

**HISTOLOGICAL STUDY OF THYROID GLAND IN CASE OF
EXPERIMENTALLY INDUCED HYPOTHYROIDISM BY
CARBIMAZOLE IN DOMESTIC FEMALE RABBITS
(*Lepus cuniculus domestica*)**

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ABSTRACT

The present study aimed to investigate the histological , histochemical changes of thyroid gland in case of induced hypothyroidism by carbimazole in domestic female rabbits .

Histological results revealed many histopathological changes compared with the control group there are hyperatrophy of follicular epithelium , hemorrhage , edema and damage in the epithelium lining of the follicles.

Histochemical results revealed alterations in normal distribution of glycoprotein inside follicles of thyroid gland in hypothyroidic groups.

INTRODUCTION

The thyroid gland is a butterfly- shaped endocrine gland lying in the neck in front of the upper part of the trachea .⁽¹⁾ The thyroid gland consist of two lobes connected by a narrow band of thyroid tissue called the isthmus , it is surrounded by a double connective tissue capsule , two pairs of parathyroid glands are located on the posterior surface of thyroid gland .⁽²⁾ The thyroid follicle or acinus , which is the structural and functional unit of the gland , it is consist of a single layer of cuboidal epithelial cells , the follicular epithelium enclosing a central lumen containing a colloid substance rich



in thyroglobulin an iodinated glycoprotein.⁽³⁾ The follicular epithelium contain scattered parafollicular cells also called C cells contain small cytoplasmic granules representing the stored hormone calcitonin which regulate calcium concentration in blood .⁽⁴⁾ Thyroid gland secret three important hormones triiodothyronine T3 ,thyroxin T4 ,and calcitonin .⁽⁵⁾The extracellular storage of thyroglobuline in the follicular lumen is essential for maintaining constant blood levels of thyroid hormones T3 and T4 .⁽⁶⁾ Thyroid function is to synthesize the hormones T3 ,T4 which are important for growth , for cell differentiation and for the control of oxygen consumption and basal metabolic rate of cells in the body .⁽⁷⁾ Hypothyroidism is a deficiency of thyroid activity , it is results from reduced secretion of both T3 and T4. ⁽⁶⁾ So ,this study was carried out in order to demonstrate the histological and histochemical affects of thyroid gland in case of induced hypothyroidism in domestic female rabbits .

MATERIALS AND METHODS

The studied animals included 32 female mature rabbits were divided into four groups: two control groups for 30 and 60 days ,two hypothyroidic groups for 30 and 60 days of treatment which were breded in the same

Environmental condition. Hypothyroidism was induced by using carbimazole (5 mg /kg bw) dissolved in water and given orally by stomach tube daily through out the experiment while the control groups received normal saline .

- Histological study :

Tissue samples were taken of thyroid gland ,these specimens were placed in fixative 10% buffered formalin immediately upon removal from the body , after tissue processing and embedding in paraffin section were cut at 6 microns thickness then the slides were stained with heamatoxylin and eosin stain .

-Histochemical study :

Paraffin section 6 microns thickness stained with periodic acid –shiffs reagent to demonstrate glycoprotein of thyroid follicles .



RESULTS

First : The results of histological study revealed histopathological alterations in thyroid gland in comparison with the control group figure (1) in case of hypothyroidism for 30 days of treatment with carbimazole figure (2) there is hyperatrophy of follicular epithelium and non homogenous colloid or cord like materials inside follicles ,congested blood vessels and hemorrhage ,however in case of hypothyroidism for 60 days of treatment with carbimazole figure (3) there is hyper atrophy of cell lining epithelium or follicular epithelium and infiltration of inflammatory cells with edema between connective tissue septa of thyroid gland and damage in the epithelial lining follicles, some follicles enlarged.

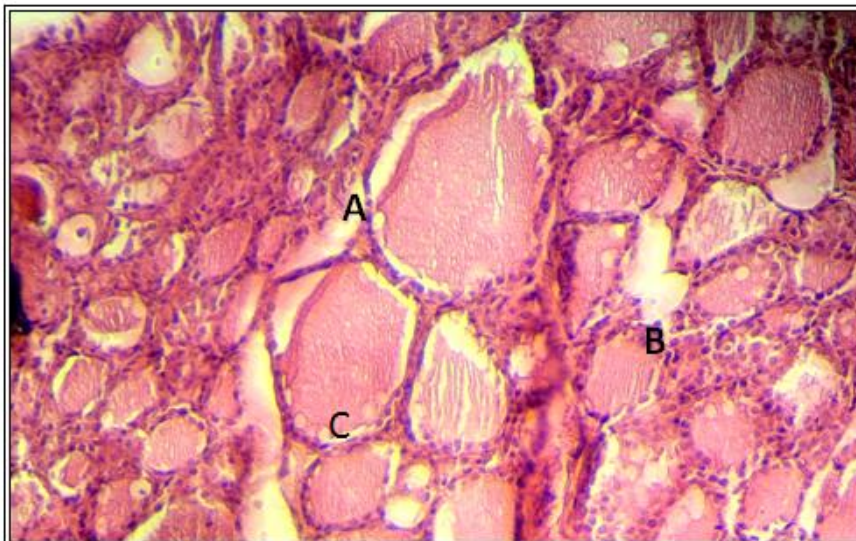


Figure (1): Section of thyroid control female rabbits showing , A – Follicles, B , parafollicular cells ,C-colloid , (H&E stain , 400 X)



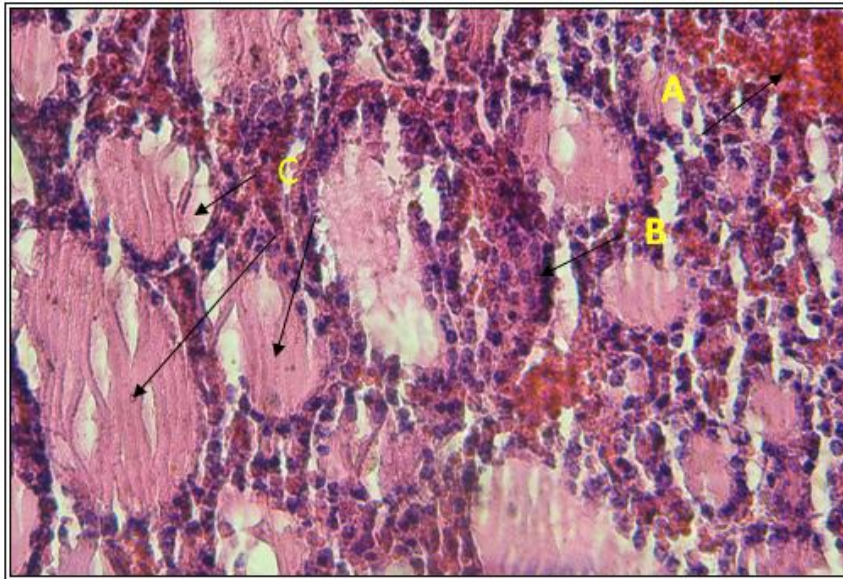


Figure (2) section of thyroid gland treated of female rabbits for 30 days showing A- hemorrhage , B-hyperatropy of follicular epithelium C-cord like colloid, (H&E stain,400 X)

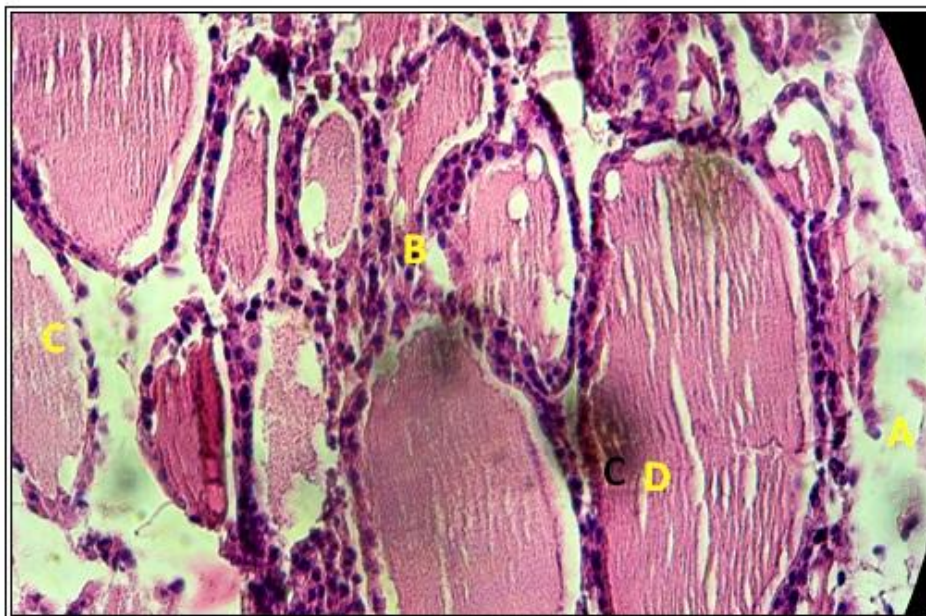


Figure (3) section of thyroid gland of female rabbits treated for 60 days showing A- edema , B-hyperatropy of follicular cell , c-damage of follicular epithelium , D- cord like colloid , (H&E stain ,400 X)



Second : Histochemical examination of thyroid gland of control rabbits show the intensity and homogenous staining of colloid figure (4) while the thyroid gland of female rabbits treated with CBZ for 30 days show decreased of normal distribution of glycoprotein inside follicles ,the non homogenous cord like materials and less intensity of colloid figure (5) also the thyroid gland of rabbits treated with CBZ for 60 days show less homogeneity of colloid or absence of colloid in some follicles figure (6) .

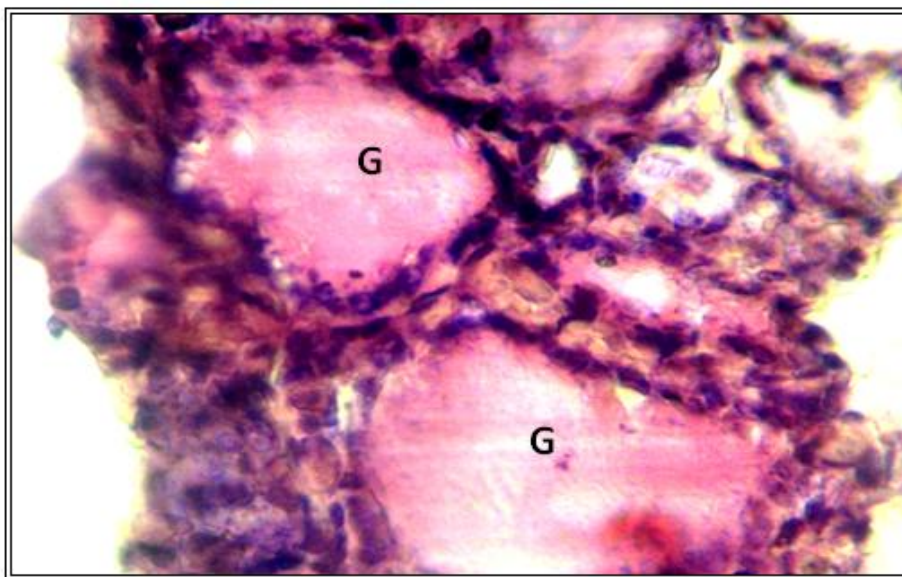


Figure (4): Section of control thyroid gland, show G-homogenous distribution of glycoprotein in thyroid follicles (PAS stain , 400 X).



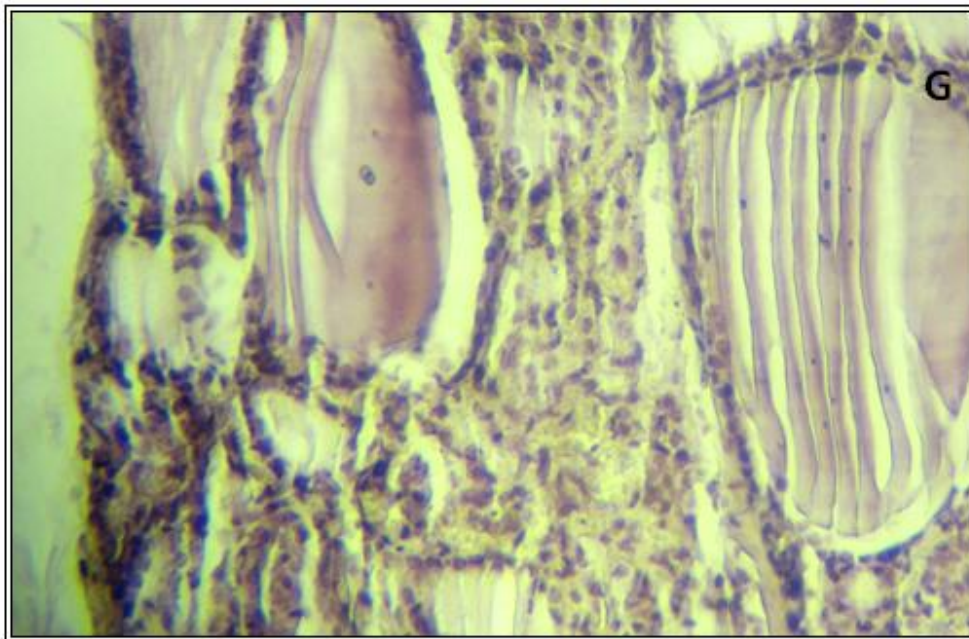


Figure (5) section of thyroid gland of female rabbits treated by CBZ for 30 days, showing G-cord like colloid , and less intensity (PAS stain ,400X)

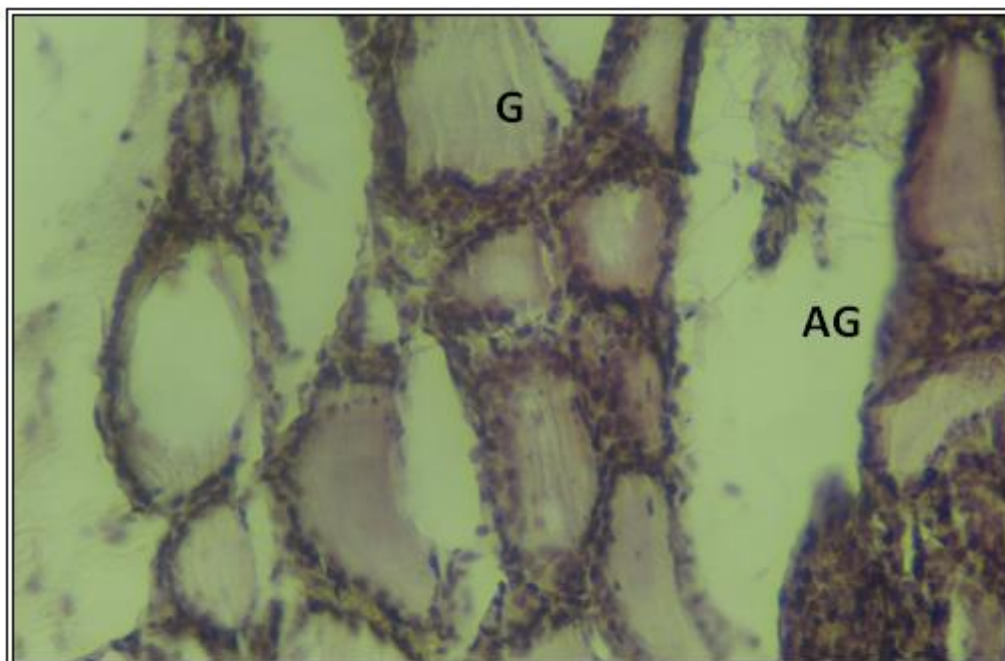


Figure (6) : section of thyroid gland of female rabbits treated by CBZ for 60 days show G- colloid less homogenisty, AG-absence of colloid in some follicles (PAS 400 X) .



DISCUSSION

The histological results of thyroid gland after induction hypothyroidism for 30 and 60 days by CBZ reveal hyperatrophy of follicular epithelium ,(8) mention that CBZ which is anti thyroid drug inhibit the formation of T3 and T4 , which stimulate the anterior pituitary gland to secrete more TSH and this hormone stimulates the growth of thyroid gland ,results hyperatrophy of follicular epithelium ,these results are in agreement with (9) found that induce hypothyroidism in mice by sodium fluoride characterized by follicular cells hyperplasia and hyperatrophy and increase in vascularity also the results are in agreement with (10) induce hypothyroidism in virgin and lactating rabbits by CBZ, and agreement with (11) (12) (13) induce hypothyroidism in male rats stimulate secretion of TSH which cause hyperatrophy of follicular cells , also agreement with (14) CBZ in human cause hyperatrophy of follicular cells . On the other hand the results reveal congested blood vessels in 30 days of treatment and hemorrhage in 60 days of treatment in thyroid tissue ,(3) mention that because inhibit T3, T4 secretion from thyroid gland in case of hypothyroidism is made to exert a negative feedback of TSH synthesis and increase secretion , this hormone stimulates the vascularization of thyroid gland and consequently the gland enlarged , TSH increase blood flow to thyroid gland and other organs and tissues (15) so this may cause destruction to the blood vessels results hemorrhage in thyroid tissue. Low level of T3 T4 lead to hypoxia that result bloody congestion hepatic dysfunction lead to blood congestion due to hypoxia (16) .

The results show edema in thyroid gland in female rabbits treated with CBZ for 60 days ,because of the destruction of large follicles of thyroid gland due to induction of hypothyroidism for long period ,some follicles appear empty without colloid which may accumulate in thyroid tissue ,in which there is increase the filtration of fluid out of the capillaries and edema due to accumulation of osmotically active mucopolysaccharides in the interstitial fluid (17)or due to change in the permeability of congested blood vessels resulting edema .low level of T3 T4 cause hepatocytes damaged lead to adema appearance (18) .



The histochemical results of thyroid gland of female rabbits treated with CBZ is made by periodic acid- schiff's reaction to demonstrate glycoprotein in thyroid follicles , colloid is rich in thyroglobulin ,which is an iodinated glycoprotein yielding a PAS positive reaction (3)(18). The results show decrease in the normal distribution of glycoprotein and non homogenous colloid and appear as cord like substances and less intensity in hypothyroidic rabbits for 30 days while in hypothyroidic rabbits for 60 days the colloid appear less intensity or absence in some follicles especially in the large follicles , Thyroid follicular epithelial cells synthesized and metabolized the thyroglobulin (19) , Antithyroid drugs which bind to the thyroglobulin may alter the setric configuration of this protein so that coupling of iodotyrosin residues can no longer occur (20) ,The colloidal materials in the thyroid gland follicles is known as thyroglobulin from which free thyroxin is librated by enzymatic action

(21). The antithyroid drugs methmazole inhabits thyroid hormone synthesis by interfering with thyroid peroxidase mediated iodination of tyrosine residues which an important step to formation throglobulin and synthesis of T3 ,T4 (22) this may cause the moderate or even negative reaction with PAS reagent .

So we concluded that induce hypothyroidism in female rabbits produced histological alterations in follicular epithelium , histochemical changes in the glycoprotein of thyroid follicles .

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دراسة نسيجية للغدة الدرقية في حالة استحداث القصور الدرقي تجريبيا في إناث الأرانب

المحلية

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الخلاصة

تهدف الدراسة الحالية التحري عن التغيرات النسيجية والكيمنوسيجية للغدة الدرقية بعد استحداث القصور الدرقي تجريبيا باستخدام عقار الكاربامازول في الارانب الاناث المحلية ، اظهرت نتائج الفحص النسيجي ظهور تغيرات نسيجية امراضية بالمقارنة مع مجموعة السيطرة حيث اظهرت فرط تنسج في الخلايا الجريبية مع حدوث نزف ووذمة في النسيج الدرقي وتحطم بالضهارة المبطنة للجريبات وبينت النتائج الكيمنوسيجية تغيرات في التوزيع الطبيعي للكلايكوبروتين في مادة الغروان داخل الجريبات عند استحداث القصور .

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