

Anti-Diabetic and Anti-Lipidemic Effects of Prickly Pear Juice Enriched with Sage or Mint Leaves Powder in Alloxan-Induced Diabetic Rats

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Abstract: Effect of Prickly pear juice enriched with Sage or Mint leaves powder on serum glucose, insulin levels and Lipid profile of relative control and diabetic rats was evaluated. The mean values of serum glucose level of positive control group were significantly ($p < 0.05$) higher than that of negative control. The mean values were 253 and 78 mg/dl, respectively. Addition of sage or mint leaves powder to Prickly pear juice caused a significant ($p < 0.05$) decrease in the level of serum glucose in comparing to positive control group. On the other hand, the best serum glucose result was observed in the group fed on Prickly pear juice with Sage (1.5%) is 175.3 mg/dl. The insulin level of negative control group were significantly ($p < 0.05$) higher than that of positive control. The mean values of insulin were 35.3 and 8.3 ($\mu\text{U/ml}$) respectively. Rats group fed on Prickly pear juice with sage 1.5% recorded the highest increase of insulin level in comparing with other treated groups. Insulin level was significantly different ($p < 0.05$). The mean value of insulin was 30.2 ($\mu\text{U/ml}$), while, the lowest value of insulin was recorded for Prickly pear juice being 27.3 ($\mu\text{U/ml}$). The results were significantly different ($p < 0.05$). The levels of total triglyceride (TG) total cholesterol (TC) in positive control groups were 171.23, 228.3 mg/dl elevated as compared with negative control group which the mean values were 102.56, 118.2 mg/dl respectively. Addition of sage or mint leaves powder to Prickly pear juice caused a reduction in serum TG, TC levels. Also, the Prickly pear juice enriched with mint or sage leaves powder (1.5%) showed higher effect in reducing the levels of TG and TC than in Prickly pear juice combined with mint or sage (1.0%). The mean value of HDL-c of positive control group (39.4 mg/dl) which showed significant ($p < 0.05$) decrease comparing with the negative control group (48.33 mg/dl). Meanwhile, data indicated that the consumption of Prickly pear juice enriched with Sage or Mint led to increase HDL-c. The highest increase in HDL-c was observed in diabetic group administrated with Prickly pear juice enriched with sage (1.5%) (59.01 mg/dl). The level of low-density lipoprotein LDL-c cholesterol in the positive control group was high, where the value was 154.66 mg /dl compared to the negative control group, where the mean value was 49.36 mg /dl. The obtained results indicated that mean values of VLDL-c of positive control group were higher than that of negative control with significant difference (34.24 and 20.51 mg/dl). Rats group consumed Prickly pear juice enriched with 1.5% mint leaves powder recorded the highest reduction of VLDL-c level (the mean value was 22.8 mg/dl).

Key words: Sage • Mint • Prickly Pear Juice • Diabetic • HDL-C • LDL-C • Insulin

INTRODUCTION

Prickly pear is an important source of phenols, in addition to having the most common antioxidant phytochemicals, such as betalains and ascorbic acid [1]. Recently, When compared between Cladodes and Fruits

of Prickly Pears. They found that its phenolic compounds concentrations were 119.66 and 123.56 mg/100 g and antioxidant activity 40.38% and 39.18 %, respectively [2]. Prickly pear seed oil has a noticeable antimicrobial activity against *Salmonella*, *Escherichia coli*, *Bacillus subtilis* and *Bacillus cereus* spores [3]. More recent, prickly pear

exhibited anti-inflammatory, anti-oxidant, antimicrobial, hypoglycemic and neuro-protective properties due to the presence of health prompting properties not only in fruit but also in its stem. Furthermore, prickly pear fruit contains vitamins, carotenoids, poly phenolic compounds, flavonoids, betalains and minerals [4]. A decrease in glycemia levels was noticed with crude and boiled blended preparations of prickly pear [5]. Also some studies have demonstrated the hypoglycemic activity of the prickly pear cactus extract on non-diabetics and diabetic-induced rats. In a study on rats, the combination of insulin and purified extract of prickly pear was found to reduce blood glucose and glycated hemoglobin levels [6]. Prickly pear due to lower blood glucose levels by 10-30 mg/dl in non-insulin-dependent diabetes (NIDDM) patients and supported the likelihood that prickly pear has a true metabolic effect in diabetics [7]. Likewise, prickly pear is amongst the majority of products recommended by Italian herbalists that may be efficacious in reducing glycemia [8]. Prickly pear produces reduction in high glucose levels in diabetics given an oral glucose load. The benefits of prickly pear thus increases over time compared to non-treated volunteers [9]. *Opuntia* spp. has 'anti-hyperglycemic' and 'anti-diabetic' properties in humans and it is prescribed in many traditional and complementary therapies around the world [10]. Observed that *Opuntia ficus indica* oil extract with these components present antioxidant and anti-free radical activity, having a potential as anticancer, anti-inflammatory, hypoglycemic, hypolipidemic and hypocholesterolemic activities [11]. Found the effect of *Opuntia ficus-indica* cladode and fruit skin extract on blood glucose and plasma insulin increments due to high-dose carbohydrate ingestion, before and after exercise. It was also found *Opuntia ficus indica* cladode and fruit-skin extract increased plasma insulin and thereby facilitated the disposal of an oral glucose load from the circulation. This reduction in blood glucose was more explicit after exercise than in a basal state [12]. Cholesterol, LDL and triglyceride plasma levels of rats were strongly reduced after 30 days of a daily administration (1 g/kg) of lyophilized cladodes of *Opuntia ficus indica* L. Mill [13]. Also, *Opuntia ficus-indica* dehydrated leaves can be consumed as a dietary supplement to improve some blood lipids parameters and risk factors in the case of metabolic syndrome [14]. Moreover, cactus fruit juice positively affects the body's redox balance, decrease oxidative damage to lipid and improve antioxidant status in diabetic rats [15]. The oral administrations of Cinnamon, Nutmeg and peppermint

extracts have beneficial effects on blood glucose levels [16]. Likewise, the mint treated diabetic rats significantly decreased the level of blood glucose and creatinine as well as increased level of insulin, glycogen and body weight. These finding demonstrated that mint possess anti-hyperglycemic activity against streptozotocin (STZ) induced diabetic rats. The anti-diabetic effect of mint compared with standard reference drug glibenclamide [17]. Also, the rats treated with mint gained more weight ($p<0.05$) and also decreased the serum concentrations of triglycerides, total cholesterol, LDL and glucose [18]. In many studies, the sage extract was found to have hypoglycemic effect in diabetic animals [19]. Also, replacing water with sage tea for 14 days decreased plasma glucose levels in the normal mice. Also, showed that a sage methanolic extract significantly reduced serum glucose level in fasted streptozotocin-induced diabetic rats without change in insulin level [20]. Likewise, Sage has been used as a traditional remedy against diabetes in many countries and its glucose-lowering affects have been demonstrated in animal studies [21]. *Salvia officinalis* might be beneficial in diabetic patients to reduce cholesterol. However higher doses might be needed to decrease fasting blood glucose and glycosylated hemoglobin [22]. The effect of aqueous and ethanol extracts of *Salvia officinalis* leaves at concentration (100 mg/kg) in dosage on albino rats for 14 days, on blood glucose, serum cholesterol and triglycerides (TG) level in induced-diabetic rats by alloxan (150 mg/kg) compared with the reference drug Glibenclamide. Also, the results showed a significant increase ($P<0.05$) in cholesterol levels compared to healthy control group as well as a significant decrease ($P<0.05$) in the level of TG of diabetic rats when treatment with aqueous and alcoholic extract of the plant leaves in comparison with the healthy control group [23]. Rat's injection with alloxan induced very highly significant elevation in mean of blood glucose levels of diabetic animals as compared with control group and sage administration groups. Diabetic rats also revealed highly significant elevation in total cholesterol (TC) triglyceride (TAG) Low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) concurrent with highly significant reduction in high-density lipoprotein cholesterol (HDL-C) as compared with control group [24]. Found that some mechanisms suggested for anti-diabetic actions of *Salvia* species extracts are as follows: activation of pancreatic beta cells, increment of insulin sensitivity and peripheral utilization of glucose, inhibition of insulinase enzyme, reduction of

glycogenolysis, decreases in the glucose absorption from intestine and increment of the synthesis of glucose in the liver. Also, It was demonstrated that flavonoids particularly quercetin, have anti-diabetic effects [25]. Also, concluded that the whole sage Essential Oil (EO) acted as a strong anti-diabetic and anti-obesity herbal sub product by delaying carbohydrate and lipid digestion, thus, decreasing glycemia, increasing liver glycogen stocking and lowering pancreatic lipase activity [26]. Recently, Mint leaves of *Mentha* species were found to possess strong antioxidant properties in vitro by displaying free radical scavenging activity [27]. The previous literature didn't reveal the effect of using Prickly Pear juice enriched with Sage or Mint leaves powder on diabetic rats, Therefore, this study aimed to evaluate the effect of feeding diabetic rats' Prickly pear juice enriched with Sage or Mint leaves powder on serum glucose, insulin levels and Lipid Profile.

MATERIALS AND METHODS

Source of Prickly Pear: Prickly pear (*Opuntia ficus indica*) was purchased from El-Arish local market, North Sinai Governorate.

Source of Herbs: Mint (*Mentha peperita*) and Sage (*Salvia officinalis*) leaves were obtained from El-Arish local market, North Sinai Governorate.

The Chemicals and Chemical Kits: Alloxan monohydrate, analytical reagent grade purchased from Sigma Chemical Co. (Sigma-Aldrich Company Ltd., UK) All used chemical kits in this study were obtained from El-Gamhouria Company for chemicals trade, Cairo, Egypt.

Preparation of Plant Material: The plant leaves of mint and sage were dried at 30-40°C by the hybrid solar convective drying system (C.C.P. Parma – Italy) then grind the leaves until it becomes a powder.

Basal Diet (Standard Diet) Preparation: The basal diet was prepared according to AIN [28], as illustrated: casein (12%) sugars (10%) sun flower oil (10%) vitamin mixtures (1%) mineral mixtures (4%) fiber (4%) starch (58.50 %) DL-methionin (0.3%) and choline chloride (0.2%).

The Induction of Experimental Diabetes: Diabetes was induces in normal healthy male albino rats by received intra-peritoneal injection dose of alloxan 150 mg/kg body weight, according to the method described by Desai and Bhide [29].

Three days after the injection of alloxan, fasting blood samples were obtained to estimate fasting serum glucose higher than 200 mg/dl rats which were considered diabetes, according to the method described by NDDG [30].

Experimental Design: Forty-two adult male white albino rats, Sprague Dawley Strain, weighing (140±10g) were used in this experiment. All rats were fed on basal diet prepared according to AIN [28], for 7 consecutive days after this adaptation period. The experiment will take 8 weeks period.

Rats Were Randomly Classified into Two Main Groups:

- Control negative group this group served as a control negative for the first and second experiments. This group consists of 6 rats and received basal diet and tap water *ad-libitum*.
- Diabetic groups these groups consist of 36 rats that were exposed to alloxan to induce diabetes as previous explained. All diabetic rats fed on basal diet and received the experimental diets and classified into main experiments as follows:

Thirty six diabetic rats were used to study the effect of supplemented with Prickly pear juice (1.0 and 1.5% W/V of mint or sage leaves) which was given orally by gavages daily for eight weeks. Dose of Prickly pear juice and their supplementation for every rat (28.56 ml/kg b.w/daily) [31], then, classified into the following:

- Positive control group (+ve) served as positive control (diabetic) for the first and second experiments. This group received standard diet and tap water *ad-libitum*.
- PPJ: Diabetic rats group was received standard diet and tap water *ad-libitum* + Prickly pear juice.
- PPJS1: Diabetic rats group was received standard diet and tap water *ad-libitum* + Prickly pear juice supplemented with Sage 1.0%.
- PPJS2: Diabetic rats group was received standard diet and tap water *ad-libitum* + Prickly pear juice supplemented with Sage 1.5%.
- PPJM1: Diabetic rats group was received standard diet and tap water *ad-libitum* + Prickly pear juice supplemented with 1.0% mint.
- PPJM2: Diabetic rats group was received standard diet and tap water *ad-libitum* + Prickly pear juice supplemented with 1.5% mint.

Blood Sampling: After fasting for 12 hours, blood samples in initial times were obtained from hepatic portal vein at the end of each experiment. Apart of blood samples were collected into a dry clean centrifuge glass tubes and left to clot in water bath (37°C) for 30 minutes, then centrifuged for 10 minutes at 4000 rpm to separate the serum, which were carefully aspirated and transferred into clean cuvette tube and stored frozen at 2°C till analysis according to the method described by Schermer [32].

Biochemical Analysis

Determination of Serum Blood Glucose and Insulin: Serum Blood glucose was estimated according to method described by Sasaki *et al.* [33], as a drop of blood from the tail using a glucometer (ACCU-CHECK, Roche, Germany). Insulin levels were estimated according to method described by Abraham *et al.* [34], Wilson and Miles [35], by using ELISA kit by Linco Research Inc, USA.

Lipids Profile

Determination of Serum Total Cholesterol: Serum total cholesterol was determined according to the colorimetric method described by Thomas [36].

Determination of Serum Triglycerides: Serum triglycerides were determined by enzymatic method using kits according to Young [37].

Determination of High Density Lipoprotein (HDL-c): HDL-c was determined according to the method described by Grodon and Amer [38].

Calculation of Very Low Density Lipoprotein Cholesterol (VLDL-c): VLDL-c was calculated in mg/dl according to Lee and Nieman [39], using the following formula:

$$\text{VLDL-c (mg/dl)} = \text{Triglycerides} \div 5$$

Calculation of Low Density Lipoprotein Cholesterol (LDL-c): LDL-c was calculated in mg/dl according to Lee and Nieman [39], as follows:

$$\text{LDL-c (mg/dl)} = \text{Total cholesterol} - \text{HDL-c} - \text{VLDL-c.}$$

Statistical Analysis: Data were statistically analyzed using a completely randomized factorial design when a significant main effect was detected; the means were separated with the Student-Newman-Keuls Test.

Differences between treatments of ($P \leq 0.05$) were considered significant using Cost at Program. Biological results were analyzed by One Way ANOVA.

RESULTS AND DISCUSSION

Effect of Prickly Pear Juice Enriched with Different Concentrations of Sage or Mint Leaves Powder on Serum Glucose and Insulin Levels of Normal Control and Alloxan-induced Diabetic Experimental Rats: Data presented in Table (1) showed that serum glucose and insulin levels of normal control and diabetic rat groups that consumed prickly pear juice fortified with sage or mint at different levels.

The mean values of serum glucose level of positive control group were significantly ($p < 0.05$) higher than that of negative control with significant difference. The mean values of serum glucose were 253 and 78 mg/dl, respectively.

Results in Table (1) also showed that addition of sage or mint to Prickly pear juice caused significantly ($p < 0.05$) decrease in the level of serum glucose compared to positive control group. On the other hand, the best result was observed in the group fed on Prickly pear juice with Sage (1.5%) being 175.3 mg/dl. These results were in agreement with those reported by researchers [20], They showed that sage extract consumption caused a reduction in serum glucose level in diabetic rats. The diet supplemented with prickly pear linked with a decrease on glucose levels [40]. A dose of dried prickly pear 2g/kg body weight caused a significant decrease in blood glucose level in diabetic rats [13]. Sage is among the plants that are claimed to be beneficial to diabetic patients. SO, indicated that sage essential oil (EO) reduced glycemia by 60% and the level of glycogen stored in the liver by 43.7% [26]. Intra peritoneal injection of ethanolic and water extracts of sage leaves significantly lowered the Fasting Blood Glucose (FBG) level in Alloxan diabetic mice [41]. Meanwhile, orally consumption of sage tea leading to lower glycemia on STZ-induced diabetic mice and rats [20].

Effect of Prickly Pear Juice Enriched with Different Concentrations of Sage or Mint Leaves Powder on Insulin Levels: Data presented in Table (1) showed also the effect the addition of Prickly pear juice with Sage or Mint on Insulin of diabetic rats. Results indicate that the insulin level of negative control group was higher than that of positive control with significant difference.

Table 1: Serum glucose and insulin levels in negative control and diabetic groups as affected by consuming prickly pear juice enriched with Sage or Mint leaves powder

Groups	Variables	
	Glucose (mg/dl)	Insulin (μ U/ml)
Control Negative (-)	78.00 ^e \pm 3.80	35.90 ^a \pm 2.30
Control Positive (+)	253.00 ^a \pm 4.50	8.20 ^d \pm 0.50
PPJ (Prickly pear juice)	243.40 ^b \pm 5.90	27.30 ^c \pm 3.40
PPJS1 (Prickly pear juice with Sage leaves powder 1.0%)	209.20 ^c \pm 6.50	29.11 ^b \pm 2.90
PPJS2 (Prickly pear juice with Sage leaves powder 1.5%)	175.30 ^d \pm 4.90	30.20 ^b \pm 3.30
PPJM1 (Prickly pear juice with Mint leaves powder 1.0%)	202.40 ^c \pm 6.50	27.40 ^c \pm 3.70
PPJM2 (Prickly pear juice with Mint leaves powder 1.5%)	186.30 ^d \pm 5.70	28.60 ^c \pm 3.10
LSD	9.11	7.30

Values are expressed as mean \pm SD, n=6, Mean \pm SD followed by different superscript within columns are significantly different at (p<0.05)PPJ: Prickly pear juice, PPJS1: Prickly pear juice with Sage 1.0%, PPJS2: Prickly pear juice with Sage 1.5%, PPJM1: Prickly pear juice with Mint 1.0%, PPJM2: Prickly pear juice with Mint 1.5%.

Table 2: Serum lipid profile levels in negative control and diabetic groups as affected by consuming prickly pear juice enriched with sage or mint leaves powder

Groups	TG (mg/dl)	TC (mg/dl)	HDL-c (mg/dl)	LDL-c (mg/dl)	VLDL-c (mg/dl)
Control Negative (-)	102.56 ^d \pm 5.30	118.20 ^e \pm 2.50	48.33 ^b \pm 1.50	49.36 ^f \pm 3.47	20.51 ^e \pm 1.10
Control Positive (+)	171.23 ^a \pm 5.90	228.30 ^a \pm 5.50	39.4 ^d \pm 2.00	154.66 ^a \pm 5.30	34.24 ^a \pm 1.10
PPJ (Prickly pear juice)	127.00 ^b \pm 5.20	181.90 ^b \pm 2.80	43.6 ^c \pm 3.40	112.9 ^b \pm 3.40	25.4 ^b \pm 1.70
PPJS1 (Prickly pear juice with Sage leaves powder 1.0%)	123.10 ^b \pm 5.00	156.30 ^c \pm 2.50	46.7 ^b \pm 3.10	84.98 ^d \pm 3.10	24.62 ^b \pm 2.10
PPJS2 (Prickly pear juice with Sage leaves powder 1.5%)	114.00 ^c \pm 4.20	139.30 ^d \pm 2.70	59.01 ^a \pm 5.70	62.19 ^e \pm 6.20	23.8 ^b \pm 1.80
PPJM1 (Prickly pear juice with Mint leaves powder 1.0%)	126.50 ^b \pm 5.00	176.20 ^b \pm 2.50	47.23 ^b \pm 3.10	103.67 ^c \pm 3.10	25.3 ^b \pm 2.10
PPJM2 (Prickly pear juice with Mint leaves powder 1.5%)	119.00 ^c \pm 4.20	145.00 ^d \pm 2.70	58.2 ^b \pm 5.70	58.3 ^e \pm 6.20	22.8 ^c \pm 1.80
LSD	9.60	6.70	6.50	8.90	3.00

Values are expressed as mean \pm SD, n=6, Mean \pm SD followed by different superscript within columns are significantly different at (p<0.05)PPJ: Prickly pear juice, PPJS1: Prickly pear juice with Sage 1.0%, PPJS2: Prickly pear juice with Sage 1.5%, PPJM1: Prickly pear juice with Mint 1.0%, PPJM2: Prickly pear juice with Mint 1.5%. TC: Total Cholesterol, TG: Triglycerides, HDL-c: High density lipoprotein, LDL-c: Low density lipoprotein, VLDL-c: Very low density lipoprotein.

The mean values were 35.3 and 8.3 μ U/ml, respectively. Results also showed that, rats group fed on Prickly pear juice with sage 1.5% recorded the highest increase of insulin level when compared with other treated groups and data were significantly different. The highest value of insulin was 30.2 μ U/ml. While, the lowest values of insulin was recorded being 27.3 μ U/ml.

Consumption of oral ethanolic extract of sage leaves potentially lowered serum glucose, triglycerides, total cholesterol and enhanced plasma insulin depending on the increasing dose on STZ diabetic rats [42].

Peppermint essential oil (PEO) has an antidiabetic effect and confirmed that by reduction of blood glucose, enhancement of insulin and C-peptide levels, improvement in pancreatic β cell structure, increased expression of insulin and Bcl-2 and improvement in hematological parameters in diabetic rats treated with PEO. This effect could be attributed to the antioxidant activity of PEO, which was observed to scavenge free radicals and increase the levels of antioxidant enzymes [43]. These results are in agreement with who indicated

that phenolic compounds and antioxidant activities of peppermint may be useful for meal planning in type 2 diabetes [44].

Effect of Prickly Pear Juice Enriched with Different Concentrations of Sage or Mint Leaves Powder on Serum Lipid Profile on Normal Control and Induced Diabetic Rats by Alloxan: Results presented in Table (2) show that the effect of addition of Prickly pear juice with Sage and Mint leaves powder on total triglyceride (TG) and total cholesterol (TC) of normal and diabetic rats (mg/dl) Results indicated that the level of TG, TC in positive control groups were (171.23, 228.3) mg/dl elevated as compared with negative control group which the mean values were (102.56, 118.2) mg/dl, respectively.

Addition of Sage and Mint leaves to Prickly pear juice caused a reduction in serum TG, TC levels. The highest effect in reducing the level of TC was observed in the diabetic groups supplemented with Prickly pear juice with Sage at level of (1.5%) the mean value was (139.3) mg/dl. The data indicated that Prickly pear juice with

additives have antilipidemic and anticholesterolemic effect and reduced levels of total triglyceride and total cholesterol in diabetic rats. The groups administrated with Prickly pear juice enriched with sage or mint showed significant increased for reducing in the levels of TG and TC.

Results in the same table showed also that, The Prickly pear juice with additives mint and sage (1.5%) showed the higher effect in reducing the levels of TG and TC than The Prickly pear juice with additives mint or sage at 1.0%.

Results their study showed a significant increase ($P < 0.05$) in cholesterol levels compared to healthy control group as well as a significant decrease ($P < 0.05$) in the level of TG of diabetic rats when treated with aqueous and alcoholic extract of the sage leaves in comparison with the healthy control group [23]. Also, prickly pear treatment was associated with significant decrease in plasma free fatty acid (FFA) and triglyceride concentrations and tissue triglyceride contents in rats [45]. These results are also in agreement with those observed that prickly pear reduced the levels of serum total cholesterol and triglyceride [46]. In addition, rat diets supplemented with prickly pear (25g/kg b.w) decreased plasma total cholesterol and total lipid [47]. Drinking of a *S. officinalis* infusion decreased the levels of cholesterol and triglycerides in the blood [48]. Furthermore, sage leaves were effective in lowering plasma cholesterol, LDL and triglycerides as well as increase HDL levels in lipidemic rats [21]. Sage water extract (SWE) reduces the level of lipid contents, increases cellular antioxidant activities and protects cardiac and testicular tissues by scavenging free radicals [49]. Observed benefits of peppermint juice in enhancement of glucose and lipid profile levels in normoglycemic Wistar rats [50].

Also, data presented in Table (2) show the effect of addition of Sage and Mint to Prickly pear juice on high density lipoprotein, low density lipoprotein and very low density lipoprotein of diabetic rats. Results showed that the mean value of HDL-c of positive control group (39.4 mg/dl) which showed significant decrease ($p < 0.05$) comparing with negative control group (48.33 mg/dl) Meanwhile, data indicated that the consumption of Prickly pear juice enriched with Sage and Mint led to increase HDL-c. The highest increase in HDL-c was observed in diabetic group administrated with Prickly pear juice enriched with sage (1.5%) (59.01 mg/dl)

The results also showed that the level of low-density lipoprotein LDL-c cholesterol in the positive control

group was high, where the value was 154.66 mg / dl compared to the negative control group, where the mean value was 49.36 mg / dl.

The obtained results indicated that mean values of VLDL-c of positive control group were higher than that of negative control with significant difference (34.24 and 20.51 mg/dl)

On the other hand, rats group consumed Prickly pear juice enriched with 1.5% mint recorded the highest reduction of VLDL-c level (the mean value was 22.8 mg/dl) when compared with other treated groups with significant difference.

Consumption prickly pear Juice caused a significant increase in HDL-c cholesterol of rats [40]. Moreover, observed that prickly pear increased the level of HDL-c [46]. In a crossover trial on 6 healthy female volunteers (aged 40-50) after 4- week sage tea consumption (infusion prepared by pouring 300 ml of boiling water onto 4 g dried leaves of sage, twice a day) led to a reduction on blood LDL-C, total cholesterol but increased blood HDL-C without hepatotoxic or other adverse effects [51]. *Salvia officinalis* tea consumption is accountable for the improvement of the lipid profile inducing a decrease on the highly atherogenic LDL-C particles and an increase in the HDL-C which may be due to the ability of sage water extract (SWE) to reduce cholesterol biosynthesis [52].

CONCLUSION

From the above results it could be concluded that fortifying prickly pear juice with different concentrations of Sage or Mint leaves powder showed a remarkable improvement in nutritional indicators such as blood glucose level, insulin and lipids profiles. Furthermore, these additives worked to reduce the risks of diabetes and thus improve health in diabetic rats.

REFERENCES

1. Zenteno-Ramirez, G., B.I. Juárez-Flores, J.R. Aguirre Rivera, M. Monreal-montes, J. Merida Garcia, M. Perez Serratos, M.Á. Varo Santos, M.D. Ortiz Perez and Rendon J.A. Huerta, 2018. Juices of prickly pear fruits (*Opuntia* spp.) as functional foods Ital. J. Food Sci., 30: 614-627.
2. El-shehy, H.R., S.S. El-Sayed, E.M. Abdel-Mawla and N.F. Agamy, 2020. Nutritional Value of Cladodes and Fruits of Prickly Pears (*Opuntia ficus-indica*) Alex. J. Fd. Sci. & Technol., 17(1): 17-25.

3. Abdel Fattah, M.S., S.E.A. Badr and A.S. Elsaid, 2020. Nutritive value and chemical composition of prickly pear seeds (*Opuntia ficus indica* L.) growing in Egypt. Int. J. Agric. Pol. Res., 8(1): 1-10.
4. Sabtain, B., R. Farooq, B. Shafique, M.M.A.N. Ranjha, S. Mahmood, G. Mueen-Ud-Din, S. Irfan, K. Shehzadi, Q. Rubab, L. Asad and M. Ishfaq, 2021. A Narrative Review on the Phytochemistry, Nutritional Profile and Properties of Prickly Pear Fruit. OpAcc J. Bio. Sci. & Res., 7(2): DOI: 10.46718/JBGSR.2021.07.000164.
5. Frati, A.C., E. Jimenez and C.R. Ariza, 1990. Hypoglycemic effect of *Opuntia ficus-indica* in non-insulin-dependent diabetes Mellitus patients. Phytotherapy Research, 4: 195-197.
6. Trejo-González, A., G. Gabriel-Ortiz and A.M. Puebla-Perez, 1996. A purified extract from prickly pear cactus (*Opuntia fuliginosa*) control experimentally induced diabetes in rats. J. Ethnopharmacol., 55: 27-33.
7. Aguilar, F.J., M. Jimenez-Estrada and R. Reyes-Chilpa, 2001. Hypoglycemic activity of root-water decoction, sesquiterpenoids and one polysaccharide fraction from *Psacalium decompositum* in mice. J. Ethnopharmacol., 69: 207-215.
8. Cicero, A.F.G., G. Derosa and A. Gaddi, 2004. What do herbalists suggest to diabetic patients in order to improve glycemic control? Evaluation of scientific evidence and potential risks. Acta Diabetologica, 41: 91-98.
9. Magos, G., D.S. Basurto and M. Lorenzana-Jiménez, 2006. Cactus utility glucose control in diabetes mellitus type 2. Rev. UNAM School Med., 49: 157-161.
10. Brinker, F., 2009. Prickly pear as food and medicine. J. Diet. Suppl., 6: 362-376.
11. Bensadón, S., D. Hervert-Hernández, S.G. Sáyago-Ayerdi and I. Goñi, 2010. By products of *Opuntia ficus-indica* as a source of antioxidant dietary fiber. Plant Foods Hum. Nutr., 65: 210-216.
12. Van Proeyen, K., M. Ramaekers, I. Pischel and P. Hespel, 2012. *Opuntia ficus indica* ingestion stimulates peripheral disposal of oral glucose before and after exercise in healthy men. Int. J. Sport Nutr. Exerc Metab., 22: 284-291.
13. Galati, E., M. Mondello, D. Giuffrida, G. Dugo, N. Miceli, S. Pergolizzi and M. Taviano, 2003. Chemical characterization and biological effects of Sicilian *Opuntia ficus-indica* (L.) Mill. Fruit juice: antioxidant and antiulcerogenic activity. J. AFOOD Cvem., 51(17): 4903-4908.
14. Linarès, E., C. Thimonier and M. Degre, 2007. The effect of Ne *Opuntia* on blood lipid parameters--risk factors for the metabolic syndrome (syndrome X) Adv. Ther., 24: 1115-1125.
15. Abd El-Razek, F.H. and A.A. Hassan, 2011. Nutritional Value and Hypoglycemic Effect of Prickly Cactus Pear (*Opuntia ficus- indica*) Fruit Juice in Alloxan-Induced Diabetic Rats. Aust. J. Basic & Appl. Sci., 5(10): 356-377.
16. Sailesh, A., 2014. The mechanism of the inhibitory action of mentholon guts smooth muscle, Br. J. Surg., 71.902.
17. Chandirasegaran, G., C. Elanchezhiyan, S. Suhasini and A. Babby, 2014. Antihyperglycemic activity of menthe piperita ethanol leaves extract on streptozotocin induced diabetic rats. International Journal for Pharmaceutical Research Scholars, 3: 1-3.
18. Mesbahzadeh, R., K. Somerville, W. Ellis, B. Whitten, T. Balfour and G. Bell, 2015. Stones in the common bile duct: experience with medical dissolution therapy, Postgrad Med. J., 61: 313-316.
19. Eidi, M., A. Eidi and H. Zamanizadeh, 2005. Effect of *Salvia officinalis* L. leaves on serum glucose and insulin in healthy and streptozotocin-induced diabetic rats. Journal of Ethno Pharmacology, 100: 310-313.
20. Lima, C.F., M.F. Azevedo, R. Araujo, M. Fernandes-Ferreira and C. Pereira-Wilson, 2006. Metformin-like effect of *Salvia officinalis*(common sage) Is it useful in diabetes prevention?. Br. J. Nutr., 96(2): 326-333.
21. Christensen, K.B., M. Jørgensen, D. Kotowska, R.K. Petersen, K. Kristiansen and L.P. Christensen, 2010. Activation of the nuclear receptor PPAR γ by metabolites isolated from sage (*Salvia officinalis* L.) J. Ethnopharmacol., 132: 127-133.
22. Behradmanesh, S., F. Derees and M. Rafieian-kopaei, 2013. Effect of *Salvia officinalis* on diabetic patients, J. Ren. Inj. Prev., 2: 51-54.
23. Khashan, K.T. and K.A. Al-Khefajim, 2015. Effects of *Salvia officinalis* L. (sage) leaves extracts in normal and alloxan -induced diabetes in white rats. International Journal of Scientific & Engineering Research, 61: 20-28.
24. Chalabi, W., S. Bilen, S. Yilmaz, M.A. Bilen and G. Biswas, 2016. Effects of dietary incorporation of tetra (*Cotinus coggygria*) extract on immune response and resistance to *Aeromonas hydrophila* in koi Carp (*Cyprinus carpio*) 7 pages. The Israeli Journal of Aquaculture- Bamidgheh., 66: 1-6.

25. Mahdizadeh, R., S. Moein, N. Soltani, K. Malekzadeh and M. Mahmoodreza, 2018. Study the molecular mechanism of salvia species in prevention of diabetic. IJPSR, 9: 4512-4521.
26. Belhadj, S., O. Hentati, M. Hammami, A. Ben Hadj, T. Boudawara, M. Dammak, S. Zouari and A. El-Feki, 2018. Metabolic impairments and tissue disorders in alloxan-induced diabetic rats are alleviated by *Salvia officinalis* L. essential oil. Biomedicine & Pharmacotherapy, 108: 985-995.
27. Brown, N., J.A. John and F. Shahidi, 2019. Polyphenol composition and antioxidant potential of mint leaves. Food Prod Process and Nutr., 1: 1-14.
28. AIN, 1993. American Institute of Purified Diet for Laboratory Rodent, Final Report; J. Nutr., 123: 1939-1951.
29. Desai, N.S. and H. G. Bhide, 1985. Hypoglycemic effect of Hantitonia Suave lens. Indian. Med., 81: 86-91.
30. NDDG, 1994. The National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes, 28: 1039-1057.
31. Abd El-Razek, F.H., E.M. El-Metwally, G.M.G. Shehab, A.A. Hassan and A.M. Gomaa, 2012. Effects of cactus pear (*Opuntia ficus indica*) juice on oxidative stress in diabetic cataract rats. Saudi Journal for Health Sciences, 1(1): Jan-Apr 2012.
32. Schermer, R.M., 1967. Radio protective effect of Mentha Piperita. J. Med. Arom. Plant Sci., 23(1A): 91-97.
33. Sasaki, T., S. Matsy and A. Sonae, 1972. Effect of acetic acid concentration on the colour reaction in the O-toluidine boric acid method for blood glucose estimation. Rinsh. Kagaku., 1: 346-353.
34. Abraham, E.C., T.A. Huff, N.D. Cope, J.B. Wilson, E.D. Bransome and T.H. Huisman, 1978. Determination of the glycosalated hemoglobin (Hb) with a new microcolumn procedure. Suitability of the technique for assessing the clinical management of diabetes mellitus. Diabetes, 27(9): 931-7.
35. Wilson, M.A. and L.E. Miles, 1977. Radioimmunoassay of Insulin in Handbook of Radio Immunoassay G.E. Abraham, Ed., M. Inc. New York, pp: 275.
36. Thomas, L., 1992. Labor and Diagnose, 4th Ed. Marburg: Die Medizinische Verlagsgesellschaft, 208.
37. Young, S.K., 1975. Studies on essential oils, Part 14. Natural preservatives for butter, J. Med. Arom. Plant Sci., 20: 735-739.
38. Grodon, R. and B. Amer, 1996. In Compendium of Indian Medicinal Plants, CDRI, Lucknow and Publication and Information Directorate. New Delhi, 1: 272.
39. Lee, C.R. and G.D. Nieman, 1996. Delayed release peppermint oil capsules (colpermin) for the spastic colon syndrome: a pharmacokinetic study, Br J. Clin Pharmacol., 18: 638-640.
40. Cho, K., E. Kim, R. Choue, M. Park, H. Jung, S. Zhang and J. Chen, 2006. Insufficient taurine in enteral nutrition for patients. Nutrition Research 26: 450-453. Cladodes in the wound- healing process. J. Hort Sci., 25: 1315-1316.
41. Alarcon, A.F.J., R.R. Roman, S.J.L. Flores and G.G. Guirre, 2002. Investigation on the hypoglycaemic effects of extracts of four Mexican medicinal plants in normal and alloxan-diabetic mice. Phytother Res., 16: 383-386.
42. Eidi, A. and M. Eidi, 2009. Antidiabetic effects of sage (*Salvia officinalis* L.) leaves in normal and streptozotocin-induced diabetic rats. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 3(1): 40-44.
43. Abdellatief, S.A., R.R. Beheiryb and S.A.M. El-Mandrawyc, 2017. Peppermint essential oil alleviates hyperglycemia caused by streptozotocin nicotinamide- induced type 2 diabetes in rats Biomedicine & Pharmacotherapy, 95: 990-999.
44. Buyukblaci, A., 2008. Determination of *in vitro* anti-diabetic effects, anti-oxidant activities and phenol contents of some herbal teas. Plant foods hum nutr. Mar; 63(1): 27-33.
45. Tohn, L., D. Butera, A.M. Pintaudi, M. Allegra and M.A. Livrea, 2005. Supplementation with cactus pear (*Opuntia ficus-indica*) fruit decrease oxidative stress in healthy humans: a comparative study with vitamin C. Am. J. Clin. Nutri. 80: 391-395, 395-398.
46. Coskuner, Y. and A. Tekin, 2003. Monitoring of seed composition of prickly pear (*Opuntia ficus-indica* L) fruits during maturation period. J. Sci. Food Agri., 83(8): 846-849.
47. Ennouri, M., E. Bourret, L.Mondolot and H. Attia, 2005. Fatty acid composition and rheological behavior of prickly pear seed oils. Food Chemistry, 93: 431-437.
48. Lima, C.F., P.B. Andrade, R.M. Seabra, M. Fernandes-Ferreira and C. Pereira-Wilson, 2005. The drinking of a *Salvia officinal* is infusion improves liver antioxidant status in mice and rats. J. Ethnopharmacol., 97: 383-389.

49. Alshubaily, F.A. and E.J. Jambi, 2018. "The Possible Protective Effect of Sage (*Salvia officinalis* L.) Water Extract against Testes and Heart Tissue Damages of Hypercholesterolemic Rats", *International Journal of Pharmaceutical and Phytopharmacological Research*, 8(1): 62-68.
50. Barbalho, S.M., A.P.M. Spada, E.P. De Oliveira, M.E. Paiva-Filho, K.A. Martuchi, N.C. Leite, R.M. Deus, V. Sasaki, L.S. Braganti and M. Oshiiwa, 2009. Menthapiperita effects on wistar rats plasma lipids. *Brazilian Archives of Biology and Technology*, 52(5): 1137-1143.
51. Sa, C., A. Ramos, M. Azevedo, C. Lima, M. Fernandes-Ferreira and C. Pereira-Wilson, 2009. Sage tea drinking improves lipid profile and antioxidant defences in human. *Int. J. Mol. Sci.*, 10: 3937-3950.
52. Elida, B., Z. Daniel, P. Payal, J. Vishal, L. Tejas, K. Inna, J. Sidney and D. Sidhartha, 2010. A novel dietary supplement containing multiple phytochemicals and vitamins elevates hepatorenal and cardiac antioxidant enzymes in the absence of significant serum chemistry and genomic changes. *Oxid. Med. Cell Longev.*, 3(2): 129-144.