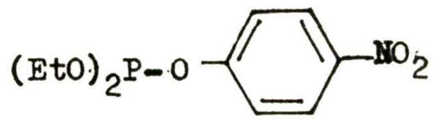
PART-I

INTRODUCTION

Every year India loses crops worth crores of rupees due to pests, insects, fungi, rodents etc. It is also reported that one third of the yearly harvest of the world worth about $75 billion is destroyed by pests, inspite of all the available means for plant protection. A large number of pesticides are marketed nationally and internationally to prevent this loss.

In general, pesticides are classified into two categories - chlorinated hydrocarbons and organophosphorus compounds. In recent years, biologically active oxygen and nitrogen heterocycles have also found use as pesticides. At one time DDT, gammaxine, etc. were used in very large quantities through out the world to protect the valuable crops. DDT or p,p-dichloro diphenyl trichloro ethane was introduced in 1942 by J.R. Geigy under the trade name Gesarol, Guesarol, Neocid etc. P. Muller et. al.[1] first observed that it has strong insecticidal properties. DDT is a potent non-systematic stomach and contact insecticide of persistence on solid surfaces but with little action on phytophagous mites.



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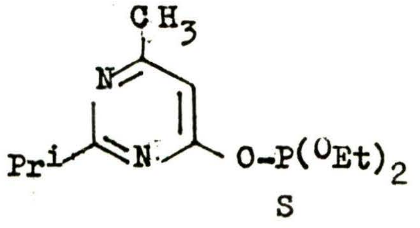
It is phytotoxic except to cucurbits and some varities of barley. One most-used organo- phosphoran is parathion, O,O-diethyl O-4-nitro phenyl phosphoro- thioate (1), prepared by the condensation of O,O diethyl phosphorochlorodithioate with sodium-4-nitro phenoxide. It is a yellow-liquid b.p.: 157-162^{o}C/0.6 Torr. Parathion is also a non-systematic contact and stomach insecticide and acaricide with some fumigrant action. It is non-phytotoxic except to some ornamentals and under certain weather conditions, to pears and some apple varieties.

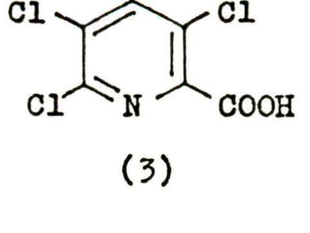
Diazinon (2), O,O diethyl O-2-isopropyl-6-methyl pyrimidine-4-yl phosphorothioate, a widely used organo phosphorus insecticide is prepared by condensing isobutyramidine with ethyl 3-oxobutyrate. It is a non-systematic insecticide with some acaricidal action. Main applications are in rice,



(2)

fruit trees, vineyards, sugar cane, horticultural crops etc for a wide range of sucking and leaf-eating insects. It is also used against flies in glass houses, mushroom houses and against flies. Toxicity is acute and oral LD_{50} for rats is 300-850 mg/kg. It is highly toxic to birds and honey bees , and also to fish.

Besides these there are few other insecticides possessing strong biocidal activities. Among these compounds are

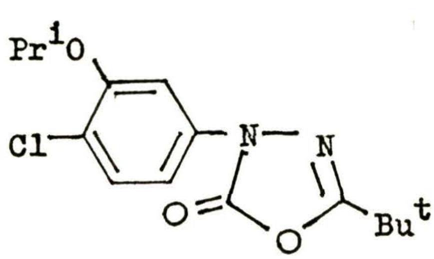


(3)

oxygen-heterocycles, nitrogen-hetorocycles, carbocycles etc.

Pictoram, 4-amino-3,5,6-trichloro picolinic acid (3) and its salts, are good systematic herbicides producing epinasty and leaf curling and are rapidly absorbed by leaves and roots. It is less toxic to fish and aquatic animals.

5-tert-butyl-3-(2,4-dichloro-5-isopropoxy phenyl) 1,3,4- oxadizol-2-one (Oxadiazon) (4) is another selective herbicide, effective against mono- and di-cotyledonous weeds.



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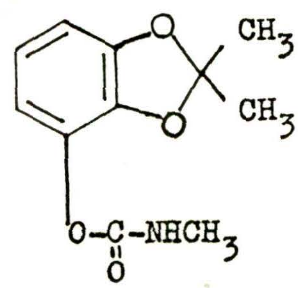
This compound is prepared by the cyclization with carbonyl chloride, of 1-(2,4-dichloro-5-isopropoxy phenyl)-2-pivalyl hydrazine, obtained by acylation of the corresponding phenyl hydrazine.

Active oxygen heterocyclcs Bendiocarb, 2,3-iso propyl- idenedioxyphenyl methyl carbamate (5) an oxygen heterocyclic insecticide, is prepared by the reaction of 2,3 isopropylidene dioxyphenol with methyl isocyanate. Bendiocarb is an insecticide acting by cholonesterase inhibition and is



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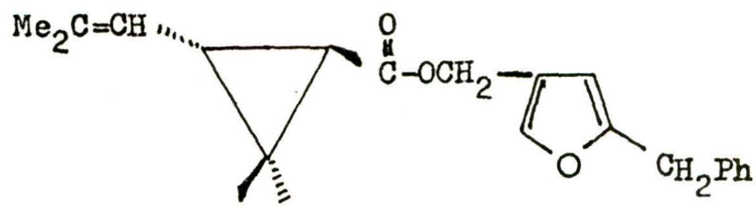
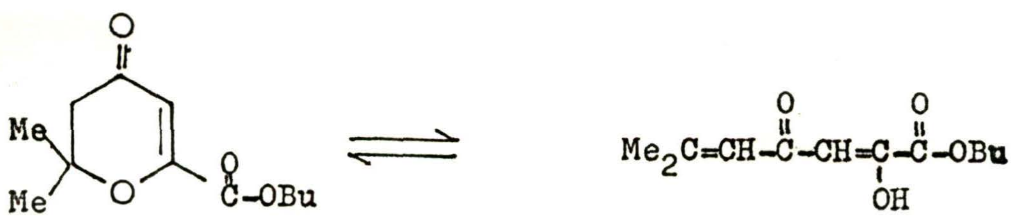


(6)

effective as a contact and stomach poison. It is active against mosquitoes, flies, wasps, cockroches etc. In agriculture, it is active against hepidoptera coleoptera and collembola and especially soil pests. The acute toxicity for most mammals lies in the range LD_{50} 34-64 mg/kg. The dietary and cumulative toxicity to the rats is low but it is too highly toxic to honey bees and LC_{50} for a range of fish species is 0.4-1.8 a.i/ L.

Bioresmethrin (6) a furan derivative is also a powerful contact insecticide first described by M. Elliott et al[2] and is widely used against flies, mosquitoes cockroches as well as plant pests. The toxicity to normal Musca domestica is 50 times that of pyrethins. Butopyronoxyl, butyl 6,6-dihydro-4-oxopyran 2-carboxy-late (7) used as insect repellent has little insecticidal activity.



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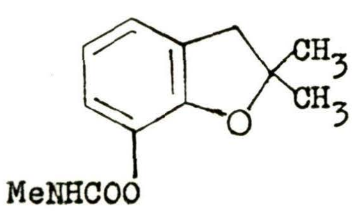
Carbofuran, 2,3-dihydro-2,2-dimethyl-benzofuran-7-yl methyl carbamate (8), is a systematic insecticide, acaricide



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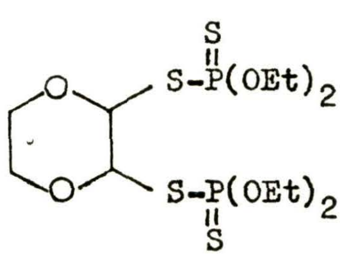

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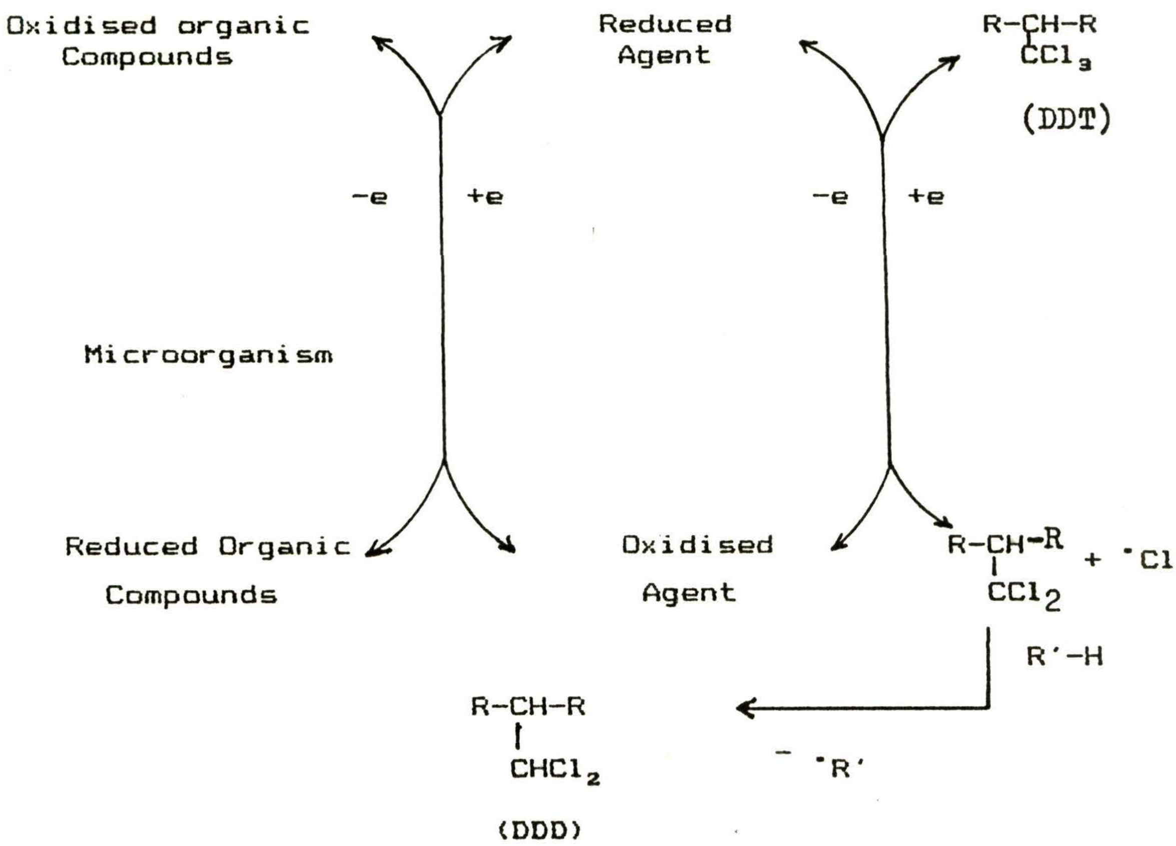
and nematocide and is applied to foliage at 0.25-1.0 a.i/ha for the control of insects and mites. Dioxathion, S,S'-(1,4 dioxane-2,3 diyl) O, O, O', O'-tetraethyl di(phosphoro dithio-nate) (9), is pre- pared by the condensation of 2,3 dichloro-1,4 dioxane with O,O-di ethyl hydrogen phosphorodithioate. It is a non-systematic insecticide and acaricide especially useful for the treatment of livestock to control the external pests including ticks. The cis- isomer is somewhat more toxic to flies and rats than the trans- isomer. LD_{50} value for male albino rats is 43 mg/kg.

It is well-known that certain efficient pesticides, have residual effect. The residual effect is sometimes, more dangerous to ecosystem. For example,DDT has a half life of nearly 20 yrs.. The residual effect of DDT creates more serious problems than the other pesticides, because these other pestcides are relatively resistant to degradation by either chemicals or biological means in the environment.

The chlorinated hydrocarbons are non-polar, relatively immobile and concentrate in biological systems Hickey et. al.[3] reported evidence of extensive contamination of a portion of Lake Michigan.

DDD is formed by the action of microorganisms on DDT is dangerous to humans also. Though the mechanism is not clear, a probable path is shown as follows:



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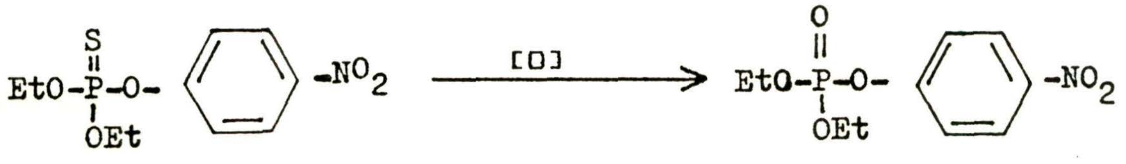
The acute oral LD_{50} for rats is 113-118 mg/kg. It is reported that DDT is actually stored in body fat and finds its way into milk. Bevenue et. al.[4] reported that the bioconcentration of DDT in the environment and its effects on reproduction of higher animals is likely to be more dangerous in future. In 1950 Fleming[5] reported that DDT was persistent in soils and that it had accumulated in amounts of 137-194 lbs/acre under trees sprayed to control Dutch Elms-disease. In the early 1950's Dewitt[6] found that feeding DDT to quail reduced the hatchability of their eggs and the viability of the chicks. Several investigators observed that DDT and other pesticides cause the death of fish and other aquatic life. The other pesticides such as endrin and dieldrin are slightly better than DDT due to their volatility. The acute oral of dieldrinLD_{50} for rats is 46mg/kg and the acute dermal LD_{50} for rats is 10-20mg/kg. Though eldrin in a two year feeding trial with rats receiving 1 mg/kg diet showed no ill effects it is highly toxic to fish.

The organophosphate, cygon has a much greater water solubility and higher vapour pressure than the chlorinated hydrocarbons and relative relatively high adsorption by soil particulate matter. The organophosphorus compounds are not readily volatilised. According to Edward[7] these do not accumulate in soil fauna like earthworms and concentrate less in birds and fish than the chlorinated hydrocarbons. Kleinman et.al.[8] reported that due to relatively high toxicity to humans, some organophosphates are more difficult to use than the chlorinated hydrocarbons. Most of the pesticides are retained in the soil by different types of mechanisms and ultimately go into water. Most of the pesticides decompose photochemically or by aerial oxidation. Thus Parathion hydrolyses or oxidises in aquatic environment to paraxon[9]



(1) (11)

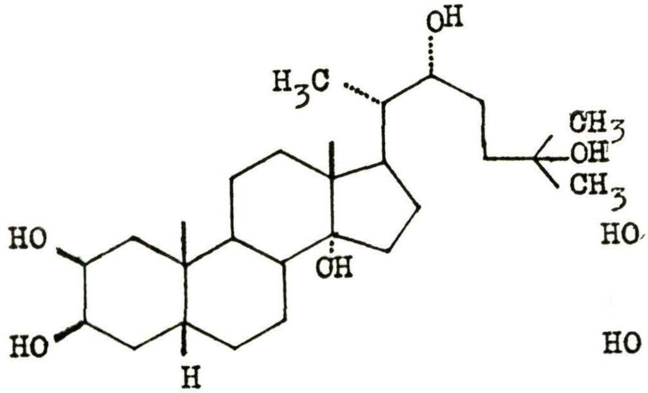
(10), which is more toxic than the parent compound to insects as well as to mammals.

The LD_{50} for male white rats is 14 mg/kg for parathion whereas for paraxon it is only 3 mg/kg. The organic herbicides are plant toxicants that have little or no effect on animals except in unusually large doses.

So, the orientation of present research should be in such a manner that the new synthetic compounds must be "tailor made" according to the general rules which relate structure to biological activity. In the past few years studies on the biology as well as biochemistry of insects and plants have yielded a completely new approach for the protection of plants using secondary plant products that may be toxic to a specific pest species yet harmless to man. This is particularly true of plant protection where the new solutions envisaged are based on the combined knowledge arising from fundamental research in biology, biochemistry, chemistry, plant and insect physiology.

Early research on the biochemistry and physiology of insects was not only the isolation of the different types of hormones but also study of the effect of different compounds on insect behavior. It is reported that nearly 400 repellents have been isolated from 700 species of orthopodes which affect the physiology and/or behaviour of insects.

Insect hormones are classified into three catagories: Peptide hormones, steroid hormones and isoprenoid



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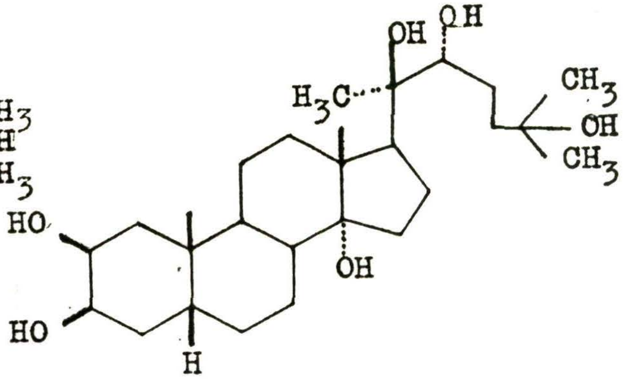
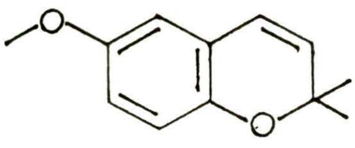


(13)

hormones. Peptide hormones are the products of neurosecretory cells. These are not used in plant protection. Ecdysones and their derivativesare steroid hormones. Ecdysone (12) 2β,3β,14α,22,25 pentahydroxy, cholest-7-ene-6-one, biochemically derived from cholesterol, is secreted from prothoracic glands. Ecdysterone (13) , (20-hydroxy ecdysone) seems to be active. Juvenile hormones (JH) are simple terpenoid esters.

A peptide hormone released from neurosecretory cells activates the prothoracic glands and initiates moulting. Prothoracic glands act as endocrine glands and produce 20-hydroxy ecdysone (13). Ecdysteron acts on the target tissues including moulting. If the corpora- allta secretes juvenile hormone (JH) before or during the secretion of ecdysone the moult will be larval. This hormone prevents the metamorphosis of immature insects by maintaining the juvenile charecter of the growing insect. In the adult female, JH has important role in stimulating the production and incorporation of yolk into the egg.

In 1976 W.S. Bower et. al.[10] isolated two new Chromenes, Precocene I (14) and Precocene II (15) from *Ageratum houstonianum*.



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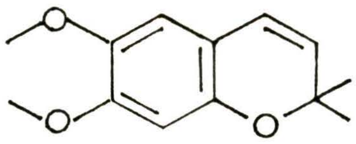

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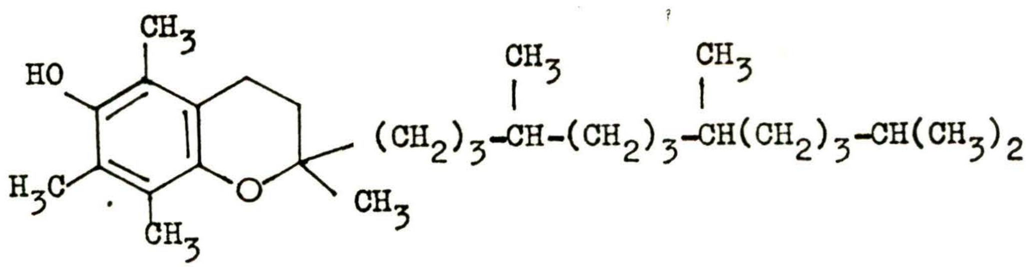
It is widely believed that Vitamine E is an anti-sterility factor. The biologically most active one is the α-tocopherol (16).



(16) (±) α-tocopherol

By comparing tocopherol with precocenes it is clear that the oxygen containing ring contains an additional double bond in precocenes and is probably responsible for its action including precocious metamorphosis[11]. The 3,4 epoxide derived via bioactivation metabolism destroys the insect corpus allatum preventing juvenile hormone production by this gland.

Thouching with Precocene I & II *Hemiptera* undergoes precocious metamophosis. The resulting precocious adult females are sterile and the adults are unable to inseminate normal females. Treatment of sterile female with JH-III results in prompt ovarian development.

Since allatal volume has been associated with JH secretion. The allatal volume of female milk-weed begins to increase on the second day and continues until the ninth day. Treatment with precocene on day one (B) results in no allatal delopment. The apllication of exogenous JH III (C) did not affect allata volume. Treatment of normal 5-day-old insects (D) with precocene II stopped the alla tal volume (fig 17). It is clear that the precocene II could prevent or stop and reverse allatal development. Evi̐dence of JH scretion in female milk-weed bugs can be followed by mesurement of the ovaries, especially the terminal oocyte length since ovarian growth is strictly dependent upon the secretion of JH. Figure 18A illustrates the time course and relative growth of the terminal oocyte. Treatment with precocene in permanent sterility (B) whereas.

JH III treatment of precocene sterilised females on fifth day induces prompt oocyte development. Precocene treatment of normal 5-day-old female about to lay eggs caused oocyte resorption and ovarian atropy. In view of the inhibition of allatal volume caused by Precocene shown previously in fig-17D, it is obvious that precocenes cause

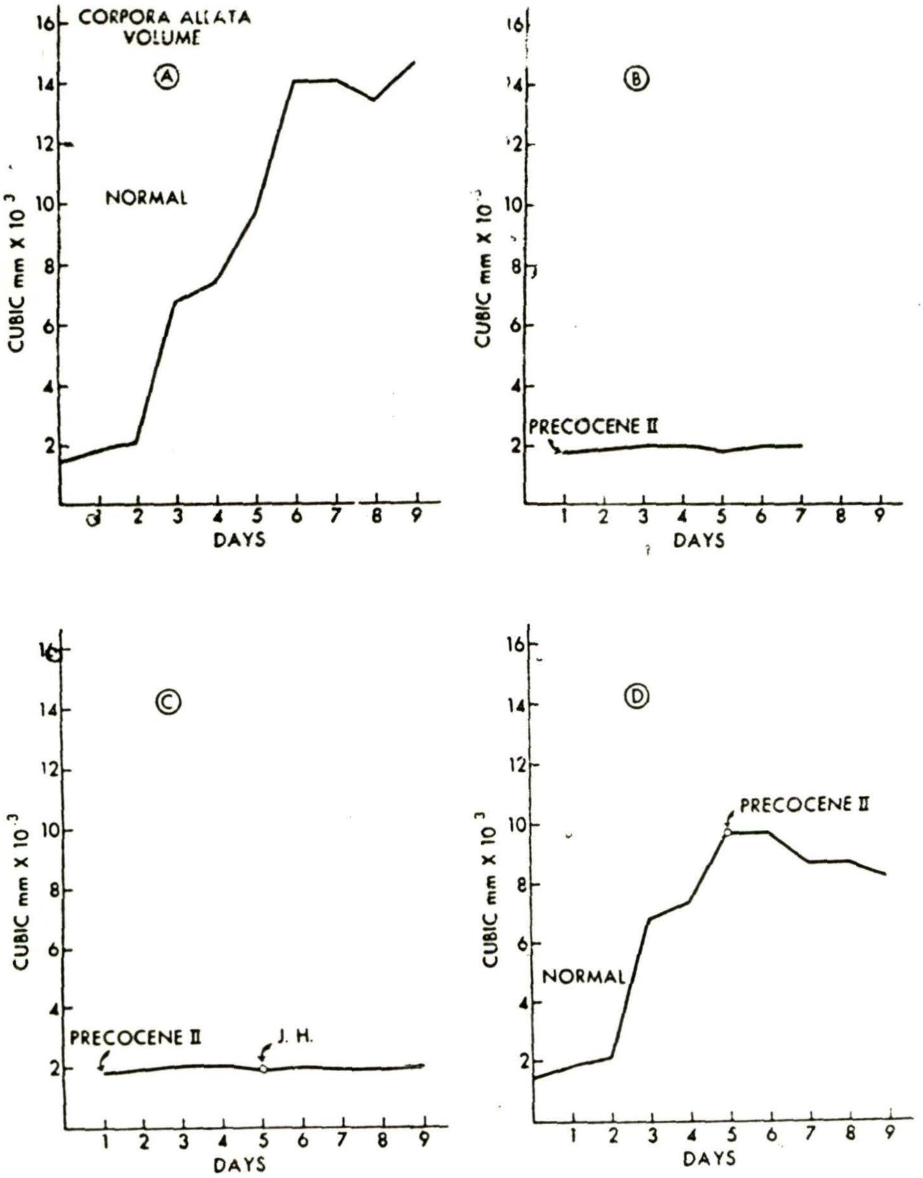


Fig 17: Effect of Precocene II on allatal Volume in female milk-weed bugs following adult eclosion.
(A) change in allatal volume in untreated female, (B) allatal volume is unchange following Precocene treatment, (C) the administration of JH III to precocen treated females does not affect the allatal volume, (D) treatment of normal developing females with precocene on day (5) stops allatal development and causes regression.

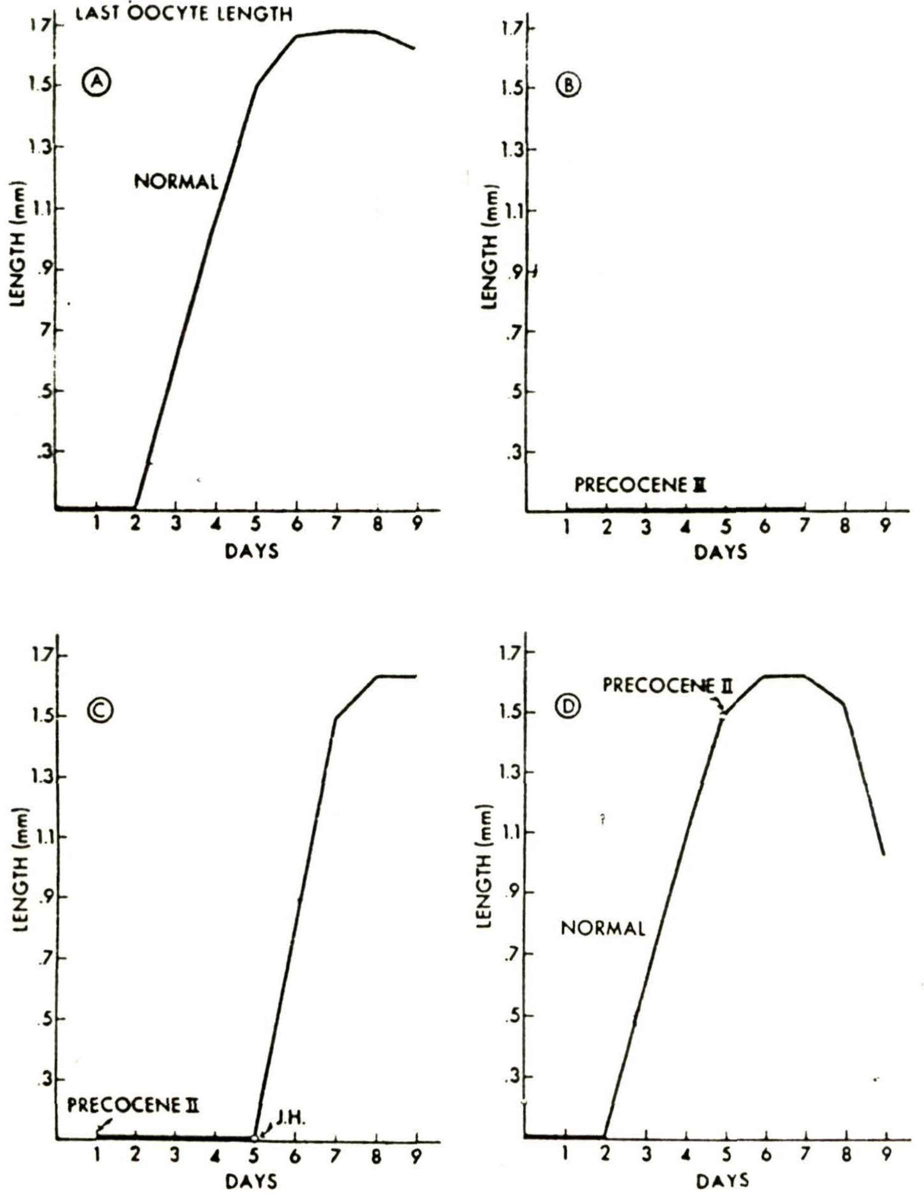


Fig:18 Effect of Precocene II on oocyte growth in female milk-weed bugs following adult eclosion.
(A) normal oocyte growth in untreated females, (B) oocyte growth is completelyprevented by Precocene treatment, (C) treatment of Precocene sterilized females with JH III on day 5 ceases rapid and complete ovarian development, (D) treatment of normal females on day 5 with Precocene stops oocyte growth promotes regression of the ovaries.

allatal regression and stop JH secretion which results in ovarian atropy.