Chapter I

Carbohydrate Metabolism
Total Carbohydrates

Results

The total carbohydrate content was estimated by method of Carroll et al., (1956). In control rats the amount total carbohydrate was found to be 50.61 mg of glucose/gm wet weight of tissue in liver and testis 32.00 mg of glucose/gm wet weight of tissue. In group-II, where the control rats were treated with Aloe vera extract the levels were increased. Group-III had showed a significantly decreased to 35.03 mg of glucose/g wet weight of tissue in liver and testis 24.00 mg of glucose/gm wet weight of tissue. In group-IV where the diabetic rats were subjected to Aloe vera extract, increased levels were found when compared to control rats.

Discussion

The liver is an important organ that plays a pivotal role in glycolysis and gluconeogenesis. It is the primary site of endogenous glucose production (Roden and Bernroeder, 2003) with a minor contribution from the testis (Cersosimo et al., 1997; Stumovvallo et al. 1997) and produce glucose either from gluconeogenesis or via glyconeolysis. Elevated endogenous glucose production is a common abnormality associated with diabetes that, concurrence with deprived pancreatic function and reduced glucose clearance, contributes to the hyperglycemia characteristic of the disease, diabetes (Wanjungot et al., 2001). Insulin regulates the metabolism by modulating the uptake utilization of glucose in target organs such as liver, testis, and adipose tissues by controlling the activities of numerous metabolic enzymes.

Partial or total deficiency of insulin causes impairment in carbohydrate metabolism that decreases activity of several key enzymes including glucokinase, phosphofructokinase and pyruvate kinase (Hikino et al., 1989). Resulting impaired peripheral glucose utilization and augmented hepatic glucose production. Glucose is transported out of the liver to increase blood glucose concentration. The content of total carbohydrate was decreased in liver and testis in experimentally induced diabetic rats. This has been many workers (Rathi, and shanmugasundaram, 1981; Vijaya Lakshmi et al. 2009). These finding suggest that Aloe vera extract has complimentary potency to develop an antihyperglycemic agent for the treatment of diabetes mellitus. Further studies are in progress to elicit the exact mechanism of antihyperglycemic action of Aloe vera extract in diabetes.
Glucose

Results

Glucose levels were estimated by a commercially available glucose kit based on the glucose oxidase method (Sigma Diagnostics, St.Louis, MO). In control rats the amount glucose was found to be 1.41 mg of glucose/gm wet weight of tissue in liver and testis 1.30 mg of glucose/gm wet weight of tissue. In group-II, where the control rats were treated with Aloe vera extract the levels were decreased. Group-III had showed a significantly increased to 1.77 mg of glucose/gm wet weight of tissue in liver and testis 1.44 mg of glucose/gm wet weight of tissue. In group-IV where the diabetic rats were subjected to Aloe vera extract, decreased levels were found when compared to control rats.

Discussion

Carbohydrate metabolism in the animal system is essentially the metabolism of glucose and of substances related to glucose in their metabolic processes. Glucose is simple sugar and is required to for energy production. The liver is mainly responsible for maintaining normal concentrations of blood glucose by its ability to store glucose as glycogen and to produce glucose from glycogen breakdown or gluconeogenic precursors. The liver is the primary site of endogeneous glucose production (Rden, and Bernoider, 2003) with a minor contribution from the testis (Cersosimo et al., 2009, Meyer et al., 2004) and produces glucose either from gluconeogenesis or via glycogenolysis. Elevated endogenous glucose production is a common abnormality associated with diabetes that, in concurrence with deprived pancreatic function and reduced glucose clearance, contributes to the hyperglycemia characteristic of the disease, diabetes (Wajngot et al., 2001) glucose over and underutilization by peripheral tissues during diabetes mellitus, which is characterized by partial or total deficiency of insulin, plays a pivotal role during the disarray of glucose metabolism leading to elevated systematic glucose (Raju et al., 2001). The rise in fasting plasma glucose in type-II diabetes is only in part due to changes in endocrine state, this is supported by studies using hyperinsulinaemic glucose clamps which show impaired suppression of hepatic glucose production by hyperglycemia Mevorach et al 1998 and by elevated insulin (Basu et al., 2004) indicating that intra
hepatic changes in glucose metabolism and in responsiveness to hyperglycemia and insulin contribute to the increase in the hepatic glucose threshold and insulin resistance.

Chronic hyperglycemia in diabetes leads to changes in expression of proteins involved in the glucose metabolism that further aggravate the metabolic imbalance (Briachard et al., 1993) a process commonly described as glucose toxicity. An example of this is that hyperglycemia promotes the induction glucose-6-phosphates which in turn lead to a further increase in hepatic glucose production (Massillon et al., 1996).

In the present study, the administration of Aloe vera extract to Alloxan-induced diabetic rats restored the levels of hepatic glucose involved in the metabolism of carbohydrate. In this context a number of other plants have been observed to have similar patterns of hypoglycemic effects (Eidi and Esmaeili, 2006). Results on the plasma insulin from pancreas; i.e. it exerts direct insulin tropic effect. Earlier studies (Achrekar et al. 1991 and Shama et al. 2006). These findings suggest that Aloe vera extract has complimentary potency to develop an antihyperglycemic agent for the for treatment of diabetes.

Glycogen

Results

Glycogen content was determined as described by (Ong and Khoo, 2000). In control rats the amount glycogen was found to be 45.22 mg of glucose/gm wet weight of tissue in liver and testis 28.00 mg of glucose/gm wet weight of tissue. In group-II, where the control rats were treated with Aloe vera extract the levels were increased. Group-III had showed a significantly decreased to 30.03 mg of glucose/g wet weight of tissue in liver and testis 18.00 mg of glucose/gm wet weight of tissue. In group-IV where the diabetic rats were subjected to Aloe vera extract, increased levels were found when compared to control rats.

Discussion

Glycogen is the primary intracellular storable form of glucose and its levels in various tissues, especially in liver, testis and skeletal muscles, are a direct reflection of insulin activity, which regulate glycogen deposition by stimulating glycogen synthase and inhibiting glycogen phosphorylase. Since Alloxan causes selective destruction of beta cells of islets of Langerhans, Resulting marked decreased insulin levelsit could be
predicted that glycogen levels in tissues liver and testis decrease as the influx of glucose in the liver is inhibited in the absence of insulin (Golden, and Okakama, 1979). During diabetes, the glycogen levels, glycogen synthase activity and responsiveness to insulin signaling are diminished and glycogen phosphorylase activity is significantly increased (Parker et al., 2004). Diabetes mellitus is known as impair the normal capacity of the liver to synthesize glycogen (Hornbrook, 1970; Whitton and Hems, 1975). However, after food; diabetic animals fail to synthesize glycogen from glucose and gluconeogenic precursors. Synthase phosphatase activates glycogen synthase resulting in glycogenesis and this activation appears to be defective in Alloxan-induced diabetic animals (Bishop, 1970; Tan and Nuttall, 1976).

In the diabetic rats, glycogen content in liver and testis were reduced by approximately 68 and 75 % respectively in comparison with non-diabetic controls (Grover et al., 2000). This is in agreement with previous studies with a similar does not Alloxan and carried for approximately same period (Ferrnmini et al., 1990). However the study of (Chen and Ianuzzo 1982) showed increased in glycogen content. The decreased hepatic contents in diabetic rats have been observed earlier by others (Grover et al., 2000). Also the decrease in hepatic glycogen observed in this study may be due to due to lack of insulin in the diabetic state and this type of Results probably due to the inactivation of glycogen synthetase system. However, this alteration glycogen content is normalized by insulin treatment Vats, and (Grover, 2004). Insulin is the main regulate of glycogenesis in liver and testis. In the present study oral administration of Aloe vera extract to Alloxan induced diabetic rats regulated the activity of glycogen metabolizing enzymes by stimulating the remnat beta cells to secrete more insulin there by normalized the altered glycogen content. Same Results were observed in extract of seed of Tamarindus indica for 7 and 14 days in diabetic rats (Maiti et al., 2004) observed graded and significant elevation in both liver and testis glycogen levels. The glycogen content was increased in both the liver and testis treatment with Aloe vera in Alloxan induced rats (Vats et al, 2003). Diabetes rats treated with casearia esculenta root brought bark liver glycogen to near normal levels, which could be due to increased secretion of insulin (Govindasamy Chandramohan et al., 2008). Thus the obtained results focus the one possible way of antidiabetogenic action of Aloe vera extract by the improvement of glycogenesis process in liver and testis.
Table 1.1: Showing Glucose, Glycogen, and Total Carbohydrate levels in Liver the Control and Experimental animals

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (Non Diabetic Rats)</th>
<th>Group II (Non Diabetic Rats + Aloe vera)</th>
<th>Group III (Diabetic Rats)</th>
<th>Group IV (Diabetic Rats + Aloe vera)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg of glucose/gm wet weight of tissue)</td>
<td>1.41 ±0.028</td>
<td>1.41 ±0.026 (-1.42)</td>
<td>1.78 ±0.027 (+25.58)</td>
<td>1.51 ±0.027 (+6.71)</td>
</tr>
<tr>
<td>Glycogen (mg of glucose/gm wet weight of tissue)</td>
<td>45.18 ±0.62 (+0.01)</td>
<td>46.30 ±1.61 (-56.93)</td>
<td>30.03 ±0.53 (-9.60)</td>
<td>44.66 ±0.61</td>
</tr>
<tr>
<td>Total Carbohydrates (mg of glucose/gm wet weight of tissue)</td>
<td>50.61 ±0.72 (+1.43)</td>
<td>51.84 ±0.71 (-39.88)</td>
<td>35.03 ±0.68 (-19.28)</td>
<td>48.66 ±0.53</td>
</tr>
</tbody>
</table>

Values are mean, ± S.D. of 6 individual rats

Values in the parenthesis are % change from that of control

Values are significantly different from control at P < 0.001
Table 1.2: showing glucose, glycogen, and total carbohydrate levels in Testis the Control and Experimental animals

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (Non Diabetic Rats)</th>
<th>Group II (Non Diabetic Rats + Aloe vera)</th>
<th>Group III (Diabetic Rats)</th>
<th>Group IV (Diabetic Rats + Aloe vera)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg of glucose/gm wet weight of tissue)</td>
<td>1.30 ±0.028 (+1.42)</td>
<td>1.31 ±0.028 (+1.42)</td>
<td>1.44 ±0.027 (+25.58)</td>
<td>1.29 ±0.024 (+6.71)</td>
</tr>
<tr>
<td>Glycogen (mg of glucose/gm wet weight of tissue)</td>
<td>28.00 ±0.71 (+1.01)</td>
<td>28.44 ±0.72 (+1.01)</td>
<td>18.00 ±0.67 (-56.93)</td>
<td>27.10 ±0.65 (-9.60)</td>
</tr>
<tr>
<td>Total Carbohydrates (mg of glucose/gm wet weight of tissue)</td>
<td>32.00 ±0.88 (+1.43)</td>
<td>31.88 ±0.82 (+1.43)</td>
<td>24.00 ±0.74 (-39.88)</td>
<td>31.10 ±0.78 (-19.28)</td>
</tr>
</tbody>
</table>

Values are mean, ± S.D. of 6 individual rats

Values in the parenthesis are % change from that of control

Values are significantly difference from control at P < 0.001
Fig: 1.1: Showing glucose levels in Liver tissue of control and experimental animals

* Significant difference from that of Diabetic Control animals P < 0.001.

Values are mean, SD: n=6

Fig: 1.2: Showing % change of glucose levels in Liver tissue of control and experimental animals

Values in the parentheses are % change
Fig: 1.3: Showing glycogen levels in Liver tissue of control and experimental animals

* Significant different from that of Diabetic Control animals P < 0.001.

Values are mean, SD: n=6.

Fig: 1.4: Showing % change of glycogen levels in Liver tissue of control and experimental animals

Values in the parentheses are % change from Control
Fig. 1.5: Showing total carbohydrate levels in Liver tissue of control and experimental animals

* Significant difference from that of Diabetic Control animals P < 0.001.

Values are mean, SD: n=6

Fig. 1.6: Showing % change of total carbohydrate levels in Liver tissue of control and experimental animals

Values in the parentheses are % change from Control
**Fig: 1.7:** Showing glucose levels in testis tissue of control and experimental animals

* Significant difference from that of Diabetic Control animals $P < 0.001$.

Values are mean, SD: $n=6$

**Fig: 1.8:** Showing % change of glucose levels in testis tissue of control and experimental animals

Values in the parentheses are % change from Control
Fig: 1.9 showing glycogen levels in testis tissue of control and experimental animals

* Significant difference from that of Diabetic Control animals P < 0.001.

Values are mean, SD: n=6

Fig: 1.10 showing % change of glycogen levels in testis tissue of control and experimental animals

Values in the parentheses are % change from Control
Fig: 1.11 showing total carbohydrate levels in testis tissue of control and experimental animals

* Significant difference from that of Diabetic Control animals $P < 0.001$.

Values are mean, SD: $n=6$

Fig: 1.12 showing % change of total carbohydrate levels in testis tissue of control and experimental animals

Values in the parentheses are % change from Control