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The Effects of Structurally Different Saponin Containing Plants on Tissue Antioxidant Defense Systems, Lipid Peroxidation and Histopathological Changes in Streptozotocin-Induced Diabetic Rats

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Abstract: The aim of this study, was to examine the effects of *Yucca schidigera*, *Quillaja saponaria* and mixture of both plants on tissue antioxidant defense systems, lipid peroxidation and histopathological changes on streptozotocin-induced diabetic rats. Animals were allocated into 5 groups of each containing 10 rats. Control (C) and Diabetic Control group (D) were fed by Standart Rat Feed (SRF). The other diabetic groups, *Yucca schidigera* group (DY), *Quillaja saponaria* group (DQ) and mix group (DQY) were fed *ad libitum* using SRF +100 ppm *Yucca schidigera* powder (Sarsaponin 30®), SRF +100 ppm *Quillaja saponaria* powder (Nutrafito®) and SRF+100 ppm *Yucca schidigera-Quillaja saponaria* powder (Nutrafito Plus®), respectively for 3 weeks. MDA levels in liver and kidney of the rats significantly increased in D group compared to control. MDA levels in DY, DQ and DQY groups significantly decreased in liver and kidney of the diabetic rats. On the other hand, the liver and kidney GSH concentrations significantly decreased in D, DY and DQY groups compared to control and DQ group. The SOD levels in liver significantly increased in DY, DQ and DQY groups compared to D group. The kidney SOD levels in D and DY group significantly decreased compared to control and other groups. On the other hand, treatment of diabetic rats with *Quillaja saponaria* and *Quillaja saponaria-Yucca schidigera* mixtures prevented the alteration in liver and kidney pathology with the return to their normal texture. Consequently, in buffering the negative impacts of increased oxidative stress in DM and in preventing or mitigating diabetic complications, it was seen that *Quillaja saponaria* was more effective than *Yucca schidigera*. Moreover, it can be considered that these plants could support the treatment of the disease by antioxidant effects.

Key words: Diabetes mellitus, saponins, oxidative stress, tissue, histopathological changes, rats

INTRODUCTION

Free radicals are very reactive chemical species, can cause oxidation injury to the living beings by attacking the macromolecules like lipids, carbohydrates, proteins and nucleic acids. Under normal physiological conditions, there is a critical balance in the generation of oxygen free radicals and antioxidant defense systems used by organisms to deactivate and protect themselves against free radical toxicity (Sies, 1991; Halliwell and Whiteman, 2004; Ramakrishna and Rama, 2007). Impairment in the oxidant/antioxidant equilibrium creates a condition known as oxidative stress. Oxidative stress is known to be a component of molecular and cellular tissue damage mechanisms in a wide spectrum of iseases (Halliwell and Gutteridge, 1998; Ramakrishna and Rama, 2007).

Diabetes Mellitus (DM), characterized by hyperglycemia and long-term complications affecting the eyes, kidneys, nerves and blood vessels is the most common endocrine disorder. Although, the underlying mechanism of diabetic complications remains unclear, much attention has been focused on the role of oxidative stress. It has been suggested, that oxidative stress may contribute to the pathogenesis of different diabetic complications (Ceriello, 2000).

Nowadays, herbal drugs are gaining popularity in the treatment of diabetes and its complications. The major merits of herbal medicines seem to be their efficacy, low incidence of side effects and low cost (Valiathan, 1998). Eddouks *et al.* (2005) that according to the World Health Organization, there are >1200 plant species worldwide used in the treatment of diabetes mellitus and substantial

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number of plant showed effective hypoglycemic activity after laboratory testing (Eddouks *et al*., 2005). A wide variety of plant species contain saponins in leaves, stem, seeds, bark, blossoms, fruit and roots (Price *et al*., 1987). When present in the diet of animals they are believed to have several negative effects. For example, dietary saponins derived from different plants have been held responsible for depression of feed intake, reduction in weight gain, accentuation of ruminant bloat, photosensitization (Cheeke, 1999), inhibition of the active uptake of nutrients (Johnson *et al*., 1986). On the other hand, saponins have also long been known to possess properties useful to man as they are the active components in a large number of traditional herbal medicine preparations. There have been reports of antiviral, antifungal, antibacterial, cholesterol lowering activity, hypoglycemic, immunostimulant, antidiabetic and antioxidant activity of saponins (Francis *et al*., 2002; Aslan *et al*., 2005). The 2 major commercial sources of saponins are *Yucca schidigera* and *Quillaja saponaria*. *Yucca schidigera* is native to the southwestern United States and Mexico. *Quillaja saponaria* is a tree native to Chile (Cheeke, 1999).

The aim of the present study, is to evaluate the effect of diet suplementation with different types of saponin containing plant sources such as *Yucca schidigera* in streoid type saponin or *Quillaja saponaria* in triterpenoid type saponin or mixture of both plants on antioxidant defense systems, lipid peroxidation and NOx levels in liver and kidneys of streptozotocin induced diabetic rats, by histopathological examination and biochemical analysis and to elucidate the mechanism involved in this effect.

MATERIALS AND METHODS

Chemicals: The chemicals used in the study were purchased from Sigma-Aldrich (Sigma-Aldrich Chemical Co. St. Louis, MO, USA).

Plant material: In our study, *Yucca schidigera* powder (Sarsaponin 30®), *Quillaja saponaria* powder (Nutrafito®) and commercial preparations consisting of mixture of both (Nutrafito Plus®) incorporating in the trial rations of our study as source of saponin, were provided from the firm Desert King International (San Diego, CA, USA). According to the information obtained from the firm, the preparations were produced without losing the phytochemicals they contained as 100% plant powder whereas, moreover, they contained also Sarsaponin 30® >8% steroidal, Nutrafito® 2.5-3.5% triterpenoidal and Nutrafito Plus® 2.5% triterpenoid and 0.5% steroidal saponin.

Animals and experimental design: Male albino Wistar rats, weighing about 180-250 g were used. They were housed under standard conditions of temperature (23±2°C), humidity and dark-light cycle (lights on from 6:00 am to 6:00 pm). The animals were maintained on standard rat feed supplied by Bil- Yem Ltd. (Turkey). Tap water was available *ad libitum*. All the animals were carefully monitored and maintained in accordance with the ethical recommendation of the University of Afyonkarahisar Kocatepe Animal Ethics Committee.

The animals were fasted overnight and diabetes was induced by a single intraperitoenal injection of a freshly prepared solution of STZ (50 mg kg^{-1} body weight) in cold 0.9% saline. The animals were allowed to drink 5% glucose solution overnight to overcome the drug-induced hypoglycemy. Control rats were injected with 0.9% saline alone. Diabetes was confirmed in STZ rats by measuring the fasting blood glucose concentration using a glucometer Accu-chek Go (Bayer, Germany) 48 h after the injection of STZ. The rats with blood glucose level >200 mg dL^{-1} were considered to be diabetic and were used in the experiment. The treatment was started on the 2nd day after STZ injection and this was considered as 1st day of treatment. The treatment was continued for 21 days.

Normal and diabetic rats were randomly divided into 5 experimental groups:

- Nondiabetic Control (C) (n = 10)
- Diabetic Control (D) (n = 10)
- Diabetes + *Yucca schidigera* (DY) (n = 10)
- Diabetes + *Quillaja saponaria* (DQ) (n = 10)
- Diabetes + Plant mix (DQY) (n = 10)

C and D groups were fed by Standart Rat Feed (SRF). The other diabetic groups, DY, DQ and DQY groups were fed *ad libitum* by SRF +100 ppm *Yucca schidigera* powder (Sarsaponin 30®), SRF + 100 ppm *Quillaja saponaria* powder (Nutrafito®) and SRF +100 ppm *Yucca schidigera-Quillaja saponaria* powder (Nutrafito Plus®), respectively for 3 weeks during the study.

Biochemical estimation: At the end of the experimental period, the rats were anaesthetized and killed by cervical dislocation. The organs including liver and kidney were collected for examination of clinical biochemistry. The tissues were collected for examination of clinical biochemistry, removed immediately and washed in ice-cold saline. Tissues were homogenized 1.40 w v^{-1} in 0.1 M phosphate buffer, pH 7.4, containing 1 mM EDTA. After centrifugation at 18000× g for 15 min at 4°C, the supernatant was extracted and kept at -30°C in advance

of assays. In the tissue, homogenates the levels of Malondialdehyde (MDA), reduced Glutathione (GSH), Superoxide Dismutase (SOD) and Nitric Oxide (NOx) were assayed. The vital organs (liver and kidney) of each rat were carefully removed. Pieces of this organs were fixed in 10% neutral formol saline for further histopathological investigations.

Determination of tissue malondialdehyde levels: The MDA levels, an index of lipid peroxidation in tissues was determined according to the method described by Ohkawa *et al.* (1979). In this method, MDA reacts with thiobarbituric acid to form a colored complex that has maximum absorbance at 532 nm. MDA levels as nmol g^{-1} wet tissue was expressed.

Estimation of tissue nitric oxide levels: Nitric oxide decomposes rapidly in aerated solutions to form stable nitrite/nitrate products (NOx). The tissues nitrite/nitrate concentration was measured by a modified method of Griess assay, described by Miranda *et al.* (2001). The principle of this assay is reduction of nitrate by vanadium combined with detection by the acidic Griess reaction. Briefly, samples were deproteinized prior to assay. The supernatants (0.5 mL) 0.25 mL of 0.3 M NaOH were added. After incubation for 5 min at room temperature, 0.25 mL of 10% (w v^{-1}) $ZnSO_4$ was added for deproteinization. This mixture was then centrifuged at 14000× g for 5 min and supernatants were used for the Griess assay. The plasma was added to 96% cold ethanol at 1.2 (v v^{-1}) and then vortexed for 5 min. After incubating for 30 min at 4°C, the mixture was centrifuged at 8000 g for 5 min and the supernatants were used for the Griess assay. One hundred micro liter of filtrated plasma was mixed with 100 μL of VCl3 and was rapidly followed by the addition of the Griess reagents, which are containing SULF 50 μL and NEDD 50 μL. The determination was performed at 37°C for 30 min. The absorbance was measured by a microplate reader (Multiskan Spectrum, Thermo Labsystems, Finland) at 540 nm. Nitrite/nitrate concentration was calculated using a $NaNO_2$ standard curve and expressed as μ M L^{-1}.

Determination of tissue reduced glutathione levels: The tissues GSH concentration was measured using the method described by Beutler *et al.* (1963). Briefly, 0.2 mL supernatant was added to 1.8 mL distilled water. Precipitating solution of 3 mL (1.67 g metaphosphoric acid, 0.2 g EDTA and 30 g NaCl in 100 mL distilled water) was mixed with haemolysate. The mixture was allowed to stand for approximately 5 min and then filtered (Whatman No. 42). Filtrate of 2 mL was taken and added into another tube and then 8 mL of the phosphate solution (0.3 M disodium hydrogen phosphate) and 1 mL DTNB were added. A blank was prepared with 8 mL of phosphate solution; 2 mL diluted precipitating solution (3-2 parts distilled water) and 1 mL DTNB reagent. A standard solution of the GSH was prepared (40 mg 100 mL^{-1}). The optical density was measured at 412 nm in the spectrophotometer. Results were communicated as mg g^{-1} wet tissue.

Determination of tissue superoxide dismutase activity: The activity of superoxide dismutase was estimated spectrophotometrically at 540 nm by a method according to Sun *et al.* (1988), using the Xanthine/Xanthine Oxidase (XOD) reaction as a source of substrate (superoxide) and reduced nitroblue tetrazolium as an indicator of superoxide. In this method, xantine-xantine oxidase was utilized to generate a superoxide flux. The absorbance obtained from Nitroblue Tetrazolium (NBT) reduction to blue formazon by superoxide was determined at 560 nm spectrophotometrically.

Histopathological estimation: After blood sampling for the biochemical analysis, the animals were sacrificed, quickly necropsied and small piecess of liver and kidneys were taken for histopathological examination. Organ samples were fixed in 10% neutral formol saline, embedded in paraffin and cut on a microtome in 4-5 μ thick and stained with hematoxylin-eosine (Allen, 1992.) then examined under light microscopy. In present study, lesions were given the histopathological picture depending on the severity of changes.

Statistical analysis: All data were presented as mean±SD for parametric variables. Parametric variables were compared using one-way analysis of variance with post-hoc analysis using the Duncan test. Data were analyzed using the SPSS® for Windows computing program (Version 10.0) and $p<0.05$, was considered statistically significant (Sokal and Rohlf, 1969).

RESULTS AND DISCUSSION

The results of biochemical determination for the experimental and the control group tissues are given in Table 1.

As shown in Table 1, the marker of lipid peroxidation MDA levels in liver and kidney of the rats significantly increased ($p<0.05$) in D group compared to control and other experimental groups. The liver and kidney GSH concentrations significantly decreased in D, DY and DQY

Table 1: MDA, GSH, SOD and NOx content in various tissues of rats

Tissue	Parameters	Control $\bar{x} \pm$ SD	D $\bar{x} \pm$ SD	DY $\bar{x} \pm$ SD	DQ $\bar{x} \pm$ SD	DQY $\bar{x} \pm$ SD
Liver	MDA (nmol g^{-1})	6.5 ± 0.64^{b}	10.85 ± 2.12^{a}	7.43 ± 1.04^{b}	7.19 ± 1.19^{b}	7.62 ± 0.95^{b}
	GSH (mg g^{-1})	25.53 ± 3.96^{a}	10.94 ± 2.10^{c}	13.00 ± 2.89^{c}	17.38 ± 3.83^{b}	13.25 ± 1.18^{c}
	SOD (U mg^{-1} protein)	0.50 ± 0.08^{a}	0.36 ± 0.06^{b}	0.44 ± 0.03^{a}	0.50 ± 0.04^{a}	0.47 ± 0.04^{a}
	NOx (μmol L^{-1})	8.49 ± 2.06^{a}	2.75 ± 0.77^{cd}	2.06 ± 1.27^{d}	4.92 ± 0.78^{b}	3.97 ± 1.72^{bc}
Kidney	MDA (nmol g^{-1})	6.85 ± 1.27^{b}	13.31 ± 5.00^{a}	8.62 ± 1.07^{b}	8.09 ± 0.72^{b}	9.28 ± 1.31^{b}
	GSH (mg g^{-1})	26.13 ± 5.6^{a}	12.52 ± 2.39^{c}	14.30 ± 3.98^{c}	19.52 ± 6.66^{b}	13.49 ± 1.50^{c}
	SOD (U mg^{-1} protein)	0.35 ± 0.06^{ab}	0.28 ± 0.37^{c}	0.32 ± 0.05^{bc}	0.35 ± 0.03^{ab}	0.39 ± 0.04^{a}
	NOx (μmol L^{-1})	5.41 ± 1.12^{a}	2.77 ± 0.94^{c}	1.84 ± 0.52^{c}	4.14 ± 0.91^{b}	2.76 ± 1.18^{c}

Values with different letters show statistically significant differences ($p<0.05$)

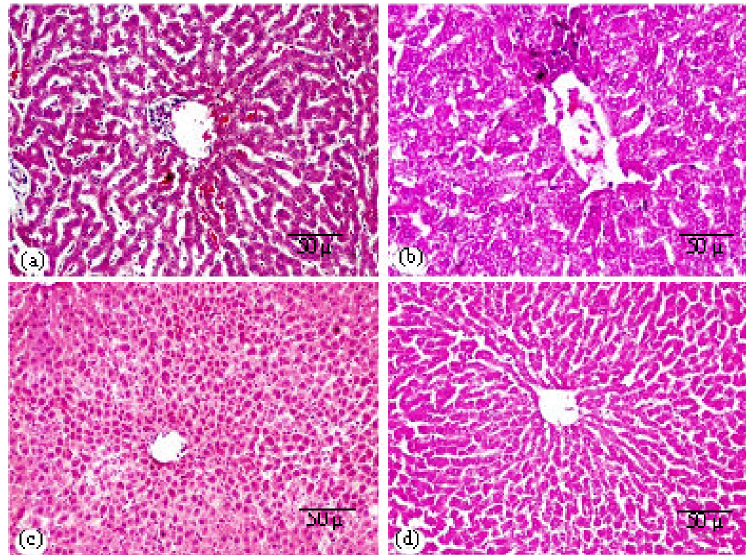

Fig. 1a: Histopathological apperence of congestion and perivascular lymphocyte infiltration in D group livers, b: Periacinar lymphocyte infiltration and slight paranchyma degeneration in DY group livers, c: Dilated liver sinusoides in DQ group livers, d: No microscopic changes were seen in DQY group livers. HE×200. Scale Bars 50 μ

groups compared to control and DQ group ($p<0.05$). The SOD levels in liver significantly decreased in D group compared to control and other groups ($p<0.05$). The kidney SOD levels in D and DY group significantly decreased compared to control and other groups ($p<0.05$). The liver and kidney NOx levels significantly decreased in D, DY and DQY groups compared to control and DQ group ($p<0.05$). Furthermore, the liver and kidney NOx level was lower in DY group as compared to the D group.

Histopathological changes in organs of experimental groups were described. In group D, parenchyma degenaration in the hepatocytes, congestion in the sinusoides and perivascular lymphocyte infiltration in the livers have been observed. There were degenarations in the proximal tubules in the cortex of kidneys, hemorrhage in the interstitial area and periglomerular lymphocytic infiltration (Fig. 1a and 2a). In DY group, mild periacinar lymphocyte infiltration and paranchyma degenarations in the livers, mild hyperemia and hemorrhage in the cortex and medulla of the kidneys were noticed (Fig 1b and 2b). In DQ group, dilatations in the liver sinusoides and degenerations of proximal tubules epithelial cells in the kidneys were seen (Fig. 1c and 2c). In DQY group, no significant histopathological changes were observed in the livers and kidneys (Fig. 1d and 2d). No abnormal macroscopic findings were detected in the other organs.

Free radicals are held responsible from pathogenesis of several diseases like DM, atherosclerosis, cell damage, cancer, myocard coronary thrombosis, hemolitic diseases and immune diseases (Fidan and Dundar, 2008). The main damage induced by free radicals results in alterations of cellular macromolecules (membrane lipids, proteins and DNA) and changes in intracellular calcium and intracellular pH, or cell death (Dorval *et al*., 2003; Fidan and Dundar, 2008). The impact made by free radicals on lipids is named as Lipid Peroxidation (LP). LP is a complicated radical chain reaction leading to the formation of various products including lipid hydroperoxides,

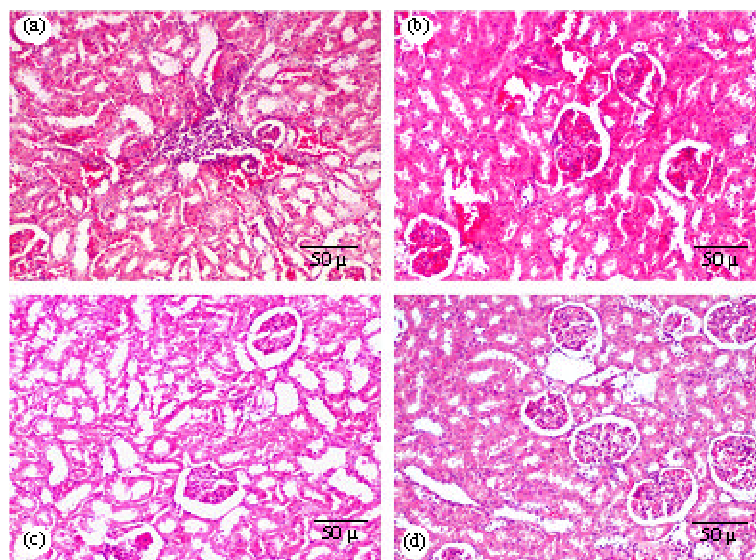

Fig. 2 a: Periglomerular lymphocyte infiltration, hemorrhage and tubular degeneration in the cortical interstitium in D group kidney, b: Periglomerular and interstitial hemorrhage in DY group kidney, c: Slight tubular degeneration in DQ group kidney, d: No microscopic changes were seen in DQY group kidney, HE×200. Scale Bars 50 μ

conjugated dienes and malondialdehyde. Detection of lipid hydroperoxides and conjugated dienes and Thiobarbituric Acid-Reactive Substances (TBARS) such as MDA, are often applied to the study of lipid peroxidation reactions (Diplock, 1994; Enginar *et al*., 2006). Since, membrane phospholipids are major targets of oxidative damage, lipid peroxidation is often the first parameter analyzed for proving the involvement of free radical damage. Thus, the presence of MDA is considered as an indicator of free-radical damage through membrane lipid peroxidation (Katz *et al*., 1996; Enginar *et al*., 2006).

The antioxidant defense system includes small molecular antioxidants, antioxidant enzymes and metal chelating agents. Halliwell and Gutteridge (1998) define an antioxidant as any substance that when present at low concentrations, compared to those of an oxidizable substrate, significantly delays, or inhibits, oxidation of that substrate. The efforts of the endogenous antioxidant enzymes to remove the continuously generated free radicals initially increase due to an induction but later enzyme depletion results, resulting in oxidative cell damage (Vidyasagar *et al*., 2004). Enzymatic scavengers like SOD, CAT, Glutathione Peroxidase (GPx), Glutathione Reductase (GR) etc. protect the system from deleterious effects of reactive oxygen species and pesticides have been reported to cause alteration in antioxidants or free radical scavenging system (Oberoi *et al*., 2007). Reduced GSH and its metabolizing enzymes provide the major defense against ROS-induced cellular damage (Celik and Suzek, 2008). GSH serves as a reductant in oxidation reactions resulting in the formation of GSSG. GSH can protect cells against the damage of ROS and free radicals that arise during conditions of oxidative stress (Loch-Caruso *et al*., 2005). Thereby, decreased GSH levels may reflect depletion of the antioxidant reserve. As a consequence of GSH deficiency, a number of related functions may be impaired such as a decrease in reducing capacity, protein biosynthesis, immune function, accumulations of lipid peroxidation products and detoxification capacity (Annuk *et al*., 2001; Sen, 2000; Hayes and McLellan, 1999).

Fidan and Dundar (2008) found that the profiles of fasting glucose levels, were significantly increased in diabetic rats compared to healthy control. Moreover, they reported that the increased level of blood glucose in diabetic rats, significantly decreased by supplementation of 100 ppm *Yucca schidigera* and *Quillaja saponaria* powder. Although, *Quillaja saponaria*-*Yucca schidigera* mixtures powder to the ration didn't decrease the fasting glucose levels in diabetic rats. The hyperglycemy in diabetes causes free radicals to be formed and the antioxidant system to become insufficient so increasing the oxidative stress (Karasu, 1999). It was found that in diabetic persons plasma and tissue LP products were much more in number than those in healthy persons of same ages whereas, in addition to this, in patients of retinopathy and angiopathy Type I DM it was observed that LP products were increased comparing to patients not having any complications. This situation puts ahead the significance of LP in development of diabetic

complications. Similar findings were obtained in diabetic animals, too (Wolf, 1993; Cother *et al*., 1992; Jain *et al*., 1990) in their study they carried out with rats, which they established diabetes with STZ, they found that the LP in erythrocytes of diabetic rats were significantly high comparing to the control group. In this study, diabetic groups were fed by 100 ppm *Yucca schidigera*, *Quillaja saponaria* and *Quillaja saponaria-Yucca schidigera* mixtures powder. GSH, SOD and MDA were evaluated for oxidative stres in liver and kidney. The results of the present study have demonstrated that 100 ppm of *Yucca schidigera*, *Quillaja saponaria* and *Quillaja saponaria-Yucca schidigera* mixtures powder supplementation decreased the MDA concentration in liver and kidney of the diabetic rats. This data shows that *Yucca schidigera* and *Quillaja saponaria* powder provides protective impact against collapsing effects of oxidation reactions. Sur *et al.* (2001) demonstrated that saponin containing plants have antioxidant properties. And this may arise due to redox potential of phenolic compounds (Cheeke *et al*., 2006). These results suggested that *Quillaja saponaria* and *Yucca schidigera* supplementation exhibited direct antioxidant properties by reducing MDA formation in diabetes mellitus and protective antioxidant effect. On the other hand, the liver and kidney GSH concentrations significantly decreased in D, DY and DQY groups compared to control and DQ group. The SOD levels in liver significantly increased in DY, DQ and DQY groups compared to D group. The kidney SOD levels in D and DY group significantly decreased compared to control and other groups. Since, the oxidative stress indicators in our study are being considered, the results best fit to physiological picture are seen in the *Quillaja saponaria* group. In buffering, the negative impacts of increased oxidative stress in DM and in preventing or mitigating diabetic complications, it was seen that *Quillaja saponaria* was more effective than *Yucca schidigera*.

Nitric oxide, a magic free radical gas molecule, has been shown to be involved in numerous physiological and pathophysiological processes. Endogenous NO is produced almost exclusively by L-arginine catabolism to L-citrulline in a reaction catalyzed by a family of nitric oxide synthases. In the 1st step, Arg is hydroxylated to an enzyme-bound intermediate Nu-hydroxy-l-arginine and 1 moL of NADPH and O_2 are consumed. In the 2nd step, NHA is oxidized to citrulline and NO, with consumption of 0.5 mol of NADPH and 1 moL of O_2. Oxygen activation in both steps is carried out by the enzyme-bound heme, which derives electrons from NADPH (Fidan *et al*., 2008; Wang *et al*., 2005). Nitric oxide is a endothelium-derivated relaxing factor as a signaling molecule in the normal physiology of mammalian (Boeckxstaens *et al*., 1991). In diabetic patients, as a result of hyperglycemy, an increase in activity of poliol path occurs. Since, the activated sorbitole path, uses NADPH for activity of aldose reductase enzyme in this path, the in-cell NADPH is being consumed. However, NADPH is required for nitric oxide synthesis. Due to such reason, the sorbitole path becoming active and eventually lack of NADPH cause NO synthesis to decrease and vascular complications of diabetes to arise (Altan *et al*., 2006). As similar to circulars telling that NO secretion from endothel is decreased in DM, it was seen that the liever and kidney nitric oxide level in our diabetic groups was decreased comparing with the control group. According to Jeon *et al.* (2000), the Korean red ginseng saponin fraction containing triterphenoide, increases the NO content. On the other hand, the liver and kidney NOx levels significantly decreased in D, DY and DQY groups compared to control and DQ group ($p<0.05$). Furthermore, the liver and kidney NOx level was lower in DY group as compared to the D group. And it is already known that *Yucca schidigera* decreases NO formation by affecting the iNOS enzyme (Cheeke *et al*., 2006). Although, *Yucca schidigera* didn't increase significantly the diminished NO level, the diminished NO level being increased significantly by *Quillaja saponaria*, makes one to think that *Quillaja saponaria* might be effective by this way in preventing angiopathys, which are among important complications of diabetes.

The liver and kidney exhibits numerous morphological and functional alterations during diabetes (Sochar *et al*., 1985). In the present study, the histological and histopathological examination of liver of diabetic rats showed parenchyma degenaration in the hepatocytes, congestion in the sinusoides and perivascular lymphocyte infiltration in the livers. Light microscopy of kidney sections of diabetic rats showed degenarations in the proximal tubules epithelial cells in the cortex of kidneys, hemorrhage in the interstitial area and periglomerular lymphocytic infiltration. In DY group, mild periacinar lymphocyte infiltration and paranchyma degenarations in the livers, mild hyperemia and hemorrhage in the cortex and medulla of the kidneys were noticed. In DQ group, dilatations in the liver sinusoides and degenerations of proximal tubules epithelial cells in the kidneys were seen. In DQY group, no significant histopathological changes were observed in the livers and kidneys. Our results indicated that treatment of diabetic rats with *Quillaja saponaria* and *Quillaja saponaria-Yucca schidigera* mixtures prevented the alteration in liver and kidney pathology with the return to their normal texture.

CONCLUSION

According to the findings, the oxidative stress indicators in our study are being considered, the biochemical results best fit to physiological picture are seen in the *Quillaja saponaria* group. In buffering, the negative impacts of increased oxidative stress in DM and in preventing or mitigating diabetic complications, it was seen that *Quillaja saponaria* was more effective than *Yucca schidigera*. Moreover, it can be considered that these plants could support the treatment of the disease by antioxidant effects.

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