Medical Science

25(114), August, 2021

Hypoglycemic and protective effects of *Boswellia carterii* against functions and structures of thyroid gland in rat model of type 2 diabetes

Dalia Domiaty[1], **Anoud Althagafi**[2], **Muna Alamoudi**[3]✉, **Haleema Al-Nahary**[1], **Saleh Fouaz Bakrshoom**[4]

To Cite:
Domiaty D, Althagafi A, Alamoudi M, Al-Nahary H, Bakrshoom SF. Hypoglycemic and protective effects of *Boswellia carterii* against functions and structures of thyroid gland in rat model of type 2 diabetes. Medical Science, 2021, 25(114), 2077-2087

Author Affiliation:
[1]Biology department, faculty of Science, Jeddah University, Jeddah, Saudi Arabia
[2]General Practitioner in Almojaheed in Primary Health Care, Ministry of Health, Makkah, Saudi Arabia
[3]Biology department, faculty of Science, University of Hail, Hail, Saudi Arabia
[4]Medical department, Zamzam Clinic, Hail, Saudi Arabia

✉**Corresponding author**
Biology department, faculty of Science, University of Hail, Hail, Saudi Arabia
Email: m.alamodi@uoh.edu.sa

Peer-Review History
Received: 09 July 2021
Reviewed & Revised: 12/July/2021 to 10/August/2021
Accepted: 12 August 2021
Published: August 2021

Peer-review Method
External peer-review was done through double-blind method.

ABSTRACT

Boswellia carterii extract has many beneficial pharmacological activities and various medicinal utilization. The scientific data about its effects on thyroid functions of type 2 diabetes is limited. This research was conducted to assess the hypoglycemic and antioxidant properties of *Boswellia carterii*. Its protective effects against type 2 diabetes induced dysfunction and structural changes of thyroid gland were also investigated. Wistar male rats (N=25) were indiscriminately allocated into four groups (N=5): G1 (Control), G2 (diabetic control), G3 (diabetic+ *Boswellia Carterii* extract), G4 (diabetic+ Metformin) and G5 (*Boswellia carterii* extract). *B. carterii* was given to G3 and G5 in a dose of 100mg/kg/BW and G4 received a dose of150mg/kg of metformin. The treatment was continuing for 6 weeks. Oxidative stress was assessed by measuring superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase (CAT), and lipid peroxidation (LPO) plus the blood glucose level (BGL) in all groups. The protective properties of the *B. carterii* extract was evaluated by estimation Thyroid stimulating hormone (TSH), triiodothyronine (T3) and tetraiodothyronine (T4) hormones and histological studies of thyroid gland. The results showed in *B. carterii* treated diabetic rats: BGL and LPO were significantly *decreased*, while SOD and CAT were significantly *increased* in comparison to the non-treated diabetic rats. Moreover, it was found that the extract has protective effects against diabetic induced (functional and structural) alterations of thyroid gland. In conclusions, this study showed that *B. carterii* extract has potential impact as hypoglycemic and antioxidant natural agents, inhibiting thyroid functional disturbance and conserving the thyroid histological architectures in the animal model of experimental type 2 diabetes.

Keywords: *Boswellia Carterii*, thyroid gland, TSH, hyperglycemia, lipid peroxidation.

1. INTRODUCTION

Diabetes mellitus is a familiar metabolic disorder categorized by hyperglycemia due to relative reduction in insulin action, insulin secretion, or both (ADA, 2009). It is accompanied with metabolic disturbance of protein, fat and carbohydrate (Jayasri et al., 2008). It was considered the most common cause of mortality and morbidity as well as challenging health problems in 21st century (Gurjeet et al., 2011; Ramesh et al., 2015). Hyperglycemia has essential role in the pathogenesis of long-date complications involved many organs such as nervous system, heart, kidneys, and small blood vessels (Chawla et al., 2016).

Diabetes mellitus has unfavorable impact on fundamental pathology with subsequent thyroid dysfunction. Pancreatic functions and the carbohydrate metabolism are in oneside regulated by thyroid, and on other side, diabetes has direct impact on thyroid itself (Wang, 2013). Thyroid dysfunctions and diabetes mellitus are considered as the major common two endocrine dysfunction faced in clinical field. Thyroid dysfunctions and Diabetes are shown to be mutually affect each other and the link between both cases have been studied (Hage et al., 2011). Knowing that thyroid hormones act on most of the cells of the body tissues and are involved in many physiological procedures, attract the attention to the agents effecting thyroid functions (Sun et al., 2008). Thyroid hormones participate in heat generation and protein, lipid, and carbohydrate metabolism (Kim, 2008). Thyroid hormones are very important for normal reproductive functions, gastrointestinal motility, and heart rate regulation as well as for the stability of motion (Bauer et al., 2008). Perturbation of thyroid functions by exogenous or endogenous agents leads to multiple subclinical consequence (Havre et al., 2008) or direct clinical effects (Dallaire et al., 2009).

Oral synthetic hypoglycemic drugs have various side effects so; the interest to use herbal therapy for curing diabetes mellitus grows up (Deng, 2012). Multiple plant extractions are utilized in folk remedy to treat diabetes mellitus (Kooti et al., 2016). Many medicinal plants are considered as a source of developing pharmaceutical entities or dietary supplement and used to provide oral hyperglycemic compounds (Wang et al., 2013). Herbal drugs have minor side-effects and minor toxicity compared to synthetic drugs (Babu and Prince, 2004). *Boswellia carterii* is one of the natural pharmaceutical plants used. Olibanum is a common name of *Boswellia carterii* from Burseraceae Family (Al-Mehdar and Albattah, 2017). Many countries like China, India, Africa and Middle East have been used *Boswellia carterii* for prevention and remedying of multiple disorders particularly chronic inflammatory disorders, anti-proliferative, anti-arthritic, and analgesic substance for treating related diseases (Hamidpour et al., 2015). In the most recent decade, the utilization of olibanum has turned out to be more common in European countries for curing several of chronic inflammatory disorders like chronic bowel diseases, arthritis, asthma, edema of peritumoral brain and other disorders (Ammon, 2006).

Furthermore, boswellic acids possess many others therapeutic properties such as anti-cancer properties through apoptotic andcytostatic effects in numerous cancer cell lines of human. Boswellic acid is one of the principal components of olibanum, a content known to have anti-neoplastic activities (Frank et al., 2009). The current study aimed to evaluate the anti-hyperglycemic and antioxidant impacts of *Boswellia carterii* (BC) against increased blood glucose caused by type 2 diabetes mellitus and reveal the functional and structural protective consequence of BC on thyroid gland against DM adverse effects.

2. MATERIALS AND METHODS

Streptozotocin

Streptozotocin was purchase from SRL, LTD, India. 0.01 M sodium citrate buffer with pH 4.5 was used to dissolve streptozotocin which freshly prepared and used within 15 minutes. An injection of 45mg/kg/body weigh was implemented (Salemi et al., 2016).

Induction of diabetes

After four weeks of high fat diet, rats banned from food for 12h then injected peritoneally with streptozotocin (45 mg/kg) (Zhang et al., 2008). To prevent hypoglycemia and improve STZ access to β cells through GLUT2 glucose transporter, the animals were given 5% sucrose solution overnight (Zhao et al., 2005). Blood samples from tail vain were used to estimate hyperglycemia seven days after STZ injection using ACCU-CHEK performa meter (Roche). The level of blood glucose is larger than 250 mg/dl were selected for the study and considered an indicator for developing Type 2 diabetic (Francis and Sudha, 2016).

***Boswellia carterii* aqueous**

Boswellia carterii is maintained from Abazear local store in Jeddah Saudi Arabia. 100 ml distilled water with 50g of dry *B. Carterii* boiled for 10 min. The mixture leaved to cool to reach room temperature then filtered. The aqueous extract with concentration of (25% w/v) preserved at refrigerator till time of use. Oral gavage is used for administration o dose of 100mg/kg/BW (Al-Mehdar and Albattah, 2017).

Metformin preparation

Dose of 150 mg/kg/day was used from Metformin hydrochloride (Shanghai Shiguibao Medicine Co., Ltd., China), and given orally to diabetic rats after dissolving in 0.9% (W/V) sodium chloride for six weeks (Akinola et al., 2012).

Experimental animals and study design

Male adult Wistar rats (N=25) with weighing 200-250 g and three-month-old were obtained from Animal House, KAU. Animals were kept in standardized rodent cages at 22±2 °C and light-dark cycle (12/12) at 22±2 °C and left for one week for acclimatization. Drinking water and the standard diet were accessible ad libitum throughout the research. All doses were given daily for six weeks orally using gastric gavage (Maway et al., 1969; Faried et al., 2014). Animals were then allocated into 5 groups (N= 5) as following:

G1: Control (C) group, which were given a vehiclenormal saline and citrate buffer.

G2: Non-treated type 2 diabetic (DM) group (diabetic control).

G2: Diabetic type 2 treated with *Boswellia carterii* extract (DM+BC) group, given orally the previously prepared BC100mg/kg/BW orally.

G4: Diabetic type 2 treated with metformin (DM+ Metf) group, given orally 150 mg/kg/B. W metformin.

G2: Normal *Boswellia carterii* extract (BC) group, given orally previously prepared BC100mg/kg (BC). The experiment was conducted during 2019-2020

Body weights

Body weight for each rat was takenusing a sensitive balance. The changes in body weight were documented week by week. Initial and final body weight at the beginning and the end of research were recorded for all animals.

Blood sampling and glucose level analyses

After six weeks, rats were banned from food for 10-12 hours. Blood sample was collected from retro-orbital venous plexus (Parasuraman et al., 2010; Parasuraman et al., 2015) using special capillary tube (5 ml, BD vacutainer, SST/Advance, UK). Serum was maintained by centrifugation of the blood for 15 min at 3000g at 4^{oC} (Hettich, Roto silent A/K, Western Germany) and kept at -80 C till the time of analysis. Serum was used to measure blood glucose, antioxidant, and hormones. To measure blood glucose, enzymatic glucose kits (Human Gesellschaft fur & Diagnostic mbH, Germany) was applied.

Hormonal assays

Serum thyroxine (T4), triiodothyronine (T3) and thyroid stimulating hormone (TSH) were analyzed using the particular enzyme-linked immunosorbent assay (ELISA) kits from (BioVision Life Science Source ™) according to manufacturer protocol.

Antioxidant assays

Diagnostic kit of MDA from (Cayman Chemical Company, Ann Arbor, MI, USA) was used to analyze lipid peroxidation (LPO). Diagnostic kit from (Cayman Chemical Company, Ann Arbor, MI, USA) was used to analyze SOD and CAT. Diagnostic kit from (Abcam, Cambridge, MA, USA) was used to analyze GPx according to manufacturer's protocol

Histological study

The thyroid gland of each rat was carefully dissected, extracted and immediatelyput in 10% neutral buffered formalin pH 7.4 for fixation. Then, the tissue samples were processed as the usual histological technique; slides were stained with H& E (Suvarna et al., 2019). The slides were examined under Motic light microscope and images were taken using AmScope microscope digital camera and the histological changes were observed.

Statistical analysis

Means and standard Error for every parameter, analysis of variance, and student's T-test at 5% significant level were taken.

3. RESULTS

Body weight

The body weight meaning fully reduced (p< 0.000) in diabetic rats in comparison to control (Table 1). However, the body weight non-significantly increased in diabetic-BC treated rats in 2nd week and significantly in 6th week compared to non-treated diabetics rats.

Table 1 Total body weight (g) in 2nd and 6th weeks comparison of different groups versus control and diabetic control.

Group	2nd week body weight (grams)	6th week body weight (grams)	Body weight changes (%)
G1 (control)	232.42±8.82	263.89±7.14	14.51+1.12
G2 (Diabetic control)	220.96±9.41*	236.94±6.47*	7.99±0.06
G3 (Diabetic +BC)	225.33±3.42	261.97±3.92#	16.38±0.68
G4 (Diabetic +Metf)	229.96±8.55	268.24±7.52#	17.41±0.98
G5 (normal BC)	260.11±2.29*	270.74±10.33	4.08±0.25

Data were expressed as mean+ Standard error

*Significant versus control, # significant versus diabetic control, @ significant versus metformin

Blood glucose levels

Blood glucose at the beginning of experiments was within normal level in all groups. After the 6th week of experiment, STZ-induces diabetic group showed significant increase in blood glucose level values reached 369.08+7.56 mg/dl compared to normal control (98.87±4.18 mg/dl) (p<0.000) (Table 2). Level of blood glucose decreased significantly after supplementation with either BC (p< 0.002) or metformin (p< 0.03) compared to diabetic, but it did not reach the level of normal control group. BC significantly decreased blood glucose level after two weeks compared to untreated diabetic group.

Table 2 Comparison blood glucose levels (mg/dl) in different studied groups in different weeks versus control and diabetic control.

Group	0-week blood glucose (mg/dl)	6th week blood glucose (mg/dl)
G1 (control)	99±1.95	98.87±4.18
G2 (Diabetic control)	99.8±1.56	369.08±7.56*
G3 (Diabetic + BC)	101±2.53	224.65±7.52*#
G4(Diabetic +Metf)	98.4±1.69	318.44±12.84*#
G5 (Normal BC)	101.89±1.36	96.53±0.78

Data were expressed as mean+ Standard error

*Significant versus control, # significant versus diabetic control, @ significant versus metformin

Antioxidant parameters

There was significant decline in level of the antioxidant enzymes including SOD (p< 0.000), GPx (p<0.02), CAT (p<0.004) and significant raise in level of lipid peroxidation (p<0.03) in diabetic group compared to control group (Table 3). Supplementation diabetic group with BC increased the SOD (p<0.04) and CAT (p<0.001) and decrease LPO (p<0.01) significantly compared to diabetic group Metformin caused increase in SOD (p<0.009) and GPX (p<0.02) and decrease LPO (p<0.05) significantly. It is well noticed that BC supplementation to normal rats resulted in marked increase in SOD (p<0.000) and CAT (p<0.007) compared to control.

Table 3 Comparison between serum levels of SOD, GPx, CAT and LPO in different studied groups versus control and diabetic control

Group	SOD (U/ml)	GPx (nmol/ml)	CAT (mmol/ml)	LPO (mmol/ml)
G1 (control)	0.73± 0.02	13.80± 0.58	70.29± 3.15	3.98± 0.17
G2 (Diabetic control)	0.54± 0.02*	11.58± 0.21*	44.03± 4.18*	4.81± 0.30*
G3 (Diabetic + BC)	0.60± 0.01*#@	12.28±0.18*	125.43±9.50*#@	3.28±0.06#
G4 (Diabetic +Metf)	0.76± 0.03#	13.45± 0.30#	34.07± 1.52*	4.11± 0.06#

G5 (Normal BC)	1.02±0.03*	14.31±0.10	94.90±3.91*	4±0.21

Data were expressed as mean+ Standard error

*Significant versus control, # significant versus diabetic control, @ significant versus metformin.

Hormonal parameters

In non-treated diabetic group, there was a meaningful raisein level of TSH ($p< 0.01$) and meaningful decline in the level of T4 ($p< 0.002$) and T3 ($p< 0.000$) compared to normal control group (Table 4). Treating diabetic rats with BC decrease the level of TSH significantly ($p< 0.02$) compared to non-treated diabetic group and the value of TSH became near normal value where no significant difference between them. The level of T4 ($p< 0.002$) and T3 ($p< 0.002$) significantly increased in the treating diabetic rats with BC compared to non-treated diabetic group even though the values of T4 and T3 did not reach the normal.

Table 4 Comparison of TSH and thyroid hormones in different studies groups versus control and diabetic control

Groups	TSH Ng/ml	T4 Pmol/l	T3 Pmol/l	T3/T4
G1 (control group)	26.2+0.52	16.82+0.54	3.72+0.03	0.22+0.01
G2 (Diabetic control)	31.16+1.23*	11.68+0.40*	2.53+0.09*	0.24+0.014
G3 (Diabetic + BC)	27.02+0.46#	12.62+0.16*#@	3.3+0.10*#@	0.26+0.01*#
G4 (Diabetic + Metf)	26+0.42#	10.58+0.42*	2.28+0.09*#	0.21+0.13*
G5 (Normal BC)	27.27+0.80	16.3+0.58	3.26+0.08*	0.20+0.004*

Data were expressed as mean+ Standard error

*Significant versus control, # significant versus diabetic control, @ significant versus metformin

Histological study

Histological structures of rat thyroid gland in control, diabetics and BC treated diabetic rats are showed in (Fig. 1). In this study BC given to normal nondiabetic rats was found to be safe and not alter normal structure of thyroid gland which looked exactly similar to that of control.

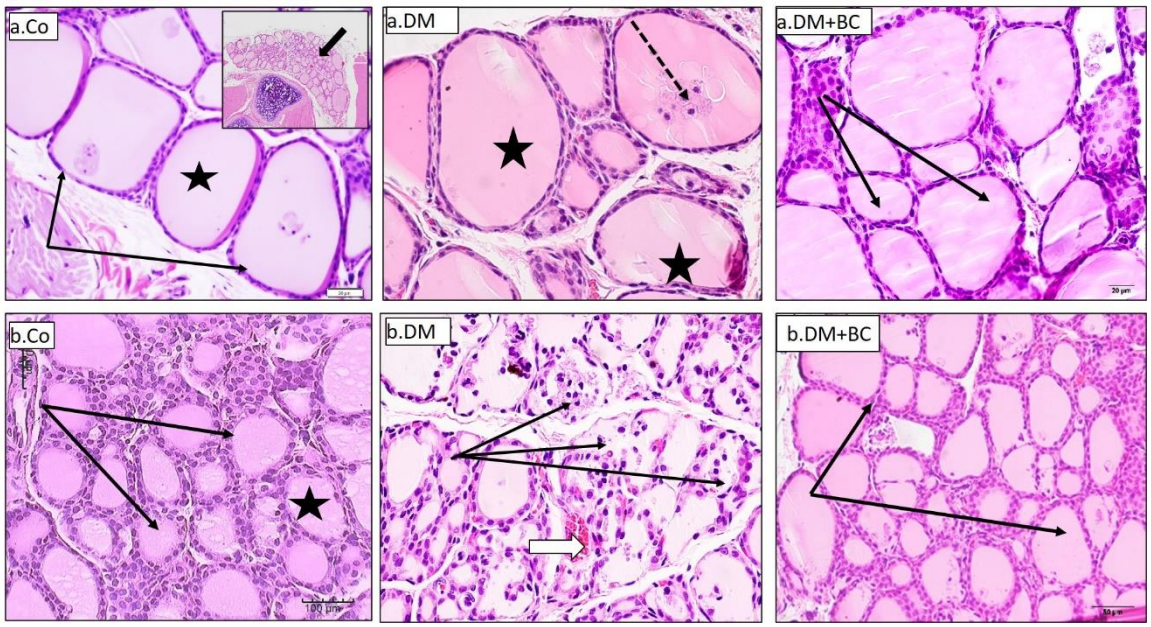

Figure 1 Paraffin sections of rat thyroid gland stained by H & E, show: G1: Control: Peripheral (a) & central (b) regions showing normal thyroid follicles (Black arrows) contain homogenous stained colloid (star) and lined by intact cuboidal to flat cells (black arrows). Colloid (stars) is stained homogenous with no vacuoles or desquamates cells. G2: Diabetes Type II thyroid: a. peripheral follicles showed desquamated squamous cells (dotted arrows). Dark stained colloid (star). b. central follicles showed marked disruption with degeneration and desquamation of lining cells with decrease colloidal staining (black arrows). slight dilated, congested capillaries (white arrow) G3: Diabetes +BC: showing nearly normal a. peripheral and b. central regular follicles with normal intact lining epithelium (arrows) similar to control.

Histological structure of control rat thyroid (CO)

In the present study, H & E-stained paraffin sections showed that rat thyroid has histological features of normal thyroid described in literature. Thyroid follicles are of varying sizes with larger ones located at the periphery. They are separated blood sanity connective tissue contains thin wall blood capillaries. The lining epithelium of follicles is intact and varies from low cuboidal to flat epithelium. Colloidal content is stained homogenously and free from any cell debris and desquamated cells.

Histological structure of Type 2 diabetic rat thyroid (DM)

Compared to control, peripheral thyroid follicles showed dark stained colloid containing desquamated cells. Central follicles showed disrupted shape, degenerated with marked desquamation of its lining epithelium (black arrows) surrounded unstained colloid (stars).

Histological structure of Type 2 diabetic rat thyroid treated with BC (DM+BC)

Thyroid glandsof type 2 diabetic rats treated with BC (100mg/kg) showing marked preservation of normal structures. Follicles in both regions looked more or less similar to control.

4. DISCUSSION

In this study, T2DM model was successfully maintained using (Zhang et al., 2008) method by practical, easily accessible, cheaper for the assessment as well as testing the effect of BC treatment on T2DM. This method is established by many researchers (Srinivasan et al., 2005; Franconi et al., 2008). The blood glucose in untreated diabetic animal was significantly high. Many causes lead to the blood glucose levels rises in T2DM. The most important cause is insulin resistance; the body is mainly ignoring its insulin secretions. Another reason is the decline in the production of insulin by the pancreas β cells. So, person with type 2 diabetes may suffer from both the deficiency in insulin secretion and insulin action (Zhang et al., 2007).

In this research, the raised blood glucose level of diabetic groups was improved with BC and metformin treatments. This finding in agree with previous studies (Khan et al., 2003; Azemi et al., 2012; Ahangarpour et al., 2014; Al-Mehdar and Albattah, 2016). The hypoglycemic properties of BC plant extracts may be due to that the remaining β-cells were stimulated to secrete insulin which lead to enhance utilizing glucose by the tissue through enhancing its uptake and metabolism or preventing hepatic gluconeogenesis, or due to the existence of pentacyclic triterpene (boswellic acid derivatives) (Al-Mehdar and Albattah, 2016). BC may have direct stimulatory effect on β cell division and / or contain non metabolizable 2-deoxy 3-Omethylglucose which blocks the diabetogenic effect (Shafrir, 2003). Moreover, BC may possess direct protective effect on β cells through its antioxidant action (Altman et al., 2004). Also, one of the possible actions of *Boswellia Carterii* is anti-hyperglycemic activity, its antioxidant property (Al-Mehdar and Albattah, 2016).

In present study, the body weight of non-treated diabetic group meaningfully declined comparing to the normal controls, our finding goes line with (Kusari et al., 2007; Eleazu et al., 2013). The lost in the body weight of diabetic rats attributed to the increase in urine excretion causing dehydration and loss of body fluid (Kusari et al., 2007), or to the breakdown of muscle due to hyperglycemia (Kusari et al., 2007) and degeneration of structural proteins (Eleazu et al., 2013) due to unavailability of carbohydrate (energy source) (Emam, 2012). Though, a meaningful raise towards normal body weight was noticed in diabetic group supplemented with *B. carterii* extracts in comparison with diabetic controls. Our results in agreement with (Al-Mehdar and Albattah, 2016) who demonstrated that the improvement in diabetic rats after the BC supplementation proves the protective influence of these extracts against the degeneration of structural and could also be due to their direct hypolipidemic activities or their indirect impact on nemarous lipid regulation systems.

One of diabetic characteristic is lipid peroxidation. Lipid peroxidation is an indicator of oxidative stress condition (Niki, 2008) and free-radical-production process led to oxidative damage of poly un-saturated fatty acid (Chis et al., 2009). In current investigation, the levels of serum lipid peroxidation were markedly increased in diabetic control in comparison with normal control rats at the same time the level of enzymatic antioxidant including SOD, GPx and CAT were decease significantly. Our results are in consistent with (Sadri et al., 2017; Mohajeri and Doostary, 2010). The level of antioxidants decreased in diabetic rats attributed to proteins glycation due to hyperglycemia (Gomathi et al., 2013) or could be due to free radical-induced inactivation of these enzymes in diabetic state (AI-Azzawie and Alhamdani, 2006). Treatment of diabetic rats with BC had reversed the activities of these enzymatic antioxidants, this means that the extracts can reduce the potential glycation of enzymes or they may reduce the production of reactive oxygen free radicals and improve the activities of antioxidant enzymes (Prabhakar et al., 2013).

Various components isolated from Boswellia resins particularly boswellic acids and their derivatives have shown multiple biological activities (Poeckel and Werz, 2006). Boswellia has been found to have a number of pharmacological actions, including anti-hyperglycemia (Azmi et al., 2012) and antioxidant properties (Borrelli et al., 2006; Azmi et al., 2012). Furthermore, it was proven that BC possesses more powerful free radical scavenger properties (Azmi et al., 2012; Mohamed et al., 2015, Masoud et al., 2017).

Thyroid hormones and insulin act synergistically in glucose uptake and disposal in peripheral tissues (Clement et al., 2002). There are numerous investigations on the association between diabetes and thyroid dysfunction, albeit with contradiction outcomes, some researches recording an association between type 2 diabetes and hyperthyroidism, while others record instead an association between diabetes and hypothyroidism (Chaker et al., 2016). Furthermore, one of the major recent and biggest cross-sectional investigation records no association between type 2 diabetes and thyroid dysfunction (Fleiner et al., 2016).

The serum level of TSH in diabetic rats was found to be significantly higher than in control rats in the current study. Our outcome is consistent with (Arshad and Hussian, 2013; Chandel et al., 2016; Hu et al., 2017; Mohamed and Abdel Gawad, 2017). T4 and T3 levels in diabetic rats, on the other hand, decreased significantly when compared to controls. Our outcome is consistent with (Zari and Attar, 2007; Daniel et al., 2015; Mohamed and Abdel Gawad, 2017). It was stated that the rate of production of T3 and T4 and the conversion of T4 to T3 in the tissue and pituitary gland are reduced in diabetic rats (Peeter, 2017). The decline in serum T3 is due to the reduction in peripheral conversion of T4 to T3. Also, insulin, an anabolic hormone, enhances FT4 level while suppresses T3 level by reducing hepatic conversion of T4–T3 (Udiong et al., 2007; Uppal *et al.,* 2013). Furthermore, low serum level of T3, T4 may be due to decreased binding protein (Goodman, 2009; Kim & Landeson, 2012). Uppal et al., (2013) revealed that there was an increase in insulin and decrease in T3 level in T2DM compared to normal healthy group which agree which our result.

According to Mohamed and Abdel Gawad (2017), DM affects thyroid function on two levels: the hypothalamus level, where it regulates TSH secretion, and the peripheral tissue level, where T4 to T3 conversion occurs. Hyperglycemia produces a reversible decrease in the activities and in the concentration of T4-5-deiodinase in hepatic tissues, as well as low serum T3 and T4 concertation. The increase of ROS is one of the contributing reasons in the hypothyroid condition seen in diabetic rats which could lead to oxidative injuries to the thyroid gland (Santos et al., 2013). The diabetic effects on the thyroid were reversed by BC treatment. BC significantly reduced the elevated level of TSH almost entirely to the level of normal control, with no significant difference between them. BC also causes a significant increase in T4 and T3 levels when compared to diabetics, though it does not reach normal levels. To the best of our knowledge, the effect of Boswellia on thyroid function has not been studied.

Ashwini et al., (2017) reported that the treatment with the *Costus pictus* extract (the extract contained pentacyclic triterpenes alpha and beta amyrins) improvement in thyroid profile. The chemical structure of Boswellia resin is identical to that of other pentacyclic triterpenes (Chevrier et al., 2005). According to Ashwini et al., (2017), *C. pictus* extract may upregulate the expression of main enzymes contribute in thyroid hormone synthesis, thyroperoxidase and 5'deiodinase, or increase the activity of these enzymes, which stimulate the thyroid gland to secrete thyroid hormones. It was also suggested that *C. pictus* extract improvement hypothyroid in rats treated with Propylthiouracil (PTU) which induced the hypothyroidism and inhibit nuclear factor-kappa B (NF-kβ) activation (Vitor et al., 2009) which led to impairment in the production of thyroid hormones (Takada and Aggarwal, 2003; Alakurtti et al., 2006).

Sarup et al., (2015) reported that the Guggulu (from Family: Burseraceae) encompasses volatile oil which comprises terpenoidal enhanced the triiodothyonine (T3) level and T3/T4 ratio. *Z*-Guggulsterone which found in guggulu responsible for significant increase in thyroid function, increase uptake of iodine by the thyroid, and enzymes involved in the synthesis of thyroid hormones and stimulate thyroid action (Sarup et al., 2015). Panda and Kar, (2005) found that guggulu improve hypothyroidism by raising the levels of triiodothyronine T3, thyroxine T4 and hepatic 5' monodeiodinase, in addition, there were activations of antioxidative enzymes in particular superoxide dismutase (SOD) and catalase (CAT) which is in agreement with our results. In this research, a histological structure correlated with biochemical results in relation to thyroid function tests. The disruption of normal thyroid morphology and the focal damage of epithelial lining of follicular cells in diabetic groups could explain the decrease in thyroid hormone serum levels with subsequent increase in TSH based on feedback mechanism (Pandit, 2017). The necrotic changes in thyroid follicle and possible of other body tissue could also explained the increased in lipid peroxidation in the serum of those animals. Lipid peroxidation and altered antioxidant defensive mechanism wasreported in diabetic patients (Tuncayengin et al., 2003). Similar changes were described by (Yetim et al., 2015) who attributed such changes to oxidative stress associated with hyperglycemic (Asmat et al., 2016). Thyroid dysfunctions were reported in persons who suffer from type 2 diabetes (Radaideh et al., 2004). The improvement and protection of thyroid morphology in diabetic rats treated with BC is most probably due to control of glycemic status and lowering of blood glucose by BC (Chaker et al., 2016). At the same time, the antioxidant activities of BC (proved here by the increase in antioxidant enzymes catalase, SOD and GPx.

5. CONCLUSION

With the stated findings, diabetes mellitus of type 2 is disorder with various deterioration effects on the thyroid gland effecting its function and structure. Using natural medicine is a hope to for many diseases to cure. *Boswellia carterii* has powerful antioxidant activities with lowering blood glucose level properties. It increases the antioxidant enzyme and the same time decrease the lipid peroxidation. Through its activities it modulates the high level of TSH and the low level of T3 and T4 hormones caused by T2DM at the same time preserve the histological structure of thyroid gland. *Boswellia carterii* can be used by T2DM patient to mitigate the deleterious s effects of diabetes

Abbreviations

BC, Bowellia Carterii; BLG, blood level glucose; SOD, superoxide dismutase; CAT, catalase; GPx, glutathione peroxidase; LPO, lipid peroxidation; TSH, thyroid stimulating hormone; T4, thyroxine hormone; T3, Triiodothyronine.

Acknowledgments

Sincere gratitude to King Fahad Research Center and King Abdul-Aziz hospital for their generosity and their helping and guidance in doing lab work. Special grateful to prof. Dr. Soad Shaker Ali in anatomy department, faculty of medicine, member 5 in Yousef Abdullatif Jameel Chair of Prophetic Medical Applications (YAJCPMA), King Abdul-Aziz University, Jeddah, Saudi Arabia who helped in reading the slides and for her guidance in histological part of the research.

Ethical approval

Ethical approval was taken from the ethic committee in King Abdul-Aziz University (Jeddah, Saudi Arabia) and according to the OECD suggestions for the proper use and care of experimental animals(Ethical approval No. HA-02-J-008).

Funding

This study has not received any external funding.

Conflict of Interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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