Therapeutic Potential of Green Tea Extract and Low Doses of γ-Irradiation on Diabetic Nephropathy of Rats

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Abstract

Introduction: Diabetic nephropathy is one of the most frequent and serious complications of diabetes mellitus. This study was designed to evaluate the effect of green tea (GT) extract and low doses of 0.5 Gy γ-radiation (R) on diabetic nephropathy (DN) of rats.

Materials and methods: Male Swiss albino rats were used in this study. DN was induced in rats using streptozotocin (45 mg/kg body weight). The rats were divided into five groups DN, DN+R, DN+GT, DN+GT+R and a sham treatment control group. Throughout the experimental period (3 and 6 weeks) animals body weight, glucose and insulin levels were evaluated. Kidney functions assay (serum urea and creatinin) were recorded. Histopathological observations in kidney tissue, DNA and glycogen intensity were also detected.

Results: Diabetic rats exhibited many symptoms including loss of body weight, increase in blood glucose level and decrease in serum insulin levels. Increase in serum urea and creatinin levels. Diabetic kidney showed a moderate renal damage, multifocal clarifications and vacuolations. Carbohydrates intensity showed a significant increase and DNA intensity showed many alterations. Improvements in glomerular and tubulointerstitial lesions were demonstrated in the diabetic rat group exposed to low doses of γ-radiation or supplemented by green tea either alone or combined in addition to amelioration in glucose, insulin urea and creatinin levels.

Conclusion: The present study demonstrates the efficacy of low doses of γ-radiation and in reducing diabetes-induced functional and histological alterations in the kidneys. The longterm control of blood glucose levels using low doses of γ-radiation or green tea either alone or combined could prevent the progression of diabetes mellitus, and therefore, nephropathy could be prevented.

Introduction

Diabetic nephropathy is one of the major microvascular complications of diabetes. The renal lesions, whether related to type 1 or 2 diabetes mellitus, are similar (Fioretto and Mauer, 2007). At present, patients with diabetes mellitus in the world were increased by millions, and the number is increasing; however, maintaining prolonged dialysis therapy is a great burden on patients both mentally and physically, and social problems, including financial issues, have also been raised. Therefore, the daily consumption of food and drink containing effective agents for the management of onset and/or progression of diabetic complications has been receiving attention to reduce the number of patients with end-stage renal failure. There is much debate over the health benefits of green tea extracts, and it is common to drink tea with meals. In the previous studies, it has been reported that green tea polyphenols have antioxidant properties, and green tea is a useful agent to protect against protein oxidation- and glycation-associated diseases (Yokozawa et al., 1996, 1997, 1998; Nakagawa and Yokozawa, 2002 and Nakagawa et al., 2002). Green tea polyphenols were also indicated as beneficial agents to manage the development of diabetic nephropathy induced by streptozotocin (STZ) injection (Yokozawa et al., 2005). Alternatively, of the catechins, (−)-epigallocatechin 3-O-gallate (EGCg) is known to be the most abundant in green tea. Recently, it has
been reported that EGCg had an antioxidant effect on creatinine (Cr) oxidation in rats with chronic renal failure and thus inhibited methylguanidine production in an adenine-induced renal failure model (Nakagawa et al., 2004).

Radiation is known to have significant effects on living organisms depending on the dose received. At higher doses, radiation destroys living materials including cells in tissue. At moderate levels, it is generally harmful but is also used for beneficial purposes including radiation therapy of cancer. At low doses, on the other hand, radiation is generally regarded as safe, and its effect, if any, is considered to be negligible. However, there have been several reports of interesting but unexpected effects of low-dose ionizing radiation on living organisms. For example, sublethal low-dose irradiation has been shown to induce an increased life span in insects (Caratero et al., 1998), increased resistance to oxygen toxicity (Lee and Ducoff, 1984), and enhancement of immune function (Yoon et al., 1998). These results have suggested the existence of significant biological effects of low-dose irradiation. Since many diseases have been shown to be caused by pathological oxidative stress, the present study examined the effects of low-dose irradiation and the dietary green tea extract in suppresses the oxidative stress of diabetic neuropathy using streptozotocin (STZ)-induced diabetic rats.

Material and Methods

Chemicals
Streptozotocin (STZ) was obtained from Sigma Chemical Co. (St. Louis, MO, USA).

Green tea extract
Green tea extract was obtained from Arab Company for Pharmaceuticals and Medicinal plants MEPACO-Egypt (Enshams El Ramil - Sharkeiya) in the form of tablets each tablet contain 300 mg of green tea dry extract. In the present study green tea extract was prepared by dissolving the tablets in distilled water at dose level 45mg/1ml/rat/day. It was administered daily by gavage.

Radiation facility:
Whole body gamma irradiation was performed at the National Centre for Radiation Research and Technology, Atomic Energy Authority (NCRRT), Cairo, Egypt, using Caesium -137 in a Gamma cell-40 Irradiator (Atomic Energy of Canada Limited, Canada). Animals were exposed to fractionated dose levels of 0.5 Gy/week of γ-radiation. The γ-radiation delivered at a dose rate of 0.61 Gy min⁻¹ for 3 and 6 weeks.

At the end of the experimental periods, animals were killed by cervical decapitation. Kidneys were removed and washed in ice-cold saline.

Experimental Design.
Adult male Swiss albino rats, weighing 120 to 130 g, were obtained from the breeding unit of the Egyptian Organization for Biological Products and Vaccines (Cairo) were used in this study. They were allowed free access to laboratory pellet chow (24.0% protein, 3.5% lipid, and 60.5% carbohydrates) and water. After several days of adaptation rats were injected intraperitoneally with freshly prepared streptozotocin (STZ) at the dose of 45 mg / kg b.w. (Chattopadhyay et al., 1997) in 0.1 M Citrate buffer of pH 4.5 (Mitra et al., 1996). Control animals were received citrate buffer alone. Induction of the diabetic state was confirmed by measuring blood glucose levels 72 h after injection of STZ. The rats whose blood glucose concentrations were > 300 mg/dl were randomly divided into four groups: DN (Diabetic group). DN+R (diabetic group exposed to 0.5 Gy/week of γ-radiation for 3 and 6 weeks). DN +GT (diabetic group supplemented by 45mg/1ml/rat/day green tea extract for 3 and 6 weeks). DN+GT+R (diabetic group supplemented 45mg/1ml/rat/day green tea extract and exposed to 0.5 Gy/week of γ-radiation for 3 and 6 weeks). A normal group of rats that underwent sham treatment was also included.

Blood Glucose
The blood glucose level was determined by glucose oxidase method using a one touch basic plus glucometer (Lifescane Ltd., California, USA).
Insulin assay
Serum insulin levels were determined by Biosource –INSEASIA according to Temple et al. (1992).

Kidney functions assay
Kidney function was assayed in the form of serum urea and creatinin assay Serum urea was determined by colorimetric test (Fawcett and Scott, 1960) using the available reagent kit. Serum creatinine was determined by kinetic test without deproteinization (Bartels et al., 1672) using the available reagent kit.

Histological and histochemical studies
Kidneys were fixed in 10% buffered formalin and embedded in paraffin for the histological and histochemical studies. Kidney sections were cut at 4 mm with a microtome and deparaffined with xylene. They were stained with hematoxylin and eosin (H–E) for the histological studies (Drury and Wallington, 1976). Feulgen reaction staining was used for DNA detection (Sheehan and Hrapchak, 1980). Periodic acid-Schiff’s (PAS) method to demonstrate carbohydrates (Hotchkiss, 1948).

Statistical Analysis
The statistical analysis was carried out using SPSS version 10 statistical programs (SPSS Inc., Chicago, IL, USA). Differences among treatments within the experiment were analyzed by one-way analysis of variance (ANOVA). Significant differences between treatment means were determined by student t-test. The results are presented as mean ± SE of five independent experiments unless stated otherwise.

Results

Effect of green tea extract and low doses of γ-irradiation on fasting glucose levels, insulin levels and body weight of diabetic rat.
Rats received STZ became diabetic at a frequency of 70%. The anti-hyperglycaemic effect of the low dose of γ-radiation and green tea supplementation either alone or combined on the fasting blood sugar levels of diabetic rats is shown in table (1). The plasma glucose levels of diabetic-induced rats significantly increased 72 h following the induction. Thus, the initial blood glucose level of the diabetic rats was 300±11.35 mg/dl compared to basal glycaemia of non diabetic control animals (86.67±2.19 mg/dl). Exposure of diabetic rats to 0.5 Gy/week of γ radiation for 3 and 6 weeks (DN +R) significantly decreased the blood glucose compared to DN group. Green tea extract at a dose of 45mg/1ml/rat/day, administered to diabetic rats, immediately after diagnosis of diabetes (DN +GT), produced a significant decrease in glucose level (P < 0.05) compared with diabetic controls. In DN + GT+R group, combined treatment of the diabetic rats by green tea and γ-radiation exposure revealed more significant decrease in fasting glucose level compared with the diabetic group. A significant decrease in insulin level was detected in the group suffered from diabetes mellitus (0.173±0.015) compared to the control level (0.322±0.012). Exposure of the diabetic animals to 0.5 Gy/week of γ-radiation (DN +R) significantly increase insulin level by increasing the period of γ-radiation exposure. Gavage intubations of the diabetic animals by 45mg/1ml/rat/day GT extract produced a more significant increase in insulin level compared to those of DN group either after 3 weeks or 6 weeks. Nearly normal level of insulin was recorded when diabetic animals treated with GT extract and exposed to 0.5 Gy/week of γ-radiation for 3 or 6 weeks of diabetic induction.

Diabetes was associated with reduced body weight when compared with the control rats. Exposure of the diabetic group to 0.5 Gy/week of γ- radiation showing some improvement in animal’s body weight either after 3 or 6 weeks compared to DN group. Gavage of the diabetic animals with GT represents a significant increase in the body weight after 6 weeks. Also gavage of the diabetic animals with 45mg/1ml/rat/day GT in addition to the exposure to 0.5 Gy/week of γ-radiation represented more significant increase in body weight after 6 weeks in compression to control and DN groups.
Table 1: Effect of green tea extract and low doses of γ-irradiation on fasting plasma glucose levels, insulin levels and body weight of diabetic rat.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Period of time</th>
<th>Control</th>
<th>DN</th>
<th>DN +R</th>
<th>DN +GT</th>
<th>DN +GT+R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>3 Weeks</td>
<td>86.67±2.19$^b$</td>
<td>300±11.35$^a$</td>
<td>107.33±3.29$^{ab}$</td>
<td>99.33±4.22$^b$</td>
<td>102.83±4.72$^b$</td>
</tr>
<tr>
<td></td>
<td>6 Weeks</td>
<td>111.50±1.50$^{ab}$</td>
<td>107.33±3.29$^{ab}$</td>
<td>99.33±4.22$^b$</td>
<td>102.83±4.72$^b$</td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>3 Weeks</td>
<td>0.322±0.012$^b$</td>
<td>0.173±0.015$^a$</td>
<td>0.199±0.018$^a$</td>
<td>0.247±0.034$^a$</td>
<td>0.224±0.006$^b$</td>
</tr>
<tr>
<td></td>
<td>6 Weeks</td>
<td>0.332±0.015$^a$</td>
<td>0.355±0.029$^b$</td>
<td>0.372±0.027$^b$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B.WT</td>
<td>3 Weeks</td>
<td>249.5±8.02$^b$</td>
<td>203±4.12$^{ab}$</td>
<td>212±4.16$^a$</td>
<td>185±4.83$^{ab}$</td>
<td>201.67±4.64$^a$</td>
</tr>
<tr>
<td></td>
<td>6 Weeks</td>
<td>157±11.14$^a$</td>
<td>174.67±8.04$^a$</td>
<td>221±14.08$^{ab}$</td>
<td>264±15.30$^b$</td>
<td></td>
</tr>
</tbody>
</table>

Each value represents the mean of 6 records ± S.E. Means with different superscripts are significantly different at the 0.05 level.

Table 2: Effect of green tea extract and low doses of γ-irradiation on serum urea (mg/l) and creatinine (mg/d) of diabetic rat.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Period of time</th>
<th>Control</th>
<th>DN</th>
<th>DN +R</th>
<th>DN +GT</th>
<th>DN +GT+R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>3 Weeks</td>
<td>148±19$^b$</td>
<td>455±35$^a$</td>
<td>296±27$^{ab}$</td>
<td>390±24$^a$</td>
<td>343±20$^a$</td>
</tr>
<tr>
<td></td>
<td>6 Weeks</td>
<td>481±25$^a$</td>
<td>177±16$^{ab}$</td>
<td>280±31$^{ab}$</td>
<td>228.5±33$^{ab}$</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>3 Weeks</td>
<td>0.33±0.13$^b$</td>
<td>0.85±0.10$^a$</td>
<td>0.55±0.09$^{ab}$</td>
<td>0.76±0.12$^a$</td>
<td>0.66±0.10$^a$</td>
</tr>
<tr>
<td></td>
<td>6 Weeks</td>
<td>0.96±0.29$^a$</td>
<td>0.49±0.08$^{ab}$</td>
<td>0.65±0.07$^{ab}$</td>
<td>0.57±0.13$^{ab}$</td>
<td></td>
</tr>
</tbody>
</table>

Legends as in table (1)
Histological results

Histological examination of the sections of kidney from normal control rat is shown in Fig. A (1). The circular areas observed in this photograph is the renal Malpighian corpuscle (†). It is composed of glomerulus surrounded by Bowman’s capsule with thin glomerular basement membranes and patent capsular space. Numerous tubules (proximal and distal) lie in the area adjacent to the glomerulus.

Kidney section of STZ-diabetic rat showed highly affected cytoplasm and nuclei of the convoluted tubules, some of the distal convoluted tubules cells appeared free from nuclei (curved arrow), others contained marginal chromatin (▼), the remnant contained pyknotict nuclei (p). Debris of ruptured cells could be detected inside the tubules (●). (Fig. A, 2) compared to kidney of non diabetic control rat.

Fig (A): photomicrographs of kidneys sections. 1: Control non diabetic rat. 2: STZ diabetic rat. Sections were stained with H&E. Magnifications X400.

When STZ-diabetic gavage administrated by GT for 3 weeks, a well developed glomerulus (↓) proximal (px) and distal (ds) convoluted tubules in kidney tissue section were detected. (Fig. B, 3) while treatment for 6 weeks showed also a well developed convoluted tubules but the glomerulus showed lobulated structure with deeply stained nuclei (→) (Fig. C, 6). Exposure of the STZ-diabetic rat to 0.5 Gy/week of γ-radiation for 3 weeks represented normal structure of the glomerulus and proximal and distal convoluted tubules (Fig. B, 4). But the exposure for 6 week showed atrophied glomeruli, widened Bowman’s space (†) with high cellularity in the visceral layer of the Bowman’s capsule (curved arrow) (Fig. C, 7).
Fig (B): photomicrographs of kidneys sections. 3: STZ diabetic rat treated by GT for 3 weeks. 4: STZ diabetic rat exposed to 0.5 Gy/week of γ-radiation for 3 weeks 5: STZ diabetic rat treated by GT and exposed to 0.5 Gy/week of γ-radiation for 3 weeks. Sections were stained with H&E. Magnifications X400.

Kidney of the diabetic rats gavage treated by GT and exposed to 0.5 Gy/week of γ radiation for 3 or 6 weeks recorded normal observations in tissue sections but small haemorrhagic areas were noted in between the convoluted tubules and the glomeruli appeared slightly congested (Fig. B, 5 and C, 8)
Histochemical studies
Deoxyribonucleic acid (DNA):
In control animals Kidney sections which stained by Fuelgen method showed that some particles containing DNA material appeared in the nuclei. In some cells of the glomerulus these particles were abundant, densely stained and scattered in the nucleoplasm, while in the other cells of the distal convoluted tubules they appeared fewer in number, faintly stained, and they were noted mainly in the nuclear periphery (Fig. D, 9). Diabetic group was observed to have a severely decreased coarse chromatin (↑) in the nuclei of cells either in the Glomerulus or in the convoluted tubules (Fig. D, 10 &10a).
Kidneys sections of STZ-diabetic rats treated with GT for 3 weeks showed remnants of nuclei (↓) and fragmented chromatin either in cells of the bowman’s capsule or convoluted tubules (Fig. E, 11). In the other hand increase in DNA stainability either in the convoluted tubules or Bowman’s capsule cells was observed whenever diabetic rats treated with GT for 6 weeks (Fig. E, 14).

Exposure of the STZ-diabetic animals to 0.5 Gy/week of γ-radiation for 3 weeks showed normal distribution of DNA particles either in cells of the glomerulus or the convoluted tubules (Fig. E, 12). Also the exposure of the STZ-diabetic animals to 0.5 Gy/week of γ-radiation for 6 weeks represented recurrence of stainable DNA nuclei either in the convoluted tubules (↑) or mesangial Bowman’s capsule cells (↓) (Figs. F, 15 & 15a). More recurrence of normally DNA abundant, densely stained particles

Fig (C): photomicrographs of kidneys sections. 6: STZ diabetic rat treated by GT for 6 weeks, 7: STZ diabetic rat exposed to 0.5 Gy/week of γ-radiation for 6 week. 8: STZ diabetic rat treated by GT and exposed to 0.5 Gy/week of γ-radiation for 6 weeks. Sections were stained with H&E. Magnifications X400.
scattered in the nucleoplasm were detected in the convoluted tubules and glomerulus cells, when STZ-diabetic animals treated with 45mg/1ml/rat/day GT in addition to the exposure to 0.5 Gy/week of \( \gamma \)-radiation either for 3 or 6 weeks (Fig. E, 13 & F16).

Fig (D): photomicrographs of kidneys sections. Sections showing the DNA content. 9: Control non diabetic rat. 10&10a: STZ diabetic rat. Feulgen method. Magnifications X 1000
Fig (E): photomicrographs of kidneys sections. Sections showing the DNA content. 11: STZ diabetic rat treated by GT for 3 weeks. 12: STZ diabetic rat exposed to 0.5 Gy/week of $\gamma$-radiation for 3 weeks 13: STZ diabetic rat treated by GT and exposed to 0.5 Gy/week of $\gamma$-radiation for 3 weeks. Feulgen method. Magnifications X 1000
Fig (F): photomicrographs of kidneys sections. Sections showing the DNA content.  14: STZ diabetic rat treated by GT for 6 weeks.  15&15a: STZ diabetic rat exposed to 0.5 Gy/week of γ-radiation for 6 week  16: STZ diabetic rat treated by GT and exposed to 0.5 Gy/week of γ-radiation for 6 weeks. Feulgen method.  Magnifications X 1000

**Glycogen content:**
The use of periodic acid schiff's (PAS) technique was done to demonstrate the presence of polysaccharides in the kidney tissues. The PAS +ve materials were mainly distributed at the brush border and basement membrane of the tubules. In this study control kidney sections represented moderate PAS positive materials in the cytoplasm and brush borders of the proximal convoluted tubules. Glomerulous was also positive to PAS reaction (fig. G17). The diabetic group kidney section appeared intensely positive to PAS reaction with moderate dense positive
 materials inside the lumen of the kidney tubules (fig. G18).

Fig. (G): photomicrographs of kidneys sections. Sections showing the glycogen content.
17: Control non diabetic rat. 18: STZ diabetic rat. PAS technique. Magnifications X 400

Exposure of the diabetic group to 0.5 Gy/week for 3 (fig. H 20) or 6 weeks (fig. I 23), showed a reduced amount of cytoplasmic glycogen, with diminished density in the basement membranes, and brush borders of the proximal convoluted tubules. Also, the glomeruli were less stained than those of the control group.

Kidney of the diabetic rats gavage treated by GT for 3 weeks (fig. H 19) or 6 weeks (fig. I 22) recorded less stained PAS reaction either in the basement membranes or the brush borders of the proximal convoluted tubules. Also the glomeruli represented some reactivity to PAS reaction compared to the diabetic group.
When STZ-diabetic animals gavage treated by 45mg/1ml/rat/day green tea in addition to the exposure to 0.5 Gy/week of γ radiation for 3 weeks (fig. H 21) recorded less stainability of PAS reaction either in the convoluted tubules or the glomeruli. However some reactivity was recorded when STZ-diabetic animals gavage treated by 45mg/1ml/rat/day green tea in addition to the exposure to 0.5 Gy/week of γ radiation for 6 weeks (fig. I 24).
Therapeutic Potential of Green Tea Extract and Low Doses of 

Fig (I): photomicrographs of kidney sections. Sections showing the glycogen content. 22: STZ diabetic rat treated by GT for 6 weeks. 23: STZ diabetic rat exposed to 0.5 Gy/week of γ-radiation for 6 week 24: STZ diabetic rat treated by GT and exposed to 0.5 Gy/week of γ-radiation for 6 weeks. PAS technique. Magnifications X 400.

Discussion

It is known that the increase in oxidative stress may result from over production of precursors to reactive oxygen radicals and/or decreased efficiency of inhibitory and scavenger systems. The stress may be amplified and propagated by an autocatalytic cycle producing tissue damage and cell death (Brownlee et al., 1998 and Hunt et al., 1993). Cell damage will in turn, result in elevated production of reactive oxygen species (ROS). In diabetes increased formation of ROS for reasons may possibly related to an increase in glucose concentrations in plasma and tissues (Brownlee, 2001; Ha and Kim, 1999) and may have a role in the pathogenesis of diabetic nephropathy. Injection of STZ in adult wistar rats induced experimental diabetes mellitus 72 h following STZ treatment (Akbarzadeh et al., 2007) and increase in plasma glucose levels was detected. Hyperglycaemia is the principal factor responsible for structural alterations at the renal level and is directly linked to diabetic microvascular complications, particularly in the kidney (Anonymous, 1993). DN group in the present study represented a decrease in insulin level, reduction in body weight, and increase in urea and creatinine levels for the relationship between diabetic nephropathy and oxidative stress. (Wagner et al. 2001) and (Mehrotra et al. 2001), suggesting that oxidative stress affected the progress of diabetic complications. The severely decreased coarse chromatin in the nuclei either in the Glomeruli or in the convoluted tubules may be due to effect of high glucose on cell proliferation or apoptosis. For DNA synthesis inhibition (Park et al., 2001 and Allen et al., 2003). Prevention of nephropathy is a very important concern and this study has been focused on low doses of γ-radiation and herbal medicines such as GT to find novel therapeutic agents for diabetic nephropathy. In this study, we found that either low doses of γ-radiation or GT treatment significantly decreased the blood
glucose level and significantly increased insulin level 3 and 6 week of diabetic induction.

Nomura (2002) used the low-dose rate gamma-irradiation to the model mice for Type II diabetes mellitus during their lifetime, measured the level of urine glucose with test slips every week, and investigated the recovery effects of the diabetes by the irradiation. Low doses of radiation, below toxic levels, may modulate various biological responses. Low dose radiation also ameliorates type I diabetes (Takahashi et al., 2000), which was caused by dysfunction of pancreatic β cells as a result of self-reactive immune responses (Yoon et al., 1998). Such stimulatory effects of radiation, referred to as radiation hormesis (Liu et al., 1987; Luckey, 1982 and Macklis and Beresford, 1991).

Green tea (Camellia sinensis; GT) is a rich source of polyphenols, particularly flavonoids, which have been shown to have numerous pharmacological effects. Studies using animal models show that GT catechins could be beneficial in suppressing high-fat diet-induced obesity by modulating lipid metabolism and providing some protection against lipid and glucose metabolism disorders implicated in type 2 diabetes (Matsumoto et al., 1993; Nakachi et al., 2000; Murase et al., 2002 and Crespy and Williamson, 2004).

Administration of GT in streptozotocin (STZ) diabetic animals drastically improved kidney function as a result of its anti-thrombogenic action, which in turn controls the arachidonic acid cascade system (Yang et al., 1999). These studies also demonstrated an improvement in the glomerular filtration rate (Yang et al., 1999 and Rhee et al., 2002, a,b). (Yokozawa et al 1999) examined variables of glomerular filtration in cisplatin (a nephropathy inducer)-treated rats and demonstrated that GT significantly decreased the serum creatinine, kidney excretion of glucose and oxidative stress in the kidney. Another study has shown that GT reduced serum glucose and creatinine levels and increased serum superoxide dismutase, suggesting that catechins influence glucose metabolism and improve kidney function by reducing oxidative stress in alloxan-treated diabetic rats (Sabu et al., 2002). Moreover, GT decreased plasma insulin levels but did not affect plasma glucose levels in an oral glucose tolerance test in normal rats (Wu et al., 2004). In contrast, (Mustata et al. 2005) have shown that GT drinking had a marginal effect on nephropathy parameters through improving renal mitochondrial defects; however, neither glycaemia nor urinary albumins were affected in GT-drinking diabetic animals. Also (Renno et al. 2008) indicate that in STZ diabetes, kidney function appeared to be improved with GT consumption which also prevents glycogen accumulation in the renal tubules, probably by lowering blood levels of glucose. Therefore, GT could be beneficial additional therapy in the management of diabetic nephropathy.

The pervious studies illustrate the normal structure detected in glomerulus’s and proximal and distal convoluted tubules, normal distribution of DNA material particles in the kidney tissue and the reduced amount of cytoplasmic glycogen of kidney tissue when STZ-diabetic gavage administrated by GT and/or exposed low doses of γ-radiation

The present results suggested the synergistic effects of combined GT and low doses of γ-radiation treatments are in agreement with the findings of (Nancy et al. 2006). They significantly lower urea and creatinine excretion rates, significantly decreased fasting glucose level , reaching to nearly of control level in insulin level, recorded normal observations in tissue section , recurrence of normally DNA abundant, densely stained particles scattered in the nucleoplasm and recorded less positive PAS reaction either in the convoluted tubules or the glomeruli. This may offer potential therapeutic benefit, which warrants clinical study for application in reducing diabetic complications. Further studies are required to examine the clinical use and exact mechanisms behind a possible effect of combined GT and low dose of γ-radiation treatments.
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الإمكانية العلاجية لمستخلص الشاي الأخضر وجرعة الإشعاع الصغيرة
لمعالجة إعتلال الكلى السكري في الجرذان البيضاء

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يعتبر الإعتلال الكلوي أحد المضايقات الخطيرة والمرتبطة على الإصابة بمرض السكر. صممت هذه الدراسة لتقدير الإمكانية العلاجية لمستخلص الشاي الأخضر وجرعة الإشعاع الصغيرة لعلاج إعتلال الكلى السكري في الجرذان البيضاء. استعمل في هذه الدراسة ذكور الجرذان البيضاء التي حققت بالإستروجين مساعدة الإصابتها بداء السكر. قسمت جرذان التجارب إلى خمسة مجموعات إحداها غير مصابة وغير معالجة وعولمت الجرذان المصاب بمرض السكر بمستخلص الشاي الأخضر وجرعة الإشعاع الصغيرة مفردة أو متجمعة. خلال مدة التجربة (3 و 6 أسابيع) تم تتبع أوزان الجرذان، مستوى السكر الصائم في الدم ومستوى الإنسولين، اليوبريا والكرياتين في السيرم. عينت كذلك التغيرات الهيستوباثولوجية، كثافة الكريات وكتلة حصص الدنا في النسيج الكلوي. أسفرت النتائج عن نقص أوزان الجرذان المصاب بداء السكر ومستوى الأنسولين في السيرم مع زيادة شديدة في مستوى السكر الصائم في الدم وكذلك مستوي اليوبريا والكرياتين في السيرم، ظهر بالنيسج الكلوي ضرر نسيجي متوسط بالإضافة إلى وجود كثرة من البولات الفارغة بالجرذان المصاب بداء السكر. زيادة كثافة السكرات كذلك أوضح النسيج الكلوي عن تغيير واضح في كثافة حصص الدنا. من الملاحظ أن علاج الفئران المصاب بمرض السكر بمستخلص الشاي الأخضر وجرعة الإشعاع الصغيرة مفردة أو متجمعة أدى إلى تحسن التركيب النسيجي وكتلة هرمون اللد 啾 بالإضافة إلى التحسن الملحوظ في مستوى السكر الصائم في الدم ومستوى الأنسولين، اليوبريا والكرياتين في السيرم. أوضح هذه الدراسة الإمكانية العلاجية لمستخلص الشاي الأخضر وجرعة الإشعاع الصغيرة مفردة أو متجمعة على الإقلال من إعتلال الكلى السكري في الجرذان البيضاء وإعادة حدوثه.