INTRODUCTION
The problem of pollution arose with the onset of human civilization and within a span of 200 years, it is magnified to such an extent that it has become a branch of deep study by scientists, chemists, engineers, biologists etc., throughout the world.

"Pollution" is defined as an undesirable change in the physical, chemical or biological characteristics of our environment that may harm human life or that of desirable species. This problem is very severe in technologically and industrially advanced countries, and less in the case of developing and under developed countries. The difference is only the magnitude in the developing countries, where the pollution problem is more confined to urban areas, comprising more industries and the population density is high compared to the rural areas where planning in respect of growth and development in relation to men and animals is in proper perspective. Human society disposes certain kinds of byproducts and waste products which are injected into the biosphere in great quantities, affect the normal functioning of ecosystem and have adverse effect on man and the fauna and flora surrounding him. Among
the various pollutants, chemical pollution of the environment occupies a pivotal place.

Chemical pollution of the environment is considered to be a major and serious problem and this is known to occur in different ways viz., organic and inorganic chemicals (Mc Kee and Wolf, 1963) oil refinery (Sood, 1999) radioactivity (Olson, 1961) and pesticides (Hayes, 1966). Recent studies on the fresh water eco-systems show the pesticides to contribute much to the chemical pollution (Brown, 1978).

1. Pesticide and its mode of pollution

Pesticides occupy a rather unique position among the many chemicals that man encounters daily, in that they are deliberately added to the environment for the purpose of killing or injuring some form of life. Ideally their injurious action would be highly specific for undesirable target organisms. In fact, however most of the chemicals that are used as pesticides are not highly selective but are generally toxic to many non-target species, including humans, and other desirable forms of life that coinhabit the environment. Therefore, lacking highly selective pesticidal action, the application of pesticides, most often be predicated on selecting quantities and manners of usage that will
minimize the possibility of exposure of non-target organisms to injurious quantities of these useful chemicals.

The first truly global environmental summit was held in Brazil in 1992. The governments in attendance agreed to work jointly to solve specific environmental problems that had a potential radical changing human existence (United Nations Environmental Programme, June 1992). Among those threats targeted for long-term planning and action was the increasing pollution produced by a group of chemicals known as persistent organic pollutants or pops.

Pesticides pose a menacing threat to the human well being in the third world countries because of their free availability, lack of adequate protection against them, improper storage, excessive and wasteful use leading to environmental pollution, and absence of safety warnings, apart from the residues finding their way into the food. In a remarkably well documented book (A growing problem pesticides and the Third World Poor) published in 1982 by Oxfam, researcher David Bull and his colleagues have reported that there are many dimensions of the problem and their findings deserve the atmost attention by planners, academicians, bureaucrats, manufacturers, dealers, public health
officials, voluntary agencies for rural development, farmers, service societies, communicators, media men, agriculturists, home-gardeners - in short, all who have something to do with the pesticides.

There are many examples of mass destruction of different crops by plant pests all over the world, leading to widespread shortage of food grains. This problem becomes much more acute in view of the increase of human population. Many economic goods such as wood, paper, products made of cotton, wool and silk, raw and crude rubber etc., are also being damaged by insect pests and microorganisms. Mites and other parasitic forms are vectors of infectious diseases and cause damage to animal husbandry. Even man is also being dangerously affected by such disease as encephalitis, typhus, sleeping sickness, filaria, malaria etc. the vectors of which are insects.

The most convenient means for controlling harmful organisms and pests is the chemical method. To meet the increased demand for food and to improve the public health, many chemicals have been used in the agricultural and public health operations to combat the ravages of pests and disease-producing organisms. The chemicals used to destroy selectively any species of pest in a biological community are
known as "pesticides". The use of pesticides sharply decreased the losses to the natural economy from various pests and the high economic efficiency achieved with the use of pesticides in agriculture and other branches of economy has favoured the rapid development of these pesticides both qualitatively and quantitatively.

The needs of the present day have intensified research interests in the use of mixture of chemical compounds for environmental protection (Morse, 1978). Studies on interaction of pesticides, herbicides or with other environmental factors and of interaction with non-toxic compounds are well documented (Livingston et al., 1974; Nimmo and Bahner 1974; Akobundu, et al., 1975; Macek, 1975; Bahner and Nimmo, 1976; Hoss et al., 1977; Dikshith et al., 1978a, b). The significance of the interaction of pesticides on induction of toxicological effects in animals is well discernible from the studies of Frawley (1965), Su et al., (1971); Cohen and Murphy (1974). The accumulation of organic pesticides in the foodchain cycle has long been worked out as the root cause of health hazards in human beings (Abbott et al., 1966; Macek 1969; Edwards 1973; Portmann, 1975; Parish et al., 1976; Hileman 1991; Rea 1992; Devis et al., 1993; Li et al., 1996; Rea 1996;
Depending on the nature of the pest intended to be controlled (an insect; parasite, fungus, rodent, weeds, soil nematodes etc.), pesticides are classified as insecticides, fungicides, rodenticides, herbicides, fumigants, molluscicides, nematicides, ascaricides etc. A detailed nomenclature and classification of pesticides with emphasis on practice in Yugoslavia was made (Mojasevic Milica, 1980). Most of these pesticides are not specific in their action. They not only kill the pest but also effect the organisms whose control is not intended. Hence a general term "biocide" has been preferred by many authors in order to emphasize the overlapping ecological effects of such compounds. Based on the chemical nature of these pesticides they are classified into three general groups:

a. Inorganic compounds including arsenicals, mercurials, borates and fluorides,

b. natural organic compounds derived from plants like nicotine, pyrethrum, rotenone and derris etc.,
c. Synthetic organic compounds like organochlorides, organophosphates and carbamates [Rudd, 1964; Mojasevic and Milica, 1980; Sanchez - Fortun and Barahona 2005; Graig et al., 2005].

2. Manufacture and consumption of pesticides

A large variety of potential pesticides are now being synthesized and used by different nations replacing the lower toxic and low potency chemicals for the pest control. In India, pesticides come into wide use around 1994. The manufacture of pesticides began in India in 1952 with the production of BHC followed by DDT. Among the South Asian and African countries, India stands second. Of the pesticides manufactured, 126 products have been registered and licensed for use in agriculture. The Government of India have issued licences for the production of 75,000 tonnes of various pesticides, out of which a capacity of 58,416 tonnes has already been achieved (Elbert and Neumen, 1996).

Over 80,000 tonnes of various pesticides are consumed by agriculture and public health agencies in India. The total installed capacity meets about 80 percent of the requirement. At present 23 units are engaged in manufacturing technical grade pesticides and
about 50 units are preparing formulations based on technical grade pesticides. In addition, about 350 small scale units undertake the manufacturing of conventional formulations. The need for certain sophisticated and expensive pesticides is being met by imports. Import of pesticides have amounted to about 3,886 tonnes during the year 1983-84 (Pesticide Information, 1984).

Eventhough production of pesticides in our country is sizeable, yet the consumption rate of pesticides per hectare is very low. The average per hectare consumption of pesticides grew from 3.2 g/ hectare during 1983-84. It is estimated that during 1984-85, production and consumption of technical grade pesticides is of the order of 58,416 tonnes for agriculture and public health operations (Visweswaraiah et al., 1975 ; Pesticides Information, 1985C) have reported that on world wide basis, yearly about 20 million tonnes of organic chemicals enter the environment.

3. CLASSIFICATION OF PESTICIDES

There is no universal phenomena regarding the classification of pesticides. Based on the target species, pesticides can be classified as
insecticides, ascaricides, helminthicides, rodenticides, molluscicides, bacteriocides, herbicides, fungicides etc.

Pesticides based on their chemical nature, are classified into three categories (Sood, 1999).

a) Inorganic compounds: borates, fluorides, arsenicals and mercurials.

b) Natural organic compounds: Organochlorides, organo-carbamates and organophosphates. In recent times, these three types are used as popular pesticides.

1. ORGANOCHLORIDES

These are basically organic compounds that have been chlorinated with several atoms of chlorine per molecule. These insecticides have very low solubility in water but are readily soluble in fats (Abbot et al., 1965). These compounds are chemically stable and show considerable persistence upon introduction into physical environment. Since these compounds are stable and persistent, they are referred to as hard pesticides (Abbott et al., 1966). These are less acutely toxic but having greater potential towards chronic toxicity. These are called as 'neuropoisons'. Some examples of these compounds are
stable and highly persistent. DDT, lindane, heptachlor, mirex, chlordan, aldrin, dieldrin, toxaphene etc., under biological magnification (Macek, 1969; Petrocelli et al., 1974)

2. ORGANOCARBAMATES

Carbamates are esters of carbonic acid \([\text{HO C}(\text{o}) \text{CNH}_2]\). Free carbamic acid is not known to occur in nature. These compounds do not accumulate in the biosystem but are rapidly degraded and eliminated. Mode of action of organocarbamates is similar to that of organophosphates by inhibiting acetylcholinesterase, neurotransmitter enzyme. Most of the carbamate compounds are used as powerful insecticides. The action of carbamate increases by the addition of small amounts of synergistic compounds.

3. ORGANOPHOSPHATES

Organophosphorus compounds contain phosphorus as the active element. These organophosphorus compounds first developed by Gerhard Schradr in Germany. The usage of these compounds is increased considerably as they are found to be less persistent and less residual in the environment. Hence the usage of organochlorides is decreased (Casarette et al., 1968; Deichmann and Mac Donald, 1971).
Due to biological biodegradability and specificity in action (Fest and Schmidt, 1973) OP insecticides became second generation chemicals. Tetra ethyl pyrophosphate (TEPP) had entered as the first organophosphate insecticide in Germany in 1946 to control pests. These are less likely to accumulate in soil or to be transferred through food chains into parts of ecosystems (Metalev et al., 1983). The sequel of enhanced production of organophosphorus insecticides with varied types and formulations like parathion, malathion and methyl parathion etc. was owing to increased developments of synthetic pesticides for use in the public health and agricultural programme (Hayes, 1963; Murphy, 1980).

Melnikov (1971) and Sood (1999) pointed out that many of the OP compounds have the disadvantage of having the relatively ion toxicity to vertebrates. But a large number of these compounds having relatively moderate or low toxicity to mammals. The suitability of OP insecticides in agriculture for the eradication of pests and insects was demonstrated by Gerhard and Schrader in Germany (O’ Brien, 1967).

Recently, more than, 1,00,000 different organophosphates have been synthesized and their insecticidal properties were evaluated (Pesticide Information, 1983). Malathion, parathion, methyl parathion,
phosphamidon, dimethoate, fenetrothiion, phorate, disulfoton, formothion, diazinon, demeton etc., come under this group. It is estimated that 50,000 of them had been synthesised in 1959 (Metcalf, 1959). The OP insecticides are of 3 types with different molecular forms namely phosphorothionates, phosphorodithionates and phosphates (Brown, 1978). Many OP insecticides are absorbed by skin and by the respiratory and gastrointestinal tracts. They are potential inhibitors of AchE (O'Brien, 1960).


The term organophosphate, covers all the toxic organic compounds containing 'phosphorous'. Most of them are considered as esters of alcohols with a phosphoric acid or as any hydrides of a phosphoric acid with some other acid (O’Brien, 1967). Generally, all the organophosphates have the following common structural features.

\[
\begin{align*}
\text{R} & \quad \text{Y} \\
\text{R'} & \quad \text{P} - \text{X} - \text{R''}
\end{align*}
\]
Where $R$ and $R_1 = \text{Usually short chain hydrocarbon (or) hydrocarbon and oxygen groups.}$

$X, Y = \text{Positions having either S (sulphur) or O (Oxygen) groups.}$

$R - X = \text{The region possessing the group that is metabolised by the insects.}$

The central phosphorous atom (P) is highly electrophilic and key to the observed physiological effects.

In the last four decades there has been an increase of the pesticides in public health operations and agriculture (Edwards, 1973; Murphy 1980; Hayes, 1982). OP compounds: Biological activity of insecticidal organophosphates is not limited to insects. They are toxic to mammals and to other organisms particularly to those in which ChE place a vital role (Carvalho et al., 1994b). The OP compounds to be used extensively because of the following reasons.

a) Greater effectiveness against some species of insects.

b) Development of resistance of some insects towards organo-chlorine compounds.

c) The present environment safety offered by organophosphates by virtue of their more rapid degradation.
Mode of action of OP is extensive and well illustrated (Verloop, 1972; Fest and Schmidt, 1973; Freed et al., 1979; Mulla and Mion. 1981). It is the only class of pesticides whose action is known in great deal at the cellular and molecular levels (O’ Brien, 1967; Biddinger and Hull, 1995).

4. MODE OF ACTION OF OP INSECTICIDE

The main qualifying character of organophosphate compounds as insecticides is based on its high anticholinergic nature. All the acidic hydrogens around the phosphorus atom in phosparic acid must be esterified and the group ‘X’ should possess a non-hydrolc like character. The organic groups may be attached directly to OP by either O₂ or N or S (Aldridge, 1981). Since acetylcholinesterase inhibiting property of many compounds have been demonstrated by several workers (Aldridge, 1950; Wilson, 1960; O’ Brien, 1967; Edwards, 1973; Murphy, 1980; Hayes, 1982).

The inhibitory effet of organophosphates on cholinsterase is the base for their biological activity (Hellenbrand and Krupka, 1970). The enzyme had two sites, a negatively charged, ‘anionic site’ which binds cationic part of the substrate and relatively non-specific ‘esteric site’
which catalyses the hydrolysis of ester linkage (Green et al., 1990). In the esteric site there are two groups viz., serine hydroxyl group and acid group. The reaction between organophosphorus compound and cholinesterase is mainly a nucleoophilic attack of serine hydroxyl on to phosphorus atom, and it is facilitated by the acid or basic group present in the esteric site, yields phosphorylated enzymes. This, then results in acetylcholine accumulation leading to neurotoxicity (O' Brien, 1967). Nachmanson and Field (1947) reported that the death of the organism occurs when the brain acetylcholinesterase is inhibited by 95%. The inhibition of acetylcholine in blood and brain during pesticide intoxication.

Ishaaya and Degheele (1998) demonstrated interference of OP toxicants with a specific membrane bound protein which has been characterised as neurotoxic esterases. Some of the commercial pesticides contain thiophosphoryl group (P=S) are usually weak inhibitors of AchE in vitro, but once activated in vivo by mixed function oxidase system, they become strong inhibitors of AchE.
5. BIOLOGICAL UPTAKE OF PESTICIDES

Mostly the pesticides can enter into the biological products through water born residues, direct or indirect uptake by ingestion of contaminated food, absorption through integument (Sood, 1999) or through particulate matter etc. Aquatic organisms can tolerate pollutants only at low concentrations. Usually polluted particulate matter adhere to the surface of the plankton which in turn are ingested by higher aquatic organisms. Some of these chemical toxicants are concentrated from water by small aquatic organisms which become concentrated in the higher organisms through the food chain cycle. This process is called “Bio-magnification”. Generally uptake of pesticides is a process involving surface absorption followed by absorption into the cells (Campos et al., 1996). In higher invertebrates, accumulation of pesticides occur by (a) ingestion of contaminated food. (b). Direct absorption from water through gills. (c) Absorption through gills and gut are reported to be considered as main routes of uptake of pesticides.

Intake of food may differ, depending upon the environmental conditions and nature of organisms but absorption through gills and gut are considered as main routes (Addison, 1976). In fishes, pesticides
enter through gills (Holden, 1962; Macek et al., 1970). The same thing happened in snails also. In crab, the principal mode of uptake of pesticides is through the gills (Holden, 1965), absorption through the integument (Kerr and Vass, 1973).

Normally the aquatic environment receives pesticides through the following routes.

a) Surface run off and sediment transport from treated soil (Gillet et al., 1970; Bauman, 1981).

b) Industrial water discharge as factory effluents.

c) Direct application as serial spray on granules to control water inhibiting pests.

d) Disposal of waste products by pesticide processing (Chowdary et al., 1981).

e) Spray drift for normal agricultural operations (Westlake and Gunther, 1966)

f) The aerial application of pesticides (Abbott et al., 1965)

g) Municipal wastes discharge as sewage effluents.

h) Agricultural wastes

i) Accidents and spills

j) Heavy rainfall immediately after aerial application of pesticides has a higher potential for pesticide transport into the water environment (Sood, 1999).
Kamanyire and Karalliedde (2004) in their review article explained OP toxicity as follows.

The ubiquitous organophosphates present a continuing health hazard in agriculture, public health eradication programmes and as chemical warfare gents. Despite significant progress in understanding the potential mechanisms of toxicity far beyond the commonly accepted mechanism of cholinesterase inhibition in intentional exposures, the precise health effects following occupational exposures are yet to be completely defined. A much greater understanding exists of the clinical features of organophosphate poisoning. These are characterized by a triphasic response involving an initial acute cholinergic phase, an intermediate syndrome (both associated with high mortality) and a disabling but non-lethal delayed polyneuropathy. The delayed polyneuropathy may occur in the absence of the cholinergic or intermediate phases. However, progress is still required in order to improve the quantification and assessment of occupational exposures and the implementation of appropriate preventive measures. Finally, evidence based guidelines for appropriate of optional therapeutic interventions following poisoning are required urgently and collaborative work with colleagues in developing countries, where the occurrence of organophosphate exposures is more frequent, may provide the answer. The above is further supported by many authors (Coggon, D. 2002; Marrs, TC. 2001, Karalliedde et al., 2003; Karalliedded and Henry 2001; Karalliedded, 2002; Moretto and Lotti 2001; Cocker et al., 2002).
6. IMPACT OF PESTICIDES ON PHYSIOLOGICAL, BIOCHEMICAL AND BEHAVIOURAL ASPECTS OF INVERTEBRATES AND VERTEBRATES

Eventhough, the organophosphates mainly have their target enzymes, they can also bring about physiological and biochemical changes in the tissues of various organisms (Kohli et al., 1975). The toxicity of pesticides depends on various factors like species and tissue specificity (Pandian and Bhaskar, 1983), temperature (Bansal and Bansal, 1980; Namiyama et al., 1980), pH (Ishaaya and Degheele, 1998), hardness of water (Pickering et al., 1962; Pandian and Bhaskar, 1983), size, time (Bansal and Bansal, 1980) and the stage of growth and development (Hithibron, 1967; Pawar et al., 1983). There is noticeable behavioural changes like irritability, loss of equilibrium and immovability leading to death, owing to pesticiede toxicity (Koundinya and Ramamurty, 1979; Jayantha Rao, 1982; Narasimhamurthy, 1983; Sambasiva Rao et al., 1985).

Invertebrates constitute a very large portion of the fauna in both aquatic and terrestrial ecosystems. From an ecological point of view these animals play an important role in food transferring or energy flow in the food chain. The disruptions caused by pesticide stress in one or more of these organisms may interfere with other interdependent components of the food chain. Mulla et al. (1981) reviewed the effect of OP on invertebrate fauna. Reduction in growth and survival of E. gracilis was reported by Moore (1970). Ishaaya and Degheele (1998) studied the effect of parathion on rotifer species, Ishaaya and Degheele (1998) reported that leech, Hirudo ripponia developed resistance to the OP compounds such as parathion and malathion on molluscs, but Lowe et al., (1970) reported more susceptibility of oysters to malathion. Ishaaya and Degheele (1998)
studied the response of the fresh water mussel, *Anodondonta cygnea* and its larvae to malathion treatment. They found that the activity of adults was significantly reduced by 10 mg/L at a 48h exposure period but the larval population were sensitive to 0.01 mg/L concentration.

Much work has been done on the biochemical effects with special reference to carbohydrate metabolism of selected biosystems inclusive of molluscs (Ramana Rao and Ramamurthy, 1980; Sastry and Sharma, 1980; Siva Prasad Rao, 1980; Pala et al., 1991) studies on oxygen consumption showed significant decrease both at whole animal and tissue level resulting in hypoxic condition (Sreenivasamurthy, 1983). Organophosphates inhibit the oxidative metabolism by inhibiting the oxidoreductase system (Sitkiewiez et al., 1980).

The studies on tissue lipid metabolic profiles of molluscs are scanty (Mullcho Pandhyay and Dehadrai, 1980; Tayyabha et al., 1981; Swami et al., 1983). In addition to carbohydrates, lipids are also affected by OP pesticides (Buchet et al., 1977). Earlier studies showed that administration of pesticides resulted in increased levels of acetoacetate and B-hydroxybutyrate (Domsche and Claussen, 1977).

Very few reports were available on the effects of organophosphate compounds on nitrogen metabolism in non-target organisms (Kabeer Ahmed et al., 1978; Park et al., 1983; Kasi Reddy, 1984). Recent studies on protein metabolism during organophosphorus poisoning showed decrease of protein content followed by increased levels of aminoacids (Kasi Reddy, 1984).
Not only that, pesticides lead to alterations and changes in the endogenous physiological process of the susceptible organisms. Neurotoxic effects also leads to changes in the biochemical functions of the organisms. Butler (1966; 1969) reported, reduced pumping rate and increased shell movements in bivalves as a response to water born pesticides residue. Costa (1970) recorded increased heart beat in the fresh water shrimp, *Cardina pristis* in response to pesticide treatment. George *et al.* (1957) have described disturbed motor coordination in the Fiddler crab, *Uca pugnax*; after their tidal maarshy environment was sprayed with strobane, DDT and BHC. Several pesticides and polychlorinated biphenyls have been tested on the behaviour and sensitivity of several species of fiddler crabs to DDT (Odum *et al.*, 1969), chlorinated hydrocarbons (Klein Limcer, 1974), dieldrin (Klein Limcer, 1974) and temephos (Ward and Howes, 1974; Ward and Bush, 1976; Ward *et al*.; 1976; Sood, 1999) their studies showed disturbances in their populations either due to mortality or in their behaviour effects upon exposure to subacute concentrations of pesticides were observed in the gold fish, *Carassius auratus* (Day *et al*., 1972).

Sreenivasulu Reddy and Ramana Rao (1985) reported changes in the respiratory metabolism of the marine crab, *Scylla serrata*, under

Decrease activity in succinate dehydrogenase was observed in the tissue of fresh water mussel pelecypod, *Lamellidens marginalis* exposed to malathion (Sood, 1999). Costa (1970) recorded increased rate of heart beat in the fresh water shrimp, *CARDIA PRISTA*, in response to pesticides. Organophosphorus insecticides are also effect the muscular system by the quick fatigue and milk weakness followed by involuntary twitching, scattered fasciculations and crams. Muscular weakness of the respiratory muscles is also observed. The effect of PCB exposure on the haemolymph content, osmotic regulation, chloride and waste fluxes in the shrimp, *Palaernoetes pugio* was observed. In crab, *Carinus magister* (Sood, 1999) and in other crustacean species, blood Mg$^{++}$ concentration is effected under methoxychlor exposed. Due to organophosphorous compounds there is a marked change in the feeding habits (Nimmo and Blackman, 1972). The OP are found to reduce the reproductive capacity and growth rates in prawn. *Macrobrachium lamorri*.  

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It is observed that vident shivering of the body followed by conclusions and paralysis with endosulfan (Cox et al., 1995 b). By industrial effluents toxicity in freshwater cat fish, the behavioural changes were observed (Cochran, 1994). It is also observed that changes in body weights, ionic fluxes of non-target organisms treated with pesticides (Verma et al., 1979; Kabeer Ahammed et al., 1981; Radhaiah et al., 1986; Aravinda Baby, 1986; Jayantha Rao et al., 1987; Usha Rani and Rmamurthy, 1987; Azarbaigh, 1988; Radhaiah, 1988), Amono acids (Natarajan, 1983; Kabeer et al., 1984; Radhaiah, 1985; Jayantha Rao et al., 1987). Proteins (Anand Swarup et al., 1981; Dubale and Mohini, 1982; Ramalingam et al., 1982; Narasimhamurthy, 1983; Azhar baigh, 1988; Radhaiah, 1988) and lipids (Madhu, 1983; Narasimhamurthy, 1983; Jayantha Rao et al., 1987) of the pesticidal exposed fish were reported.

OP compounds are known for their inhibitory effect on the activity of Achesterases. Inhibition of brain AchE on different fish species was reported by different authors. Lethal and sublethal effects of methylparathion on AchE were studied by Coppage et al., (1975) a Lagodon rhombodies. Coppage and Mathews (1974) studied the short term effects of malathion, and parathion on brain AchE activity of spot,
Leistomus xanthurus, pinfish, Lagodon rhombodies, Micropogon undulatus, sheeps head minnows, Cyprinodon variegatus. The activities of other enzymes like acid and alkaline phosphataes, aminotransferases and oxidative enzyme like succinate dehydrogenase, lactate dehydrogenase and glutamin dehydrogenase and ATP ase are also known to be altered by organophosphorous compounds. Altered activities of alkaline phosphotase, acid phosphotase, pyruvic dehydrogenase, succinate dehydrogenase and ATPase were reported by Sastri and Kavana Sharma (1980) with diazinon in Ophiocephalus punctatus. Dalela et al., (1978) reported the inhibition of acid phosphotase of liver, kidney, muscle of Channa gachua exposed to rogor. Lipid esposition was observed in fish liver due to Dylox CR. Serum glucose level was increased after the administration of malathion, dipterex and DDVP to carp (Bermudez et al., 1991).

Induced hyperglycemia with methyl parathion in the murrel, Chenna punctatus was reported by organophosphorous pesticides can also affect the membrane permeability and active transport mechanism. Sublethal parthion treatment reduced haemocytes, number of erythrocyte and leucocytes in the blood of Notimigonus crysoleucars (Rao et al., 1999).
In crustaceans the synthetic organic pesticides reduce molting process particularly in crab and prawn (Nagabhushanam et al., 1983). The pesticides are known to cause hyperexcitability followed by rapid swimming and vigorous movements of pleopods in shrimps (Sarojini and Gyananath, 1983). Crustaceans show considerable changes in the rate of respiration at a whole animal and tissue levels, when exposed to different pesticides (Chandrasekhar and Natarajan, 1982; Dasaratharamaiah, 1984; Sreenivasulu Reddy and Ramana Rao, 1985). Many enzymatic and biochemical changes were observed in different crustaceans subjected to acute or chronic exposures. Enzymes like ATPase, acetylcholinesterase, succinate dehydrogenase, malate dehydrogenase, isocitrate dehydrogenase, cytochrome-c-oxidase were inhibited under sumithion intoxication in Oziotelphusa senex senex (Sreenivasulu Reddy et al., 1982b; Bhagyalakshmi et al., 1984).

In arthropods, the mode of action of organophosphorus pesticide include inhibition of the AchE (Bhagyalakshmi, 1981).

Phenthoate, a compound of organophosphorous family was selected for the present study. The structure and properties of phenthoate are dealt with in "Materials and methods".
7. NON-ENZYMIC REACTIONS OF ORGANOPHOSPHATES

The two important non-enzymic reactions of the OP compounds are hydrolysis and isomerization which alters the essential biological properties (O'Brien, 1967).

All organophosphates are susceptible to hydrolysis, where the hydroxide ion is responsible for the hydrolysis. The mechanism involves the attack of OH\(^{-}\) (hydroxide) group on the phosphorous atom. This is called nucleophilic attack i.e., negatively charged OH\(^{-}\) group attacking positively charged phosphorous. The more positive the site, the more effective is the attack. The rate of hydrolysis can be determined by the properties of the group attached to the phosphorous. Some groups are electrophilic (electron with drawing groups) which make phosphorous more positive, and which makes the atoms more negative. The susceptibility of organophosphorous pesticides mainly depends on the electrophilic character of the groups attached to phosphorus. Any chemical or metabolic change that modifies electrophilic character will alter the susceptibility. Because O is more susceptible than S, the conversations of these groups influence the susceptibility of hydrolysis (O'Brien, 1971). Many compounds like amino acids, hydroxamic acids,
chlorine, inorganic phosphates and copper and molybdate ions promote
the hydrolysis of organophosphate (O'Brien, 1960).

The other non-enzymic process is isomerization. The commonest
isomerisation is the thiono-thiolo group, where the sulfur changes from
the thiono (\(=S\)) to the thiolo (\(-S-\)) form. This process is slow at room
temperatures and occurs rapidly at high temperatures. Isomerizations
are effective in converting \(P=S\), to \(P=O\) form which increase the
susceptibility to hydrolysis. This also increases the potency against

8. METABOLISM OF ORGANOPHOSPHOROUS PESTICIDES

Literature on the metabolism of different organophosphorous
compounds is very extensive and some of the investigations are like the
metabolism of malathion in cow, hen and white mouse on the
metabolism of sumithion and methyl parathion in mouse and housefly,
metabolism of dimethoate in insects and mammals (Kruger \textit{et al.},
1960), in cow (Dauterman, 1971), sheep and guinea pig (Uchida \textit{et al.},
1964).
Based on toxicity, the metabolism of OP pesticides, can be divided into two types (1) Activate metabolism (2) Degradative metabolism. In the activative metabolism, crucial conversion of the latent compound to the direct inhibitor of cholinesterase take place, while in the degradative metabolism conversion of the harmful compounds to the harmless compounds takes place.

9. INHIBITORY ACTION OF ORGANOPHOSPHATES

The OP compounds inhibit cholinesterase by combining (phosphorylating) with the active site of the enzyme. The inhibitory potency (interms of I50) of the OP compounds is decided not only by its two alkyl substitutes (methyl or ethyl), but also by the third larger substituent (hetero cyclic phenyl or aliphatic phenyl), which constitutes the leaving group, and is subjected to hydrolysis after phosphorylation (Brown, 1978). The inhibitory effect of the OP compounds on cholinesterase is the basis for their biological activity (Hellenbrand and Krupka, 1970). The AchE has two active sites (Wilson, 1971), an anionic site and an esteric site which contains a serine residue (Wilson, 1960). During attack the leaving group of organophosphate is replaced by the cholinesterase. The reaction is progressive, since, the extent of inhibition is more with time (O'Brien, 1971).
1. Carbohydrate metabolism

It is reported that chronic and acute poisoning of sheep and chickens by the organophosphate insecticides like thiophos, chlorophos, and methylnitrophos is accompanied by profound changes in carbohydrate metabolism (Yasnova, 1969). Siva Prasada Rao (1980) reported that the total carbohydrate content decreased considerably throughout the time-course study in methylparathion (an organophosphate pesticide) exposed fish, Tilapia mossambica tissues. The decrease in the tissue carbohydrates signified its utilization possibly to meet higher energy demands under OP pesticide stress condition of the carbohydrates, glycogen decreased rapidly indicative of its immediate utilization by the tissues. It also suggests that such of those carbohydrates that are convertable or related to glycogen are being trapped extensively to meet the energy demands under OP pesticide impact. Ostroukhova (1965) reported increased glycolytic activity and decreased glycogen content in the liver of fish, while Yakushko (1969) observed that a single oral dose of 70/mg DDT / kg body weight (20% of LC₉₅) to rats stimulated glycolysis in the liver cytoplasm. Since anoxia and hypoxia is known to increase carbohydrate
consumption (Dezwaahm and Zandee, 1972; Siva Prasada Rao, 1980; Bhagyalakshmi, 1981; Satyaprasad, 1983; Srinivasulu Reddy, 1986), the depletion might be due to the prevalence of hypoxic condition (Omkar et al., 1984; Srinivasulu Reddy et al., 1986). The decrease in the glycogen content in the OP exposed tissues also suggest high energy demand in pesticide treated animals possibly to meet the enhanced protein (enzyme) synthesis (Kabeer Ahmed Sahib, 1979; Siva Prasada Rao, 1980; Bhagyalakshmi, 1981; Srinivasulu Reddy and Ramana Rao, 1986). In consonance with the decrease in the tissue total carbohydrate and glycogen contents, the tissue glycogen level also decreased on time course basis. In invertebrates particularly in crustaceans, Srinivasulu Reddy et al. (1982a, b), Bhagyalakshmi et al. (1982) have reported BHC and Sumithion to produce hyperglycemic effect in the field crab, *Ozitelphusa senex senex*, under lethal and sublethal concentrations. Srinivasulu Reddy (1986) suggested that the direct contribution from the tissue glycogen through glycogenolysis or through the breakdown of anthrone positive substances likely to yield glucose in the case of prawn, *Metapenaeus monoceros* under phosphamidon induced stress. Since haemolymph in crustaceans is the circulating fluid, the glucose present in the haemolymph will be directly taken up by the tissues. A rapid decrease for the OP pesticide exposure periods confirms this
suggestion. It is observed that each tissue exhibits differential response and sensitivity to OP toxicity. Therefore, the requirement of glucose or glycogenic precursors is a *sine qua non* which depends on tissue physiological necessity and the intensity of the OP toxic stress. Decrease in the blood or haemolymph glucose level has been demonstrated under starvation, stress and pesticide toxicity in different aquatic animals (Huggins and Munday, 1968; Hohnke and Scheer, 1970; Siva Prasada Rao, 1980; Bhagyalakshmi, 1981; Chang and O'Connor, 1983).

The phosphorylase enzyme system occupies a strategic position in the glycolytic pathway. This enzyme exists in two forms, namely active tetrameric phosphorylase 'a' and inactive phosphorylase 'b'. Total phosphorylase 'ab' represents the activities of both 'a' and 'b' (Cowgill, 1956). In phosphamidon exposed prawn tissues, a rapid elevation in phosphorylase 'a' activity levels followed by a very notable decrease in phosphorylase 'b' activity levels is observed (Srinivasulu Reddy, 1986; Srinivasulu Reddy and Ramana Rao, 1988 a,b).

Aldolase is an important enzyme of the glycolytic pathway. It converts phosphorylated hexoses to triosephosphates. The aldolase
favours not only the operation of glycolysis but also glycerol synthesis. Under OP pesticide exposure (Phosphamidon), there is a rapid increase in aldolase activity of the tissues. This indicates a rapid breakdown of the phosphorylated hexoses to triosephosphates possibly accelerates the glycolytic pathway for further oxidation of the metabolites (Srinivasulu Reddy, 1986).

Though the tissue pyruvate content decreased under phosphamidon exposure, yet every tissue still has considerable store of pyruvate when compared to the tissue lactic acid, indicative of its contribution from other sources like aminotransferase. The NAD+ dependent LDH activity in the tissues decreased, confirming less conversion of lactate to pyruvate. The tissue lactic acid content increased in phosphamidon exposed prawns. Since, an increase in the tissue and haemolymph NH₃ and non-protein nitrogen (NPN) content was observed (Vijayalakshmi, 1987) and that it may result in a shift in the intracellular pH and also acid-base balance, it is construed, that to some extent the tissue lactic acid may help to neutralize the alkaline effects of NH₃ and also to maintain acid-base balance within the physiological limits (Srinivasulu Reddy, 1986).
2. **Protein metabolism**

The soluble proteins progressively increased throughout the time course study in the organophosphate insecticides exposed tissues. The increase in the soluble proteins suggest enhanced protein synthesis; Kabeer (1979) confirmed the occurrence of protein synthesis by 14C amino acid incorporation in fish, *Tilapia mossambica* exposed to malathion. Since soluble proteins represent enzymes, hormones and free peptides, it is likely that an increase in tissue soluble proteins should represent an increase in the synthesis of some enzymes. Siva Prasada Rao (1980) confirmed an increase in the activities of some enzymes, which might possibly be due to an increase in the synthesis of these enzymes.

The insoluble protein fractions showed fluctuations in the organophosphate exposed tissues. Siva Prasada Rao (1980) confirmed the presence of non-significant and less significant values in water insoluble protein fractions of the OP exposed tissues in teleost, *Tilapia mossambica*, Varley (1969) suggests that these proteins which constitute the structural element of the cells that makeup the respective tissues are less sensitive to the impact of methyl parathion.
Siva Prasada Rao (1980) observed a steady and significant increase in the tissue of free amino acid pool of OP exposed tissues. This increase in the tissue free amino acid pool should either be due to the breakdown of proteins as a consequence of enhanced proteolytic activity, to be again used for the resynthesis of new types of proteins to copeup with the altered conditions or there should be recycling of ammonia through deamination followed by transmination for the synthesis of both amino acids and ketoacids, wherein, the keto acids find its way into the TCA cycle and the amino acid to be used for protein synthesis.

The activity of tissue aminotransferases (AAT & AIAT) increased in the OP exposed animals. Since, the enzymes concerned with the transmination are distributed in almost all the tissues, it is but natural that the increased FAA content may be channelled for energy yielding and other synthetic purposes.

3. Lipid metabolism

The Lipids are also effected by the OP pesticides (Bhatia and Venkata Subramanian, 1972). The total lipid and phospholipid contents progressively decreased in the OP exposed tissues. The decrease in the total lipids could either be due to increased lipolysis (Satya Prasad et al.,
personal communication, 1980) or due to a reduction in the fatty acid synthesizing enzymes (Bhatia and Venkata Subramanian, 1972). The phospholipids seems to be decreased rapidly. Since they are actively degradable among lipids (Harper et al., 1978), suggests of its immediate utilization for energy purposes.

Curiously, the free fatty acids increased in the OPE tissues. This increase suggests an increased lipolysis under MP impact and this agrees with decreased total lipid and phospholipid contents.

The total cholesterol content increased in the OPE tissues shows increased diversion of acetyl CoA to acetoacetate for the synthesis of cholesterol, since administration of OP insecticides, increases acetoacetate and - hydroxy butyrate contents (Domsche and Claussen, 1977). This diversion can be expected as a possibility of acetyl-CoA accumulation, since TCA cycle enzymes are inhibited under OPI impact. The acetyl-CoA produced through segmented - oxidation and from glycolysis may produce more ketone bodies, particularly acetoacetate which acts as a precursor for cholesterol biosynthesis. Since the OP insecticides are known to inhibit the metabolism of steroids (Kupfer, 1969), the increase in the cholesterol content might also be due to the non-utilisation of cholesterol for the synthesis of steroidal hormones, resulting in its accumulation in the tissues.