AIMS & OBJECTIVES OF PRESENT STUDY

3.0 Aims & Objectives of present study :

Diabetes is tackled by diet control, oral hypoglycaemics and insulin injection. Sulphonylureas act primarily by stimulating the beta cells of the islets of Langerhans of pancreas to release stored insulin. They are, therefore; ineffective in totally insulin deficient patients and for successful therapy probably require about 30% of normal beta cell function.

Biguanides reduce absorption of carbohydrates from the gut and increase the utilisation of glucose in peripheral tissues, provided insulin is present and they reduce hepatic gluconeogenesis.

Both groups of drugs are only effective in the presence of insulin. Long term administration of these drugs probably cause cardiovascular morbidity.

Insulin's drawbacks :

1. Promotes allergic reaction.
2. Hypoglycaemia leading to coma and death.
3. Lipoatrophy at the injection site.
4. Injectable preparation.

So it is seen that inspite of diabetes being a burning threat to population all over the world there are drawbacks of therapy and no existing biochemical marker which is directly proportional to the severity of the disease is available.

A number of laboratory studies in animals and epidemiological studies relating to humans have appeared that attempt to link decreased selenium status with increased incidence of cancer [136] and its use as an anticarcinogenic agent has been studied in detail [137, 138, 139, 140 & 141]. Selenium is in GroupVI A of the Periodic Table and has properties intermediate between those of a metal and non-metal. Selenium has a highly specific metabolism and its functional role has been well documented. Selenium (Se), being an integral part of the enzyme glutathione peroxidase is the first line of defence in protecting various cells from injurious consequences, Glutathione peroxidase plays an important role in preventing lipid degradation and membrane disordering [142, 143 & 144]. Recent studies have suggested that in a cell free system glucose can enolize and reduce molecular oxygen radicals [145, 146 & 147] and hyperglycaemia may cause peroxidative injury to membranes. This prompted us to focus our attention on the possible hidden role of selenium as a therapeutic agent since selenium prevents the initiation of peroxidation of membrane lipids and free radical attack.

A few interesting points emerge from the recent studies on diabetes. Many workers have already stated the role of selenium for normoglycaemia in experimental diabetic mice. There are few more reports which showed the effect of selenium on different antioxidants in mice. There are only few reports which stated the effect of selenium on the parameters of different metabolic pathways as well as on the liver microenzyme system.

In the light of the above literature review the present work was aimed towards the understanding of the response of different metabolic pathways under selenium treatment in diabetic mice. Efforts will also be given to draw a correlation between the response of these parameters with the prominent antioxidants like catalase, glutathione.

Mice were made diabetic by intraperitoneal injection of streptozotocin. Selenium was fed to the diabetic mice. It was observed that normoglycaemia occurs after a certain period of time. This time period varies directly with the dose of selenium. Three doses in multiple of ten were taken. These doses were much lower than the toxic dose of selenium. A dose response study of the different parameters were observed to find out the overall normalization effect of selenium in experimental diabetes.

The following parameters were studied :

1. Glucose
2. Glucose 6 Phosphatase
3. Glucose 6 Phosphate dehydrogenase
4. Succinic dehydrogenase
5. Lactic acid
6. Pyruvic acid
7. Glycogen
8. Lactate dehydrogenase
9. Urea
10. L.D.L.
11. H.D.L.
12. V.L.D.L.
13. Cholesterol
14. Triglyceride
15. UDP Glucoronyl transferase
16. Cytochrome p 450
17. Catalase
18. Mono Amine Oxidase
19. Acetyl choline transferase
20. Fibrinogen
21. Glutathione
22. Glutathione s transferase
23. Glutathione reductase
24. Lipid peroxidation
25. HMG CoA reductase
26. Protein
27. Selenium
28. Vanadium
29. Chromosome preparation
30. Histology of pancreas

3.1 Plan of Work :

The following plan of works were undertaken during the course of investigations.

Phase-I : Selection of Experimental animals :

Seven to eight weeks old inbred male swiss mice, average weight of each being 20 ± (SD2) gm were taken.

Phase-II : Mode of treatment :

Mice were injected intraperitoneally 65 mg/kg body weight of streptozotocin (Sigma, USA) dissolved in 0.5 M citrate buffer (pH 4.5).

Phase-III : Design of experiments :

The details of experimental design is given in the scheme below :