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Novel insecticides: A potential tool for the management of insect pest

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Abstract
Development of selective properties insecticides that act on biochemical sites present in particular insect groups, but their properties are different from other insecticides. Aim of this study is the discovery of compounds that affect the hormonal regulation of molting and developmental processes in insects *viz.*, ecdysone agonists (tebufenozide and methoxyfenozide), juvenile hormone mimics (pyriproxyfen and fenoxycarb), and chitin synthesis inhibitors (benzoylphenyl ureas and buprofezin). Insect nicotinic acetylcholine receptor such as imidacloprid, acetamiprid, and thiamethoxam has been introduced for the control of aphids, whiteflies, and other insect species. Novel compound pyradalyl (S-1812) has found to act selectively on lepidopterans and thrips. Neuroactive chemicals have played major role in management of insect pests in crops, their judicious uses led to several problems like insect resistance, secondary pest outbreaks, destruction of natural enemies', residue and resurgence. Now days the focus is laid down on development of new green chemistries insecticides having novel biochemical target for controlling pest, understand mode of action and resistance management. The mechanism of these insecticides targeting of a molecular target site present in pest on an enzyme form that is different from other organism. In recent years, several new insecticide groups having new chemistries *viz.*, neonicotinoids, oxadiazines, diamides etc. are developed and commercialized for controlling pest. Novel insecticides will play a greater role in controlling pest because they are target specific in pest having no toxicity on non-target pest (environment friendly and toxicologically safer), high efficiency in pest control, and resistance management.

Keywords: Novel insecticide, natural enemies, resistance, pest management

Introduction
There is a great role of conventionally used neuroactive insecticides in managing insect pest population because these are broad spectrum [1]. Repeated use of neuroactive insecticide *viz.* problems in insect pest population management like insecticides resistance, pest resurgence, secondary pest outbreak, and residue related problems and toxic effect on human beings [2]. Replacement of conventionally used neuroactive insecticides became necessity of existence to manage insect pest population. Emphasis is laid in searching green chemistry insecticide with different mode of action. Newly discovered molecules are insect pest specific affect the specific biochemical sites present in the particular insect groups, having different properties present in other insecticides [3]. They have different mode of action, so there is no impact of developed resistance mechanism in insect pest and act as rotational alternatives, provide unique selective chemicals for controlling insect pests and give more desirable control in insect pest management [3]. These newly discovered insecticides have very less toxic effect on non-target pest, natural enemy, mammals and environment due to their green chemical origin and minimum doses for their application [2].
There are three major principal approaches has recognized in resistance management. These are moderate use of insecticides lower dose of insecticides, increasing the efficiency of chemical toxic effect on target pest through increasing uptake of chemical by adding attractant or inhibiting detoxifying enzymes of resistant insect and use of various insecticides mixture or through application of alternate insecticides having different modes of action in pest management [4]. Newly discovered novel insecticides have different mode of action affect development of insects through inhibiting chitin synthesis, juvenile hormone mimics, and ecdysone agonists. Some compounds developed those have toxic effect on selective insect groups through biochemical sites activity inhibition or enhancement like respiration

(diafenthiuron) acetylcholine receptor activating (Neonicotinoids) or GABA receptor (Avermectins) [3].

Resistance: Pesticide resistance is the decreasing the effectiveness of a pesticide against a pest population that was previously susceptible. According to IRAC 2007 [5] there are number of ways of insecticide resistance development:-

Behavioral resistance: In this kind of resistance insects become aware regarding the presence of toxic substance on plants and avoid feeding [4].

Penetration resistance: Insects modify their exoskeleton that reduces insecticide penetration from cuticle to insect body [5].

Target-site resistance: in this type of resistance insects genetically modify the target site where the insecticide act that avoids insecticide interaction to the site of its action and prevents or decreases their effectiveness [1].

Metabolic resistance: Insects quickly detoxify the particular insecticide, through increasing metabolic activity like excretion which transport insecticides from digestive system and avoid chemical toxic effect. Resistance became major problem against conventionally used insecticides such as organophosphates, carbonates, pyrethroids due to their repeated application and same mode of action. To prevent or delay resistance problem have necessity to develop insecticide with different mode of action [6]. All newly developed novel insecticides are having different mode of action, they are less toxic effect on mammals, environment and relatively safe to natural enemies.

The aim of this reviews for the mode of action of different groups of novel or newer insecticides and use them to avoid/delayed the resistance development in insect-pest.

Different group of novel insecticides and their mode of action

1. Insecticides with synthetic origin
2. Insecticides derived from soil microorganisms / macrocyclic lactones
3. Insect growth regulators

1. Different classes of Insecticides with synthetic origin

Neonicotinoids: These are synthetic organic insecticides has developed through modification of natural products have both chemical and biological properties. In modern crop protection Neonicotinoids insecticides are the fastest growing class of insecticides. They are mainly systemic in nature rapidly absorbed by plants majorly for managing piercing sucking and certain chewing insect pest. Due to their systemic mode of action they are move rapidly to growing tip of plants and provide long term protection from target insect pest. In insect nervous system nicotinic aetylcholine receptor (nAChRs) is the main target site of Neonicotinoids insecticides [7]. Neonicotinoids insecticides are applied at low doses, highly target specific, hence low risk of non-target organism and environment, make them important class of insecticide for controlling insect pest and resistance [8].

Oxadiazines: To overcome problems like resistance development in insect pest a new insecticide originated from different class of chemistry Oxadiazines has been developed. Oxadiazines a broad-spectrum insecticide that acts as sodium channel blocker, have trans laminar movement into mesophyll of plants. Insects dye due to binding of insecticide molecule on sodium channel and blocking flow of sodium ion through exposure of spray fluid or ingestion of chemical treated plant parts. Immediately after ingestion of chemical molecule feeding cessation occurs paralyze insects and kill. Oxadiazines have minimal impact on birds, earthworms and aquatic organism [9].

Diamides: Diamides new class insecticides developed that act on ryanodine receptor a novel target in insect pest management. Muscle contraction kill the insects occur due to release of stored calcium from sarcoendoplasmic reticulum [10].

Ketoenols: To manage phytophagous resistant mite and insect pest population ketoenols new novel insecticides, acaricides developed. ketoenols inhibit acetyl CoA – Carboxylase major enzyme involved in fatty acid biosynthesis in mites and insect. Ketoenols majorly developed to manage mites, whitefly, aphid and other sucking pests [11].

Phenylpyrazoles: Phenylpyrazoles insecticides highly effective in managing mites and insects population through targeting on the GABA gated chloride channel, [12]. Mite and insects killed due to blockage of GABA gated chloride channel an ionotropic receptor.

Pyridine: Pyridine group of insecticides play great role in managing sucking insect pest mainly aphid, whitefly, plant hopper being systemic and Trans laminar activity in plant system. Pyridine Insecticides highly target specific. Due to obstruction of stylet penetration result of insecticide affect cessation of feeding in insect cause starvation and death [13].

Flonicamid: Flonicamid a novel insecticide contain pyridinecarboxamide compound highly effective against hemipterous and thysanopterous insect pest. Flonicamid cause inhibition of stylet penetration in plant tissue. Insects unable to take food due to inhibition of stylet penetration, continue till death of insects resulted from starvation, [14].

METI: METI insecticides and acaricides have great role in managing insects and mites population. METI insecticides and acaricides inhibit the mitochondrial electron transport in insect, mites [15]. They are highly effective in controlling mites and sucking pest population.

Tetrazines: Tetrazines is a highly effective acaricides against phytophagous mites and has no harmful impacts on environment and predatory mites. Tetrazines a contact acaricides have ovicidal properties as well as enter into mtes through ingestion due to translaminar properties, [16].

Thiazolidinones: It is used to control mites, thrips and leafhoppers due to their broad spectrum toxic effect on egg, larva and nymphal stage. These are highly effective in management of mite's population [17] and applied at any growth stage of plants.

Nereistoxin: It is a broad-spectrum insecticide effective in controlling sucking and chewing insect pest at all development stages [18]. It blocks the activity of nicotinic acetylcholine receptor channel of insects.

Formamidines: Having both acaricidal and insecticidal properties used to control red spider mite, two spotted spider mites, aphid, leaf miners and scale insects [19]. It effect on the basis of adrenoreceptors agonists and inhibition of enzyme monoamine oxidase.

2. Insecticides derived from soil microorganisms / macrocyclic lactones

These insecticides are derived from the natural or biological sources mostly from present in the soil. These insecticides have not much harmful effect on environment and human beings. Four classes of insecticides are developed in this group: - Avermectins, Milbemycins, Spinosyns, Pyrrole Insecticides.

Different classes of Insecticides derived from soil microorganisms / macrocyclic lactones

Avermectins: Insecticide are isolated from soil actionmycete microorganism *Streptomyces avermitilis* through fermentation. Avermectin is broad spectrums chemical have contact as well as stomach poison to mites and insects. Avermectin act on GABA-gated chloride channels receptor of insect nervous system. Avermectin kill the target organism due to increasing flow of chloride ions into cells [20]. Abamectins: - derived from eight molecules from soil microorganism. Abamectin shown multiple effect on insect its effect on GABA-gated chloride channels and glumate-gated chloride channels. Abamectin insecticide has broad spectrum contact and translaminar action on plants. These are highly toxic to mites, chewing and sucking insect pest. Insects are died due to paralyze and stop feeding. Emamectin Benzoate: - this class of chemical derived from the Streptomyces bacteria natural fermentation. This chemical is highly effective in controlling lepidopteran insects. Contact and translaminar properties of chemical in plants make them highly effective in controlling sucking and contact pests also increase their effect on plants. It disrupts neurotransmitter that leads to irreversible paralysis in insects [21].

Milbemycins: It derived from *Streptomyces hygroscopicus* subsp. *Aureolacrimosus* soil microorganism. Milbemycins have stomach and contact action in controlling mite's population. This chemical is safe for non-target pest due to non-persistent activity in environment [20].

Spinosyns: These bioinsecticides derived from macrocyclic lactones produced by soil actinomycete, *Saccharopolyspora spinosa through* fermentation. These classes of insecticides are effective for controlling lepidopteran, thysanopteran and dipteran pest. Primary target of spinosyns is binding sites on nicotinic acetylcholine receptors and GABA gated ion chloride channels secondary target that disrupt acetylcholine neurotransmission [22].

Pyrrole insecticides: It derived from dioxapyrrolomycin, isolated from a strain of *Streptomyces fumanus*, a natural product. It mainly toxicant on stomach but also some affect when comes in contact with insects. It is a broad spectrum in control of lepidopteran, thysanopteran, coleopteran and mite pest. Pyrrole insecticides uncouple oxidative phosphorylation at mitochondrial level and disturb the ATP production that causes death of arthropod [23].

3. Insect growth regulators

IGRs (insect growth regulators):- insect growth regulators affect insect growth and development. These insecticides classified as growth regulators or hormone mimics. They have not toxic effect on insects but they affect the normal functioning of target pest through interfering with physiological process of growth development like abnormalities that suppress survival of insects and their progeny. They destroy insect life cycle on their egg and larval developmental stage, preventing insect to becoming adult ultimately, they unable to reproduce [24].

Toxic effect of neuroactive insecticide on mammals due to their similar target sites on insects and mammals. To avoid toxic effect of insecticides on mammals it's desirable to develop insecticides having different target site that don't match with mammals [3]. IGRs insecticides have different target site that don't match with mammals and is therefore grouped correspondingly on their mode of action as chitin synthesis inhibitors that are inhibition of cuticle formation; juvenile hormone mimics (affect insect hormones). Insects exoskeleton made up of chitin and for development insect goes under metamorphosis. In metamorphosis insects replace older exoskeleton with new one developed beneath them through shedding. All process of metamorphosis controlled by hormones. IGRs effect chitin synthesis and hormone development.

IGRs are developed based on the life cycle of the insects that is how the insects reproduce, develop, function and grow. Mainly the IGRs developed based on two manners. In one manner insects are exposed to IGRs and their effect on insects functioning and behavior was observed. Those IGRs chemicals shown desirable result were developed. In second manner hormones required during development process was observed and chemicals are developed to synthesize those hormones for disturbing normal growth and development of insects [25]. By application of IGRs some insects may killed due to hormonal imbalance or due to alternation of their normal development and functioning. Other insects died due to insects' biochemical pathways regulation or inhibition.

Different classes of Insect growth regulators insecticides

Benzylphenylureas: benzylphenyl ureas IGRs developed insecticide widely used in controlling insect pest due to their safety to environment and non-target organism. It inhibits chitin biosynthesis due to that insect unable to moult cause abnormal cuticular deposition [26]

Buprofezin: It is effectively used to control organophosphates resistant insect pest. It inhibits chitin biosynthesis in homopteran insect. They are highly effective in controlling sucking pest [27].

Triazine: It is highly effective at low dose in controlling resistant dipteran insect pest. Its target specificity and translaminar properties make less toxic effect to natural enemies [28].

Diacylhydrazines: It accelerates molting process through disrupting insect hormonal system by deactivating ecdysteroidal of the ecdysone receptor [24]. Occurrence of incomplete and premature moult kills insects due to desiccation and starvation.

Juvenile Hormone analogues/mimcs: Juvenile Hormone analogues/mimcs cause hormonal imbalance in insects. Suppress activity like embryogenesis, metamorphosis and adult formation. These are highly effective in controlling final instar larvae due to blocking of larval-pupal metamorphosis [29].

Role of novel insecticide in resistance management

Newly discovered novel insecticides have very less harmful effect on human health and natural enemies. They are highly selective to target pest. These newly discovered novel insecticides overcome the problems like insecticides resistance caused due to conventionally used Op, carbamate and pyrethroid insecticides, [30]. According to insecticide resistance action committee (2007) [5], resistance in insect pest can be effectively delayed or prevented by application of alternate insecticide having different mode of action.

Problems like resistance, resurgence, residue and environmental safety emerged due to use of neuroactive chemical insecticides in pest management [2]. These ordinary used neuroactive insecticides are replaced by green chemistries insecticides having novel mode of action in pest controlling and resistance management. Efficacy of insect growth regulator on organophosphate resistant 3rd and 4th instar larvae of mosquito studied at different geographic locations. No resistance is seen in any of the evaluated insect growth regulator and Triflumuron was highly effective from all tested insecticides [31]. Study suggests use of IGR in mosquito population control due to resistance developed in conventionally used insecticides.

Repeatedly using a chemical with same mode of action tends to develop resistance in insect pest [32]. Newer classes' chemicals contain natural toxicant those are toxicologically and environmentally safer molecules. As per the guideline of the IRAC sucking pest working group (2015) resistance in insect pest has occur due to application of higher or lower dose of group 4 insecticide than recommended on label rates to avoid this resistance emergence in insect use recommended dose of insecticides [33]. For one generation of insect pest spray of group 4 insecticide and for next generation of insect pest spray of alternate insecticide having different mode of action break resistance development. In unavailability of insecticide having different mode of action rotates subgroups of 4A, 4C and 4D.

Novel insecticides with different modes of action have better control over target pest. Insecticides resistance managed by using insecticides with different modes of action and their less frequently application [3]. Insecticide resistance managed by using mixture of two or more chemicals having different mode of action. Neonicotinoids insecticides are nicotinic acetylcholine receptor agonists and in insect central nervous system bind strongly to nicotinic acetylcholine receptors. Binding of insecticides causes nervous stimulation at lower dose and at higher dose causes receptor blockage, paralysis and death. Neonicotinoids help in preventing resistance due to their alternative mode of action than conventionally used organophosphate, carbamates and pyrethroid insecticides [7].

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