CHAPTER 2

REVIEW OF LITERATURE
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2.1 History:

Following many pioneering studies in basic insect endocrinology during 1930s and 40s, the discovery of chemical structure of naturally occurring juvenile hormone (Roller et al., 1967) provided the impetus for development of related compounds for insect control. As early as 1934, Wigglesworth described the endocrine function of the corpus allatum (ca) in the blood sucking bug, *Rhodnius prolixus* Stal (Wigglesworth, 1934 and 1936). During his parabiosis experiments, Wigglesworth demonstrated that joining a nymph in the penultimate or an earlier instar with a nymph at the beginning of the last larval instar, results in partial or total suppression of the metamorphosis without preventing an increase in size. In this way VI instar giant nymphs (an additional instar) were produced which eventually changed after another moult into a giant imago in case of *R. prolixus*. Conversely, removal of the ca of the younger nymph by decapitation resulted in a miniature precocious imago. To this humoral factor of the corpus allatum Wigglesworth (1940) named as juvenile hormone (JH) (Novak 1975).

Several investigators, later, established this discovery in other groups of insects: Bounhiol (1938) and Piepho (1939) for lepidoptera, Pfulgfelder (1939) for
Orthoptera. Hadorn and Neel (1938) for Diptera and Radtke (1942) for Coleoptera. Piepho (1950) found that the hormonal action of these glands were order non-specific irrespective of the type of metamorphosis characteristic of the order. It has also been shown that transplants of adult corpora allata in to allatectomised (Fukuda, 1962 and Roller, 1962) and intact larvae (Fukuda, 1963) could duplicate the action of larval corpora allata.

Williams (1956) first made an attempt to elucidate the chemical nature of the juvenile hormone (JH) using ether extracts of male abdomens of saturniid *Hylophora cecropia* (Linn).

The chemical structure of the juvenile hormone (JH) was determined by Roller *et al.* (1965) and Williams (1965). Later Roller *et al.* (1967); Meyer *et al.* (1968); Judy *et al.* (1973) and Bergot *et al.* (1980) isolated four homologous structures having identical morphological activities. For convenience, they were designated as JHI, JHII, JHIII and JHO respectively. However, these compounds differ in physiological activities as demonstrated by a large number of assays (Dahm *et al.*, 1976; Luscher and Lanzrein 1976; Roussel, 1977).

Subsequently, many chemically different compounds from non insect sources were found to possess similar biochemical activities like the JH homologues, popularly.
known as Juvenile hormone analogue or Juvenoids (Schneiderman and Gilbert, 1958; Williams et al., 1959; Schneiderman et al., 1960; Slama, 1962; Poduska et al., 1971; Slama, 1971; Pallos et al., 1971; Rogers and Mouville, 1972; Saxena and Srivastava, 1972; Henrick et al., 1973; Ohsumi et al., 1985; George et al., 1989; Mohsen et al., 1989).

2.2 Metabolism. Transportation and Degradation:

The entire biosynthetic pathway of JH occurs within ca (De Kort and Granger, 1981). With one interesting exception, the accessory reproductive glands of the adult male H. cecropia (Linn) (Dahm et al., 1976), other tissues are unable to synthesize JH.

Basic pathways for JH bio-synthesis were illustrated first by Slade and Zibbit (1971 and 1972). Subsequent works on JH metabolism dealt with expanding early observations to variety of insects done by several workers (Ajami and Riddiford, 1971 and 1973; Metzler et al., 1971 and 1972; Tobe and Pratt, 1974; Hammock, 1975; Tobe and Saleuddin, 1977; Pratt et al., 1978; Hammock and Quistad, 1981; Sparagana et al., 1984; Bhaskaran et al., 1986).

Whitemore and Gilbert (1972), Kramer et al. (1974), Dahm et al. (1976) and Peterson et al. (1977) have studied the transportation mechanism of the JHs from the site of
origin to the target cells. In that they have described two classes of carrier proteins: (a) low affinity high molecular weight lipo-protein and (b) high-affinity low molecular weight protein, present in the haemolymph of insects and carries the JH from point to point.

Slade and Zibitt (1972) were the first to establish two main degradative pathways of JH, one mediated by esterase and the other by mixed function oxidases (MFO). Detail catabolic pathways of excretory mechanisms of JH in different insect groups have also been demonstrated by a number of other authors (Whitemore et al., 1972; Weirich et al., 1973; Slade and Wilkinson, 1974; Yu and Terriere, 1974; Kramer et al., 1977; Wilson and Gilbert, 1978; Mitsui et al., 1979; Sparks and Hammock, 1980).

The metabolism of different Juvenoids and their metabolites have been examined in many Dipteran insects (White, 1972; Solomon, 1975; Rowlands, 1976, Edwards et al., 1988).

2.3 Mode of action and Biochemical effects:

Various theories have been put forward to explain the mode of action of JH, some obviously contradictory (Wigglesworth, 1936; Novak, 1975; Laufar and Borst, 1983). Recently Yamamato et al (1988) have suggested a membrane
protein mediated effect of Juvenile hormone that involves calcium and Kinase C.

JHa seems to act through some general changes in the metabolism or cell division. All these proceed very well in the absence of JH during metamorphosis (Slama, 1971). Compounds similar to isoprenoid JHa are known to form bimolecular lipid-protein membranes (Hanahan et al., 1960) and the direct effect JHa may be to affect membrane permeability (Bauman, 1968; Wigglesworth, 1969; Bauman, 1969). Other theories suggest that the mode of action of JHa may lie in their ability to block the depression, transcription or utilization of fresh genetic information (Slama and Williams, 1966a; Lezzi and Gilbert, 1969 Laufer and Holt, 1970).

Engelmann (1972) have reported enhance RNA synthesis after JH application and Farinha et al. (1988) have published that influence of JH treatment on DNA synthesis can be activated or inhibited depending on the physiological condition of the larvae at the moment of the Juvenile hormone application.

Engelmann (1969 and 1972) and Engelmann et al. (1971) found the de novo production of a specific protein in the serum of adult Leucophaea maderae (Fabricius) and Sarcophaga bullata Parker females treated with JH and JHa. Besides
these studies, many literatures dealing with influences of JHs and JHas on the protein contents of insects during the development have been published. Fristrom et al. (1976) and Breccia et al. (1977) have demonstrated the inhibition of protein synthesis after the application of JHs and JHas. Keeley (1978). Beenakkers (1983). Steele (1983) and Roseler and Roseler (1988) have postulated a dual role of Juvenile hormone in fat body metabolism: (1) induction of protein synthesis and (2) inhibition of lipogenesis (Vitelloiogenin). Ismail and Fouad (1985) have found inhibition of protein synthesis in Chrysomia albiceps (Wiedman) pupae treated with JHas. Kajiura and Yamashita (1989) have observed stimulated synthesis of the female specific, storage protein in male larvae of silk worm Bombyx mori Linn treated with JHa. Gadallah et al. (1989) have demonstrated decreased in total protein content during embryogenesis after treatment of A. (P.) arboreous (Acari: Argasidue) with JH III. Similar results were also reported in the ixodids Dermacentor andersoni Stiles by Bactor and Kamel (1977) and in Hyalomma dromedarii Koch by Kamel et al. (1982). Keeley and Mo Kercher (1985) have shown marked increase of total ovarian protein content of B. discoidalis after injection of JH. Beck and Feir (1989) have got no significant effect on the total protein content of Oncopeltus fasciatus (Dallas) after treating with JH. Conspicuous changes have been observed by different investigators in the glycogen metabolism after the
application of JH and JHa during the development of insects. Downer et al. (1976) have demonstrated depletion of glycogen after the treatment of mosquito pupae with JHas. Similar observations were shown by Ismail and Fouad (1985) in C. albiceps. Klowden and Chambers (1989) in Ae. aegypti. Roseler and Roseler (1986 and 1988) in bumble bee B. terrestris. Gilbert (1967) investigated changes in the lipid content of the ovaries and fat body of L. maderae and found that lipid synthesis by a mating ovary was enhanced by JH application in vitro. Morohoshi and Kiguchi (1969), Stephen and Gilbert (1970), Morohoshi and Fugo (1972) and Morohoshi et al. (1972) have studied various aspects of the effects of JH on lipid and other metabolism in Bombyx. Regarding the effect of JHa on the lipid contents during the metamorphosis of different insects, the most important publications are of Downer et al. (1976) and Mazomenos and Fytizas (1985).

Sehnal (1972) carried out a systematic study of the effects of JH on the oxygen metabolism during larval and pupal development in Galleria mellonella (Linn). No effect of ca implantation was observed in the penultimate larval instar but implantation in the last larval instar was followed by a distinct increase in metabolism in the specimens which changed to supernumerary larvae.

Schmialek and Drews (1965) and Emmerich et al. (1965) have discussed about the effect of JHa on the
respiratory enzymes. dehydrogenase, transaminase enzyme systems. Postlethwaith and Gray (1975) and Sahata (1975) have demonstrated inhibition of acid phosphatase activity in the ovary of *Drosophila melanogaster* Meiger and flight muscle of Douglas fire beetle, *Dendroctonus pseudotsugae* Hopko. Beck and Feir (1989) have reported that JH have no effect on acid phosphatase activity of milk weed bug. Ziegler et al. (1979) and Roseler and Roseler (1986) have found low activity of UDP-glucose:glycogen 4-L-D-glucosyl transferase after the injection of JH to *B. terrestris*. Phosphorylase activity, but, does not get affected by the exogenous application of JH to insects. Topical application of JH III to the tick *A. (p.) arboreus* during embryogenesis had no differences in activity and isoenzyme pattern of malic acid dehydrogenase (MDH), Lactic acid dehydrogenase (LDH), Acetyl choline esterase (AchE) and Alkaline phosphatase (ALP) (Gadallah et al., 1989).

2.4 Morphological and Histological effects:

Exogenous application of JH and JHa to the last larval instar causes severe morphogenetic anomalies that appear to be the mixture of larval and adult characteristics or supernumerary larvae or incomplete emergence of adults from the pupal exuviae or albino pupae (Williams, 1956; Wigglesworth, 1961; Slama and Williams, 1966; Bowers et al., 1966; Spielman and Skaff, 1967; Sacher, 1971; Bhaskaran, 1972; Schaefer and Wilder, 1972; Jacob and Schoof, 1972; Madhavan, 1972; Madhavan, 1972; Schaefer and Wilder, 1972; Jacob and Schoof, 1972; Madhavan,
1973; Postlethwaith. 1974; Arias and Mulla. 1975; Sehnal and 
Zdarek. 1976; Eshita and Kurihara. 1977; Sharma et al.. 1979; 
a and b: Yodbatra et al.,. 1985: Saxena and Sumithra. 1985: 
Amalraj et al.,. 1988: Mohsen et al.. 1989; Kramer et al., 
1989).

reported that the sensilla of the antennal maxillary palp and 
labial palp and abdominal tergits are affected by the JHs and 
JHas in Leucophae madrae (Fabricius). Periplaneta americana 
(Linn) and Blatta germanica (Linn).

Slama and Williams (1966a) first demonstrated that 
the JHa disrupts embryogenesis. when applied exogenously to 
insect eggs. This effect was subsequently shown by many 
authors for different JHs and JHas and found to be potent 
ovicides than the conventional contact insecticides 
(Riddiford and Williams. 1967: Matolin. 1970. Ascher and 
Sehnal (1965 and 1968) studied the effect of JH on the growth
and morphogenesis of internal organs during the development of insects, where they have demonstrated that application of extra JH to the early of the last larval instar completely inhibits metamorphosis but later application resulted in a series of transitions between larval and imaginal shape of the brain and the other organs. Similar results were also reported by Hlinak 1968. Mouze and Schaller 1971. Mouze 1971 and Riddiford 1972. Chudakova and Bokharova-Messener (1968) have shown that the flight muscles of insects ripen without JH whereas exogenous supply of JH and JHa causes rapid degeneration. Awad and Mulla (1984a) have described that the application of the JHa (Cyromazine) to M. domestica affected the muscles causing vesiculation, change of shape, dystrophy, disruption of tonofibrillae but no noticeable histological change was observed in Cx. quinquefasciatus (Awad and Mulla 1984b).

The influence of ca hormone on the development of egg in the ovaries was first shown by Wigglesworth (1936). Subsequently many experiments have been done to analyse the effects of JH and JHa on the morphogenesis of the egg and egg maturation (Masner et al., 1968; Rohdendorf and Sehnal, 1972; Socha, 1974). They have shown that the implantation of ca or administration of JHa at the beginning of the adult emergence and during the egg laying period, inhibits the morphogenesis of the gonads and various deformities in the ovarioles.
Penzlin (1965) and Needham (1965) found that the JH also influenced the regeneration process of insects. Many literatures are available on the various ways in which JH acts in instincts of various insects especially as regard to mating behaviour and migration (Pener, 1965; Barth, 1965; Zdarek and Slama, 1968; Engelman and Barth, 1968; Strong, 1968; Pener, 1968; Adams and Hintz, 1969; Meola and Readio, 1987 and 1988).

Remarkable changes have been observed in the colouration of both larval and adult insects following experimentally interference with JH production (Roussel, 1967 and Truman et al., 1973).

2.5 Aphid Juvenile hormones (JHs) and polymorphism:

Aphids show photoperiodically controlled parthenogenetic/gamic and alate/apterous polymorphism (Hille Ris Lambers, 1966; Lees, 1966; Behura, 1978).

During 1970's the physiological mechanisms involved in regulating this sort of typical polymorphism in aphids received much attention. Staal (1975) and Mittler et al. (1976) have advocated that Juvenile hormones control this polymorphism in aphids.

Hardie (1981a) first established that all the three naturally occurring Juvenile hormones (JHs) have effects on
the parthenogenetic/gamic polymorphism in *A. fabae* Scopoli, where they mimicked long day conditions by inducing parthenogenetic forms. However, the JH's differed in potency in the order JH I > JH II > JH III. This result was obtained even at JH doses below the threshold level for appearance of oviparous/viviparous intermorphs. Hardie (1981 b) further demonstrated the induction of apterisation in the aphid *A. fabae* by topical application of natural JHs. But the activity is in the order JH I > JH II > JH III.

In holocyclic aphids parthenogenetic generation of females during spring and summer are followed by production of males and sexual females in the short days and lower temperature in autumn. Mittler *et al.* (1979) have shown that the photoperiodic induction of males could be prevented in *Myzus persicae* (Sulzer) by treatment with Kinoprene, a juvenile hormone analogue while the anti JH compound preocene III has been reported to induce production of males in the same species (Hales and Mittler, 1981 and 1983). Hardie and Lees (1985) found in *M. viciae* and *A. fabae* that the type of female progeny deposited by short day reared mothers can be reversed by continuous low level exposure to Kinoprene and JH I, with the result of normal Parthenogenetic females in place of expected oviparae.

According to Hardie (1987), the role of Juvenile hormone in metamorphosis is terminated during the third
(Penultimate) larval instar in aphids where adult characters are determined by low or zero titres. Such a strategy enables juvenile hormone to take on precocious gonadotropic function during the fourth larval instar and results in the regulation of the Parthenogenetic morphs under long day conditions. But earlier studies of Hardy (1974), Mittler et al. (1976), Kohno and Takaoke (1977) and Hardie and Lees (1985) had reported that juvenile hormones and their analogues increase the rate of reproduction and total fecundity in aphids. Hales and Mittler (1988) have proposed two threshold levels of juvenile hormone: a low threshold which is assumed to exceed in aphids that undergo four larval instars as in normal, before attaining adulthood, and an upper threshold which is assumed to exceed in aphids under long day conditions and permits all the oocytes to be ovulated as females. Any fall in JH titer below the upper threshold results in the ovulation of males.

Hardie et al. (1985) have quantitated the circulating JHs of *M. viciae* and *A. fabae* at different physiological conditions. Different levels of JH III were detected (0.12 ± 0.03) ng/g in long day forms and 0.04 ± 0.01 ng/g in short day forms), but such a small difference could not clear the context of hormonal regulation of morph determination and left with the possibility that some other juvenilising factor may exist excluding the existing known JHs of aphids (Wigglesworth, 1969).
2.6 Effects on reproduction:

Juvenile hormone / JHa administration in the early phases of gametogenesis, inhibits the process (Manser, 1967; Rohdendorf and Sehnal, 1973; Socha, 1974; Moore and Taft, 1975; Gaaboub et al., 1981 and Iwanaga and Kanda 1988). The sensitive period for this inhibitory effect is, in general, earlier than for follicle stimulation. In some of the insects studied, it comes at the beginning of the adult stage, in others in the pupal instar or (in exopterygota) in the last larval instar. It includes the whole period of gametogenesis from the first oogonia and spermatogonia up to the maximum sex cells.

In anautogenous *Ae. aegypti*, Lea (1963 and 1969) demonstrated the removal of ca within 1 hour of adult emergence, prevented yolk deposition and follicular growth after a blood meal, but when the operation was delayed for 2 - 3 days, egg maturation occurred following blood ingestion. Similar results were also obtained by Gwadz and Spielman (1973). Masler et al. (1980), Kelly et al. (1981), Borovsky (1981), Borovosky et al. (1985), Klowden (1987), Matinez and Hagedorn (1987) and Klowden and Chambers (1989) for both autogenous and anautogenous mosquitoes.

Complete inhibition of reproduction was shown to result from low doses of IGRS applied during the differentiat
ion of follicular epithelial cells prior to adult ecdysis in a wide range of species (MetWally et al., 1972; Rhodendorf and Sehnal, 1972). Besides these studies effects of JHAs on the fertility and fecundity in various insect species have been analysed (Hatakoshi et al., 1985 and 1986; Keil and Othman, 1988).

Male sterilisation, although sometimes observed after JHa application (Tang and Tseng, 1971; Amos et al., 1978) does not appear to be very obvious. However, Daseo (1972) found a reduction of fecundity through the treatment of male codling moth with 1 μg of farnesyl methyl ether. External and Internal morphogenetic effects can influence mating and other reproductive functions directly or indirectly. A well known example is the inhibition of male genital rotation in Diptera, leading to inability to mate. Sometimes only pronounced shortening of adult longevity seems responsible for reduced fecundity (Staal, 1975).

2.7 Insect Control Potential of JH and JHAs:

William (1967) first proposed the insect control potential value of JH and JHAs. Since then a large number of studies relating to the laboratory and field efficacy of JHs/JHAs have been undertaken against a wide range of insect pests (Ascher and Nemny, 1976; Slama and Maid El-Din, 1977; Flint et al., 1977; Johnson et al., 1978 and Retnakaran, 1982).
Effective control of some stored product pests has been achieved by the application of JHas (Strong and Dickman 1973, Kramer and Mc Greger 1978; Mc Greger and Kramer, 1979).

Efficacy of various juvenile hormone analogue formulation in the control of vector and non-vector mosquito species (Cx. quinquefasciatus, Cx. p. molestus, Forskal, Cx. tarsalis, Cx. sallinarius Coquillett, Cx. p. palle\textsuperscript{s} Coquillett, An. quadrivmaculatus Say, An. stephensi, Ae. aegypti, Ae. taeniorhynchus (Weidman), Ae. sollicitans (Walker), Ae. (Ochlerotatus) detritus (Haliday). \textit{Toxorhynchites rutilus rutilus} (Coquillett) have been evaluated extensively both in the laboratory, field and in various mosquitogenic conditions in different parts of the world(Jacob and Schoof, 1971; Jacob. 1972; Schaefer and Wilder. 1972; Hsieh and Steelman. 1974; Sharma \textit{et al}.., 1977; Boonluan panthumachinda and Pimpa Wattanachai. 1978; Self \textit{et al}.., 1978; Raj \textit{et al}.., 1978; Rathburn \textit{et al}.., 1979; Mulla and Darwasheh. 1979; Pridansteva \textit{et al}.., 1980; TenHouten \textit{et al}.., 1980; Das \textit{et al}.., 1981; Burgess and chetwyn. 1983; Tiwari and Saxena. 1984 Wexner. 1984; Darviet \textit{et al}.., 1985: Estrada and Mulla \textit{et al}.., 1986; Amalraj \textit{et al}.., 1988 ; Mulla \textit{et al}.., 1989; Mullingan and Schaefer, 1990).

2.8 Effects on non target-organisms and toxicity:

Studies so far been done, presented no such serious deleterious effects against the non target organisms.
Miura and Takahashi (1974) reported that in field tests copepods showed some susceptibility at the dose of $0.025$ lb Ai/acre, but they concluded that the rates used for mosquito control are probably safe to use in irrigated pastures. Northland and Mulla (1975) reported that repeated treatment of Altosid EC4 to experimental ponds at the rate of $0.1$ ppm ($0.27$ lb/acre) reduced abundance of several arthropod prey and predator species. Steelman et al. (1975) found a reduction in *Tropisternus* spp adult population caused by four IRGS including Altosid. Finney et al. (1977) have shown no effects on diving beetles (Coleoptera) and Zooplankton (Copepoda). The coleoptera were presented by four dytiscid species: *Potamonectes cerisyi* Aube, *Coelambus parallelogrammus* Ahr, *Hydroporus limbatus* Aube and *Hydaticus leander* Rossi. The copepods were represented by Cyclopidae cyclops spp. Breaud et al. (1977) have discussed the effects of IGRs on the natural populations of aquatic organisms in Louisiana intermediate marsh habitat. The acute effects of Methoprene on non target organisms have been demonstrated (Dunn et al., 1974; Takahashi and Miura 1975). The IGR diflubenzuron exhibits larvicidal activity against several anthropophilic and pestiferous black fly species (Lacey and Mulla, 1977 and 1978). Lacey and Mulla (1978) compared the efficacy of diflubenzuron with other juvenoids against *Simulium vittatum* Zetterstedt (Diptera: Simulidae). Case and Washino (1978) have got no population fluctuations of the aquatic organisms

Even though the information is lacking on the metabolism of JH. it appears to have very low toxicity in mammals (Siddall and Slade. 1971; Slade abd Zibbit. 1972). The metabolism of diflubenzuron have been analysed and the metabolic process has been described by Sparks and Hammock (1979). Diflubenzuron was extensively metabolized and readily excreted in rats, sheep and cattle. if given orally (Ivie, 1977, 1978). Significant degradation of diflubenzuron by fish as well as other components of aquatic eco-system like fungi and bacteria has been reported by Metcalf and Sanborn (1975) and Brooth and Ferrel (1977).

Dimilin has low acute mammalian toxicity, but did not affect the growth and organ histopathology (Ferrel and
Verloop, 1975; Miller et al., 1979). Bishai and Stoolmiller (1979) have demonstrated that diflubenzuron is neither cytotoxic nor inhibits the synthesis of complex carbohydrates in mammalian cells.

2.9 Development of resistance to IGRs:

Very few species have shown development of resistance to IGRs (Dyte, 1972; Rowland and Dyte, 1979). The process of accumulation of resistance was very slow (Georghiou et al., 1978; Brown and Brown 1980; Maas et al., 1981). Resistance and cross resistance to insect growth regulators was perhaps due to minimal penetration of the IGRs like Dimilin or higher rate of metabolism in resistant individuals (Plappa and Vinson, 1973; Georghiou et al., 1978; Sparks and Hammock, 1983; Waker and Wood 1986).