Chapter 5

INVOLVEMENT OF PARASYMPATHETIC AND SYMPATHOADRENAL SYSTEM ON PROTEIN AND LIPID CONTENT, ACTIVITIES OF TRANSPORT ENZYMES AND AMINOTRANSFERASES IN RAT LIVER

Hypoglycaemia is a potent stimulator of the sympathetic nervous system, which in turn, increases the level of glucagon, epinephrine and norepinephrine in plasma (Katagiri et al., 1982; Vinik and Glowniak, 1982). They regulate glucose homeostasis through glycogenolysis and gluconeogenesis by apparently influencing the enzyme activities of tissues. Glucagon plays a primary role in glucose counterregulation during hypoglycaemia (Shi et al., 1996). Thus, the control of total body glucose utilization is multifactorial. This response is interfered in individuals with sympathetic neuropathy and may be responsible for the early symptoms of hypoglycaemia.

More recently the importance of adrenergic mechanisms to whole body glucose economy has been thoroughly appreciated in human models of prolonged hypoglycaemia (DeFeo et al., 1991a; Fanelli et al., 1992). Combined alpha and beta adrenergic blockade accentuated the severity of insulin hypoglycaemia and this occurred as a consequence of two mechanisms- inhibition of the rebound increase in hepatic glucose production that normally occurs despite sustained hyperinsulinaemia (Sacca et al., 1979b) and as potentiation of insulin action on tissue glucose uptake. Insulin sensitivity can be separated into two component and liver has been reported to be much more sensitive to the effects of insulin than are peripheral tissues (Rizza et al., 1981). Both in vivo and in vitro observations suggest that hyperinsulinaemia usually inhibits gluconeogenesis (Exton, 1972).
The endocrine glands function to a large extent in maintaining relatively constant states (homeostasis) in internal fluid environment of the body. They generally cooperates with the nervous system in effecting exteroceptive and interoceptive stimuli and in order to do so they must be subjected to complex control systems which regulates their output of secretions. For example, activation of sympathoadrenal system, results in release of large quantities of catecholamine which may have direct suppressive effect on insulin secretion.

Catecholamine and adrenocorticosteroid secreted from adrenal gland are involved in metabolic, thermoregulatory, reproductive and many other physiological changes taking place in birds (Ghosh, 1980; Holmes and Cronshaw, 1980). The physiological effect of catecholamine are mediated by both alpha and beta adrenergic receptors. Of which, beta adrenergic effects of catecholamine are known to be mediated by an increase in intracellular cyclic AMP whereas activation of alpha adrenergic receptors does not increase cyclic AMP in hepatocyte (Exton, 1980). The alpha and beta receptors mediated function in adult rat liver have been shown to be mediated by corticosteroids and thyroid hormone (Chan et al., 1979; Barney et al., 1980).

Catecholamine can also act indirectly by stimulating an increase in glucagon release via actions on alpha adrenergic receptors. Glucagon in turn may also act on hepatocyte to increase intracellular cAMP concentration and glucose release (Foster and Mc Garry, 1992) by enhancing hepatic glycolysis and gluconeogenesis (Hutson et al., 1976; Saiton, 1976) and therefore preventing the organism from the fatal effects of low blood sugar level. Catecholamine cause a significant reduction in plasma insulin levels (Hooper et al., 1994) and the importance of catecholamines in counterregulation of insulin induced hypoglycemia has long been demonstrated in several animals (Sacca et al., 1975, 1977; Mc Donough, 1989).

In the current study, the interplay of glucagon, epinephrine and norepinephrine on metabolic activities of liver has been emphasized by using sympatholytic agent, guanethidine sulphate. Guanethidine affects the innervation of adipose tissue (Hussein et al., 1975), pancreas (Woods, 1972), and salivary gland (Eccher et al., 1977) as well as other tissues and when chronically administered the compound produces an apparently permanent depletion of postganglionic somata and adrenergic terminals (Johnson and O'Brien, 1976). Guanethidine causes inhibition of oxidative phosphorylation as it inhibit mitochondrial
metabolism *in vitro*, the inhibition of the retrograde transport of NGF (nerve growth factor) and the inhibition of polyamine biosynthesis. Also, the interaction of parasympathetic and sympathoadrenal system has been figured out by hampering cholinergic supply and adrenal secretions along with sympathectomy.

**MATERIAL AND METHODS**

Adult male albino rats of Charles Foster strain weighing around 150-200 gm were used for the present study. Rats were acclimatized to standard laboratory conditions for a week, with ad libitum food and water. They were divided into six groups for respective treatments, with six 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  HEMICAL SYMPATHECTOMY + VAGOTOMY (CSX + VGX)  
GROUP VI  CONTROL CHEMICAL SYMPATHECTOMY + SHAM VAGOTOMY (CSS + VGS)  

After 28 days of respective treatments overnight fasted rats were sacrificed. Liver was excised quickly, blotted and preserved in freezer. It was latter weighed and homogenates of different grades were prepared in respective mediums for the estimation of various parameters.

The tissue protein content was assayed by the method of Lowry *et al* (1951) and expressed as mg protein/100 mg wet tissue/30 minutes. Acid and alkaline phosphatases were estimated by the method of Linhardt and Walter (1963) and expressed as μmoles of PNP released/mg protein. Activity of AST and ALT was estimated by the method of Bergmeyer and Bernt (1963) and expressed as Karmen units/mg protein/minute. Na⁺-K⁺-ATPase activity was estimated by the method of Post and Sen (1967) as μg phosphorous released/mg protein/10 minutes. The lipid content was measured by the wet method of Folch *et al* (1957) and calculated as mg lipid/100mg tissue.
Statistical Analysis

Student's 't' test was employed for the statistical analysis of the data and p value <0.05 was considered statistically significant.

RESULTS

Data elucidated following parasympathetic and sympathoadrenal manipulations is depicted in table 5.1, 5.2 and figure 5.1-5.5, respectively.

Liver protein and lipid content increased significantly in chemical sympathectomized rats (p<0.02 and p<0.01, respectively; Figure 5.1A & B). This increase was more remarkable in rats subjected to chemical sympathectomy and adrenalectomy together. In these rats, protein content increased by 64% and lipid by 45% respectively (Table 5.2). Whereas, in CSX + VGX rats both protein and lipid stores declined to significantly (Protein-p<0.05; lipid-p<0.02), compared to the sham treated rats.

Both, acid and alkaline phosphatase activity decreased to significance p<0.01 and p<0.001 respectively in rats subjected to chemically sympathectomy singly and in combination with adrenalectomy (Table 5.1). However, activity of both these phosphatase increased significantly in CSX + VGX rats. The increase of alkaline phosphatase activity (p<0.02; Figure 5.2B) was concomitant compared to acid phosphatase (p<0.05; Figure 5.2A).

Activity of membrane bound enzyme, Na⁺-K⁺-ATPase increased in all the three conditions (Figure 5.3). In rats subjected to CSX singly and in combination with adrenalectomy (CSX + ADX), the increase was marginal (p<0.05). But, in rats treated for chemical sympathectomy and vagotomy together (CSX + VGX), Na⁺-K⁺-ATPase activity increased significantly by 34% (p<0.02; Figure 5.5).

Activity of both the transaminases (ALT & AST) decreased markedly after guanethidine injections alone (CSX) and together with adrenalectomy (CSX + ADX). Moreover, the decrease in alanine aminotransferase activity was profound (p<0.01; Figure 5.4A) than aspartate aminotransferase (p<0.02; Figure 5.4B). Whereas, in CSX + VGX rats, ALT and AST activity increased to 141.4 ± 6.88 and 107.4 ± 6.83, compared to the activity of control group rats 115.4 ± 5.60 and 88.8 ± 4.09, respectively (Table 5.1).
Table 5.1 Levels of protein, lipid and activities of phosphatases and transaminases 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</th>
<th>Chemical Sympathectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sham</td>
<td>Experimental</td>
<td>Sham</td>
</tr>
<tr>
<td>Protein (mg/100 mg Wet Tissue)</td>
<td>27.46±1.46</td>
<td>35.05±2.11</td>
<td>24.79±1.27</td>
</tr>
<tr>
<td>Lipid (mg lipid/100 mg Non Fat Dry Tissue)</td>
<td>4.09±0.203</td>
<td>5.35±0.306</td>
<td>4.10±0.204</td>
</tr>
<tr>
<td>Acid Phosphatase (µM PNP released/mg Protein/30 Min.)</td>
<td>1.22±0.084</td>
<td>0.81±0.06</td>
<td>1.29±0.073</td>
</tr>
<tr>
<td>Alkaline Phosphatase (µM PNP released/mg Protein/30 Min.)</td>
<td>0.135±0.007</td>
<td>0.090±0.005</td>
<td>0.125±0.005</td>
</tr>
<tr>
<td>Na⁺-K⁺-ATPase (µg P released/mg Protein/10 Min.)</td>
<td>14.92±0.65</td>
<td>19.89±1.44</td>
<td>16.33±0.78</td>
</tr>
<tr>
<td>Alanine Transaminase (Karmen units/mg Protein/Min)</td>
<td>122.0±7.04</td>
<td>88.0±4.09</td>
<td>124.4±6.33</td>
</tr>
<tr>
<td>Aspartate Transaminase (Karmen units/mg Protein/Min)</td>
<td>93.60±4.71</td>
<td>74.80±3.99</td>
<td>88.60±4.60</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 5.2  Percentage change (compared to controls) in protein, transaminases and transport enzymes in the liver of 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>Protein (mg/100 mg Wet Tissue)</td>
<td>28° ** ↑</td>
<td>64 *** ↑</td>
<td>20 * ↑</td>
</tr>
<tr>
<td>Lipid (mg/100mg Non Fat Dry Tissue)</td>
<td>31 *** ↑</td>
<td>45 **** ↑</td>
<td>28 ** ↓</td>
</tr>
<tr>
<td>Acid Phosphatase (μM PNP released/mg Protein/30 Min.)</td>
<td>34 *** ↓</td>
<td>33 *** ↓</td>
<td>14 * ↑</td>
</tr>
<tr>
<td>Alkaline Phosphatase (μM PNP released/mg Protein/30 Min )</td>
<td>33 **** ↓</td>
<td>29 **** ↓</td>
<td>21 ** ↑</td>
</tr>
<tr>
<td>Na⁺-K⁺-ATPase (μg P released/mg Protein/10 Min.)</td>
<td>33 * ↑</td>
<td>28 * ↑</td>
<td>34 ** ↑</td>
</tr>
<tr>
<td>Aspartate Aminotransferase (Karmen units/mg Protein/Min.)</td>
<td>28 *** ↓</td>
<td>30 *** ↓</td>
<td>23 ** ↑</td>
</tr>
<tr>
<td>Alanine Aminotransferase (Karmen units/mg Protein/Min.)</td>
<td>20 ** ↓</td>
<td>20 ** ↓</td>
<td>21 * ↑</td>
</tr>
</tbody>
</table>

*Values corrected to nearest whole number; * p< 0.05; ** p< 0.02; *** p< 0.01; **** p< 0.001
Figure 5.1 Levels of Protein and Total Lipid in the Liver of rats subjected to chemical sympathectomy (CSX) singly and in combination with adrenalectomy (CSX+ADX) and vagotomy (CSX+VGX).

(A) Protein

(B) Total Lipid

* p < 0.05; ** p < 0.02; *** p < 0.01; **** p < 0.001.
Figure 5.2 Activities of Alkaline Phosphatase and Na⁺-K⁺-ATPase in liver of rats subjected to chemical sympathectomy (CSX) singly and in combination with adrenalectomy (CSX+ADX) and vagotomy (CSX+VGX).

(A) Alkaline Phosphatase

(B) Acid Phosphatase

* p < 0.05; ** p < 0.02; *** p < 0.01; **** p < 0.001.
Figure 5.3 Activity of $\text{Na}^+\text{-K}^+\text{-ATPase}$ in the liver of rats subjected to chemical sympathectomy (CSX) singly and in combination with adrenalectomy (CSX + ADX) and vagotomy (CSX + VGX)
Figure 5.4 Activities of Aspartate and Alanine Transferase in liver of rats subjected to chemical sympathectomy (CSX) singly and in combination with adrenalectomy (CSX+ADX) and vagotomy (CSX+VGX)

\[ \text{Karmen units/mg Protein/Min.} \]

\[ \text{Aspartate Aminotransferase} \]

\[ \text{Alanine Aminotransferase} \]

\[ \text{CSX} \quad \text{CSX + ADX} \quad \text{CSX + VGX} \]

\[ \begin{array}{c}
\text{Control} \\
\text{Experimental}
\end{array} \]

\[ * p < 0.05; ** p < 0.02; *** p < 0.01. \]
Figure 5.5 Percentage change in hepatic protein, lipid, and activities of phosphatases and transaminases in rats subjected to chemical sympathectomy singly (A) and in combination with adrenalectomy (B) and vagotomy (C).
DISCUSSION

Hypoglycaemic condition following guanethidine induced chemical sympathectomy (chapter 3) is also associated with impaired amino acid and lipid metabolism, and also glucose sensing mechanism of pancreatic alpha cells. This could be due to suppressed sympathetic tone and in turn glucagon release. The liver protein metabolism and nitrogen loss would also be obstructed/foiled as a result of sympathectomy. Uptake of amino acids by the liver is enhanced, thereby increasing the tissue protein content compared to control group where sympathetic system is unaffected. In addition, glucagon’s lipolytic action is also blocked in sympathectomized rats, resulting high liver lipid content (Parikh, 1992).

Several investigators (Nair et al., 1987; Couet et al., 1990) have recently speculated that the loss of amino acids is concentrated in the splanchnic bed, which consists of both liver and gastrointestinal tissues. Splanchnic nerve activation stimulates the release of glucagon, cortisol and aldosterone (Bornstein et al., 1990). Of which, cortisol causes an accumulation of amino acid in the liver (Quinlan et al., 1982). Also, the lipolytic action of glucagon is enhanced especially in presence of glucocorticoids (Hermier et al., 1991). But obstruction of the sympathetic tone and adrenal hormone secretion by subjecting to chemical sympathectomy and adrenalectomy simultaneously would hinder the proteolytic and lipolytic actions of glucagon and corticoids. In such cases the influence of parasympathetic system on the metabolism gets emphasized overtly. Insulin decreases plasma amino acid concentrations (Carlstein et al., 1966; Zinneman et al., 1966). This reduction appears to be due to both enhanced peripheral uptake and suppressed cellular release of amino acids, resulting in increased protein stores in the liver. In addition, insulin also manifest its antilipolytic effect (Samols et al., 1965), which could be cause of increased lipid stores in the liver of CSX + ADX rats.

However, following surgical trauma, an obligatory loss of protein and lipid emerges (Kinney et al., 1968). In addition, corticoids also reduces reabsorption of glucose by the kidney. The overall result is hyperglycaemia and glucosuria. A similar glycaemic state is manifested by performing chemical sympathectomy and vagotomy simultaneously. Here, the major influence on metabolic activities is through adrenal hormones. In rats it has been demonstrated that the release of NE and E from adrenal medulla is under neuronal and non-
neuronal control (Khalil et al., 1988). The amino acids released in response to adrenal hormones are utilized in gluconeogenic pathways. Also, the local production of cytokines within the adrenal gland with the medulla as a potential source and the cortex as a target, chromaffin cells may also play an important role in mediating glucoregulatory activities.

In addition to above discussed protein metabolism, lipid metabolism is also influenced by neural and hormonal interplay. Sympathetic regulation is through glucagon and parasympathetic through insulin. Insulin being a potent inhibitor (Nurjhan et al., 1986) and glucagon a weak stimulator of lipolysis in man, any effect of glucagon on lipolysis is most likely to be noted only when insulin is low or absent. But, with both insulin and perhaps glucagon also becoming low in CSX + VGX rats conditions would favour the lipolysis, thereby increasing the FFA in the circulation, which would serve as the substrate for gluconeogenic activity and the marginal hyperglycaemic state.

Over and above, dietary amino acids flux and those from labile protein necessitates regulation of protein turnover. But, a continuous supply of amino acids is also required to replace irreversible losses through gluconeogenesis, systemic transmethylation reactions and other metabolic pathways. Transport of amino acids is governed by certain membrane bound enzymes. Alkaline and acid phosphatases as phosphomonoesterases subserve a variety of processes requiring the mobilization of phosphate radicals or entails dephosphorylation as steps in anabolism, catabolism and transport of ions (Moog, 1946). They also aid in the biosynthesis of carbohydrate, proteins and lipids and in growth and differentiation processes (Moog, 1946).

Of both the phosphatases, acid phosphatase being the membrane bound lysosomal enzyme serves a vital role in the regulation of metabolites across the membrane. In CSX and CSX + ADX animals, the persisting parasympathetic tone influences proteogenesis through the secretion of insulin. This in turn, reduces the autophagy and proteolysis. Also, the transport of amino acids across the hepatocyte must have decreased which could be the reason for the reduced acid phosphatase activity in these rats.

In liver, where lysosomal alterations have been extensively studied, it is reviewed that autophagy and proteolysis are enhanced by amino acid or insulin lack (Mortimore and Ward,
Therefore, obliterated insulin secretion due to suppressed parasympathetic tone, in individuals operated for vagotomy along with guanethidine induced chemical sympathectomy enhances amino acid mobilization through protein breakdown. Also, in suppressed insulin secretion, hepatic lysosomes have been shown to contain increased amounts of cytoplasmic proteins and degradation products (Mortimore and Ward, 1976). This could result in increased cellular autophagy through simultaneous increase in acid phosphatase activity.

Boden et al. (1990) using in vivo nitrogen excretion technique have shown that glucagon aids in amino acid disposal by increasing hepatic intracellular amino acid transport across the membrane. Alkaline phosphatase has influential role in regulating plasma membrane permeability and glucose homeostasis. Enhanced alkaline phosphatase activity favors the transport of metabolites by the hepatocyte, which in turn serve as a substrate for gluconeogenic activity. This could be the reason for marginal hyperglycaemic condition in rats treated for chemical sympathectomy and vagotomy simultaneously.

On the contrary, the decreased glucagon concentration in response to suppressed adrenergic system in rats treated for chemical sympathectomy singly and in combination with adrenalectomy would diminishes the mobilization of amino acids across the hepatocyte. This is depicted by reduced alkaline phosphatase activity in these individuals and presence of large stores of amino acids in the hepatocyte as mentioned previously.

In addition, the membrane bound Na⁺-K⁺, Ca²⁺, and Mg²⁺ dependent ATPases as energy transducers couple the hydrolysis of ATPases to the transport of Na⁺, K⁺, Ca²⁺ and Mg²⁺ ions across the plasma membrane. These ions act as cofactors in various cellular biochemical reactions and their concentration is of functional validity. Of these, Na⁺-K⁺ ATPase is a widely distributed enzyme whose activity is regulated in a tissue-specific fashion by a variety of factors (Frambrough et al., 1994) such as pituitary-dependent and independent hormones, peptide hormones and neurotransmitters e.g. dopamine (Gick et al., 1988). This enzyme uses the energy released from ATP hydrolysis to maintain osmotic balance and to produce electrochemical gradient of Na⁺ and K⁺ across the plasma membrane (Skou, 1957), thereby maintaining the membrane potential to excitable neural and muscle cells. It is involved in reabsorption of Na⁺ in the kidney (Schwartz et al., 1975; Jrgansen, 1982) and in salivary glands (Hosoi et al., 1989; Kurihara et al., 1990). Enhanced activity of Na⁺-K⁺-ATPase, in
rats subjected to chemical singly (CSX) and in combination with adrenalectomy (CSX + ADX) and vagotomy (CSX + VGX) suggests the increased rate of hepatic metabolic reactions through the ionic transport mechanism and flow coupled transport of glucose and amino acids across hepatic cell membrane.

Low blood sugar level is usually accompanied by an increase in the circulating concentration of glucagon and the glucocorticoids (Exton, 1972). These hormones regulate the hepatic gluconeogenic pathway (Exton, 1972) and the amino acid transport is a rate determining step for the pathway (Mallette et al., 1969a,b). The effect of glucagon on glucregulatory pathway is multifocal and the glucocorticoids although exerting little effect by themselves, amplify the effects of glucagon (Exton, 1972). The overall effect is exerted on the stimulation of A system (Lecam and Frey et al., 1976) which is largely responsible for the transport of L-alanine (Quinlan et al., 1982). Nevertheless, converse results obtained in individuals treated for chemical sympathectomy due to suppressed stimulus for glucagon release. Also, suppressed sympathetic tone in conjunction with adrenal abrogation in CSX + ADX rats reduces the uptake of amino acids by the liver (Malliinson et al., 1974; Boden et al., 1977) through A system. The persisting parasympathetic tone was depicted by low alanine transaminase activity.

Apart from the above discussed glucregulatory mechanisms, the parasympathetic tone regulates the metabolic activities in varied ways. Historically, insulin and glucose are thought to work in concert to maintain glucose homeostasis. Insulin and glucose may also be closely linked in the regulation of plasma amino acids and by inference protein homeostasis. During euglycaemia, insulin is known to decrease plasma amino acid concentrations (Carlsten et al., 1966; Zinneman et al., 1966), primarily through its inhibition of protein breakdown (Jefferson et al., 1974; Lundholm et al., 1981; Flakoll et al., 1989) and via an increased intracellular amino acid transport (Manchester, 1970). But, these insulin triggered activities are suppressed in vagotomized rat.

Hyperglycaemia, caused by increased gluconeogenic activity has been demonstrated to influence protein metabolism (Flakoll et al., 1994). An increase in any hepatic synthetic function may result from either an increase in substrate delivery to the liver or a change in the hepatic kinetics of the processes. Amino acids mainly alanine being the important substrate
for gluconeogenesis have noticeable control on the glycaemic pathways. Increased alanine transaminase activity in rats operated for chemical sympathectomy and vagotomy concurrently, probably reflect an accelerated peripheral release of amino acids (alanine) through enhanced proteolysis. Further, which could be utilized as a substrate for glucose producing pathways, in turn rendering marginal hyperglycaemia. Also, alanine also act as an important negative allosteric effector of glycolysis (Quinlan et al., 1982). Therefore, glucose uptake from the circulation is hindered. This is in accordance with enhanced alanine transferase activity and the marginal hyperglycaemic condition in rats treated for chemical sympathectomy and vagotomy together.

Aspartate amino transferase is ubiquitous pyridoxal phosphate-dependent enzyme. The cytosolic AST is expressed at approximately the same level in all tissues and carries both a house keeping function as well as tissue specific, hormonally regulated, metabolic functions. However, it is specifically regulated by glucocorticoids in liver and kidney but not in other tissues (Pave-Preux et al., 1990). Therefore, its hormonal regulation is tissue specific. Insulin prevents the effects of glucocorticoids on cytosolic aspartate amino transferase and decreased transcription from all sites but with preferential inhibition of the most induced ones. This is in agreement with chemically sympathectomized rats, where insulin level has increased. Thereby, resulting in low AST activity through its subdued effect on glucocorticoid. Similarly, lack of adrenal hormones with simultaneous increase in insulin in rats treated for chemical sympathectomy and adrenalectomy together amplifies the decrease in AST activity. However, the asserted/endured glucocorticoids enhanced the aspartate amino transferase activity in response to obliterated sympathetic and parasympathetic system (CSX + VGX rats). Concluding the operation of gluconeogenic activity, parallel to the alteration in membrane permeability.

A multitude of intrinsic physiologic relationships of components of autonomic nervous system and adrenal hormones regulate and fine tune carbohydrate homeostasis in complex way. It can be concluded that the metabolic status is under the influence of adrenergic and cholinergic innervations in the liver respectively. Also, adrenal hormones have a discernible role in liver metabolism. Sympathetic neuropathy by guanethidine reduces proteolysis, and helps in controlling hyperglycaemic condition to some extent by obliterating gluconeogenic pathways. This regulatory control can be enhanced by obstructing adrenal hormone influence
on metabolism. Furthermore, it can be concluded that on gluconeogenic mechanisms the effect of cholinergic nerves is more pronounced than adrenergic. Thereby, vagus has a salient role in the maintenance of normoglycaemic state or glucose homeostasis.