EVALUATION OF ANTIOXIDANT PROPERTIES OF IMMATURE PALMYRA PALM FRUITS EXTRACT STUDIED IN HIGH FAT DIET FED- LOW DOSE STREPTOZOTOCIN INDUCED EXPERIMENTAL TYPE 2 DIABETES IN RATS

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ABSTRACT

Borassus flabellifer Linn. commonly known as the palm tree is an erect and celestial tree with more than 800 distinct uses. The immature palmyra palm fruits have been traditionally used for the treatment of diabetes and its major secondary complications. In the absence of absolute reports in the literature, the present study was aimed to evaluate the antidiabetic and antioxidant properties of the immature fruits in high fat diet fed – low dose streptozotocin induced experimental type 2 diabetes rats. Phytochemical screening revealed the presence of therapeutically important phytochemicals and the momentous levels of phenolic and flavonoid content. HFD fed and low dose STZ induced type 2 diabetic rats showed extensively altered levels of important biochemical parameters such as fasting blood glucose, insulin, hemoglobin, and glycosylated hemoglobin and the levels were reverted to the physiological range after oral treatment with fruits extract at a concentration of 400mg/kg/b.w/rat/day for 30 days. Since chronic hyperglycemia induced oxidative stress has been implicated in the etiology of diabetes mellitus, the extent of oxidative stress markers and the status of enzymatic and non enzymatic antioxidants were assayed. The treatment with immature fruit extract decreased the oxidative stress markers and improved the levels of both of enzymatic and non enzymatic antioxidants. The efficacy of the fruit extract was comparable with metformin. From the data obtained, it may be concluded that the observed significant antioxidant properties of the fruits extract may be responsible for its antidiabetic properties.

INTRODUCTION

Experimental and clinical reports demonstrated that the chronic hyperglycemia-induced oxidative stress chiefly contributes to the development and progression of diabetes and its secondary complications (Asmat et al., 2016). Free radicals with an unpaired electron in the valency orbit are generated disproportionately in chronic hyperglycemia through glucose oxidation, non-enzymatic glycation of proteins, activation of transcription factors and oxidation of glycated proteins (Maritim et al., 2003). Oxidative stress is a patho physiologic process wherein the generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) overwhelms the cells inherent antioxidant defenses, damaging vital cellular macromolecules, including lipids, proteins, nucleic acids and membrane-bound polyunsaturated fatty acids and they play a significant role in the impairment of cellular architecture and metabolic dysfunctions (Young and Woodside, 2001). Additionally, the pancreatic β-cells, due to the feeble intrinsic antioxidant availability, succumb to the excessive ROS that behave in a sporadic and destructive manner (Wang and Wang, 2017).

Hyperglycemia induces diabetic complications via free radical generation by any one of these four hypotheses: (i) increased polyol pathway flux, (ii) increased advanced glycation end-product formation, (iii) activation of protein kinase isoforms C and (iv) increased hexosamine pathway (Giacco and Brownlee 2010;Loren et al., 2005; Forbes et al., 2008). Chronic hyperglycemia also increases the circulating concentration of cytokines. It is a fact that the antidiabetes drugs, such as insulin, metformin, thiazolidinediones, gliclazide analogs, α-glucosidase inhibitors, glucagon like peptide-1, receptor agonists and dipeptidyl peptidase-4-inhibitors, although with extremely different mechanisms of action, possess antioxidant properties in addition to their hypoglycemic properties (Sena et al., 2010). However, most of the currently available drugs for the treatment of diabetes elicit undesirable side effects in addition to the development of resistance after prolonged use. In spite of great advancements in the field of science and tech-
ology in the early diagnosis and prognosis, the maintenance of normoglycemia in diabetic patients remains a task for the clinicians. Hence the search for novel drugs capable of controlling the oxidative stress and hyperglycemia effectively at a low dose continues.

**Borassus flabellifer** Linn (“Arecales”) is a monopodial, tall and cephalic tree widely known for its large, fan-shaped leaves (Morton, 1988). The trees can live up to more than 100 years. It is commonly referred to as the “tree of life” with more than 800 established uses including food, beverage, fiber, medicinal and timber (Ramachandran et al., 2004; Arulraj and Augustine, 2008). India stands first in the world in terms of its possession of Palmyra palms with a population of more than 125 million (Vengaiah et al., 2012) and out of this nearly 60% are in Tamil Nadu (Ankita et al., 2018). Above all, due to the special contemporary significance, this tree is pronounced as the official tree of Tamil Nadu in 1978 (Saravanya and Kavitha, 2017). The fruits are stomachic, sedative, laxative and aphrodisiac in nature useful in hyperdipsia, dyspepsia, flatulence, skin diseases, haemorrhages, fever and general impediment (Davis and Johnson, 1987). Palmyra fruits pulp reported to have antioxidant activity (Pathberiya and Jansz, 2010). In traditional medicine, the extract of immature palm fruits has been widely used for the treatment of diabetes and its secondary complications (Uluwaduge et al., 2005; Uluwaduge et al., 2006). Recently, we have reported the in vitro antioxidant and antimicrobial properties of immature palm fruits (Renuka et al., 2018, Renuka et al., 2019). In the present study, it is aimed to evaluate the antidiabetic and antioxidant properties of immature palm fruits extract in the High Fat Diet fed and Low Dose Streptozotocin induced experimental type 2 diabetes in rats.

**MATERIALS AND METHODS**

**Chemicals and drugs**

Streptozotocin (STZ) was procured from Sigma Chemicals, St Louis, USA. All other chemicals and reagents used in the present study were of analytical grade obtained from SRL chemicals, Bombay, India.

**Plant material**

The immature Palmyra palm fruits (prior to the development of endosperms) that have weighed between 30 to 50 gm were collected from the trees near Chengalpet, Tamil Nadu during December. The plant material was authenticated by a qualified taxonomist at the Centre for Advanced Studies in Botany, University of Madras and a voucher specimen was deposited for future reference.

**Preparation of the fruits extract**

The immature fruits were washed thoroughly and then rinsed in distilled water. The fruits were cut into thin slices and dried in an electric oven and powdered in an electrical grinder. The powdered fruits were stored in an airtight container at 5°C until further use. To selectively remove the lipids from the powdered fruits, petroleum ether (60-80°C) was used as solvent. The delipidated fruits extract was subjected to soxhlation using ethanol. The ethanolic extract of the fruits was filtered, dried and weighed and the yield was around 26%.

**Phytochemical screening**

The ethanolic extract of immature palm fruits was subjected to phytochemical screening such as alkaloids, flavonoids, glycosides, saponins, tannins, phytosterols, triterpenoids, anthraquinones and phenols (Harbone, 1998, Kokate et al., 2001). The experiments were conducted in triplicates to substantiate the findings.

**Toxicity and dosage fixation studies**

The acute toxicity of immature palm fruits extract was studied in control rats according to OECD guideline 423 (OECD, 2000). Graded doses of fruits extract dissolved in water and administered orally and the animals were observed continuously for the first 2 hours followed by every hour up to 6 hours and daily thereafter for fourteen days for any signs of morbidity, mortality and behavioral changes.

Similarly based on the reports available in the literature, graded doses of immature palm fruits (100, 200, 300, 400, 500 mg/kg b.w.) were administered to HFD – low dose STZ induced diabetic rats for various periods of treatment (Pradeep et al., 2014). From the data obtained, the optimum dosage was fixed as 400 mg/kg b.w. for 30 days.

**Experimental animals**

Male Wistar rats weighing about 160–180 g, procured from Tamil Nadu Veterinary and Animal Sciences University, Chennai, India, were housed in clean, sterile, polypropylene cages (38×23×15 cm) under standard vivarium conditions. The animals were allowed free access to standard rat chow diet (Hindustan Lever Ltd., India) or high fat diet as the case may be and water ad libitum. The composition of the standard rat diet includes 5% fat, 21% protein, 55% nitrogen-free extract and 4% fiber (w/w) with adequate minerals and vitamins for the animals. The animals were acclimatized to the laboratory conditions for two weeks before the commencement of experiments. The animal experiments were performed according to the regulations laid down by the Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA) as well as Institutional Animal Ethics Committee Guidelines.

**High fat diet fed – low dose streptozotocin induced diabetes**

The rats were divided into two dietary regimens either by feeding normal or high fat diet for two weeks (Suman et al., 2016). After two weeks of dietary manipulation, the groups of rats fed with HFD were injected intraperitoneally with a low dose of STZ (35 mg/kg b.w) dissolved in 0.1M ice cold citrate buffer, pH 4.5(Ramachandran et al., 2011). One week after STZ injection, the rats were analyzed for fasting blood glucose levels. The rats with fasting blood glucose (FBG) >250mg/dl that exhibited random hyperglycemia and glycosuria were chosen for further studies. The rats were allowed to continue to feed on their respective diets until the end of the experiments.

**Experimental Protocol**

The animals were divided into four groups, comprising a minimum of six animals in each group as follows:
RESULTS AND DISCUSSION

The preliminary phytochemical analysis forms the basis for the quantitative estimation, extraction and identification of therapeutically active constituents present in various parts of medicinal plants. The qualitative analysis of the fruits extract evidenced that the immature fruits contain most of the imperative bioactive principles which readily accounts for its folklore therapeutic and beneficial claims. The results obtained are in accordance with the earlier reports on mesosperms (Singchail et al., 2015; Sarkodie et al., 2015).

The total phenolic and flavonoid contents in the immature fruits extract were found to be 104.00 ± 0.02 μg gallic acid equivalents/100mg of fruits extract and 98.45 ± 0.03 μg quercetin equivalents/100mg of fruits extract, respectively. Phenols are considered as important plant constituents because of their free radicals scavenging ability which in turn due to the presence of one or more hydroxyl groups in them (Kumar et al., 2013). Similarly, flavonoids are an important group of polyphenols widely distributed among the plant flora containing a benzopyrone that is used as antioxidants or free radicals scavengers (Somit et al., 2013). The significant levels of total phenolic and flavonoid contents provide further evidence for the presence of biologically active phytoingredients in the ethanolic extract of immature palm fruits (Renuka et al., 2018).

The results of the toxicity and dosage fixation studies revealed that the fruits extract is non-toxic up to 2 g/kg b.w. and the fruit extract showed dose-dependent hypoglycemic activity in HFD-STZ diabetic rats. Based on the results obtained, the optimum dosage was fixed as 400 mg/ kg.b.w./rat/day for 30 days.

The levels of fasting blood glucose, glycosylated hemoglobin, plasma protein, blood urea, uric acid and serum creatinine were determined by standardized methods. Plasma insulin and C-peptide were assayed using ELISA kit for rats (Linco Research, Inc., USA). The presence of urine sugar was detected using urine strips (Diastix). Assay of key enzymes of carbohydrate metabolism

ASSAY OF BASIC BIOCHEMICAL PARAMETERS

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IN VIVO ANTIOXIDANT ASSAY

The levels of lipid peroxides (Ohkawa et al., 1979), hydroperoxides (Jiang et al., 1992) and protein carbonyls were determined in plasma, pancreatic and liver homogenates. The activities of enzymatic antioxidants such as Superoxide dismutase (SOD) (Misra and Fridovich, 1972), catalase (CAT) (Takahara et al., 1960), Glutathione Peroxides (Gpx) (Rottruck et al., 1973), Glutathione S transferase (GST) (Habig et al., 1974) were assayed in the pancreatic and hepatic homogenates of control and experimental groups of rats. The levels of non enzymatic antioxidants such as vitamin C (Omaye et al., 1979), vitamin E (Desai, 1984), ceruloplasmin (Ravin, 1961) and GSH (Sedlak and Lindsay, 1968) were also estimated.

STATISTICAL ANALYSIS

All the data obtained were grouped and statistically evaluated with the aid of SPSS 16.0 software. Hypothesis testing methods included ‘One-way analysis of variance’ followed by ‘least significant difference test’ was used. A value of P < 0.05 was considered to indicate statistical significance. All results were expressed as mean ± Standard error mean (S.E.M) for six rats in each group.

RESULTS AND DISCUSSION

Phytochemical analysis shows the presence of biologically active phytochemicals such as alkaloids, flavonoids, glycosides, saponins, tannins, phytosterols, and phenols in the immature palm fruits extract. Phytochemicals may be defined as the ecologically derived non-nutrient bioactive compounds synthesized by the plants in order to protect them from environmental stress and pathogenic microbes. Interestingly, these phytochemicals possess the ability to exert pharmacological as well as several beneficial effects on human health. The preliminary phytochemical analysis forms

<table>
<thead>
<tr>
<th>Groups</th>
<th>Control</th>
<th>Diabetic</th>
<th>Diabetic + Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Blood Glucose (mg/dl)</td>
<td>90.26 ± 4.55</td>
<td>267.65 ± 21.63</td>
<td>104.35 ± 9.33</td>
</tr>
<tr>
<td>Hemoglobin (%)</td>
<td>13.74 ± 0.55</td>
<td>11.34 ± 0.55</td>
<td>11.02 ± 0.55</td>
</tr>
<tr>
<td>Plasma Insulin (µU/ml)</td>
<td>12.5 ± 1.45</td>
<td>11.70 ± 1.79</td>
<td>11.05 ± 1.79</td>
</tr>
<tr>
<td>Urine sugar</td>
<td>Nil</td>
<td>+++</td>
<td>++</td>
</tr>
</tbody>
</table>

Units are expressed as mg/dl for blood glucose, g/dl for hemoglobin, % hemoglobin for HbA1c, µU/ml for plasma insulin and urine sugar in experimental groups of rats after 30 days of experimental period.
insulin, +++ indicates more than 2% sugar. Results are expressed as mean ± S.E.M [n=6]. One-way ANOVA followed by post hoc test LSD. Values are statistically significant at *P<0.05. The results were compared with a Control rats, b Diabetic control rats.

Tables 2, 3, 4 and 5 show the levels of lipid peroxides, hydroperoxides and protein carbonyls in plasma, pancreas, liver and kidney tissues of control and experimental groups of rats. The significant increase observed in the levels of oxidative stress markers was declined upon treatment with fruits extract and the efficacy was comparable with metformin.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Lipid peroxides</th>
<th>Hydroperoxides</th>
<th>Protein carbonyls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>3.45 ± 0.21</td>
<td>8.7 ± 0.40</td>
<td>5.48 ± 0.31</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>7.2 ± 0.30*</td>
<td>18.89 ± 2.65</td>
<td>11.59 ± 2.56*</td>
</tr>
<tr>
<td>Diabetic + palm fruits extract</td>
<td>4.45 ± 0.30*</td>
<td>11.80 ± 1.86</td>
<td>7.06 ± 0.78*</td>
</tr>
<tr>
<td>Diabetic + metformin</td>
<td>3.92 ± 0.27*</td>
<td>10.71 ± 1.10</td>
<td>6.45 ± 0.78*</td>
</tr>
</tbody>
</table>

Units are expressed as: mM/ml for lipid peroxides; 10^-5 mM/dl for hydroperoxides; nM/mg of protein for protein carbonyls. Values are presented as mean ± S.E.M for six rats in each group. One-way ANOVA followed by post hoc test LSD. Statistical significance was compared within the groups as follows: a Control rats, b Diabetic control rats; Values are statistically significant at *P<0.05

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<th>Protein carbonyls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>36.54 ± 2.56</td>
<td>13.10 ± 0.71</td>
<td>4.18 ± 0.28</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>49.21 ± 5.89**</td>
<td>25.04 ± 1.51**</td>
<td>9.15 ± 1.65**</td>
</tr>
<tr>
<td>Diabetic + palm fruits extract</td>
<td>41.00 ± 2.60**</td>
<td>16.89 ± 1.98**</td>
<td>6.81 ± 0.55**</td>
</tr>
<tr>
<td>Diabetic + Metformin</td>
<td>39.65 ± 2.98**</td>
<td>15.65 ± 0.31**</td>
<td>5.89 ± 0.98**</td>
</tr>
</tbody>
</table>

Units are expressed as: mM/ 100 g of wet tissue for lipid peroxides and hydroperoxides; nM/mg of protein for protein carbonyls. Values are given as mean ± S.E.M for six rats in each group. One-way ANOVA followed by post hoc test LSD. Statistical significance was compared within the groups as follows: a Control rats, b Diabetic control rats; Values are statistically significant at *P<0.05

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<th>Protein carbonyls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.37 ± 0.12</td>
<td>47.42 ± 4.09</td>
<td>4.51 ± 0.32</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>2.31 ± 0.65*</td>
<td>65.10 ± 6.03*</td>
<td>8.20 ± 0.56*</td>
</tr>
<tr>
<td>Diabetic + palm fruits extract</td>
<td>1.76 ± 0.17*</td>
<td>56.64 ± 3.02*</td>
<td>5.15 ± 0.39*</td>
</tr>
<tr>
<td>Diabetic + Metformin</td>
<td>1.63 ± 0.21*</td>
<td>49.65 ± 3.98*</td>
<td>4.98 ± 0.32*</td>
</tr>
</tbody>
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Units are expressed as: mM/ 100 g of wet tissue for lipid peroxides and hydroperoxides; nM/mg of protein for protein carbonyls. Values are given as mean ± S.E.M for six rats in each group. One-way ANOVA followed by post hoc test LSD. Statistical significance was compared within the groups as follows: a Control rats, b Diabetic control rats. Values are statistically significant at *P<0.05

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</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.05 ± 0.073</td>
<td>50.10 ± 3.18</td>
<td>3.75 ± 0.30</td>
</tr>
<tr>
<td>Diabetic control</td>
<td>2.65 ± 0.20*</td>
<td>85.50 ± 3.80*</td>
<td>5.47 ± 0.89*</td>
</tr>
<tr>
<td>Diabetic + palm fruits extract</td>
<td>1.96 ± 0.13*</td>
<td>59.28 ± 3.58*</td>
<td>4.82 ± 0.55*</td>
</tr>
<tr>
<td>Diabetic + Metformin</td>
<td>1.52 ± 0.12*</td>
<td>56.11 ± 4.40*</td>
<td>4.24 ± 0.48*</td>
</tr>
</tbody>
</table>

Lipid peroxidation is a free radical induced spontaneous process involving a source of secondary free radical, which subsequently act as the second messenger or can directly react with other biomolecules such as carbohydrate, proteins, lipids and DNA and thereby causing irreversible biochemical as well as molecular lesions (Robertson, 2004; Robertson and Harmon, 2006). However, lipid peroxidation primarily takes place in polyunsaturated fatty acids which contain one or more double bonds located in the cell membranes and it often proceeds with a cascade of radical stimulated chain reactions. Hydroxyl radical is known to initiate oxidative stress and remove hydrogen atom, thus generating lipid free radicals and subsequently converted into diene conjugates. Further, by the addition of oxygen, it forms a peroxyl radical which is highly reactive radicals and attacks another fatty acid forming lipid hydroperoxide (LOOH) and a new radical. Thus, lipid peroxidation is disseminated. Due to lipid peroxidation, a number of compounds such as alkanes, malonaldehyde and isoprostanes are formed. These compounds are used as markers in lipid peroxidation assay and their levels have been verified in many diseases such as neurodegenerative diseases, ischemic reperfusion injury and diabetes.

Likewise, the excessive generation of cytotoxic and highly reactive oxidative stress markers such as lipid peroxides, hydroperoxides and protein carbonyls causes oxidative damage to proteins as well as DNA and the reduced the levels of both cellular non-enzymatic and enzymatic antioxidant levels in diabetic conditions that increase the severity of organ dysfunction resulting in decreased insulin synthesis, secretion and finally resulting in β cell death. In the present study, the elevated levels of lipid peroxides, hydroperoxides and protein carbonyls were significantly altered upon oral administration of fruits extract which demonstrates the significant free radical scavenging property of fruits extract in hyperglycemia mediated oxidative stress.

Tables 6, 7 and 8 depict the activities of enzymatic antioxidants such as SOD, catalase, Gpx and GST in pancreatic, hepatic and renal tissues of control and experimental groups of rats. The diminished activities of the above enzymes in all the three tissues of the diabetic group of rats were improved after oral treatment with fruits extract. The observed decrease in the levels of plasma non-enzymatic
The activities of enzymes are expressed as: 50% of inhibition of epinephrine autoxidation/min for SOD; mM of hydrogen peroxide decomposed/min/mg of protein for catalase; mM of glutathione oxidized/min/mg of protein for GPx; U/min/mg of protein for GST.

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(Takemoto et al., 2009). Catalase enzymatically processes hydrogen peroxide into oxygen and water. Catalase deficiency results in oxidative stress leading to β-cell dysfunction. Additionally, the β - cells are rich in mitochondria and thus this organelle might be a source of ROS (Goth and Eaton, 2000).

Gpx, a selenium-containing peroxidase is linked to the detoxification of hydrogen peroxide and lipid peroxide by using GSH as a hydrogen donor and acts as a peroxynitrite reductase. Gpx is a relatively stable enzyme, but it may be inactivated under conditions of severe oxidative stress. Inactivation of this enzyme may occur through glycation governed by prevailing glucose concentration (Rahbani-Nobar et al., 1999). Persistent hyperglycemia increases oxidative stress through diverse mechanisms; the defective antioxidant function of Gpx is a hallmark in the diabetic state. The low activity of Gpx could be directly explained by the low content of GSH found in patients with type 2 diabetes, since GSH is a substrate and cofactor of Gpx. Increased activity of GR may be a compensatory response to oxidative stress. Changes in glutathione peroxidase and glutathione reductase activity may be considered an adaptation of antioxidant defense against ROS. However, the altered levels of enzymatic antioxidants were improved upon fruits extract treatment indicating the effective antioxidant as well as tissue protective nature of fruits extract.

Vitamin C, a hydrophilic antioxidant sequesters the singlet oxygen radicals, stabilizes the hydroxyl radical and regenerates reduced vitamin E back to the active state. On the other hand Vitamin E, a lipophilic antioxidant transfers its phenolic hydrogen to a peroxyl free radical of peroxidized polyunsaturated fatty acids, thereby block the radical chain reaction and averting the peroxidation of membrane lipids (Opara, 2002). Ceruloplasmin is a powerful non-enzymatic antioxidant that inhibits lipid peroxidation by binding with copper. The observed decline in plasma ceruloplasmin in diabetic rats may be due to elevated lipid peroxidation which was normalized upon treatment with fruits extract.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Reduced glutathione (mg/100 g wet tissue)</th>
<th>Pancreas</th>
<th>Liver</th>
<th>Kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>23.00 ± 0.72</td>
<td>48.10 ± 2.13</td>
<td>36.10 ± 1.52</td>
<td></td>
</tr>
<tr>
<td>Diabetic</td>
<td>11.10 ± 0.35</td>
<td>35.90 ± 0.98</td>
<td>20.09 ± 0.70</td>
<td></td>
</tr>
<tr>
<td>Diabetic + palm</td>
<td>17.52 ± 0.24</td>
<td>41.06 ± 2.42</td>
<td>30.60 ± 1.38</td>
<td></td>
</tr>
<tr>
<td>fruits extract</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic +</td>
<td>19.79 ± 0.62</td>
<td>42.50 ± 1.94</td>
<td>32.00 ± 0.80</td>
<td></td>
</tr>
<tr>
<td>Metformin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Units:** mg/100 g of wet tissue. Values are given as mean ± S.E.M for six rats in each group. One-way ANOVA followed by post hoc test LSD. Statistical significance was compared within the groups as follows: *Control rats; †Diabetic control rats. Values are statistically significant at *P*<0.05

The pancreatic, hepatic and renal GSH (Table 10) in the experimental diabetic group of rats were improved to the physiological range after treatment with fruits extract as well as metformin. Reduced glutathione (GSH), a tripeptide, γ-Lglutamyl -L-cysteinylglycine, is present in all mammalian tissues at 1–10 mm concentrations (the highest concentration in the liver) as the most abundant nonprotein thiol that defends against oxidative stress (Lu, 2013). GSH is known to maintain SH groups of proteins in a reduced state, participate in amino acid transport, detoxify foreign radicals, act as a coenzyme in several enzymatic reactions and also prevent tissue damage (Tsai et al., 2012). It is an effective antioxidant present in almost all living cells and is also considered as a biomarker of redox imbalance at the cellular level (Rizvi and Chakravarthy, 2011). Decreased GSH level is a contributory factor in the oxidative DNA damage in type 2 diabetes mellitus (Dincer et al., 2002). Hyperlipidemia, inflammation and altered antioxidant status associated with diabetes mellitus accompanied by a decreased GSH/GSSG ratio (Das et al., 2012). Altered GSH status is involved in β-cell dysfunction and in the pathogenesis of long-term morbidities of diabetes. Similarly, the lowered GSH levels observed in diabetic rats were increased upon oral administration of fruits extract further amplified the antioxidant potential of fruits extract. Several studies reported that treatment with antioxidants reduces the development of pathological complications aroused out of oxidative stress in diabetes (Sadi et al., 2008; Pazdro and Burgess, 2010). Thus the data obtained clearly evidenced the antioxidant properties of the fruits extract next to its antidiabetic efficacy.

**CONCLUSION**

The observed decrease in the levels of fasting blood glucose, glycosylated hemoglobin, urea, uric acid, creatinine and oxidative stress markers such as lipid peroxides, hydroperoxides and protein carbonyls along with a concomitant increase in the levels of both enzymatic and non enzymatic antioxidants in the diabetic rats treated with the fruits extract revealed the noteworthy antidiabetic and antioxidant properties of the fruits extract which in turn may be due to the presence of pharmacologically important phytochemicals present in the immature palmyra palm fruits extract.

**Conflict of interest statement**

The authors declare that there is no conflict of interest.

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