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EVALUATION OF REDUCING ACTIVITY OF FLAXSEED OIL IN STREPTOZOTOCIN INDUCED DIABETIC CARDIOMYOPATHY IN RATS

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ABSTRACT: Diabetic cardiomyopathy (DCM) describes diabetes-associated changes in the structure and function of the myocardium. Flaxseed oil, an antioxidant, improve cardiac function which may an increase in myocardial antioxidant enzyme activities and a decrease in lipid peroxidation in the diabetic rats. This study was done to evaluate the effect of flaxseed oil on Diabetic Cardiomyopathy and the mechanisms behind it. In this study, Wister rats were used and those rats were induced diabetes by a dose of streptozotocin(STZ) through intraperitoneal. In those rats flaxseed oil orally administrated 300 or 500 mg/kg/day respectively for 30 days. Biochemical test were used for the evaluation of metabolic profile and myocardial enzyme. The result were obtained that flaxseed oil have potential role to alleviate diabetic cardiomyopathy as it has potent antioxidant property because of linoleic and alpha linoleic contents. In streptozotocin-induced diabetes, there is a decrease in antioxidant enzyme activities and an increase in myocardial lipid peroxidation. It is suggested that diabetic cardiomyopathy is found if there is decrease of antioxidant so that antioxidant therapy like flaxseed oil may be useful in improving cardiac function in diabetes.

KEYWORDS: Diabetes cardiomyopathy, Flaxseed oil, oxidative stress, antioxidant.

I.INTRODUCTION

When the heart muscle changes in size, the condition is called cardiomyopathy. The heart muscle becomes stiff and thick. [Grundy et.al. (1, 2)] Sometimes muscle tissue can be converted into scar tissue. In this situation it becomes difficult for the heart pumping blood and sending it to the rest of the body. [Rubler et al. (3)] The heart hardly makes blood pump, due to which it becomes weak, which in some people can cause heart failure and other problems such as fluid buildup in the ankle, lungs, legs, heart valve problems.[Aneja.et.al (4)] Cardiomyopathy has four types such as Dilated, restrictive, hypertrophic and arrhythmogenic right ventricular dysplasia. [Kannel et al. (5)]

It occurs rarely or in this muscle tissue in the lower right heart ventricle is changed into a damaged group of cells and results in rhythmic problems commonly caused by genetic mutations. Rest three types will be discussed in later phases. [Cohn et al. (6-8)]

Flaxseed is one of the most powerful plants on the earth. Various evidences suggested that it can help decrease the possibilities of heart disorder, cancer, stroke, and also diabetes. For a small seed that has been around for centuries, this is a rather long thing to do. [Zhou et al. (11)]

Flaxseeds were grown in Babylon as early as 3000 BC. In the 8th century, King Charlemagne suggested that he passed laws requiring his subjects to accept them, particularly on the health benefits of flaxseed. Now, thirteen centuries later, some experts said that we have preliminary research to support Charlemagne's suspicions. [Lee et al. (12, 13)]

II.METHODOLOGY

Animals

Male Wister rats (animal facilitation centre R.V Northland Institute, Dadri, Greater noida) weighing between 200-250gm. All the animals were 3-4 months old at the start of study. Total 24 rats were used and they were categorized into five different groups with each group having 6 rats. Animals were housed at 22±2°C and allowed free access to food and water ad libitum. 12hrs dark and 12hrs light conditions were maintained. The protocol was approved by IAEC and caring of animals were performed as per the CPCSEA guidelines (**Registration Number: 1149/PO/ERe/S/07/CPCSEA**).

Chemicals and drugs

The chemicals were used spironolactone, metformin and flaxseed oil obtained from Sigma Adrich company USA, vestige healthcare

Group 1 – Control Rats (normal saline)

Group 2 – Disease induced group (STZ 65mg/kg body weight on 1st day)

Group 3 – Disease induced (STZ on 1st day) + Metformin (200mg/kg) (For 30 days)

Group 4 – Disease induced (STZ on 1st day) + Flaxseed oil (300mg/kg/day) (For 30 days)

Group 5 - Disease induced (STZ on 1st day)) + Flaxseed oil on high dose (500mg/kg/day) (For 30 days)

Daily body weight and clinical signs for toxicity and weekly feed consumption were recorded.

Procedure

Animals were acclimatized for one week before starting of the experiment.

On day 0, rat were fasted for 12-hour, after which 65mg/kg streptozotacin (STZ) dissolve in 0.1M citrate buffer (ph-.4.5) were administered intra peritoneal.

The rats were fasted again 12-h at day six following streptozotacin administration. The level of blood glucose was measured by collecting blood from the tail vein. The blood glucose level of >350/dl were screened for further experiments. The blood glucose level were measured by using a glucometer (Accu Check)

For the experiments, the rats were divided into five groups. Each group contains 6 rats.

The control group were treated orally with vehicle formulation daily till the experiment completed. Rats in other groups were treated with respective formulations till completion of experiment (30 days)

Determination of SOD activity, MDA,

Xanthine oxidase method was used to evaluate the SOD activity in plasma and myocardium as per kit's instruction. The method is depending on that superoxide anion reaction can be inhibited with hydroxylamine to develop nitrite. The quantity of SOD can be defined by formula provided in kit.

Results of SOD in plasma and myocardium were defined as nitrite unit per millilitre (NU/ml) and nitrite unit per milligram protein (NU/mg protein) respectively. Lipid peroxidation provides the final product as MDA. Lipid peroxidation limit can be defined with quantity of MDA. Thiobarbituric Acid Method was used to evaluate the MDA in plasma and myocardium as per the kit's instruction. As per method that MDA reacts with thiobarbituric acid to produce a red complex with high absorbance at 532nm. This method can be used to evaluate the quantity of MDA. MDA results in plasma and myocardium were defined as nanomoles per millilitre (nmol/ml) and nanomoles per milligram protein (nmol/mg protein) respectively.

Lactate dehydrogenase

Lactate dehydrogenase (LDH) activity were defined spectrophotometrically (UV-160, Shimadzu) in a blinded manner by an automatic biochemistry analyser. The density of the solution for LDH was checked at 492 and for CK at 340nm.

III.RESULTS**Table 1** Effect of Flaxseed Oil on MDA, GSH, SOD and LDH Levels.

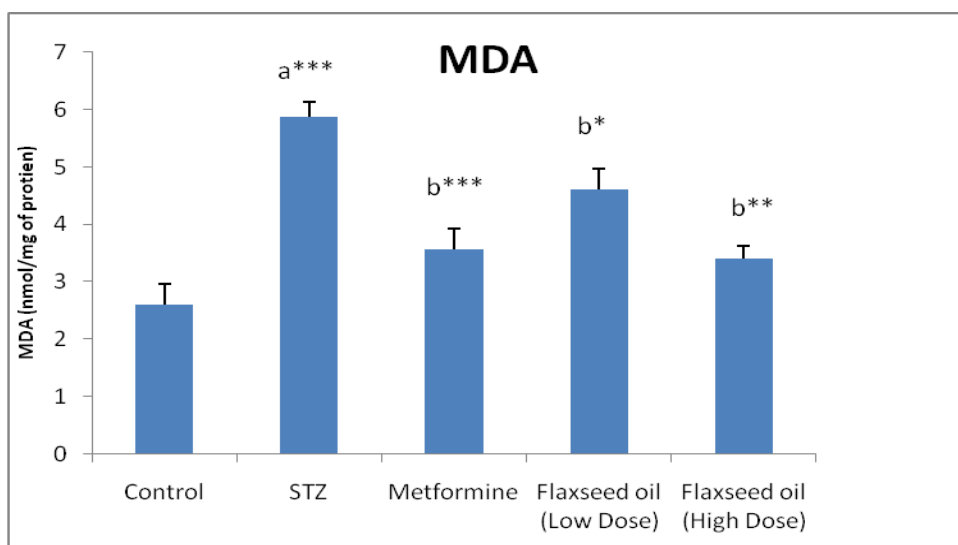
| Groups | MDA(nmol/mg of protein) | GSH(μ mol/mg of protein) | SOD(NU/mg of protein) | LDH(IU/L) |
|--------------------------|-------------------------|-------------------------------|-----------------------|-------------------|
| Control | 2.60 \pm 0.36 | 2.92 \pm 0.10 | 364.48 \pm 10.69 | 181.66 \pm 4.21 |
| STZ | 5.87 \pm 0.25*** | 1.18 \pm 0.99 | 215.5 \pm 3.94 | 381.97 \pm 4.32 |
| Metformin | 3.56 \pm 0.35*** | 2.64 \pm 0.07 | 325.4 \pm 5.63 | 273.38 \pm 9.82 |
| Flaxseed Oil (Low Dose) | 4.61 \pm 0.56* | 1.37 \pm 0.04 | 306.85 \pm 4.56 | 308.14 \pm 7.51 |
| Flaxseed Oil (High Dose) | 3.40 \pm 0.22** | 2.71 \pm 0.08 | 348.63 \pm 8.44 | 270.18 \pm 6.78 |

Values are expressed as Mean \pm SEM. *** p <0.001, ** p <0.01. a vs. Control, b vs. STZ.



Effect of Flaxseed oil on MDA level in STZ induced Diabetic cardiomyopathy in rats.

Figure 1 showing a comparison of MDA level in the control, STZ, Metformin, Flaxseed Oil (Low Dose) and Flaxseed Oil (High Dose). Control group shows normal appearance although STZ show increase in MDA level. FO (300mg/kg) show decrease in MDA level as compare to STZ. FO (500mg/kg) show decrease in MDA level as compare to FO (300mg/kg). Metformin show decrease in MDA level, as compared to FO (300mg/kg).

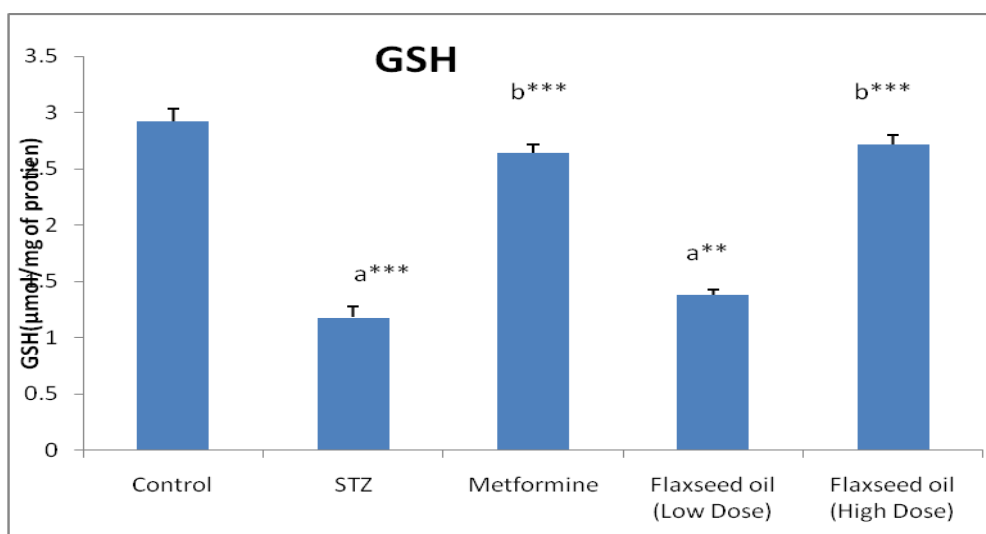


Values are expressed as Mean ± SD. ***p<0.001, **p<0.01. a vs. Control, b vs. STZ.

Figure 1: Effect of Flaxseed oil on MDA level in STZ induced Diabetic cardiomyopathy. Values are expressed as means ± SD. Statistical analysis was done using one way ANOVA and Tukey test.

Effect of Flaxseed oil on GSH level in STZ induced Diabetic cardiomyopathy in rats.

Fig 2. Showing a comparison of GSH level in the control, STZ, Metformin, Flaxseed Oil (Low Dose) and Flaxseed Oil (High Dose). Control group shows normal appearance although STZ show decrease in GSH level. FO (300mg/kg) show increase in GSH level as compare to STZ. FO (500mg/kg) show increase in GSH level as compare to FO (300mg/kg). Metformin show increase in GSH level, as compared to FO (300mg/kg).

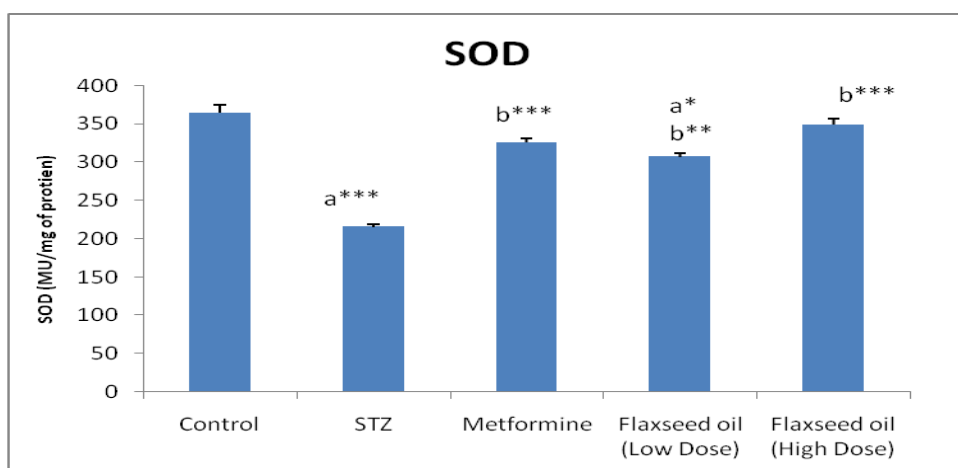


Values are expressed as Mean ± SD. ***p<0.001, **p<0.01. a vs. Control, b vs. STZ.

Figure 2: Effect of Flaxseed oil on GSH level in STZ induced Diabetic cardiomyopathy. Values are expressed as means ± SD. Statistical analysis was done using one way ANOVA and Tukey test.

Effect of Flaxseed oil on SOD level in STZ induced Diabetic cardiomyopathy in rats.

Fig 3 Showing a comparison of SOD level in the control, STZ, Metformin, Flaxseed Oil (Low Dose) and Flaxseed Oil (High Dose). Control group shows normal appearance although STZ show decrease in SOD level. FO (300mg/kg) show increase in SOD level as compare to STZ. FO (500mg/kg) show increase in SOD level as compare to FO (300mg/kg). Metformin show increase in SOD level, as compared to FO (300mg/kg).

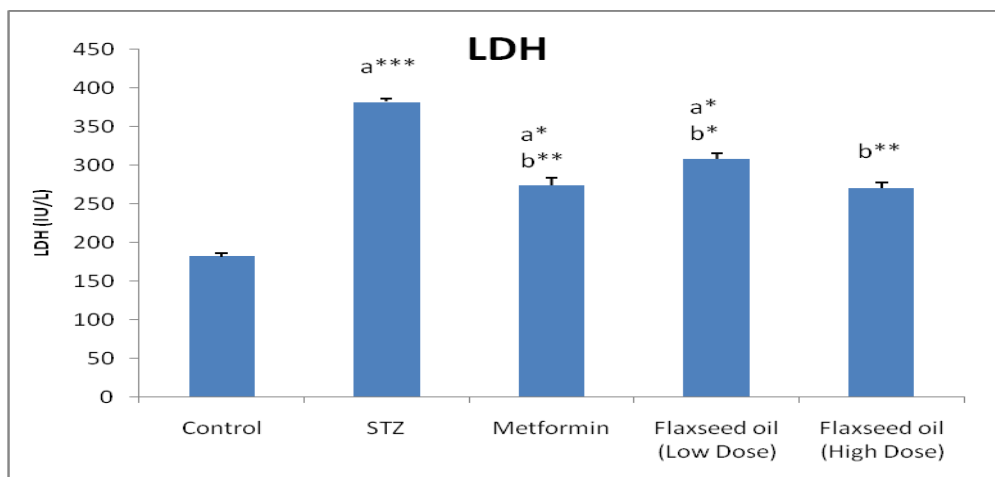


Values are expressed as Mean ± SD. ***p<0.001, **p<0.01. a vs. Control, b vs. STZ.

Figure 3: Effect of Flaxseed oil on SOD level in STZ induced Diabetic cardiomyopathy. Values are expressed as means ± SD. Statistical analysis was done using one way ANOVA and Tukey test.

Effect of Flaxseed oil on LDH level in STZ induced Diabetic Cardiomyopathy in rats.

Fig1 Showing a comparison of LDH level in the control, STZ, Metformin, Flaxseed Oil (Low Dose) and Flaxseed Oil (High Dose). Control group shows normal appearance although STZ show increase in LDH level. FO (300mg/kg) show decrease in LDH level as compare to STZ. FO (500mg/kg) show decrease in LDH level as compare to FO (300mg/kg). Metformin show decrease in LDH level, as compared to FO (300mg/kg).



Values are expressed as Mean ± SD. ***p<0.001, **p<0.01. a vs. Control, b vs. STZ.

Figure 4: Effect of Flaxseed oil on LDH level in STZ induced Diabetic cardiomyopathy. Values are expressed as means ± SD. Statistical analysis was done using one way ANOVA and Tukey test.

IV. CONCLUSION

Flaxseed oil have potential role to alleviate diabetic cardiomyopathy as it has potent antioxidant property because of linoleic and alpha linoleic contents. In streptozotocin-induced diabetes, there is a decrease in antioxidant enzyme

activities and an increase in myocardial lipid peroxidation. It is suggested that diabetic cardiomyopathy is found if there is decrease of antioxidant so that antioxidant therapy like flaxseed oil may be useful in improving cardiac function in diabetes. Flaxseed oil attenuates complications of DCM in rats. Reduction in oxidative stress markers as indicators of protective effects of Flaxseed oil, but exact mechanism(s) of this protection needs further investigations.

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