WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 10, 1219-1232. Research Article ISSN 2277– 7105

REGULATION OF TYPE-II DIABETES TREATMENT WITH *ALOE VERA* EXTRACT ON LIPID METABOLISM STATUS IN LIVER ALLOXAN INDUCED MALE RATS

Ravi Naik Mude*

Department of Zoology, Sri Venkateswara University, Tirupati - 517502, India.

Article Received on
23 July 2015,

Revised on 16 Aug 2015,
Accepted on 05 Sep 2015

***Correspondence for Author**
Ravi Naik Mude
Department of Zoology, Sri Venkateswara University, Tirupati - 517502, India.

ABSTRACT

To investigate the protective use of ethanolic extract of *Aloe vera* on cholesterol, lipid peroxidation, Triglycerides levels in diabetic male Albino-rats. The protective effect of *Aloe vera* in Experimental was evaluated in this study. Three months old male wistar rats were divided into 4 groups (n=6) namely: Control, Control + *Aloe vera* (300 mg/ kg body weight), diabetic (Alloxan 40 mg/kg body weight), (diabetic + *Aloe vera* (300 mg/kg body weight) the experimental period was 21 days. In the present study the work was undertaken to evaluate the potential anti hyper lipid anemic effect of *Aloe vera* leaf extract in liver tissue of Alloxan induced diabetes rats. The levels of cholesterol, lipid peroxidation, Triglycerides in liver tissue were increased significantly in diabetic rats. In case of, Diabetic + *Aloe vera* leaf extract to present the development alteration in lipid metabolism status in liver tissue maintained near normal while comparing with non diabetic rats.

KEYWORDS: Diabetes, *Aloe vera*, Alloxan, Lipid metabolism, Rats.

INTRODUCTION

Diabetes mellitus is a serious health problem being the third greatest cause of death all over the world. It is associated with a large number of lipid abnormalities. Diabetes mellitus results in hyperglycemia and is characterized as type-1, in absolute insulin deficiency or type-2 in insulin resistance due to receptor insensitivity to endogenous insulin.[1] Control of blood glucose levels in only one goal of a healthy food plan for people with diabetes. A diet for those with diabetes should also help achieve and maintain a normal body weight as well as prevent heart and vascular disease, which are frequent complications of diabetes.[2]

Hyperlipidemia is a complication associated with diabetes mellitus,[3] due to qualitative and quantitative abnormalities in lipoproteins. Hyperglycemia in diabetes leads to over production of free radicals and these contribute to the development of diabetic nephropathy.[4] A number of epidemiological investigations have shown a clear association between dietary saturated fat and atherosclerosis.[5] The analysis of fatty acids composition in blood and tissue lipids has lately gained renewed interest to study the pathogenesis of metabolic disease. Fatty acids of the adipose tissue are a major supply for the plasma fatty acids pool.[6] The liver utilizes plasma fatty acids in building up the different plasma lipids and lipoprotein.[7] that is implicated in the different metabolic reactions in health and disease.[8] Recent decades have shown a resurgent interest in traditional plant treatments for diabetes. Plants often contain substantial amounts of antioxidants including Alfa-tocopherol (Vitamin E) carotenoids, ascorbic acid (Vitamin C), flavonoids and tannis.[9] And it has been suggested that antioxidant action may be an important property of plant Medicines used in diabetes. *Aloe vera* is a perennial plant belonging to the family of Liliaceae, which includes about 360 species.[10] Toxonomists now refer to Aloe barbadensis as *Aloe vera.*[11] Clinical evaluations have revealed that the pharmacologically active ingredients are concentrated in both the gel and rind of *Aloe vera* leaves the present study was designed to evaluate the effects of *Aloe vera* leaf get extract a tissue (liver) lipid metabolism status in rats with Alloxan induced diabetes.

MATERIALS AND METHODS

Selection of Animals

Wistar strain albino rats (180±20g) were obtained from Indian Institute of science, Bangalore. The rats were housed in clean polypropylene cages having six rats cage and maintained under temperature controlled room (26±20C) with a photo period of 12 hours light and 12 hours dark cycle. The rats were fed with a standard rat pellet diet and water adlibitum. The study was carried out according to guidelines for the care and use of laboratory animals and approved by the Institutional Animal Ethical Committee at Sri Venkateswara University, Tirupathi, India. (Regd. No.438/01a/CPCSEA, Dt: 17-07-2001, and its resolution no. 08/2012-2013/ (i)/a/ CPCSEA/IAEC/SVU/MBR-MRN/dt. 02-07-2012).

Chemicals

The entire chemical used in the present study were Analar Grade (AR) and obtained from the following scientific companies: Sigma (ST. Louis, MO, USA), Fischer (Pitrsburg, PA, USA), Merck (Mumbai, India), Ranbaxy (New Delhi, India), Qualigens (Mumbai, India).

Induction of Diabetes

The rats were injected intraperitonial with Alloxan monohydrate (Span chemical Co.Mimbai) dissolved in sterile normal saline at a dose of 40 mg/kg body weight. After injection, they had a free access to food and water was given 5% glucose solution to drink, overnight to counter hypoglycemic shock. The animals were considered as diabetic, if their blood glucose values were above 250 mg/dl on the third day After Alloxan injection the treatment was continued for 21 days.

Preparation of *Aloe vera* extract

The fresh *Aloe vera* was locally and authenticated by botanist in the department of Botany, S.V.University, and Tirupathi. *Aloe vera* solid gel in the center of the leaf was collected and homogenized resulting, mucilaginous, thick and straw colored homogenate was obtained and lyophilized. Then the lyophilized sample was extracted using 95% ethanol. The filtrate was collected and evaporated to dryness under reduced pressure in a rotary evaporator at 60°C. The residue was stored in dry sterilized small containers at 4°C until further use. A Suspension which is the form customarily usual in folk medicine was prepared by dissolving suitable amount of ethanol free extra of *Aloe vera* leaf gel to get the desired concentration. The dosing schedule used was once per day. The extracts were administered orally, daily to different groups of rat at a dose of 300 mg/kg body weight.

Experimental design

Rats were randomly divided into four groups of six animals in each group.

Group-1: Control rats

Group-2: Control + *Aloe vera* (300mg/kg body weight of *Aloe vera*)

Group-3: Diabetic rats (40mg/kg body weight of Alloxan)

Group-4: Diabetic + *Aloe vera* extract (300mg/kg body weight in ethanol solution daily. Once in a day by an intragastic tube for 21 days)

After completion of 21 days treatment the animals were sacrificed by cervical dislocation and the liver tissue was excised at 4°C .The tissue was washed with ice-cold saline, and immediately stored in deep freeze at 80° C for further biochemical analysis.

Biochemical analysis and Enzymatic assays

Triglycerides (TG - Triacylglycerol)

Triglycerides were estimated by the method of, (12) with slight modifications as given below. Triglycerides were assayed by hydrolyzing them to glycerol and the liberated glycerol was determined.

Tissue homogenates were prepared in $1NH_2SO_4$ and to it 4 ml of chloroform was added 0.5 ml of tissue homogenate was taken. To it 0.5 ml of $1NH_2SO_4$ and 4 ml of chloroform were added. The contents were centrifuged at 1000 rpm for 15 min 0.5 ml of chloroform layer was taken and to it 0.4 ml of methanol and 0.1 ml of alkaline barium solution were added and the contents were heated for 30 min at 80°C, the total volume was made up to 1 ml with $2NH_2SO_4$ and centrifuged for 10 min at 1000 rpm 0.5 ml of this supernatant was taken and to it 0.1 ml of sodium periodate was added and shaken well for 1 min, 0.1 ml of sodium arsenate and 5 ml of chromotrophic acid reagent was added and heated for 30 min and cooled. The samples were read at 575 nm in Spectrophotometer against the reagent blank. The results were finally expressed in mg of triglycerides / gram wet weight of the tissue.

MDA content [Lipid Peroxidation (LP)]

This assay is used to determine MDA levels as described by.(13) The Liver tissue was homogenized (5% - w/v) in 50 mM phosphate buffer (pH 7.0) containing 0.1 mM EDTA, The homogenates were centrifuged at 10,000 rpm for 10 min at 0°C in cold centrifuge. The separated supernatant part was used for the estimation. 200 µl of the tissue extract was added to 50 µl of 8.1% sodium dodecyl sulphate (SDS), vortexed and incubated for 10 min at room temperature. 375 µl of 20% acetic acid (pH 3.5) and 375 µl of thiobarbituric acid (0.6%) were added and placed in a boiling water bath for 60 min. the samples were allowed cool at room temperature. A mixture of 1.25 ml of butanol: phyridine (15:1) was added, vortexed and centrifuged at 1000 rpm for 5 min. The colored layer (500 µl) was measured at 532 nm using 1, 1, 3, 3-tetraethoxypropane as a standard. The values were expressed in µ moles of malondialdehyde formed / gram wet weight of the tissue.

Total Cholesterol

The total cholesterol content was estimated using Liebermann Burchard reaction as described by. (12) The liver tissue was homogenized in isopropanol. The contents were centrifuged at l000 rpm for 15 min. 0.5 ml of supernatant was taken and to it 4 ml of cholesterol reagent was added. Then the contents were heated at 90°C for 15 min. After cooling, the samples were read at 560nm in

spectrophotometer against the reagent blank. The results were finally expressed in mg of total cholesterol/gram wet weight of the tissue.

Statistical analysis

The data has been analyzed by using one-way Analysis of Variance (ANOVA) followed by Dunnet's-test and 'P' value < 0.001 was considered significant. The data were presented as Mean ± S.D. And analysis was carried out by using SPSS 16.0.1 program.

RESULTS

Total Cholesterol

In control rats the amount triglycerides was found to be 65.72 mg of cholesterol/gm wet weight of tissue in liver. In group-II, where the control rats were treated with *Aloe vera* extract the levels were in decreased. Group-III had showed a significantly increased to 82.10 mg of cholesterol /gm wet weight of tissue in liver. In the group-IV where the diabetic rats were subjected to *Aloe vera* extract, decreased levels were found when compared to control rats.

Lipid Peroxidation

In control rats the amount of lipid peroxidation was found to be 40.02 μ moles of malondialdehyde formed/gm wet weight tissue in liver. In group-II, the levels were decreased. In case of group-III the levels were increased, in group- IV where the diabetic rats were subjected to *Aloe vera* extract, decreased levels were found when compared to control rats.

Triglycerides

In control rats the amount triglycerides was found to be 1.902 mg of triglycerides/gm wet weight of tissue in liver. In group-II, where the control rats were treated with *Aloe vera* plant extract the levels were decreased. Group-III had showed a significantly increased to 3.92 mg of triglycerides/gm wet weight of tissue in liver. In group-IV where the diabetic rats were subjected to *Aloe vera* extract, decreased levels were found when compared to control rats.

Table: Showing Cholesterol, Lipid peroxidation, Triglycerides Levels in Liver of Control and Experimental animals

Parameter	Group I (non diabetic rats)	Group II (non diabetic rats + *Aloe Vera*)	Group III (diabetic rats)	Group IV (diabetic rats + *Aloe Vera*)
Cholesterol (µ moles of total cholesterol/gram wet weight of tissue)	65.72±9.198	62.83±9.200 (-6.35)	82.10±7.100 (+31.60)	60.99±6.140 (-23.65)
Lipid peroxidation (µ moles of lipid peroxidation formed/ gm wet weight of tissue)	40.02±10.000	37.20±9.268 (-14.18)	58.02±9.072 (+80.56)	29.02±6.472 (-9.69)
Triglycerides (mg of triglycerides/gm wet weight of tissue)	1.90±0.142	1.20±0.120 (-6.79)	3.92±0.440 (+148.11)	1.20±.0.126 (+97.59)

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

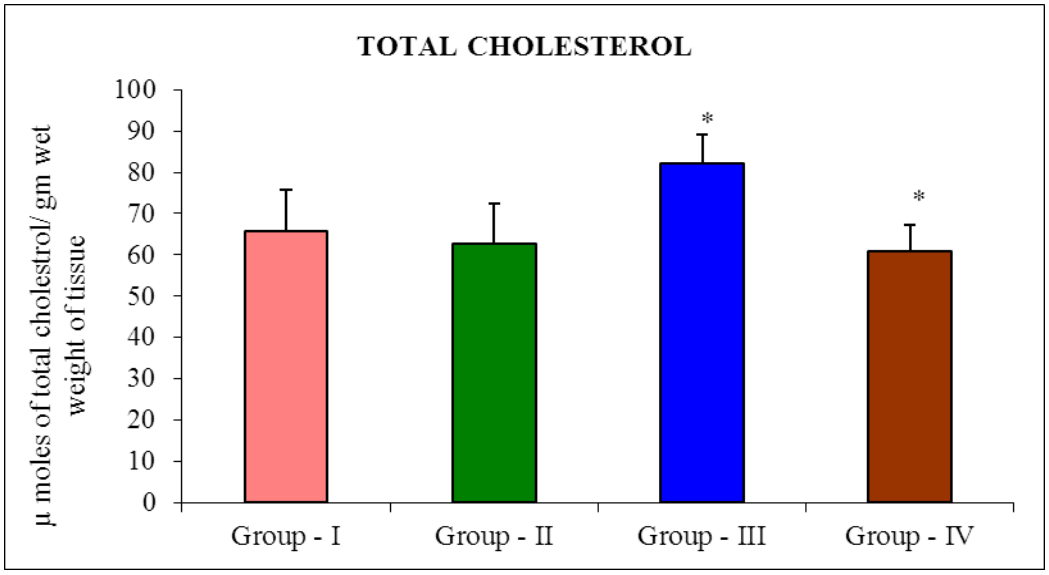

Fig: 1.1 Showing Total Cholesterol levels in Liver tissue of control and experimental animals

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

Values are mean, SD: n=6

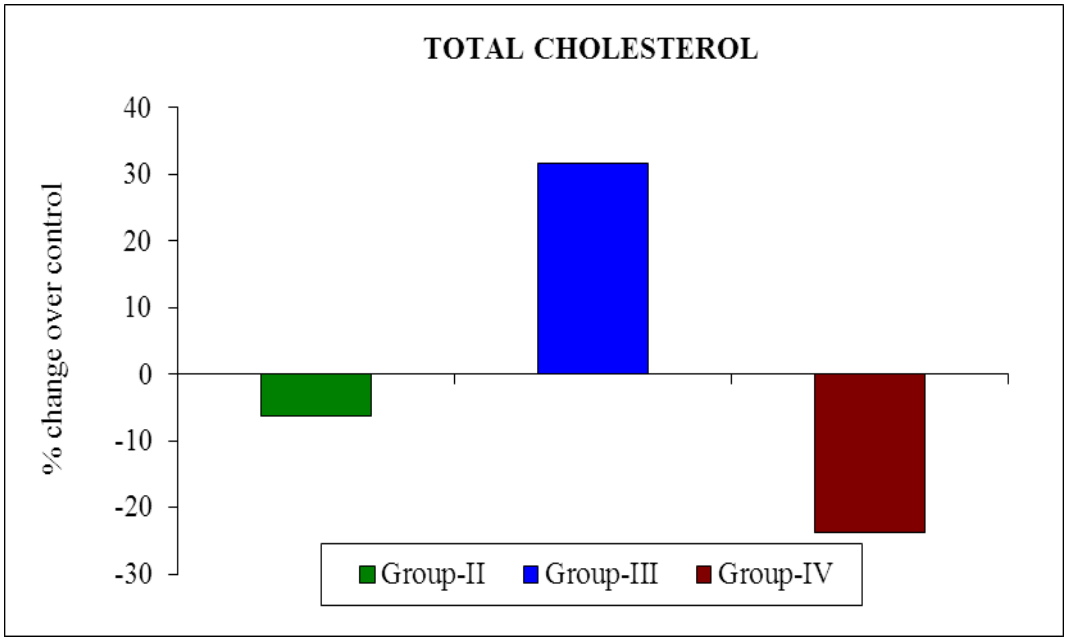

Fig: 1.2 Showing % change of Total Cholesterol levels in Liver tissue of control and experimental animals.

Values in the parentheses are % change from Control

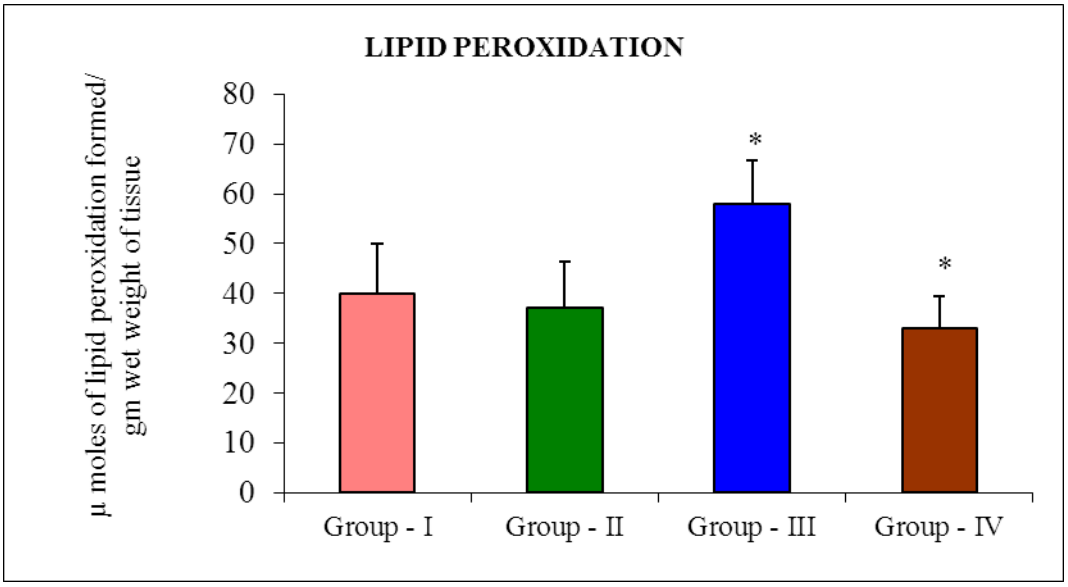

Fig: 2.1 Showing Lipid peroxidation levels in Liver tissue of control and experimental animals

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

Values are mean SD: n=6

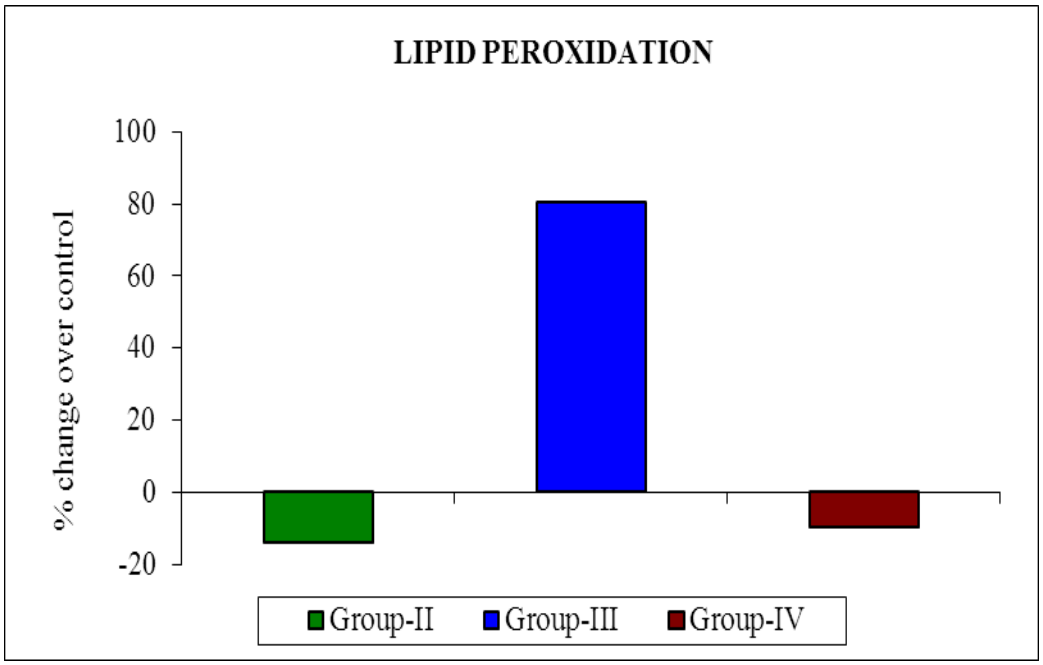

Fig: 2.2 Showing % change of Lipid peroxidation levels in Liver tissue of control and experimental animals.

Values in the parentheses are % change from Control

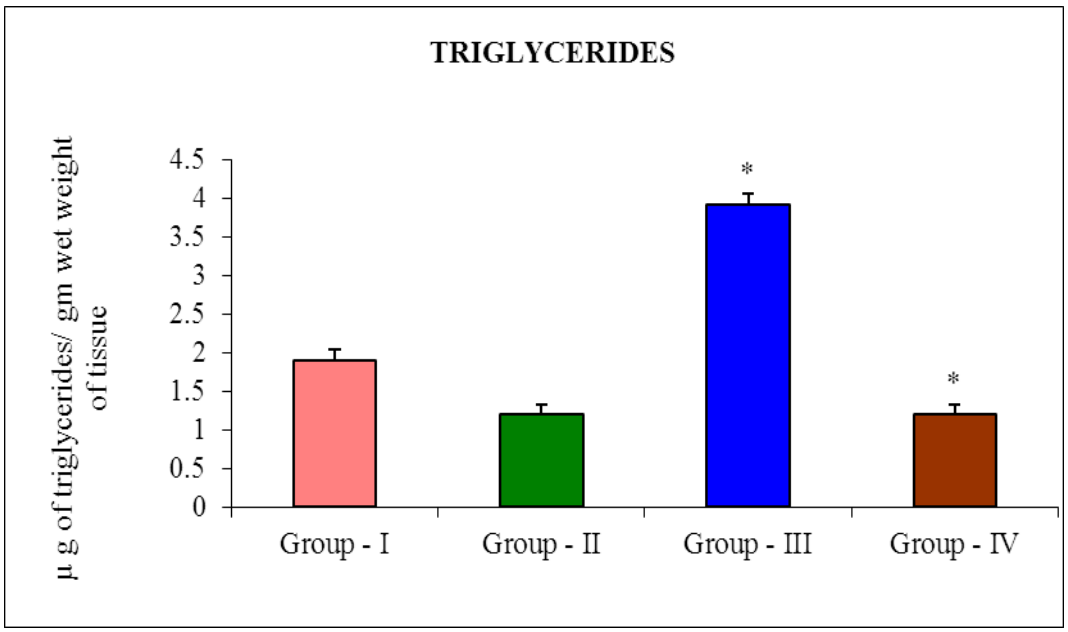

Fig. 3.1 Showing Triglycerides levels in Liver tissue of control and experimental animals

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

Values are mean, SD: n=6

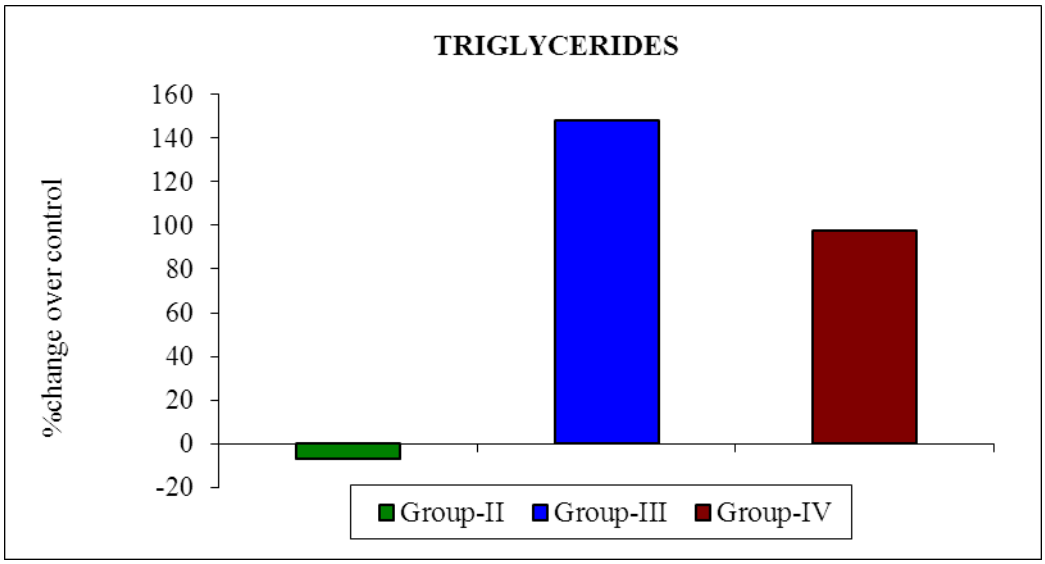

Fig: 3.2 showing % change of Triglycerides levels in Liver tissue of control and experimental animals

Values in the parentheses are % change from Control.

DISCUSSION

Cholesterol is an amphipathic lipid present in tissue (liver) and in plasma lipoproteins either as free cholesterol with a long chain fatty acid or as cholesterol ester. It is synthesized in many tissues from acetyl Co-A.[14] It forms a precursor for all steroids in the body such as corticosteroids, sex-hormones, bile acids and vitamin-D.[15] Cholesterol and its esters are used for biosynthesis of membrane lipoprotein layers and several metabolically active compounds. The localization of cholesterol may also be attributed to the architectural and physiological functions of the tissue.[16] The major functions of cholesterol in the membrane lipid by layer are to act as a stabilizer of membrane structure and its stability to promote hydrophobic interactions among fatty acid chains. Cholesterol has neuroprotective functions also.[17] But the mechanism responsible for the neuroprotective effects of cholesterol was not clearly known,[17] suggested at least two possibilities: (a) The presence of cholesterol in membranes may cause a hindrance in radical chain propagation; (b) Oxides of cholesterol may increase the order of bilayer and maintain this order after oxidative insult. In the present study, the metabolic of total cholesterol has been investigated so as to understand the implication of this steroid in liver tissue of normal control, plant extract treated, and diabetes induced and in diabetic rats treated with plant extract.

In normal rats cholesterol levels were well regulated as the insulin production is normal. Apart from the regulation of carbohydrate metabolism, insulin also plays an important role in the metabolism of lipids. Insulin is potent inhibitor of lipolysis since it inhibits the activity of

the hormone sensitive lipases in adipose tissue and suppresses the release of free fatty acids.[18] Due to this inhibited activity of lipases, lipolysis decreases and results in less free fatty acids in to the circulation. Decreased fatty acids concentration decreases the β-oxidation of fatty acids, resulting in regulated levels of acetyl CoA and cholesterol. In plant extract treated rats the total cholesterol content in liver were decreased. This was due to the hypocholestemic effects of plant extract by the inhibition of cellular cholesterol synthesis.

Alloxan induced diabetic rats had showed increased total cholesterol levels. There were many reports on elevated levels of total cholesterol content in diabetic rats. During diabetes, enhanced activity of lipase enzymes increases lipolysis and releases more free fatty acids in to the circulation.[19] Increased fatty acids concentration also increases the β-oxidation of fatty acids, producing more acetyl Co-A and cholesterol during diabetes. These effects may be due to higher activity of cholesterol biosynthesis enzymes and/or high levels of liposysis.[20]

Oxidative stress that leads to an increased production of reactive oxygen species (ROS) and finally cellular lipid peroxidation has been found to play an important role in the development of diabetes mellitus.[21] Lipid peroxidation one of the cellular features of chronic diabetes. In diabetes, it is thought that hypoinsulinemia increases the activity of the enzyme such as fatty acyl coenzyme-a oxidase, which initiates beta-oxidation of fatty acids, resulting in lipid peroxidation.[22] Increased lipid peroxidation impairs membrane function by decreasing membrane fluidity and changing the activity of membrane-bound enzymes and receptors.[23] Moreover, lipid peroxide-mediated tissue damage has been observed in the development of both type-I and II diabetes mellitus and insulin secretion is closely associated with lipoxygenase-derived peroxides. The increased lipid peroxidation leads to cellular infiltration and islet cell damage in type-I diabetes In view of the importance of lipid peroxides in diabetic stress, lipid peroxidation was studied in the present investigation with respect to plant extracts treated, diabetic (Alloxan induced) and diabetic rats with plant extract treatment.

In the present results the formation of TBARS, a product of lipid peroxidation reaction, was significantly increased in diabetic tissues, as reported earlier.[24, 25] This increased lipid peroxides formation during diabetes has been shown to disturb the anatomical integrity of the membrane, leading to inhibition of several membrane bound enzymes.[26, 27] reported that lipoic acid restore the inactivity of membrane ATPase enzymes by inhibiting the lipid peroxidation in high glucose treated human erythrocytes. The reduction in the activity of Na+/K+ ATPase observed in diabetic tissue may be due to the membrane peroxidation

damage induced by increased lipid peroxidation status. Lipid peroxidation may bring about protein damage and inactivation of membrane bound enzymes either through direct attack by free radicals or through chemical modification by its end products, malondialdehyde and 4-hydroxynonenal.[28]

In Alloxan induced diabetic rats, MDA level was increased significantly. Alloxan treatment induces lipid peroxidation through the generation of free radicals in high concentration. This free radical stress gets amplified gradually and is propagated by an autocatalytic cycle of metabolic stress, tissue damage and cell death, leading to further increase in free radical production and MDA. Lipid peroxidation is a complex process initiated by reactive radicals, such as the hydroxyl radical, which causes biological damages including atherosclerosis, liver diseases.[29] The triglycerides or so called neutral fats are esters of the ethanol, glycerol and fatty acids. Acylglycerols in the form of triacylglycerols constitute majority of lipids in the body. They are the major lipids in fat deposits and in food.[15] These play a major role in lipid transport, storage and in various physiological conditions such as obesity, diabetes, hyper lipopoteinemia.[14] Triglycerides are stored in adipose tissue and within muscle cells.[30] The present investigation was planned to investigate the effect of Alloxan induced diabetic and diabetic rats with *Aloe vera* treatment on the amount of triglycerides. There was a significant increase in the total triglyceride levels of Alloxan induced diabetic rats.

In the present study triglyceride content was increased in the liver is tissue of diabetic rats. An increase in triglycerides and cholesterol in rat myocardium was reported after Alloxan injection. The concentration of lipids such as cholesterol, Triglycerides etc, were significantly higher in diabetic rats than in control groups a variety of rearrangements in metabolic and regulatory mechanisms due to insulin deficiency are responsible for the observed accumulation of lipids.[31] In the present study triglyceride content was decreased in diabetic rats treated with plant extract**.** Furthermore the accumulation of triglycerides and long chain fatty actyl coenzyme (CoA) in the liver leads to a reduction in insulin mediated metabolic syndrome.[32] 3-hyroxy-3-methylgultaryCoA reductase catalyses the rate limiting step in cholesterol biosynthesis and its activity was found to be significantly increased in the liver of diabetic rats.[33] The increase in liver cholesterol in diabetic rats observed in the present study could be due in liver triglycerides, in diabetic rats after treatment with *Aloe vera* extract. This reduction may be attributed to increased clearance and decreases production of the major transporters of endogenously synthesized and triglycerides**.** The overall effect of the presence of

reactive oxygen species leads to hyperlipidemia as there is an accumulation of triglycerides and cholesterol, due to damage to pancreatic islets and liver cells.

CONCLUSION

The effect of the ethanolic of *Aloe vera* on liver tissue in lipid profiles due to reduction enzymes in activities of diabetic rats. Further studies are in progress in *Aloe vera* and thick role in controlling diabetes.

ACKNOWLEDGEMENT

I express my special thanks to University Grant commission (UGC) for financial support by awarding Rajiv Gandhi National Fellowship (RGNF) during my research work.

REFERENCES

1. El-Hilaly J, Adil T, Zafar H J and Badiaa L. A. Hypoglycemic, hypocholesterolemic and hypotriglyceridemic effects of continuous intravenous infusion of a lyophilized aqueous extract of ajugaiva I. Schreber whole plant in steptozotocin-induced diebetic rats. Pak J Pharma Sci., 2007; 20(4): 261-268.
2. Melzig MF and Funki I. Inhibitors of Alfa amylase from plants, a possibility to treat diabetes mellitus type – 2 by phytotherapy? Wien med Wochenschr., 2007; 157: 320-324.
3. Miller CJ, Dunn EV and Hashim 1B. Glycemic index of 3 varieties of dates. Saudi Med. J., 2002; 23(5): 536 – 538.
4. Sharma S, Kulkarni SK and Chopra K. Curcumin, the active principle of turmeric (curcuma longa), ameliorates diabetic nephropathy in rats. Clin Exp pharmacol physiol., 2006; 33(10): 940 – 945.
5. Shekelle RB, Shryock AM, Paul O, Lepper M, Stamler J, Liu S and Raynor WJ Jr. Diet, Serum Cholesterol and death from coronary heart disease. The western study N Engl. J Med., 1981; 304: 65-70.
6. E.Berry, J.Hirsch, J.Most, D.Mc Namara, and J Thornton, "The relationship of Dietary fat to plasma lipid levels as studied by factor analysis of adipose tissue fatty acid composition in a free living population of middle aged American men", AM. J. Clin. Nutr., 19786; 44: 220-231.
7. J.Triscari, N.Koral, B.Levin, and A. Sullivan, "Changes in lipid metabolism in diet – induced obesity", Metabolism., 1985; 34(6): 580 – 587.

8. T. Pischon, H. Boeing, and K.Hffman, "General and abdominal adiposity and risk of death in Europe", N.Engl. J med., 2008; 359(20): 2105-2120.
9. Larson RA: the antioxidants of higher plants. Phyto-chemistry., 1988; 27: 969-978.
10. Klein AO, Penneys N: *Aloe vera*, J Am Acad Dermatology., 1988; 18: 714 – 720.
11. Coats BC, Ahola R: *Aloe vera* the silent Healer: a modern study of *Aloe vera* Dallas, 1979.
12. Natelson S, Total cholesterol procedure Liebermann-Burchard reagent. In: Techniques of clinical chemistry. Charles, C. Thomas publishers, Springfield, Illinois, USA, 3rd edn., 1971;p.263.
13. Ohkava H, Ohishi N, Yagi K. Assay for lipid peroxidation in animal tissues by thiobarbituric acid reaction. Animals of Biochemistry., 1979; 95: 351-358.
14. Murray, R.K., Granner, D.K., Mayes, P.A. and Rodwell, V.W. 2000. Harper's Biochemistry, Lang Medical book, 25th edition. Appleton and Lange, Prentice Hall Publ, New Jersey, USA.
15. Nelson, D.L. and Cox, M. M. 2001. Lehninger Principles of Biochemistry 23rd edition, MacMillan Press Ltd., Hampshire, UK. P-873.
16. Gurr MI James WP. Studies on the body composition, fat distribution, and fat cell size and number of 'Ad', a new obese mutant mouse. *Br J Nutr., 1979;* 41(1): 211-21.
17. Parasassi T, Giusti A M, Raimondi M, Ravagnan G, Sapora O, Gratton E. Cholesterol protects the phospholipid bilayer from oxidative damage. *Free Radic Biol Med., 1995;* 19(4): 511-6.
18. Loci AS, Shaabha M, Khazraji AL, Husain A, Twaija A. Hypoglycemic effect of a valuable extract of artemicisia herb Alba II. Effect of a valuable extract on some blood parameters in diabetic animals. *J Ethnopharmacol.*, 1994; 43: 167-171.
19. Agardh CD, Bjorgell P, Nilson EP. The effect of tolbutamide on lipoproteins, and lipoproteinlipase and hormone sensitive lipase *Diabetes Res Clin Pract., 1999;* 46: 99-108.
20. Mallick, C., Rajkumar, M. and Gosh. D. Comparative Study on Antihyperglycemic and Antihyperlipidemic Effects of Separate and Composite Extract of Seed of Eugenia jambolana and Root of Musa paradisiaca in Streptozotocin-induced Diabetic Male Albino Rat. *Iranian Journal of Pharmacology & Therapeutics., 2006;* 5: 27-33.
21. Pari L, Latha M. Antidiabetic effect of Scoparia dulcis: effect on lipid peroxidation in streptozotocin diabetes. *Gen Physiol Biophys.*, 2005; 24: 13–26.

22. Rahimi R, Nikfar S, Larijani B, Abdollahi M. A review on the role of antioxidants in the management of diabetes and its complications. *Biomed Pharmacother., 2005;* 59: 365–73.
23. Soon YY, Tan BK. Evaluation of the hypoglycemic and anti-oxidant activities of Morinda officinalis in streptozotocin-induced diabetic rats. *Singapore Med J., 2002;* 43: 077–85.
24. Maiorino M, Coassin M, Roveri A, Ursini F. Microsomal lipid peroxidation: Effect of vitamin E and its functional interaction with phospholipids hydroperoxide glutathione peroxidase. Lipids., 1989; 24: 721–726.
25. Nandhini TA, Anuradha CV: Inhibition of lipid peroxidation, protein glycation and elevation of membrane ion pump activity by taurine in RBC exposed to high glucose., 2003; 336(1–2): 129–135.
26. Rauchova H, Ledvinkova J, Kalous M, Drahota Z. The effect of lipid peroxidation on the activity of various membrane-bound ATPases in rat kidney. *Int J Biochem Cell Biol., 1995;* 27(3): 251–225.
27. Jain SK, Lim G. Lipoic acid decreases lipid peroxidation and protein glycosylation and increases (Na+/K+- and Ca++-ATPase activities in high glucose-treated human erythrocytes. *Free Radic Biol Med., 2000;* 29(11): 1122–1128.
28. Halliwell B and Gutteridge JMC. Lipid peroxidation, oxygen radicals, cell change and antioxidant therapy. The Lancet., 1984; 23: 1396-1397.
29. Suematsu, T., and Abe, H. 1982. Liver and serum lipid peroxide level in patients with liver diseases. *Lipid Peroxides in Biology and Medicine.* Yagi, K., ed., *Academic Press, New York,* 285-293.
30. Palmer, W. K. Hormonal regulation of myocardial lipolysis. *Med. Sci. Sports. Exercise., 1983;* 15: 331-335.
31. Rajalingam, R., Srinivasan, N., Govindarajulu, P. Effect of Alloxan induced diabetes on lipid profiles in renal-cortex and medulla of mature albino rats. *Indian JExp Biol., 1993;* 31: 577-9.
32. Moller DE. New drug targets for type 2 diabetes and the metabolic syndrome: A review. *Nature., 2001;* 414: 821-7.
33. Al-Shamaony L, Al-Khazraji SM, Twaji HAA. Hypoglycemic effect of Artemisia herbal Alba. II Effect of a valuable extract on some blood parameters in diabetic animals. *J. Ethanopharmacol.,* 1994; 43: 167-171.