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RESEARCH ARTICLE

Hypoglycemic Effect Of Zingiber officinale On Hepatocytes Of Alloxan Induced Charls foster Rats

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Abstract

Background: Diabetes is a chronic metabolic disease, characterized by elevated blood glucose level. Diabetes in adults is more increasing in developing country. Ginger is the richest source of antioxidants having free radicals scavenging properties due to its component gingerols. The present study is designed to study hypoglycemic effect of *Zingiber officinale* on hepatocyte of diabetic *Charls foster* rats.

Methods: Aqueous rhizome extract of *Zingiber officinale* (200 mg/kg/b.w/day) is administered orally to diabetic group of rat for eight weeks. Serum was collected for biochemical assay and liver tissues were collected for hepatocyte study.

Results: It causes decrease in glucose up to normal level. Ginger restores SGPT and Lipid peroxidation effectively. Urea, Uric acid and creatinine were also restored effectively on administration of *Zingiber officinal.* The restoration was increased with increased duration of exposure. Ginger causes marked restoration in hepatic cells and central veins. It maintains both cytoplasm and chromatin material of hepatic cells of diabetic rat. Cytoplasm is restored more effectively in comparison to nucleus.

Conclusion: *Zingiber officinal* plays active role in protection of hepatic cell of diabetic rats and maintains its normal integrity.

Introduction

Diabetes is a chronic metabolic disease, characterized by elevated blood glucose level [1]. An estimate shows that the adult population of world will increase 35 % and number will increase 64% from 1995- 2025 and prevalence of diabetes will increase to 35% and number will increase by 122 %[2]. Now a day's diabetes is increasing, it was 135 millions in 1995 and expected to reach 300 million in 2025. India, China and United State will have the largest diabetic people in the year 2025. According to a report India has 30 millions diabetic people[3] in 2003 and will reach 46.1 million in 2025 [4].

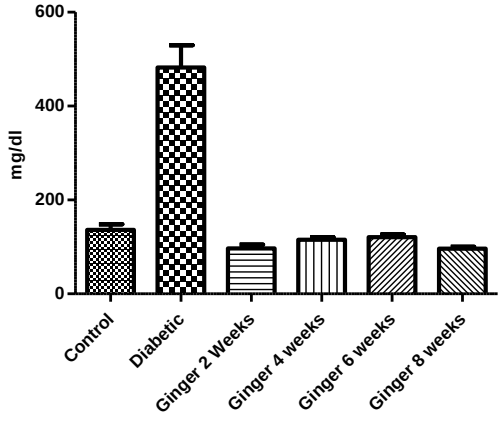
Liver is an important organ for hepatic metabolism of insulin, recent studies revealed that diabetes mellitus may cause liver disease like non-alcoholic fatty liver disease, chronic viral hepatitis, hemochromatosis, alcoholic liver disease, and cirrhosis. Non-alcoholic fatty liver disease is considered the most common cause of cryptogenic cirrhosis[5]. Diabetic nephropathy is the most common cause of chronic renal failure and end-stage kidney disease in the United States and is linked with increased cardiovascular mortality and morbidity [6].

Zingiber officinale is one of the most commonly consumed herbs with an array of application in traditional medicines. It has some properties like hyperglycemic, insulinotropic and hypolipidemic in human[7]. Ginger contains phytochemical substances such as (n)-gingerol, zingerone, and (n)-shogaol [8] which function as an antioxidant and anticancer agent [9]. It has also been used to treat stomach aches, diarrhea, nausea, asthma, respiratory disorders, [10] headaches, rheumatism and colds. Ginger is the richest source of antioxidants having free radicals scavenging properties due to its component gingerols [11]. It also exhibit anti-tumorogenic activity due to its active component and is effective in controlling colorectal, gastric, ovarian, liver, and skin cancers [12,13].
The present study is designed to study hypoglycemic effect of *Zingiber officinale* on hepatocyte of diabetic *Charls foster* rats.

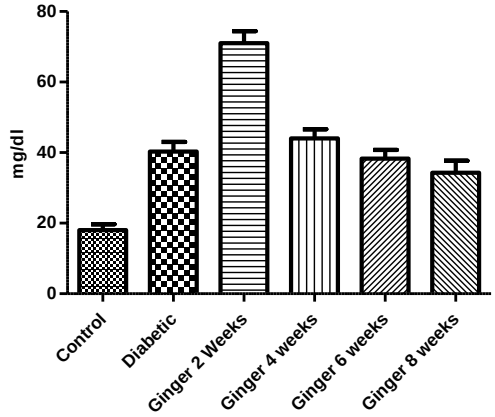
METHODS

Animals: The rat (*Charls foster*) was reared in our laboratory. The age group of rat selected for the study was 12 weeks old with 200±10 gm. b.w.
Chemicals: Alloxan, manufactured by Loba Chemie Pvt. Ltd, Mumbai was utilized for the experiment.
Aqueous rhizome extract of *Zingiber officinale* is administered orally by Gavage method to diabetic group of rat. Fresh rhizome of *Zingiber officinale* was purchased from local herbal store in Patna, India. The identity of the rhizome of *Zingiber officinale* was confirmed by Dr. Ramakant Pandey (Botanist), Department of Biochemistry, Patna University, Patna, Bihar, India. Approval for this study was taken from Institutional Animal Ethics Committee of the Mahavir Cancer Institute and Research Centre.
Study groups & sampling: The control group of 6 rats received distilled water orally. The 'treatment' groups (n=6) received alloxan 125 mg/kg b.w by intra-peritoneal method once followed by eight weeks administration of aqueous rhizome extract of *Zingiber officinale* (200 mg/kg/b.w/day) orally by Gavage method. Animals were sacrificed after the scheduled treatment. Serum was collected for SGPT, Creatinine, Urea, Uric acid, lipid peroxidation and glucose estimation. The Liver from all the animals were removed and washed three times in isotonic saline (0.85 v/w %) and fixed in neutral formalin for Light Microscope (LM) study.

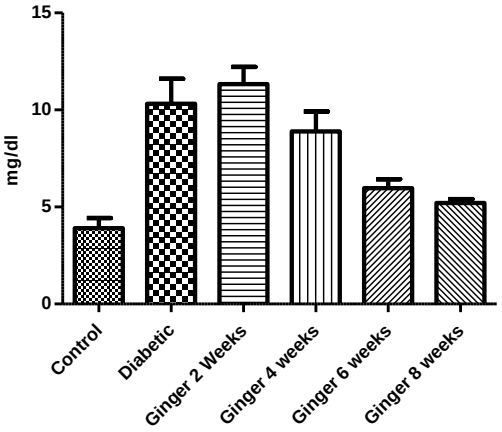
Graph-1: Glucose Level in Different Groups of Rat



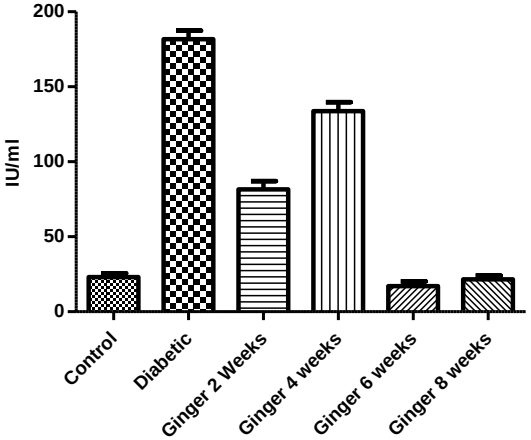
Graph-2: Urea Level in Different Groups of Rat



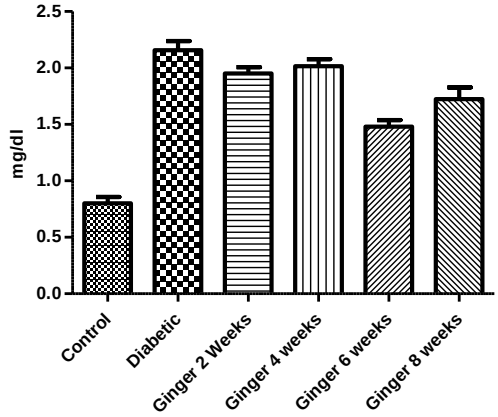
Graph-3: Uric Acid Level in Different Groups of Rat



Graph-4: SGPT Level in Different Groups of Rat



Graph-5: Creatinine Level in Different Groups of Rat



Graph-6: Lipid peroxidation Level in Different Groups of Rat

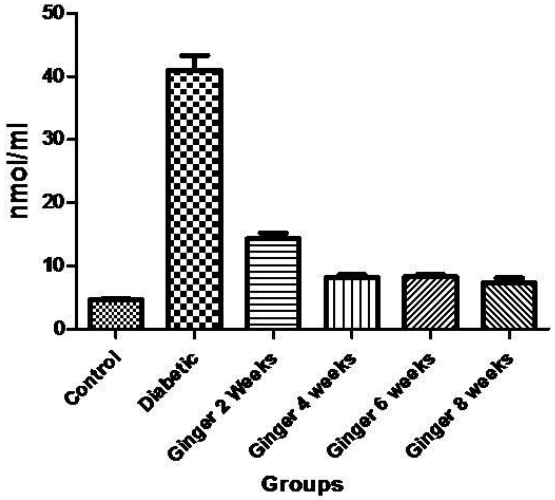


Figure – 1: shows liver of control rat with distinct hepatic cells, central vein is also normal in shape, hepatic veins are normal in structure.

Figures

Figure – 1

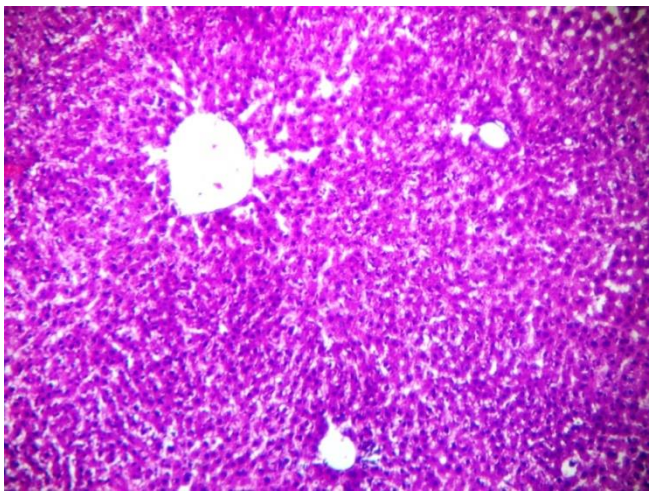


Figure – 2: shows liver of control rat with distinct hepatic cells, nucleus and cytoplasm of hepatic cells are well distributed.

Figure – 2

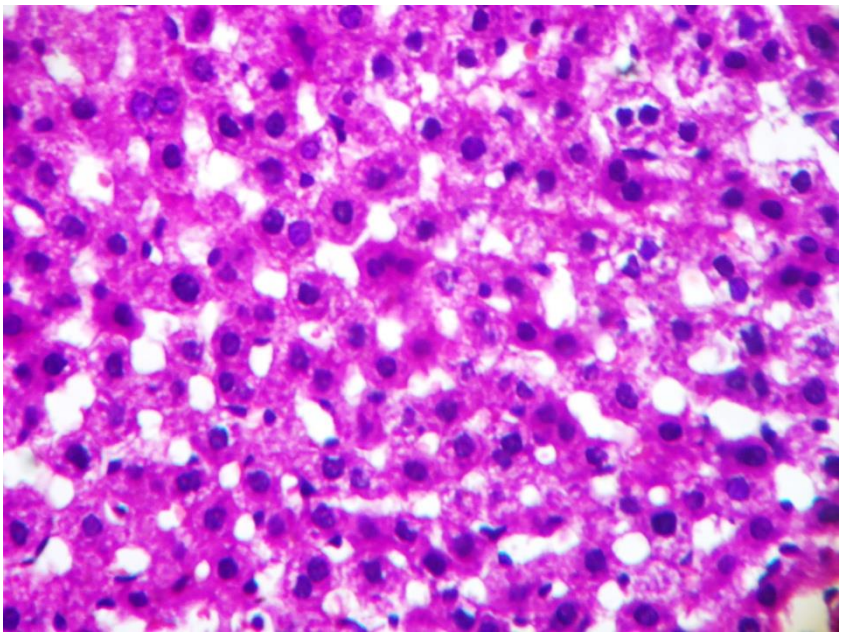


Figure – 3: shows liver of diabetic rat with degeneration in hepatic cells. Many vacuolated spaces were observed. Degenerated cytoplasm was also visible. Central vein is degenerated with rudiments of cytoplasm. Fragmented nucleus was also observed.

Figure – 3

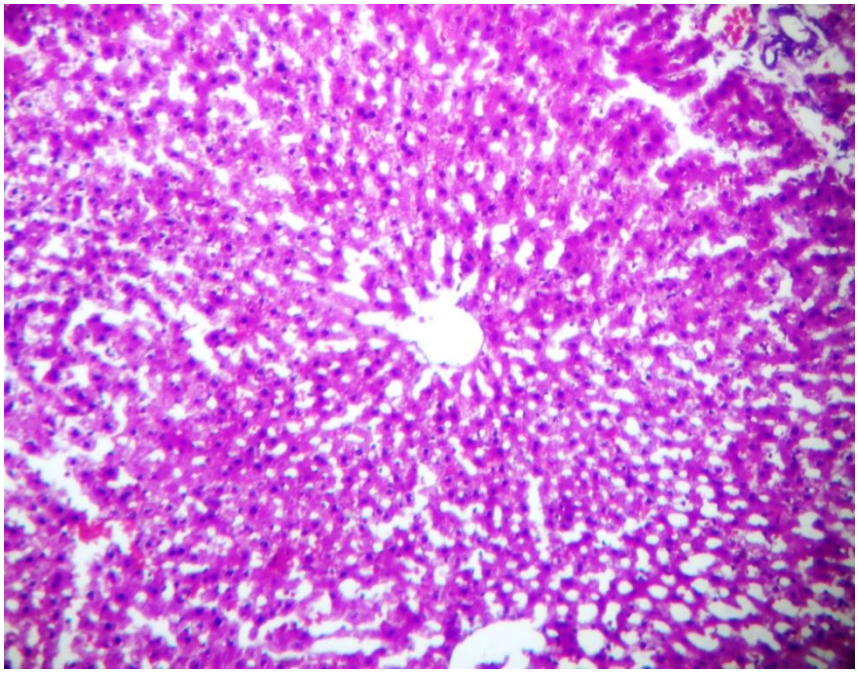


Figure – 4: shows liver of diabetic rat with degeneration in hepatic cells. Fragmented nuclei were observed. Vacuolated chromatin is also visible. Vacuolization is frequent in hepatic cells with degenerated cytoplasm.

Figure – 4

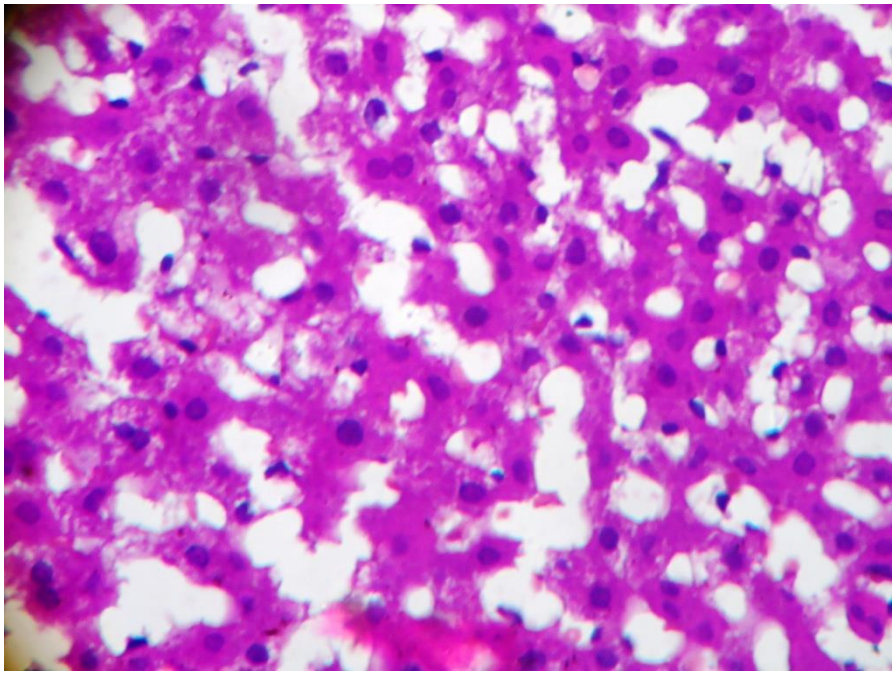


Figure – 5: shows liver of diabetic rat followed by two weeks administration of *Zingiber officinale* with degeneration in hepatic cells. Many vacuolated spaces were observed. Degenerated cytoplasm were observed with clustered nuclei.

Figure – 5

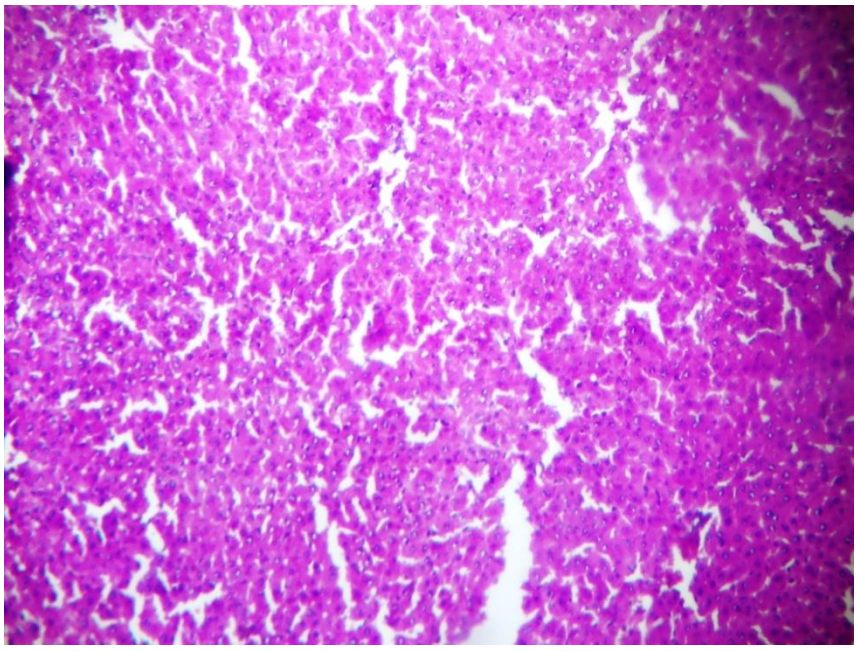


Figure – 6: shows liver of diabetic rat followed by two weeks administration of *Zingiber officinale* with vacuolated chromatin in hepatic cells. Clustered nuclei were observed in cytoplasm. Many vacuolated spaces were observed.

Figure – 6

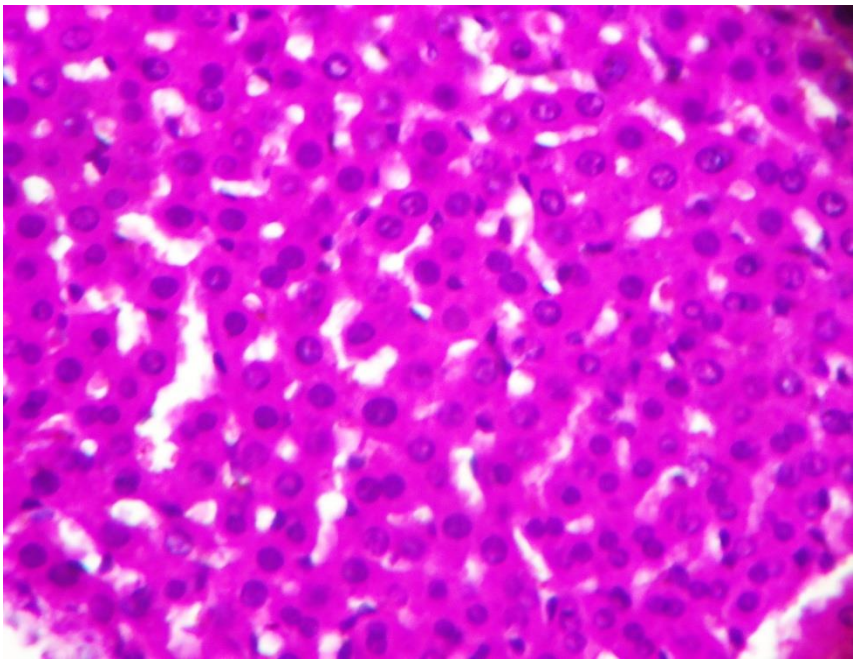


Figure – 7: shows liver of diabetic rat followed by four weeks administration of *Zingiber officinale* with frequent vacuolization. Clustered nuclei were observed in hepatic cells. Degenerated central vein and hepatic veins were observed.

Figure – 7

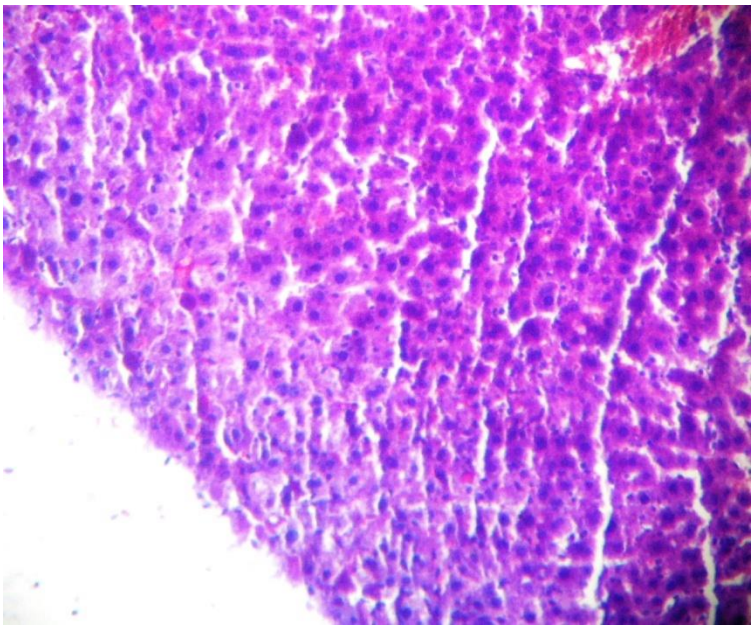


Figure – 8: shows liver of diabetic rat followed by four weeks administration of *Zingiber officinale* with many vacuolated spaces in hepatic cells. Clustered and fragmented nuclei were observed in hepatic cells. Degenerated hepatic vein was observed.

Figure – 8

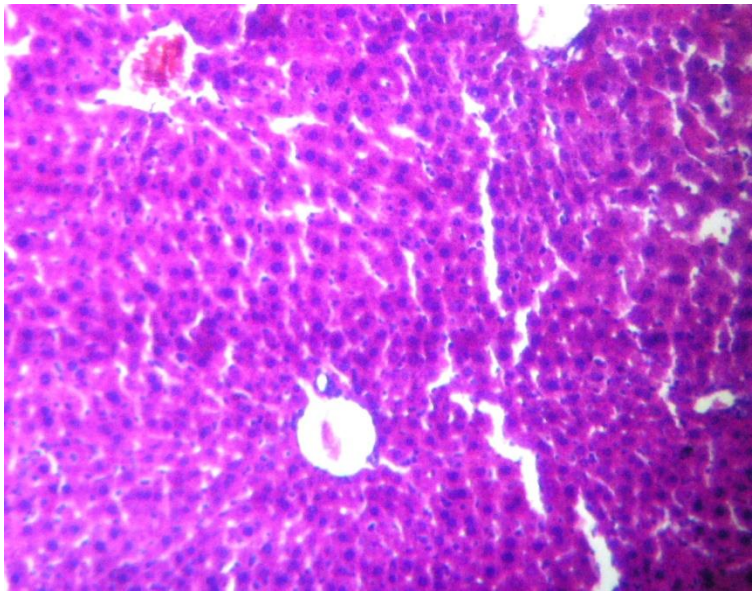


Figure – 9: shows liver of diabetic rat followed by six weeks administration of *Zingiber officinale* with restoration in hepatic cells. Least vacuolization were observed. Restoration in cytoplasm was more effective.

Figure – 9

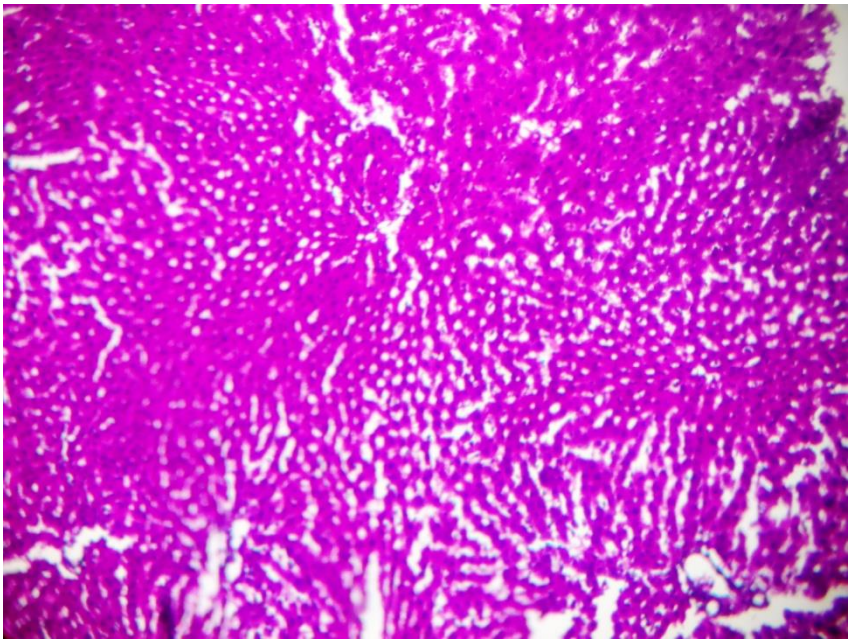


Figure – 10: shows liver of diabetic rat followed by six weeks administration of *Zingiber officinale* with restoration in chromatin material of hepatic cells. Clustered nuclei were observed. Degenerated cytoplasm was observed with clustered nuclei.

Figure – 10

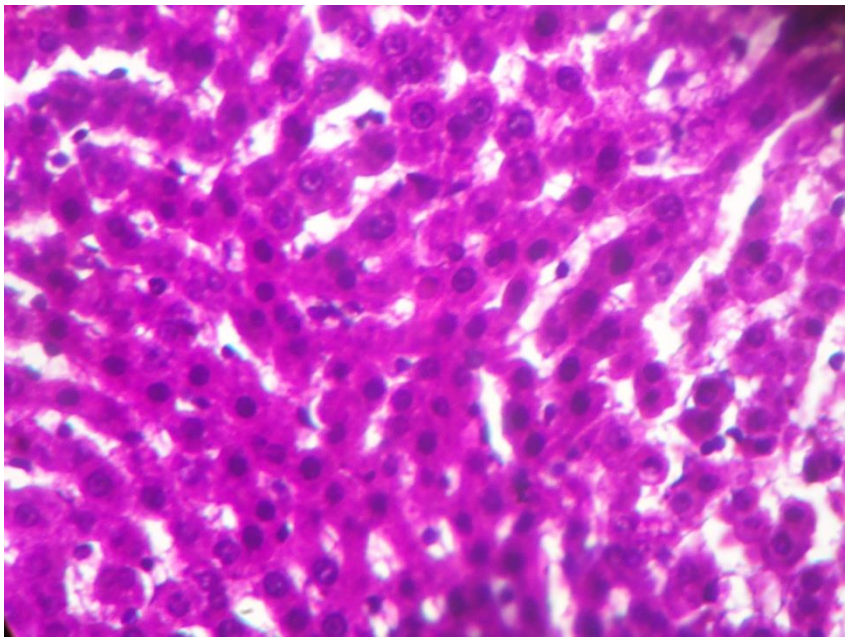


Figure – 11: shows liver of diabetic rat followed by eight weeks administration of *Zingiber officinale* with restoration in hepatic cells.. restoration in cytoplasm and nuclear material was observed.

Figure – 11

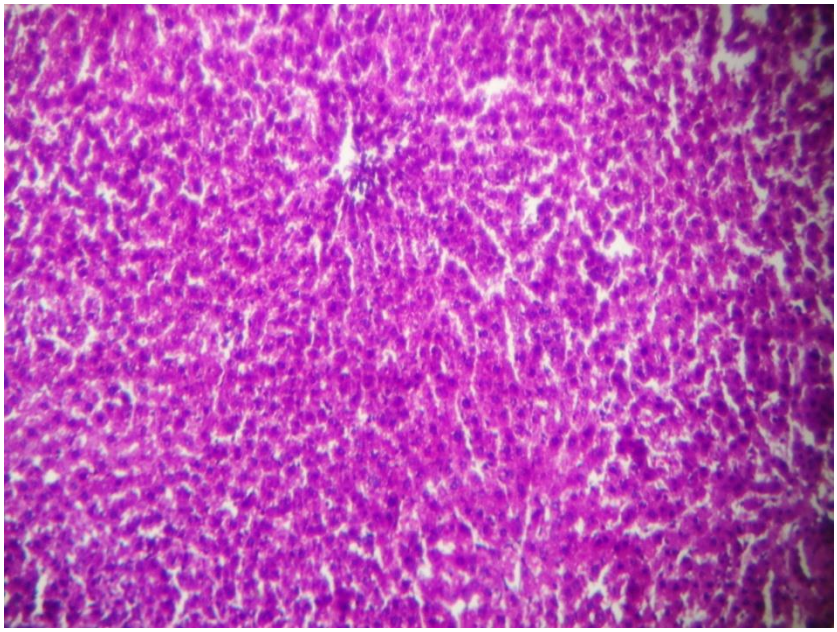
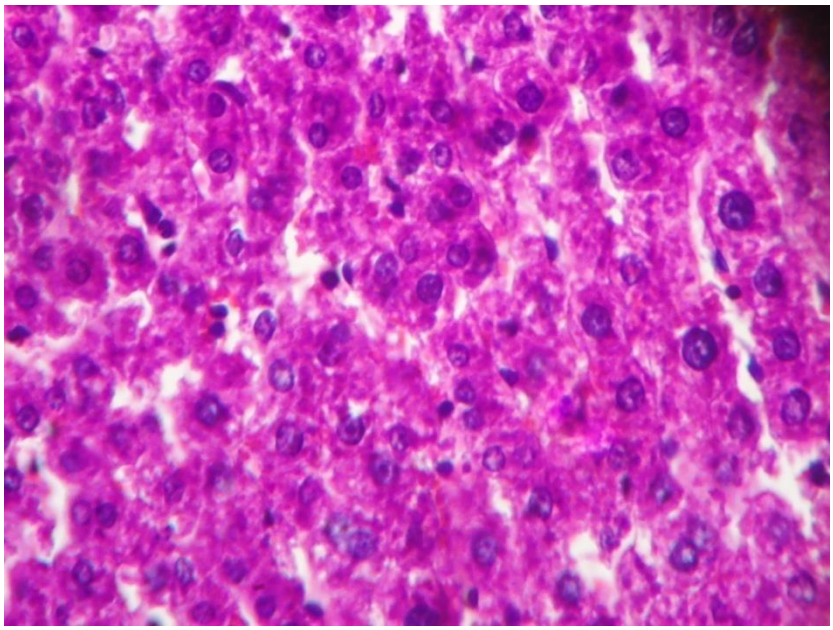


Figure – 12: shows liver of diabetic rat followed by eight weeks administration of *Zingiber officinale* with restored chromatin in hepatic cells. Well organized hepatic cells were observed. Cytoplasm was restored to greater extent.

Figure – 12



RESULTS

Changes in blood biochemistry

Glucose level in control group of rat was 136.3 ± 11.84 mg/dl. In diabetic group of rat glucose level was 482.0 ± 47.51 mg/dl. Glucose level was 96.67 ± 8.11 mg/dl, 115.3 ± 5.20 mg/dl, 120.7 ± 5.54 mg/dl and 96.33 ± 3.84 mg/dl in *Zingiber officinale* two weeks, four weeks, six weeks and eight weeks administered group of rats (Graph: 1).

Urea level in control group of rat was 18.00 ± 1.73 mg/dl. In diabetic group of rat urea level was 40.33 ± 2.72 mg/dl. Urea level was 71.00 ± 3.46 mg/dl, 44.00 ± 2.64 mg/dl, 38.33 ± 2.40 mg/dl and 34.33 ± 3.38 mg/dl in *Zingiber officinale* two weeks, four weeks, six weeks and eight weeks administered group of rats (Graph: 2).

Uric acid level in control group of rat was 3.90 ± 0.52 mg/dl. In diabetic group of rat uric acid level was 10.32 ± 1.28 mg/dl. Uric acid level was 11.33 ± 0.88 mg/dl, 8.9 ± 1.01 mg/dl, 5.967 ± 0.46 mg/dl and 5.2 ± 0.20 mg/dl in *Zingiber officinale* two weeks, four weeks, six weeks and eight weeks administered group of rats (Graph: 3).

Serum Glutamic Pyruvic Transaminase (SGPT) level in control group of rat was 23.00 ± 2.64 IU/ml. In diabetic group of rat SGPT level was 181.7 ± 5.78 IU/ml. SGPT level was 81.67 ± 5.48 IU/ml, 133.7 ± 6.11 IU/ml, 17.00 ± 3.21 IU/ml and 21.50 ± 2.50 IU/ml in *Zingiber officinale* two weeks, four weeks, six weeks and eight weeks administered group of rats (Graph: 4).

Creatinine level in control group of rat was 0.8 ± 0.057 mg/dl. In diabetic group of rat creatinine level was 2.157 ± 0.08 mg/dl. Creatinine level was 1.950 ± 0.05 mg/dl, 2.017 ± 0.06 mg/dl, 1.480 ± 0.05 mg/dl and 1.723 ± 0.10 mg/dl in *Zingiber officinale* two weeks, four weeks, six weeks and eight weeks administered group of rats (Graph: 5).

Lipid peroxidation (malondialdehyde) level in control group of rat was 4.667 ± 0.14 nmol/ml. In diabetic group of rat lipid peroxidation level was 41.00 ± 2.30 nmol/ml. Lipid peroxidation level was 14.33 ± 0.88 nmol/ml, 8.167 ± 0.44 nmol/ml, 8.333 ± 0.33 nmol/ml and 17.300 ± 0.80 nmol/ml in *Zingiber officinale* two weeks, four weeks, six weeks and eight weeks administered group of rats (Graph: 6).

Changes in Liver morphology

Liver of control rat show distinct hepatic cells, central vein is also normal in shape, hepatic veins are normal in structure (Figure: 1). Well defined hepatic cells, nucleus and cytoplasm of hepatic cells are well distributed (Figure: 2). Liver of diabetic rat show degeneration in hepatic cells. Many vacuolated spaces were observed. Degenerated cytoplasm was also visible. Central vein is degenerated with rudiments of cytoplasm. Fragmented nucleus was also

observed (Figure: 3). Liver of diabetic rat show fragmented nuclei. Vacuolated chromatin is also visible. Vacuolization is frequent in hepatic cells with degenerated cytoplasm (Figure: 4). Liver of diabetic rat followed by two weeks administration of *Zingiber officinale* show degeneration in hepatic cells. Many vacuolated spaces were observed. Degenerated cytoplasm was observed with clustered nuclei (Figure: 5). Vacuolated chromatin in hepatic cells were observed. Clustered nuclei and many vacuolated spaces were clearly observed (Figure: 6). Liver of diabetic rat followed by four weeks administration of *Zingiber officinale* show frequent vacuolization. Clustered nuclei were observed in hepatic cells. Degenerated central vein and hepatic veins were observed (Figure: 7). Clustered and fragmented nuclei were observed in hepatic cells. Degenerated hepatic vein was observed (Figure: 8). Liver of diabetic rat followed by six weeks administration of *Zingiber officinale* show restoration in hepatic cells. Least vacuolization were observed. Restoration in cytoplasm was more effective (Figure: 9). Restoration in chromatin material of hepatic cells was observed. Restoration in cytoplasm was observed (Figure: 10). Liver of diabetic rat followed by eight weeks administration of *Zingiber officinale* show restoration in hepatic cells. Restoration in cytoplasm and nuclear material was observed (Figure: 11). Restored chromatin in hepatic cells and well organized hepatic cells were observed. Cytoplasm was restored to greater extent (Figure: 12).

DISCUSSIONS

The diabetes associated complications include retinopathy, neuropathy, nephropathy and atherosclerosis[14]. Atherosclerosis includes coronary artery disease, leading to myocardial infarction or angina, stroke and intermittent claudication as well as diabetic foot[15]. Diabetic nephropathy is one of the most common micro vascular complications of diabetes[16] defined as rise in urinary albumin excretion rate, often associated with an increase in blood pressure, but without evidence of other causes of renal disease. In present study we also observe increased level of Urea, Uric acid and creatinine to greater extent. Hepatic cell degeneration in diabetic group of rat were observed with increase in liver function test.

Hyperglycemia leads to an increase in serum glycated proteins [17] along with alterations in other atherogenic risk factors and disturbances in Mineral metabolism is also noticed. Lipid peroxidation level was increased many fold in diabetic group of rat.

The charecteristic taste of ginger is due to its compound 6-gingerol. Active gingerol can be converted into shogaols, zingerone and paradol [18]. Zingeron and shogaols are found in small amount in fresh ginger but in larger amount in dried ginger. Ginger shows strong antibacterial and antifungal activity. It gives powerful stimulatory effect on heart muscle to stimulate blood circulation to the body [19]. It also prevents the increased cholesterol level [20]. *Zingiber officinal* causes decrease in glucose to normal level. Ginger restores SGPT effectively. Urea, Uric acid and creatinine were also restored effectively on administration of *Zingiber officinal.* Lipid peroxidation was also restored to some extent. The restoration was increased with increased duration of exposure.

A study in Denmark revealed that ginger reduces inflammation and arthritis. One of the features of inflammation is increased oxygenation of arachidonic acid which results in the production of prostaglandin and leukotrienes [21] and anti-inflammatory effect of ginger could be by inhibiting prostaglandin and leukotriene biosynthesis [22].

The liver is an important organ which is actively involved in many metabolic functions and is the frequent target for a number of toxicants [23]. Unfortunately most of the drugs have side effects on liver and sometimes causes hepatic failure. Ginger diet can restore biochemical parameter on normal levels and also maintain the integrity of liver and protect it from damage [24]. We also find that *Zingiber officinal* administration causes marked restoration of hepatic cells and maintain its integrity. It restores both cytoplasmic material and nuclear material effectively.

Thus it is evident from study that *Zingiber officinal* plays active role in maintaining glucose level of diabetic rat. It maintains liver function tests and kidney function test effectively to normal level in diabetic *Charls foster* rats. Lipid peroxidation level is also restored to normal level. Ginger causes marked restoration in hepatic cells and central veins. It maintains both cytoplasm and chromatin material of hepatic cells of diabetic rat. *Zingiber officinal* plays active role in protection of hepatic cell of diabetic rats and maintains its normal integrity.

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