoxy)propan-2-yloxy]pyridine**.**

Pyriproxyfen is a pyridine-based pesticide that is effective against a variety of arthropods. It was introduced to the U.S. in 1996 to protect cotton crops against whitefly. It has also been found helpful in protecting other crops also. It is also used as a prevention for fleas on household pets. It belongs to insecticidal class U.

Mode of action: It is a juvenile hormone analogue, preventing larvae from developing into adulthood and thus rendering them unable to reproduce. It prevents them from maturing into reproductive adults, causes morphological abnormalities, and disrupts the normal development of immature stages of insects, leading to sterility or death [60].

Formulations: 10% EC (Admiral®), 0.5% G (Sumilarv®)

Environmental impact: Pyriproxyfen is moderately volatile and has low water solubility but does not readily adsorb onto soil surfaces. Measured residue concentrations have been reported to decline by 50% in 24 hours in treated ponds. Pyriproxyfen adsorbs onto suspended organic matter and remains biological activity for up to two months after an initial application. Its persistence in water in the absence of organic matter declines with increasing temperature and sunlight exposure [60].

24) Cyclic Ketoenols

Spirotetramat: IUPAC: cis-4(ethoxycarbonyloxy)-8-methoxy-3-(2,5-xylyl)-azaspiro [4, 5] dec-3-en-2-one.

Spirotetramat is a novel insecticide belonging to the chemical class of ketoenols a tetronic acid derivative [61]. It belongs to insecticidal class III.

Mode of action: It interferes with lipid biosynthesis, leading to the death of the target insect-pest immature stages within two to ten days after application. Spirotetramat inhibits acetyl CoA carboxylase, a key enzyme in fatty acid biosynthesis. The active constituent is against a broad spectrum of sucking insects, including aphids, scales (soft and armored), mealybugs, whiteflies, psyllids, and selected thrip species [61].

Formulations: S.C. (Movento®)

Environmental impact: Studies were conducted to evaluate

the compatibility of spirotetramat 150 OD with beneficial organism's *viz*., *Trichoderma viridae*, *Beauveria bassiana* and *Pseudomonas fluorescens.* Spirotetramat was incompatible with *T. viridae*, *B. bassiana* but relative compatibility was significantly better than other insecticides. Spirotetramat was highly compatible with *P. fluorescens* and did not inhibit it even at higher doses. Spirotetramat was considered relatively safer for honeybees [62].

Future Challenges

We need to develop more and more new molecules that are effective at low dosages and have high efficacy and quick knockdown effect, low mammalian toxicity, relatively safer formulations for humans and non-target organisms, less leaching potential, and which are less harmful to beneficial species. Also, as the residue analysis techniques are becoming more and more technologically advanced, it is becoming more and more challenging to develop new chemicals which leave significantly less residue in the environment. So, more innovations are required to develop new chemicals which are satisfactory from residue analysis methods. More innovative technology is needed in the methods of application of pesticides. There is a need to minimize the residue load in the ecosystem.

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