Results

BODY WEIGHT

In the beginning of the experiment, the body weight of all the rats was within the normal range. Body weight of hypoglycemic neonatal rats was decreased significantly (p<0.001) in 10th day when compared to control. After treatment with glucose, *Bacopa monnieri* and Bacoside A alone and in combination for 10 days, the body weight was significantly reversed (p<0.001) when compared with hypoglycemic neonatal rats (Table-1).

BLOOD GLUCOSE LEVEL

Blood glucose levels of all rats before insulin administration and treatment was within the normal range (100 – 120 mg/dl). 10 days after treatment, hypoglycemic neonatal rats showed a significant decrease (p<0.001) in blood glucose when compared to control (Table-2a).

Blood glucose level was monitored from day 1 to day 10. Blood glucose level of all rats at time 0 min, before insulin administration, was within the normal range. Insulin administration in rats led to a significant decrease (p<0.001) in blood glucose level 240 min after administration, when compared to control group. Glucose, *Bacopa monnieri* and Bacoside A treatments alone and in combination were significantly reversed (p<0.001) the increased blood glucose level when compared to hypoglycemic neonatal group (Table-2b).
Results

CEREBRAL CORTEX

Real Time PCR amplification of Dopamine D1 receptor mRNA in the cerebral cortex of control and experimental rats

Gene expression of Dopamine D1 receptor subtype mRNA showed significant down regulation (p<0.001) in the cerebral cortex of hypoglycemic neonatal rats and rats treated with glucose when compared to control. In H+B, H+D, H+G+B and H+G+D groups, there was significant up regulation (p<0.05, p<0.01, p<0.001) In all the treatment groups, H+G, H+B, H+D, H+G+B and H+G+D groups there was a significant reversal of the gene expression to near control (p<0.01, p<0.001, p<0.001, p<0.001, p<0.001) when compared with hypoglycemic neonatal and glucose treated group (Figure-1, Table-3).

Real Time PCR amplification of Dopamine D2 receptor mRNA in the cerebral cortex of control and experimental rats

Gene expression of Dopamine D2 receptor subtype mRNA showed significant up regulation (p<0.001) in the cerebral cortex of all the experimental groups and an up regulation of when compared to control. H+G showed significant reversal (p<0.001) when compared to the neonatal hypoglycemic group. In H+B, H+D, H+G+B and H+G+D groups there was a significant reversal of the gene expression (p<0.001) when compared with both the H and H+G group (Figure-2, Table-4).

Scatchard analysis of Dopamine D1 receptor using [3H] SCH 23390 binding against SCH23390 in the cerebral cortex of control and experimental rats

Scatchard analysis of Dopamine D1 receptor using [3H] SCH 23390 binding against SCH 23390 in the cerebral cortex of hypoglycemic neonatal rats and H+G groups showed a significant (p<0.001) decrease in $B_{max}$ compared to control rats. H+G+D showed no difference when compared to control. This showed decreased Dopamine D1 receptor density in the cerebral cortex of
hypoglycemic neonatal rats. $K_d$ showed no significant difference. Significant reversal in the $B_{\text{max}}$ was observed in treatment groups: H+B, H+D, H+G+B and H+G+D ($p<0.001$) when compared with glucose treatment and neonatal hypoglycemic groups (Figure-3,4 Table-5, 6).

**Scatchard analysis of Dopamine D2 receptor using $[^3H] \text{YM-09151-2}$ against sulpiride in cerebral cortex of control and experimental rats**

Scatchard analysis of Dopamine D2 receptor using $[^3H] \text{YM-09151-2}$ binding against sulpiride in the cerebral cortex of hypoglycemic neonatal rats and H+G groups showed a significant ($p<0.001$) increase in $B_{\text{max}}$ compared to control rats. $K_d$ showed no significant difference. Significant reversal in the $B_{\text{max}}$ was observed in all the other treatment groups: H+B, H+D, H+G+B and H+G+D ($p<0.001$) when compared with glucose treatment and neonatal hypoglycemic groups (Figure-5,6 Table-7, 8).

**Dopamine D1 receptor subtype antibody staining in control and experimental groups of rats using confocal microscope**

Dopamine D1 subtype specific antibody staining in the cerebral cortex showed a significant decrease ($p<0.001$) in mean pixel value in the hypoglycemic neonatal rats and H+G treated group when compared to control. H+B and H+D groups significantly reversed ($p<0.001$) the mean pixel value when compared with hypoglycemic neonatal rats and H+G treated group. H+G+B and H+G+D treatment showed prominent down regulation ($p<0.05$) when compared when compared to control and a significant reversal ($p<0.001$) when compared to hypoglycemic neonatal rats and glucose treated rats (Figure-7, Table-9).

**Dopamine D2 receptor subtype antibody staining in control and experimental groups of rats using confocal microscope**

Dopamine D2 subtype specific antibody staining in the cerebral cortex showed a significant increase ($p<0.001$) in mean pixel value in the hypoglycemic neonatal rats and H+G treated group when compared to control. H+B and H+D
(p<0.05, p<0.001) groups showed significant up regulation when compared to control and significantly (p<0.001) reversed mean pixel value when compared with the H and H+G groups. H+G+B and H+G+D treatment showed no significant change when compared to control but, showed prominent reversal (p<0.001) when compared with the H and H+G groups (Figure-8, Table-10).

cAMP content in the cerebral cortex of control and experimental rats

cAMP content showed significant decrease (p<0.001) in the cerebral cortex of hypoglycemic neonatal rats and compared to control rats. H+G treated group showed no reversal when compared to neonatal hypoglycemic group. There was a significant reversal (p<0.001) in cAMP content of the treatment groups: H+B, H+D, H+G+B and H+G+D to near control levels when compared with H and H+G groups. (Figure -9, Table-11).

IP3 content in the cerebral cortex of control and experimental rats

IP3 content showed significant decrease (p<0.001) in the cerebral cortex of hypoglycemic neonatal rats compared to control rats. H+G treated group showed no reversal when compared to neonatal hypoglycemic group. There was a significant reversal (p<0.001) in IP3 content in all the treatment groups H+B, H+D, H+G+B and H+G+D to near control levels when compared with neonatal hypoglycemic rats and glucose treated rats. (Figure -10, Table -12).

Real time PCR amplification of Phospholipase C mRNA in the cerebral cortex of control and experimental rats

Gene expression of Phospholipase C mRNA showed significant up regulation (p<0.001) in the cerebral cortex of hypoglycemic neonatal rats and H+G group when compared to control. In H+B group and H+D groups there was an up regulation of the gene expression (p<0.05) when compared control and showed significant reversal (p<0.001) when compared to the H and H+G groups. In the combination treatment groups, H+G+B and H+G+D there was no significant change when compared to control, but showed significant reversal of
the gene expression levels to near control (p<0.001) when compared with the H and H+G groups (Figure -11, Table -13).

Real time PCR amplification of CREB mRNA in the cerebral cortex of control and experimental rats

Gene expression of CREB mRNA showed significant (p<0.001) up regulation in the cerebral cortex of hypoglycemic neonatal rats and H+G group when compared to control. In H+B and H+D groups there was a significant up regulation (p<0.001) when compared to control and significant (p<0.001) reversal of the gene expression to near control levels when compared with hypoglycemic neonatal and the glucose treated groups. In the combination treatment groups, H+G+B and H+G+D there was a up regulation of the gene expression levels (p<0.001) when compared to control and a significant reversal (p<0.001) when compared with H and H+G groups (Figure-12, Table-14).

Real Time PCR amplification of GLUT 3 mRNA in the cerebral cortex of control and experimental rats

Real-time PCR gene expression of GLUT 3 showed significant decrease (p<0.001) in the cerebral cortex of hypoglycemic neonatal rats when compared to control group. H+G group showed a marked up regulation (p<0.001) compared to control and hypoglycemic neonatal groups. H+B, H+D, H+G+B and H+G+D treatment showed a significant (p<0.001) up regulation when compared to control. These groups showed a prominent reversal of gene expression (p<0.001) when compared to the H and H+G groups (Figure -13, Table-15).

Real Time PCR amplification of Akt -1 mRNA in the cerebral cortex of control and experimental rats

Real time PCR gene expression of Akt -1 showed significant (p<0.001) up regulation in the cerebral cortex of hypoglycemic neonatal rats when compared to control and H+G group. In H+B, H+D and H+G+D treated groups showed a significant (p<0.001) reversal of the gene expression to near control levels when
Results

compared with hypoglycemic neonatal group. In the combination treatment group, H+G+B, there was no significant change with respect to control and showed a marked reversal (p<0.001) of the gene expression levels when compared with H and H+G groups (Figure-14, Table-16).

Real Time PCR amplification of TNF-α mRNA in the cerebral cortex of control and experimental rats

Real-time PCR gene expression of TNF-α in the cerebral cortex of neonatal hypoglycemic rats showed a significant down regulation (p<0.001) when compared to the control and H+G groups. The other treatment groups: H+B, H+D, H+G+B and H+G+D showed a significant down regulation (p<0.001) when compared to control and also significantly reversed (p<0.001) the altered gene expression when compared with H and H+G groups to near control levels (Figure-15, Table-17).

Real Time PCR amplification of GDNF mRNA in the cerebral cortex of control and experimental rats

Real-time PCR gene expression of GDNF showed significant down regulation (p<0.001) in the cerebral cortex of hypoglycemic neonatal rats and all the other treatment compared to control rats. The GDNF gene expression was significantly reversed (p<0.001) in H+B, H+D, H+G+B and H+G+D treatment groups when compared with hypoglycemic and glucose treatment groups (Figure-16, Table-19).

Real Time PCR amplification of BDNF mRNA in the cerebral cortex of control and experimental rats

Real-time PCR gene expression of BDNF showed significant down regulation (p<0.001) in the cerebral cortex of hypoglycemic neonatal rats and all the other treatment compared to control rats. There was a significant reversal (p<0.001) of BDNF gene expression in the H+B, H+D, H+G+B and H+G+D groups when compared to the H and H+G groups. (Figure -17, Table -19).
Real Time PCR amplification of NF-κB mRNA in the cerebral cortex of control and experimental rats

Real-time PCR gene expression of NF-κB showed significant down regulation (p<0.001) in the cerebral cortex of all the groups of neonatal rats when compared to control rats. The H+B, H+D and the combination treatment groups H+G+B and H+G+D groups, showed a marked (p<0.001) reversal of the gene expression when compared to both the hypoglycemic and H+G groups (Figure-18; Table-20).

Real Time PCR amplification of SOD mRNA in the cerebral cortex of control and experimental rats

Real-time PCR gene expression of SOD showed significant decrease (p<0.001) in the cerebral cortex of H and H+G group, and a significant (p<0.001) increase in the H+B, H+D, H+G+B and H+G+D groups when compared to control. The treatment groups, H+B, H+D, H+G+B and H+G+D groups showed a significant (p<0.001) reversal of the SOD gene expression when compared to hypoglycemic neonatal rats and glucose treated group (Figure-19; Table-21).

Real Time PCR amplification of GPx mRNA in the cerebral cortex of control and experimental rats

Real-time PCR gene expression of GPx showed significant down regulation (p<0.001) in the cerebral cortex of hypoglycemic neonatal rats, H+G, H+D and H+B groups and the H+G+B and H+G+D groups showed a significant (p<0.001) up regulation when compared to control rats. There was a significant reversal (p<0.001) in GPx gene expression in the following treatment groups: H+B, H+D, H+G+B and H+G+D, when compared to H and H+G groups (Figure-20; Table-22).
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Real Time PCR amplification of Bax mRNA in the cerebral cortex of control and experimental rats

Real-time PCR gene expression of Bax showed significant up regulation (p<0.001) in the cerebral cortex of H, H+G, H+B and H+D groups when compared to control rats. H+G+B and H+G+D groups showed no significant change when compared to control. There was a significant reversal (p<0.01) in Bax gene expression in H+B, H+D, H+G+B and H+G+D groups compared to H and H+G (Figure-21, Table-23).

Real Time PCR amplification of caspase 8 mRNA in the cerebral cortex of control and experimental rats

Real-time PCR gene expression of caspase 8 showed significant up regulation (p<0.001, p<0.001, p<0.01) in the cerebral cortex of hypoglycemic neonatal rats, H+G and H+B group compared to control rats. The H+D group showed no change when compared to control. There was a significant reversal (p<0.001) in Caspase 8 gene expression in H+D, H+G+B and H+G+D groups when compared to H and H+G groups (Figure-22, Table-24).
CORPUS STRIATUM

Real Time PCR amplification of Dopamine D1 receptor mRNA in the corpus striatum of control and experimental rats

Gene expression of Dopamine D1 receptor subtype mRNA showed significant down regulation (p<0.001) in the corpus striatum of hypoglycemic neonatal rats and H+G groups when compared to control. H+B and H+D groups and the combination treatment groups, H+G+B and H+G+D showed a marked reversal (p<0.001) of the gene expression to near control levels, when compared with hypoglycemic neonatal group and H+G group (Figure-23, Table-25).

Real Time PCR amplification of Dopamine D2 receptor mRNA in the corpus striatum of control and experimental rats

Gene expression of Dopamine D2 receptor subtype mRNA showed significant up regulation (p<0.001) in the corpus striatum of all the other experimental groups when compared to control. In H+B, H+D, H+G+B and H+G+D groups there was a significant reversal (p<0.001) of the gene expression when compared with hypoglycemic neonatal group and H+G group (Figure-24, Table-26).

Scatchard analysis of Dopamine D1 receptor using [$^3$H] SCH 23390 binding against SCH23390 in the corpus striatum of control and experimental rats

Scatchard analysis of Dopamine D1 receptor using [$^3$H] SCH 23390 binding against SCH 23390 in the corpus striatum of hypoglycemic neonatal rats and H+G groups showed a significant (p<0.001) decrease in $B_{\text{max}}$ compared to control rats. $K_d$ showed no significant change. Significant (p<0.001) reversal in the $B_{\text{max}}$ was observed in treatment groups: H+B, H+D H+G+B and H+G+D groups when compared to glucose treatment and neonatal hypoglycemic groups (Figure- 25, 26 Table- 27, 28).
Scatchard analysis of Dopamine D2 receptor using $[^3]H$ YM-09151-2 against sulpiride in corpus striatum of control and experimental rats

Scatchard analysis of Dopamine D2 receptor using $[^3]H$ YM-09151-2 binding against sulpiride in the corpus striatum of hypoglycemic neonatal rats and H+G groups showed a significant ($p<0.001$) increase in $B_{max}$ compared to control rats. Significant reversal in the $B_{max}$ was observed in treatment groups: H+B, H+D, H+G+B and H+G+D ($p<0.001$) when compared with glucose treatment and neonatal hypoglycemic groups (Figure- 27,28 Table- 29, 30).

Dopamine D1 receptor subtype antibody staining in the corpus striatum of control and experimental groups of rats using confocal microscope

Dopamine D1 subtype specific antibody staining in the corpus striatum showed a significant decrease ($p<0.001$) in mean pixel value in the hypoglycemic neonatal rats, H+G, H+B and H+D treated groups when compared to control. The treatment groups, H+B, H+D, H+G+B and H+G+D significantly ($p<0.001$) reversed mean pixel value when compared with the H and H+G groups (Figure- 29, Table-31).

Dopamine D2 receptor subtype antibody staining in the corpus striatum of control and experimental groups of rats using confocal microscope

Dopamine D2 subtype specific antibody staining in the corpus striatum showed a significant increase ($p<0.001$) in mean pixel value in the hypoglycemic neonatal rats, H+G groups when compared to control. The treatment groups H+B, H+D, H+G+B and H+G+D treatment showed prominent reversal when compared with both the H and H+G treated rats (Figure-30, Table-32).

cAMP content in the corpus striatum of control and experimental rats

cAMP content showed significantly decreased ($p<0.001$) in the corpus striatum of hypoglycemic neonatal rats, H+G, H+B and H+D groups when compared to control. Both H+G+B and H+G+D groups showed no prominent change when compared to control. There was a significant reversal ($p<0.001$) in
cAMP content in H+B, H+D, H+G+B and H+G+D treatment groups when compared with the neonatal hypoglycemic rats and glucose treated rats (Figure-31, Table-33).

**IP3 content in the corpus striatum of control and experimental rats**

IP3 content showed significantly increased (p<0.001) in the corpus striatum of hypoglycemic neonatal rats, H+G and H+D group when compared to control rats. H+B, H+G+B and H+G+D treatment groups showed no marked change when compared to control. H+B, H+G+B and H+G+D treatment showed prominent reversal to near control levels when compared to both the H and H+G groups. (Figure -32, Table -34).

**Real time PCR amplification of Phospholipase C mRNA in corpus striatum of control and experimental rats**

Gene expression of Phospholipase C mRNA showed significant up regulation (p<0.001) in the corpus striatum of hypoglycemic neonatal rats and H+G group when compared to control. The groups, H+B and H+D also showed a significant (p<0.01, p<0.05) up regulation, whereas the H+G+B and H+G+D groups showed no apparent change when compared to control. In H+B, H+D, H+G+B and H+G+D groups, there was a significant reversal of the gene expression levels to near control (p<0.001) when compared with hypoglycemic neonatal group and H+G group (Figure -33, Table -35).

**Real time PCR amplification of CREB mRNA in the corpus striatum of control and experimental rats**

Gene expression of CREB mRNA showed significant (p<0.001) up regulation in the corpus striatum in the groups H when compared to control. H+G showed no prominent change when compared to hypoglycemic group. Also the group H+G+D showed no prominent change when compared to control. It was observed that in the groups, H+B, H+D, H+G+B and H+G+D the gene expression
levels were significantly (p<0.001) brought down when compared with H and H+G groups (Figure -34, Table -36).

**Real Time PCR amplification of GLUT 3 mRNA in the corpus striatum of control and experimental rats**

Real-time PCR gene expression of GLUT 3 showed significant down regulation (p<0.001) in the corpus striatum of hypoglycemic neonatal rats when compared to control rats. H+G group showed a marked up regulation (p<0.001) compared to both the neonatal hypoglycemic and the control rats. All the other treatment groups, H+B, H+D, H+G+B and H+G+D prominent up regulation (p<0.05, p<0.05, p<0.01, p<0.01) in GLUT 3 gene expression when compared to control. The treatment groups, H+B, H+D, H+G+B and H+G+D showed a marked reversal (p<0.001) when compared to both the H and H+G groups (Figure-35, Table-37).

**Real Time PCR amplification of Akt -1 mRNA in the corpus striatum of control and experimental rats**

Real time PCR gene expression of Akt -1 showed significant (p<0.001) up regulation in the corpus striatum of all the groups H, H+G, H+B, H+D, H+G+B and H+G+D groups when compared to control. It was also observed that in H+B, H+D, H+G+B and H+G+D groups there was a marked reversal of the gene expression levels (p<0.001) when compared with H and H+G groups (Figure-36, Table-38).

**Real Time PCR amplification of TNF-α mRNA in the corpus striatum of control and experimental rats**

Real-time PCR gene expression of TNF-α showed significant down regulation (p<0.001) in the corpus striatum of H, H+G and H+D groups when compared to control. The groups H+B, H+G+B and H+G+D showed no significant change when compared to control. In H+B, H+D, H+G+B and H+G+D treated hypoglycemic neonatal rats, there was significant (p<0.001) reversal of
Results

TNF-α gene expression when compared to hypoglycemic neonatal and H+G rats respectively (Figure-37, Table-39).

**Real Time PCR amplification of GDNF mRNA in the corpus striatum of control and experimental rats**

Real-time PCR gene expression of GDNF showed significant down regulation (p<0.001) in the corpus striatum of hypoglycemic neonatal rats and H+G group compared to control rats. The GDNF gene expression was significantly reversed (p<0.001) in H+B, H+D, H+G+B and H+G+D treatment groups of rats when compared with hypoglycemic neonatal rats and glucose treatment groups (Figure-38, Table-40).

**Real Time PCR amplification of BDNF mRNA in the corpus striatum of control and experimental rats**

Real-time PCR gene expression of BDNF showed significant down regulation (p<0.001) in the corpus striatum of all the groups of rats compared to control rats. There was a significant reversal (p<0.001) in BDNF gene expression in H+B, H+D, H+G+B and H+G+D groups to near control levels when compared to the H and H+G groups (Figure-39, Table-41).

**Real Time PCR amplification of NF-κB mRNA in the corpus striatum of control and experimental rats**

Real-time PCR gene expression of NF-κB showed significant down regulation (p<0.001) in the corpus striatum of hypoglycemic neonatal rats compared to control rats. The treatment groups H+G, H+B, H+D, H+G+B and H+G+D showed a significant (p<0.001) up regulation in the gene expression levels when compared to control and hypoglycemic neonatal rats. There was a significant reversal (p<0.001) in NF-κB gene expression in H+B, H+D, H+G+B and H+G+D (p<0.001) groups when compared to hypoglycemic neonatal rats and neonatal hypoglycemic group treated with glucose (Figure-40, Table-42).
Real Time PCR amplification of SOD mRNA in the corpus striatum of control and experimental rats

Real-time PCR gene expression of SOD showed significant down regulation (p<0.001) in the corpus striatum of neonatal rats group. No significant change was observed in the H+G group compared to neonatal hypoglycemic group. There was a marked reversal (p<0.001) in SOD gene expression in hypoglycemic neonatal rats treated with *Bacopa monnieri* and Bacoside A and the combination treatments, H+G+B and H+G+D groups, when compared to hypoglycemic and H+G group (Figure-41, Table-43).

Real Time PCR amplification of GPx mRNA in the corpus striatum of control and experimental rats

Real-time PCR gene expression of GPx showed significant down regulation (p<0.001) in the corpus striatum of hypoglycemic neonatal rats, H+G, H+B and H+D groups when compared to control rats. The groups H+G+B and H+G+D also showed an apparent down regulation (p<0.05, p<0.01) when compared to the control group. There was a significant reversal (p<0.001) in GPx gene expression in hypoglycemic neonatal rats treated with *Bacopa monnieri* and Bacoside A alone and H+G+B and H+G+D groups when compared to H and H+G groups (Figure-42, Table-44).

Real Time PCR amplification of Bax mRNA in the corpus striatum of control and experimental rats

Real-time PCR gene expression of Bax showed significant up regulation (p<0.001) in the corpus striatum of all the groups when compared to control rats. There was seen to be a significant reversal (p<0.01) in Bax gene expression in hypoglycemic neonatal rats treated with *Bacopa monnieri* and Bacoside A alone, and the combination treatment groups, H+G+B and H+G+D compared to hypoglycemic neonatal rats and the glucose treated group (Figure-43, Table-45).
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Real Time PCR amplification of caspase 8 mRNA in the corpus striatum of control and experimental rats

Real-time PCR gene expression of caspase 8 showed significant up-regulation (p<0.001) in the corpus striatum of hypoglycemic neonatal rats, H+G, H+B and H+D groups compared to control rats. There was a prominent reversal (p<0.001) in Caspase 8 gene expression in H+B, H+D, H+G+B and H+G+D groups compared to H and H+G groups (Figure-44, Table-46).
CEREBELLUM

Real Time PCR amplification of Dopamine D1 receptor mRNA in the cerebellum of control and experimental rats

Gene expression of Dopamine D1 receptor subtype mRNA showed significant down regulation (p<0.001) in the cerebellum of hypoglycemic neonatal rats, H+G, H+B, H+D, H+G+B and H+G+D groups when compared to control. Both the individual treatment groups, H+B and H+D and the combination treatment groups, H+G+B and H+G+D there was a significant reversal of the gene expression levels (p<0.001) when compared with hypoglycemic neonatal group and H+G group (Figure-45, Table-47).

Real Time PCR amplification of Dopamine D2 receptor mRNA in the cerebellum of control and experimental rats

Gene expression of Dopamine D2 receptor subtype mRNA showed significant up regulation (p<0.001) in the cerebellum of hypoglycemic neonatal rats and the treatment groups H+G, H+B and H+D when compared to control. There was no significant up regulation of the gene expression (p<0.001) in the H+G+B and H+G+D groups when compared to control. H+D, H+G+B and H+G+D (p<0.01, p<0.001, p<0.001) showed a significant decrease of the gene expression levels when compared with hypoglycemic neonatal group and H+G group (Figure-46, Table-48).

Scatchard analysis of Dopamine D1 receptor using \[^{3}H\] SCH 23390 binding against SCH23390 in the cerebellum of control and experimental rats

Scatchard analysis of Dopamine D1 receptor using \[^{3}H\] SCH 23390 binding against SCH 23390 in the cerebellum of hypoglycemic neonatal rats showed a significant decrease in B\(_{\text{max}}\) (p<0.001) and increase in K\(_{d}\)(p<0.001) compared to control rats. This showed decreased Dopamine D1 receptor density in the cerebellum of hypoglycemic neonatal rats. No Significant reversal in the B\(_{\text{max}}\) was observed. K\(_{d}\) showed significant was observed in all the other treatment
groups: H+B (p<0.001) and H+G+B (p<0.001) when compared with control groups (Figure- 47,48 Table- 49, 50).

Scatchard analysis of Dopamine D2 receptor using $[^3]$H YM-09151-2 against sulpiride in cerebellum of control and experimental rats

Scatchard analysis of Dopamine D2 receptor using $[^3]$H YM-09151-2 binding against sulpiride in the cerebellum of hypoglycemic neonatal rats, H+G, H+B, H+D and H+G+D groups showed a significant (p<0.001) increase in $B_{\text{max}}$ and $K_d$ compared to control rats. This showed an increased Dopamine D2 receptor density in the cerebellum. H+G showed a significant reversal (p<0.001) compared to hypoglycemic group. The treatment groups: H+B, H+D, H+G+B and H+G+D groups showed prominent reversal (p<0.001) in $B_{\text{max}}$ and $K_d$ when compared with glucose treatment and neonatal hypoglycemic groups (Figure-49,50 Table-51, 52).

CAMP content in the cerebellum of control and experimental rats

CAMP content showed significant decrease (p<0.001) in the cerebellum of all groups of rats compared to control. The individual treatment groups, H+B and H+D and combination treatment groups H+G+B and H+G+D treatment showed prominent reversal to near control levels when compared with both the neonatal hypoglycemic rats and the glucose treated rats (Figure-51, Table-53).

IP3 content in the cerebellum of control and experimental rats

IP3 content showed significant increase (p<0.001) in the cerebellum of hypoglycemic neonatal rats, H+G, H+B and H+A treated groups compared to control rats. There was no significant change observed in IP3 content in H+G+B and H+G+D treatment compared to control. A prominent reversal to near control levels was observed in H+B, H+D, H+G+B and H+G+D when compared with H and H+G groups. (Figure -52, Table -54).
**Results**

**Real time PCR amplification of Phospholipase C mRNA in cerebellum of control and experimental rats**

Gene expression of Phospholipase C mRNA showed significant upregulation (p<0.001) in the cerebellum of all groups except H+G+B and H+G+D when compared to control. In the treatment groups, H+B, H+D, H+G+B and H+G+D there was a marked reversal of the gene expression levels to near control (p<0.001) when compared with hypoglycemic neonatal group and H+G group (Figure -53, Table -55).

**Real time PCR amplification of CREB mRNA in the cerebellum of control and experimental rats**

Gene expression of CREB mRNA showed significant (p<0.001) downregulation in the cerebellum of H, H+G, H+B and H+D groups when compared to control. Combination treatment groups, H+G+B and H+G+D showed no significant down regulation when compared to control group. In H+B, H+D, H+G+B and H+G+D groups there was a significant reversal of the gene expression to near control levels (p<0.001) when compared with hypoglycemic neonatal group H+G groups (Figure -54, Table -56).

**Real Time PCR amplification of GLUT 3 mRNA in the cerebellum of control and experimental rats**

Real-time PCR gene expression of GLUT 3 showed a significant upregulation (p<0.001) in the cerebellum of all groups of rats when compared to control rats. H+G group showed a marked increase (p<0.001) compared to neonatal hypoglycemic rats. All the other treatments with *Bacopa monnieri* and Bacoside A: H+B, H+D, H+G+B and H+G+D significantly (p<0.001) increased the GLUT 3 gene expression when compared to the hypoglycemic neonatal rats (Figure-55, Table-57).
**Real Time PCR amplification of Akt -1 mRNA in the cerebellum of control and experimental rats**

Real time PCR gene expression of Akt -1 showed significant down regulation in the cerebellum of both hypoglycemic neonatal rats (p<0.001) and H+G group (p<0.001) whereas the H+B, H+D, H+G+B and H+G+D showed a significant up regulation (p<0.001) when compared to control. In H+B, H+D H+G+B and H+G+D groups there was an significant increase of the gene expression levels (p<0.001) when compared with H and H+G groups (Figure-56, Table-58).

**Real Time PCR amplification of TNF-α mRNA in the cerebellum of control and experimental rats**

Real-time PCR gene expression of TNF-α showed significant up regulation (p<0.001) in the cerebellum of all the neonatal groups of rats compared to control. Treatment using *Bacopa monnieri* and Bacoside A: H+B, H+D, H+G+B and H+G+D significantly reversed (p<0.001) the altered gene expression when compared with hypoglycemic neonatal rats and glucose treated rats (Figure-57, Table-59).

**Real Time PCR amplification of GDNF mRNA in the cerebellum of control and experimental rats**

Real-time PCR gene expression of GDNF showed significant down regulation (p<0.001) in the cerebellum of hypoglycemic neonatal rats and H+G group and in the H+B and H+D groups (p<0.05) compared to control rats whereas H+G+B and H+G+D treatment showed no marked change when compared to control. The GDNF gene expression was significantly (p<0.001) reversed in H+B, H+D, H+G+B and H+G+D treatment to near control levels when compared with hypoglycemic and glucose treatment groups (Figure-58, Table-60).
**Results**

Real Time PCR amplification of BDNF mRNA in the cerebellum of control and experimental rats

Real-time PCR gene expression of BDNF showed significant down regulation (p<0.001) in the cerebellum of all the groups of rats when compared to control. There was a significant reversal (p<0.001) in BDNF gene expression in the treatment groups: H+B, H+D, H+G+B and H+G+D groups when compared to H and H+G groups (Figure-59, Table-61).

Real Time PCR amplification of NF-κB mRNA in the cerebellum of control and experimental rats

Real-time PCR gene expression of NF-κB showed significant down regulation (p<0.001) in the cerebellum of hypoglycemic neonatal rats and H+G group compared to control rats. In H+B, H+D and H+G+D groups also there was seen to be a significant down regulation (p<0.05) compared to control. The gene expression was significantly (p<0.001) reversed in H+B, H+D, H+G+B and H+G+D groups when compared to hypoglycemic and H+G groups (Figure-60, Table-62).

Real Time PCR amplification of SOD mRNA in the cerebellum of control and experimental rats

Real-time PCR gene expression of SOD showed significant down regulation (p<0.001) in the cerebellum of hypoglycemic neonatal rats, H+G, H+B, H+D, H+G+B and H+G+D groups compared to control. There was a significant reversal (p<0.001) in SOD gene expression in hypoglycemic neonatal rats treated with *Bacopa monnieri* and Bacoside A and the combination treatments, H+G+B and H+G+D groups, (p<0.001) when compared to hypoglycemic neonatal group. Also a marked (p<0.001) reversal was observed in groups H+D, H+G+B and H+G+D compared to H+G group. H+B showed no prominent change when compared to H+G (Figure-61, Table-63).
Real Time PCR amplification of GPx mRNA in the cerebellum of control and experimental rats

Real-time PCR gene expression of GPx showed significant down regulation (p<0.001) in the cerebellum of all the experimental groups except H+G+B, compared to control rats. There was a significant reversal (p<0.001) in GPx gene expression in hypoglycemic neonatal rats treated with H+B, H+D, H+G+B and H+G+D groups when compared to hypoglycemic neonatal group. A significant (p<0.001) reversal was observed in groups H+B, H+G+B and H+G+D compared to H+G group. H+D is shown to no prominent change when compared to H+G (Figure-62, Table-64).

Real Time PCR amplification of Bax mRNA in the cerebellum of control and experimental rats

Real-time PCR gene expression of Bax showed significant up regulation (p<0.001) in the cerebellum of all the experimental groups except in H+G+D when compared to control rats. There was a significant reversal (p<0.001) in Bax gene expression in H+G, H+B, H+D, H+G+B and H+G+D groups compared to neonatal hypoglycemic group. In H+D, H+G+B and H+G+D groups, a significant (p<0.001) reversal in Bax gene expression was observed when compared to H+G group. (Figure-63, Table-65).

Real Time PCR amplification of caspase 8 mRNA in the cerebellum of control and experimental rats

Real-time PCR gene expression of caspase 8 showed significant down regulation (p<0.001) in the cerebellum of hypoglycemic neonatal rats and H+G group compared to control rats. There was a significant reversal (p<0.001) in Caspase 8 gene expression in the treatment groups H+B, H+D, H+G+B and H+G+D groups to near control levels compared to H and H+G groups (Figure-64, Table-66).
Results
BRAIN STEM

Real Time PCR amplification of Dopamine D1 receptor mRNA in the brain stem of control and experimental rats

Gene expression of Dopamine D1 receptor subtype mRNA showed significant down regulation (p<0.001) in the brain stem of all experimental groups when compared to control. In H+B, H+D, H+G+B and H+G+D there was a significant reversal of the gene expression levels (p<0.001) when compared with hypoglycemic neonatal group and H+G group (Figure-65, Table-67).

Real Time PCR amplification of Dopamine D2 receptor mRNA in the brain stem of control and experimental rats

Gene expression of Dopamine D2 receptor subtype mRNA showed significant up regulation (p<0.001) in the brain stem of all the experimental groups when compared to control. In the treatment groups, H+B, H+D H+G+B and H+G+D there was a significant reversal (p<0.001) of the gene expression levels when compared with hypoglycemic neonatal group. The dopamine D2 receptor mRNA expression showed a significant reversal in H+B (p<0.01), H+D (p<0.001), H+G+B (p<0.001) and H+G+D (p<0.001) when compared to H+G group (Figure-66, Table-68).

Scatchard analysis of Dopamine D1 receptor using $[^3]$H SCH 23390 binding against SCH23390 in the brain stem of control and experimental rats

Scatchard analysis of Dopamine D1 receptor using $[^3]$H SCH 23390 binding against SCH 23390 in the brain stem of hypoglycemic neonatal rats showed a significant (p<0.001) decrease in $B_{\text{max}}$ and significant increase in $K_d$ (p<0.01) compared to control rats. This showed decreased Dopamine D1 receptor density in the brain stem of hypoglycemic neonatal rats. Significant reversal (p<0.05) in the $B_{\text{max}}$ was observed in treatment groups: H+B, H+D, H+G+B and H+G+D when compared with glucose treatment and neonatal hypoglycemic groups (Figure- 67,68, Table- 69, 70).
Scatchard analysis of Dopamine D2 receptor using $[^3]$H YM-09151-2 against sulpiride in brain stem of control and experimental rats

Scatchard analysis of Dopamine D2 receptor using $[^3]$H YM-09151-2 binding against sulpiride in the brain stem of hypoglycemic neonatal rats and H+G groups showed a significant (p<0.001) increase in $B_{\text{max}}$ compared to control rats. $K_d$ showed no significant change. This showed increased Dopamine D2 receptor density in the brain stem of hypoglycemic neonatal rats. Significant reversal in the $B_{\text{max}}$ was observed in treatment groups: H+B, H+D, H+G+B and H+G+D groups showed prominent reversal (p<0.001) when compared with glucose treatment and neonatal hypoglycemic groups (Figure- 69,70, Table- 71, 72).

cAMP content in the brain stem of control and experimental rats

cAMP content showed significant decrease (p<0.001) in the brain stem of all experimental groups except H+G+D group when compared to control rats. There was a significant reversal (p<0.001) in cAMP content in hypoglycemic neonatal rats treated with Bacopa monnieri and Bacoside A and H+G+B and H+G+D to near control levels when compared to hypoglycemic neonatal groups glucose treated rats (Figure-71, Table-73).

IP3 content in the brain stem of control and experimental rats

IP3 content showed significant increase (p<0.001) in the brain stem of all experimental groups except H+G+D group when compared to control rats. There was a significant reversal (p<0.001) in IP3 content in H+B, H+D, H+G+B and H+G+D groups to near control levels when compared with glucose treated rats (Figure -72, Table -74).

Real time PCR amplification of Phospholipase C mRNA in brain stem of control and experimental rats

Gene expression of Phospholipase C mRNA showed significant up regulation (p<0.001) in the brain stem of all experimental groups except H+G+D
group when compared to control rats. In the groups, H+B, H+D, H+G+B and H+G+D there was a significant reversal of the gene expression (p<0.001) when compared with hypoglycemic neonatal group and H+G group (Figure -73, Table - 75).

**Real time PCR amplification of CREB mRNA in the brain stem of control and experimental rats**

Gene expression of CREB mRNA showed significant up regulation in the brain stem of all the experimental groups when compared to control. In the individual treatment groups, H+B and H+D and In the combination treatment groups, H+G+B and H+G+D there was a significant reversal of the gene expression levels (p<0.001) when compared with H and H+G groups (Figure -74, Table -76).

**Real Time PCR amplification of GLUT 3 mRNA in the brain stem of control and experimental rats**

Real-time PCR gene expression of GLUT 3 showed significant decrease (p<0.001) in the brain stem of hypoglycemic neonatal rats, H+G+B and H+G+D groups when compared to control rats. H+G, H+B and H+D groups showed a marked up regulation (p<0.001) compared to control rats. H+G, H+B, H+D, H+G+B and H+G+D showed a significant (p<0.001) reversal when compared to the neonatal hypoglycemic group. (Figure-75, Table-77).

**Real Time PCR amplification of Akt -1 mRNA in the brain stem of control and experimental rats**

Real time PCR gene expression of Akt -1 showed significant(p<0.001) down regulation in the brain stem of hypoglycemic neonatal rats, H+G, H+B and H+D groups when compared to control. In the treatment with *Bacopa monnieri* and Bacoside A, H+B and H+D groups and in the combination treatment groups, H+G+B and H+G+D there was a significant reversal of the gene expression levels (p<0.001) when compared with H and H+G groups (Figure-76, Table-78).
Results

Real Time PCR amplification of TNF-α mRNA in the brain stem of control and experimental rats

Real-time PCR gene expression of TNF-α showed significant down regulation (p<0.001) in the brain stem of H, H+G and H+B groups when compared to control. Treatment using All the treatment groups, H+B, H+D, H+G+B and H+G+D treatment significantly reversed (p<0.001) the altered gene expression to near control levels when compared with hypoglycemic neonatal group and H+G group (Figure-77, Table-79).

Real Time PCR amplification of GDNF mRNA in the brain stem of control and experimental rats

Real-time PCR gene expression of GDNF showed significant down regulation (p<0.001) in the brain stem of all the experimental groups compared to control rats. The GDNF gene expression was significantly reversed (p<0.001) in H+B, H+D, H+G+B and H+G+D treatment when compared with hypoglycemic and glucose treatment groups (Figure-78, Table-80).

Real Time PCR amplification of BDNF mRNA in the brain stem of control and experimental rats

Real-time PCR gene expression of BDNF showed significant down regulation (p<0.001) in the brain stem of all the experimental groups compared to control rats. There was a significant reversal (p<0.001) in BDNF gene expression in H+B, H+D, H+G+B and H+G+D groups, the gene expression was reversed back when compared with hypoglycemic and glucose treatment groups (Figure-79, Table-81).

Real Time PCR amplification of NF-κB mRNA in the brain stem of control and experimental rats

Real-time PCR gene expression of NF-κB showed significant down regulation (p<0.001) in the brain stem of all the experimental groups compared to control rats.
control rats. There was a significant reversal to near control levels (p<0.001) in NF-kB gene expression in hypoglycemic neonatal rats treated with *Bacopa monnieri* and Bacoside A alone: H+B, H+D and in combination: H+G+B and H+G+D groups, when compared to hypoglycemic and H+G group (Figure-80, Table-82).

**Real Time PCR amplification of SOD mRNA in the brain stem of control and experimental rats**

Real-time PCR gene expression of SOD showed significant down regulation (p<0.001) in the brain stem of H, H+G, H+B, H+D, H+G+B and H+G+D groups. In the treatment groups: H+B, H+D, H+G+B and H+G+D groups, the gene expression was significantly reversed (p<0.001) when compared to hypoglycemic and H+G group (Figure-81, Table-83).

**Real Time PCR amplification of GPx mRNA in the brain stem of control and experimental rats**

Real-time PCR gene expression of GPx showed significant down regulation in the brain stem of hypoglycemic neonatal rats (p<0.001), H+G (p<0.001) and H+B (p<0.01) group compared to control rats. H+D and H+G+D showed a significant (p<0.01) up regulation compared to control. There was a significant reversal (p<0.001) in GPx gene expression in hypoglycemic neonatal rats treated with *Bacopa monnieri* and Bacoside A alone and in combination, H+G+B and H+G+D when compared to H and H+G groups (Figure-82, Table-84).

**Real Time PCR amplification of Bax mRNA in the brain stem of control and experimental rats**

Real-time PCR gene expression of Bax showed significant up regulation (p<0.001) in the brain stem of all the experimental groups compared to control rats. H+B, H+D, H+G+B and H+G+D groups showed significant reversal
Results

(p<0.001) of the Bax mRNA levels compared to H and H+G groups (Figure-83, Table-85).

**Real Time PCR amplification of caspase 8 mRNA in the brain stem of control and experimental rats**

Real-time PCR gene expression of caspase 8 showed significant up regulation (p<0.001) in the brain stem of hypoglycemic neonatal rats, H+G, H+B, H+D groups compared to control rats. There was a significant reversal (p<0.001) in Caspase 8 gene expression in H+B, H+D, H+G+B and H+G+D groups when compared to H and H+G groups (Figure-84, Table-86).