Thermoregulation, Heart Rate and Body Weight as Influenced by Thyroid Status and Season in the Domestic Rabbit (*Lepus cuniculus*)

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Abstract: The aim of this study was to investigate the effects of thyroid status and seasonal change in thermal environment on rectal temperature (Tr), respiratory rate (RR), heart rate (HR) and body weight (BW) in male rabbits. Thyroxine, T4 (30 µg/ kg BW /day) injected subcutaneously was used to induce hyperthyroidism and carbimazole, (CBZ) (30 mg / animal /day) administered orally, was used to induce hypothyroidism. During summer, (T4) treatment increased significantly (Tr), (RR), (HR) and decreased significantly (BW) compared with (CBZ). In all groups, (Tr) and (RR) values were higher and (BW) values were lower in summer compared to respective winter values. The group receiving (T4) had higher (Tr) in summer compared to winter. The control and (CBZ) treated group had higher and (T4) treated group had lower (HR) during winter compared to respective summer values. (T4) treatment significantly increased (HR) compared with control and (CBZ) values in summer. (T4) treated group had lower mean (BW) and (CBZ) treated group had higher mean (BW) compared to the respective control values; the mean (BW) was significantly lower with (T4) compared to the control. For all groups, the mean (BW) values were higher during winter. The findings have implications in therapy of thyroid disorders in mammals.

Key words: Rabbits · Thyroid status · Season · Thermoregulation · Heart rate · Body weight.

INTRODUCTION

Mammalian species including rabbits are exposed to variable environmental thermal loads which affect their physiological responses. Animals kept at high temperature develop mechanisms to adapt to heat stress. The mechanisms include the hormones which regulate energy metabolism which declines in heat acclimated animals [1}. Thyroid hormones play a fundamental role in obligatory and adaptive thermogenesis [2]. Experimental evidence supports an essential role for thyroid hormones in thermogensis of mammals [3-6] and they are considered as key hormones in controlling metabolic heat production in homeothermic animals [7,8].

Changes in environmental temperature stimulate alterations in thyroid stimulating hormone (TSH) secretion and in the serum concentrations of thyroid hormones and their metabolism [9, 10]. Most small mammals respond to cold exposure by augmenting thyroid mediated processes [11, 12] which increase basal metabolism and heat production [13]. Conversely, the serum levels of thyroid hormones tend to be lower during exposure of mammals to warm environments. Prior studies have reported a decrease in plasma concentrations of thyroid hormones associated with increase in ambient temperature in rats [14] and rabbits [15]. This response is considered as an adaptive mechanism to reduce metabolic heat production [1, 16]. A decrease in metabolic heat production improves the heat tolerance and survival of mammals in hot environments. Elevated ambient temperature is also associated with reduction in voluntary food intake and a decrease in mobilization of body reserve [17, 18].

The purpose of the present study was to investigate the effects of thyroid status and seasonal change in thermal environment under tropical conditions on thermoregulation, heart rate and body weight responses in the domestic rabbit. This is of particular interest as thyroid hormones are known to have marked influence on growth, thermoregulation, metabolism and reproductive functions in mammals.

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MATERIALS AND METHODS

Animals and Feeding: Thirty six adult healthy male rabbits were used in the study. The animals were subjected to thorough clinical examination and kept in the laboratory animal house of the Department of Physiology at Shambat. The initial mean body weights of rabbits were 1.22±0.02 and 1.31±0.01 Kg in summer and winter, respectively. In both seasons, the animals were kept for an adaptation period of 2 weeks; this was followed by an experimental period of 25 days. Animals were fed fresh alfalfa (CP: 162.7 g/kg; ME: 7.1 MJ/kg) and sorghum grains (CP: 132.3 g/Kg; ME:14.4 MJ/Kg) ad libitum and allowed free access to tap water. The same experimental protocol was performed during summer (June-July, 2006) and winter (December, 2006-January, 2007).

Induction of Hyper- and Hypothyroidism: The results obtained from a series of investigations were utilized in determining the appropriate dose for induction of hyperthyroidism by administration of thyroxine (T4) and hypothyroidism using carbimazole (CBZ). In each season,18 rabbits were randomly assigned to three groups of 6 animals each. Group (A)served as control; group (B) animals received a daily dose of sodium L-thyroxine (T4, Eltroxin, Glaxo,Wellcome., Germany) 30 µg/kg BW/day injected subcutaneously to induce hyperthyroidism; group (C) animals received daily an oral dose of the antithyroid drug carbimazole (CBZ, Neomercazole, Roche products Ltd., England) 30 mg/ animal/day administered orally to induce hypothyroidism.

Measurements of Rectal Temperature (Tr), Respiration Rate (RR), Heart Rate (HR) and Body Weight (BW): During the experimental period, the representative body-core temperature of rabbits, rectal temperature (T_r) was measured by a digital clinical thermometer (Hartman–United Kingdom). The tip of the thermometer was inserted to a depth of approximately 4 cm into the rectum and (T_r) was measured with an accuracy of ±0.1°C. The respiratory rate (RR) (was measured by visually counting the flank movements for one minute using a stopwatch, the measurement was done when the animal was sitting quietly and breathing regularly. The heart rate (HR) was obtained by monitoring the heart sounds for one minute using a stethoscope. The measurements of (Tr), (RR) and (HR) were done every 3 days at 8.00 a.m. The body weight (BW) of the animals was measured to the nearest ±1.0 g using a standard balance (Every-United Kingdom). The (BW) was measured on days 13 and 25 at 9.00 a.m.

Climatic Conditions: The data for climatic conditions prevailing during the experimental period in summer and winter were obtained from the local meteorological station. The mean ambient temperature, (Ta) during summer was 33.96±1.07 °C, mean relative humidity, (RH) was 32.0±4.43%. During winter, mean (Ta) was 21.78 ± 2.91°C; (RH) was 28.72 ± 5.17%.

Statistical Analysis: The experimental data were subjected to standard methods of statistical analysis using statistical analysis system [19]. Analysis of variance (ANOVA) test as factorial completely randomized design was used to examine the effect of the thyroid status and seasonal change in thermal environment on thermoregulation, (HR) and (BW) of rabbits. The experimental data are expressed as mean values ±standard deviation (SD). The separation of means was done by Duncan Multiple Range Test.

RESULTS

Rectal Temperature (T_r): During summer (Fig. 1), the initial (T_r) values ranged from 39.9 to 40.2 °C. The general pattern indicates that the group of rabbits receiving (T4) had higher and the group receiving (CBZ) had lower (T_r) values compared to the control group. The treated groups had significantly higher (T_r) values compared with control group at day 3 (P< 0.05) and day 6 (P< 0.01). The group of rabbits receiving (T4) had significantly higher (T_r) values compared with the control at day 9 (P< 0.05) and day 12 (P< 0.01). At days 21 and 24, the group receiving (T4) had higher (P< 0.05) (T_r) values compared to respective values obtained for the group of rabbits receiving (CBZ).

During winter (Fig. 2), the initial values of (Tr) ranged from 39.1 to 39.2 °C. For all groups, there was gradual increase in (T_r) during the experimental period. However, the elevation was more pronounced for the group of rabbits receiving (T4). The (T4) group had higher (T_r) compared with the control at day 3 (P< 0.05), day 12 (P< 0.01) and days 21 and 24 (P< 0.05). The group receiving (CBZ) had lower (P< 0.05) (T_r) values compared to respective values obtained for the group of rabbits receiving (T4) at days 9 and 18.

Fig. 3 shows the effects of thyroid status and season on (T_r) at day 24. For all experimental groups, the mean values of (Tr) were higher during summer compared to the respective winter values. The group receiving (T4) had higher (P< 0.05) (T_r) in summer compared with winter value.
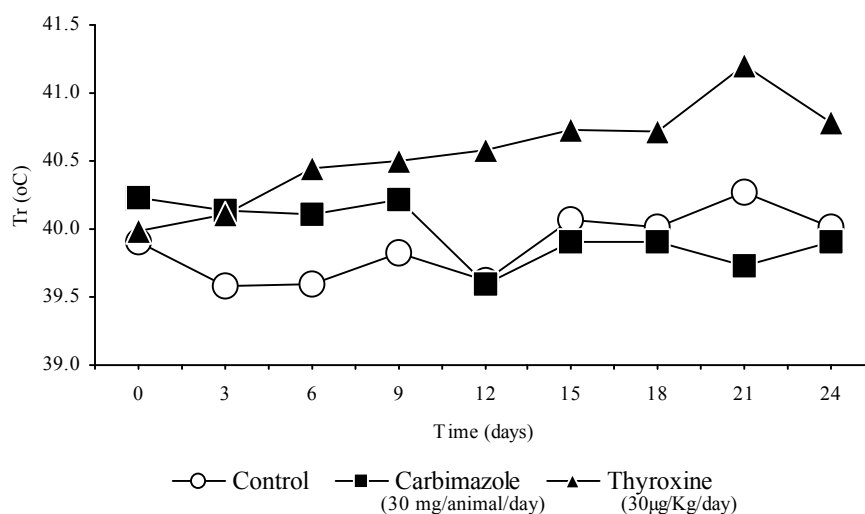
Fig. 1: Effect of thyroid status on rectal temperature (Tr) in male rabbits during summer
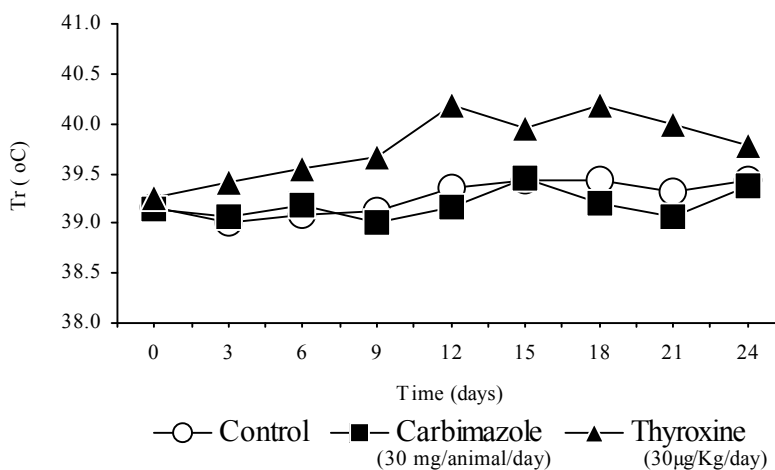

Fig. 2: Effect of thyroid status on rectal temperature (Tr) in male rabbits during winter
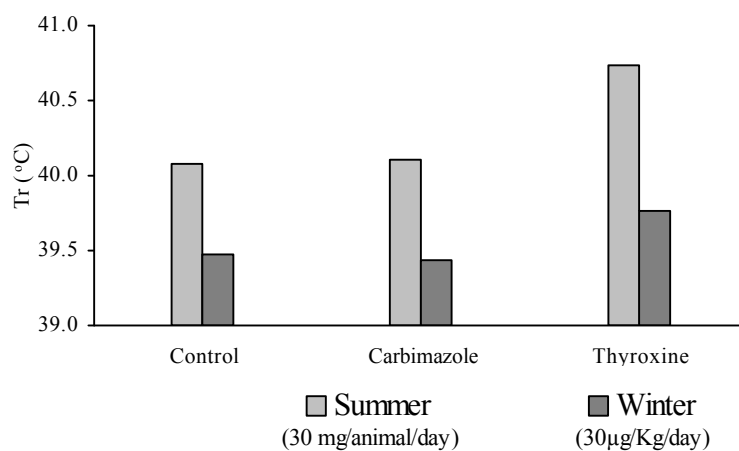

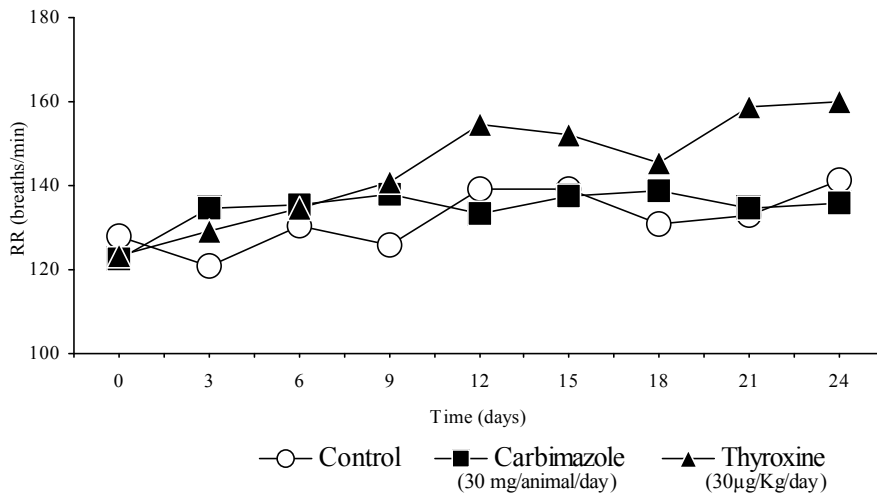Fig. 3: Effects of thyroid status and season on rectal temperature (Tr) in male rabbits (Day 24)

Fig. 4: Effect of thyroid status on respiratory rate (RR) in male rabbits during summer
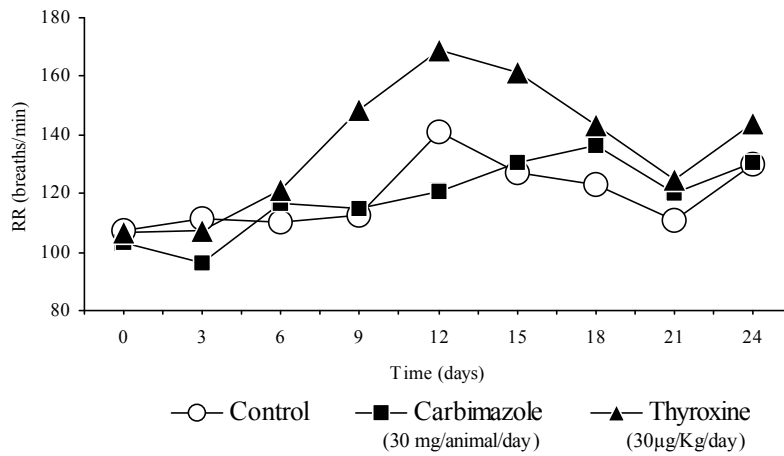
Fig. 5: Effect of thyroid status on respiratory rate (RR) in male rabbits during winter
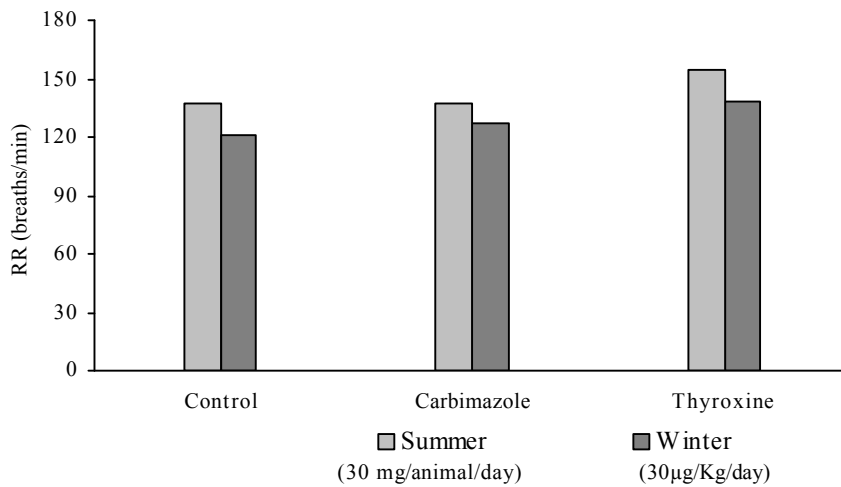
Fig. 6: Effects of thyroid status and season on respiratory rate (RR) in male rabbits (Day 24)
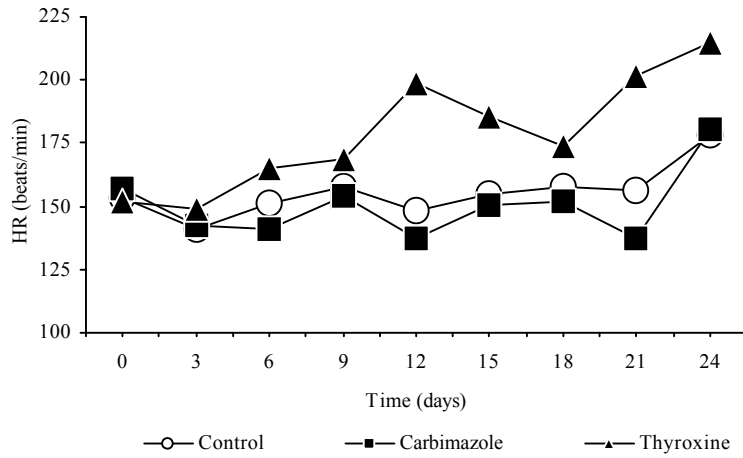
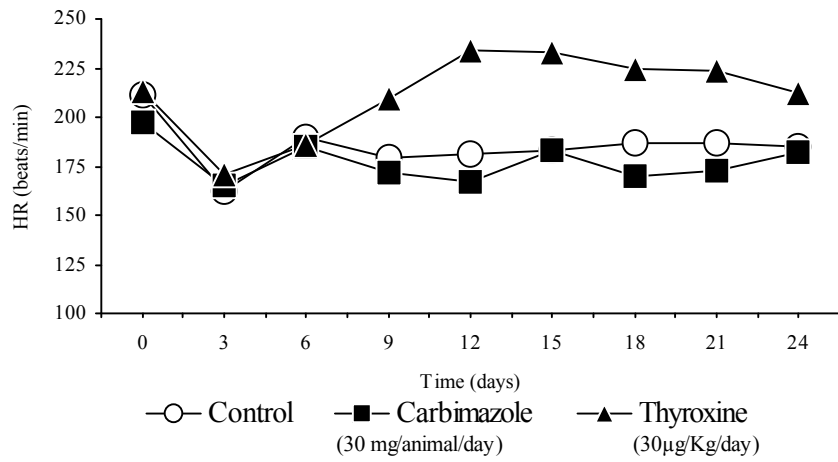Fig. 7: Effect of thyroid status on heart rate (HR) in male rabbits during summer

Fig. 8: Effect of thyroid status on heart rate (HR) in male rabbits during winter
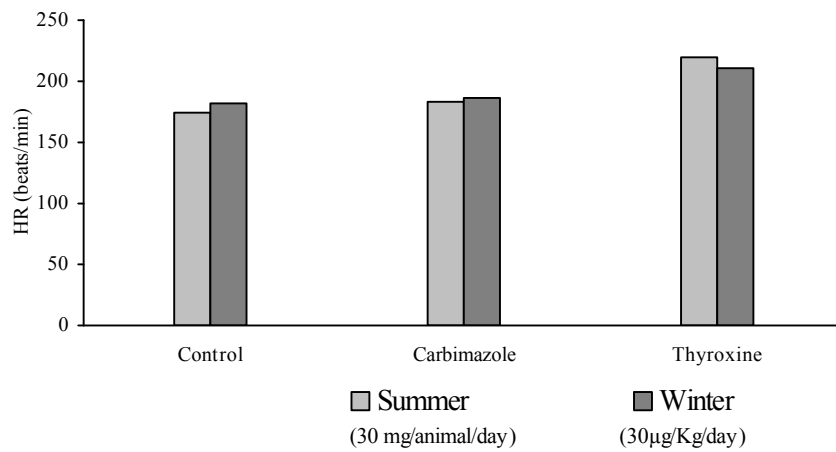
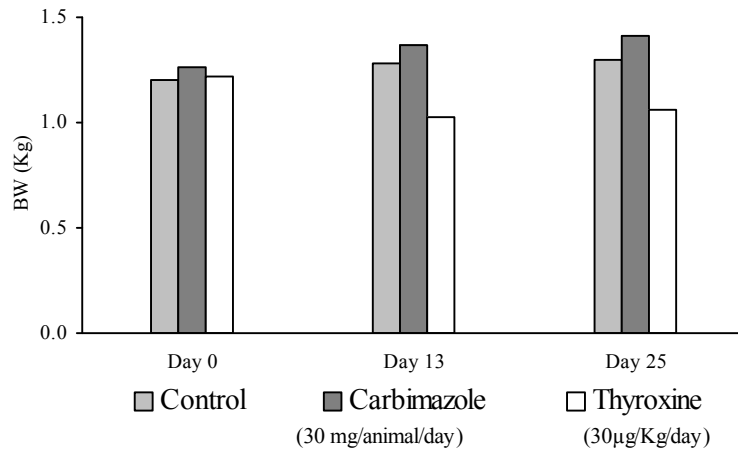Fig. 9: Effects of thyroid status and season on heart rate (HR) in male rabbits (Day 24)

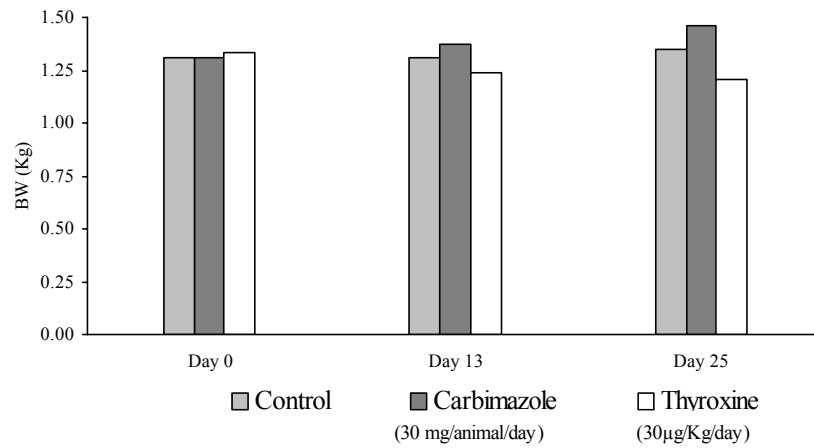Fig. 10: Effect of thyroid status on the mean body weight (BW) in male rabbits during summer

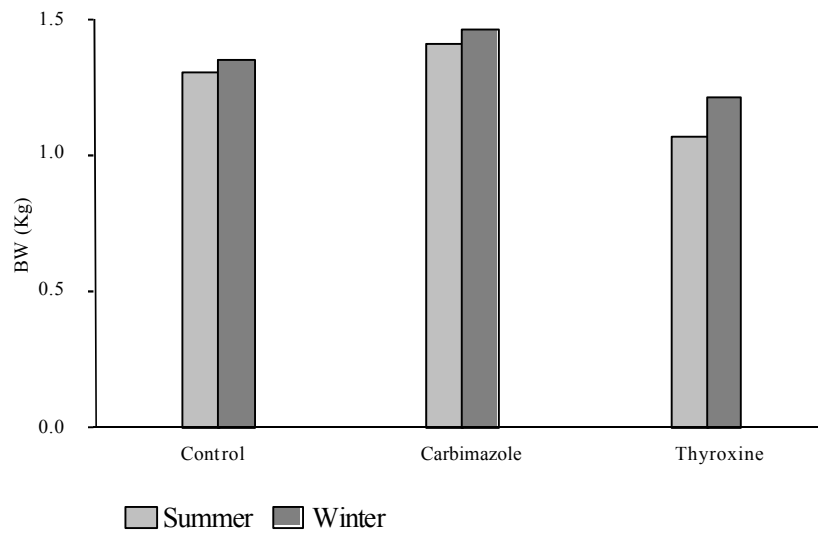Fig. 11: Effect of thyroid status on the mean body weight (BW) in male rabbits during winter

Fig. 12: Effects of thyroid status and season on mean body weight (BW) of male rabbits (Day 24)

Respiration Rate (RR): During summer (Fig. 4), the initial values of (RR) ranged from 122 to 128 breaths /min. For all groups, there was gradual increase in (RR) during the experimental period. However, the increase was more pronounced for the group receiving (T4). The treated groups had higher (P< 0.05) (RR) values compared with the control at day 9. At day 24, the (T4) treated group had higher (P< 0.05) (RR) value compared to the group receiving (CBZ).

During winter (Fig. 5), the initial values of (RR) range was 103 -107 breaths /min. The control group and the group receiving (T4) showed progressive increase in (RR) until day 12. Thereafter, both groups showed decline in RR until day 21. The group receiving (CBZ) showed progressive increase in (RR) until day 18 and subsequently declined. At day 9, the group of rabbits receiving (T4) had higher (P< 0.01) (RR) values compared with the (CBZ) treated and control group. At day 12, the (T4) treated group had higher (P< 0.05) (RR) value compared with the group receiving (CBZ). The (T4) treated group had higher (P< 0.05) (RR) value compared with the control at day 15.

The mean values of (RR) of control and treated groups were higher during summer compared with the respective winter values (Fig. 6).

Heart Rate (HR): During summer (Fig.7), the initial values of (HR) were almost similar for experimental groups. All groups maintained low (HR) values until day 9. Thereafter, the control and (CBZ) group showed low but fluctuating values of (HR). The (T4) group showed an increase in (HR) at day 12, followed by a decline until day 18 and then progressive increase until the end of the experimental period. At day 6, the (T4) group had higher (P< 0.01) (HR) value compared with (CBZ) treated group. The group of rabbits receiving (T4) had significantly higher /HR) value compared to the control and (CBZ) group at days 12, 15, 21 and 24 (P< 0.001, P< 0.05, P< 0.001 and P< 0.01, respectively).

During winter (Fig. 8), the (HR) of the experimental groups decreased from an initial similar value of about 200 beats /min to a low value of 165 beats/min at day 3 and then an increase to 185 beats/min at day 6. Thereafter, the control and (CBZ) group maintained lower values compared to the (T4) group until the end of the experimental period. The (T4) group had significantly higher (HR) values compared to the respective values of the control and (CBZ) group at days 9, 12, 15, 18, 21 and 24 (P< 0.01, P< 0.001, P< 0.001, P< 0.01, P< 0.01 and P< 0.05, respectively).

Fig. 9 shows that at day 24, the control and (CBZ) group had slightly higher (HR) values during winter compared to the respective summer values. However, for the (T4) group, (HR) was higher during summer.

Body Weight (BW): Generally, the (T4) group had lower mean (BW) and the (CBZ) group had higher mean (BW) compared to the respective control group values. During summer (Fig. 10), the (T4) group of rabbits had lower mean (BW) at days 13 (P< 0.001) and 25 (P< 0.05). However, during winter (Fig. 11) there was no significant difference between the mean (BW) values of control and treated groups of rabbits. Fig. 12 shows that generally all experimental groups had higher mean (BW) values during winter compared with respective summer values.

DISCUSSION

The results indicate that the changes in thyroid status produced by administration of (T4) and (CBZ) and the season related thermal load influenced thermoregulation in rabbits. The higher rectal temperature (T_r) of (T4) treated rabbits (Figs.1,2) is clearly related to the calorigenic effect of exogenous (T4) which maintains a critical role in the control of body temperature by stimulation of thermogenesis and regulation of cellular metabolism [20].Thyroid hormones are involved in thermoregulation by increasing oxygen consumption and internal heat production [21]. Also thyroid hormones increase energy release by activating Na^+/K^+-ATPase [22] and (ATP) turnover, which lead to an increase in body temperature. The decrease in (T_r) of the group of rabbits receiving (CBZ) (Figs.1 and 2) is related to decrease in the levels of thyroid hormones and consequent reduction in energy expenditure. It has been reported [23] that oral administration of methimazole was associated with lowering of concentration of (T4) and increased TSH in rats. Lack of thyroid hormones reduces energy expenditure which leads to a marked decrease in cold tolerance of humans [6].

The higher (Tr) values reported for the control and treated groups in summer are attributed to decrease in thermal gradient and consequent decline in sensible heat loss at high environmental temperature during summer. The current result is in agreement with previous findings in rabbits [24] and pigs [25, 26. For the (T4) treated group, the significantly higher (T_r) in summer compared to winter value (Fig. 3) is attributed to the additive effects of elevated thermal load and the calorigenic effect of (T4). In studies performed on rabbits [15] and pigs [1], exposure

to high ambient temperature was associated with an increase in (Tr) despite reduction in food intake and the rate of secretion of thyroid hormones. However, the present results indicate that the seasonal change in thermal environment had no significant effect on (T_r) in (CBZ) treated rabbits. This could be related to slow responses of rabbits to (CBZ) dose; (CBZ) inhibits thyroid hormone synthesis, but it does not affect deiodinase activity [27,28]. Since the synthesis rather than the release of hormones is affected, the onest of the effect of (CBZ) is slow, often requiring 3-4 weeks before stores of (T4) are depleted [29].

The administration of (T4) to rabbits resulted in higher (RR) values in summer and winter (Figs. 4 and 5); administration of (CBZ) had no effect on summer values, but the winter value was slightly higher compared to the respective untreated control value (Figs. 4 and 5). The higher value of (RR) obtained with (T4) could be attributed to thermally stimulated increase in pulmonary ventilation that augmented evaporative heat loss. In rabbits exposed to high ambient temperature, increase in metabolic heat production led to an increase in respiratory evaporative water loss by panting [24].

The higher (RR) values in summer compared to the respective winter values are related to increase in ambient temperature which was associated with increase in body temperature (Fig. 6). The rabbits increased respiratory water loss by increasing (RR) in order to dissipate the internal heat. Heat stress is usually associated with a marked increase in (RR) in rabbits [15, 24]. The higher (RR) values of rabbits in summer compared to winter values in (T4) treated animals may be attributed to combined effects of (T4) and ambient temperature on body core temperature which stimulated increase in (RR) during summer. For the group of rabbits receiving (CBZ), the (RR) was higher during summer compared to winter; this is likely related to the effect of high ambient temperature during summer despite decline in thyroid gland activity.

The increase in (HR) of rabbits with (T4) treatment in summer (Fig. 7) and winter (Fig. 8) is consistent with the physiological effects of thyroid hormones on cardiovascular system which include lowering of systemic vascular resistance, increase of cardiac output and increase in blood volume [30]. It has been indicated [31] that the increase in (HR) in hyperthyroidism resembles a state of increased adrenergic activity, despite normal or low serum concentrations of catecholamine. The thyroid hormone (T3) increases cardiac output by affecting tissue oxygen consumption [32]. The haemodynamic changes typical of hypothyroidism are opposite to those of

hyperthyroidism [33]. Many studies reported that hyperthyroidism shows a hyperdynamic circulation with increased cardiac output, heart rate, pulse pressure and blood pressure and decreased vascular peripheral resistance, whereas the hypothyroid state is associated with low cardiac output, heart rate, pulse pressure and blood pressure and elevated vascular peripheral resistance [33-35]. Hypothyroidism was associated with a decrease in (HR) in rabbits and rats [36] while administration of (T3) increased the heart rate in rats [37].

The (HR) of the control and (CBZ) treated groups was higher during winter compared with the respective summer values (Fig. 9). This response is related to elevation of metabolic demands of rabbits on exposure to the cold environment coupled with a relative increase in the level of thyroid hormones which enhance the responses of the heart to catecholamines.

Rabbits receiving (T4) had higher (HR) in summer than winter (Fig. 9). Exogenous (T4) and elevated ambient temperature during summer led to an increase in body core temperature and moderate hyperthermia. Dissipation of surplus internal heat necessitated modulation in cardiovascular responses that included peripheral vasodilatation and increase in (HR).

The metabolic changes associated with alteration in thyroid status of rabbits influenced the mean body weight (BW) of rabbits. During summer, the mean (BW) of rabbits receiving (T4) was lower and that of (CBZ) treated group was higher compared with control group (Fig. 10). During winter, a similar pattern indicated that the mean (BW) of the group receiving (T4) was lower and that of (CBZ) treated group was higher compared with the control group (Fig. 11). The decrease in mean (BW) associated with exogenous (T4) is related to an increase in metabolic rate and negative nitrogen balance associated with stimulation of protein catabolism. In rats, researchers demonstrated that thyroid hormones caused reduction in (BW) via an increase in metabolic rate [38,39]. Previous studies [29] indicated that hyperthyroidism in humans led to an increase in basal metabolic rate and negative nitrogen balance and hypothyroidism was associated with decrease in (BMR) and slightly positive nitrogen balance.

The mean (BW) of rabbits receiving (T4) was markedly lower in summer compared with the respective winter value (Fig. 12). This could be attributed to the increase in body core temperature which causes a decrease in food intake. In rabbits exposed to hot environment, decrease in (BW) was associated with decrease in food intake [40]. During the experimental period, the (CBZ) treated rabbits had slightly higher gain

in (BW) during summer compared with the gain in winter. This could be a response to decrease in level of thyroid hormones related to (CBZ) treatment and exposure to hot environment during summer which led to a decrease in metabolic rate and heat dissipation to the environment.

CONCLUSION

The studies indicate that in rabbits the chemical regulation of thyroid can be induced by administration of T4 and CBZ. The alterations in thyroid status are associated with changes in thermoregulation, heart rate and body weight and the responses are modulated by thermal environment. The results have implications in monitoring therapy of thyroid disorders in mammals.

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