WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 2, 775-792. Research Article ISSN 2277– 7105

COMPARATIVE HYPOGLYCEMIC EFFECT OF *CUMINUM CYMINUM AND GINGIBER* OFFICINALE ON DIABETIC MICE

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Article Received on
24 Nov. 2019,
Revised on 14 Dec. 2019,
Accepted on 04 Jan. 2020,
DOI: 10.20959/wjpr20202-16577

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ABSTRACT

Diabetes is the world's oldest disease, described in historical records of civilizations such as those found in ancient Egypt, Persia, and India (Holt, 2004). The incidence of diabetes is rapidly increasing in world at alarming rate. High blood glucose levels over time can causes damage of blood vessels, resulting in serious health complications such as high blood pressure, heart disease, stroke, blindness, kidney failure, and amputations. Cumin is the most common flavouring agent in India. Cumin has been used as anti-inflammatory, diuretic, carminative, and antispasmodic, in the treatment of toothaches and epilepsy and also as an aid for treating dyspepsia, jaundice, diarrhea, flatulence, and indigestion. Ginger is a strong antioxidant substance and may either mitigate or prevent generation of free radicals and also very useful in cases of ulcerogenesis due to its antioxidant activities. In the present study, diabetic mice were treated with C*uminum cyminum* and *Zingiber officinale* whereas Diabetic control group were treated with distilled water for 16 weeks. Diabetic mice were treated with C*uminum cyminum* @ 80 mg/kg body weight and with *Zingiber officinale* @ 80 mg/kg body weight for 16 weeks. The treatment with *Zingiber officinale* restored glucose level up to 106 mg/dl while the glucose level was up to 123 mg/dl in *Cuminum cyminum* administered mice group. Uric acid and SGPT were effectively restored by 16 weeks' administration of *Cuminum cyminum*. Hepatic cells were also observed in restored condition in *Cuminum cyminum* administered group. It is concluded from the study that *Cuminum cyminum* restored glucose level LFT and KFT effectively in diabetic mice. It also restored hepatic cells and sinusoid effectively, while *Zingiber Officinale* restored

glucose and urea levels effectively. Uric acid and SGPT level were not restored effectively in ginger administered mice group. The present study suggests that *Cuminum cyminum* acts effectively on LFT/ KFT and histology of liver of diabetic mice in comparison to *Zingiber Officinale* administered group.

KEYWORD: LFT, KFT, Sinusoid, diuretic, dyspepsia.

INTRODUCTION

Diabetes is the world's oldest disease, described in historical records of civilizations such as those found in ancient Egypt, Persia, and India (Holt, 2004). The incidence of diabetes is rapidly increasing in world at an alarming rate (Huizinga and Rothman, 2006). The World Health Organization states that 347 million people worldwide were suffering from diabetes in 2008, which equates to 9.5%. The age standardized prevalence of type-2 diabetes was 12.1%. The prevalence was the highest in Hyderabad (16.6%), followed by Chennai (13.5%), Bengaluru (12.4%), Kolkatta (11.7%), New Delhi (11.6%) and Mumbai (9.3%) (Premalatha *et al*., 2000). High blood glucose levels over time can cause damage blood vessels, resulting in serious health complications such as high blood pressure, heart disease and stroke, blindness, kidney failure, and amputations (National Diabetes Statics Report 2014). The risk of cardiovascular disease increases continuously with rise in fasting plasma glucose levels (Singh *et al.*, 2013 and Danaei *et al.*, 2006). Diabetic neuropathy is a syndrome which encompasses both the somatic and autonomic divisions of the peripheral nervous system. There is, however, a growing appreciation that damage to the spinal cord (Selvarajah *et al*., 2006).

Cumin is most common flavouring agent in India. Cumin has been used as anti-inflammatory, diuretic, carminative, and antispasmodic, in treatment of toothaches and epilepsy and also as an aid for treating dyspepsia, jaundice, diarrhea, flatulence, and indigestion (Rebey *et al*., 2012). Seeds of *Cuminum cyminum* are carminative, aromatic, stimulant, and cooling in effect, (Hanif *et al*., 2012). The presence of phytoestrogens in cumin has shown the anti-osteoporotic effect of reduced urinary calcium excretion, augmentation of calcium content and mechanical strength of bones (Vanithakumari, 1987). Cumin seed is enriched source of iron which is required for the synthesis of haemoglobin (Silja *et al*., 2008). Cumin helps in decreasing hypoglycemia and high blood glucose level by stimulating the secretion of hormone insulin in diabetic patients (Chaudhary et al, 2014).

Ginger is a strong antioxidant substance and may either mitigate or prevent generation of free radicals and also very useful in cases of ulcerogenesis due to its antioxidant activities (Gull *et al*., 2012; Kim *et al*., 2007). It helps to reduce atrial blood pressure by blocking calcium channel or by acting on muscarinic receptor (Ozgoli and Goli, 2009). Ginger is reported to be useful in treating inflammation in Rheumatoid arthritis and Osteoarthritis patients (Srivastava *et al*., 1994). Aqueous extract of ginger (200 mg/ 400 mg/kg) is known to reduce acetaminophen induced hepatotoxicity and also decrease ALT, AST and ALP levels (Ajith *et al*., 2007).

The present study is designed to find comparative hypoglycemic effect of *Cuminum cyminum and Gingiber officinale* on liver and kidney function and on histology of liver tissues in diabetic mice.

MATERIALS AND METHODS

Animals: - The mice (*Mus musculus*) were reared in animal house. The mice selected for the study were 12 weeks old with 30±2 gm body weight. The mice were housed at controlled environmental conditions i.e. at 22±2ºC temperature, 50±10% relative humidity and 12h dark-light cycle. All experiments were conducted as per the guidelines of CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals).

Chemicals: - Alloxan, purchased by Loba chem Pvt. Ltd., Mumbai was utilized for the experimental design.

Medicinal plants used: - Aqueous seed extract of C*umimum cyminum* @ 80 mg/kg b.w. and aqueous rhizome extract of *Zingiber officinale* @ 80 mg/kg b.w. Was orally administered to diabetic group of mice. Fresh seeds of C*uminum cyminum* and *rhizome of Zingiber officinale* were purchased from herbal store in Patna, India and identified by botanist.

Diabetic control group mice were treated with distilled water while diabetic mice were treated with C*uminum cyminun* and *Zingiber officinale* separately for 16 weeks. Animals were sacrificed on 4^{th}, 8^{th}, 12^{th} and 16^{th} week of C*uminum cyminum* and *Zingiber officinale* administration. Blood were collected from the sacrificed mice for biochemical analysis while tissues of liver were fixed formalin for microscopic examination.

RESULTS

Glucose: In control group glucose level was 90.67 ± 1.45 while in diabetic group it was 213.3 ± 6.36. In the group administrated with *Cuminum cyminum* for 4 weeks, 8 weeks, 12 weeks and 16 weeks, it was 161.3±12.34, 155.8± 20.38, 138.01±9.75 and 123.7 ±1.202 respectively and in *Zingiber officinale* administered group, it was 157.8± 11.53, 144.3± 7.63, 129.7±14.58 and 106.0 ± 2.64 for 4 weeks, 8 weeks, 12 weeks and 16 weeks' period of administration respectively (Text figure -1 & 2).

Urea: - in control group urea level was 106.0 ± 2.64 while in diabetic groups it was 73.00 ± 2.51. In *Cuminum cyminum* 4 weeks, 8 weeks, 12 weeks, and 16 weeks administrated groups, it was 50.33 ±1.45, 45.33 ± 0.88, 41.33± 1.76 and 39.67 ± 2.02 respectively. In *Zingiber officinale* 4 weeks, 8 weeks, 12 weeks, and 16 weeks administrated groups it was 42.00 ± 1.15, 41.33 ± 1.20, 40.67 ± 2.02 and 40.67 ± 2.02 respectively (Text figure -3 & 4).

Uric acid: - In control group uric acid level was 16.33 ± 0.88 while in diabetic group it was 73.00 ± 2.51. In *Cuminum cyminum* 4 weeks, 8 weeks, 12 weeks, and 16 weeks administrated groups it was 8.90 ± 0.063, 7.96 ± 0.062, 6.147 ± 0.031, and 5.037 ± 0.034 respectively. In *Zingiber officinale* 4 weeks, 8 weeks, 12 weeks, and 16 weeks administrated groups it was 10.12 ± 0.151, 9.70 ± 0.057, 9.66 ± 0.08 and 9.70 ± 0.057 respectively (Text figure -5 & 6).

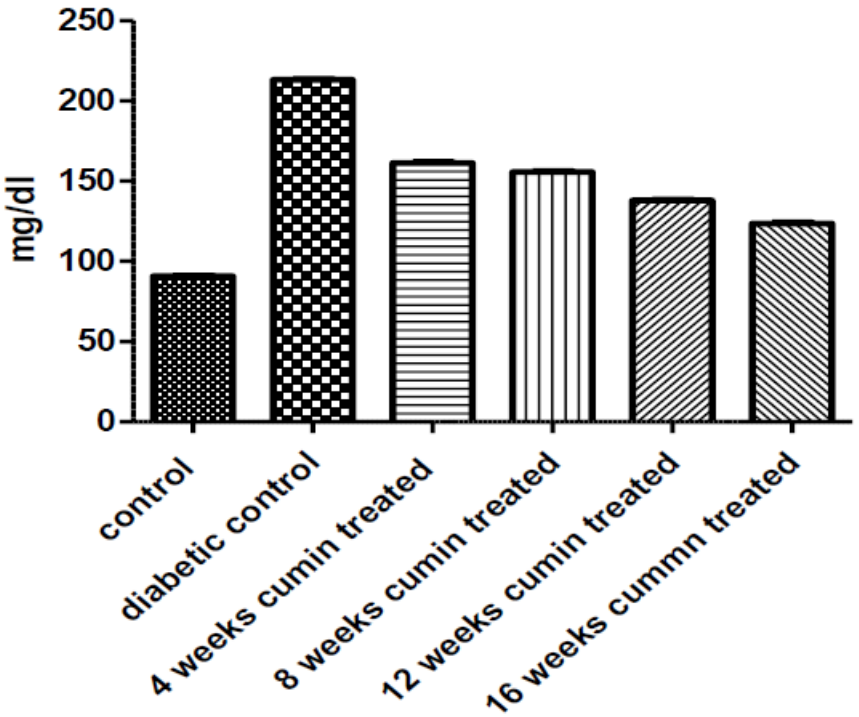
SGPT: - control group SGPT level was 19.67 ± 1.202 U/ml while in diabetic group it was 191.3 ± 2.84.00. In *Cuminum cyminum* 4 weeks, 8 weeks, 12 weeks, and 16 weeks administrated groups it was 79.67 ± 6.36, 59.33 ± 1.856, 50.00 ±3.786 and 43.00 ± 1.528 respectively. In *Zingiber officinal* 4 weeks, 8 weeks, 12 weeks, and 16 weeks administrated groups it was 121.3 ± 2.028, 108.0 ± 1.73, 100.3 ± 2.028 and 99.00 ± 1.155 respectively (Text figure -7 & 8).

Liver of control mice showed well defined hepatic cell with normal cytoplasmic and nuclear material. Central vein was also normal in structure (Figure -1). Liver of diabetic mice showed fragmented nuclear material of hepatic cells having degenerated cytoplasm with vacuolization (Figure -2).

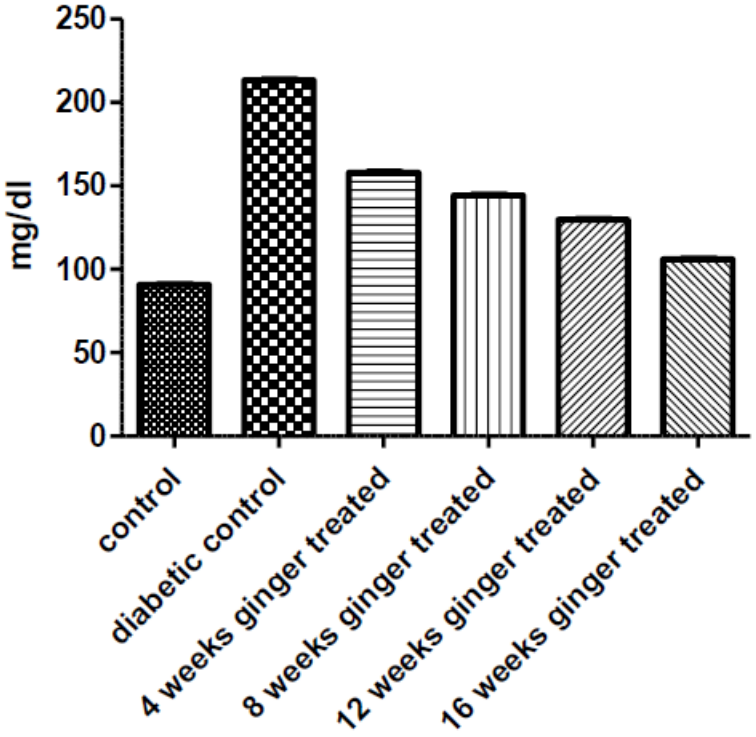
Liver of diabetic mice administered with *Cuminum cyminum* for 4 weeks showed clustered

nuclei in hepatic cells with few fragmented nuclei and many vacuolated (Figure -3). Liver of diabetic mice administered with *Cuminum cyminum* for 8 weeks showed many vacuolated spaces in hepatic cells (Figure -4). Liver of diabetic mice administered with *Cuminum cyminum* for 12 weeks showed degenerated cytoplasm & nucleus of hepatic cells with many vacuolated spaces (Figure -5). Liver of diabetic mice administered with *Cuminum cyminum* for 16 weeks showed restoration in nuclear material to some extent (Figure -6).

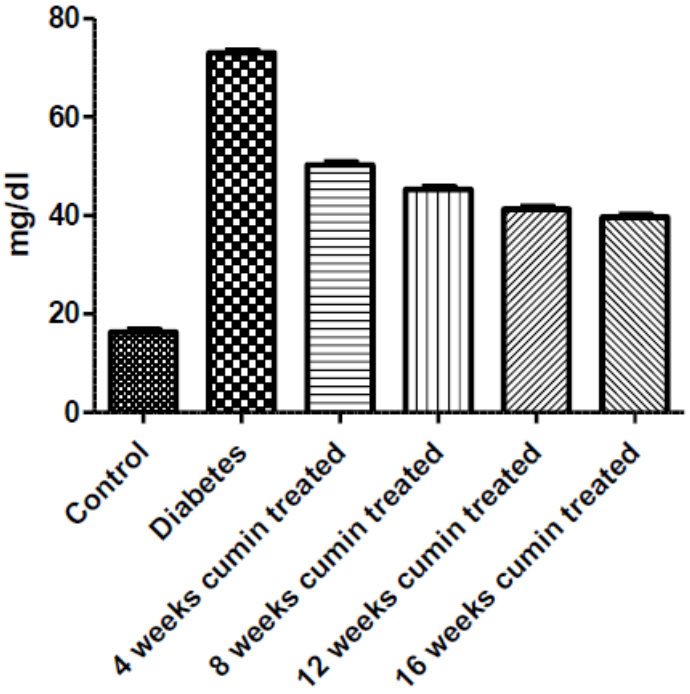
Liver of diabetic mice administered with *Zingiber officinale* for 4 weeks showed little restoration in central vein with rough inner walls and fragmented nuclear material were also observed (Figure -7). Liver of diabetic mice administered with *Zingiber officinale* for 8 weeks shows degenerated hepatic cells, multiple nucleated hepatic cells in cytoplasmic spaces (Figure -8). Liver of diabetic mice administered with *Zingiber officinale* for 12 weeks showed fragmented nuclear material in multi nuclear hepatic cells with degeneration of cytoplasmic and nuclear material (Figure -9). Liver of diabetic mice administered with *Zingiber officinale* for 16 weeks showed restoration in nuclear material to some extent as few vacuolated space was also observed (Figure -10).



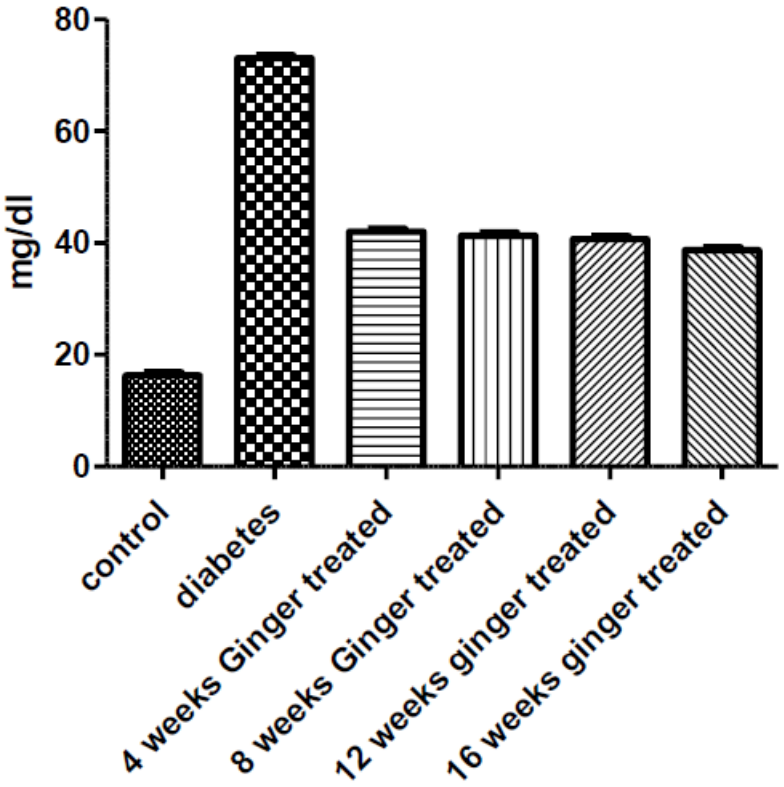
Text Figure 1: Glucose level in different group of mice.



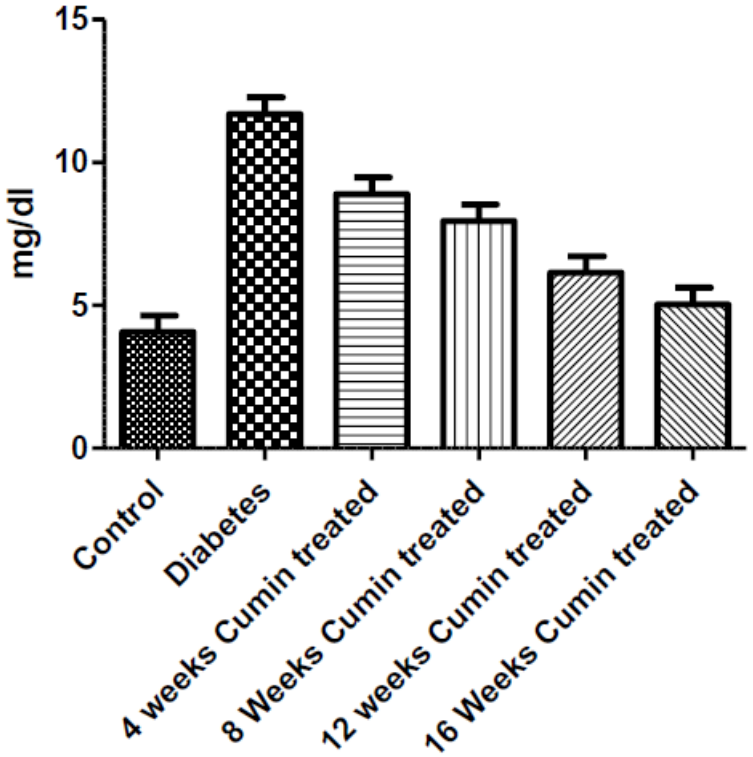
Text Figure 2: Glucose level in different group of mice.



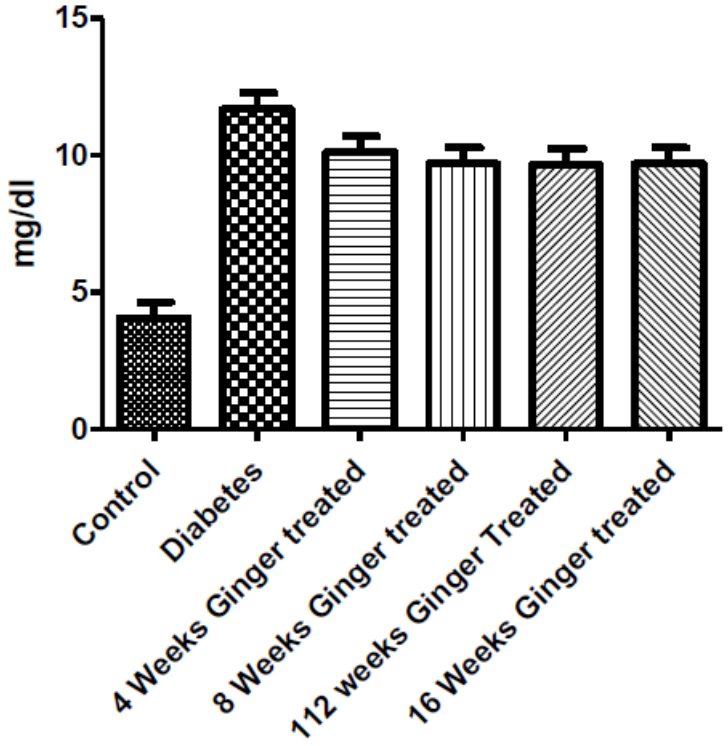
Text Figure 3: Urea level in different group of mice.



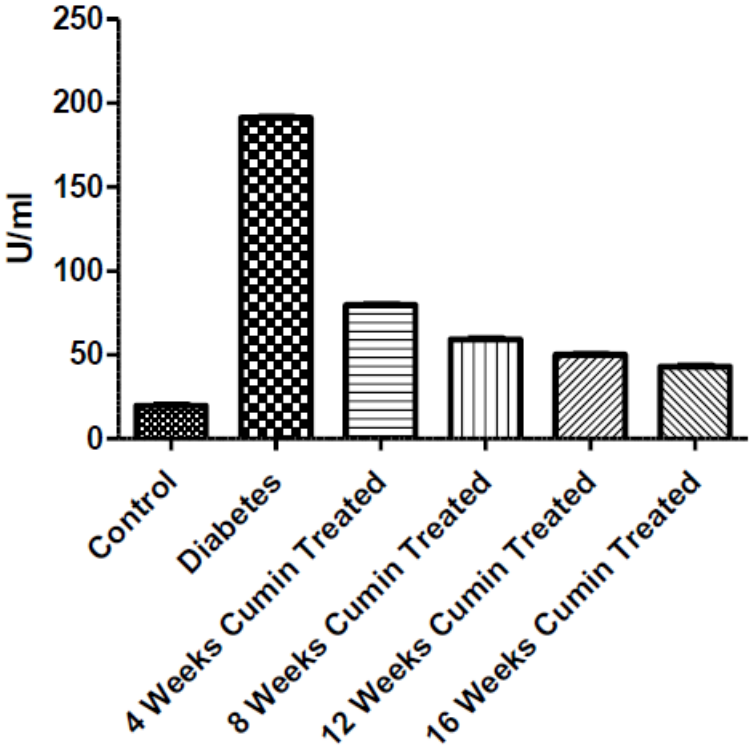
Text Figure 4: Urea level in different group of mice.



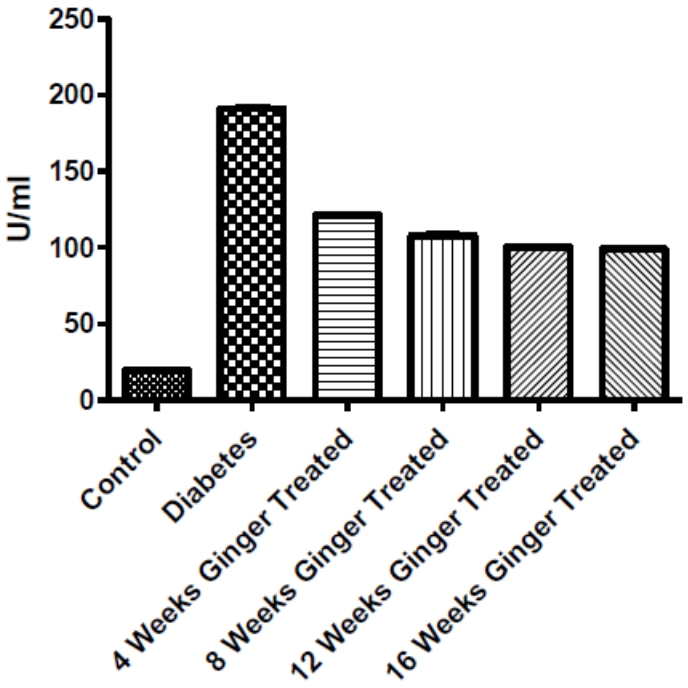
Text Figure 5: Uric acid level in different group of mice.



Text Figure 6: Uric acid level in different group of mice.



Text Figure 7: SGPT level in different group of mice.



Text Figure 8: SGPT level in different group of mice.

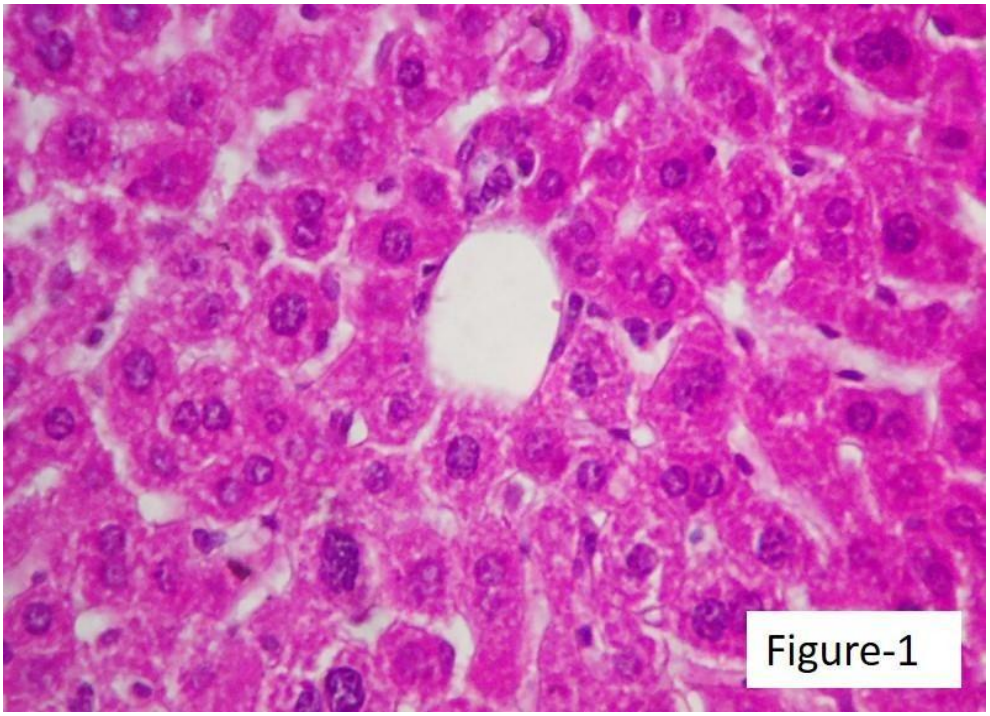


Figure 1: Liver of control mice shows well define hepatic cell both Cytoplasmic and nuclear material are normal. Central vein was also normal in structure. 600X.

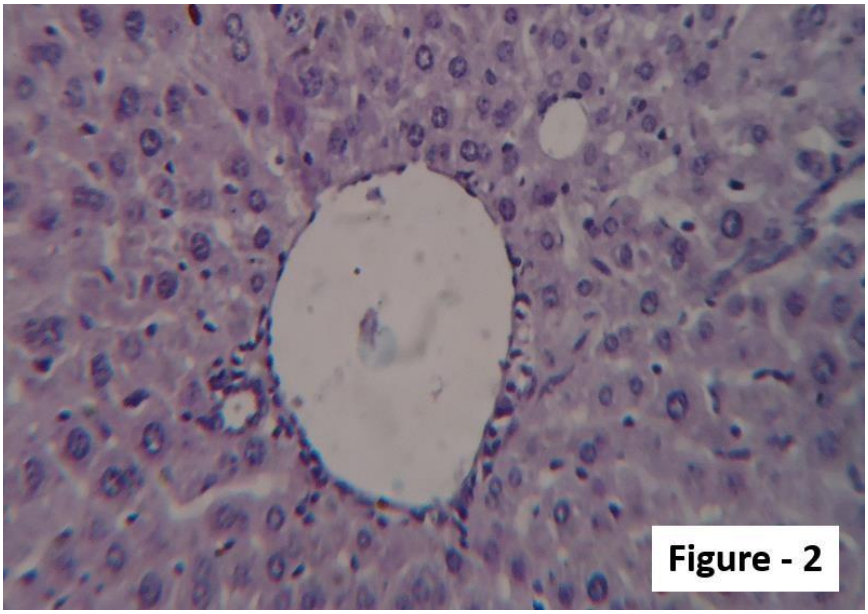


Figure 2: Liver of diabetic mice shows fragmented nuclear material of hepatic cells degenerated cytoplasm were observed with vacuolization. Signet ring nucleus was also evident.

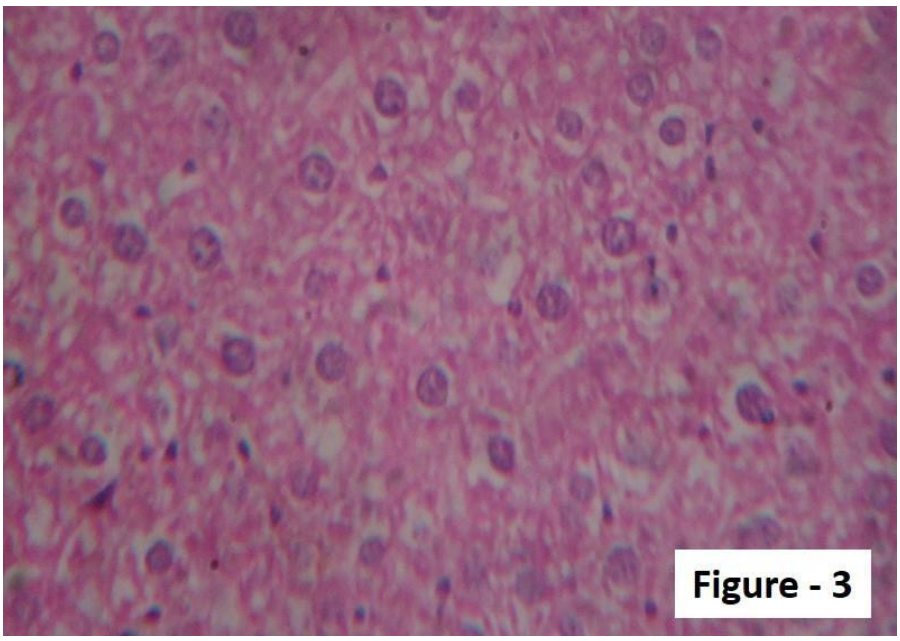


Figure 3: Liver of diabetic mice administered with *Cuminum cyminum* for 4 weeks shows clustered nuclei in hepatic cells few fragmented nuclei were also observed many vacuolated space were seen in hepatic cells.

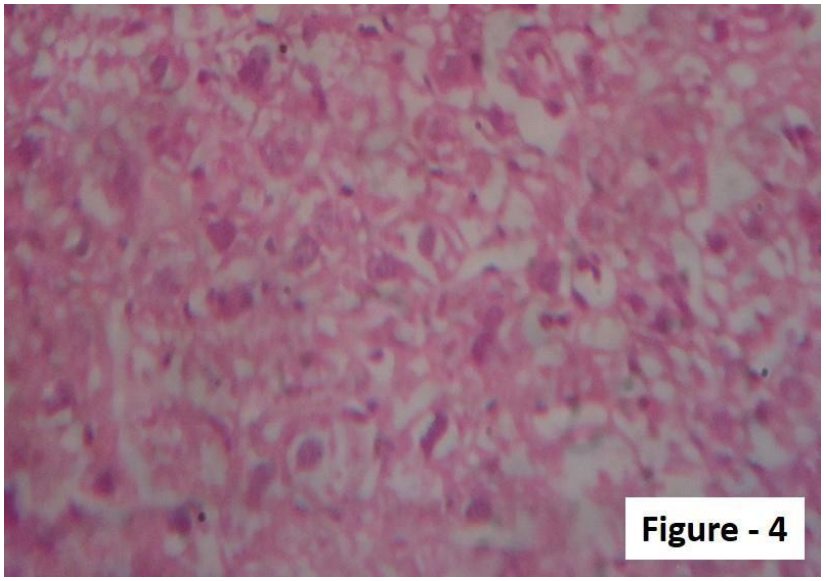


Figure 4: Liver of diabetic mice administered with *Cuminum cyminum* for 8 weeks shows many vacuolated spaces in hepatic cells fragmented nuclei were observed degenerated cytoplasm of hepatic cell were also observed.

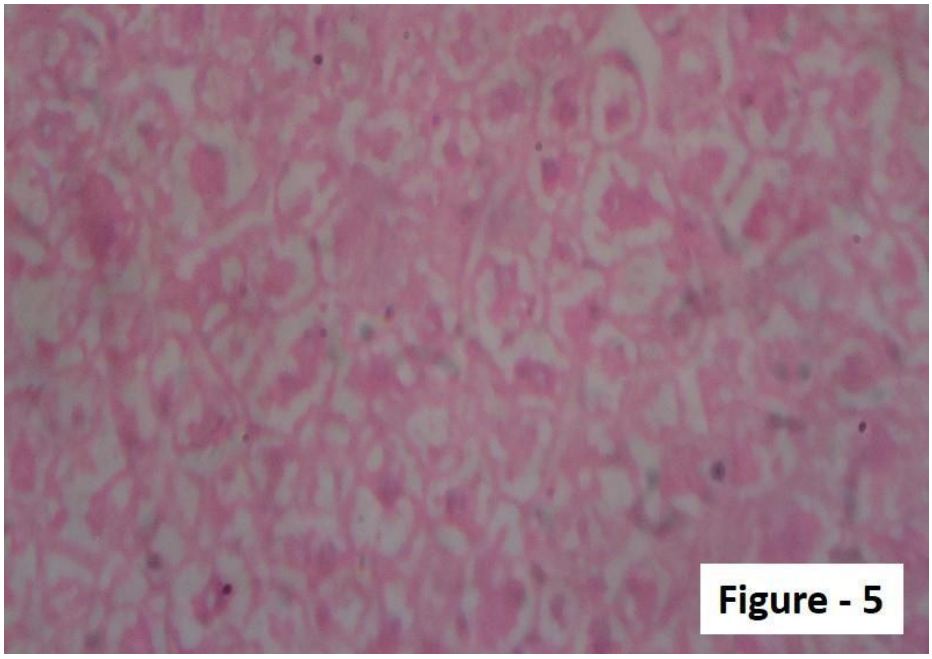


Figure 5: Liver of diabetic mice administered with *Cuminum cyminum* for 12 weeks shows degenerated cytoplasmic & nucleus of hepatic cells with many vacuolated spaces.

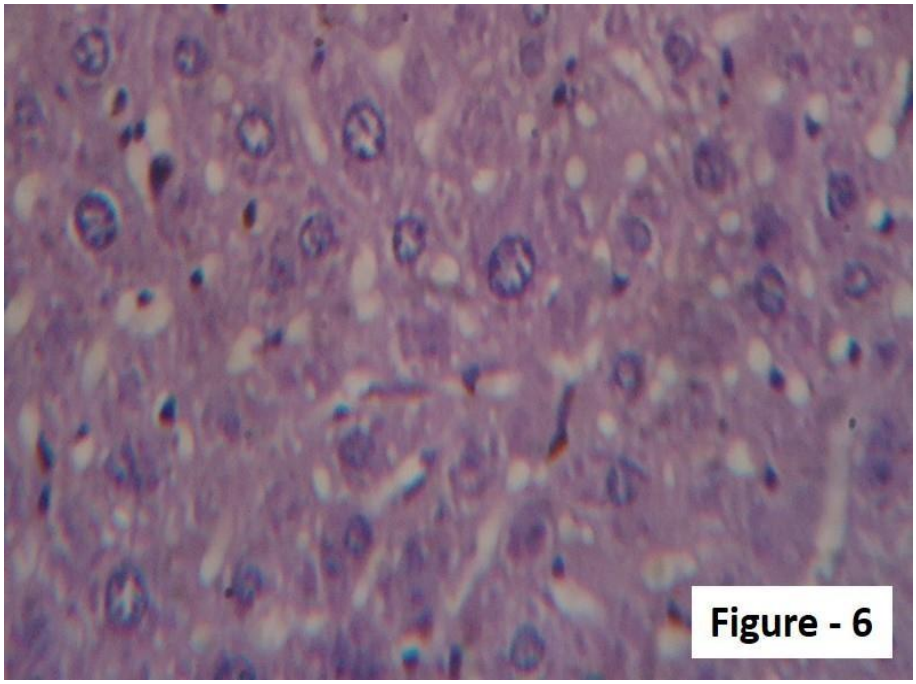


Figure 6: Liver of diabetic mice administered with *Cuminum cyminum* for 16 weeks showing restoration in nuclear material to some extent many vacuolated space were observed in hepatic cells multinuclear hepatic cells were observed.

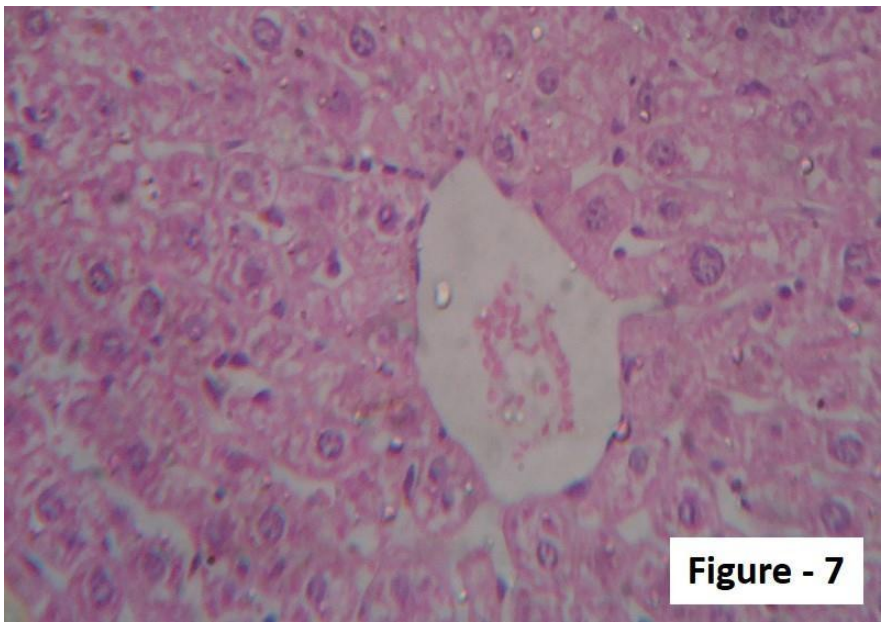


Figure 7: Liver of diabetic mice administered with *Zanziber officinal* for 4 weeks shows little restoration in central vein with cirrated inner walls fragmented nuclear material were also observed with many vacuolated spaces.

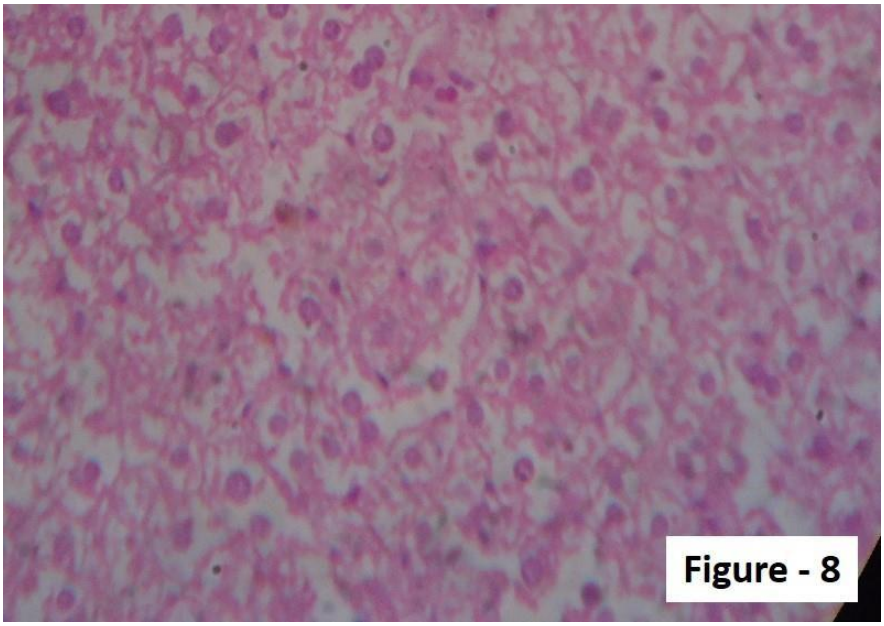


Figure 8: Liver of diabetic mice administered with *Zingiber officinale* for 8 weeks shows degenerated hepatic cells, multiple nucleated hepatic cells were observed many vacuolated space were observed in cytoplasmic spaces.

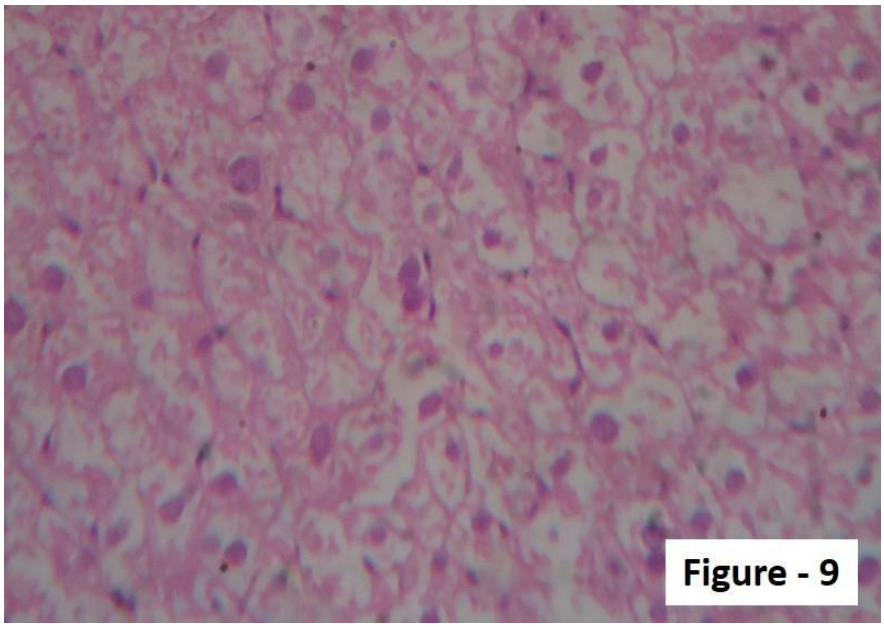


Figure 9: Liver of diabetic mice administered with *Zingiber officinale* for 12 weeks shows fragmented nuclear material with multi nuclear hepatic cells many vacuolated space were observed in hepatic cells denoted complete degeneration of cytoplasmic and nuclear material.

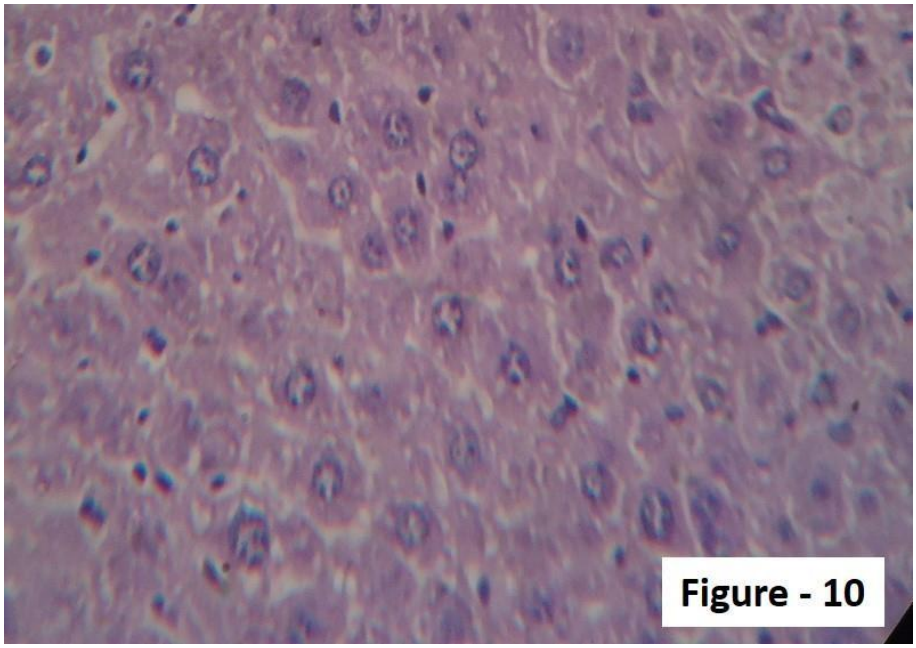


Figure: 10 Liver of diabetic mice administered with *Zingiber officinale* for 16 weeks shows restoration in nuclear material to some extend few vacuolated space were observed with degenerated cytoplasmic material of hepatic cells.

DISCUSSION

Diabetes can damage blood vessels, resulting in serious health complications such as high blood pressure, heart disease and stroke, blindness, kidney failure and amputations (National Diabetes Statics Report 2014). Diabetes also causes nephropathy and anomalies in peripheral nervous system. There is, however, a growing appreciation that damage to the spinal cord (Selvarajah *et al, 2006*). Diabetes is a chronic disorder of glucose metabolism occur due to dysfunction of insulin secretion from pancreatic β cells (Rahim. and Jamal, 2009). In the present study, increase in level of SGPT, uric acid and urea, and degeneration in hepatic cells were observed in diabetic group. Ginger enhances blood circulation throughout the body by stimulating the heart muscle and by diluting circulating blood. This enhances cellular metabolism and helps to relief cramp and tension (Gong et al., 1989; Pecoraro et al., 1998; Frisch et al., 1995; Yamahara et al., 1989; Ernst and Pittler, 2000; Chaiyakunapruk et al., 2006). There are many studies which prove hypotensive effect of ginger when it was given at 0.3-3 mg/kg. It helps to reduce atrial blood pressure by blocking calcium channel or by acting on muscarinic receptor (Ernst and Pittler, 2004; Portoni et al., 2003; Ozgoli and Goli, 2009; Vutyavanich et al., 2001). We observed effective restoration in SGPT, urea, and uric acid in our study. Effective restoration was also observed in hepatic cells and central vein.

Cumin promotes bile secretion and stimulates detoxification of harmful substances in order to keep our liver healthy (Kaur and Sharma, 2012). Cumin seeds have been also used by patients to suppress coughs, disintegrate renal calculi and retard the carcinogenic process (Hosseinzadeh et al., 2007). Dietary cumin also countered other metabolic alterations as revealed by lowered blood urea level and reduced excretions of urea and creatinine by diabetic animals (Willatgamuva, 1998). Cuminaldehyde and cuminol increases insulin secretion many folds. The insulinotrophic action of both components was glucose-dependent and due to the closure of the ATP-sensitive K channel and the increase in intracellular Ca^2 concentration (Patil, 2013). In our study cumin shows effective restoration in liver function and kidney function test. Hepatic nuclei and cytoplasmic material are effectively restored.

CONCLUSIONS

From the present study, it is concluded that *Cuminum cyminum* restored glucose level LFT and KFT, and hepatic cells and sinusoid effectively in diabetic mice, whereas *Zingiber officinale* restored only glucose and urea levels effectively. Uric acid and SGPT level are not restored effectively in ginger group. Thus it is evident from the study that *Cuminum cyminum* acts effectively on LFT- KFT and histology of liver of diabetic mice in compared to *Zingiber officinale* administered mice group.

ACKNOWLEDGEMENTS

Authors sincerely thank Mahavir Cancer Sansthan and Research Center for allowing us to undertake the present work and also for providing laboratory and infrastructure facilities. We also thank to all technical staff and animal house staff of the Mahavir Cancer Sansthan and Research Center and staff of P. G. Department of Biotechnology, T. M. Bhagalpur University for their support for this study.

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