DISCUSSION
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The biochemical demonstration of occurrence of dopamine (DA) in the brain (Montagu, 1957; Carlsson et al., 1958, Bertler and Rosengren, 1959) and its intraneuronal localization (Carlsson et al., 1962) initiated extensive studies on the organisation of central dopaminergic neuron systems (Anden et al., 1966; Dahlastroom and Fuxe, 1965). Most of our current knowledge of the projections of dopamine neurons has been due to the development of sensitive biochemical (Thierry et al., 1973a,b) and histochemical (Hokfelt et al., 1976, 1977) techniques which have helped in localisation of termination areas of DA neurons in the central nervous system.

Dopamine agonists have provided a relatively new lead in research of more effective anti-parkinsonian drugs. The ones known and employed so far, are not free from troublesome adverse effects, although being highly expensive and the search for safer agent which can be synthesized more easily still continues. The use of anti-cholinergic agents in the treatment of Parkinson's disease has been largely empirical. A variety of anti-parkinsonian drugs inhibit dopamine uptake into striatal synaptosomes of rat. (Coyle and Snyder, 1969). Amantadine may possess a similar property upon dopamine neurons (Parkes, J.D., 1970b). Amphetamine acts by causing
release of dopamine from neurons and stores. At present we do not know which type of drug—the directly acting agonist or the indirectly acting releaser or uptake blocker with long/short duration of action is more useful in treating parkinsonism.

Evidence implicating brain dopamine in psychotic disorders is mainly considered as hypothetical. In particular, the hypothesis that drugs used in treatment of schizophrenia owe their effectiveness to their ability to antagonize the effects of dopamine at receptor sites in CNS has been supported by recent experimental evidences (Caeese et al., 1978; Kendler et al., 1983).

Dopamine receptors in the brain have been studied extensively in vitro (Brown et al., 1976) and in vivo (Baudry et al., 1977). The possibility of existence of multiple categories of dopamine receptors has been considered in recent articles. (Kebabian and Calne, 1979; Gulati and Dhawan, 1984; Sidhu et al., 1986; Claus and Anderson, 1987). Numerous functions are affected and regulated by dopaminergic receptors. The animal behaviour is also influenced by agents acting on dopaminergic receptors. The behavioural effects produced as a result of dopamine receptor stimulation are stereotype.
(Eranst, 1965, 67; Srimal and Shawan, 1970; Dhawan et al., 1974), hypermotility (Carlsoon, 1975; Woodrulf et al., 1974, 1976), sexual behaviour (Kamberic et al., 1971) and self stimulation (Simon et al., 1977). Dopaminergic receptor mechanisms also take part in control of autonomic functions like cardiovascular (Goldberg, 1972), respiration, growth hormone release (Lai et al., 1973) and emesis (Cannun, 1975). Furthermore, dopamine inhibits the adenylyl cyclase from prolactin secreting human pituitary adenomas (Camills et al., 1978). Dopamine-receptors not associated with adenyl cyclase activity also exist (e.g. dopaminergic "autoreceptors" on the nigro neostriatal neurons). The presence of both functionally and pharmacologically distinct types of dopamine receptors within the mammalian brain may have great impact upon both, in situ in the aetiology of disorders and the design of drugs required for treatment of central dopamine disorders (Cools and Van Rossum, 1976, 1980, Colls, 1977; Dandia and Biswat, 1985; Calark and Smith, 1981; Margaret et al., 1987; Adjeroud et al., 1986).

The results of the present study describe the effects of dopamine on CNS in laboratory animals and the experiments undertaken to account for their mechanism of action at these sites.
Immobility in mice:

In the present study, a slightly modified "behaviour despair swimming test" of Porsolt, et al., 1977 was employed. As some mice hardly exhibited the immobile posture, the mice were forced to swim twice. Mice showing a duration of immobility of constant range were selected first, then it was repeated again for immobility. It was found that mice treated in this system showed a significantly longer duration of immobility at the second swimming period than at the first. This prolongation seems to be the result of "learning" during the first swim as escape was impossible. Similar observation have been reported by Porsolt, et al., 1977a, Iao et al., 1984. We also reconfirmed the ability of imipramine (20mg/kg) an uptake blocker to reduce the duration of immobility. These results indicate that the present system is basically similar to that of Porsolt et al. (1977a).

Porsolt et al., (1979) have speculated that a decrease in the level of catecholamines leads to an increase in the duration of immobility. Costa et al., 1975 reported similar results, that diazepam decreases the turn over of catecholamines. In the present study it was found that the drugs which tend to increase the levels, or availability of dopamine, i.e. apomorphine, L.dopa, amphetamine and SK & F 38393 decrease the immobility whereas, dopamine receptor blocking agents and depletor of catecholamines increase the immobility.
In conclusion, the present results tentatively indicate that the dopaminergic system plays a role in appearance of immobility.

**Study related to yawning behaviour of different dopamine agonists:**

Schizophrenic morbidity has been reported to be reduced by low doses of apomorphine (Corsini et al., 1971; Smith et al., 1977). Such low doses of apomorphine are considered to stimulate selectively dopamine autoreceptors (Strombom, 1976), leading to a decrease of dopamine release. In humans, it has been found that a low non-emetic dose of apomorphine induces yawning (Corsini et al., 1977). Apomorphine also induce yawning in rats (Mogilincka, and Klime-k, 1977), and the behaviour is believed to reflect autoreceptor stimulation (Yamada and Furukawa, 1980).

The present study confirmed the finding that in very low doses, apomorphine induces yawning (Mogilincka and Klime-k, 1977; Yamada and Furukawa, 1980). Pimozide, a specific dopamine receptor blocking drug inhibited this effect in a dose dependent manner, giving and evidence for the involvement of dopamine in the yawning response and its possible mediation by autoreceptors. It is not possible that the
response could be due to stimulation at peripheral dopamine receptors since domperidone does not antagonise apomorphine induced yawning.

Further it was observed that L.dopa in doses at 50, 100, 150 and 200 mg/kg, amphetamine in doses at 1, 2, 5 and 10 mg/kg produced dose dependent increase in yawning upto the period of 40 minutes, comparable with those of a low doses of apomorphine, whereas SK & F 38393, a novel dopamine agonist failed to elicit this response. Our data supports the idea that yawning behaviour may be used as an index of dopamine autoreceptor stimulation. Using this model it was found that L.dopa, amphetamine and apomorphine possess autoreceptor stimulating properties whereas SK & F 38393 is devoid of this feature.

**Dopaminergic system in aggressive behaviour:**

Apomorphine is considered to be a specific agonist of dopaminergic receptors (Andén et al., 1967). It can be argued that apomorphine induce aggressive behaviour by activating central dopaminergic receptors. The involvement of brain dopamine in the aggressive response is substantiated by the finding that L-dopa, the precursor of catecholamines, elicits the aggressive response. Furthermore in the present study it was found that dopaminergic agonists (i.e. amphetamine
and SK & F 38393) enhance aggressive behaviour in reserpine-apomorphine aggressive (RAA) model.

Dopamine receptor blocking drugs like pimozide, haloperidol, metaclopramide and neuroleptic agent like chlorpromazine blocked the reserpine-apomorphine fighting behaviour (Table-6). These results strongly support the contention that central dopaminergic receptors are essential for the fighting responses. Our results support the results of other workers who have studied different pharmacological models of aggressive behaviour (Richardson and Iacobowitz, 1972; Thoa et al., 1972a).

Apomorphine induces the aggressive response only when the brain catecholamines are depleted by reserpine. Reserpine depletes brain catecholamine levels to about 20% of normal in 4 hours.

There is strong evidence in support of the development of supersensitivity of dopaminergic post-synaptic receptors in the CNS (Thornburg and Moore, 1975). Central dopamine receptors acquired a supersensitivity on reserpinization (Ungarstedt, 1971). In the present study, a similar mechanism can be postulated for the enhanced aggressive response seen after pretreatment with reserpine.
Other possibilities must also be considered, for example, reserpine treatment can alter other transmitter systems which interact with dopaminergic neurones such as NA, Ach or L-glutamate (Palmer et al., 1976; Jain et al., 1985). Furthermore, the finding that the supersensitivity developed in the dopamine receptor after denervation of the dopaminergic neurons is associated with an increase in susceptibility of DA sensitive adenylated cyclase to agonists (Misashi et al., 1976), suggests that cAMP acts as second messenger in the central dopaminergic system. Therefore, it can be postulated that cAMP linked dopamine receptors are involved in behavioural responses.

When imipramine was given for 3 days followed by reserpine, given 4 hr before the apomorphine challenge the fighting response was blocked. However, when reserpine was given for 3 days followed by imipramine, given 4 hr before the apomorphine challenge, fighting tendency was induced in animals. In the first case imipramine could raise the effective concentrations of catecholamine at the receptor sites by blocking active re-uptake, whereas in the later situation it possibly could not do so.

In conclusion, aggressive behaviour appears to be mediated specifically through dopaminergic mechanisms. Acetylcholine, noradrenaline or 5-hydroxytryptamine appears to act as inhibitory in the aggressive behaviour.
Isolation syndrome in mice:
The isolation is known to produce aggressive behaviour. The aggressive behaviour developed after a period of 6 weeks. The dopamine receptor antagonists—pimozide, haloperidol or metoclopramide inhibited the post-isolation syndrome. Since isolation syndrome reflects psychoneurosis in human beings, it can be concluded that dopamine antagonists may be useful in such an aggressive human condition.

Dopamine agonists on haloperidol induced catalepsy:
In the present study employment of different doses of dopamine agonists have thrown some light on the role of dopaminergic system in haloperidol induced catalepsy. Dose dependent paradoxical effects on spontaneous motor activity have been ascribed to reflect difference in agonist activity for presynaptic autoreceptors and postsynaptic dopamine receptor (Stromberg, 1976).

The behavioural effects such as hypermotility and stereotype are considered to be the effects mediated by post synaptic dopamine receptors, which are blocked by a known striatal dopamine antagonist, haloperidol (Von Rossum 1969). The predicted anti-cataleptic effects of apomorphine, L.dopa, amphetamine and SK & F 38393 in different doses were observed. It was concluded that these four dopaminergic agonists produced dose-dependent responses through post-synaptic dopamine receptors.
Role of dopamine in sleep:

Involvement of dopamine in sleep has been speculated by various workers. Green and Iverson (1972) reported that haloperidol and promethazine reduces sleeping time. It was also suggested that dopamine receptor activity of nigrostriatal and mesolimbic dopaminergic system is involved in cortical activation and behavioural arousal (Gillin et al., 1978). Results of the present investigation support these findings. It was found that ethanol induced sleeping time was significantly potentiated by dopaminergic agents and decreased by dopaminergic blocking agents.

In the data obtained in our study, prostaglandin E\textsubscript{1}, (50ng/kg and 100ng/kg, i.p.) produced significant potentiation (P < 0.001) of pentobarbitone sleeping time in mice, rats and chicken. Animals receiving PGE\textsubscript{1} before pentobarbitone sodium (100mg/kg), became quiescent, huddled together in corner and closed the palpebral fissure. In this study we observed significant decrease in sleeping time (P < 0.001) in the presence of dopaminergic receptor blocking drugs like haloperidol (4mg/kg), pimozide (0.5mg/kg) and metaclopramide (5mg/kg), whereas 5-HT, \(\alpha\) and \(\beta\)-receptor blockers failed to shorten the sleeping time.
Catecholamine release from nerve endings can be inhibited by PGE$_1$ (Hedquist, 1970; Shio et al., 1971; Boonyaviro and Gutam, 1975). It is possible that the mechanism of PGE$_1$-induced potentiation of barbiturate sleeping time is due to a supersensitivity to post-synaptic dopamine receptors that develops as a result of inhibition of dopamine release from the nerve endings by PGE$_1$.

REM sleep deprivation sensitizes the brain, the effect which may be mediated through dopamine (Carlini et al., 1977). This REM sleep deprivation enhances central effects of apomorphine (Tufix et al., 1978). These workers suggested the underlying mechanism to be explained in terms of supersensitivity of brain dopamine receptors.

Dopamine and temperature regulation:

The catecholamines acting on the anterior hypothalamus, bring about changes in body temperature which are species-dependent. Dopamine (DA), the metabolic precursor of the neurotransmitter, nor-adrenaline, has not yet found a place in the monoamine models of thermoregulation. This may be attributed to the following observations, (1) DA evokes only mild change in body temperature compared to the intense effect of noradrenaline. (2) The nature of temperature response in different species to both amines is identical. The present results support the role of dopamine in thermo-regulatory mechanism.
ICV injection of the specific DA agonist, apomorphine has been shown to produce hypothermia in rats and this was blocked by the specific antagonist, pimozide (Kruk, 1972), conflicting reports like hyperthermia and hypothermia have been reported after icv injection of DA (Cruk, 1972). In the present study the effects of DA, apomorphine, SK & F 38393 and L.dopa were investigated for their effects on the rectal temperature. The effects of DA receptor blocking agents, haloperidol and pimozide, on the effects of these drugs acting at DA receptor have also been determined. Our results are in favour of what has been reported by Kruk (1972).

From the results obtained in the present study, it was observed that dopamine, in the doses employed, produces a fall in rectal temperature. Pimozide and haloperidol had no significant effect on body temperature when given alone, however when administered along with dopamine (5 µg and 10 µg in rats icv) they reversed its action (i.e. from hypothermia to hyperthermia). In a similar manner other agonists i.e. apomorphine 2.5, 5 and 10 mg/kg, SK & F 38393, 5 and 10 mg/kg and L.dopa in doses of 100, 200 and 300 mg/kg respectively produced dose dependent decrease in body temperature and this hypothermic effect was antagonized by the dopamine receptor blocking drugs i.e. Pimozide 0.5 mg/kg and haloperidol
4mg/kg. In another series, hyperthermia was induced in rats by injection of T.A.B. vaccine as this agent is known to be a potent hyperthermic in nature. The dopamine agonists under reference were able to produce hypothermic action in T.A.B. vaccine treated rats and this action was not seen when animals were simultaneously pretreated with 0.5mg/kg. Pimozide or 4mg/kg haloperidol, suggesting the involvement of central biogenic amine, dopamine, in the hypothalamic nuclei in thermoregulation.

Dahlstrom et al. (1961) suggested that depletion of presynaptic catecholamine may result in hypersensitive postsynaptic receptors in a manner analogous to the phenomenon of decentralization supersensitivity described in peripheral adrenergic systems (Trendelenberg, 1963). However, it was observed in the present study that drugs which increase brain concentration of dopamine (e.g. nialamide, or cocaine) potentiated the hypothermic effect of all dopamine agonists, whereas all these agents failed to elicit hypothermic response in rats pretreated with reserpine.

Thus it appears that increase in concentration of dopamine and not the postsynaptic dopamine receptor supersensitivity is responsible for the hypothermic effect. Furthermore, in the pigeons, the dopamine receptors stimulated
by apomorphine and mediating hypothermia appear to be distinct from adrenoceptor because they are blocked by pimozide and not by phenoxybenzamine or propranolol. The receptors mediating stereotype are also distinct from the adrenoceptors and involved in addition, tryptaminergic receptors. Rotrosen et al., (1972) have shown that tryptaminergic receptors are not involved in the regulation of stereotype in rat. Finally, from data observed in the present study, on the basis of pharmacological evidence presented here, dopamine receptors may be distinct from other receptors. This finding is supported by the observation of many investigators that dopamine receptors are preferentially blocked by DA antagonist such as pimozide and haloperidol (Fuxe and Slogust, 1972, Kurk, 1972), suggesting that dopaminergic receptors have important mediator/modulator role to play in thermoregulation.

Food intake:

The role of central adrenergic and 5-hydroxytryptaminergic system in regulation of food intake is well documented (Booth, D.A., 1968; Setler, et al., 1978 and Samanin et al., 1977). 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 ascribed to its dopaminergic activity (Carlson, 1970). Carruba et al. (1980) demonstrated a decrease in food intake in rats pre-treated with mazindol, piribedil and bromocriptine.
In the present study it was observed that dopamine agonists amphetamine (5mg/kg) apomorphine (10mg/kg), L-dopa (200mg/kg), decreased food intake associated with decrease in body weight. The action was antagonised by specific dopamine blockers haloperidol (4mg/kg) or pimozide (0.5mg/kg). This supports the role of dopaminergic system in the regulation of food intake.

SK & F 38393, is a new dopamine receptor agonist (Janssen et al., 1968), which does not share some of the central actions of other dopamine agonists like apomorphine and amphetamine as it does not produce emesis, decreased prolactin activity and stereotype behaviour (Setler et al., 1978; Girdhar et al., 1982). It was found to decrease food intake in rats. Pimozide in the dose used selectively blocks dopamine receptors (Anden et al., 1970; Janssen et al., 1968) and completely abolished the action of SK & F 38393 on food intake. Researches in developing new anorectic drug is directed to minimizing the central side effects while preserving the anorectic activity. SK & F 38393 does not seem to produce the excitation, emesis, stereotype behaviour or decrease in prolactin activity (Setler et al., 1978) and Spontaneous Motor Activity (Girdhar et al., 1982). The site of action, therefore remains intriguing.
Role of dopamine in drinking behaviour of rats:

During the 1960's, the idea that serotonin or dopamine was involved in ingestive behaviour arose because 5-hydroxy-tryptophan (5-HTP) administered peripherally altered both food and water intake of the rat (Joyce and Morsovsky, 1964). The role of dopaminergic system in the regulation of drinking and food intake has been demonstrated in the central effects of amphetamine ascribed to its dopaminergic activity (Calissun, A., 1970). Further Goldman and Lehr (1967) have reported the inhibition of the dipsogenic effect by the injection of propranolol. However, studies with central dopamine are lacking and the role of central dopaminergic mechanisms in drinking behaviour is still controversial.

In the present investigation, no apparent change in water intake was observed, following i.c.v. administration of saline, but i.c.v., dopamine in dose of 100 μg significantly (P<0.01) increased the water intake. Pimozide (50 μg/rat i.c.v.) has no direct effect on water intake but it blocked the effect of dopamine on water intake. Furthermore apomorphine and SK & F 38393 when given i.c.v. in dose of 100 μg produce same effect like dopamine and this action was also significantly blocked by prior treatment of rats with pimozide (i.c.v.), indicating that the central dopaminergic receptors are involved and are excitatory for water intake in rats.
Dopaminergic system and its involvement in analgesia:

Numerous attempts have been made to link the central effects of morphine with neurotransmitters in the brain (Clouet, 1971; Way, 1972), but this evidence is often confusing. The observation that reserpine alters the antinociceptive action of morphine (Fenessy and Lee, 1971) prompted us to investigate the involvement of dopamine in analgesic action of morphine.

Both the MAO inhibitors, nialamide and mangiferin, are reported to produce marked potentiation of morphine analgesia in albino rats, the effect being substantially greater with nialamide (Bhattacharya et al., 1980). They also found that reserpine-induced inhibition of nialamide potentiation of morphine was significantly reversed by pretreatment with 5-HTP and not by L-dopa suggesting that the potentiation involves brain monoamines and not dopamine.

In the present study it was found that L-dopa, apomorphine, SK & F 38393 and amphetamine exhibited analgesic activity in well tolerated doses, whereas, pimozide exhibited no such activity when each drug was studied by tail flick method. Our results are not in accordance with the views of Hidelberger and Erspamer (1975).
Present results are consistent with data of Watanahle et al. (1969), who reported a potentiation of analgesic activity of morphine by sodium-dl-ethyl dithocarbamate, a dopamine B-hydroxylase inhibitor, which produces a rise in dopamine concentration in the mouse brain. The antinociceptive action of morphine was reduced by pretreatment with pimozide indicating that dopaminergic mechanism is involved in the antinociceptive effect of morphine. It can be postulated that the enhanced efficacy of morphine after L-dopa appears to be mediated solely by the central dopamine receptors. These results suggest that brain DA may be an important and potent modulator of analgesic action of morphine.

In another set of experiments, effect of dopamine agonists are studied on acetic acid induced stretch episodes in mice, as well as by Bianchi's tail clip methods. L-dopa was found to have significant analgesic activity in the doses which have been used by many other investigators to increase the brain catecholamine levels (Latti and Porter, 1970; Way, 1972). In the present study, L-dopa in doses of 100mg/kg, 200mg/kg and 300mg/kg produced a significant increase in the reaction time as compared to normal reaction time (i.e. without drug treatment), in the same animals. The increase in reaction time produced by L-dopa was found to be dose dependent. The maximum effect was observed at 15 and 30 minutes after drug administration.
Further, L-dopa, when given along with the morphine (5mg/kg i.p.) was found to enhance the analgesic activity of morphine (P < 0.001). Similar type of results were obtained with all other dopamine agonists studied (i.e. SK & F 38393, apomorphine and amphetamine).

Dopamine turn over is suppressed by either morphine administered systemically or B-endorphine injected intracerebrally (Deyo et al., 1979). Since in our study, L-dopa enhanced the analgesic action of morphine, the possibility that an increase of dopaminergic activity could occur in brain areas associated with opiate receptors implicated in morphine analgesia can not be ruled out, other possibility could be that morphine can alter the distribution or release of dopamine in the brain.

The results of present study also support the contention of Major and Pleuvry (1980) that morphine analgesia in rats depend on relative brain concentrations of dopamine.

**Morphine dependence:**

Morphine dependence has been induced in rats by the intraperitoneal administration of drug (Drawbagh and Lal, 1976). Injection of antagonist naloxone in morphine dependent rats has been reported to result in the production of withdrawal signs, i.e. jumping, wet dog shaking, writhing, ptosis and eye twitching (Blesing et al., 1973).
Our results are in agreement with observations of Khan and Dandiya (1983) and Menon and Loh (1975) that the appearance of writhing, wet dog shaking declines when the dominant sign like jumping appears on withdrawal of morphine in dependent mice.

Dopamine has been ascribed a significant role in the production of morphine dependence and withdrawal (Wood and Richard, 1982; Genc et al., 1983). Ferrai and Baggio (1982) proposed that lisuride aergolic derivative modulates withdrawal signs by stimulation of dopamine receptors in central nervous system. Wood and Richard (1982) have suggested that in rats, morphine appears to act exclusively at the presynaptic opiate receptors on dopaminergic nerve endings in the striatum and activation of these receptors results in enhanced dopamine synthesis. In present study dopamine agonists like L-dopa, apomorphine, d-amphetamine and SK & F 38393 aggravated the phenomenon of jumping. Dopamine receptor blockers and depletors i.e. pimozide and reserpine respectively were effective in preventing the withdrawal signs particularly the "Jumping" whereas 5HT and histaminergic blocking agents cyproheptadine and mepyramine respectively failed to do so. Imipramine increases the availability of dopamine, potentiating the jumping response has been suggested by Wood and Richard (1982). This finding indicates that the occurrence of withdrawal signs of morphine dependence like jumping, writhing are functions of elevated dopaminergic activity.
Psychopharmacological aspects of dopaminergic system:

Involvement of brain catecholamines and serotonin in the learning process is fairly well documented. It is reported that amphetamine facilitates learning in animals (Kulkarni, 1968). However, various workers failed to support this view (Stein, 1964; Broze and Moore, 1966; Fuxe and Hanson, 1967; Leonard, 1969; Barar et al., 1980).

In our study also dopaminergic drugs did not antagonize the conditioned avoidance response in Cook's pole climbing apparatus, Y-maze, as well as in obstruction box.

The concepts of dopaminergic mediation in drug-induced stereotype is well established (Randrup and Munkvad, 1970). The extensive studies conducted with number of pharmacological agents in animals have clearly demonstrated that induces compulsive syndrome should influence the brain dopaminergic system by one or other mechanism. It was postulated that production of stereotyped behaviour of drugs under study is due to stimulation of dopaminergic receptors in the striatum as it was also reported by Randrup and Munkvad, 1966; Fog et al., 1967, where as the locomotor effect of these drugs was due to activation of dopaminergic receptors in the nucleus accumbens (Kelly et al., 1975; Van Rossum et al., 1977; Iversen and Koob, 1977). The effects of dopaminergic agents has
also been studied by Van Rossum et al., 1970; Dandya and Bapna, 1967; and Kulkarni and Dandya 1972. In our study amphetamine apomorphine and L-dopa were found to induce stereotyped behaviour which was antagonized by dopaminergic blockers like haloperidole, pimozide and chlorpromazine. Methysergide, propranolol, clonidine, cyproheptadine and cimetidine failed to alter the stereotype behaviour. This results further substantiate the involvement of dopamine in stereotype behaviour. It is however not clear why SK & F 38393 failed to produce any stereotype behaviour. In our study we have observed that SK & F 38393 is devoid of central effect like stereotype behaviour as also reported by Pendelton et al., 1978.

In mice "swimming test" we observed a decrease in the tone and the spasticity with agents like L-dopa (200mg/kg), SK & F 38393 (5mg/kg), apomorphine (5mg/kg) and amphetamine (5mg/kg). Reserpine (5mg/kg, i.p.) failed to produce any change in normal muscle activity and tone of animals. The studies thus indicate the role of dopamine system in maintainance of tone muscle and spasticity of muscle.
Role of dopaminergic amines in diabetes:

The hyperglycaemic effect of adrenaline based upon glycogenolysis and decreased peripheral glucose utilization is well known (Ellis, 1956; Hagen and Hagen, 1964). With regard to the site of action of dopamine, which does not seem to have been investigated previously probably on the assumption that it would be the same as for adrenaline. Our results tentatively suggest that central dopaminergic system may play a key role in controlling the blood glucose level.

It is observed that dopamine i.c.v. 10 ug and dopamine 20mg/kg i.v. produced hyperglycemia in normally fed rats. In 18 hours fasted rats dopamine and its agonists produced more pronounced hyperglycaemia. Pimozide (1mg/kg) did not produce any effect, however it antagonized the hyperglycemic effect of L-dopa, apomorphine and SK & F 38393. After pretreatment with nialamide the hyperglycemic response was potentiated by L-dopa.

Injection of L-dopa did not alter alloxan induced hyperglycemia in rats. However, pimozide prevented alloxan-induced hyperglycemia in rats. These results suggest that central dopaminergic mechanisms may be involved in alloxan induced diabetes mellitus.
Glybenclamide which has been shown to have a direct effect on the beta-cells of the pancreas, resulting in insulin release, failed to lower the dopamine induced hyperglycemia when given shortly after dopamine, whereas dopamine did not elicit the usual hyperglycemia when glybenclamide was injected shortly before dopamine. This interaction of the two drugs further indicates that dopamine is able to interfere with the insulin release mechanism.

Little information is available on blood glucose level changes evoked by other drugs interfering with the formation, storage and release of dopamine. The results of this study provide some evidence for the concept that dopamine produces effects partly on the pancreatic beta cells by interfering with insulin releasing mechanisms for its hyperglycemic effect.