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The Potential Effect of the Black Seed (Niagella Sativa) Extract on Heamato-Biochemical Profile on Streptozotocin (STZ) – Induced Diabetic Mice

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Annotation: Context: Diabetes is related with both hematological and biochemical complications. Combination medical treatment has been recommended as a strategy to decrease the influence of these-related complications. Aim: This study was designed to investigate the protective effects of Nigella sativa seed extract (NSSE) on some hemato-biochemical parameters in streptozotocin (STZ)- induced diabetic mice. Method: Streptozotocin (STZ)-induced diabetic mice received medication with Nigella sativa seed extract at doses of 125, 250 and 500 mg/kg or glibenclamide, once a day for 4 weeks. Specimens from blood were taken on day 28 for hematological and biochemistry analysis. The many hematological indices that were examined were , red blood cell count (RBCs), hemoglobin (HB) mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH),packed cell volume (PCV), mean corpuscular hemoglobin concentration (MCHC) and platelets count (PC), the total white blood cell count (WBC) was evaluated, in addition to a differential count of white blood cells, including lymphocytes, neutrophils, monocytes and eosinophils. On other hand, serum biochemical indices analyzed were serum glucose level (Glu), blood urea nitrogen (BUN), cholesterol (Chol), serum creatinine (Crt) ,bilirubin "bile pigment" (Bil), serum protein and enzymes level, alanine phosphate (ALP),alanine transaminase (ALT) ,aspartate transaminase

(AST) total protein (TP) and albumin (ALB). Results: The results showed that Nigella sativa seed extract (NSSE) had positive benefits on hematological profile including, packed cell volume (PCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red blood cells (RBC), among others, while also dramatically lowering blood glucose and cholesterol levels. In addition, it reduced both kidney and liver damage, among other diabetes effects, and might have liver-protective activities. Conclusions: According to the results of this current study, Nigella sativa seed extract (NSSE) significantly effects on certain hemato-biochemical investigations, in comparison with metformin identified as guideline anti- hyperglycemic medication. Subsequently, the herbal extracts under current inquiry could have a role in alleviating the risk of certain chronic complications associated with diabetes.

Keywords: Diabetes mellitus (DM), Nigella sativa seed extract, metformin, hematology, serum blood biochemistry.

Introduction

Throughout history, medicinal plants have been utilized for their biological properties, such as th eir anti-inflammatory, antioxidant, and wound healing properties, to treat a wide range of illnesses (Ullah *et al*., 2020). Certain archeological results approve the fact that therapeutic plants have been used profitably Since ancient times (Leonti *et al*., 2020). According to data from the World Health Organization, approximately 75% of the global population still rely on the usage of therapeutic herbs. This results from the fact that these plants are readily available and reasonably priced, particularly in the developing countries (Salmerón *et al*., 2020). A member of the Ranunculaceae family, *Nigella sativa* (NS), sometimes referred to as black cumin, is an annual flowering plant that is found throughout India, north Africa besides the middle east (Hossain *et al*., 2021). Black cumin is widely recognized for having a wide range of benefits, including analgesic, immunomodulatory, diuretic, and anti-inflammatory properties (Islam., 2016). Free radicals are usually formed during biochemical processes; if the body produces more of them than the innate antioxidant system can handle, this could be detrimental (Dalli *et al*.,2021). Several advantageous pharmaceutical characteristics have been ascribed to it, including anti-diabetic effectiveness (Maideen., 2021), antiobesity (Namazi *et al*., 2018), antihyperlipidemic (Shrivastava *et al*.,2023) , antimicrobial (Shafodino *et al*.,2022) antiviral (Shamim *et al*., 2019) , and nephroprotective activities (Hannan *et al*., 2021). Extracts of *Nigella sativa* have established significant antihyperglymic characteristics in mice with Streptozotocin-induced diabetes. Such effectiveness include protectiveand therapeutic activities on pancreatic efficiency, principally and via modifying oxidative stress and maintaining the structural integrity of β-cells, *Nigella sativa* has been showed to improve serum insulin levels whereas effectually reducing hyperglycemia related with diabetes

(Adam *et al*., 2022).

In our current research, we examined the potential toxic effects of *Nigella sativa* seed extracts (NSSE) on some heamatology and serum chemistry of the streptozotocin- diabetic mice.

Materials and methods

Chemicals

To induce diabetes, nicotinamide (NA) and streptozotocin (STZ) and were purchased from Sigma Company (USA).

Preparation of metformin

Glucophage® (metformin hydrochloride), a product of Minapharma Co., Ltd., Egypt. A dosage of 300 mg/kg body weight (BW) was given orally to diabetic mice.

Plants and different extracts preparation *Nigella sativa* seed extract (NSSE)

Firstly, *Nigella sativa* seeds were sourced from a local market in Iraq, and a professional botanist thoroughly verified the species' scientific classification and identification. In brief, 250 grams of dried *N. sativa* seeds were soaked in one liter of 90% methyl alcohol while being shaken for five days, then the resulting methanol extracts were stored in a refrigerator. A rotatory evaporator device was used to evaporate methanol. To make a 20% solution, 20 g of the semisolid *N. sativa* extract was suspended in 100 mL of distilled water with 2 mL of tween 80 (a suspension agent).

Qualitative screening of phytochemicals of *Nigella sativa* extract NSSE

The *N. sativa* seeds extracts were investigated for their phytochemical constituents following established protocols (Srinivasan, 2018). General reactions were used in the experiment to identify the existence or absent of important phytochemicals within the extract.

Experimental animals and care

A total of 54 healthy male albino mice with a body weight of 20–30 g were utilized in the present study. Experimental mice were acquired from the animal house of Biotechnology Research Center of AL-Nahrain University. The experimental mice were housed in groups of six mice each in polyacrylic cages, which were retained under regular laboratory settings in a room with a 12-hour artificial light/dark cycle, maintained at a steady temperature of 24±2 1C, and with a relative humidity of 55±10%. They had unrestricted access a typical dry pellet mea and water. Prior to the experimentation starting, the mice were acclimated to the lab environment for ten days.

Diabetes induction

In order to induce experimental diabetes, Streptozotocin (Sigma-Aldrich Chemie Gmbh Munich, Germany) was administered intraperitoneally for 4 days at a dose of 55 mg/kg after being liquefied in sterile citrate buffer (0.05 mol/L sodium citrate, pH 4.5). According to Arbab *et al*. (2018), the experimental mice were observed for 14 days, and those whose blood glucose levels over 400 mg/dl were classified as diabetic**.**

Biochemical investigations

Blood specimens
were centrifuged at 3000 rpm for 5 minutes to extract blood plasma for biochemical assessments.

Hematological assays

The blood specimens were subjected to hematological investigation via an automatic blood cells analyzer (2800 Hematology Auto Analyzer), which assessed different criteria such as hemoglobin concentration (Hg), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), white blood cell (WBC), and red blood cell (RBC).

Experimental groups and study strategy

After a day of diabetic induction, the experimental mice had been divided randomly and equally into 6 groups, each group comprising six mice as detailed follow:

Group I (normal control):Non-diabetic mice (euglycemic) receiving saline throughout the course of the study(n = 6).

Group II (negative control group)**:**Diabetic mice(but untreated -fed normal fat diet)(n = 6).

Group III (positive control group): Diabetic mice receiving metformin, an anti-diabetic medication at dosage of 300 mg/kg) (n = 6).

Group IV: Diabetic mice receiving NSSE at dosages of 125 mg/kg (n = 6).

Group V: Diabetic mice receiving NSSE at doses of 250 mg/kg (n = 6).

Group VI: Diabetic mice receiving NSSE at doses of 500 mg/kg (n = 6).

300 mg/kg of metformin with 125, 250 and 500 mg/kg of N. sativa seed extract (NSSE) were administrated orally on a daily basis for a period of 28 days, in accordance with earlier research, the dosage selection was carried out (Sherkatolabbasieh *et al*., 2017).

Statistical assessment

The data from this study were analyzed using the mean and standard error of the mean (Mean ± SEM). The Mean ± SEM of six repeats were submitted to Duncan's multiple variety assessment to compare the effects of the extracts against all control groups. A significance level of $P < 0.05$ was measured for the indicators evaluated.

Results

Phytochemical quantitative analysis

The results of the present study showed that *Nigella sativa* seed extract (NSSE) is great reservoirs of medicinally active ingredients (phytochemicals).

Table 1: Quantitative determination of compound in *Nigella sativa* seed extracts (NSSE).

No.	Phytochemicals	Presence (+) and absence (-) in NSSE
1.	Flavonoids	++
2.	Carotenoids	-
3.	Alkaloids	+
4.	Phenols	+
5.	Tannins	++
6.	Steroids	+
7.	Terpenoids	+

(-) Negative reaction,(+) positive reaction and (++) strong positive reaction

Effects of the Nigella sativa extracts (NSSE) on hematological indices

Red blood cells (RBCs)

Table 2 shows a significantly difference (p>0.05) in the mean red blood cell counts (RBCs) of all diabetic mice as compared to the control mice. Moreover, mice that treated with NSSE at both doses of 250 mg/kg (5.17±1.57) and 500 mg/kg (5.12±1.37) have the least RBCs count. The mean red blood cell count of all diabetes treated mice did not differ significantly from that of the diabetic untreated mice.

Haemoglobin (HB)

There was a significant decrease (p>0.05) in hemoglobin concentration (Hb) of diabetic mice was observed when compared to the euglycemic mice. Moreover, hemoglobin concentration of all

treatment groups were reduced in comparison with negative control mice with significant reductions detected in mice that treated by NSSE at 250 (8.51±0.44) and 500 mg/kg (7.72±0.55) (Table 2).

Hematocrit (HCT)

There was a significant decrease ($p>0.05$) in every hyperglycemic animals in contrast to standard samples, with the most marked decrease showed in the animal that treated with NSSE at the dose of 250 mg/kg (26.11±5.48b). The diabetic animals without treatment had the least decrease observed (27.59±2.37). No significant difference was observed between mice treated with metformin and the other experimental groups (Table 2).

Mean corpuscular volume (MCV)

As shown from (Table 2), MCV levels of all experimental animals that treated with the NSSE at different doses were insignificantly ($p>0.05$) decreased in comparison with control animals. On the contrary, animals treated with metformin and the diabetic animals without treatment had increased MCV levels, where both groups showed (66.19±0.94 and 63.77±0.83) respectively.

Mean corpuscular haemoglobin (MCH)

The mean MCH of the control mice was higher than that of all mice that administered with the NSSE at different doses except for mice that administered with 500 mg/kg (19.38±2.33). MCH of control mice were lower than that of mice administered with metformin and diabetic mice without treatment (Table 2).

Mean corpuscular haemoglobin concentration (MCHC)

As presented in (Table 2), the mean MCHC levels of mice treated with NSSE at 250 mg/kg and 500 mg/kg were higher as compared to both control and diabetic untreated groups, where both groups showed (35.91±0.11 and 34.31±0.19) respectively. Additionally, the mice that administered with metformin exhibited a were insignificantly ($p>0.05$) increased MCHC levels when compared with control mice.

Platelets count (PC)

Exception for animals that treated with NSSE at 125 mg/kg(1.85±0.11), which showed a slight decrease, platelet counts (PC) in all experimental groups, as seen in (Table 2), increased non-significantly ($p>0.05$) when compared to the control mice.

Table 2: Effect of *Nigella sativa* extracts NSSE on RBCs and related indices.

Parameters	Experimental groups					
	Control	Diabetic	Diabetic metformin	NSSE 125 mg/kg	NSSE 250 mg/kg	NSSE 500 mg/kg
RBC 7 (X106 µL)	7.11 ± 1.68 ^{a}	5.79±1.32 ^{b}	5.81±1.36 ^{b}	6.21±1.51 ^{b}	5.17±1.57 ^{b}	5.12±1.37 ^{b}
HB (g/dl)	12.6±1.43^{a}	9.24±0.41^{bcd}	9.74±1.57^{b}	8.62±0.11^{cd}	8.51±0.44^{d}	7.72±0.55^{cd}
HCT (%)	36.87±0.18^{a}	27.59±2.37^{c}	25.42±2.66^{c}	26.32±1.35^{c}	26.11±5.48b^{c}	26.69±2.45^{c}
MCV (*fl*)	57.75±1.55^{abc}	66.19±0.94^{a}	63.77±0.83^{ab}	58.19±8.83^{bc}	55.72±0.13^{ab}	58.77±0.83^{ab}
MCH (ρg)	18.11±0.39 ^{abc}	21.64±1.72^{a}	22.12±0.71^{ab}	15.18±0.14^{abc}	15.98±1.18^{c}	19.38±2.33a^{b} c
MCHC (g/dl)	32.76±1.18^{bcd}	32.69±1.44^{bc} d	32.81±2.21^{bc} d	32.14±2.13^{bc}	35.91±0.11^{d}	34.31±0.19^{cd}
PLT (105/µl)	2.65±1.32^{ab}	1.48±1.38^{ab}	2.81±1.61^{ab}	1.85±0.11^{a}	1.91±0.32^{ab}	1.81±1.13^{ab}

Values in the same column with different letters are considerably different at $p>0.05$ (mean ± SEM; n=5). Red blood cell =RBC; Hemoglobin=HB; Packed Cell Volume= PCV; Mean Corpuscular Volume =MCV ;Mean Corpuscular Haemoglobin=MCH; Mean corpuscular hemoglobin concentration = (MCHC) ; Mean Count of platelets= PLT.

Total white blood cells count (WBCs)

According to the current data concerning white blood cell count, the mean WBCs of animals treated with NSSE were insignificantly higher ($p>0.05$) than those of the control group. Moreover, animal treated with metformin exhibited a slight decline in the WBCs percentage (1.33±0.34), but diabetic untreated mice showed a significant decrease in WBC percentage (0.62 ±1.13) than that of all other experimental groups (Table 3).

Differential white blood cells count

Lymphocytes percentage

The percentage of lymphocytes as shown in (Table 3) exhibited a non-significant ($p>0.05$) change in mice that treated with NSSE as compared to the normoglycemic mice. Nevertheless, diabetic untreated mice (71.19±2.31), exhibited a significant increase compared to the normoglycemic mice, whereas mice treated with metformin had a lower lymphocyte percentage (59.25±0.91) (Table 3).

Neutrocytes percentage

Percentage of the neutrophils (neutrocytes) of mice that treated with metformin (36.2±3.44) having higher neutrophil percentage than that of all other groups. Conversely, diabetic untreated mice significantly had the least neutrophil percentage. Control mice had (33.9±3.19) of neutrophil which was non-significantly ($p>0.05$) higher than that observed in NSSE at 250 mg/kg which had the least percentage of neutrophil (26.6±1.31) (Table 3).

Monocytes percentage

As shown in (Table 3), the difference was not statistically significant ($p>0.05$) in the average percentage of monocytes among all treatment groups in comparison to normal control, untreated diabetic group besides diabetic metformin with the exception of the mice treated with NSSE at 250 mg/kg (2.22±0.27).

Eosinophil percentage

For eosinophils as presented in (Table 3), roughly the same pattern as for monocytes was seen, where there was no statistically significant variation in the average eosinophil count ($p>0.05$) of the experimental groups than those of all control groups.

Table 3: Effect of Nigella sativa extracts NSSE on WBCs and differentials.

Parameters	Experimental groups					
	Control	Diabetic	Diabetic metformin	NSSE 125 mg/kg	NSSE 250 mg/kg	NSSE 500 mg/kg
WBC (X103 µL)	1.36±1.15^{a}	0.62 ±1.13^{b}	1.33±0.34^{a}	1.55±0.14^{a}	1.81±0.11^{a}	1.62±0.65^{a}
Lymphocyte (%)	68.19±2.21^{b} abc	71.19±2.31^{a}	59.25±1.91^{c}	67.71±2.20 ^{abc}	73.27±2.12^{ab}	72.33±2.29 ^{ab}
Neutrophil (%)	33.9±3.19^{ab}	22.7±3.38^{c}	36.2±3.44^{a}	31.29±3.32^{abc}	26.6±1.31^{bc}	27.9±4.91^{bc}
Monocyte (%)	2.39±1.16^{a}	2.51±0.22^{a}	1.12±0.28^{a}	2.98±0.14^{a}	1.24±0.17^{a}	2.22±0.27^{a}
Eosinophil (%)	2.22±0.41^{a}	2.12±0.29^{a}	2.99±1.81 ^{a}	1.29±0.71^{a}	2.92±2.25^{a}	3.52±0.29^{a}

Values in the same column with different letters are considerably different at $p>0.05$ (mean ± SEM; n=5).

NSSE on some biochemical indices

Serum glucose level (Glu)

The levels of serum blood glucose as shown in (Table 4) of mice treated with NSSE was significantly ($P<0.05$) lower than that of the both diabetic control (391.27±24.35) and metformin (167±11.31) treated mice groups. However, it was similar with that showed in the euglycemic mice especially at 250 mg/k (102.11±0.33 mg/k) .

Blood urea nitrogen (BUN)

As presented in (Table 4), the BUN levels of animals administrated with extracts or metformin did not change significantly from those of normoglycemic mice ($p>0.05$). Nevertheless, diabetic untreated mice had considerably higher BUN concentrations in comparison with euglycemic mice.

Creatinine (Crt)

For creatinine (Crt) as shown in (Table 4), roughly the same pattern as for urea nitrogen (BUN) was seen, where there was no discernible statistically significant variation ($p>0.05$) in the mean of Crt as regard of the experimental groups as compared to control groups.

Cholesterol (Chol)

Mean cholesterol levels of NSSE and metformin of administrated animals was significantly decreased ($P>0.05$) as compared to the diabetic untreated mice, Nonetheless, the decline was not statistically significant when compared with euglycemic animals (Table 4).

Bilirubin (Bil)

The results as shown in (Table 4) exhibited a non-significant difference ($p < 0.05$) in mean bilirubin levels of all treated groups as compared to the euglycemic control. However, the diabetic untreated mice exhibited considerably elevated bilirubin levels.

Table 4: Effect of Nigella sativa extracts NSSE on some biochemical indices

Parameters	Experimental groups					
	control	Diabetic	Diabetic metformin	NSSE 125 mg/kg	NSSE 250 mg/kg	NSSE 500 mg/kg
BUN (mg/dl)	14.77 ± 0.22^{ab}	12.17 ± 0.97^{a}	12.29 ± 1.18^{ab}	13.09 ± 0.61^{ab}	12.19 ± 2.22^{ab}	13.88 ± 1.52^{ab}
Crt (mg/dl)	2.59 ± 0.18^{a}	1.33 ± 0.27^{a}	2.72 ± 0.13^{b}	1.66 ± 0.09^{a}	2.41 ± 0.13^{a}	1.98 ± 0.15^{a}
Chol (mg/dl)	68.91 ± 2.11^{a}	81.61 ± 2.21^{b}	50.29 ± 2.85^{a}	54.59 ± 0.11^{a}	48.98 ± 8.45^{a}	60.74 ± 2.12^{a}
Bil (mg/dl)	1.92 ± 0.15^{b}	0.32 ± 1.12^{a}	0.29 ± 0.18^{ab}	0.69 ± 0.03^{ab}	0.25 ± 0.11^{ab}	0.71 ± 0.12^{b}

Mean ± SEM; n=5; Values with different alphabets in the same column are significantly different at $p>0.05$; Gluc = Glucose; BUN = Blood Urea Nitrogen; Crt= Creatinine; Chol = Cholesterol; Bil = Bilirubin.

Effect of different extracts on hepatic marker enzymes

Alanine phosphate (ALP)

As displayed in (Table 5), mice treated with NSSE treatments exhibited a significantly increased ALP levels. Likewise, mice administered with metformin and diabetic untreated mice both had noticeably higher ALP levels than the euglycemic group.

Alanine transaminase (ALT)

Exception of diabetic untreated animals, which were considerably ($p<0.05$) higher (34.49 ± 0.23) than normoglycemic mice, no statistically notable difference ($P > 0.05$) was observed in the mean ALT values among any of the sampels. Additionally, ALT level of diabetic untreated animals (46.13 ± 1.12) was also significantly higher in comparison to the all treated groups (Table 5).

Aspartate transaminase (AST)

As depicted in (Table 5), our findings indicate that the average AST numerical value for every experimental groups exhibited a notably ($p>0.05$) decreased in comparison with normal controls. On the converse, diabetic untreated mice (61.31 ± 1.08) showed an elevation in AST levels in comparison with treatment groups and the euglycemic controls.

Total protein (TP)

The average protein content (TP) as shown in (Table 5) was not statistically significant ($p>0.05$) decreased in all mice treated by NSSE except for mice that administered with 125 mg/kg dose

(7.43±0.12) which was significantly decreased than those of other treated groups. Nonetheless, there was a significant reduction noted in untreated diabetic mice (7.11±0.28) comparing to the normal group. In addition, mice treated with metformin (7.21±1.81) likewise displayed a marked reduction in total protein in comparison with euglycemic animals.

Albumin (ALB)

In comparison to the euglycemic control mice, the average albumin levels were not significantly reduced ($p > 0.05$) in the animals treated by NSSE formula and metformin treatments. However mice treated with metformin(5.61±0.27) exhibited a significantly decrease in the mean albumin than those of other experimental groups (Table 5).

Table 5: Effect of *Nigella sativa* extracts NSSE on hepatic marker enzymes

Parameters	Experimental groups					
	control	Diabetic	Diabetic metformin	NSSE 125 mg/kg	NSSE 250 mg/kg	NSSE 500 mg/kg
ALP (IU/L)	115.81±0.77^{ab}	155.52±1.81^{c}	150.14±1.25^{a}	157.13±0.22^{a}	131.00±8.62^{ab}	148.00±11.26^{a}
ALT (IU/L)	32.21±1.19^{a}	46.13±1.12^{b}	29.12±0.52^{a}	33.18±1.21^{a}	32.21±1.11^{a}	34.49±0.23^{b}
AST (IU/L)	59.11±0.56^{a}	61.31±1.08^{c}	55.45±0.19^{ab}	55.00±0.16^{b}	57.67±1.45^{b}	56.31±1.27^{b}
TP (g/dl)	8.50±0.05^{a}	7.11±0.28^{c}	7.21±1.81^{b}	7.43±0.12^{b}	8.12±0.21^{ab}	8.26±0.12^{ab}
ALB (g/dl)	7.81±1.22^{a}	8.23±0.67a	5.61±0.27^{b}	7.11±1.11^{a}	7.77±0.18^{a}	8.49±0.26^{a}

Mean ± SEM; n=5; Values with different alphabets in the same column are significantly different at $p>0.05$; ALP = Alanine phosphate; ALT = Alanine transaminase; AST = Aspartate transaminase; TP = Total protein; Alb = Albumin.

Discussion

In the current research, in order to find the existence of medicinally active constituents, phytochemical screening was accomplished by analyzing *N. sativa* seeds extracts (NSSE). This qualitative screening test showed different results in different extracts of N. sativa. Treatment of diabetic mice with different extracts of *N. sativa* extracts showed improvement in many parameters.

Results showed that, oral administration of NSSE greatly affected all hematological parameters. It led to decrease in RBCs count, Hb, PCV, MCV, MCH and PC values. These results are in agreement with the findings of earlier researcher, including that of Yonus *et al*. (2020), who perceived a drastic decline in red blood cell (RBC) count, haemoglobin (Hb) levels, hematocrit (HCT) and hemoglobin concentration per red blood cell (MCHC) in diabetic mice. Clinically, sideroblastic anemia, thalassemia, iron insufficiency, and lead poisoning are associated with decreased MCV and MCHC levels (De Souza., 2023). The results of the current study demonstrated that the anemia showed in extracts mice group may be physiologically caused via iron insufficiency. Current results were in accordance to those that were stated by Ibrahim et al.(2020).The platelet count, on the other hand, increased; nonetheless, this is consistent with our findings regarding the indices of white and red cells, which indicate of the anemia occurrence (Cho *et al*.,2013).

In return, the percentage of white blood cells (WBCs) significantly decreased in the untreated-diabetic mice, but showed a non-significant increase in the extracts groups. It was noticed in the present study that, lymphocyte counts were particularly increased, this was in line with literature findings of Giudice and Selleri, (2022), who pointed out the possibility that this increase might suggest an enhanced immune response, similar to that observed in the sickness of serum and different immune syndromes. Conversely, a decreased in the count of neutrophil indicates a heightened susceptibility to infection, a condition commonly linked to neutropenia (Klein., 2020). Current data were in accordance to those that were stated by Özsan *et al*. (2024).

In the present study results revealed that administration of experimental extracts to diabetic mice significantly decreased blood glucose and increased plasma insulin level. These outcomes was supported a previous report done by Khan and Zaidi, (2024).This result suggests that N. sativa extracts possesses antidiabetic potential which may be attributed to the chemical constituents of the extracts (Li *et al*., 2022). Nonetheless, the exact process by which the extracts have its anti-diabetic properties is still being studied, but can be hypothesized that some of the phytochemicals present may contribute to this (Maideen., 2021).

According to Arifianto *et al*. (2020), the serum blood urea nitrogen (BUN) and creatinine (Cr) values were significantly increased in diabetic untreated mice, which could potentially indicate renal damage. The main metabolite produced the breakdown of the protein turnover is urea, whereas the breakdown of creatine in muscle tissue leads to the creatinine production (Peng *et al*.,2021). The same observations have been made by (Razmpoosh *et al*.,2020).

Van Rooyen *et al*., (2011) stated that the elevated cholesterol levels observed in untreated diabetic mice can be attributed to the metabolic alterations associated with diabetes. These conditions often lead to a reduction in high-density lipoprotein (HDL), while promoting an increase in triglycerides (TG) and low-density lipoprotein (LDL).This imbalance ultimately results in a rise in total cholesterol levels.

Diabetes, as previously stated, is associated with increased hemolysis; as a result, there will be an increase in the excretion of heme, a by-product of hemolysis. Our theory that there was some grade of elevated heme excretion is further supported by the increase in bilirubin levels observed in all experimental groups in the recent investigation.

It is evident from biochemistry assays that diabetes is linked to altered liver function, which is characterized by a marked decrease in total protein and its constituents, particularly albumin, in addition to an increase in the production of hepatic enzymes. Current result displays that the extracts had a more profound liver-protective effect action compared to that of glyburide medications "glibenclamide". Generally, proteins of plasma are predominantly produced via liver cells and hepatic impairment is characteristically marked by decreased protein synthesis alongside reduced activity of key liver-specific enzymes, for instance alkaline phosphatase (ALP) besides alanine aminotransfarase (Adeyemi *et al*., 2015). Increased expression of aspartate transaminase (AST) is more specific for biliary tract damage, obstruction or infection (Khan *et al*., 2021) which was markedly increased in diabetic untreated mice. In the present study, serum concentration of total protein (TP) and albumin (ALB) decreased in all mice administered with the extracts except for the high concentrations of both extracts. The current finding is consistent with earlier research. (Talebi *et al*.,2021).

Conclusions

The finding of this study indicate that *Nigella sativa* extracts possesses hypoglycemic and hypolipidemic effects in STZ-induced diabetic mice and indicate that this extracts might be an excellent adjuvant support in the treatment of diabetes and its complications particularly when it is used for a longer period.

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