SUMMARY AND CONCLUSIONS
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Research in psychopharmacology over the past two decades indicates that brain catecholamines play an important role in mediation of different CNS functions. In the present study the effects of dopamine as well as its agonists and antagonists were studied on the central nervous system.

1. The drugs which tend to increase the levels, or availability of dopamine, like apomorphine, L-dopa, amphetamine and SK & F 38393 decrease the immobility whereas, dopamine receptor blocking agents such as pimozide, haloperidol, metoclopramide and depletor of catecholamines, reserpine increased the immobility. The present results tentatively indicate that the dopaminergic system play a role in appearance of immobility.

2. Very low doses of apomorphine induce yawning. Yawning in rats is believed to reflect stimulation of dopaminergic autoreceptors. Further L-dopa and amphetamine produced dose dependent increase in yawning upto the period of 40 mins., comparable with a low doses of apomorphine, whereas SK & F 38393 a novel dopamine failed to elicit this response. This yawning effect was inhibited by pimozide, a specific dopamine receptor blocking agent but remained unaltered in the presence of domperidone.
3. Dopaminergic agonists i.e. amphetamine, L.dopa and SK & F 38393 enhanced aggressive behaviour in reserpine apomorphine aggressive model whereas, dopamine receptor blocking drugs like pimozide, haloperidol, metoclopramide and neuroleptic agent like chlorpromazine blocked the reserpine-apomorphine fighting (R.A.A.). Furthermore, imipramine successfully antagonised the R.A.A. responses. Imipramine could not antagonise the R.A.A. behaviour when reserpine was administered daily for 3 days. These results suggest that central dopaminergic receptor are essential for the fighting responses.

4. The results obtained in the present study favour that dopaminergic system is responsible for aggressive behaviour which developed due to isolation. The dopamine receptor antagonists namely pimozide, haloperidol and metoclopramide inhibited the post-isolation syndrome. An isolation syndrome is reflection of psychoneurosis in human. It can be concluded that dopamine antagonists may be useful in such a human condition.

5. The predictal anti-cataleptic effects of apomorphine, L.dopa, amphetamine and SK & F 38393 in different doses were observed, and concluded that these responses of dopamine agonists are produced through post-synaptic receptors.
6. Pentobarbitone-induced "barbiturate sleeping time" was potentiated by PGE\textsubscript{1}. There was a significant decrease in the sleeping time in the presence of dopaminergic receptor blocking drugs, like haloperidol, pimozide, and metoclopramide, whereas, 5HT\textsubscript{1} blockers failed to shorten the sleeping time. REM sleep deprivation sensitized the brain effects which may be mediated through dopamine. This REM sleep deprivation enhanced central effects of apomorphine. The results of present study suggest that supersensitivity of post synaptic dopamine receptors may be involved in sleep mechanism.

7. Furthermore for the potentiating effect of dopaminergic stimulant agents on ethanol hypnosis, at present it can only be speculated that dopamine receptor activity of the nigrostriatal and mesolimbic dopaminergic system is involved in cortical activation and thus to potentiate the depressant action of ethanol.

8. DA injected intracerebroventricularly into rats, caused a fall in the rectal temperature. Similar effect was seen with intraperitoneal injection of dopamine agonists. The temperature changes induced by these drugs were virtually abolished by dopamine receptor blocking agents, haloperidol, pimozide and metoclopramide.
In another design dopamine agonists under reference were able to produce hypothermic action in TAB vaccine treated rats, and this action was not seen when animals were simultaneously pre-treated with dopamine receptor blocking agents. Furthermore, it was observed in present study that drugs which increase brain concentration of dopamine (e.g. nialamide, cocaine) potentiated the hypothermic effect of all dopamine agonists, whereas, these all agents failed to elicit hypothermic responses in animals pre-treated with reserpine.

Thus it appears that increase in concentration of dopamine and not post-synaptic dopamine receptor supersensitivity is responsible for the hypothermic effect, suggesting that dopaminergic receptors have important mediator/modulator role to play in thermoregulation.

9. Dopamine agonists amphetamine, apomorphine, L-dopa, and SK & F 38393 decrease food intake associated with decrease in body weight. The actions were antagonised by dopamine receptor blockers like haloperidol, and pimozide.
10. In our study no apparent change in water intake was observed, following i.c.v. administration of saline but i.c.v. dopamine significantly increased the water intake, pimozide has no effect on water intake but it blocked the effect of dopamine on water intake. So the dipsogenic effect of dopamine was significantly blocked by prior i.c.v. pimozide treatment of rats, indicating that dopaminergic receptors are involved and are stimulatory in nature.

11. The antinociceptive action of morphine was enhanced by dopaminergic stimulation and reduced by dopaminergic blockade. L.dopa, SK & F 38393 and apomorphine exhibited analgesic activity of their own. It was concluded that dopaminergic mechanism are involved in morphine-induced analgesia.

12. Nalorphine/naloxone precipitated jumping and other withdrawal syndrome in morphine dependent mice/rats was found to be increased in presence of dopamine agonists and dopamine receptor blockers and depletors (i.e. pimozide and reserpine respectively) were effective in preventing the withdrawal signs particularly "jumping". This confirmed the involvement of dopaminergic mechanism in morphine dependence.
13. In our study amphetamine, apomorphine, L.dopa were found to induce stereotyped behaviour whereas, in mice "swimming test" a decrease in the tone and spasticity of muscles was observed with the help of dopamine stimulating agents. Reserpine failed to produce any change in normal muscular activity and tone of animals. The studies thus indicate the role of dopamine system in maintainance of the tone of muscle and spasticity of muscle. Furthermore, in our study I have observed that SKF 38393 is devoid of central effects like stereotype behaviour.

14. Dopamine i.c.v. and i.v. produced hyperglycemia in normally fed rabbits and rats. Pimozide did not produce an effect on blood glucose level, however, it antagonized the hyperglycemic effect of L.dopa, apomorphine and other agonists of dopamine. After pre-treatment with nialamide the hyperglycemic response was potentiated by L.dopa. Furthermore, pronounced response in treatment to L.dopa and this action is antagonised in the presence of pimozide treated animals.

From the results enumerated above it is suggested that hyperglycemic effect of L.dopa and other dopamine agonists is mediated through dopamine in the brain, although,
how L-dopa potentiates the hyperglycemic effect more powerfully, in alloxan treated animals is not understood but this use is through the involvement of dopaminergic system in CNS as exerts at least part of its hyperglycemic effects on the pancreatic beta cells by interfering with insulin release mechanisms.

For the physiologist, the pharmacologist and the clinician it is a question of interest to know how dopamine is involved in the pathophysiology of the brain.

Our study leads to postulate that dopaminergic nervous system play modulatory/mediator role in various CNS functions. New actions and ideas concerning its possible involvements in pharmacological actions are emerging all the time, and the views set out in this thesis must necessarily, be regarded as provisional and tentative.