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Research Article

Thyroxine Accelerates Healing of Acetic Acid-Induced Gastric Ulcer in Rats

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Abstract

Studies have shown that disturbed thyroid states may predispose the gut to ulcer formation, suggesting that thyroid hormones play important roles in gastroprotection. It is not known however if the gland and its principal hormones affect the processes leading to the healing of already formed gastric ulcers. Therefore this study was designed to investigate the effects of thyroid hormones on healing of acetic acid induced gastric ulcer. Male albino rats (160 – 200g) were divided into four groups viz: control, thyroidectomised, thyroidectomised with thyroxine treatment (100µg/kg/day) and Sham operated animals treated with thyroxine. After 35 days of drug treatment and/or surgery, ulcer was induced in stomach of animals using acetic acid. Ulcer healing was assessed 3, 7 and 10 days post-ulcer induction. Ulcer area was measured by planimetry. Blood cells were counted and tissue regeneration was studied using histology technique. Ten days post ulcer induction, thyroxine treatment significantly increased the rate of ulcer healing ($0.81 \pm 0.02 mm^2$/day) when compared with control ($0.46 \pm 0.05\ mm^2$/day) while thyroidectomy significantly reduced the rate of ulcer healing ($0.28 \pm 0.05 mm^2$/day). Thyroxine treatment increased the rate of clearing of inflammatory cells, fibroblast proliferation, collagen deposition and epithelial cell proliferation while thyroidectomy delayed these processes. Thyroxine treatment significant increased while thyroidectomy decreased white blood cell on day 7. We conclude that thyroid hormones accelerate gastric ulcer healing by accelerating inflammatory and proliferative phases of healing and increased white blood count during healing while thyroidectomy delayed these processes.

Keywords: *gastric ulcer healing, thyroxine, inflammation, blood cells*

Introduction

The gastrointestinal tract is a rapidly renewing part of the body. Several substances taken as food, drinks and drugs expose the gut to agents which cause cell loss through surface cell exfoliation (Konturek, 1988). Cell proliferation, cell migration, angiogenesis and other processes considered very important in ulcer healing are known to be intricately controlled by interplay of many factors which regulate cell formation and growth.

Several reports are available on the role of thyroxine in the healing of damaged tissues of the body. Talmi *et al.*, (1989) reported that thyroxine treatment accelerated healing of laryngeal fistula in postoperative *hypothyroid* patients. Accelerated healing of experimental myocardial infarction in rats was also reported by Kranz *et al.*, 1976. It was reported that thyroid hormones accelerated skin wound healing (Lennox and Johnston, 1973), stimulated epidermal proliferation, dermal thickening, and hair growth (Safer *et al.*, 2001, Safer, 2005). Mehregan and Zamick (1974) reported that additional thyroid hormone stimulated the rate and quality of wound healing in euthyroid rats while hypothyroidism retarded wound healing on the skin 2-fold relative to euthyroidism (Lennox and Johnston, 1973; Safer *et al.*, 2004). However, Pirk *et al.* (1974) noted no change in wound healing with euthyroid hamsters receiving thyroxine (ip). Cannon (1994) reported that hypothyroidism did not diminish wound strength in pigs, and Ladenson *et al.* (1984) failed to detect wound-healing deficits in hypothyroid humans after surgery. It therefore follows that there is no general rule on the action of thyroid hormones on healing in damaged tissues.

Gastric ulcer is a deep defect in the gastric wall penetrating the entire mucosal thickness and the muscularis mucosa (Tarnawski, 2000). Pathophysiology of ulcer is due to an imbalance between aggressive factors (acid, pepsin, *H. pylori* and non steroidal anti-inflammatory drugs) and local mucosal defensive factors (mucus bicarbonate, blood flow and prostaglandins) (Hoogerwerf and Pasricha, 2001). Gastric ulcer healing consists of reconstruction of mucosal architecture and is a dynamic, active process of filling the mucosal defects with epithelial and connective tissue cells. Ulcer healing process includes inflammation, tissue formation (granulation tissue formation, angiogenesis, and re-epithelialization), and tissue remodeling (Tarnawski 2000). All these processes are controlled by growth factors, transcription factors and cytokines (Tarnawski 1993, Vanwijck, 2001).

Thyroxine has been reported to reduce the formation of stress ulcer when given before stress (Koyunca *et al*, 2002) and reduces the formation of indomethacin-induced ulcer (Oluwole and Saka 2008). These reports suggest that thyroid hormones play a role in gastric ulcerogenesis.

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However, there is a dearth of information about the effects of these hormones the processes leading to the healing of already formed gastric ulcers. Therefore this study was designed to investigate the effects of thyroid hormones on healing of acetic acid induced gastric ulcer in albino Wistar rats.

Materials and Methods

Drug and Animals: Levothyroxine was purchased from Octavis, Barnstaple, UK, thiopentone sodium was purchased from Rotex Medica, Germany and procaine penicillin was obtained from China Medical Medicines, Guorui Pharmaceuticals Co. Ltd.

Male albino Wistar rats (160 -200g) were obtained from animal house, College of Medicine, University of Ibadan, Nigeria. They were randomly divided into four groups with adequate matching of weight. They were kept in wired cages and fed with standard commercial rat diet and tap water *ad libitum*.

Drug Treatment and Animal Grouping: Animals in control group were sham operated euthyroid animals. The other groups were untreated thyroidectomised animals (THx), thyroidectomised animals treated with thyroxine (THx+T_4) and euthyroid animals given thyroxine (T_4).

A chronic thyroxine treatment was used as previously described by Olaleye and Elegbe (2005). A dose of 100µg/day was given for 35 days using esophageal cannula.

Surgical procedure:

Sham operation: The animals were anaesthetised using 50mg/kg thiopentone sodium. A midline incision was made in the neck region, the thyroid gland was exposed, but the thyroid gland was left intact. The incision was sutured back, cleaned with procain penicillin and the animals were returned to standard diet and tap water.

Thyroidectomy: The animals were anaesthetized using thiopentone sodium (50mg/kg). A midline incision was made in the neck region, the skin was bilaterally retracted, the fascia and the muscle covering the thyroid gland were carefully removed and the thyroid gland was then extirpated. Care was taken so that the parathyroid glands were not removed. The incision was sutured back, dabbed with procain penicillin and the animals were returned to standard diet and tap water.

*Measurement of Plasma Thyroxine (T_4), Triiodotyronin (T_3) and Thyroid Stimulating Hormone TSH***:** After 35 days of drug treatment and post surgery, plasma T_4, T_3 and TSH were measured using radioimmunoassay technique.

Ulcer induction: After 35 days of drug treatment and/or surgery, ulcer was induced in the stomach of animals. The rats were fasted for 18 h before ulcer induction. Gastric ulcers were induced by the method of Wang *et al.,* (1989) with slight modifications. Animals were anaesthetised using 50mg/kg thiopentone sodium. Laparatomy was performed and stomach was exposed. Acetic acid (0.5 ml, 80% vol/vol) was applied to the serosal surface of glandular portion of the stomach for 1 minute using a 2ml syringe barrel that has been cut and smoothed. The acid was removed by aspiration and the area was washed with sterile saline. The abdomen was suture closed. Thereafter, the animals were returned to standard diet of laboratory chow and tap water.

Assessment of ulcer healing: On days 3, 7 and 10 after ulcer induction, five animals were randomly picked from each group and blood was collected from each rat via the orbital artery for blood cell count. Red and white blood cell counts were done using a method previously described by Lewis *et al*., (2006).

Each animal was then sacrificed by cervical dislocation and the stomach was removed, opened along greater curvature, rinsed with normal saline, pinned on a wax block. Transparent paper was placed over ulcer area and the ulcer area was traced out. The area of ulceration was converted to units of square millimeters using 1mm by 1mm paper grid. The rate of healing per day on day 7 was calculated as:

(Ulcer area on day 7 – ulcer area on day 3) divided by 7

The rate of healing per day on day 10 was calculated as:

(Ulcer area on day 10 - ulcer area on day 3) divided by10

Histological study

Histological slides were prepared according to the methods previously described by Ogihara and Okabe (1993). Stomachs were fixed with 10% formalin. At autopsy, small pieces of tissue, including ulcers, were embedded in paraffin and sectioned at 5µm in an automated microtome. Haematoxylin and eosin staining technique was done. Tissues were examined for inflammation, exudates, formation of granulation tissue, regeneration of the ulcerated mucosa and the different types of cells.

Statistical Analysis

Results were expressed as Mean ± SEM, the difference between the means was determined using independent sample Students t-test. The level of statistical significance was $p<0.05$.

Results

Plasma Thyroxine, Triiodotyronin and Thyroid Stimulating Hormone: After 35 days of drug treatment and surgery, thyroidectomy significantly reduced the plasma level of T_3 and T_4 ($p< 0.01$, 0.01 respectively), therefore the animals were hypothyroid. Thyroxine treatment (Sham + T_4) significantly increased the plasma level of T_3 and T_4 ($p< 0.001$, 0.001 respectively), therefore the animals were hyperthyroid. Thyroidectomy also significantly increased the level of TSH in plasma ($p< 0.01$), while thyroxine treatment decreased the TSH level ($p< 0.05$) as shown in Table 1.

Effects of altered thyroid states on Ulcer Area: Three days after ulcer induction, ulcer area was significantly higher in thyroxine-treated animals than in control and thyroidectomised animals ($p < 0.01$). However by day 7, ulcer area had reduced in both control and thyroxine-treated groups but the reduction was not significant in thyroidectomised animals. By day 10-post induction, ulcer area was reduced in all groups of animals ($p < 0.05$) (Table 2).

Table 1:
Plasma level of Thyroxine, Triiodothyronine and Thyroid Stimulating Hormone

Groups	T_3 (µg/dl)	T_4 (µg/dl)	TSH (µu/ml)
Control	3.9 ± 0.2	3.8 ± 1.0	0.96 ± 0.006
THx	1.0 ±0.1^{xx}	1.1±0.1^{xx}	2.12±0.012^{xx}
THx +T_4	3.7 ± 0.4	4.3± 0.7	0.86 ± 0.005
T_4	13.4±1.05^{xxx}	11.5±1.1^{xxx}	0.620±0.080^{x}

N= 5, value are mean ± SEM
^{X}Significant compared with control group at P < 0.05
^{XX}Significant compared with control group at P < 0.01
^{XXX}Significant compared with control group at P < 0.001

Figure 1 shows that on day 10 after ulcer induction, thyroxine treatment significantly increased the rate of healing (0.81 ± 0.02 mm^2/day) ($p < 0.01$) as compared with control (0.46 ± 0.05mm^2/day), while thyroidectomy significantly reduced the rate of healing (0.28 ± 0.05mm^2/day) ($p < 0.05$) as compared with control.

Histology Result

Three days after ulcer induction, ulcer was observed in the gastric mucosa of all groups of animal. In control animals, histology showed that there were abundant neutrophils (both intact and degenerate), congested blood vessels, swollen epithelial cells at the margin, hemorrhage and neovascularization at the serosal surface (Plate 1A and 1B).

Table 2
Ulcer Area in Animals after Ulcer Induction

Groups	Day 3 (mm^2)	Day 7 (mm^2)	Day 10 (mm^2)
Control	8.0 ± 0.4	4.8 ± 0.4^{xx}	3.4± 0.2^{xxx}
THx	8.5 ± 0.4	7.0 ± 0.5	5.7 ± 0.4^{x}
THx +T_4	13.7± 0.2^{aa}	7.8 ± 0.4^{xxx}	6.1± 0.3^{xxx}
T_4	13.5± 0.2^{aa}	7.6 ± 0.7^{xxx}	5.4± 0.2^{xxx}

N= 5, value are mean ± SEM
^{aa}Significant compared control on day 3 at p < 0.01
^{X}Significant compared with animals in same group on day 3 at p < 0.01;
^{XX}Significant compared with animals in same group on day 3 at p < 0.001;
^{XXX}Significant compared with animals in same group on day 3 at p < 0.0001

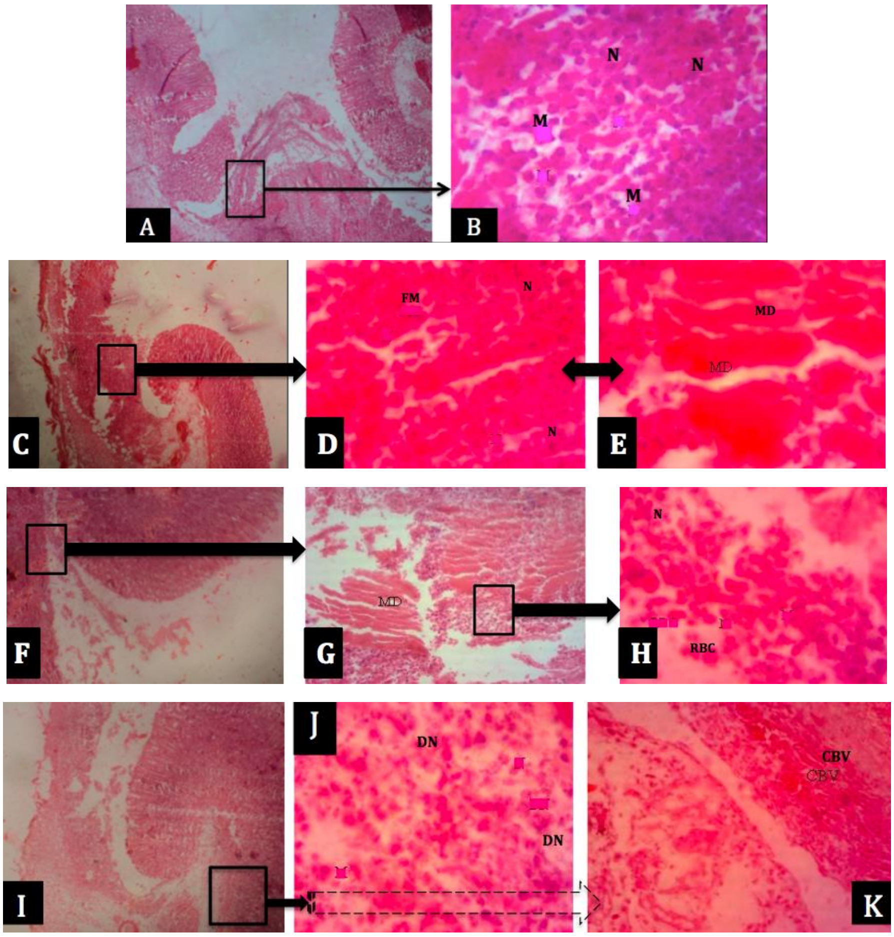
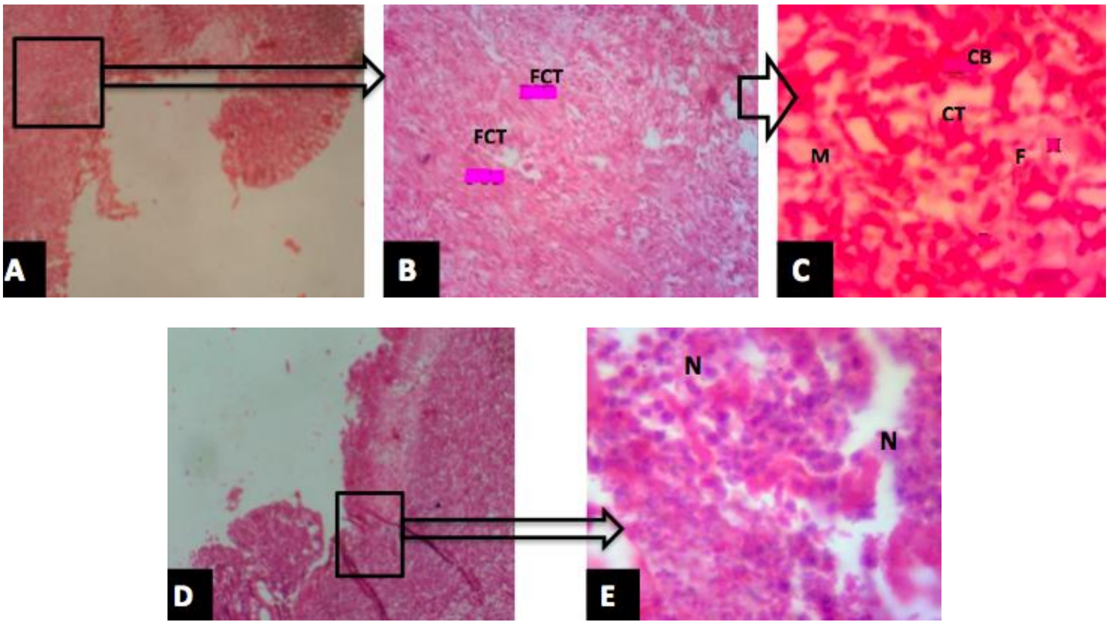


Plate 1:
Ulcerated gastric mucosa on Day 3 after ulcer induction in Control (1A, x40 and 1B, x400), thyroidectomised (1C, x40, 1D, x400 and 1E, x400) ; Thyroidectomised + T4 (1F, x40, 1G, x400 and 1H, x400) and thyroxine-treated ((1I, x40, 1J, x400 and 1K, x400) rats. *N = Neutrophil; M = Macrophage FM = Fibrin Mesh; MD = Muscle Degeneration; RBC = Red Blood Cells; DN = Degenerate neutrophil; CBV = Congested Blood Vessels*



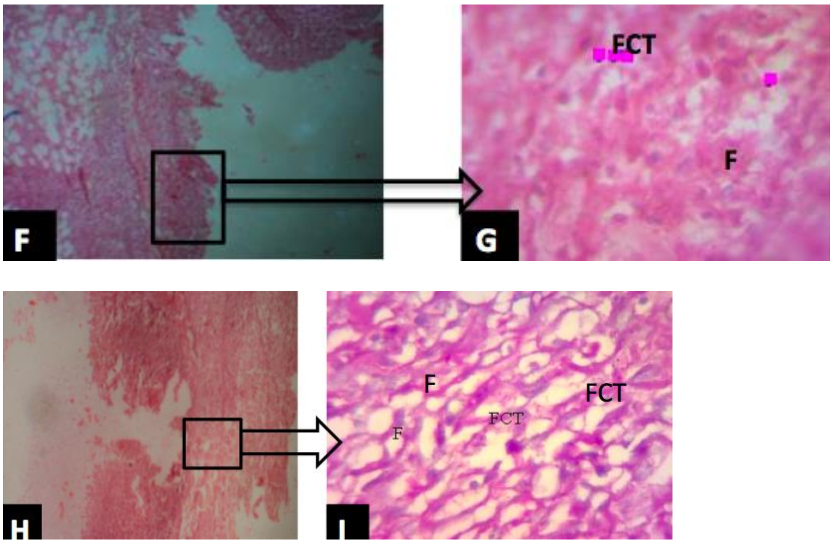


Plate 2:
Ulcerated gastric mucosa on Day 7 after ulcer induction in Control (1A, x40, 1B, x400 and 1C, x400), thyroidectomised (1D, x40, 1E, x400); Thyroidectomised + T4 (1F, x40 and1G, x400) and thyroxine-treated ((1H, x40 and 1I, x400) rats.
N = Neutrophil;
M = Macrophage
FM = Fibrin Mesh;
MD = Muscle Degeneration;
RBC = Red Blood Cells;
DN = Degenerate neutrophil;
CBV = Congested Blood Vessels,
FCT = Fibrous Connective Tissue,
F = Fibroblast,
CT = Connective Tissue

Inflammatory cells were observed to be more abundant in thyroidectomised animals (Plate 1C, 1D and 1E), while inflammatory cells were observed to be less in thyroxine treated animals as compared with thyroidectomised animals (Plate 1I, 1J and 1K). Neutrophils were also abundant in ulcer bed of thyroidectomised animals given thyroxine supplementation (Plate 1F, 1G and 1H).

By the seventh day post ulcer induction, neutrophils and macrophages were still present in ulcer bed of control animals, but not as much as on day 3. Fibroblasts were young, having plump and large nucleus with few plasma cells, fibrous connective tissues were haphazard (Plate 2A, 2B and 2C).

In thyroidectomised animals, there was purulent exudate in ulcer bed with massive neutrophils infiltrating the muscularis mucosa, abundant macrophages, fibrin trapping lymphocytic cell, abundant lymphocytic cells, few plasma cells and gut associated lymphoid tissue (nodular) with few fibroblasts (Plate 2D and 2E).

In hyperthyroid animals, few neutrophils were observed in ulcer bed, with hyperplastic epithelial cells and neovascularization at the epithelial surface. Fibrous connective tissues were present, but not well organized, blood vessels were forming (Plate 2H and 2I).

Plates 3A and 3B showed that inflammatory cells were still present in ulcer bed 10 days after ulcer induction although not massive in control animals. Fibroblasts were present and debris had not been cleared. In thyroidectomised animals, inflammatory cells were still abundant in the gastric mucosa. However submucosa layer was filled with fibrous connective tissues (Plate 3C, 3D and 3E). Result showed macrophages, fibroblasts with fibrous connective tissues in thyroidectomised animals given thyroxine supplementation by day 10 (Plate 3F. 3G and 3H), while Plates 3I. 3J and 3K showed that in thyroxine treated animals, there was marked regeneration of epithelial cells, focus of degenerate neutrophils at the epithelial junction with the gastric lumen, hyperplastic cells, and abundant fibroblasts.

Effects of thyroxine treatment and thyroidectomy on blood cell count after ulcer induction

Effect of thyroidectomy and thyroxine treatment on Packed Cell Volume (PCV) after Ulcer Induction: In control group PCV was 40.4 ± 1.0% by day 3. There was no significant change on day 7, but by day 10, PCV significantly increased (50.2 ± 0.9%) as compared with value on days 7 and 3 ($P < 0.01$).

Thyroxine treatment significantly increased packed cell volume by day 7 (44.2 ± 0.6%) ($p < 0.01$) and 10 (47.0 ± 0.5%) as compared with the value on day 3 (38.0 ± 1.6%) ($p < 0.001$). Thyroidectomy increased PCV only on day 10 (47.4 ± 0.4%) as compared with value on day 3 (43.2 ± 1.2%) ($p < 0.05$). Thyroxine replacement therapy also boosted PCV count as in the hyperthyroid animal; PCV in this group was significantly increased on days 7 ($p < 0.05$) and 10 ($p < 0.01$) respectively (Figure 2).

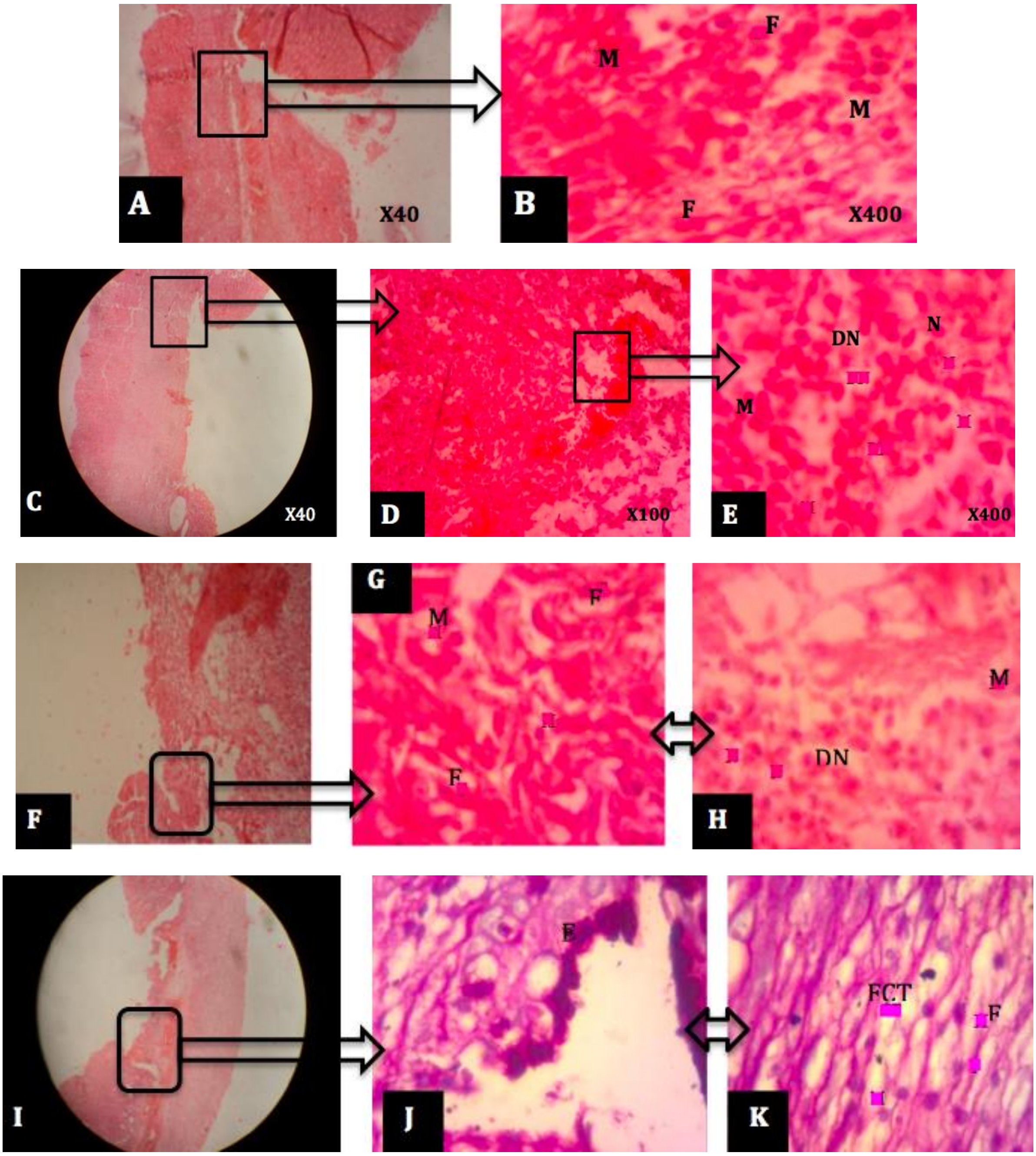


Plate 3:

Ulcerated gastric mucosa on Day 10 after ulcer induction in Control (1A, x40 and 1B, x400), thyroidectomised (1C, x40, 1D, x100 and 1E, x400) ; Thyroidectomised + T_4 (1F, x40, 1G, x400 and 1H,x400) and thyroxine-treated ((1I, x40, 1J and 1K, x400) rats.

N = Neutrophil; , M = Macrophage , FM = Fibrin Mesh; , MD = Muscle Degeneration; , RBC = Red Blood Cells; DN = Degenerate neutrophil; CBV = Congested Blood Vessels, FCT = Fibrous Connective Tissue, F = Fibroblast, CT = Connective Tissue, E-Epithelial Cell

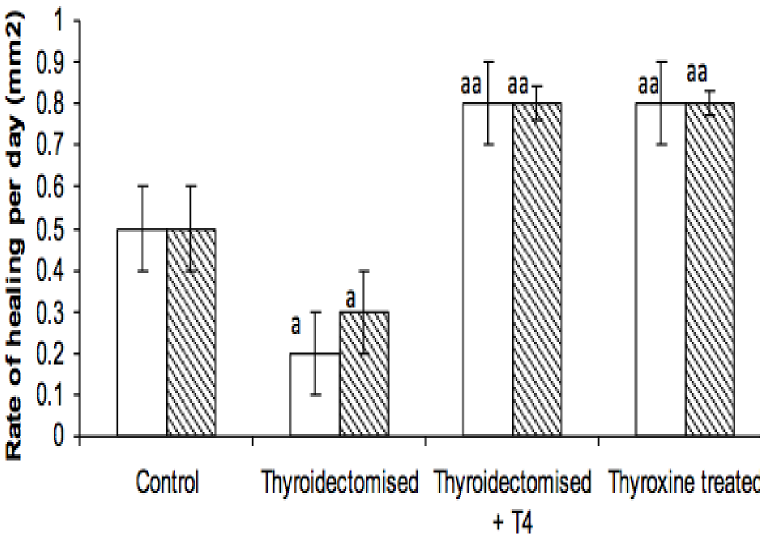


Figure 1
Rate of Healing of Gastric Ulcer in Thyroidectomised and Thyroxine Treated Animals; Each bar represents mean ± SEM of five rats per group. Clear bars = day 3, harshed bars = day 10)
a= significant compared with animals in Control group on same day at p < 0.05
aa= significant compared with animals in Control group on same day at p < 0.01)

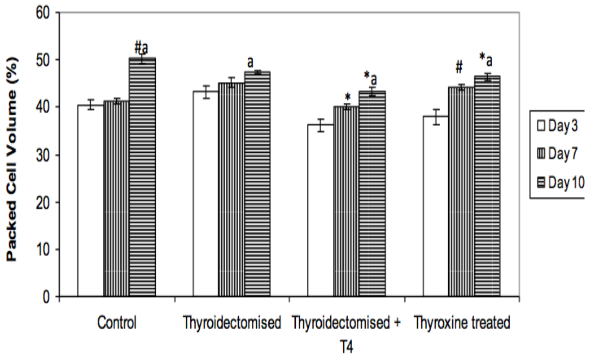


Figure 2:
Packed cell volume in animals after ulcer induction in thyroxine treated and thyroidectomised rats, n = 5, Values are mean ± SEM;
**= significant compared with animals in same group the previous day of assessment at p < 0.05*
#= significant compared with animals in same group the previous day of assessment at p < 0.01; a= significant compared with animals in same group on day 3 at p < 0.01

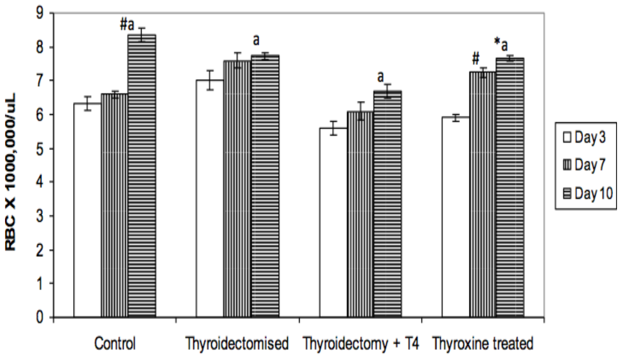


Figure 3:
Red blood cells in animals after ulcer induction in thyroxine treated and thyroidectomised rats; n = 5, Values are mean ± SEM;
**Significant compared with animals in same group the previous day of assessment at p < 0.05*
[#]Significant compared with animals in same group the previous day of assessment at p < 0.01; [a]Significant compared with animals in same group on day 3 at p < 0.01

Effect of Thyroidectomy and Thyroxine Treatment on Red Blood Cell Count (RBC) after Ulcer Induction: In control animals, RBC count was significantly increased (p< 0.01) on day 10 as compared with value on days 7 and 3 respectively. Thyroxine treatment significantly (p< 0.01) increased RBC count on days 7 and 10 respectively. Thyroidectomy also caused a significant (p< 0.01) increase in RBC count only on day 10 compared with day 3. Thyroxine replacement therapy also caused significant (p< 0.01) increase in RBC count only on day 10 compared with day 3 (Figure 3).

Effect of thyroidectomy and thyroxine treatment on White Blood Cell Count after Ulcer Induction: Thyroxine treatment significantly (p<0.01) increased white blood cells (WBC) count on day 7 after ulcer induction as compared with value on day 3, but on day 10, WBC count significantly (p < 0.01) dropped as compared with value on day 7, to a value not significantly different from the value on day on day 3. White blood cells also increased significantly (p < 0.0001) in control animals on day 7, but also dropped significantly (p< 0.01) on day 10 as compared with day 7 to a level still higher (p < 0.01) than the value on day 3. In thyroidectomised animals there was no significant increase in WBC count on day 7, but value significantly (p<0.01) increased on day 10. Thyroxine replacement therapy also significantly (p< 0.01) increased WBC count on days 7 and 10 respectively as compared with day 3 (Figure 4).

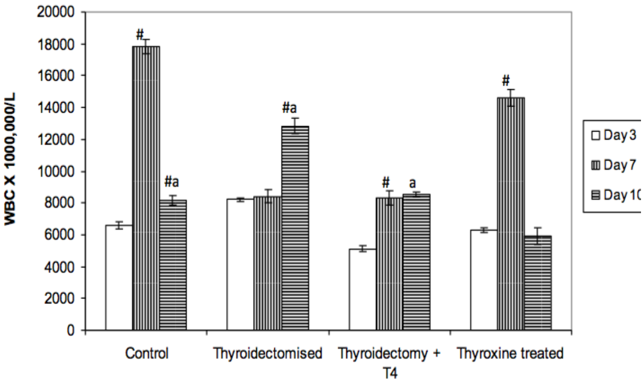


Figure 4:
White blood cells in animals after ulcer induction in thyroxine treated and thyroidectomised rats. N = 5, Values are mean ± SEM *#= significant compared with animals in same group the previous day of assessment at p < 0.0001; a= significant compared with animals in same group on day 3 at p < 0.01*

Discussion

Thyroid hormone exerts a broad range of effects on almost all systems of the body. It affects the cardiovascular (Klein and Levey, 2000), neuromuscular (Schwartz *et al*, 1997), respiratory, gastrointestinal system, growth and development (Cabello and Wrutniak, 1989). Thyroid hormones notably increase basal metabolic rate of all cells of the body except in the adult brain and spleen (Moreno *et al.*, 2002). In the gastrointestinal tract, thyroxine treatment increases basal and histamine stimulated gastric acid output and increased parietal cell mass (Adeniyi and Olowookorun, 1989, Rafsanjani *et al*, 2003). Thyroxine stimulates the biochemical process involved in cell growth and mitotic activity of cells especially, in the crypts of digestive system in rat (Adeniyi and Olowokorun, 1989), and thyroxine plays an important role in gastric development (Tseng and Johnson, 1986). On the other hand, thyroidectomy decreases gastric acid secretion and parietal cell mass (Adeniyi and Olowookorun, 1989).

Results of the present study shows that thyroxine treatment accelerated the rate of healing gastric ulcer while thyroidectomy delayed gastric ulcer healing. Results also showed the presence of ulceration in the gastric mucosa of animals on day 3 after inducing ulcer using acetic acid. Macroscopic observation of the formed ulcers on day 3 revealed that ulcer area was significantly larger in thyroxine treated animals than in control; all animals had a significant reduction in ulcer area on day 10. However, the rate of healing was significantly higher in thyroxine treated rats as compared with control animals, while thyroidectomy significantly reduced the rate of healing. This effect of thyroid hormone on ulcer healing is in line reports that thyroid hormones accelerate healing in the heart (Kranz *et al.*, 1976), skin (Safer, 2005, Lennox and Johnston, 1973) and after surgery (Erdogan *et al.*, 1999).

Ulcer healing is an active process that involves various stages: inflammatory, proliferative and scar formation. In this study, thyroid hormone treatment accelerated the healing processes observed in each stage of healing, while thyroidectomy slowed down the processes. There was faster rate of clearing of inflammatory cells in thyroxine treated animals. Fibroblast proliferation, collagen deposition and epithelial cell proliferation (proliferative phase) began earlier in hyperthyroid animals than in control animals, while thyroidectomy prolonged the inflammatory phase with less collagen synthesis - there was still massive inflammatory cells in thyroidectomised animals on day 10. This delay in healing in thyroidectomised animals corresponds with the report of Zimmermann *et al*., (2009)**.** The presence of debris and necrotic tissue slows down rate of healing (Ekmektzoglou and Zografos, 2006). Ulcer healing requires interactions between different tissues and cell types to achieve restoration of the normal mucosal architecture. Studies have indicated a pivotal role for the extracellular matrix (ECM) in wound repair (Mikami *et al.*, 1994), not only by providing the support for the regenerating cells (Domschke *et al.*, 1993), but also by creating the environment necessary for cellular interactions (Zern *et al.*, 1993). Fibrillar collagens, in particular, are important for the generation of wound strength (Shahina *et al*, 1997). Therefore the faster rate of healing observed in thyroxine treated animals might be due to the ability of thyroid hormones to increase the formation of connective tissue, which increased the strength of healing ulcer and also create an enabling environment for healing to occur. The rapid proliferation of cells observed in thyroxine treated rats might also be due to the ability of thyroxine to increase mitotic activity and stimulate growth (Adeniyi and Olowookorun, 1989). The faster rate of healing observed in thyroxine treated animals might also be due to the ability of thyroxine to increase blood flow and angiogenesis (Davis *et al.*, 2004, Davis *et al.*, 2009). The increase blood flow is important in supplying oxygen and nutrient to the healing mucosa (Tarnawski 2001, Guo *et al*., 2002). While the slower rate of healing in thyroidectomised animals might be due to decrease blood flow to the gastric mucosa. Previous studies reported that thyroidectomy decreased blood vessel density in rat brain (Schlenker *et al.*, 2008) and heart (Liu *et al.*, 2008), therefore there might be a slower rate of delivery of nutrients and growth factors to the ulcerated gastric mucosa of thyroidectomised rats. The faster rate of healing observed in thyroxine treated animals might be due to increase in metabolic activity of cells involved in healing, while thyroidectomy decreased metabolic activity of cells in the body.

Thyroxine treatment significantly increased packed cell volume and red blood cell count on days 7 and 10 as compared with day 3 after surgery and ulcer induction. This is in agreement with previous studies that thyroxine stimulates erythropoiesis via a direct, beta 2-adrenergic receptor-mediated stimulation of red cell precursors, and an indirect, erythropoietin-mediated mechanism (Sullivan and McDonald, 1992). An increase in red blood cells might result in increased delivery of oxygen to healing ulcer site, which is important for healing to take place. The increase in PCV and RBC count in thyroidectomised animals was only significant on day 10, thus a slower response of erythropoiesis. This might be as a result of low metabolic rate in the bone marrow. Low red blood cells might result in inadequate delivery of oxygen to the healing tissue, hence causing slow rate of healing. Result of this study showed that there was a significant increase in white blood cell count in control and thyroxine treated rats on day 7 as compared with day 3, but on day 7 the change in WBC in thyroidectomised animals was not significant. The increase in WBC count in control and thyroxine treated rats might be responsible for the faster rate of healing in these groups of animals when compared with the thyroidectomised animals. White blood cells are responsible for helping the body to heal. They do this by ingesting materials that need to be removed from the body. These materials include: old red blood cells, debris from body tissues and dead cells in the body. However, if the white blood cells in the body are low, they might likely be unable to remove materials from the body that could be toxic if left to remain, promoting the possibility of complications for the patient who is trying to heal. It is known that the process of tissue repair involves a biological response whereby the body's cellular defense mechanisms are recruited to the damaged area with accompanying vascular and neural responses (Mann *et al.*, 1995). Moreover, white blood cell counts have been used to monitor progress of healing in patients (Haffor, 2010). On day 10 after ulcer induction WBC significantly dropped in both control and thyroxine treated animals, showing that these cells had accomplished their functions, while on day 10, WBC count had just significantly increased in thyroidectomised animals, revealing a slower WBC response to injury in this group.

In conclusion, thyroxine accelerates gastric ulcer healing by accelerating the inflammatory and proliferative phases of healing and by increase white blood cells response during injury while thyroidectomy delays ulcer healing by slowing down these processes.

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