

Original Article

Evaluation of Antihyperglycemic Potential of Homeopathic Medicines *Insulinum 6CH*, *Pancreatinum 6CH* and *Uranium nitricum 6CH* in Streptozotocin-induced diabetic Rats

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Abstract

Introduction *Diabetes Mellitus* is an emerging endocrine and metabolic disorder which has affected millions of people globally. Homeopathic system of medicine uses ultra-molecular doses for treatment of *Diabetes Mellitus*. Homeopathic medicines are prepared from plant, mineral, sarcodes, nosodes and animal parts. *Insulinum 6 CH*, *Pancreatinum 6 CH* and *Uranium nitricum 6 CH* are used in homeopathy for treatment of *Diabetes Mellitus*. However, no preclinical studies have been investigated for the anti-diabetic effect and its safety. **Methods** Homeopathic medicines *Insulinum 6CH*, *Pancreatinum 6CH* and *Uranium nitricum 6CH* (10^{12}) dilution factor were used to examine antihyperglycemic effects in streptozotocin induced diabetic rats. After 28 days of treatment, bodyweight, Hematology, Biochemistry (serum glucose, urea, creatinine, SGPT, SGOT, ALP, Triglyceride and HDL-cholesterol), Oral Glucose Tolerance Test, HbA1C with histopathology of (Liver, Kidney, Pancreas) were measured. **Results** After Streptozotocin induction, the animals have shown significant increase in the fasting blood glucose level ($p < 0.01$) as compared to normal control animals. Treatment with homeopathic medicine *Insulinum 6CH*, *Pancreatinum 6CH* and *Uranium nitricum 6CH* potency showed significant decrease in levels of Glucose ($p < 0.05$), OGTT, Total protein ($P < 0.001$), ALP ($P < 0.05$), Cholesterol ($P < 0.001$), SGPT ($P < 0.001$), SGOT ($p < 0.01$), Urea, HbA1C as compared to diabetic animal. **Conclusions** In the present study homeopathic medicine *Insulinum 6CH*, *Pancreatinum 6CH* and *Uranium nitricum 6CH* potency exhibit antihyperglycemic effects in streptozotocin induced diabetic rats.

Keywords: Antihyperglycemic, Homeopathy, Mineral, Streptozotocin, Sarcodes

Introduction

Diabetes mellitus (DM) is a metabolic disorder impacting gradually on the lifestyle and health of patients all over the globe. DM is triggered by dysfunction of beta cells of pancreas which leads to decrease the production of hormone insulin and/or increased resistance to the action of insulin in the peripheral tissues with initial impaired glucose tolerance and can further lead to severe symptoms. Long standing history of DM leads to serious complication like Diabetic Retinopathy, Diabetic Nephropathy, Diabetic Neuropathy etc., needing immediate medical attention (1).

The oral antihyperglycemic agents are routinely prescribed and found effective in managing high blood sugar levels. Metformin is always preferred as first line of oral antihyperglycemic agent, with other options available for second line of oral antihyperglycemic agents when the recommended dosage of metformin gets resistance which consist of sulphonylureas, thiazolidinediones (TZD),



Alpha-glucosidase inhibitors, dipeptidyl peptidase-4 (DPP-IV) inhibitors and sodium glucose co-transporter 2 (sglt2) inhibitors (2). However, these drugs in their long term consumptions have been associated with side effects like abdominal discomfort, metallic taste, diarrhea, loss of appetite etc. Consequently, there is a need for discovering new drugs with safety profiles and minimal side effects for management of DM (3).

Homeopathic medicine in ultra- high dilution doses are used for the treatment of various metabolic disorders (4). This science works on the 'principal of similar' i.e 'Similia similibus curentur' which was discovered by a German physician Samuel Hahnemann (1755 – 1843) (5). The use of animal models with various targeted biomarkers are introduced in understanding the scientific evidence-based actions of the homeopathic medications (6). Homeopathic medicines are prepared from various sources like plants, animals, minerals, sarcodes, nosodes, imponderabilia etc.

Syzygium jambolanum and *Cephalandra indica* in its homeopathic preparations have been investigated for its antioxidative stress effects and antidiabetic effects in preclinical studies, both in vitro and in vivo (7,8,9).

Sarcodes and mineral source medicine in homeopathy is also prescribed for the management of DM. Sarcodes are a source of homeopathic preparation from healthy animal tissues and secretion from glands which contain biological molecules with specific physiological functions in human. Sarcodes are studied under preparation from whole endocrine glands e.g *Thyroidinum*, preparation from healthy secretion and enzyme e.g *Insulinum*, preparation from extract e.g *Pancreatinum* and other miscellaneous e.g *Cholesterinum*. For the management of DM in clinical practice *Insulinum 6CH*, *Pancreatinum 6CH* and *Uranium nitricum 6CH* are used in homeopathy. However, there had been no experimental studies conducted with these sources in homeopathy for evaluating its pharmacological activities.

The aim of this research study is to evaluate the antihyperglycemic potentials of homeopathic medicines *Insulinum 6CH*, *Pancreatinum 6CH* and *Uranium nitricum 6CH* in streptozotocin induced diabetic rats.

Materials and Methods

Materials and study settings

The chemicals and reagents used in this study were of analytical grade and were procured from DELTA LAB. The study was conducted at APT RESEARCH FOUNDATION S.N.36/1/1, M.N.199, VADGAON KHURD, PUNE 411041, MAHARASHTRA, INDIA. The study was approved by Institutional animal ethical committee (IAEC) with approval number RP34/1718 approval date 8/ august/ 2017.

Homeopathic remedies

Homeopathic remedies (*Insulinum 6CH* (Ethanol content: 90%), *Pancreatinum 6CH* (Ethanol content: 90%) and *Uranium nitricum 6CH* (Ethanol content: 90%) were procured from GMP approved pharmaceutical manufacture St. George Co. P. vt. Ltd, Mangalore, India. The following mentioned potencies were identified by APT Research study personnel as physical state: Liquid, Colour: Colourless, Quantity: 100ml and were preserved in amber color glass bottles kept at room temperature.

Dose selection and preparation



Systematic review was conducted with search key words as Homeopathy, Homoeopathy, Diabetic rats and in vivo. Based on previous studies through published literature we selected the dose for the study as 62 µl for 100gm of animal weight i.e. 620 µl/ kg of the Homeopathic medicines (Ethanol content: 90%) to check its efficacy. Glibenclamide was used at a concentration of 10mg/kg bw. So, the glibenclamide was suspended in distilled water to obtain the concentration of 1 mg/ml.

Induction of Diabetes

Streptozotocin (STZ) was given at dose of 30 mg/kg bw subcutaneously in Citrate buffer (pH 4.5). So for 30 animals (200 g weight) the STZ was suspended in citrate buffer to obtain the concentration of 6mg/ml. After streptozotocin induction, the animals have shown significant increase in the fasting blood glucose levels ($p < 0.01$) as compared to Normal Control animals. The surviving rats showing more than 300mg/dl blood glucose were selected for this experiment (10).

Animal and Animal care

Healthy male Sprague Dawley rats, weighting between 150 to 180g were used for this study. The rats were housed in their cages for five days prior to start of dosing in the experimental room after veterinary examination. Room temperature maintained between $22 \pm 3^{\circ}\text{C}$, relative humidity 50-60 % and illumination cycle set to 12 hours light and 12 hours dark. Three rats per cage housed in polypropylene cages with stainless steel grill top, facilities for food and water bottle, and bedding of clean paddy husk. Pelleted feed by APT RESEARCH FOUNDATION. Potable water passed through 'AquaGuard' water filter was provided *ad libitum* in plastic bottles with stainless steel sipper tubes. Experiments were conducted following the guidelines of Institutional Animal Ethics Committee (IAEC).

Experimental design

Initially 36 rats were administered Streptozotocin at a dose of 30mg/kg subcutaneously to undergo induction of *Diabetes mellitus*. The surviving rats showing more than 300mg/dl blood glucose were divided into 5 groups excluding Normal Control:

Group 1(NC): Normal Control (No treatment)

Group 2(DC): Disease Control (STZ 30mg/kg s.c.)

Group 3(STD): Diabetic rats +Marketed Standard drug (Glibenclamide 10mg/kg)

Group 4(T1): Diabetic rats + *Insulinum* 6CH potency

Group 5(T2): Diabetic rats + *Pancreatinum* 6CH potency

Group 6(T3): Diabetic rats + *Uranium nitricum* 6CH potency

At the end of the study blood was withdrawn of the fasted animals. After collection, blood was allowed to stand for 30 minutes and then the serum was separated by Centrifugation at 2500 rpm for 10 minutes using an Eppendorf cooling centrifuge. The clear supernatant obtained was then used for biochemical estimations using commercial kits (Coral Biosystems, India).

After streptozotocin (STZ) induction, the animals have shown significant increase in the fasting blood glucose levels ($p < 0.01$) as compared to Normal Control animals (Table 2). These animals were then randomly divided into five groups viz. Disease control (DC), Standard group (STD) and T-1, T-2 and T-3 respectively.

Experimental Parameters

Serum blood glucose, Oral Glucose Tolerance Test (OGTT), HbA1c – (glycosylated haemoglobin) and body weight estimation

Serum blood glucose, oral glucose tolerance test (OGTT) and HbA1c – (glycosylated haemoglobin) were performed. Blood samples were obtained from the tail vein under mild ether anesthesia. Briefly, rats were fasted overnight and the baseline blood glucose was determined next day with the help of an automated glucometer (Accucheck active) (11,12). Body weight gain was measured before and after the completion of experiment.

Measurement of lipid profile, total protein and hematological parameters

Serum lipid profile like serum levels of triglycerides (TG)(13), total cholesterol (TC)(14) and high density lipoprotein cholesterol (HDLc)(15) and total protein (16) were estimated biochemically using specific kits in this concern. Hematological parameters like red blood count (RBC), haemoglobin (HGB), haematocrit (HCT), platelet (PLT), white blood cells (WBCs), and white blood cell differential counts were also estimated.

Organ weight, Liver and kidney parameters

The concentration of Urea (17), Creatinine (18), SGPT and SGOT levels (19) and ALP (Alkaline phosphatase) (20) were estimated biochemically using specific kits in this concern. The organ-to-body weight ratio was determined by comparing the weight of each organ with the final body weight of each rat.

Histopathology

After euthanasia, animals were dissected out and the pancreas, liver and kidney were fixed in 10% formalin for monitoring necropsy or adverse effect of the treatment. The tissues were then processed by undergoing a series of steps that includes fixation, dehydration, clearing, wax impregnation, embedding & subsequent sectioning on the microtome (21, 22). The histopathology was conducted at INNOVET DIAGNOSTIC LABORATORY (SPECIALIZED VETERINARY PATHOLOGY LABORATORY) Registration No. MSVC-6589, Kothrud, pune, Maharashtra, India.

Statistical Analysis

The results were analyzed for statistical significance by one-way ANOVA and were expressed as Mean \pm SEM (n = 6) by using Graphpad prism 5 version Bonferroni post-test (Compare all pairs of column test). P values < 0.05 and less were considered as statistically significant.

Results

Effect of Homeopathic medicines on body weight



Body weight was measured weekly during the study period of 28 days. There was statistical change observed in the body weights of animals as compared to DC on Day 14 ($p<0.01$) and Day 21 ($p<0.01$) for T-1; Day 14 ($p<0.001$), Day 21 ($p<0.001$) and Day 28 ($p<0.01$) for T-2; Day 14 ($p<0.001$), Day 21 ($p<0.001$) and Day 28 ($p<0.001$) for T-3.(Table 1).

Table 1 - Body weight

Group	0 Day (Mean \pm SEM)	7 th Day (Mean \pm SEM)	14 th Day (Mean \pm SEM)	21 st Day (Mean \pm SEM)	28 th Day (Mean \pm SEM)
NC	199.3 \pm 19.7	204.2 \pm 20.4	207.5 \pm 20.2	216.8 \pm 19.9	236.8 \pm 25.1
DC	206.5 \pm 24.6	202.3 \pm 22.4	170.0 \pm 36.7	180.0 \pm 25.2	189.6 \pm 27.4
STD	192.7 \pm 18.1	179.3 \pm 32.3	174.2 \pm 42.8	186.3 \pm 37.8	207.2 \pm 43.9
T1	194.7 \pm 34.2	220.8 \pm 32.8	231.8 \pm 28.6	236.5 \pm 25.7	*241.3 \pm 23.9
T2	220.7 \pm 11.3	232.7 \pm 10.0	242.1 \pm 17.0	245.2 \pm 22.4	*252.2 \pm 20.9
T3	220.0 \pm 17.9	227.3 \pm 16.5	240.0 \pm 12.7	251.0 \pm 22.6	*263.0 \pm 30.2

Values are expressed in mean \pm SEM (n=6 in each group). Data were analyzed by one-way ANOVA. Results compared with disease control showed ($p<0.01$) significant for T1, ($p<0.001$) significant for T2 and ($p<0.001$) significant for T3.

Effect of homeopathic medicine on glucose level

The Glucose levels were weekly monitored in all animals. On 28th day, the glucose levels were found to be significantly decreased ($p<0.01$) in T-1, T-2 and T-3 group in comparison with DC and STD. (**Table 2**) The oral glucose tolerance test was performed on Day 14 and Day 28. On 28th day there was statistically significant ($p<0.05$) reduction in the glucose levels of T-1, T-2, T-3 group animals at 2nd hr as compared to DC and STD (**Table 3**).

Table 2 -Glucose (mg/dl)

Group	0 Day (Mean \pm SEM)	7 th Day (Mean \pm SEM)	14 th Day (Mean \pm SEM)	21 st Day (Mean \pm SEM)	28 th Day (Mean \pm SEM)
NC	120.7 \pm 2.8	123.5 \pm 3.3	120.8 \pm 4.4	120.2 \pm 3.4	115.2 \pm 7.9
DC	357.0 \pm 23.0	351.8 \pm 31.8	341.7 \pm 44.5	296.4 \pm 43.1	354.6 \pm 51.9
STD	357.7 \pm 68.6	331.3 \pm 58.0	291.7 \pm 48.1	276.0 \pm 66.9	275.7 \pm 48.4
T1	331.2 \pm 102.0	301.3 \pm 117.7	272.8 \pm 115.6	147.5 \pm 101.9	*241.3 \pm 134.7
T2	330.8 \pm 67.5	246.7 \pm 89.2	213.6 \pm 60.8	153.0 \pm 40.6	*93.8 \pm 20.2
T3	332.3 \pm 50.8	269.2 \pm 56.5	253.2 \pm 71.0	234.2 \pm 80.5	*108.8 \pm 104.6

Values are expressed in mean \pm SEM (n=6 in each group). Data were analyzed by one way ANOVA. Result showed ($p<0.01$) significant for T-1, T-2 and T-3 as compared to STD and DC.

Table 3 -Oral Glucose Tolerance Test (mg/dl)

Day	Hours	NC	DC	STD	T1	T2	T3
14 th	0 hr	120.8±4.4	341.7±44.5	291.7±48.1	243.5±87.9	225.6±54.7	268.8±46.1
	½ hr	145.8±4.9	437.2±38.9	400.7±77.7	328.0±105.8	471.7±11.0	540.8±134.4
	1 hr	137.8±4.0	393.5±35.0	329.5±80.3	292.9±96.7	347.3±30.2	453.0±125.8
	2 hr	125.5±3.4	348.0±48.4	299.0±78.4	258.8±97.5	289.5±54.9	339.7±53.1
28 th	0 hr	115.2±7.9	354.6±51.9	275.7±48.4	241.3±134.7	93.8±20.2	108.8±104.6
	½ hr	146.2±5.3	477.0±95.6	362.6±69.3	357.5±194.4	251.2±76.8	453.2±205.4
	1 hr	135.3±4.7	414.8±80.1	327.8±51.8	312.3±165.1	191.0±73.7	368.2±158.6
	2 hr	120.3±8.4	366.6±61.8	284.7±49.1	*274.3±154.8	*112.4±13.7	*258.8±105.1

Values are expressed in mean ± SEM (n=6 in each group). Data were analyzed by one way ANOVA. Result showed (p<0.05) significant for T-1, T-2 and T-3 as compared to STD and DC.

Effect of homeopathic medicine on biochemical parameters

At the end of the study blood was collected for hematology and serum was analyzed for various parameters viz. Creatinine (Figure 1), Total Protein (TP) (Figure 2), Alkaline Phosphatase (ALP) (Figure 3), Cholesterol (CHOL) (Figure 4), Triglycerides (TGL) (Figure 5), Serum glutamic pyruvic transaminase (SGPT) (Figure 6), Serum glutamic-oxaloacetic transaminase (SGOT) (Figure 7), High-density lipoproteins (HDL) (Figure 8) and Urea (Figure 9). In hematological parameters there was no statistically significant change observed in all groups when compared to DC (Table 4). There was no significant change observed in levels of Creatinine, triglycerides and HDL in any treatment when compared to DC and NC. Further, levels of Total protein found to be increased in DC compared to NC while with T-1 (p<0.001), T-2 (p<0.01), T-3 (p<0.001) it reduced to normal levels when compared to DC.

Table 4 - Hematology

Groups	WBC (10 ³ /μl)	RBC (10 ⁶ /μl)	HGB (g/L)	HCT (%)	PLT (10 ³ /μl)
NC	7.5±0.7	8.0±0.4	13.4±1.2	41.7±4.0	616.7±91.3
DC	7.5±0.5	7.1±0.6	11.9±0.6	39.3±2.2	489.2±57.2
STD	7.6±0.5	7.8±0.4	13.0±0.7	41.5±1.7	528.2±74.0
T1	7.6±0.1	8.1±1.7	13.9±2.5	42.2±8.3	409.5±105.5
T2	7.4±0.3	8.5±0.5	15.2±1.8	43.4±3.5	460.4±60.9
T3	7.4±0.5	8.1±1.4	14.5±2.8	41.7±7.5	444.6±136.2

Values are expressed in mean ± SEM (n=6 in each group). Data were analyzed by one way ANOVA. No significant changes seen in hematological parameters when compared with disease control. WBC: White blood cell, RBC: Red blood cell, HGB: Haemoglobin, HCT: Hematocrit, PLT: Platelets

Similarly, ALP levels were increased in DC while treatment T-1 ($p<0.001$), T-2 ($p<0.01$) and T-3 ($p<0.05$) restored it. Cholesterol levels were also found to be elevated in DC and found to be restored on treatment with T-1 ($p<0.01$), T-2 ($p<0.001$) and T-3 ($p<0.001$). DC showed increased levels of SGPT treatment and it was depleted with treatment of T-1 ($p<0.01$), T2 ($p<0.01$) and T3 ($p<0.001$). In similar manner, SGOT levels were also found to be decreased in T-1 ($p<0.05$), T-2 ($p<0.05$) and T3 ($p<0.01$) treated groups when compared to DC. Urea levels found to be increased in DC while treatment with T-1 ($p<0.05$) and T-2 ($p<0.01$) the levels were restored back to normal. Levels of glycosylated hemoglobin (HbA1c) were elevated in DC and found to be restored with T-1 ($p<0.01$) and T2 ($p<0.001$) treatment (Figure 10).

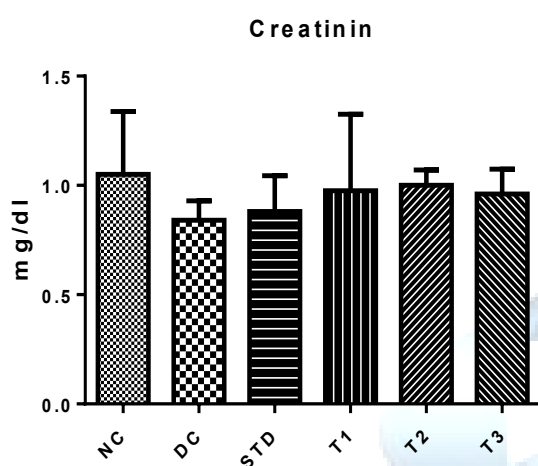


Figure 1

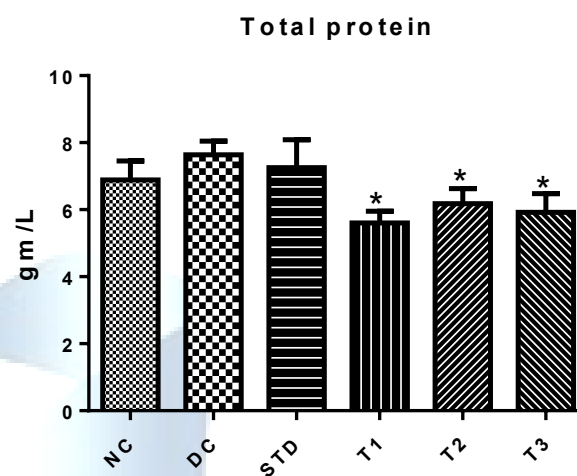


Figure 2

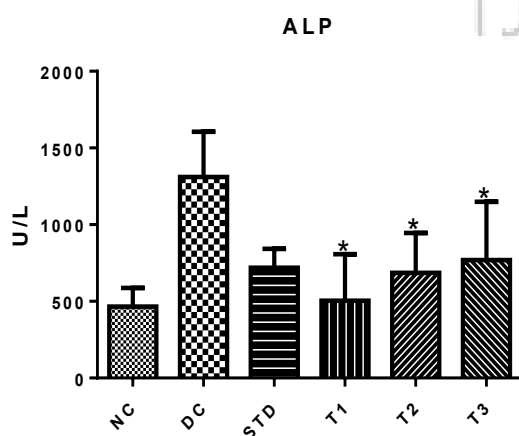


Figure 3

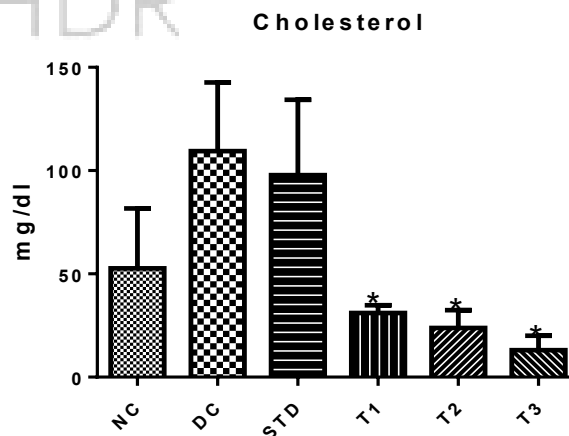


Figure 4

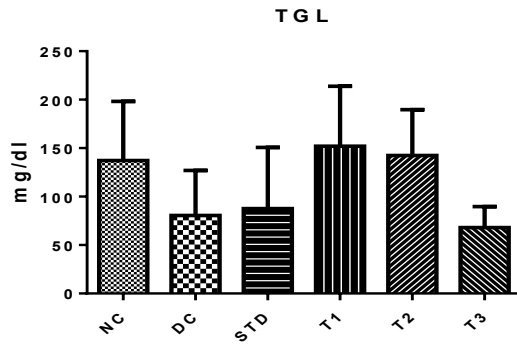


Figure 5

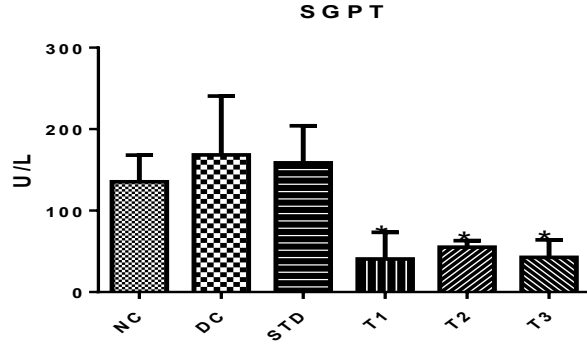


Figure 6

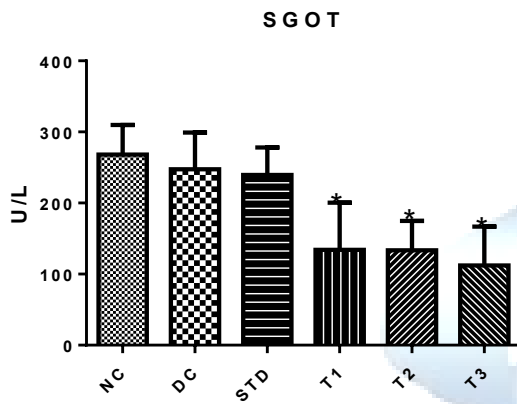


Figure 7

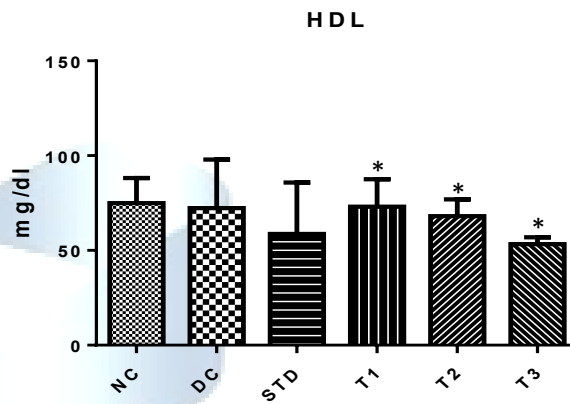


Figure 8

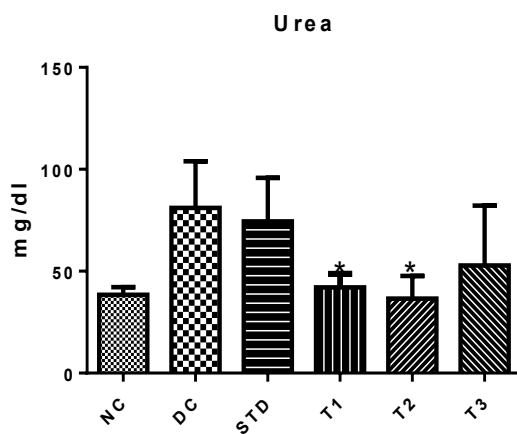


Figure 9

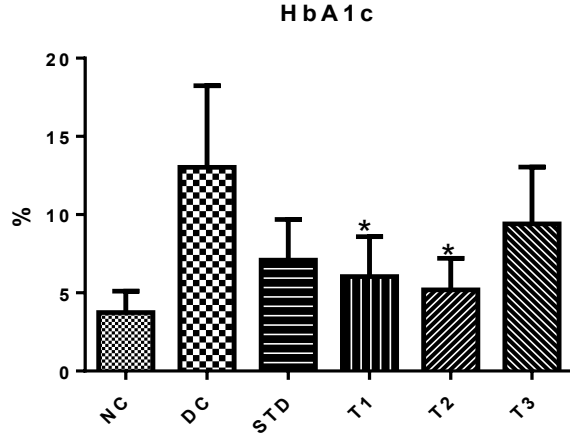


Figure 10

Values are expressed in mean \pm SEM (n=6 in each group). Data were analyzed by one-way ANOVA. Results showed significant changes for T-1 ($p<0.001$), T-2 ($p<0.01$) and T-3 ($p<0.001$) in TP; Significant changes in ALP for T-1 ($p<0.001$), T-2 ($p<0.01$) and T-3 ($p<0.05$); Significant changes in CHOL for T-1 ($p<0.01$), T-2 ($p<0.001$) and T-3 ($p<0.001$); Significant changes in SGPT for T-1 ($p<0.01$), T2 ($p<0.01$) and T3 ($p<0.001$); Significant changes in SGOT for T-1 ($p<0.05$), T-2 ($p<0.05$) and T3 ($p<0.01$); Significant changes in Urea for T-1 ($p<0.05$) and T-2 ($p<0.01$); Significant changes in HbA1c for T-1 ($p<0.01$) and T2 ($p<0.001$).

Effect of homeopathic medicine on relative organ weight

The relative organ weight data has also shown non-significant changes in the organ weights of animals in comparison with DC (Table 5).

Table 5 - Relative Organ weight (gm)

Groups	Adrenals	Heart	Kidneys	Liver	Spleen	Lungs	Gonads	Brain	Pancreas
NC	0.039 \pm 0.010	0.366 \pm 0.032	0.753 \pm 0.107	3.675 \pm 0.419	0.407 \pm 0.113	0.817 \pm 0.212	0.887 \pm 0.268	0.689 \pm 0.074	0.246 \pm 0.067
DC	0.043 \pm 0.014	0.397 \pm 0.049	1.081 \pm 0.268	4.513 \pm 0.600	0.510 \pm 0.047	0.612 \pm 0.128	0.995 \pm 0.538	0.741 \pm 0.119	0.266 \pm 0.073
STD	0.038 \pm 0.014	0.353 \pm 0.051	0.974 \pm 0.198	4.480 \pm 0.711	0.446 \pm 0.050	0.969 \pm 0.591	0.845 \pm 0.273	0.715 \pm 0.170	0.221 \pm 0.054
T1	0.031 \pm 0.005	0.359 \pm 0.121	0.770 \pm 0.109	3.671 \pm 0.617	0.361 \pm 0.055	0.683 \pm 0.158	0.854 \pm 0.206	0.709 \pm 0.195	0.330 \pm 0.087
T2	0.035 \pm 0.008	0.396 \pm 0.045	0.891 \pm 0.062	3.939 \pm 0.882	0.371 \pm 0.065	0.653 \pm 0.095	1.234 \pm 0.163	0.609 \pm 0.065	0.324 \pm 0.062
T3	0.031 \pm 0.004	0.481 \pm 0.080	0.899 \pm 0.124	3.581 \pm 0.810	0.371 \pm 0.073	0.569 \pm 0.168	1.114 \pm 0.171	0.597 \pm 0.120	0.248 \pm 0.067

Values are expressed in mean \pm SEM (n=6 in each group). Data were analyzed by one-way ANOVA. No significant changes seen in relative organ weight when compared with DC.

Histopathology of Liver

DC had focal degenerative changes in the hepatic parenchyma with presence of cellular swelling and karyomegaly of hepatocytes as compared to NC. STD showed normal hepatic parenchyma with normal histomorphology of hepatocytes and portal vascular tissue, minimal focal congestion of portal vessel and focal degenerative changes of few hepatocytes only as compared to disease control, while T-1, T-2 and T-3 showed normal hepatic parenchyma with normal histomorphology of hepatocytes arranged in cord like manner around central vein with presence of normal sized nucleus and intact cellular border but focal congestion of portal vessel and focal occasional degenerative changes of few hepatocytes only (Figure 11).

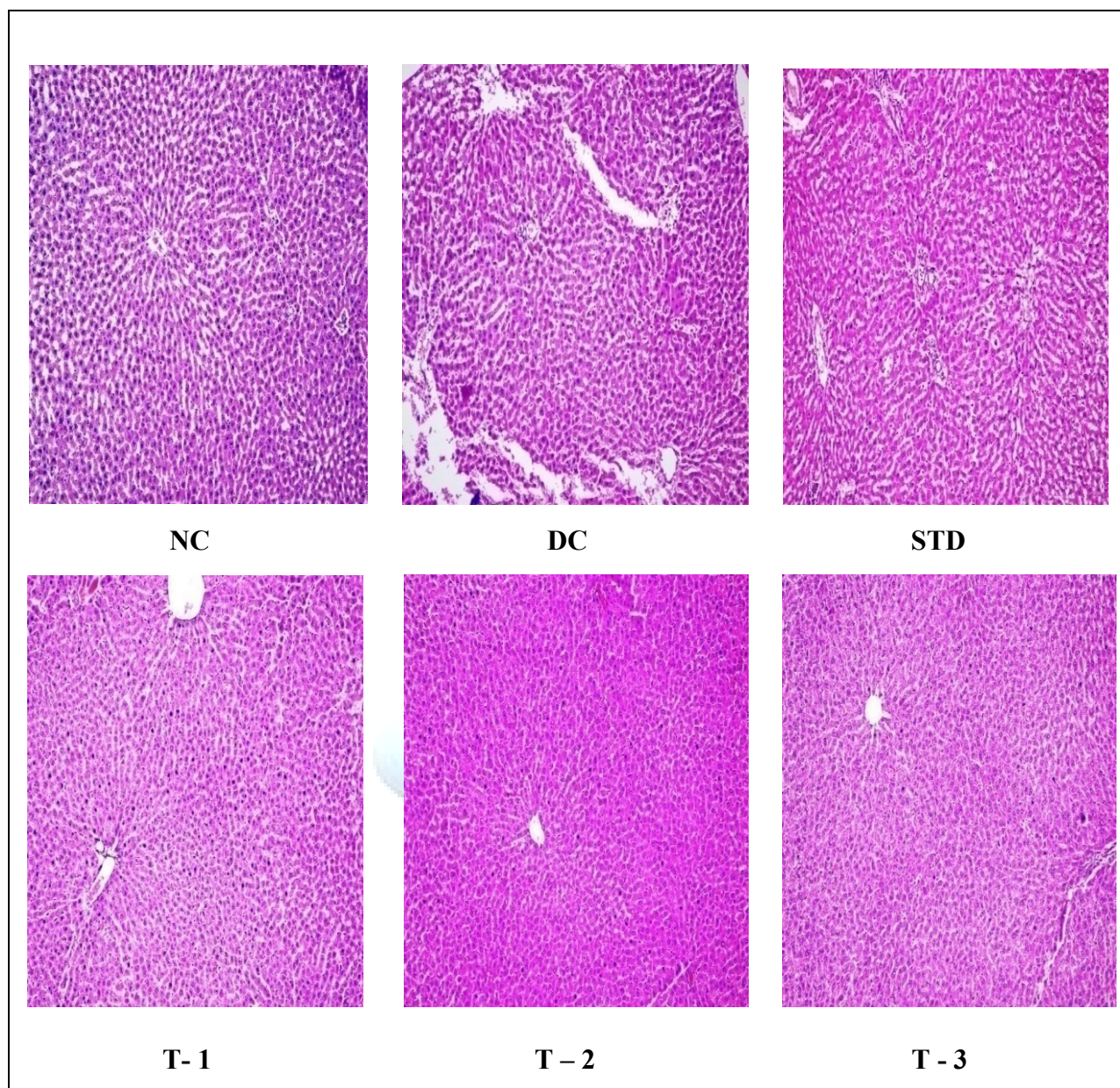


Fig. 11 – Histopathology of Liver

Histopathology of Kidney

DC had focal congestion of vessels in renal parenchyma, diffuse foci of cellular swelling of renal tubules with presence of granular cytoplasmic changes in the epithelium of tubules with these there was eosinophilic cellular debris in the lumen of few renal tubules in cortical region with degenerative foci of nephrosis and nephritis of renal focal atrophic changes of glomeruli. STD showed normal histomorphology of glomeruli and renal tubules with intact cellular features and intact nucleus in tubules. Minimal focal congestion of vessels in renal parenchyma and focal areas of cellular swelling of renal tubules with presence of granular cytoplasmic changes in the epithelium of tubules is noticed as compared to DC. While T-1 showed normal histomorphology of glomeruli and renal tubules with

intact cellular features and intact nucleus in tubules with minimal focal congestion of vessels in renal parenchyma and focal area of cellular swelling of renal tubules with presences of granular cytoplasmic changes in the epithelium of tubules as compared to disease control. T-2 and T-3 showed normal histomorphology of glomeruli and renal tubules with intact cellular features and intact nucleus in tubules with absence of degenerative or necrotic or inflammatory changes in the section compared to DC (Figure 12).

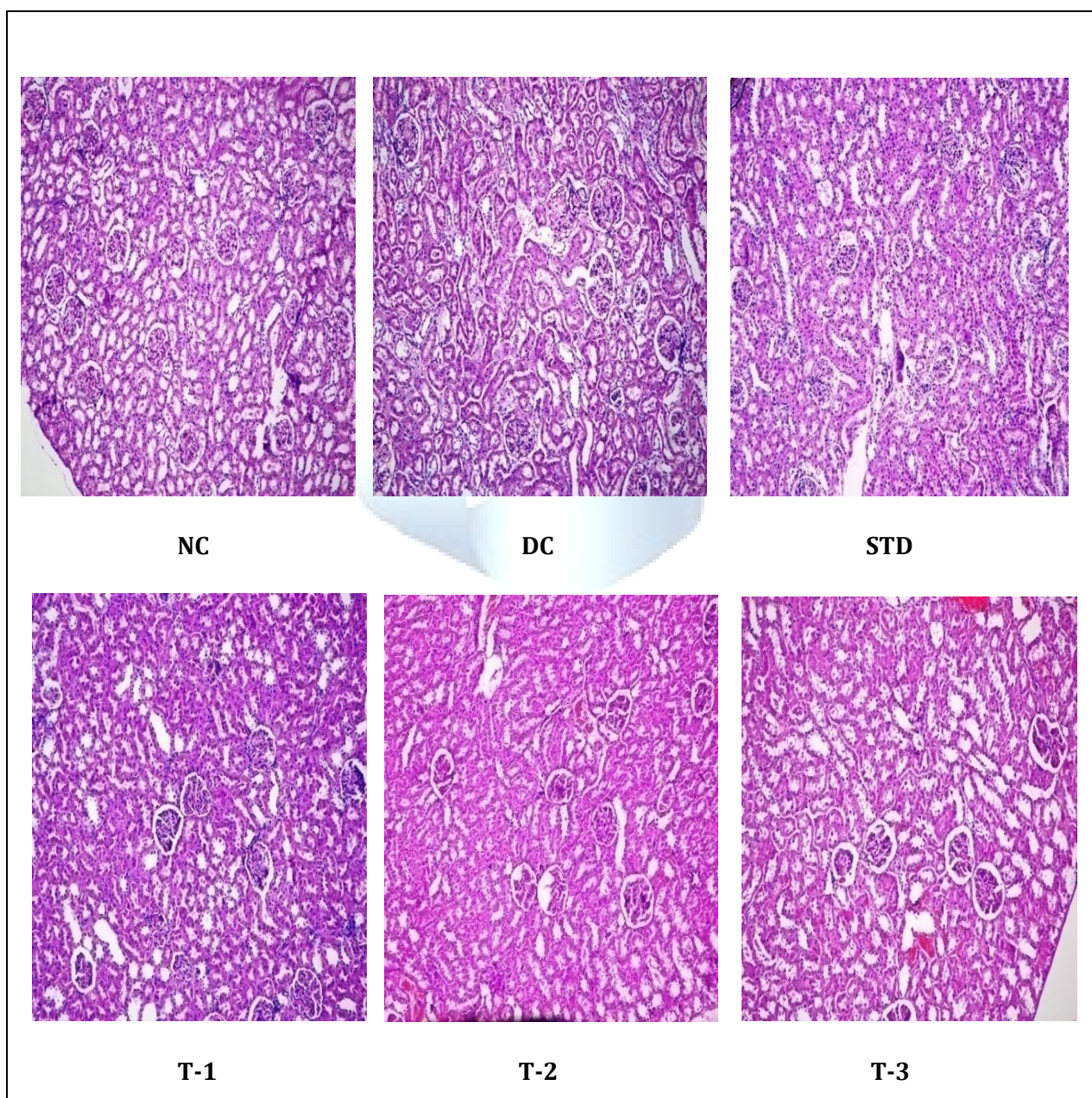


Fig. 12 – Histopathology of Kidney

Histopathology of Pancreas

DC had diffuse foci of degenerative changes of endocrine pancreas with loss of beta cells in the islets of Langerhans with cellular swelling of beta cells with degenerative vacuolar changes was noted in many islets. Reduced number of beta cellular mass in the islets was noted, focal atrophic changes of few beta cells were also noted in few islets. STD showed few focal degenerative vacuolar changes in beta cells with normal histopathology of exocrine and endocrine pancreas. Numerous islets of Langerhans were observed in the section with adequate number of beta cells of normal histomorphology with intact cellular borders and nucleus (Figure 13).

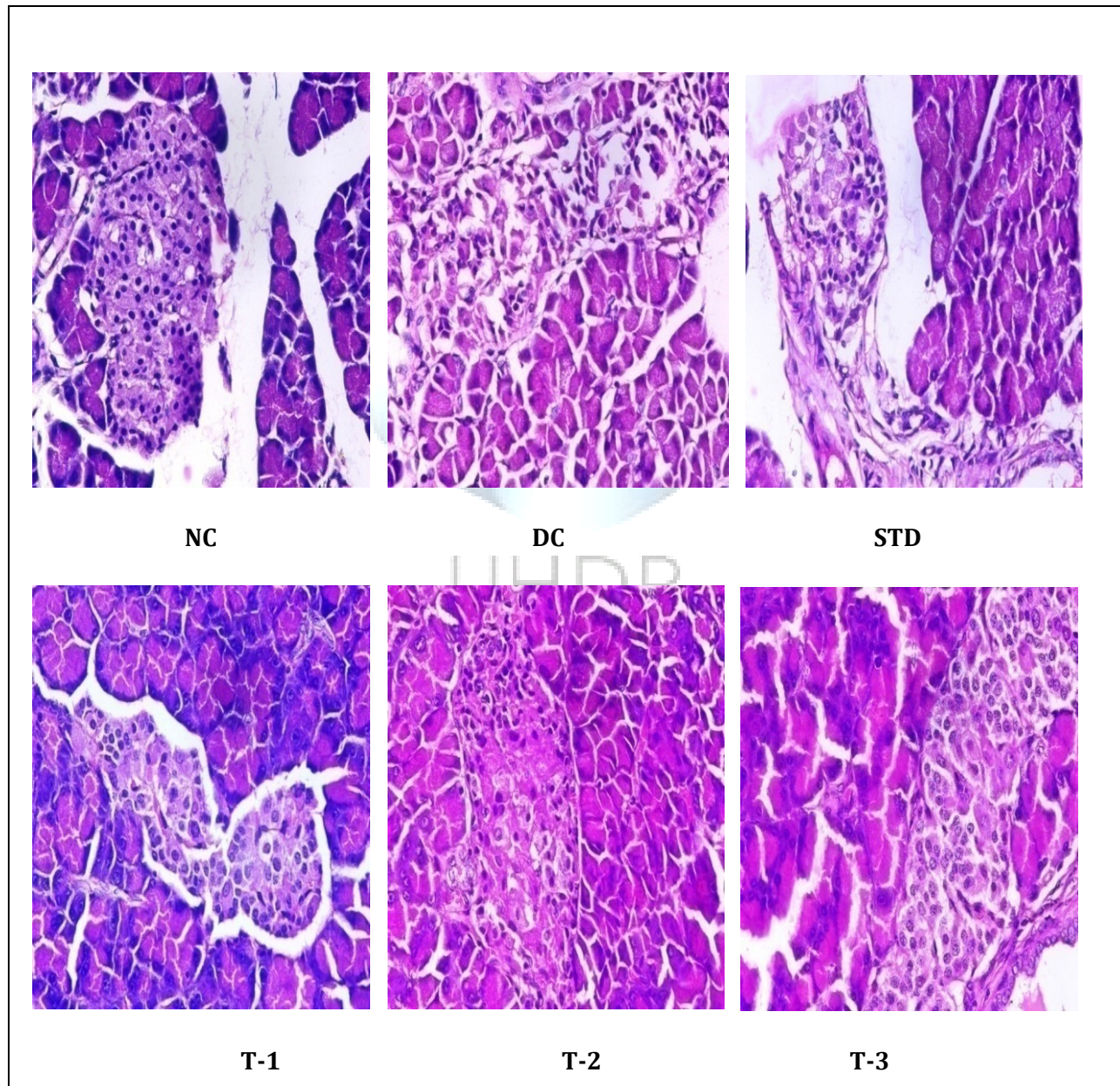


Fig. 13 - Histopathology of Pancreas

Absence of inflammatory changes or degenerative changes in both endocrine and exocrine pancreatic tissue was observed when compared to DC. T-1, T-2 and T-3 showed normal histopathology of exocrine and endocrine pancreas with numerous islets of Langerhans were observed in the section with adequate number of beta cells of normal histopathology with intact cellular borders and nucleus. Absence of inflammatory changes or degenerative changes in both endocrine and exocrine pancreatic tissue with few focal degenerative vacuolar changes noted in beta cells only as compared to DC.

Discussion

In our study blood glucose level in STZ induced diabetic rats was lowered after administration of *Insulinum* 6CH (T-1), *Pancreatinum* 6CH (T-2) and *Uranium nitricum* 6CH (T-3) orally. STZ causes swelling in pancreas leading to degeneration in Langerhans islet beta cells which shows conditions of hyperglycemia, hypoinsulinemia and hyperlipidemia (23). Diabetic state caused by STZ is due to generation of free radicals and nitric oxide which impair the function of beta cell (24). The hypoglycemic activity of T-1, T-2 and T-3 might be due to glucose uptake metabolism via inhibition of hepatic gluconeogenesis in adipose tissue (25, 26), the remaining pancreatic beta cells might have stimulated the secretion of insulin. No changes were significant in haematological parameters in STD, T-1, T-2, T-3 when compared to DC.

In diabetic rat, deficiency of carbohydrate for the energy metabolism might have resulted in degradation of structural protein and fats leading to reduction in body weight (27). T-1, T-2 and T-3 showed the blood glucose stabilization effect which prevented the loss of body weight in diabetic rats.

STZ causes massive destruction of pancreatic beta cells which leads to generation of free radicals through oxidation of excessive glucose therefore increasing the HbA1c levels (28). In our study T-1, T-2 and T-3 significantly reduced the HbA1c level in diabetic rats and it might be due to its antioxidative activity (29).

Long term effect of diabetes leads to secondary complications like dyslipidemia which was often discussed during these past decades (30, 31). During diabetes the level of SGPT, SGOT, TP, ALP, CHOL increase and the HDL level decline significantly (32). The abnormal concentration of serum lipids might have arisen due to disturbances in hormone sensitive enzyme, lipase. Since insulin deficiency leads to increase in its concentration which allows the mobilizations of free fatty acid from peripheral fat repository (33). The administration of T-1, T-2 and T-3 significantly restored SGPT, SGOT, TP, ALP, CHOL and HDL levels to their normal values in diabetic rats and it might be due to its lipids lowering activity (34). Therefore, T-1, T-2 and T-3 have significant role against diabetes associated complications.

Conclusion

Based on the above results it can be concluded that homeopathic medicines *Insulinum* 6CH, *Pancreatinum* 6CH and *Uranium nitricum* 6CH exhibit antihyperglycemic effects in streptozotocin induced diabetic rats. Further studies are ongoing in differentiating the exact mechanisms of action of the above-mentioned homeopathic medicines.

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Conflicts of Interest

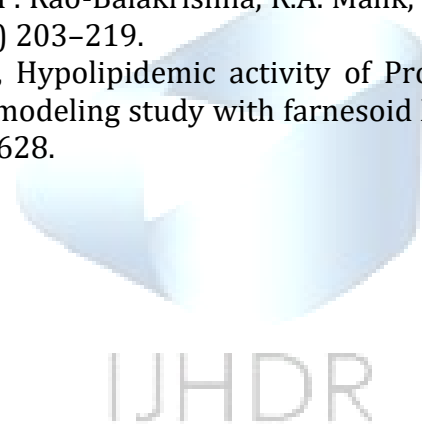
Authors declare no any conflicts of interest

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