Serotonin (5-Hydroxytryptamine, 5-HT) is known to be an important biogenic monoamine which has been isolated from the animal tissues. Biogenic amines are biologically active substances derived from amino acids. These monoamines are produced both centrally and peripherally in the nervous system. Those produced in the brain act as neurotransmitters and can modulate neural functions. For the first time serotonin was recognized in the mammalian blood, hence the name 'Serotonin' was given.

Studies on 5-HT have assumed great significance in the recent years (Haigler & Aghajanian, 1977; Mandell & Knapp, 1977; Sloviter et al., 1978 etc.). The presence of 5-HT in the non-nervous tissues of vertebrates and invertebrates has also been reported (Welsh, 1969). It is found in enterochromaffin cells of the gut, blood platelets, and mast cells of the vertebrates and in the case of invertebrates nonnervous sources of 5-HT are excretory organs of crustaceans and molluscs, and many venom producing structures like posterior salivary glands of some species of octopus and venom glands of many social wasps and many spiders.

Serotonin in central nervous system (CNS):

The presence of serotonin is detectable in most of the brain areas (Fischer et al., 1970; Saavedra, 1977). Its topographical localization in CNS has been investigated by histo-fluorescence and immunohistochemical methods and its concentra-
tion has been determined by biochemical methods. In the adult brain, most of the amine synthesis and storage in the monoamine neurons is localized in the nerve terminals. The distribution of brain 5-HT between soluble cytoplasmic and bound particulate forms has been assessed using subcellular fractionation techniques (Tissari & Raunus, 1975).

The serotonergic cells of the nervous system appear to contain all of the precursor compounds, enzymes, and cofactors necessary for the synthesis and degradation of the neurotransmitter. It is well known now that serotonin is synthesized from Tryptophan (Trp) by the process of hydroxylation, followed by decarboxylation. Release of 5-HT molecules into brain synapses has been reported in vivo following electrical stimulation (Aghajanian et al., 1966). Once released, some synaptic molecules of 5-HT are taken up again by presynaptic nerve terminals, and are deaminated and oxidised by the enzyme monoamine oxidase (MAO) to form biologically inactive metabolite, 5-Hydroxyindole-acetic acid (5-HIAA), and other molecules of released transmitter interact with receptors of the postsynaptic membrane to complete the process of neurocommunication. 5-HT is also synthesized in the nerve endings and then is transferred to the storage particles after synthesis. Serotonin receptors have been found in the brain (Haigler & Aghajanian, 1977), and its molecules appear to be stored intracellularly in at least two distinct pools, although the evidence is indirect (Shields & Eccleston, 1973; Lytle & Wurtman, 1976). It was also postulated that small pool was situated at the nerve ending and represented the
part of 5-HT which was functionally active, being released by the nerve impulse. The release of 5-HT from the nerve endings is shown to be affected by 5-HIAA levels (Reinhard & Wurtman, 1977), calcium (Lane & Aprison, 1977), L-5-Hydroxytryptophan (L-5-HTP), \( \alpha \)-methyl-D-tyramine and elevated Potassium ions (McBride & Aprison, 1976).

The activity of the enzymes involved in the metabolism of 5-HT is also measured by sensitive methods (Bender & Coulson, 1972; Joh et al., 1975; Kizer et al., 1975). Direct information of biochemical structure and regional and subcellular localization of these enzymes has been restricted by limited success in obtaining purified forms of the enzymes.

Over the past few years the emphasis is given to the examination of the factors regulating synthesis of 5-HT in the nervous system. Nutritional manipulations, Psychotropic drugs, and drugs affecting protein binding of Trp in the plasma and brain Trp levels, are receiving the attention of the workers (Fernstrom & Wurtman, 1971; Graeme-Smith, 1971; Tagliamonte et al., 1971; Paoletti et al., 1975). Trp is an essential amino acid and cannot be synthesized in the body, hence brain Trp can originate only from the lysis of brain proteins and from circulating Trp derived from the diet or other tissue pools. Experimental manipulations that markedly alter Trp levels available to the body can raise or lower brain 5-HT levels, e.g., Concentration of 5-HT is depressed in the brains of the animals given diets with little or no Trp (Modigh, 1975; Miller et al., 1977; Fernstrom & Hirsch, 1977). So physiological control of brain 5-HT synthesis
may normally be coupled with Trp levels. Serotonergic neurons
have have a high affinity for Trp uptake (Mandell & Knapp, 1977).
Trp uptake process is a drug sensitive, regulatory variable in
the control of 5-HT biosynthesis.

Hormonal regulation of neurotransmitter metabolism in
mammalian brain has not been extensively studied. Some attempts
have been made to relate glucocorticoids to brain 5-HT metabo-
lishm (Neckers & Sze, 1975; Yuwiler et al., 1978), and it is
proposed that glucocorticoids may directly act on nerve terminals
in regulation of 5-HT synthesis through an activation on uptake
of Trp.

The interest of the investigators has been shifted to the
processes of neurotransmitter release, uptake, turnover and
synthesis of 5-HT in the nervous system. The effects of certain
drugs which interfere with the metabolism of 5-HT have been
studied in detail. The metabolic pathway of 5-HT is well estab-
lished in the case of mammals. The first rate limiting step
of hydroxylation has been shown to be inhibited by Para-chloro-
phenylalanine (PCPA) in the vertebrates both in vivo and in vitro
(Koe & Weissman, 1966). The enzyme of degradative pathway,
MAO, is known to be inhibited by Nialamide, iproniazid and actomol.
Reserpine has been found to deplete 5-HT from the neural elements
by blocking storage process (Hiripi & Salanki, 1973). These
drugs have also shown remarkable effects on the behavior of the
animals. In the case of invertebrates also the effects of these
drugs on 5-HT metabolism have been investigated upto some extent
(Hiripi & Salanki, 1973), although most of the information is available from the studies on the higher animals.

Serotonin metabolism is also sensitive to narcotics like cocaine which is supposed to affect the turnover of 5-HT (Friedman et al., 1975; Lallemant & Bralet, 1976). After acute cocaine administration particulate Tryptophan hydroxylase activity is decreased but cocaine induced decrease in 5-HT synthesis is due to Trp uptake inhibition and not by direct inhibition of Tryptophan hydroxylase enzyme (Knapp & Mandell, 1972; Larson & Takemori, 1977). The turnover of 5-HT is known to be affected by Morphine (Bhargava & Matwyshyn, 1977; Warwick et al., 1977; Haigler, 1978; Snelger & Vogt, 1978; Bhargava, 1979; Weil-Fugazza, 1979), and Apomorphine (Weiner et al., 1975; Grabowska, 1976; Grabowska-Ander & Smialowski, 1977).

Brain monoamines are also affected by acute and chronic exposure to ethanol (Rawat, 1974; Tabakoff & Boggan, 1974). A significant increase in brain Trp was reported after acute ethanol administration (Pohorecky et al., 1978) and also an elevation in 5-HIAA was reported which might be as a result of impairment of 5-HIAA transport out of the brain (Tabakoff et al., 1975).

Serotonin metabolism is known to be influenced by a number of metal ions like lithium (Poitou et al., 1974; Collard & Roberts, 1977), cadmium (Rastogi et al., 1977), and calcium (Knapp et al., 1975).
The presence and metabolism of 5-HT have been identified in a number of lower animals like in certain molluscs (Twarog, 1954; Aiello & Guideri, 1966; Hiripi, 1968), and also in certain insects (Welsh & Moorhead, 1960; Colhoun, 1963).

**Functional significance:**

More attention has been paid on the functional aspects of 5-HT in the higher animals. Considerable experimental efforts continue to be directed towards the elucidation of the relationship between the activity of monoamines and specific functions. Both biochemical and pharmacological methods have been applied to the studies on the relationship between serotonergic mechanisms and centrally mediated actions. Attempts have been made to correlate levels of 5-HT and its principle metabolite, 5-HIAA, in various body tissues to specific clinical signs of CNS dysfunctions.

Serotonin has many important roles in normal physiological functions (Chase & Murphy, 1973). Apart from its role in neurotransmission in the CNS, it has been known to act as a chemical transmitter in taste organs (Morimoto & Sato, 1977) and in peripheral chemoreceptors (Sapru & Krieger, 1977). Serotonin is supposed to be a growth promoting or regulatory factor for embryonal brain (Ahmad & Zamenhof, 1978; Lauder & Krebs, 1978), and it is found during early embryogenesis and may function as a modulator of cellular differentiation (Baker & Quay, 1969). Many evidences have been accumulated for the role of Serotonin as a mediator in several types of behavior (Kostowski et al.,
1968; Wise et al., 1970; Aprison & Hingtgen, 1972; Ellison & Bresler, 1974; Subrahmanyan, 1975a; Torre et al., 1975; Smith et al., 1976; Costa et al., 1977; Ramaekers et al., 1977; Giambalvo & Snodgrass, 1978; Sloviter et al., 1978a; Sloviter et al., 1978b; Coleman, 1979; Silbergeld et al., 1979), even in early stages of life (Isaacson et al., 1977). Correlations have been made between 5-HT and the complicated processes like mood and emotions (Schildkraut & Kety, 1967; Ladisick, 1977; Mandell & Knapp, 1979).

Physiological changes in animals when exposed to the following are generally mediated by nervous and endocrine systems. Many procedures like cold water swimming, hypothermia, hyperthermia, pain, trauma, immobilization, electric shock etc. cause alterations in monoamine contents of the brain. Stress has important effects on brain 5-HT metabolism and thus leads to affective disorders (Curzon, 1971; Subrahmanyan, 1977). Hole (1972) reported that P-chlorophenylalanine treatment of rats during first week of life resulted in brain damage as evidenced by significant reduction in brain weight.

Serotonin levels are closely related to the mental retardation (Pare et al., 1960; Partington et al., 1973; Cohen et al., 1977; Oikawa et al., 1978).

5-HT is directly or indirectly involved in determining pain threshold and in regulating peripheral or behavioral response to painful stimuli (Armstrong et al., 1952; Harvey & Lints, 1971; Messing & Lytle, 1977; Schlosberg & Harvey, 1978;
Boada et al., 1979; Telner et al., 1979). Decreased 5-HT levels after certain lesions (Lints & Harvey, 1969), & Trp poor diet (Messing et al., 1976) to increased pain sensitivity can be reversed by 5-HTP treatment.

Migraine headache is a genetic disorder of a central, antinociceptive, serotonergic system in discrete areas of the brain, leading to abnormal disposition to sensing pain (Sicuteri et al., 1961; Sicuteri et al., 1973; Sicuteri, 1974; Welch et al., 1977). Sicuteri formulated the idea that a biochemical lesion associated with 5-HT metabolism may lead to pain.

Serotonin depletion also affected the sexual behavior of the animals (Sicuteri et al., 1975; Ballo, 1977; Everitt & Fuxe, 1977). PCPA can stimulate sexual behavior and sexual activity can be decreased by 5-HTP injection (Ferguson et al., 1970; Gessa & Tegliamonte, 1974). In the case of female rats serotonin is found to have a role in control of ovulation (Laasetwar, 1972; Wilson et al., 1977; Alsalti, 1979), and in suckling in weaning age rats (Williams et al., 1979).

It has been suggested that Biogenic amines are directly involved in hypothalamic control of body temperature (Feldberg & Myers, 1963; Sheard & Aghajanian, 1967; Myers & Waller, 1975; Komiskey & Rudy, 1977; Lin, 1978; Lin et al., 1978; Lin et al., 1978; Pyornila et al., 1978; Lin et al., 1979; Slater et al., 1979) even during early postnatal maturation (Goodrich & Choy, 1978).
Biogenic amines play a physiological role in the control of blood pressures (Bhargava & Tangri, 1959). 5-HT has a tonic (constrictive) influence on the blood vessels (Anthony, 1975; Martins et al., 1978), so it acts as a vasoconstrictor.

Feeding behavior of the animal is also known to be governed by serotonergic mechanisms (Blundell & Leshem, 1975; Blundell & Latham, 1979; Samanin et al., 1977; Samanin et al., 1977; Staykova et al., 1979).

Serotonin plays an important role in sleep mechanism (Jouvet & Renault, 1966; Torda, 1967; Ursin, 1976; Jacobs, 1978; Slater et al., 1978). Sleep is a result of the succession of two different stages, (1) slow wave sleep (SWS), & (2) Paradoxical sleep (PS) or Rapid eye movement (REM) sleep, respectively. Producing a decrease in 5-HT, Reserpine supressed slow wave sleep for 6-8 hours, and Paradoxial sleep for one day. Most of the MAO inhibitors have a selective and long lasting suppressive effect upon Paradoxial sleep without interfering with SWS, so MAO could be involved in transition from SWS to PS.

A depletion in brain 5-HT and 5-HIAA levels leads to depression (Goodwin & Post, 1975), and brain 5-HT levels are also related to the tension (Bhargava et al., 1979; Navafelix & Hong, 1979).

The role of 5-HT has been established in hormonal secretion in the mammals (Smythe, 1977; Woolf & Lee, 1977) especially in Prolactin release (Kamberi et al., 1971; Tindale, 1974; Clemens et al., 1977; Clemens et al., 1978; Lamberts & Macleod, 1978;
Advis et al., 1979; Garthwaite & Hangen, 1979; Koenig et al., 1979; Kruleh et al., 1979), secretion of growth hormone (Smythe et al., 1979), Luteinizing hormone release (Kamberi et al., 1970; Coen & Mackinnon, 1976; Gallo & Moberg, 1977; Hery et al., 1978; Coen & Mackinnon, 1979), and Thyrotrophin release (Jordan et al., 1978; Jordan et al., 1979).

During some pathological conditions also biogenic amines play important roles (Subrahmanyan, 1975), like elevated 5-HT levels induce myoclonus (Klawans et al., 1973; Vanwoert & Sethy, 1975), and in cerebral oedema (Mohanty et al., 1979). An increase in 5-HT levels in the brain stem has a depressant influence on respiratory mechanism in cats (Armijo & Florez, 1974) and also causes head twiching in mice (Corne et al., 1963).

It is evident from the literature available that Serotonin plays a very important role in a number of physiological processes apart from its major role in neurotransmission. Most of the work has been done in the case of higher animals and mammals especially. In the case of lower animals evidences are there to support the action of 5-HT as neurohumoral agent (Welsh, 1954; 1957). Serotonin has a role in nervous control of periodic activity in the case of fresh water mussel (Salanki, 1963), also in the contraction of molluscan smooth muscle (Twarog, 1954; Hidaka et al., 1967) and in ciliary activity of Mytilus gill (Aiello, 1957). Serotonin-sensitive Adenylate cyclase has been reported in mammalian brain (Hungen et al., 1975; Enjalbert et al., 1977; Fillion et al., 1979), and 5-HT
has been shown to be capable of increasing the accumulation of C-AMP in the brain slices (Daszuta et al., 1979). The presence of Serotonin-Sensitive Adenylate cyclase has been reported in the lower animals also like in certain molluscs (Wollemann & Rozsa, 1975), in Aplysia (Shimarhard & Tauc, 1977), Mytilus (Haley et al., 1978), and in annelid CNS (Robertson & Osborne, 1979). 5-HT sensitive Adenylate cyclase has been found in the homogenate of cockroach thoracic ganglion, so 5-HTP has been supposed to activate nerve cord phosphorylase via C-AMP, producing a glycogenolytic effect in Periplaneta (Hart & Steele, 1969). In the brain the most important function of cyclase system is the control of glycolysis. Serotonin increases glycolysis following its administration (Leonard, 1975).

Evidences are there in the literature to support that Serotonin is an important biogenic monoamine, acts as a neurotransmitter in the nervous system of most of the vertebrates and invertebrates, and also involved in a number of complicated processes like behavior, mood and emotions. For a detailed investigation of the metabolism and turnover of 5-HT in the nervous system, the main goal is to have a sensitive assay method that permits the measurement of 5-HT and its metabolites.

Extensive work has been done in this area and a number of sensitive assay procedures have been evolved like liquid chromatography (Sasa & Blank, 1977; Sasa et al., 1978; Troschutz & Roder, 1978; Sasa & Blank, 1979), Gas chromatography (Zambotti et al., 1975; Sunol & Gelpi, 1977), Liquid cation exchange
(McCaman et al., 1972), 0-Phthalaldehyde method (Leiva & Schwartz, 1976; Jacobowitz & Richardson, 1978), Mass fragmentography (Artigos & Gelpi, 1979), P-dimethylaminocinnamaldehyde method (Baumann, 1975), Radiometry (Nixon, 1972; O'Brien & Spector, 1975; Recasens et al., 1977; Ilan et al., 1978), and fluorometric techniques (Redlich & Glick, 1969; Enerback & Jarlstedt, 1975; Ciarlone, 1976; Aleksandrov et al., 1977; Geyer et al., 1978; Schofield & Wreford, 1979). Among the various types of methods used by the investigators, improved fluorometric method of Fischer & Aprison (1972) has been preferred by many.

Keeping in view the above review in mind, the present work is an attempt to study 5-HT metabolism in the nervous system of Periplaneta americana. Since significantly large quantities of 5-HT are found in the cockroach nervous system, this served as an extra incentive to study 5-HT in the cockroach.

Stomatogastric nervous system:

Stomatogastric nervous system arises during embryonic development from the dorsal wall of stomodaeum which later acquires connections with the brain. It consists of a frontal ganglion, joined by bilateral connections to anterior surface of the brain, and which sends back the median recurrent nerve. Behind the brain is a pair of corpus cardia, likewise nervous in origin, connected by the nerves to protocerebrum. The frontal ganglion, hypocerebral ganglion and gastric nerves form a Stomatogastric nervous system in strict sense, and contains both sensory and motor neurons and controls the movement of heart
and gut generally. Corpus cardiacum and corpus allatum constitute neurosecretory or endocrine system. Most of the physiological functions of neurotransmitters are mediated by endocrines (Klemm, 1976).

The frontal ganglion is an important part of the stomatogastric nervous system in the case of Periplaneta, but its functional significance is not known with certainty. Since it is known that this ganglion is an autoactive tissue (our unpublished observations), its significance for the insect is not yet established. In the area of electrophysiology of the frontal ganglion of the cockroach, not much work has been done so far. The presence and functional significance of any neurotransmitter in the frontal ganglion of the cockroach participating in the autoactivity have not been known till now. For the above reasons, we decided to analyse the spontaneous electrical activity and physiologically active neurotransmitter of this ganglion. It is known that the changes affecting nervous impulses and receptor sensitivity are reflected through the changes in the rate of synthesis and turnover of involved neurotransmitter (Carlsson et al., 1972).

The entire work was done with the cockroach, Periplaneta americana. It has been devided into 3 chapters:

Chapter I: deals with studies on quantitative distribution of Trp and Protein in the brain under normal functional conditions. It also includes the studies on the effect of certain 5-HT metabolism interfering drugs on the brain levels of Trp and Protein. These drugs include P-chlorophenylalanine, Reserpine & Nialamide.
Chapter II: deals with the quantitative distribution of 5-HT along with its principle metabolite, 5-HIAA, in the brain. The levels of brain 5-HT and 5-HIAA have been estimated under normal conditions and also after administration of certain drugs (P-chlorophenylalanine, Reserpine, & Nialamide) which are known to interfere with normal 5-HT metabolism.

Chapter III: deals with the identification of 5-HT and electrophysiological studies in the frontal ganglion. The presence and distribution of the involved neurotransmitter have been investigated qualitatively and quantitatively by paper chromatographic method and fluorometric technique, respectively. Circadian variations of the activity of the frontal ganglion along with the levels of involved neurotransmitter Serotonin have also been studied. The spontaneous electrical activity of the frontal ganglion has been measured. Utilizing the frontal ganglion, electrophysiological studies have been performed to test different neurotransmitters and certain amino acids which are suspected to act as neurotransmitters. The effect of these transmitters and amino acids has been studied on the spontaneous electrical activity of the frontal ganglion, and involved neurotransmitter has been identified as Serotonin. To further confirm the above findings, the effects of three specific drugs which interfere with serotonin metabolism, on the electrical activity of the frontal ganglion have also been investigated. These drugs are P-chlorophenylalanine, Reserpine, and Nialamide.