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Article : JUVENOIDS AND ANTI-JUVENOIDS AS THIRD GENERATION PESTICIDE TO CONTROL LEPIDPOTERAN FIELD CROP PESTS

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Introduction:

Mass awareness regarding the detrimental effects of excessive use of pesti cide was generated only after the publication of 'silent spring'
(Carson,1962) which made it imperative to consider some environment frien dly, safe and compatible alternatives.
In the last two decades or so juvenoids have opened new vistas in that res pect. These insecticides are very much target specific,
effective in small quantities and often decompose quickly (Ware,1994)
.These attributes will reduce the pesticide
inputs and conserve our natural flora and fauna
. In holometabolous insects like Lepidoptera, only in absence of juvenile hor mone the last larval instar undergo a pupal moult by the action of ecdysone. Juvenile hormone prevents any precocious development of imaginal disks, and control the morphological,
ultrastructural and physiological changes that occur during shedding of epide rmis i.e.ecdysis.
This ecdysis and moulting are dependent upon regulation of gene expression with different titers 20-ecdysone in absence or presence of JH
(.Riddiford,1996).

So,
compounds that mimic the the action of juvenile hormone will disrupt met amorphosis and lead to various deleterious effects upon exogenous applicati on(Sparks 1990&
Dhadialla,1998).Reversely juvenile hormone antagonists like imidazoles that a ct as juvenile hormone
esterase inhibitors or JH biosynthesis inhibitors like trifluromethyl ketones c

an curb pest infestation by misregulating the larval development(Stenerson,2004).

Of all the groups of insects probably lepidopteran group inflicts maximum economic injury.Virtually all the staple crops of the world like rice, wheat, maize, cotton are infested by these insects. They are also a potent pest of forestry.The adults as well as larvae can cause severe damage.And among all the lepidopteran, the agricultural crop pests are the most infamaous. The current text will give general overview of juvenoid and anti-juvenoid mediated lepidopteran pest control with special emphasis on stem borers.

Disruption of metamorphosis as a pest controlling system :

By a series of transformations like physiological, morphological and biochemical larvae get converted to adults and this process is called 'metamorphosis' which is controlled in holometabolous insects by interplay of two principal hormones , one sesquiterpenoid JH and other steroid moulting hormone, 20- ecdysone. Ecdysteroids are secreted from prothorasic glands(PTG) that lies on the dorsa l surface of the larval trunks in the in the prothorasic segments. Upon stimulation of the protorasicotropic hormone (PTTH) from the brain , the gland secrete ecdysone into haemolymph, which is hydrolysed into the active hormone ,20-hydroxyecdysone.

On the other hand juvenile hormone is secreted by a pair of tiny glands called corpora alllata (CA) attached to the base of the brain. Corpora allata in its turn is under the scanner of allatostatins secreted by the neurosecretory cells in brain (Sindhu *et al* 2001).So anything that mimics juvenile hormone or acts as an analog of ecdysone or antagonists of both can be applied to create 'meta morphic catastrophe'. This promted to utilize hormone mimics or analogs as insecticide.

Juvenile hormone mimics and analogs as insecticide:

Dr. K. Slama and C. williams working with European linden bug (*Pyrrhocoris apterus*) a Heteroptera, at first had seen that bugs did not develop normally and a fully grown bug had many larval characters and died before attainment of maturity. The cause was found to be 'american paper towels' placed in the cages to hide the insects. Subsequently the paper was shown to contain a chemical substance called 'p aper factor' that interferred with the normal development of the larvae. The chemical nature of the paper factor was then deciphered after isolation and was found to act as juvenile hormone.(.Slama et al, 1967).This discovery led to the search for more synthetic and natural substan ces with juvenile hormone activity.The paper factor is a methyl ester of mo nocyclic sesquiterpene called juvabione(Stenerson,2004).
Since the numerous JH anlogs have been tested for insectidal activity (Retnakaran et al,1996 & Dhadialla et al, 1998).
Most of the JH s are basically terpenoid derivatives. The most active ones are methoprene and hydroprene. Soon several highly active compounds that have less aparent similarity with JH have been synthesised, they are non terpenoidal juvenoids such as fenoxycarb(registered as INSEGAR^{r} ,LOGIC^{r} , TORUS^{r} etc), pyriproxyfen(registered as KNACK^{r}, SUMILARV^{r} ADMIRAL^{r}), diofenolan (CGA 59205,AWARE, CIBA etc).

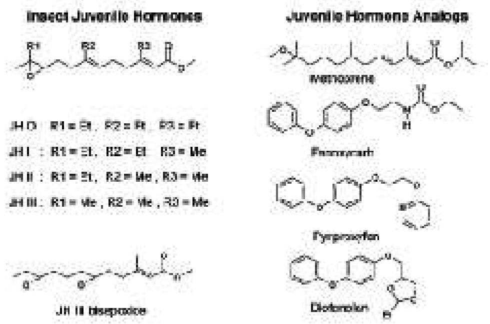

Fig: Terpenoidal and non terpenoidal juvenile hormones

Molecular basis of juvenile hormone action:

How juvenile hormone acts at the molecular level was an elusive question till early 2000. The best characterised system of JH action has been described for ovarian follicle cells of Rhodnius prolixus & Locusta migratoria (Sevela et al 1995). In them JH widens inter-follicular spaces in the epithelium which is due to activation of Na^+ /K^+ ATP ase and subsequent shrinkage of cells that promotes vitellogenin uptake. It seems that JH mediates the above action by protein kinase C (Sevela & Davey 1990).Probably JH interacts with the nuclear receptors in the fat bodies of L. migratoria and in the epidermis of Manduca sexta (Braun et al, 1995& Riddiford 1987).But the puzzle of molecular basis of JH action was solved after a rep ort appeared in the Journal of Insect Physiology by T.G.Wilson 2004. The report depicted effects of JH is due to interference with the expression or action of certain genes, particularly the the broad complex (BR-C) transcription factor gene , that direct changes during metamorphosis(Wilson,2004).

, Therefore JHAs or JH antagonists cause misexpression of BR-C which then leads to improper expression of one or more downstream effector genes controlled by BR-C gene products. Developmental caricatures like enlarged larva, intermediate larva, inability to emerge as adult are the end results.

Effect of JH analogs or JH mimic on Lepidoptera :

Most of the work of JH mimics and JH analogs since its discovery were actually centred around stored grain pest (Mohandas et al , 2006& Mandal ,2001). But some JH analogs also have been tested against the deadliest group of insects, Lepidoptera.

It has been mentioned earlier that in holometabolous insects like Lepidoptera larval-pupal molt is induced by 20- hydroxyl ecdysone in absence of JH. So the presence of JH at wrong time can cause permanent formation,larval-pupal, and larval adult intermediates.

It can affect hatching of eggs in Earias vitella (Noctuidae:Lepidoptera), a serious cotton pest(Mandal & Choudhury, 1984).Fecundity and fertility can also be lowered in this pest by juvenoids (Gelbic et al, 1984)

From early 1970s, reports started pouring about the control of lepidopteran pests by juvenoids. In then year 1975 two juvenile hormone analogs ZR-515& ZR-518 were tested alone and combindly with several synergists against 2-day old pupae of susceptible (s) and fenitrothion resistant (r) strains of Egyptian cotton leaf worm Spodoptera littoralis. The resistant strain was more sensitive to the action of the two hormones when compared to the susceptible strain (El-guindy et al, 1975).Erhan Kocak et al ,1976 found that , when one day old pupae of Spodoptera littoralis, an important pest of cotton and vegetables in Turkey were treated with methoprene and 1 day old eggs wre dipped in methoprene pupa – adult intermediates occurred.

When Spodoptera littoralis larvae was administered with isopropyl 11-methoxy-3,7,11, trimethyl-2,4,-dodecadienoate, one of most active juvenoid, in very small amount 0.8 1^1/4g amount, the treated larvae grew much bigger than untreated control. Eventually giant nonviable pupae or larval-pupal intermediates were produced (Sehnal et al, 1976).

One of the nonterpenoidal Juvenoid, pyroproxyfen was applied to 0-day old pupae of the tobacco cut worm, Spodoptera litura and oviposition came to a standstill. The oviposition stimulating factor in the haemolymph of mated untreated female was blocked by pyriproxyfen(Hatakoshi ,1992).It was also shown by Hatakoshi et al in 1992 that pyriproxyfen was much more potent agent in inducing supernumerary larvae than methoprene and JH1 when injected into last larval stage of S. litura .

Similarly in southwesrern cornborer, Diatraea gradiosella Dyar(Lepidoptera; Pyralidae), topical application of juvenile hormone induced prolonged larval diapause. A high parcentage of spotted non- diapause larvae treated with a single dose of JH mimic moulted into an immaculate morph and became dormant. On the other hand when diapause larvae were treated with JH mimic, it reversed to spotted morph but remained dormant. So, JH mimic can be utilized to disrupt the seasonal phenology of pest insects by causing larval dormancy (Chippendale et al,1976).

In the rice stem borer, Chilo suppresalis the switchover from larval to pupal epidermal commitment was studied on integument tissue in the last larval instar in Grace's medium containg 0.01-0.05 microgram/ml 20-hydroxyl ecdysone.But when juvenile hormone II was added in the medium 3 ng/ml completely inhibited the switchover which showed potential use of JH mimics and analogs to disrupt moulting and metamorphosis (Imito et al 1982).

The light brown apple moth;Epiphyas postvittana, when fed with juvenile hormone analog ZR-619(11- methoxy-3,7,11 trimethyl 2E, 4E dodecadienethiolate),produced .pronounced morphological changes in the head, antennal structures after instar v. Deformation of pupal and adult structures, particularly in the genitalia and wings were also found (Singh et al,1979).

It has been seen that application of another JH analog fenoxycarb during 2nd and 4th larval instar in Ostrinia nubialis increased the duration of 5th larval instar (Gadennc et al,1990). Similarly when Choristoneura fumiferana , eastern spruce budworm, were treated with fenoxycarb larval- pupal intermediates were produced. Wing-disks evaginated precociously and deformed pupae were the end result(Muly e et al ,1989 & Hicks et al,1992).
The above report corroborates with the findings of Heliothis viriscens, tobacco budworm(Man champ et al,1989) and Epiphyas postvittana ,light brown apple moth mentioned earlier.

The diapause programming of Sesamia nonagroides , rice stem borer was associated with increase of JH titer from about 20 to 50 nM in the 4th and 5th instar larvae. So perfect extra larval molt associated with a body weight increase can be induced in the non diapausing larvae w ith a JH analog.(Eagaguirre et al, 2005)

Mohandass et al in 2006 reported when larvae of wandering phase Indian meal moth (Lepidoptera: pyralidae) were exposed for maximum duration to hydroprene , the developmental time and mortality increased manifold.

In the cotton fields also pyriproxyfen and fenoxycarb can be potent weapon in IPM strate gy (Horowitz et al,1999).

A very interesting case of sex specific supression of gene expression of vitellogenin gene was found in Lymantria disper by JH analog. It was seen that vitellogenin transcript of 5.3 kb long hybridising to 2.5 kb cDNA clone was suppressed in 5 day old instar treated on day 2 with doses of jh analog (Adamczyk et al,1996).

One, new compound 1,3,4 oxidazole containing 2,11-pyridazin-3-one.application to many lepidopteran larvae showed anti-feedant activity and the toxic effect was found due to JH hormone effect pyradazinone.(Huang et al,2003).

Of late, in 2011 it has been shown in pistachio leaf white borer Ocneria te rebinthina(Lepidoptera:Lymantriidae), a minor pest of pistachio trees that pyri proxyfen treatment prolongs the longevity of the last larval instar with 20 to 30 days respectively, 9 days longer than control. It was also seen that treated larvae moulted to malformed prepupae and supernumerary larvae.(Moghadam et al,2001).

Anti- juvenile hormone agents as insecticide against lepidopteran pests:
After the discovery of juvenoids and JH mimics the thought of the reverse principle i.e. anti-JH hormone was inspired. Actually anti-JH are not hormones but the chemicals which lead to JH deficiency syndro mes.

Anti – juvenile hormone esterase(JHE) agents as insecticide:

In the final growing larval stage of tobacco budworm, cotton leafworm, spotted cutworm and beet armyworm,there is a rapid decline in the JH titer which initiates physiological &
behavioural changes before pupation and adult development. This decline is a ssociated with degradation of JH hormone by JH esterase as well as reduction of biosynthesis(Gilbert et al,2000 & Wogulis et al,2006). A group of chemical inhibitors of JH
esterase called trifluoromethyl ketone sulfides administratation in the final lar val stadium of Manduca sexta, (
tomato hornworm can block all blood juvenile hormone esterase activity and cause a delay in the time of metamorphosis.(Yehia et al,1985)..

Alpha-
thioalkyl substituted trifluoropropanones, an analog of trifluoromethyl ketones were found to be the most potent
inhibitor of juvenile hormone esterase in cabbage looper,Tricoplusia ni (hubner), (Lepidoptera: Noctuidae) (Linderman et al,1989).

Some lepidopteran pests were also controlled at least in the laboratory condi tion by by developing a fast acting recombinant baculovirus insecticide by cr eating a virus which expresses high level of JHE activity in the insect in in appropriate times.(Bonning & Hammock,1993). It has been shown by Hirai et al ,2002 that one imidazole KK-42 acts as JHE antagonist in Bombyx mori , one lepidopteran insect .
Fenvalerate can also act as JHE inhibitor when tested in Diamondback moth. When they fed on host plants pretreated with fenvalerate at the concentration s equivalent toLC_{20} ,LC_{50}, and
LC_{80} ,the pupation rate, pupal weight, adult emergence rate were declined as compared to non treated plants (Wei et al,2010).

JH biosynthesis inhibitors as insecticide:

Two compounds were discovered with JH biosynthesis inhibitor activity and they are aryl-pyradyl-thiosemicarbazones and 1,5-
disubstituted imidazoles specially active against lepidopteran(Barton et al,1989 & kuwann et al,1985).Prococenes that inhibit the development
of insect corpora allata are utilized against lepidopteran herbivorous crop pe sts as well(Williams et al,1967 & Szczcpanik et al,2005).

Conclusion and future prospects:

Insect juvenile hormone control several physiological processes including mo rphogenesis, development , reproduction in lepidopteran insect pests.
So, compounds that interact with JH, act like JH, inhibit JH biosynthesis or interfere with its catabolism are utilized as insecticides, specially against lepidopteran caterpillars of tobacco bud worm, corn borers, rice stem borers and cotton borers.

As our knowledge of interaction of JH with its receptor protein will expand, it is expected that some newer chemicals will come into the scene with more target specificity.

Inhibitors of JH biosynthetic activity can be a very potent insecticide. Resea rches in that regard have already made discovery of compounds such as arylpyridyl-thiosemicarbazones and 1,5-disubstitutedimidazoles which inhibit JH biosynthesis.
Another approach to disrupt JH biosynthesis can be the utilization of allatomodulatory neuropeptides(Sindhu et al ,2001,Noriega et al,2006 & Sheng et al,2001). These neuropeptides affect the biosynthesis of JH at corpora allata.
So identification of allatomodulatory peptide receptors, elucidation of their m echanism of signal transduction and deciphering which enzymes these peptide s actually inhibit will open up new avenues for designing JH biosynthesis inhibitors.

Juvenile hormone acid methyl transferase(JHAMT) is an enzyme that converts JH acids to inactive precursors of JH to active JH at the final step of JH biosynthesis pathway
.JHAMT enzyme is developmentally regulated in a few lepidopteran insect s pecies,like Manduca sexta (Bhaskaran et al,1990).So, by transcriptionally suppressing JHAMT gene expression JH biosynthesis can be terminated.

A deeper insight in the insect endocrinology and molecular basis of gene ex pression could pave the way to generate new strategies to intervene life cycl e of lepidopteran pests.

Interfering with JH metabolism is another aspect of lepidopteran pest control . Lesser or increased titer of JH at wrong time can lead to anomalies of insect development. Juvenile hormone esterase is a potent weapon in that regard. JHE brings about JH break down. So, JHE have been targeted to design such pesticides. With the advent of rDNA technology Bonning et al,1995 has made a fast acting recombinant bacculovirus, that expresses a m odified form of JHE, not active with respect of its function of JH catalysis. Alteration of specific residues of JHE that disrupted lysosomal targeting dra matically increased the insecticidal activity of that enzyme, the same recombinant JHE in the baculovirus vector with the altered residues can be tested for some other lep idopteran pests as well.

And when in future the cloned DNA sequences encoding receptors that mediate the action of JH will be available, it can be utilized for in vitro target site assays for JH along with whole insect assays and in this way new compounds that mimic JH action will certainly be discovered. So, it is recommended to try to utilize these JH mimics like fenoxycarb and pyriproxyfen or anti-juvenoid like imidazoles on large scale to control some of the major pests of rice in India , such as Scirphophaga incertulus, Sesamia inferens or Chilo supressalis in th e laboratory and field conditions as well.

But the common limitation of juvenoids that one will have to keep in min d , is that they prolong unwanted destructive instars of many other pest spec ies which needs to be taken care off greatly.

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