CHAPTER
SUMMARIES
CHAPTER 1
This study was carried out to see the effect of the aqueous extract of a combination of *Ocimum sanctum* (Tulsi) and *Pterocarpus marsupium* (Indian kino or Bija sar) on markers of carbohydrate metabolism, glycemic status, tissue protein content, markers of lipid metabolism (Total cholesterol, LDL, HDL, VLDL), enzymic (SOD, Cat, GPx, GST) and non enzymic (GSH, Vit-C) and Level of lipid peroxidation markers of oxidative stress, western blot and histopathological observations on pancreas. Adult albino female rats weighing 150-200gm were made diabetic by single intraperitoneal injection of alloxan (120 mg / Kg body weight). The alloxanised animals were left for 7 days for onset of diabetes. Animals having blood glucose level greater than 300 were selected for further experimentation with the extract mixture for 15 days. Animals were sacrificed on 16th day and all parameters were assessed.

The combination of PM and OS (PM + OS) used in the present study for a short duration of 15 days had a potent hypoglycemic effect in severely diabetic animals as the glycemic levels showed a decrease from 470% high in diabetic animals to 250%. More significant was the change in serum insulin titre which showed a recovery to just about 11% of control animals in extract treated diabetic animals compared to 54% deficit in diabetic animals. The histological observation showed greater number of β cells in PM+OS extract treated diabetic rats suggesting the possible therapeutic potential of the extract to promote proliferation of surviving β cells (consequent to alloxan destruction of β cells) and/or regeneration of islet β cells. The favourable
influence of the extract mixture in combating diabetic hyperglycemia was well confirmed by the greater glucose tolerance and insulin sensitivity in extract administered diabetic rats. Glucose elevation rate (E) which essentially provides an index of glucose tolerance is much higher in diabetic animals (9.1mg/min) and significantly lesser in PM+OS treated diabetic animals (5.8mg/min) as against identical lower E values of 1.21 and 1.11 mg/min in control and extract treated control rats respectively. The extract treated diabetic rats also show greater insulin sensitivity as seen by the 53% decrease in blood glucose as against the mere 7.6% decrease in extract treated control rats. The increased activity of glucose-6-phosphatase in the liver of diabetic rats is effectively countermanded by treatment with PM+OS extract. The observed decrease in tissue protein contents can be related with increased protein catabolism and the entry of amino acids into liver feeding the pathway of gluconeogenesis in diabetic rats. Total GLUT 4 expression in the muscle of diabetic animals is significantly decreased and administration of PM+OS extract mixture has been found to be very effective in not only reversing the decline in GLUT 4 expression but even registered an upregulated expression much above the level found in non diabetic animals. This encouraging result on GLUT 4 expression provides ample evidence for the efficacy of the PM + OS extract on glucose uptake at the molecular level. Diabetic animals showed elevated serum lipid profile and tissue lipid and cholesterol contents. The present study on PM+OS combination extract in this context shows very potent effect in maintaining hepatic cholesterol content.
and serum triglycerides, VLDL and HDL levels to near normal non diabetic state while lowering serum cholesterol and LDL to even below the non diabetic control levels. In the present study, evaluation of oxidative stress in the form of levels of LPO, non enzymatic (GSH) and enzymatic (SOD, Cat, and GPx) antioxidants in liver, muscle and kidney has depicted an increase in LPO and decrease in antioxidants ranging from 30%-5% at an average, indicating co existence of metabolic disturbances and oxidative stress in diabetic animals. Interestingly, oxidative stress in diabetic animals is paralleled with an increase in serum corticosterone level. Further, the present study has also recorded significant increment in serum markers of hepatic (SGPT- 207%, SGOT- 286%, ALP- 130%, ACP- 48%) and renal (Urea - 309%, Creatinine - 50%) damage in diabetic rats. Results of the present study strongly justify the usage of a combination therapy with PM+OS mixture and meet the objective of achieving a holistic amelioration and cure of diabetes as, the PM+OS extract mixture has not only succeeded in effecting glycemic regulation with rectification of dyslipidemia but also in restoring the antioxidant levels to the pre diabetic status. Herbal preparations are ideal candidates of choice and in this context, the present combination of PM and OS provide compelling evidences for a holistic efficacy in amelioration of all diabetic manifestations/dysregulations.
CHAPTER 2
The present study deals with Of the two doses of melatonin used, low dose of melatonin had significant hypoglycemic effect compared to the weaker effect of high dose in diabetic animals as the glycemic level showed a decrease from 420% high (average of fasted and fed) in diabetic animals to 106% in D+M_L animals. The decrease in D+M_H on the other hand was only 372%. This differential dose dependent effect of melatonin in diabetic animals is well corroborated by the observed 5% hypoglycemic effect of M_L as compared to 12% hyperglycemic effect of M_H in non diabetic control rats. Lower doses of melatonin had potent hypoglycemic effect on diabetic animals suggesting augmented glucose clearance. Despite the fact that insulin levels were lower in melatonin treated diabetic rats, the histological observations suggested a cytoprotective and regenerative effect of melatonin, more clearly seen with the high dose. The present study provides evidence for decreased hepatic and muscle glycogen phosphorylase activity and hepatic glucose -6-phosphatase activity for the observed hypoglycemic and glycogenic effects by low dose of melatonin in both non diabetic and diabetic animals. The favourable influence of low dose of melatonin is also reflected in the observed tissue protein conserving effect. Though both doses of melatonin showed a generalized lipid lowering effect; high dose of melatonin was relatively more effective in lowering serum cholesterol fractions with increase in tissue cholesterol contents in diabetic animals. However, hypotriglyceridemic effect was more potently seen in diabetic animals treated with low dose of melatonin. Evaluation of oxidative stress in terms of levels of LPO, non-enzymatic (GSH) and enzymatic (SOD, Catalase and GPx)
antioxidants in liver, muscle and kidney has depicted an increase in LPO and decrease in antioxidants ranging from 30% to 50% at an average, indicating coexistence of metabolic disturbances and oxidative stress in diabetic animals. Oxidative stress in diabetic animals paralleled with an increase in serum corticosterone level and, high dose of melatonin substantially restored corticosterone level to a non-diabetic level. In conclusion, it can be inferred that melatonin has holistic effect on various facets of deleterious characteristic of type I diabetes. The findings also suggest employment of melatonin in a sequentially graded dosage for holistic control of diabetic manifestations with an eventual low dosage to providing glycemic regulation and, a later higher dose therapy to completely nullify the oxidative stress and hepatic and renal dysfunctions.
CHAPTER 3

Hyperglycemia, a characteristic hallmark of diabetes can not only lead to the generation of free radicals but also impair endogenous antioxidant defense system. Any treatment for diabetes should address the aspect of ameliorating oxidative stress apart from glycemic control. With this objective, adult albino female rats were made diabetic by a single intraperitoneal injection of alloxan (120 mg / Kg body weight). After 7 days, onset of diabetes in the alloxanised animals was confirmed by blood glucose level greater than 300 mg / dl. Further experiments were conducted for 15 days under a photoperiodic schedule of LD 13:11. The present study was designed to assess the potential hypoglycemic effect of PM+OS extract(PM+OS) with the favourable effect of high dose (10 mg / Kg BW) of melatonin (MH) on the associated alterations by simultaneous administration of melatonin along with supplementation with PM+OS extract in diabetic rats at 18:00 hrs. Favourable influence of PM.OS+MH was manifested in the greater glucose tolerance and insulin sensitivity. As against an increase of 89 % or 81% of glycemic level in PM.OS treated or MH treated diabetic animals respectively on glucose challenge, the increment in PM.OS +MH treated diabetic animals was a mere 57% . Similarly, the glycemic level at the end of 120 mts of glucose challenge was only 30% higher than the basal zero level in PM.OS +MH rats as against 55% and 63% higher levels in PM.OS and MH treated rats respectively. Obviously, the PM.OS+MH rats show a better and more potent glucose tolerance compared to extract or melatonin treatment alone suggesting an additive or synergistic effect of extract and melatonin in not only inducing insulin release on glucose challenge but also in increasing
sensitivity to insulin. Total GLUT 4 expression in the muscle of diabetic animals is significantly decreased and administration of PM.OS+MH recovered GLUT 4 level by 18%, more than the 12% increment in GLUT 4 level shown by control animals treated with PM.OS+MH. Oxidative stress in terms of levels of LPO, non-enzymatic (GSH) and enzymatic (SOD, Catalase and GPx) antioxidants in liver, muscle and kidney has depicted an increase in LPO and decrease in antioxidants ranging from 30% to 50% at an average, indicating coexistence of metabolic disturbances and oxidative stress in diabetic animals. The findings of the present study provide strong evidence for maximal antioxidant effect of PM.OS +MH with the levels of almost all the tissue antioxidants and LPO being completely reversed and in most cases, the levels even better than the control levels. Despite the fact that both PM.OS and MH have powerful antioxidant effect; a combination of both PM.OS and MH has manifested an additive effect. Except for ALP and ACP, all other serum markers of hepatic and renal functions showed maximal ameliorative effect in diabetic animals treated with PM.OS+MH. In conclusion, it can be surmised that a combination therapy with PM.OS+MH has maximal additive effect on a holistic basis on all facets of manifestations associated with type I diabetes. A combination of natural agents (herbal extract of PM+OS) and an endogenous antioxidant principle of animals and man (Melatonin) seem to be an ideal and most potent therapeutic preparation for holistic amelioration of multiple diabetic manifestations and metabolic dysregulation.
The present study was taken up to assess the role of sub-chronic exposure to an environmentally relevant realistic dosage of Cadmium in type – I diabetes of type – II diabetes. Female adult albino rats of Wistar strain were treated with cadmium (5.18 mg / Kg body weight) for 45 days. On 46th day rats were made diabetic by a single intraperitoneal injection of alloxan (120 mg / Kg body weight). After 7 days, onset of diabetes in the alloxanised animals was confirmed by blood glucose level greater than 300 mg / dl. Further experiments were conducted for 15 days under a photoperiodic schedule of LD 13:11. Pre-treatment with cadmium showed disturbed glucose homeostasis with attendant changes in carbohydrate metabolism coupled with decrease in food and water intake. Disturbance in carbohydrate metabolism was indicated by altered metabolite load of tissues as marked by decreased protein and glycogen contents and increased cholesterol store, and increased glycogenolysis (marked by increased phosphorylase activity) and gluconeogenesis (marked by increased G-6-phosphatase activity). Poor glucose clearance subsequent to a glucose challenge under GTT was seen with cadmium pre treatment (0.48/ min in control v/s 0.13/ min in Cd animals) There was significantly lower glucose elevation rate in IRT subsequent to insulin induced decrease in glucose level in Cd exposed animals. Elevated oxidative stress was marked by increased LPO, decreased antioxidant (both non enzymatic and enzymatic) levels and serum markers of hepatic and renal damage. Decreased corticosterone level together with increased E2 level and reduced P4 level were some of the hallmark changes in serum hormone profile of Cd- exposed animals. Overall the present results are novel
and interesting to open out more searching investigations on animal models of type 1 diabetes with a history of prior Cd exposure.
As an extension to the previous study on the role of cadmium in type - I diabetic complications, the present study involving simultaneous administration of a combination of methanolic extract of *Ocimum sanctum* and *Pterocarpus marsupium* with cadmium was tried out to assess its ability to offset the detrimental effects of Cd in both non diabetic and diabetic animals 45 days prior to diabetic induction. To this end, serum hormones (insulin, corticosterone, estradiol, progesterone), metabolites and enzymes of carbohydrate metabolism (G-6-Pase, phosphorylase, glucose, glycogen), enzymic (SOD, Cat, GPx) and nonenzymic antioxidants (GSH), serum markers of hepatic and liver damage, as well as lipid profile, were assessed in female albino rats of wistar strain. Treatment with the extract mixture for 15 days after 45 days of Cd exposure shows complete protective effect against all Cd induced alterations except for minimal effect on tissue glycogen depletion, serum markers of hepatic and renal damage and insulin titre. Favourable glycaemic responses were observed with greater insulin sensitivity and an increased serum insulin titer which showed a recovery to just about 11% of the control animals as against 64% deficit in Cd+D animals. Histological observation of pancreas showed robust islets with greater number of β cells. The extract mixture of PM+OS was very potent in combating the cumulative effect of both Cd and diabetes and maintain tissue cholesterol contents and serum TG, LDL, VLDL and HDL levels to near normal together with sparing effect on enzymic and non enzymic antioxidants. Overall, extract mixture of PM+OS showed significant protective effect on the cumulative alterations induced by Cd and diabetes.
In the absence of any reported study on prior cadmium exposure at a natural environmental dosage and subsequent diabetic induction and the therapeutic potential of melatonin, the present study was taken up to assess the holistic effect of melatonin on diabetic manifestation in a background of Cd exposure, in the wake of its previously seen antioxidant and antidiabetic properties. To this end, female adult albino rats of wistar strain were treated with cadmium (5.18 mg / Kg body weight) for 45 days. On 46th day rats were made diabetic by a single intraperitoneal injection of alloxan (120 mg / Kg body weight). After 7 days, onset of diabetes in the alloxanised animals was confirmed by blood glucose level greater than 300 mg / dl. Melatonin (10 mg / kg body weight) was administered to experimental animals for 15 days under a photoperiodic schedule of LD 13:11 and glycaemic status, markers of oxidative stress, markers of carbohydrate and lipid metabolism together with serum hormone levels were investigated in control and treated experimental groups. The results revealed a paradoxical set of observations of increased oxidative stress together with increased glycogenolysis, gluconeogenesis and tissue cholesterol content but reduced protein content and decreased serum insulin titre and elevated lipid profile; all changes suggestive of exacerbation of diabetic manifestations, but with lowered glycaemic and serum corticosterone levels. Animals administered with melatonin given for fifteen days after an exposure to Cd for 45 days had 22% hypoglycaemic effect. Apart from restoring the parameters of oxidative stress, M was adept in reversing the increased serum levels of hepatic and renal toxicity markers due to Cd induced tissue damage in keeping with the cytoprotective effects of M
discussed earlier. Treatment with melatonin in Cd+D animals exerted greater hyporegulatory effect as seen by the further lowered glycaemic status and significantly higher glucose clearance rate in GTT (1.35 Vs 0.86) and significantly greater glucose clearance rate in IRT (5.38 Vs 2.23). From the observed protective effects of melatonin on Cd, diabetes or Cd+D induced oxidative stress, it is gleaned that, greater the compromised antioxidant status (as seen in Cd+D), greater the effect of melatonin. Overall, the results of the present investigation shows that, melatonin has significant protective effect on the cumulative alterations induced by Cd and diabetes, though the differential effects of melatonin in conjunction with Cd or Cd induced effects provide opportunities for more searching investigations to unreveal the underlying intricacies.
CHAPTER 7

As an extension to previous investigation on prior cadmium treatment on exacerbation of diabetic manifestations, (chapters 5, 6) the therapeutic efficacy of an extract mixture of *Pterocarpus marsupium* (PM) and *Ocimum sanctum* (OS) along with melatonin (M) in reversing the Cadmium-diabetes combination induced additive manifestation is studied. In this behest, the present investigation was designed to evaluate the relative efficacy of PM+OS mixture and M in combination as against the previously observed individual efficacies of the two. To this end, female adult albino rats of *wistar* strain were treated with cadmium (5.18 mg / Kg body weight) for 45 days. On 46th day rats were made diabetic by a single intraperitoneal injection of alloxan (120 mg / Kg body weight). After 7 days, onset of diabetes in the alloxanised animals was confirmed by blood glucose level greater than 300 mg / dl. Melatonin (10 mg / kg body weight) + methanolic extract of *Ocimum sanctum* and *Pterocarpus marsupium* was administered to experimental animals for 15 days under a photoperiodic schedule of LD 13:11. Animals were sacrificed on 16th day of and glycaemic status, markers of oxidative stress, markers of carbohydrate and lipid metabolism together with serum hormone levels were investigated in control and treated experimental groups. Both, Cd and Cd+D, were characterized by increased glycogenolysis, gluconeogenesis and peripheral glucose uptake. Protective action of E+M was very potent against hepatic glycogenolysis, as revealed by the maximal decrease in glycogen content and glycogen phosphorylase activity. Although the combination is significantly effective even against Cd and Cd+D induced muscle glycogenolysis, its efficacy was slightly lesser compared to E alone. Decreased
tissue lipid content, hypertriglyceridemia and hypercholesterolemia with elevated LDL and VLDL levels characteristic of Cd and Cd + D animals was reversed by E + M combination. A combination of E and M was able to complement each other and control the cumulative oxidative stress and hepatic and renal dysfunctions caused due to Cd and D most effectively. Diabetes and Cd+D associated oxidative stress has been noted to be accompanied by higher titers of corticosterone (Chapter 4), which seems to be significantly lowered to a hypocorticalic level by treatment with E+M. In conclusion, it can be summarized that, a combination therapy, with an extract mixture of Pterocarpus marsupium and Ocimum sanctum and melatonin, is ideal for combating all effects of Cd toxicity and diabetes on a holistic basis on all facets of diabetic manifestations compounded by metal toxicity and, worthy of further therapeutic studies using this mixture.
Exercise has now been increasingly thought of as a therapeutic approach in various metabolic disorders like diabetes and obesity due to its low cost and non-pharmacological actions. However physical activities are also likely to contribute to oxidative damage and prove contra to maintenance of health. The present study was performed to study the effect of swimming exercise on type – I diabetes rat model. To this effect, adult albino rats were made diabetic by a single intraperitoneal injection of alloxan (120 mg / kg body weight). After a duration of 7 days, induction of diabetes was checked by blood glucose level of 300 mg / dl or higher. Control and experimental animals were subjected to swimming exercise for a further duration of 15 days and upon sacrifice various parameters related to glycaemic status, carbohydrate metabolism, lipid metabolism, enzymic and non enzymic markers of oxidative stress and serum markers of hepatic and renal dysfunction, were evaluated. Experimental paradigm of 15 days of swimming exercise showed no change in glycaemic status in overnight starved non diabetic rats while the glycaemic status of the fed state showed milder hyperglycaemia. However, the same schedule in diabetic rats showed normoglycaemia in the starved state and milder reduction in glucose level in the fed state. The average of fed and fasted state reveals no change in the glycaemic status of the exercising non diabetic rats compared to non exercised ones. However, in diabetic rats, the average glucose level is significantly lowered in exercised rats compared to non exercised ones. Apparently, mild exercise has a favourable influence in diabetic animals in lowering the glucose level. Increased glucose uptake and glycogenesis observed in the
present study adequately support the significant decrement in cytosolic GLUT 4, suggestive of increased membrane insertion and glucose influx. No increase in lipid peroxidation was observed with swimming exercise; however there was significant decrement in catalase activity in liver, muscle and kidney and GSH depletion in Kidney along with an increase in serum corticosteroid. Significant increase in GLUT-4 level was observed in exercised diabetic animals compared to non exercised diabetic animals. Overall, the findings suggest a favorable influence of exercise in gluco regulation, lipid profile and oxidative stress in animals with type 1 diabetes. Based on these, exercise may be considered as of greater therapeutic value in diabetic manifestations.
The present study attempts to assess a combination effect of a low dose of melatonin and swimming in amelioration of diabetic manifestations on a holistic basis. To this effect, adult albino rats were made diabetic by a single intraperitoneal injection of alloxan (120 mg / kg body weight). After a duration of 7 days induction of diabetes was confirmed by blood glucose level of 300 mg / dl or higher. Control and experimental animals were subjected to swimming exercise of 30 minutes duration daily and administration of low dose of melatonin (1 mg / kg body weight) for a duration of 15 days and upon sacrifice various parameters related to glycemic status, carbohydrate metabolism, lipid metabolism, enzymic and non enzymic markers of oxidative stress and serum markers of hepatic and renal dysfunction were evaluated. The present holistic evaluation on the effect of a combination of melatonin (M) and swimming exercise (S), on various facets diabetic manifestations, has shown an overall beneficial effect with some effects resembling those of exercise, others of melatonin and of others as a accumulative additive effect of both melatonin and exercise. Remarkably, the effect of M+S in lowering glycaemic status of starved non-diabetic animals was, significantly greater in comparison to M or S alone. The hepatic and muscle glycogen contents also showed significant increase. Glucose uptake and glycogenesis was augmented as seen by the decrease in cytosolic GLUT 4 levels and increased tissue glycogen loads. Observed increase in serum triglyceride coupled with significant depletion of tissue lipids has been taken to suggestive increased lipid mobilization in the wake of exercise-induced increase in energy demand. Simultaneous melatonin treatment protected against exercise-
induced decrease in GSH content and Catalase and SOD activities and maintained
the delicate balance of prooxidant to antioxidant ratio. In conclusion, the present
observations tend to suggest an overall favourable, cumulative, additive influence of
S and M in glucoregulation, lipid profile and hepatic and renal function in animals
with Type I diabetes. Based on these, a combination of exercise and melatonin may
be of therapeutic value in ameliorating diabetes manifestations.
The plants for the present studies was selected on the basis of their anti-diabetic property, as these plants are consumed by the local people for treatment of diabetes also supported by literature survey. Plants like Annona squamosa (Annonaceae), Cassia fistula, Coccinia indica, Mangifera indica, Ocimum sanctum, Lagerstroemia, and Murraya koenigii used in the present study have blood glucose lowering effect in the diabetic animals and some of them have an anti-lipidemic and cholesterol lowering effects. A major objective of selecting these plants is that they are commonly available with minimal or no cost of procurance and hence very cost effective. The efficacy of this PE has also been evaluated in combination with swimming exercise in rats rendered diabetic as exercise was found to be beneficial in containing diabetic complications as described previously (Chapter 8). To this effect adult albino rats were made diabetic by a single intraperitoneal injection of alloxan (120 mg / kg body weight). After a duration of 7 days induction of diabetes was checked by blood glucose level of 300 mg / dl or higher. Control and experimental animals were subjected to swimming exercise and PE for a further duration of 15 days and upon sacrifice various parameters related to glycemic status, carbohydrate metabolism, lipid metabolism, enzymic and non enzymic markers of oxidative stress and serum markers of hepatic and renal dysfunction were evaluated. The results of the present study showed significant favorable effect of both in non-diabetic as well as diabetic rats. In terms of glycaemic regulation, neither PE nor PE+S showed any significant effect either on fasting or fed glycaemic level in non-diabetic animals while, both were equally effective in minimizing diabetic
hyperglycemia to the same extent. The reduction in diabetic glycaemic level observed with PE alone or in combination with S was however lesser than that observed with S or M (melatonin) alone or even in combination (chapters, 2, 8 & 9). In DC animals both PE and S+PE improved insulin status. There was an increased hepatic and muscle glycogen content in both NC and DC animals either treated with PE or also subjected to exercise. The increased tissue glycogen load and glucose clearance from blood are paralleled by significant decrement in tissue glycogen phosphorylase activity. There was decrement in cytosolic GLUT 4 level in NC.PE and NC.S+PE whereas significant increment in GLUT 4 expression was seen in DC.PE and DC.S+PE animals over that of the low level in DC animals. Amongst the markers of lipid metabolism, apparently, PE increased tissue cholesterol breakdown while a combination of S+PE favored tissue cholesterol deposition in non-diabetic animals. PE had positive influence on the status all enzymic and non enzymic antioxidants. Overall, the present study provides support and evidence for consideration of a therapeutic approach combining the beneficial effects of a polyherbal preparation in association with adaptive physical activity for effective management of diabetic complications as suggested by the present observations of efficient glycaemic regulation, carbohydrate and lipid metabolisms, oxidative stress and renal and hepatic dysfunction in Alloxan induced rat model of Type I diabetes.
As an extension to the experimental paradigms used in the preceding chapters, in the present study multi-dimensional therapeutic approach for combating experimentally induced Type I diabetes using polyherbal therapy with melatonin supplementation and an exercise regimen (S+M+PE). The major objective was to see whether the combination is more beneficial than the therapy given alone. To this effect adult albino rats were made diabetic by a single intraperitoneal injection of alloxan (120 mg / kg body weight). After a duration of 7 days induction of diabetes was checked by blood glucose level of 300 mg / dl or higher. Control and experimental animals were subjected to swimming exercise together with administration of melatonin and PE for a further duration of 15 days and upon sacrifice various parameters related to glycemic status, carbohydrate metabolism, lipid metabolism, enzymic and non enzymic markers of oxidative stress and serum markers of hepatic and renal dysfunction were evaluated. Results revealed a differential response in the form of much better glyceamic regulation and lowered tissue lipid and cholesterol load though with certain degree of renal oxidative stress and abnormal renal function and a marginally higher serum levels of cholesterol and lipid. The glucose clearance rates of DC,S+M+PE animals under both glucose challenge and exogenous insulin were much greater than both NC and DC animals. Observed increase in insulin levels in both NC and DC animals subjected to S+M+PE was an indicative of observed near normal glucoregulation with combination therapy. S+M+PE exerted favorable influence on glucose uptake and utilization by way of increased insulin titer and sensitivity as well as up regulation of
IRS 1 and GLUT-4. In contrast to non-diabetic animals, diabetic ones were more sensitive to S+M+PE treatment schedule as marked by the significant depletion in tissue lipid and cholesterol contents as well as anti hypertriglyceridimic and hypercholesterolemic effects. The present study involving a combination therapy seems to cause some oxidative stress as marked by significant decrement in Cat and SOD activities of liver, muscle and kidney along with GSH depletion with no increase in LPO. Increase in serum corticosterone level could be speculated to be contributor of oxidative stress. In conclusion it can be said that S+M+PE is an effective combination therapy exerting powerful glucoregulatory and antilipidemic effects but with some incompetence in containing sub adaptive swimming exercise induced oxidative stress and hepatic and renal dysfunctions. A properly worked out intensity and duration dependent adaptive exercise schedule is likely to overcome these shortcomings. Such an exercise schedule needs to be then studied in conjunction with melatonin supplementation and PE treatment.
BIBLIOGRAPHY


Masters BA, Kelly EJ, Quaife CJ, Brinster RL, Palmiter RD.. Targeted disruption


Murase, H., Moon, J.H., Yamauchi, R., Kato, K., Yoshikawa, T., Terao, J. Antioxidant activity of a novel vitamin E derivative, 2-(alpha- D-


- Noyan, T., Sadik – Yalçınkaya, A., Ramazan Şekeroğlu, M., Dülger, H., Balaharoğlu, R. Antioxidant Effects of Pentoxifylline and Melatonin in the


Ploug, T., Stallknecht, B.M., Pedersen, O., Kahn, B.B., Ohkuwa, T., Vinten, J., Galbo, H., Effect of endurance training on glucose transport capacity and


Sharmila Banu, M., G., Kumar, G., Murugesan, A.G. Effects of leaves extract of Ocimum sanctum L. on arsenic-induced toxicity in Wistar albino rats. Food and Chemical Toxicology; 47 490–495 (2009).


Sukh Dev. Review: Environmental Health Perspectives, Volume 107, Number 10, October (1999).


Vinuthan, M. K., Girish Kumar V., Ravindra.J. P., Jayaprakash., Narayana, K. Effect of extracts of murraya koenigii leaves on the levels of blood glucose


