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Research Article

Effects of soybean seed on some biochemical parameters and pancreas weight in streptozotocin-induced diabetic rats

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Abstract

Objectives: Diabetes mellitus is a group of chronic diseases in which the body has problems with the use or production of glucose, the main source of energy for metabolism. This condition can affect the metabolism of carbohydrates, fats, and proteins, potentially leading to chronic hyperglycemia (high blood sugar levels). The present study investigated the effects of soybean (Glycine max L.) seed extract on various biochemical parameters and pancreas weight in Wistar rats with experimental diabetes.

Methods: The study consisted of five groups of rats: control, diabetic, and treated (100, 200, and 400 mg/kg extract). To induce diabetes in rats, Streptozotocin (STZ) was administered through intraperitoneal injection (35 mg/kg). The rats were orally given water-soluble extracts at the indicated quantities once daily for four weeks. Venous blood was collected from the animals via heart puncture, after which the animals were sacrificed. Biochemical parameters, including blood glucose, were measured using an autoanalyzer.

Results: In diabetic rats, there was a significant increase in serum glucose concentration ($p<0.05$). However, treatment with soybean resulted in a significant reduction ($p<0.05$) of the elevated glucose concentration in the treated diabetic rats. It is noteworthy that the glucose concentrations were still significantly higher ($p<0.05$) than those of the control group. Biochemical parameters, including urea, AST, SGPT/ALT, cholesterol, triglycerides, glucose, LDL-cholesterol, and VLDL-cholesterol, were lower in the treated groups than in the diabetic control group and were considered significant ($p<0.05$). Moreover, it was observed that the HDL-cholesterol parameter was significantly higher than that of the diabetic control group ($p<0.05$), while the creatinine parameter was not found to be statistically significant ($p>0.05$).

Conclusion: The results suggest that soybean treatment may have a positive impact on certain biochemical parameters in diabetic rats. These findings are consistent with previous reports on the health benefits of soybean. It can be inferred that G. max may have a hypoglycemic effect in diabetic rats and could potentially mitigate the complications of diabetes mellitus.

Keywords: Biochemical parameters, diabetic rats, Glycine max (L), soybean seed

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Diabetes is a disease caused by lack of insulin secretion, insulin resistance, or both [1, 2]. It has been observed that disorders related to the metabolism of carbohydrates, fats, and proteins may arise due to either insufficient insulin secretion or decreased tissue sensitivity to insulin. As a result, chronic hyperglycemia is a commonly observed symptom [2]. Diabetes is a disease with acute and chronic complications. Indeed, in long-term complications, functional disorders or de-

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ficiencies are observed in organs such as eyes, heart, kidney, and brain [3]. Indeed, it is also associated with cardiovascular disorders resulting from changes in plasma lipid and lipoprotein profile [4].

Two types exist: type I diabetes mellitus, which requires insulin for treatment, and type II diabetes mellitus, which can be managed without insulin. The first is an autoimmune disorder resulting from the selective destruction of insulin-secreting beta (β) cells. The second is peripheral insulin resistance and impaired insulin secretion [5].

Diabetes mellitus is a very common disease affecting people living in developed and developing countries. WHO reports that the disease is a leading cause of death [1]. Within the next 25 years, it is predicted to become one of the world's leading causes of death [3].

Diabetes treatment is a global problem and an effective treatment method without side effects has not been developed yet [1, 6]. Over the past few years, plant-based drugs have become more preferred due to their fewer side effects and natural origin when compared to synthetic chemical drugs [1, 2, 7]. According to the literature, there are more than 400 medicinal plants used worldwide to treat diabetes mellitus. However, only a select few have undergone scientific authentication for their hypoglycemic activity [8, 9].

Soybean (Glycine max) is an annual plant that is commonly cultivated in many parts of the world and belongs to the Fabaceae family [10]. Millions of people take soybean products because of their high nutritional value. Soybean is high in protein, fat, and minerals like phosphorus, calcium, iron, and soluble fiber. It is therefore beneficial for diabetics and reduces the risk of developing diabetes. Thanks to the flavonoids it contains, it has also been reported to decrease the risk of cardiovascular problems by reducing triglycerides, blood cholesterol, low-density lipoprotein (LDL), and blood pressure [1, 9, 11].

Streptozotocin (STZ) is a kind of compound obtained from Streptomyces achromogenes bacteria and is toxic to beta cells producing pancreatic insulin, especially in mammals. It is used to initiate diabetes mellitus in experimental animals [12].

The aim of the study was to investigate the effects of soybean (Glycine max L.) seed extract on pancreatic weight and various biochemical indices, including urea, creatinine, AST, ALT, cholesterol, triglycerides, glucose, LDL, HDL, and VLDL, in Wistar rats with experimental diabetes.

Materials and Methods

This research has been accepted by The Selçuk University Faculty of Veterinary Medicine Experimental Animal Production and Research Center Ethics Committee (Resolution number: 2015/67).

Plant material

Soybean seeds used in the experiment were obtained from a market in Konya, Turkey, and confirmed by Selçuk University Agriculture Faculty. Soybean seed extract was prepared with some modifications according to the method suggested by Badavi et al. [13]. Firstly, the seeds were powdered before use. The seed powder was soaked in 60% methanol for three days at room temperature and stirred three times daily. Subsequently, the mixture was filtered using a few layers of cloth, and the resulting filtrate was dried at room temperature (25–30°C) to evaporate the methanol, resulting in soybean extract in powder form. The extract was dissolved in distilled water according to treatment group doses and administered orally via gavage needle once a day.

Animals

Twenty-five female Wistar rats weighing 210±10 g were obtained from KONÜDAM Animal Center in Necmettin Erbakan University in Konya, Turkey. The rats were accommodated in a controlled environment with a temperature of 22±1 °C and 62% humidity, following a 12-hour light/12-hour dark schedule. An adaptation period of 15 days was allowed before the commencement of the experiment. For a period of 15 days, they were provided with water ad libitum and fed a basal diet.

Experimental inducement of diabetes mellitus

Animals in all diabetic groups in the study (Group 2, 3, 4, 5) were fed a high-fat diet for 2 weeks [14]. Then, diabetes was induced in these animals, which had been fasted, with a single intraperitoneal injection of streptozotocin (STZ) (35 mg/kg body weight) dissolved in citrate buffer (pH 4.5). The high-fat diet was continued until the end of the experiment in these animals. Two weeks after STZ treatment, non-fasting rats with a blood glucose level of 300 mg/dL were diagnosed with type 2 diabetes. The chemicals were purchased from Sigma (MO, USA). Also, animals in the control group (Group 1) continued to be fed a basal diet.

Experimental design and treatment

Rats were separated into five groups of 5 rats each. Group 1: Rats of the control group. Group 2: Control rats with diabetes. Group 3: Diabetic rats treated with 100 mg/kg dose of soybean extract. Group 4: Diabetic rats treated with soybean extract at a dose of 200 mg/kg. Group 5: Diabetic rats treated with 400 mg/kg dose of soybean extract. All treatments were given once a day for four weeks. When finished, the animals were euthanised and the next procedure was started.

Biochemical analysis

Using a sterile syringe, blood samples were taken by cardiac puncture. The samples were then placed in the appropriate sterilized microcentrifuge tube and allowed to clot. Serum was recovered after centrifugation at 3000 rpm at 25°C for 15 minutes. Serum samples were immediately assayed for blood glucose, total cholesterol, HDL, LDL, VLDL, triglycerides, urea, creatinine, aspartate transaminase (AST), and alanine transaminase (ALT) using commercially available colorimetric diagnostic kits on an autoanalyzer (Biotecnica Instruments,

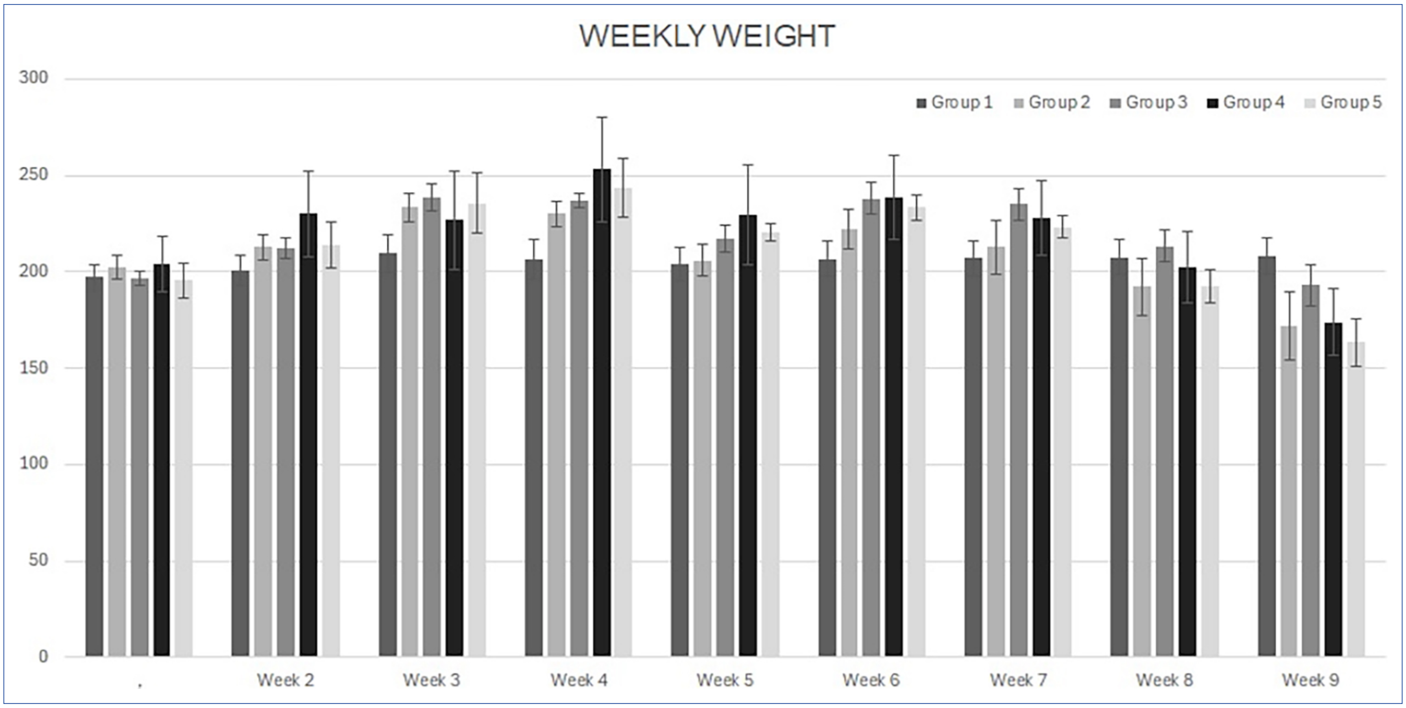

Figure 1. The average weight changes of the experimental animals.

BT3000 Plus, Italy).

Determination of pancreas weights

After euthanasia, their pancreas was carefully removed, their weight was measured and noted.

Statistical analysis

Results are expressed as mean±SD. One-way repeated measures analysis of variance (ANOVA) with Tukey's post hoc test was used to analyse differences between groups. The Statistical Package of Social Service (SPSS, version 22.0) was used for statistical analyses. A p-value of less than 0.05 was defined as statistically significant.

Results

Weight change results

The weights of the experimental animals used in the study were monitored weekly throughout the experiment, and the average weight changes are summarized in Figure 1. While there was not much difference in the average weight gain of the animals in the control group, there was a significant increase in the weights of the other groups until STZ application. It was determined that their weight decreased significantly in the week after STZ application ($p \leq 0.05$).

Biochemical analysis results

Table 1 shows mean blood glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol, triglyceride, urea, creatinine, aspartate aminotransferase (AST), and aminotransferase (ALT) in each of the five rat groups. Compared to the control group, the serum glucose concentration was significantly increased in the diabetic control group ($p<0.05$). This is an indication of an efficient induction of diabetes. Treatment with soybean significantly reduced glucose levels in the treated rats ($p<0.05$), but glucose levels were still significantly higher ($p<0.05$) than in the controls.

A statistically significant increase in serum cholesterol and serum triglycerides ($p<0.05$) was observed in the diabetic control group compared to the control group. After four weeks of treatment with soybeans, a reduction in cholesterol levels was noted, and surprisingly, the greatest reduction was seen at the dose of 200 mg/kg extract. Serum triglyceride levels were also observed to be very low ($p<0.05$) after soy treatment compared to the control group, which was very high in the diabetic control group.

LDL-cholesterol and VLDL-cholesterol levels were significantly increased ($p<0.05$), while HDL-cholesterol was decreased ($p<0.05$) in diabetic rats compared to controls. LDL cholesterol and VLDL cholesterol were significantly reduced, whereas HDL cholesterol was significantly increased ($p<0.05$) in diabetic rats treated with soybean for four weeks. However, this increase in the level of HDL cholesterol was not as great as the increase in the control group.

The parameters of ALT, AST, and Urea were significantly increased in the serum of diabetic groups ($p<0.05$). These values were found to be below the control group level in all treatment groups at the end of 4 weeks. The parameter creatinine, however, was not considered significant ($p>0.05$).

Pancreas weights results

Table 1. The effect of soybean extract on some serum biochemical levels of diabetic rats

Groups	Control Mean±SD	Diabetic control Mean±SD	100 Mg/Kg extract Mean±SD	200 Mg/Kg extract Mean±SD	400 Mg/Kg extract Mean±SD	p	Range
Parameters							
Glucose (mg/dl)	93.90±6.71	434.20±35.1	309.18±63.4	229.72±18.1	113.58±38.7	<0.05	82.68–170.36
Urea (BUN) (mg/dl)	13.40±1.34	15.82±0.38	11.48±0.36	7.92±1.46	7.06±2.06	<0.05	13.5–24.5
Creatinine (mg/dl)	0.40±0.10	0.54±0.89	0.60±0.10	0.43±0.30	0.42±0.14	>0.05	0.30–0.60
AST(UI/l)	155.20±27.7	181.02±26.0	132.12±14.7	128.00±11.6	125.82±16.5	<0.05	29.34–72.16
ALT (U/l)	67.22±16.08	131.00±18.8	55.48±8.63	43.96±3.76	46.72±9.63	<0.05	62.75–126.65
Triglyceride (mg/dL)	88.38±4.98	335.40±16.7	285.26±12.6	52.28±20.21	49.12±6.63	<0.05	26.78–65.88
Cholesterol (mg/dl)	54.96±7.75	71.80±2.04	47.58±9.24	37.40±5.54	59.40±7.60	<0.05	62.47–104.13
LDL (mg/dl)	11.52±0.50	24.88±4.70	21.58±3.68	17.60±6.65	9.24±0.82	<0.05	12.21–27.36
HDL (mg/dl)	72.78±9.96	30.96±4.35	22.18±3.03	39.86±14.56	39.12±11.46	<0.05	37.00–68.73
VLDL (mg/dl)	26.11±6.75	67.32±22.89	45.56±23.42	25.94±13.66	24.31±1.85	<0.05	5.05–13.16

SD: Standard deviation; AST: Aspartate transaminase; ALT: Alanine transaminase; LDL: Low-density lipoproteins; HDL: High-density lipoproteins; VLDL: Very low-density lipoprotein.

According to the data obtained, pancreatic weight (0.80±0.28 g) in diabetic rats was lower than that of control rats (1.12±0.23 g) ($p<0.05$). In addition, pancreas weight in all treatment groups was significantly higher than in the diabetic group. The biggest rise was observed in the 400 mg/kg extract group (1.40±0.07 g) (Fig. 2).

Discussion

This study was designed to examine possible effects of soybean seed extract on several biochemical parameters in the serum of STZ-induced diabetic rats. STZ is a broad-spectrum antibiotic that has a cytotoxic effect on the insulin-producing beta cells in the pancreatic islets [12]. It is thought that STZ is a glucose analogue that enters the cell via the glucose transporter GLUT2 and causes DNA alkylation and apoptosis in β-cells [15]. It is, therefore, often used to induce diabetes mellitus in experimental animals. In this study, it was found that serum glucose values increased in STZ-treated animals. Soybeans contain high levels of isoflavones and fiber, which enhance metabolic processes [16]. In the studies presented by some researchers, it is reported that the isoflavones contained in soybeans are effective in reducing glucose levels [17–19]. However, it has also been reported that soluble fibers obtained from soybeans show resistance to digestion and absorption and can, therefore, be used to control glucose absorption and rising blood sugar levels in diabetes [20]. Gupta et al. [3] showed in their study that soybean extract orally administered to diabetic animals reduced blood glucose levels up to 5.97%. It has also been reported that isoflavone intake in the diet can prolong lifespan and increase glucose tolerance capacity in normal mice [21]. In this study, soybean treatment significantly reduced elevated serum glucose concentration, and this reduction was most effective in the high-dose group when evaluated among the administered doses. Based on these results, it seems that soy isoflavones may have a positive effect on the overall metabolism of diabetic animals. In dia-

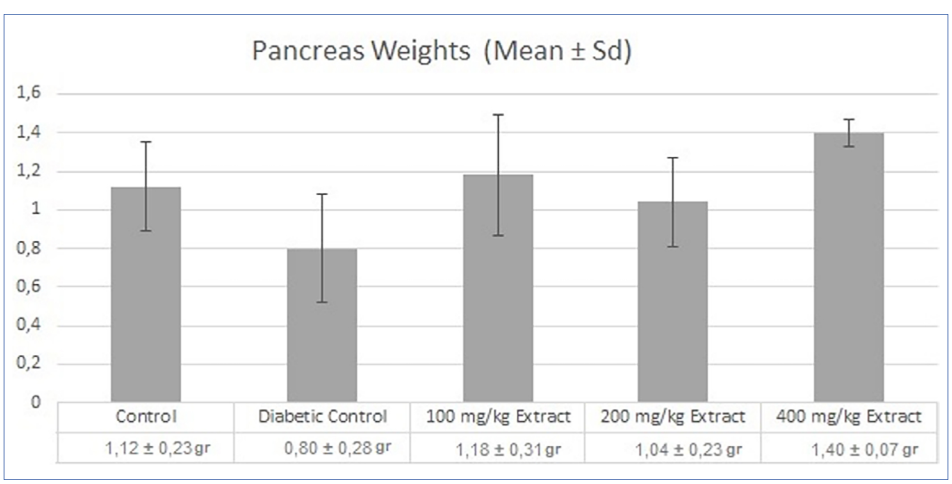

Figure 2. Mean pancreatic weight changes in the studied groups.

Sd: Standard deviation.

betes mellitus, not only carbohydrate metabolism is impaired, but also lipid and protein metabolism are significantly altered. Elevated serum total cholesterol and triglycerides are typical indicators of diabetes mellitus [22]. Insulin is essential for the inhibition of hormone-sensitive lipase and the activation of lipoprotein lipase. Therefore, mobilization of free fatty acids from peripheral fat stores increases in diabetes, and serum total triglyceride levels increase [23]. Total cholesterol and LDL levels increase in diets containing high levels of saturated fats [24]. There have been reports that the phytoestrogens and saponins in soybeans could be involved in the regulation of serum cholesterol levels [25–27]. Khushk et al. [28] assessed the non-diabetic potency of soybean extracts (chloroform and alcohol) in alloxan-induced diabetic rabbits. The extracts were shown to cause a substantial reduction in serum cholesterol levels. Consistent with these studies, in the present study, STZ-induced diabetic rats treated with soybean extract showed a significant decrease in serum cholesterol levels. This reduction was greatest at a dose of 200 mg/kg. Some studies have shown that there was no significant change in triglyceride levels after a soy-based diet [27, 29]. On the other hand, Ristić Medić et al. [30] found a 29% reduction in triglyceride levels after 12 weeks of treatment with soybeans in type 2 diabetics with hypertriglyceridemia. In this study, soybean extract was found to reduce triglyceride levels, and this reduction was less than in the control group at doses of 200 and 400 mg/kg.

Serum concentrations of LDL, HDL, and VLDL are essential for whole-body metabolism [31]. Dyslipidemia in type 2 diabetes is characterized by low levels of HDL, elevated LDL, and serum triglycerides associated with VLDL [32]. Soybean proteins, especially glycine and β-conglycinin, may be responsible for lower cholesterol concentrations by increasing bile acid production and excretion through feces [33]. This may lead to a shift in the hepatic cholesterol system to provide more cholesterol for bile acid deficiency and may also lead to increased LDL receptor activity by a mechanism that causes a decrease in total blood cholesterol concentration [34]. Previous studies have shown soy protein to lower cholesterol, triglycerides, and low-density lipoprotein (LDL) levels in people with diabetes and in healthy people and have shown similar effects in rats and rabbits [35–37]. Isoflavone compounds found in soybeans, such as genistein, cause less and smaller fat cells to be produced [9]. Lee [38] reported that a 60 mg/100 g genistein diet increased serum HDL cholesterol levels in diabetic rats. In this study, high levels of LDL were observed in the diabetic group after STZ administration, while low levels of HDL were detected. However, it was determined that there was a significant decrease in LDL and VLDL concentrations after different doses of soybean seed extract compared with the untreated diabetic control group. HDL concentration increased in the 200 and 400 mg/kg treatment groups.

Urea plays an important role in the metabolism of nitrogenous compounds and is a waste product of dietary protein. This organic compound is filtered into urine by the kidneys [39]. Uric acid is found in the cytosol and in soluble compounds found in the blood. It is synthesized mainly from purines based on adenine and guanine. Uric acid is found in all tissue compartments except the lipid phase [40]. Hyperuricemia is caused by increased uric acid. The uric acid is transported to the liver and is released into the bloodstream. Kidney function is related to glomerular filtration and tubular secretion of serum creatinine [41]. In health problems such as diabetes, kidney cells are damaged, urea levels in the blood increase, and creatinine levels increase. Therefore, the function of the kidney is reduced [42]. Soybean seeds contain phenolic compounds called flavonoids, and some studies have reported that soy protein helps prevent kidney disease in people with diabetes [27]. Kudou et al. [43] reported that in alloxan-induced diabetic rats, administration of soybean seeds reduced plasma creatinine and blood urea levels. In the present study, soybean seed extract significantly ($p<0.05$) decreased serum urea levels in STZ-induced diabetic rats, but serum creatinine levels were statistically insignificant ($p<0.05$).

Insulin clearance and the production of inflammatory cytokines take place mainly in the liver. It has an important role in the maintenance of normal fasting and postprandial glucose concentrations [44]. ALT and AST enzymes are well-known markers of liver injury. Serum levels are high because these enzymes are thought to leak from the cytosol into the bloodstream as a result of liver tissue damage [12]. Previous studies have shown increased serum AST and ALT levels in diabetic rats fed a high-fat diet and treated with low-dose STZ [45]. Bai et al. [46] have suggested that soybean may have a role to play in the enhancement of glucose and lipid homeostasis and liver function in T2DM. In this study, it was determined that soybean treatment decreased serum ALT and AST levels compared to control in all doses administered. Based on these data, it can be said that soybean has protective effects on hepatic dysfunction of type 2 diabetic rats.

One of the most important causes of diabetes is beta cell dysfunction in the pancreas [47]. In the studies conducted with various imaging methods, it was determined that the pancreas volume of patients with diabetes decreased [48, 49]. In this study, it was determined that the pancreas weight of the STZ-treated diabetes group decreased, while the pancreas weight increased in the soybean extract treatment groups. This increase was the highest at a dose of 400 mg/kg. Based on these results, it can be said that soybean may cause improvement in pancreatic cells.

Conclusion

Soybeans have a very high concentration of lysine. They also contain abundant amounts of essential amino acids such as histidine, isoleucine, leucine, phenylalanine, tyrosine, tryptophan, and valine. For this reason, it is considered to be a cost-effective and easily accessible supply of protein. When all our results were evaluated in general, soybean treatment showed a positive effect on some biochemical parameters in diabetic rats. These findings lend support to reports of the beneficial and health-promoting effects of soybeans. Furthermore, it can be concluded that G. max is hypoglycemic and reduces the complications of diabetes mellitus in diabetic rats.

Ethics Committee Approval: The study was approved by The Selçuk University Faculty of Veterinary Medicine Experimental Animal Production and Research Center Ethics Committee (No: 2015/67, Date: 29/07/2015).

Authorship Contributions: Concept – E.A., H.A.; Design – E.A., H.A., E.G.M.; Supervision – E.A., H.A.; Fundings – E.A.; Materials – E.A., E.G.M.; Data collection &/or processing – E.G.M., D.E.K.; Analysis and/or interpretation – E.G.M.; Literature search – E.G.M.; Writing – E.G.M.; Critical review – E.G.M., E.A.

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