Diabetic hyperglycaemia results both from the impairment of glucose uptake by the liver and peripheral tissues and from the overproduction of glucose through the activation of liver gluconeogenesis (Taylor and Agius, 1988; McGarry, 1992). Both hyperglycaemia and its long term metabolic consequences affect peripheral nerves and that axons, myelin, Schwann cells, interstitial cells, vessels and the perinurium are all damaged in the cause of symmetrical polyneuropathy. The pathogenesis of diabetic neuropathy is not explainable by any single mechanism and that development of neural lesions is linked to extraneural systemic complications. It appear likely that local functional and anatomical features interact with systemic abnormalities, to produce the complex of neurologic disturbances.

Studies by Trutnov and Thoenen (1967) made a remarkable discovery that an isomer of norepinephrine namely, 6-hydroxydopamine (6-OHDA), produced a destruction of the terminal ground plexus of peripheral sympathetic noradrenergic neurons. Following this observation, several studies have been done using 6-OHDA, which selectively destroys the nerve terminals leaving the cell bodies intact (Theonen and Trazer, 1973). Reciprocal changes in gluconeogenic enzyme activity in kidney and liver by VMH lesion following 6-OHDA treatment were also observed by Nagai et al (1982). It prevents the neural stimulation of glucose release (Lautt and Wong, 1978a). Apart from 6-OHDA, several other drugs are known to have antiadrenergic effect viz., vinblastine, guanethidine, guanoxan etc, which vary in their mode of action and dosage required to have antiadrenergic effect.
Amongst guanedinium adrenergic neuron blocking agent, guanethidine is widely employed. It was used as an antihypertensive drug (Burnstock and Costa, 1975) more than 20 years ago (Leishman et al., 1959; Dollery et al., 1960) and is still useful in the treatment of severe or resident hypertension (Kunes and Jelinek, 1979; Antonaccio et al., 1980). Its toxic effect was found to be selective for sympathetic postganglionic neurons in neonatal and adult rats by affecting the catecholamine uptake pump (Johnson and Manning, 1984). This drug primarily influences the cell bodies rather than axons (Heath and Burnstock, 1977; Anoop, 1993). The chronic administration or high dose of guanethidine to newborn or adult causes destruction of peripheral sympathetic neurons (Mills et al., 1986), without affecting other cell types of central adrenergic system (Johnson and O’Brien, 1976; Kvetnansky et al., 1979) due to the blood brain barrier because it is highly ionized at physiological pH (Butler et al., 1994).

Guanethidine itself could bind either covalently or noncovalently to a neuronal membrane protein as a hapten to form an antigen. Therefore, the antisympathetic action of guanethidine is immune-mediated (Manning et al., 1983), which was first suggested by Jensen-Holm and Juul (1971). Several immunosuppressive agents (gamma radiation, cyclophosphamide, azathioprine), each of which produces immunosuppression by a different mechanism, protect against guanethidine induced sympathectomy in the rats.

The toxic effect of guanethidine is pH dependent. It is directly proportional to the pH. At lower pH, it does not evoke toxic effect. But, at pH 7.4-7.6 and above it causes complete destruction of cell bodies (Johnson and Aloe, 1974; Anoop, 1993). Thereby, adrenergic neurons were destroyed but cholinergic systems were left completely intact. Thus, guanethidine might have a general toxic effect through inhibition of mitochondrial respiration. It inhibits oxidative phosphorylation in mitochondria of rat liver (Manning et al., 1982), thereby unable to generate ATP and sequester Ca\(^{2+}\) into mitochondria. This enhanced Ca\(^{2+}\) to a cytotoxic level (Juul and Send, 1973), causes complete absence of nerve endings supporting the concept of drastic loss of ganglion cells which inhibits normal growth in the animal (Klein, 1979a; b).

Adrenocorticosteroids secreted from adrenal gland are involved in metabolic, thermoregulatory, reproductive and many other physiological changes taking place in body
Guanethidine treatment also reduced adrenal sensitivity to ACTH, thus affects adrenocortical activity and reduces corticosterone secretion in adult rats (Kleitman and Holzwarth, 1985). In rats and several other vertebrates guanethidine also induces norepinephrine depletion (Eranko and Eranko, 1971; Angeletti and Levi Montaldini, 1972; Burnstock and Costa, 1975). Plasma NA levels in guanethidine treated rats were reduced by at least 85% (Butler et al., 1994), by 70% in stressed Sprague-Dawley rats (Kvetnansky et al., 1979) and by more than 80% in normotensive Sprague-Dawley rats (Lo et al., 1991).

Manipulation of sympathoadrenal system by performing chemical sympathectomy and adrenalectomy simultaneously, emphasizes the influence of parasympathetic component of autonomic nervous on the glucoregulatory activities of liver. The fact that insulin and acetylcholine are interdependent (Mondon and Burton, 1971), led to a suggestion that parasympathetic neuropathy can cause diabetes (Lautt, 1979a). The counterregulation of glycaemia is elucidated by subjecting chemical sympathectomy and vagotony simultaneously.

MATERIAL AND METHODS
Adult male albino rats of Charles Foster strain weighing between 150-170 gms were taken for the present investigation. Rats were maintained in standard laboratory conditions of 12L:12D hrs with ad libitum food and water. After acclimatizing for a week to human handling, rats were divided in six groups with ten animals in each group.

GROUP I CHEMICAL SYMPATHECTOMY (CSX)
GROUP II CONTROL CHEMICAL SYMPATHECTOMY (CSS)
GROUP III CHEMICAL SYMPATHECTOMY + ADRENALECTOMY (CSX + ADX)
GROUP IV CONTROL CHEMICAL SYMPATHECTOMY + SHAM ADRENALECTOMY (CSS + ADS)
GROUP V CHEMICAL SYMPATHECTOMY + VAGOTOMY (CSX + VGX)
GROUP VI CONTROL CHEMICAL SYMPATHECTOMY + SHAM VAGOTOMY (CSS + VGS)

After respective treatments, on 29th day overnight fasted rats were sacrificed. Blood was collected by puncturing the jugular vein and was centrifuged in a refrigerated centrifuge for 20 minutes at 3000rpm to obtain the serum. It was stored in the deep freeze and was used to estimate glucose and for hormone assay. Immediately after sacrificing, liver was excised.
quickly, blotted and freeze-dried. Homogenate of different concentrations in respective medium were prepared for various estimations employing various under mentioned methods.

The blood glucose level was estimated by the method of Glucose oxidase kit (1969) and the amount of glucose was estimated as mg glucose/100ml blood. Tissue glycogen content was assayed by the method of Seifter et al. (1950). The amount of glycogen was expressed as mg glycogen/100 mg tissue. Glycogen synthetase activity was assayed by the method of Leloir and Goldemberg (1962) and glycogen phosphorylase by the method of Cori et al. (1943) modified by Cahill et al. (1957). The enzyme activities were expressed as μmoles of UDP formed/mg protein and μmoles of phosphorous released /mg protein/10 minutes, respectively. Method of Harper (1963) was employed to measure the Glucose-6-Phosphatase activity and expressed as μmoles of phosphate released/mg protein/15 minutes. Lactate dehydrogenase activity was estimated by the method of King (1971) modified by Varley (1975) and expressed as μmoles of lactate oxidized/mg protein/15 minutes. Succinate dehydrogenase activity was estimated by the method of Nachlas et al. (1960) and the enzyme activity was expressed as μg formazan formed/mg protein/60 minutes. Acetyl cholinesterase activity was assayed by the method of Ellman et al. (1961) and expressed as μmoles of acetylcholine iodide hydrolyzed/mg protein/60 minutes.

Statistical Analysis
Data was analysed statistically employing Student's ‘t’ test and p value less than 0.05 was considered statistically significant.

RESULTS
The data procured after various treatments (CSX, CSX + ADX and CSX + VGX) are represented in Table 4.1, 4.2 and Figure 4.1-4.5 respectively.

Rats treated for chemical sympathectomy singly and in combination with adrenalectomy (CSX + ADX), resulted a pivotal decrease in blood glucose level (Figure 4.1A). In CSX rats it decreased by 28% whereas in CSX + ADX it decreased by 44% (Table 4.2). On the contrary, a marginal increase in blood glucose level was noticed after performing chemical sympathectomy and vagotomy together (p<0.05).
In CSX rats, the tissue glycogen content increased significantly (p<0.01; Figure 4.1B) along with the increase in glycogen synthetase activity (Figure 4.2A). Similarly, in CSX + ADX rats both glycogen content and glycogen synthase activity decreased significantly (p<0.01 and p<0.001, respectively). But, in rats subjected to chemical sympathectomy and vagotomy together, the liver glycogen level and glycogen synthetase activity declined by 18% and 25%, respectively (Figure 4.5).

Phosphorylase activity increased slightly in sympathectomized rats but the response was reverse in other treatments. Rats treated for chemical sympathectomy and adrenalectomy simultaneously showed decreased phosphorylase activity (p<0.01) and this decrease was less significant (p<0.05) in CSX + VGX rats (Figure 4.2B).

Glucose-6-phosphatase and lactate dehydrogenase activities decreased following chemical sympathectomy singly (CSX) and in combination with adrenalectomy (CSX + ADX). However, in CSX + ADX rats, more significant decrease in G-6-Pase (p<0.001; Figure 4.3A) and LDH (p<0.01; Figure 4.3B) activity was observed. On the contrary, after subjecting to chemical sympathectomy and vagotomy together, glucose-6-phosphatase and lactate dehydrogenase activity increased slightly (p<0.05).

Succinate dehydrogenase activity increased in all the conditions. However, in rats subjected to chemical sympathectomy and adrenalectomy together, increase in SDH activity was minor (35.81± 1.90) compared to control group rats (29.17 ± 1.58). Whereas, in chemical sympathectomized rats singly (CSX) and in combination with vagotomy (CSX + ADX) it increased significantly (p<0.02; Figure 4.4A).

Acetylcholinesterase activity increased pivotally following chemical sympathectomy singly (p<0.01) and in combination with adrenalectomy (p<0.001) (Figure 4.4B). But, it decreased concomitantly in rats subjected to chemical sympathectomy and vagotomy together (0.061 ± 0.005) compared to the control group rats (0.122 ± 0.01) (Table 4.1).
Table 4.1 Levels of serum glucose, hepatic glycogen, and activities of key enzymes of carbohydrate metabolism and acetyl cholinesterase in the liver of male albino rat subjected to chemical sympathectomy singly and in combination with vagotomy and adrenalectomy.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Chemical Sympathectomy</th>
<th>Chemical Sympathectomy + Adrenalectomy</th>
<th>Chemical Sympathectomy + Vagotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sham</td>
<td>Experimental</td>
<td>Sham</td>
</tr>
<tr>
<td>Glucose (mg/dL Serum)</td>
<td>123.19± 8.20</td>
<td>89.13***</td>
<td>121.02± 8.95</td>
</tr>
<tr>
<td>Glycogen (mg/100 mg Wet Tissue)</td>
<td>1.24± 0.112</td>
<td>1.74**</td>
<td>1.30± 0.092</td>
</tr>
<tr>
<td>Glycogen Synthase (µM UDP/mg Protein/10 Min.)</td>
<td>0.108± 0.0071</td>
<td>0.152***</td>
<td>0.118± 0.0073</td>
</tr>
<tr>
<td>Glycogen Phosphorylase (µM P released/mg Protein/10 Min.)</td>
<td>120.72± 8.27</td>
<td>150.92*</td>
<td>124.62± 9.62</td>
</tr>
<tr>
<td>Glucose-6-Phosphatase (µM PO4, released/mg Protein/15 Min.)</td>
<td>0.30± 0.008</td>
<td>0.24***</td>
<td>0.29± 0.009</td>
</tr>
<tr>
<td>Lactate Dehydrogenase (µM Lactate oxidized/mg Protein/15 Min.)</td>
<td>99.88± 6.57</td>
<td>73.45**</td>
<td>100.57± 6.55</td>
</tr>
<tr>
<td>Succinate Dehydrogenase (µg Formazan formed/mg Protein/60 Min.)</td>
<td>28.96± 1.69</td>
<td>37.37**</td>
<td>29.17± 1.58</td>
</tr>
<tr>
<td>Acetyl Cholinesterase (ACCh hydrolyzed/mg Protein/Min.)</td>
<td>0.127± 0.011</td>
<td>0.197***</td>
<td>0.141± 0.007</td>
</tr>
</tbody>
</table>

* Values are expressed as mean ± SEM of 6 experiments; * p< 0.05; ** p< 0.02; *** p< 0.01; **** p< 0.001
Table 4.2 Percentage change (compared to controls) in serum glucose, hepatic metabolites, and enzymes of carbohydrate metabolism and acetyl cholinesterase in rats subjected to sympathectomy singly and in combination with vagotomy and adrenalectomy.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sympathectomy</th>
<th>Sympathectomy + Adrenalectomy</th>
<th>Sympathectomy + Vagotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dl Serum)</td>
<td>28*** ↓</td>
<td>44 **** ↓</td>
<td>24 * ↑</td>
</tr>
<tr>
<td>Glycogen (mg/100 mg Wet Tissue)</td>
<td>40 *** ↑</td>
<td>44 *** ↑</td>
<td>18 * ↓</td>
</tr>
<tr>
<td>Glycogen Synthase</td>
<td>41 *** ↑</td>
<td>59 **** ↑</td>
<td>25 ** ↓</td>
</tr>
<tr>
<td>(μM UDP/mg Protein/10 Min.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycogen Phosphorylase</td>
<td>25 * ↓</td>
<td>37 *** ↓</td>
<td>25 * ↑</td>
</tr>
<tr>
<td>(μM P released/mg Protein/10 Min.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose-6-Phosphatase</td>
<td>20 *** ↓</td>
<td>38 **** ↓</td>
<td>13 * ↑</td>
</tr>
<tr>
<td>(μM PO₄ released/mg Protein/15 Min.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactate Dehydrogenase</td>
<td>26 ** ↓</td>
<td>28 *** ↓</td>
<td>24 * ↑</td>
</tr>
<tr>
<td>(μM Lactate oxidized/mg Protein/15 Min.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Succinate Dehydrogenase</td>
<td>29 ** ↑</td>
<td>23 * ↑</td>
<td>27 ** ↑</td>
</tr>
<tr>
<td>(μg Formazan formed/mg Protein/60 Min.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetyl Cholinesterase</td>
<td>55 *** ↑</td>
<td>46 **** ↑</td>
<td>50 **** ↓</td>
</tr>
<tr>
<td>(ACH hydrolyzed/mg Protein/Min.)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Values corrected to nearest whole number; * p < 0.05; ** p < 0.02; *** p < 0.01; **** p < 0.001.
Figure 4.1 Levels of serum glucose and liver glycogen in rats subjected to chemical sympathectomy (CSX) singly and in combination with adrenalectomy (CSX + ADX) and vagotomy (CSX + VGX)

(A) Glucose

(B) Glycogen

* p < 0.05; *** p < 0.01; **** p < 0.001.
Figure 4.2 Activities of Glycogen Synthase and Glycogen Phosphorylase in the liver of rats subjected to chemical sympathectomy (CSX) singly and in combination with adrenalectomy (CSX + ADX) and vagotomy (CSX + VGX).

(A) Glycogen Synthase

(B) Glycogen Phosphorylase

* p < 0.05; ** p < 0.02; *** p < 0.01; **** p < 0.001.
Figure 4.3 Activities of Glucose-6-Phosphatase and Lactate Dehydrogenase in the liver of rats subjected to chemical sympathectomy (CSX) singly and in combination with adrenalectomy (ADX) and vagotomy (VGX)
Figure 4.4 Activities of Succinate Dehydrogenase and Acetyl Cholinesterase in the liver of rats subjected to chemical sympathectomy (CSX) singly and in combination with adrenalectomy (ADX) and vagotomy (VGX).

(A) Succinate Dehydrogenase

(B) Acetyl Cholinesterase

* p < 0.05; ** p < 0.02; *** p < 0.01; **** p < 0.001.
Figure 4.5 Percentage change in levels of serum glucose, hepatic glycogen, and activities of key enzymes of carbohydrate metabolism and acetyl cholinesterase in the liver of rats subjected to sympathectomy singly (A), and in combination with adrenalectomy (B) and vagotomy (C).
DISCUSSION

Glucose can be mobilized from the liver in response to anesthesia, surgery or reflex nerve stimulation (Jarhult, 1975; Lautt and Cote, 1977). High blood glucose is caused by lesser utilization of the sugar by peripheral tissues as well as overproduction by the liver (Lavoie and Werve, 1991). This hyperglycaemic condition can be prevented by stimulation of parasympathetic nerves selectively. Usage of large doses of alpha or beta receptor blockers prevent simultaneous sympathetic activation (Lautt and Wong, 1978a), thereby causing parasympathetic nerve stimulation and a rapid decrease in hepatic glucose output (Lautt and Wong, 1978b). Similar low blood sugar level was observed in the guanethidine induced sympathectomized rats which suppresses the sympathetic system completely by destroying the adrenergic neurons. The persisting parasympathetic system gets stimulated resulting in a rapid decrease in glucose output, as well as priming the liver for insulin action. Activation of hepatic glucose uptake in conjunction with insulin, causes hypoglycaemia.

Previous studies using adrenalectomized rats (Watanable et al., 1990) have indicated that glucocorticoid may play a role in the regulation of glucagon receptor expression. Even adrenal catecholamine produce hyperglycaemia in response to surgery (Lautt and Cote, 1977). However, in rats subjected to sympathectomy and adrenalectomy together reduced levels of glucocorticoids and catecholamines and relative insulin excess in addition to suppressed sympathetic tone. This favours the reduced glucose output from hepatocytes resulting a definite decrease in blood sugar level. This hypoglycaemic response following chemical sympathectomy and adrenalectomy simultaneously, shows that the neural hyperglycaemic control in the liver is sympathetic in origin (Lautt, 1979b; 1980b).

Nevertheless, hepatic parasympathetic nerves are known to have direct effect on hepatic glucose uptake (Shimazu, 1971; 1974; Lautt and Wong, 1978a), whereas enhanced glucose output induced by direct stimulation of the hepatic nerve results from activation of alpha adrenergic receptors (Lautt, 1979a). However, when both adrenergic and cholinergic system was blocked marginal hyperglycaemia was observed which could be mainly due to the release of catecholamine from adrenal medulla. It is anticipated that the reduction in the hyperglycaemic response of vagotomized rats that had also undergone chemical
sympathectomy was due to removal of the sympathetic nerves rather than to removal of hepatic afferent nerves.

In the past decade, it has become clear that adrenergic receptors of both alpha and beta classification can produce glycogen breakdown and glucose release from livers of fasted rats, rabbits and cats in vitro (Sherline et al., 1972; Kuo et al., 1977) by increasing levels of 3'-5'cAMP with subsequent activation of phosphorylase kinase (Shimazu and Amakawa, 1968; 1975). Sympathetic blockade by antisympathetic drugs reverses this response. Glycogen stores of the liver increases along with a simultaneous increase in glycogen synthase activity. Whereas phosphorylase activity decreased suggesting reduced glycogen degradation.

Acute trauma or stress results in the activation of both the adrenal glands and the hepatic sympathetic nerves (Lautt, 1980b) in turn activation of glycogen phosphorylase (Lautt, 1979b). This response in turn results in a rapid, short lived release of glucose due to glycogen breakdown. Prolonged stress results in adrenal catecholamine stimulation of glucose release due to glycogen breakdown but perhaps primarily due to increased gluconeogenesis (Lautt, 1980a). This neural and hormonal induction of hepatic glycogen metabolism occurs via different pathways.

In the absence of adrenal glands, the hepatic sympathetic nerves are reflexly activated and can produce an early release of glucose in response to surgical trauma (Lautt, 1980a). But, bilateral adrenalectomy and total sympathectomy simultaneously prevented this hyperglycaemic response (Jarhult, 1975; Louis-Sylvestre et al., 1980a) by altering the glucose mobilizing pathways adn by increasing the glycogen stores of the liver increased concomitantly.

Studies using hepatocytes monolayers have established that insulin stimulated glycogen synthesis from glucose and gluconeogenic precursors when present as the sole hormone (Agius et al., 1993). Insulin is involved in both the acute and the chronic regulation of glycogen synthetase and phosphorylase, the key regulatory enzyme of glycogen metabolism. Low insulin level that followed vagotomy (parasympathetic nerve ablation) have an opposite effect on the glycogen metabolism. It decreases the glycogen synthetase activity, thereby decreasing the tissue glycogen. But performing chemical sympathectomy and
vagotomy simultaneously could not nullify the glycogenolytic effect of vagotomy completely. This is attenuated by decreased glycogen synthase and increased glycogen phosphorylase activity favouring enhanced glycogen breakdown and in turn reduced glycogen stores in the liver of these rats.

Glucose influx into microsomes is tightly linked to glucose-6-phosphatase activity, while glucose efflux may occur independent of hydrolysis. Activation of vagal fibers in response to both chemical sympathectomy singly and in combination with adrenalectomy (CSX + ADX) increases the uptake of glucose by a "pull mechanism" as evinced by decreased glucose-6-phosphatase activity. This in the glucoregulatory mechanisms favours enhanced glycogenesis and reduced gluconeogenesis.

The synthesis of glucose from lactate is another specialized property of the hepatic parenchymal cell. This process is coordinated by various hormones, substrates and cofactors (Exton, 1972). Insulin and glucagon have especially important physiologic roles in the modulation of this phenomenon. Suppressed sympathetic tone reduced lactate dehydrogenase activity therefore does not provide substrate for gluconeogenesis, in turn, could be a cause for low blood sugar level. Suppressed sympathetic tone and adrenal hormone secretion following treatment with guanethidine and surgical bilateral adrenalectomy activates the parasympathetic control over carbohydrate metabolism. Persisting insulin hinders the utilization of lactate as a glucogenic substrate, in turn resulting into the low lactate dehydrogenase activity.

A fall in the rate of metabolism, stimulates counter regulatory response. This rate can be maintained with lactate, delaying the neurohormonal responses (Sauer and Dauchy, 1994). Abrogation of parasympathetic nerves in vagotomized rats reduces insulin level and thus, the metabolic activities are under the influence of sympathetic system and endocrine hormones from adrenals, pancreas etc. This may result in enhanced lactate dehydrogenase activity, and could be maintaining the regular supply of substrate for glucogenic activity, thereby causing hyperglycaemic condition. But, performing chemical sympathectomy and vagotomy together rats could not diminish the response completely. The still persisting adrenal glands have influential role on the maintenance of marginal hyperglycaemia through lactate dehydrogenase activity.
The measurement of SDH which is a key enzyme of TCA cycle, would be a reliable index of the oxidative metabolism and the production of ATP molecules of any metabolically active organ. Increase in SDH activity indicates that the mitochondrial function, particularly TCA cycle operation has increased. The enhanced TCA cycle can also support the active synthesis of lipids, glycogen etc. (Patel et al., 1979). It could be summarised that in CSX + ADX rats pathways leading to the synthesis are activated after suppression of sympathetic nerves and secretion of hormones along with adrenergic neurotransmitters. However, the increased succinate dehydrogenase activity after chemical sympathectomy + vagotomy indicates that the enhanced TCA cycle might be providing substrates for the operation of gluconeogenic cycle. This could be the influence of adrenal hormones.

An increased or decreased nervous activity at any site could be inferred through studies on the strength of the AchE activity. Intensity of which fluctuates according to the amount of acetylcholine secreted by nerve endings. Acetylcholine released all along the sinusoidal linings in the liver could stimulate all the hepatocyte to take up glucose (Mondon and Burton, 1971). The sinusoidal linings also exhibit a very significant localization of AchE which could inactivate the Ach very quickly. Previous invivo studies have shown that AchE is more in response to elevated acetylcholinesterase release in the liver (Pilo and Patel, 1978b), which in turn could stimulate the uptake of glucose. Similar results of enhanced AchE activity was observed after treating for chemical sympathectomy alone and chemical sympathectomy + adrenalectomy together. In these individuals, the persisting parasympathetic system is involved in the glucoregulatory activities. Increased acetylcholine release in regard to above treatment could bring about the glucose uptake by the hepatocytes and be the reason for hypoglycaemic condition.

Acetylcholine (Ach) and norepinephrine are the classic transmitters of parasympathetic and preganglionic sympathetic neurons and in postganglionic neurons respectively. Mondon and Burton (1971) clearly demonstrated that the acetylcholine or choline in the presence of insulin significantly enhanced the uptake of glucose and deposition of glycogen by the liver in rats. But, inhibition of Ach release and insulin secretion following the suppression of parasympathetic tone in chemical sympathectomy + vagotomy would prolong the action of Ach on the plasma membrane due to Ach accumulation (Pilo and Patel, 1978b), which is inferred by low AchE activity.
From the present results it can be concluded that parasympathetic and sympathoadrenal autonomic activation mediate glucagon responses to hypoglycaemia in a redundant fashion, such that interfering with either autonomic subdivision would alter glucagon response. Glucagon is mainly involved in the glucose mobilizing activities and its expression would result in high blood sugar level. However, hyperglycaemia or diabetic condition can be controlled by guanethidine. But, blood glucose level tended to reduce drastically when both chemical sympathectomy and adrenalectomy is performed simultaneously.