INTRODUCTION AND SPECIFIC GOALS OF INVESTIGATION
The demonstration of the natural occurrence of a pharmacologically potent substance has always prompted an intensive investigation of the role of the agent in the physiological and pharmacological processes of the organism. Dopamine, once known as an intermediate precursor in the biosynthesis of noradrenaline and adrenaline, has rapidly established itself as an important putative neurotransmitter substance in understanding the mechanism of large number of important neuropsychopharmacological facts.

The first evidence that dopamine has a role different from other sympathomimetic amines was presented by Holtz and Credner (1942). They reported that dopamine differed from adrenaline in that it showed vasodepressor effects with species differences. Inability of conventional blocking agents to attenuate the vasodepressor effect of dopamine suggested that dopamine is acting on a unique vascular receptor. Bertler et al. (1959) reported that highest concentration of dopamine was present in localized areas of the brain and was unaccompanied by similar concentrations of noradrenaline. The interest for the role of dopamine further arose mainly with discovery that striatal dopamine concentrations are deficient, in brain of patients with Parkinson's disease (Ehringer et al., 1960), and the dramatic
improvement noticed in Parkinsonian patients with L-dopa, the precursor of dopamine, has been a reward for the physicians. From then, for the physiologists, pharmacologists and clinicians, it is a question of interest to know how dopamine is involved in the pathophysiology of brain.

Research in psychopharmacology over the past two decades indicates that brain catecholamines play an important role in mediation of different CNS functions like analgesia, temperature regulation, behavioural changes, sleep, body weight, water intake, addiction, aggressive behaviour etc. At the present state of development in this field, a large amount of evidence is consistent with the notion that several CNS drugs act through catecholaminergic and serotonergic mechanisms. The involvement of dopaminergic mechanism in these CNS functions has been focussed by various workers (Calcull, et al., 1971; Puri and Lal, 1975; Carlini and Lindsey, 1974; Gianutsos et al., 1974; Cox and Synder, 1969). The basic of their findings, in general, has been the measurement of the content of dopamine or its metabolites in CNS.

Recently various types of dopamine receptors have been identified both centrally as well as peripherally (William, et al., 1979), and various dopamine agonists and antagonists
such as amphetamine, apomorphine, SK & F 38393, L. dopa, pimozide, haloperidol, metoclopramide, domperidone etc. are now available. In view of the above mentioned facts, present investigation was undertaken to study the role of dopamine in CNS functions using various dopamine agonists and antagonists.

**SPECIFIC GOALS OF INVESTIGATION**

(1) The effect of dopamine agonists and antagonists on the motor activity in mice and rats:

Rats or mice when forced to swim in a restricted space from which they cannot escape, will after an initial period of vigorous activity, adopt a characteristic immobile posture in which they remain floating in water. Porsolt et al (1977) suggested that the immobile behaviour could serve as a screening model for antidepressants and showed that immobility was reduced with anti-depressants.

Chlorpromazine and RO 1284, a reserpine like compound, in rats increase immobility. Less attention has been paid to this enhancement of immobility. In an attempt to identify some of the biochemical processes underlying immobility, in particular the enhancement of immobility in mice, we investigated the effect of variety of pharmacological agents known to modify neurotransmission in dopaminergic system.
(2) Psychopharmacological aspects of dopaminergic system:

Involvement of brain catecholamines and serotonin, in the learning process is fairly well documented. In turn, amphetamine facilitate learning in animals (Kulkarni, 1968). On the contrary, some studies have failed to support this view (Leonard, 1969). In the present study we have studied the effects of dopaminergic agonists the learning behaviour using stereotype behaviour, locomotor activity, food reward test and study in maze as well as in maternal behaviour test, dopamine agonists and antagonists were studied to established the role of dopamine in central nervous system.

(3) Study related to yawning behaviour in rats:

Schizophrenic morbidity has been reported to be reduced by low doses of apomorphine (Corsini et al., 1977; Smith et al., 1977). Apomorphine also induces yawning in rats (Mogilnicka, and Klimerk, 1977), and the behaviour is believed to reflect autoreceptor stimulation (Yamada and Furukawa, 1980). The present study was undertaken to investigate the yawning dose response to different dopamine agonists and its sensitivity towards pimozide (0.5mg/kg), a specific dopamine receptor blocking drug and domperidone (2mg/kg) believed to effect the peripheral dopamine receptors.
(4) Pharmacological characterisation of central dopaminergic receptors in aggressive behaviour:

It is well known that apomorphine triggers a severe form of aggressive behaviour in rats pretreated with cataleptic doses of reserpine, whereas apomorphine elicits only stereotype in non-reserpinised rats. The present study was undertaken for pharmacological analysis of the neurohumoral mechanisms involved in the reserpine-apomorphine model of aggressive behaviour.

(5) Effect of different dopamine antagonists on isolation syndrome in mice:

This study was carried out in view of the interesting query as to how aggressive behaviour is related to brain dopamine level. Apomorphine, a dopamine receptor agonist (Anden et al., 1967) exhibits central stimulant effects in various animal species. We also studied the effects of various dopamine antagonists in isolated aggressive mice.

(6) Role of dopamine in sleep:

It has been reported that both prostaglandins and 5-hydroxytryptamine have some role in the regulation of sleep. Parkes (1957) showed that chlorpromazine and reserpine prolonged the sleeping time caused by pentobarbitone and this effect was correlated with change in body temperature.
The present study was prompted by the eagerness to learn about the involvement of brain dopaminergic system in sleep mechanism. In our study, the "barbiturate sleeping time" test was performed. Attempt was made to correlate brain dopamine level with PGF1 induced potentiation of barbiturate sleeping time in mice, rats and in chickens.

(7) Dopamine and Temperature Regulation:
ICV injection of the specific dopamine agonist, apomorphine has been shown to produce hypothermia and this was blocked by specific antagonist pimozide (Kruk, 1972). Conflicting effects of hypothermia and hyperthermia have been reported after ICV injection of dopamine (Kruk, 1972). In the present study the effects of dopamine, apomorphine, amphetamine, L.dopa and SK & F 38393 were investigated on the rectal temperature. The effects of dopamine receptor blocking agents, pimozide, haloperidol on the effects of these drugs acting at dopamine receptors have also been determined.

(8) Anorectic effect:
The role of central adrenergic and 5-hydroxytryptaminergic system in the regulation of food intake is well documented (Booth, et al., 1973; Samanin, et al., 1972; 1973 and Setter, et al., 1978). The role of dopaminergic system in the
regulation of food intake has been demonstrated in recent studies and some of the central effects of amphetamine are also described to its dopaminergic activity (Carlsson, et al., 1970). The studies were undertaken to investigate the effects of various dopamine agonists and antagonists on food intake and associated change in body-weight.

(9) Role of dopamine in drinking behaviour of rats:

It is clear from the work which emanates from various studies that catecholamines and 5-hydroxytryptamine can modify drinking behaviour. There is some evidence, but so far less secure, that dopamine is concerned in the brain biochemistry of food intake and drinking behaviour. The interest in the present study has arisen from the known presence of dopamine in the brain, and this study was carried out to establish the possible role of dopaminergic mechanism in drinking behaviour.

(10) Dopaminergic system and its involvement in analgesia:

Many workers have attempted to assign specific functions of catecholamines in the CNS demonstrating their presence in different areas of brain. Vedernikov and Afrikanow (1969) have reported that pre-treatment with reserpine reduced the analgesic activity of morphine and same was observed by
This prompted us to investigate the involvement of dopamine in analgesic action of morphine and its mediator role. The purpose of investigation was to study the effect of altered concentration of dopamine on the antinociceptive action of morphine.

(11) Dopamine and addiction:
Dopamine has been ascribed a significant role in the production of morphine dependence and withdrawal (Wood and Richard, 1982; Genget, et al., 1983). Wood and Richard (1982) have suggested that in rats morphine appears to act exclusively at the pre-synaptic opiate receptors of dopaminergic nerve endings in the striatum and activation of these receptors result in enhancement of dopamine synthesis. In the present study we have studied the effects of dopamine agonists and antagonists on morphine dependence by the method described by Way et al. (1969).

(12) Role of dopaminergic amines in diabetes:
The hyperglycemic effect of L-dopa has been known since 1927 (Hi rai and Gomdo). Holtz and Credner (1944) showed that it was only the Levo-isomer of dopa which produced hyperglycemia and which was decarboxylated to dopamine in the living organism. From this observation Holtz and Credner (1944) postulated that dopamine and not
dopa caused the observed hyperglycemia. A more thorough investigation of the mechanisms of the hyperglycemia following dopa and dopamine administration appears to be lacking. In the present investigation we have studied the effects of dopaminergic agents on alloxan diabetic rats.