Hypoglycemic regulation of Nogo A Gene in Cerebral Cortex and CPS 1 enzyme in Liver and Kidney of Streptozotocin Induced Diabetic Rats

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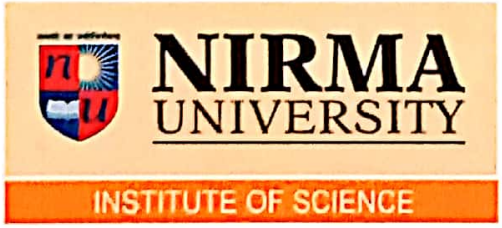

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Certificate

This is to certify that the thesis entitled "**Hypoglycemic regulation of Nogo A Gene in Cerebral Cortex and CPS 1 enzyme in Liver and Kidney of Streptozotocin Induced Diabetic Rats"** submitted to the Institute of Science, Nirma University in partial fulfillment of the requirement for the award of the degree of M.Sc. in Biotechnology is a faithful record of research work carried out by **Radhika Patel (13MBT023)** under the guidance of **Dr. Amee K Nair.** No part of the thesis has been submitted for any other degree or diploma.

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ABSTRACT

Tight regulation of glycemic level during insulin therapy often leads to recurrent hypoglycemia in diabetic patients which subsequently trigger cascade of events leading to cell death even after glucose normalization. Decreased blood sugar levels cause energy deprivation in cell leading to functional mitochondrial impairment. Carbamoyl phosphate synthetase 1 (CPS1) is an intra-mitochondrial, rate-limiting enzyme of the urea cycle vital for the removal of excess urea from cells. Mitochondrial damage and dysfunction is involved in the pathogenesis of hyperglycemia and hypoglycemia. We hypothesized that specific activity of CPS-1 would correlate with impaired mitochondrial function in the liver and kidney during diabetic and hypoglycemic condition with disease progression. Diabetes (D) was induced in Wistar rats by single intrafemoral dose (50mg/kg body weight). D+I group received daily 2 doses (1IU/Kg body weight) of insulin. Hypoglycemia was induced by 1.5 IU/kg body weight and 10IU/kg body weight subcutaneously daily in control (C+IIH) and diabetic rats (D+IIH) respectively. Increased CPS 1 activity was observed in liver and kidney of diabetic rats. Increased CPS 1 activity indicates increase in urea excretion to manage ammonia production due to excessive protein metabolism and increased deamination of amino acids as a substrate for gluconeogenesis during diabetes. Insulin decreases excessive protein metabolim and deamination of amino acids to form substrate – ammonia for urea cycle. Still, increased CPS 1 activity in liver and kidney of hypoglycemic rates was observed. This might be to deal with ammonia load occur due to degradation of elevated levels of monoamine - epinephrine by the action of monoamine oxidase enzyme during hypoglycemic condition. Increase activity of CPS 1 is an indirect measure of increased production of Urea. Urea is reported to cross blood brain barrier (BBB) very slowly and increases permeability of BBB by changing osmotic environment of brain. Hence, we hypothesized that increased activity of CPS 1 during hyperglycemic and hypoglycemic condition leading to increased production of urea which alters BBB permeability and causes myelin damage in brain. Nogo A is CNS neurite growth inhibitor is down regulated in D and no change is observed in hypoglycemic group of rats. But to get significant results this experiment need to be repeated.