1. INTRODUCTION

Pentazocine, a synthetic opiate known for its clinical importance is a product of benzomorphan series. Pentazocine has few side effects, and consequently widely used as a non-addicting and effective analgesic. Chemically it is \([2-(3,3\text{-dimethylallyl}-2'\text{-hydroxy}-5,9\text{-dimethyl-6,7-benzomorphan})]\) having a wide spectrum of actions in human beings and animals. The efficacy of pentazocine approximates to that of morphine (Laurence and Bennett, 1980).

Sternadel et al., (1976) have found pentazocine as an obstetrical anesthetics. Moir, (1977) has reported the usage of pentazocine as an analgesic in the control of labour pain. Showalter, (1980) and Jasinski et al., (1970) have observed the pentazocine in combination with tripillemamine abused by human beings in the absence of heroin.

Several authors have reported that the administration of pentazocine resulted in the alterations of certain biochemical events. Gilbert and Martin (1976) have observed that pentazocine showed agonism for kappa and sigma receptors and antagonism for mu receptors. Bowen et al., (1993) have found that pentazocine exhibited much higher affinity for sigma receptors which are either be related to or to modulate the functions of the drug metabolizing enzymes like monoamine oxidase A (Itzhak et al., 1991) and cytochrome 450 (Ross, 1991 and Klein et al., 1991). Bowen et al., (1993) have concluded that
pentazocine produced certain physiological, behavioural, biochemical effects through sigma receptors.

The effect of pentazocine as well as other opioids on the biochemical components of different tissues like brain, liver, kidney, testis and serum has received considerable attention in recent years. The activation of foetal and neonatal receptors by morphine or heroin has been shown to affect the development of nervous system with concomitant reduced body weight at birth, behavioural deficit and increased rate of mortality (Wilson et al., 1978 and 1979; Vathy et al., 1985; Hammer et al., 1989). The works of Hui et al., (1978) Ricalde and Hammer (1990) and Seatrix and Hammer (1993) showed that as a consequence to opioid administration the formation of cortical neuron dendrite would be impaired and cell maturation and proliferation might be restricted suggesting the possible inhibition of DNA synthesis.

The effect of pentazocine on DNA content will be of interest. Field et al., (1977) estimated the content of DNA in brain tissue of normal and addicted mother rats and found significant difference between the two. In the light of these observations a study of DNA content not only in brain tissues but also in other tissues like liver, kidney and testis is considered significant.

The work of Kornblum et al., (1987) in neonatal rat brain revealed that morphine, an opiate significantly affected the DNA synthesis. Stein-Martin and Hauser (1990) studied opioid dependent growth of glial cultures and found the suppression of DNA synthesis by met-enkephalin. Isayama et al., (1991) found
in the retina of developing rat that the exposure of opioid affected neuronal and thymidine incorporation and DNA synthesis.

One of the biochemical components known to be affected by opiates like pentazocine is protein. Retz and Steele (1972) have reported that the administration of natural opiates like morphine in the dosages of 30mg/kg to rats resulted in 80% decrease in the rate of secretory and nonsecretory protein synthesis in the liver.

The work of Peters (1977) revealed that chronic methadone treatment caused a deficiency in the rat brain development showing a marked decrease in its protein and RNA contents. Subsequent studies of Hui et al., (1978) confirmed that chronic administration of low doses D-L. methadone (2mg/kg) to neonatal mice resulted in the deficit of RNA and protein synthesis in the brain, heart, liver, and skeletal muscle. The work of Wassef and Smith (1980) showed that injection of pentazocine in young mice in dosages of 20mg/kg resulted in the decrease of protein synthesis in tissues studied by them. They also suggested that such inhibition of protein synthesis might lead to adverse effect on growth in mice. This was also evident from the work of Gandhi et al., (1983) who administered pentazocine in young rats and observed a significant inhibition of growth.

On the other hand Tiwari et al., (1989) who administered pentazocine with the dosages of 30mg/animal observed a tremendous increase in the total protein content of serum. Shushikoa (1992) has also observed an increased rate of protein synthesis in the brain and kidney tissues after the administration

DiGiulio et al., (1995) observed that the exposure to morphine reduced the expression of synapsin-I mRNA throughout the brain suggesting that the perinatal morphine might affect the synaptic maturation in the brain. Gorio et al., (1996) reported that morphine exposure greatly reduced the expression of brain synapsin-I mRNA in hippocampus, dentate gyrus, cerebral cortex and olfactory bulb of brain tissue. Gorio et al., (1996) showed that the expression of mRNA brain derived neurotrophin factors and neurotrophin III was unaffected by perinatal morphine exposure. Toa et al., (1993) studied the interaction of the mu opiate receptors and G-protein and found that its interaction was altered by chronic morphine treatment.

The Opiates have been shown to cause hyperglycemia (Ipp et al 1978). They are known to influence glucose homeostasis. In several studies carried out in animals, morphine has been found to increase plasma glucose level. (Radosevich et al., 1984; May et al., 1988; Bossone and Hannan 1991). Johansen et al., (1992) reported on increase in plasma glucose and lactate in adult pigs after morphine administration. These metabolic changes have been shown to be accompanied by behavioural excitation.

The work of Tiwari et al., (1989) is of interest. These authors injected pentazocine lactate with dosages of 30 mg / animal and found that glucose level of blood increased to $4.85 \pm 0.16$ from $3.05 \pm 0.06$ at 48 hours after administration. However, after 120 hours it declined to $3.39 \pm 0.11$. In the
light of these observations, it is of interest to investigate the effects of pentazocine on blood glucose level. Studies on tissue glucose content in relation to opiates have been made by a few authors.

The work of Tamura et al., (1990) indicated that the administration of pentazocine 3mg or 10mg/kg to normal mice was found to increase the cerebral glucose content. They also reported the effect of pentazocine on cerebral tissue glucose content.

Hypoglycemia is rarely seen after morphine administration. It has been reported after intrathecal administration of morphine, Brase et al., (1990) suggested that this hypoglycemic effect might be the result of increased uptake and metabolism of glucose by skeletal muscle. It would be of interest to investigate the effect of pentazocine on blood glucose level.

Mule's (1970) work showed that rats exposed to morphine for two hours exhibited a significant rise in phosphatidyl choline and phosphatidyl ethanolamine biosynthesis. Thureson-Klein et al., (1978) reported increase in the hepatic triglyceride content on exposure to morphine. Sun et al., (1978) also reported alterations in the hepatic metabolism consequent to morphine exposure. These authors suggested that morphine might disrupt hepatocellular membrane components like phosphoglycerides and inhibited oleol co-enzyme A; acyl glycerophosphate choline, a key enzyme in the metabolism of membrane phosphoglycerides. The work of Kigoshi and Kousaku (1982) showed that tumour cells treated with pentazocine contained lower levels of triglycerides and esters as compared with the tumour cells incubated alone. In
addition, the fatty acid pattern of triglyceride and cholesterol esters differed markedly between the two suggesting the effect of pentazocine on these chemical components.

The work of Lamb and Dewey (1980) on mice exposed to morphine exhibited rapid and significant increase in hepatic triglyceride content. In the light of these informations it is of interest to investigate the effect of opiates like pentazocine on the lipid content of rat tissues. If opiates could enhance organic contents, it is reasonable to expect changes in the related enzyme activity.

There is an indication of such a possibility from the work of Weinstock (1971) and Datta et al., (1971). The later authors reported a selective lowering of choline esterases activity after administration of morphine. Bhargava and Way (1972) reported that AChE activity decreased in the striatum after chronic treatment with morphine. Zequal et al., (1974) reported that AChE activity decreased in the striatum after similar treatment with morphine sulphate. Field et al., (1977) found that the pups of methadone addicted mother rats had lower brain AChE compared with normal one. On the other hand, none of the sigma ligands had any effect on AChE and acetylcholine transferase activity in the rat frontal cortex (Matsuno et al., 1993) Although a considerable information on the effect of opioids like morphine on estrase isoenzymes is available, very little is known regarding the effect of other opioids like pentazocine on these enzymes. Since pentazocine is widely used clinically, a study of known dosages of pentozocine and its effect on esterases
on different tissues is expected to throw light on this problem. Not only esterases but also other enzymes like phosphatases deserve attention. Majumdar (1993) reported increased alkaline phosphatase activity after subacute toxicity. In the light of this observation, it would be of interest to investigate the effect of pentazocine on phosphatases.

The other enzymes known to be affected by opiates are SGOT and SGPT. The work of Chang and Ho (1978) indicated that the morphine exposure rapidly elevated mouse serum SGOT and SGPT levels. Hence a study of pentazocine administration and its effects on these enzymes is considered significant. It would be of interest whether effect of pentazocine on biochemical components is reflected on the histology of tissues.

Histological and Histochemical changes due to drug like pentozocine have been reported by several authors. Meola et al., (1980) observed pentazocine induced neuromuscular syndrom in addicted patients. They further reported muscle fibre atrophy due to pentozocine injection.

The work of Hsu et al., (1992) showed membrano proliferative glomerulonephrities with tubulo interstitial nephrities. Immunoflourecent study by these authors revealed granular deposition of C-3 and IgM is mesengial and glomerular capillary wall.

Danialsen et al., (1994) observed fibrosis, multiple irregular ulcers and scars surrounded by hyper pigmentation on the upper and lower extremities
of pentazocine addicted persons. They also reported pronounced tissue
destruction and inflammation at the injection sites.

From the foregoing observations it is clear that pentazocine has
significant effects on the histology of the tissues. A study of administration of
pentazocine and consequent changes in the histology of the tissues may help
understanding the specific effect of this analgesic drug on different tissues of rat

In the light of foregoing information, the aims of the present
investigation are

1. to estimate the DNA, RNA, protein, lipid contents of different
tissues like brain, liver, kidney and testis.
2. to study of the activities of enzymes like alkaline and acid
phosphatases, esterases
3. to analyse the esterases isozymes qualitatively.
4. to estimate the glucose, lipid and triglyceride contents of rat
serum
5. to study the histology of the tissues.

It is felt that this study in control and pentazocine administered
rats may help to understand the effects of clinically important
drug like pentazocine and its manifestations.