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Catecholamines potentiate the effect of thyroid hormone on intestinal absorption of glucose in the rat

SB Olaleye and RA Elegbe
Department of Physiology, College of Medicine, University of Ibadan, Ibadan, Nigeria.

Summary
The study is to investigate the role of catecholamines on the increased absorption of glucose from the gut by thyroxine, the effect of graded doses of adrenaline and noradrenaline on glucose absorption was studied in euthyroid (ET), hyperthyroid (TH-) and hypothyroid rats (Thx). Glucose absorption was deduced *in vivo* from intestinal segment perfused with Kreb's bicarbonate solution containing 5.6mM glucose and *in vitro* using the everted sac technique. *In vivo*, basal glucose absorption was significantly increased in the hyperthyroid and decreased in the hypothyroid rats (1.97 ± 0.19mM/g, P<0.01, and 0.92 ± 0.10 mM/g, p<0.05 respectively) when compared with the euthyroid group (1.34 ± 0.15mM/g). Adrenaline (20mg/dl – 80mg/dl) increased glucose absorption in a dose dependent manner in all the groups. However, the responsiveness of the gut glucose absorption to adrenaline (as evidenced by the dose producing half- maximal absorption or ED_{50}) was reduced by thyroidectomy (ED_{50} = 26.09 mg/100ml) and increased by chronic thyroxine treatment (ED_{50} = 11.13mg/100ml) The ED_{50} in the euthyroid animals was 14.6mg/100ml. *In vitro*, glucose absorption from the isolated segments in both Thx and TH- rats were significantly reduced (P<0.05). Incubation of the isolated intestinal segments with graded doses of adrenaline caused a significant and dose related increases in glucose absorption. However thyroidectomy shifted the dose-response curve for glucose uptake from the isolated intestinal sac incubated with adrenaline to the right of the curve for euthyroid rats. It is concluded that catecholamines may play a role in the increase in intestinal absorption by thyroid hormones.

Keywords: *Thyroid hormone, thyroidectomy, adrenaline, noradrenaline, catecholamine, glucose absortion, intestine*

Résumé
Le role des catécholamines sur l'augmentation de l'absorption du glucose dans l intestin par la tyroxine a été évalué. L'effect des doses titrées d'adrenaline et nonadrenaline sur l'absorption du glucose était étudié dans l'euthyroide(ET), hyperthryroide(TH) et l'hypothyroide (Thx) des rats. L'absorption du glucose était déduite *in vivo* sur des segments intestinal perfusés avec une solution de bicarbonade de Krebs contenant 5.6mM de glucose et *in vitro* utilisant la technique du sac everté. *In vivo*, l'absorption basal du glucose était significativement élevée dans l' hyperthyroide et décrut dans l'hypothyroide du rat(1.94 +-0.19mM/kg, P<0.01 ; 0.92+-0.01mM/kg, P<0.05 respectivement) quand comparé avec le groupe d'eurothyroide(1.34+-0.15mM/kg). L'adrenaline (20-80μg/dl) augmentait l'absorption du glucose en maniére de dose dependente a tous les groupes. Cependant, le taux du glucose a l'adrenaline était réduit par la thyrodectomie(DE_{50}= 26.09 μg/100 ml) et augmentait avec un traitement chronique de tyroxine(DE_{50}= 11.13μg/100ml).La dose effective a 50(DE50) au groupe d'eurothyroide était de 14.6μg/100ml). *In vitro*, l'absorption du glucose sur les segments isolés chez les Thx, et le TH étaient significativement réduite (P<0.05). L'incubation des egments a des solutions titrees d adrenaline causait des augmentation significative d'absorption du glucose. Cependant , la thyrodectomie baissait la courbe concentration du glucose –dose d'adrenaline vers la droite sur les segments incubés aux rats d'eurothyroide

Introduction

The relationship between the thyroid gland and gastrointestinal functions has been recognized for long. Thus, thyroid hormones have been reported to influence a number of gastrointestinal functions [1]. An impairment of sugar handling by the gut is a common feature of hyperthyroidism [2]. It is generally agreed that thyroid hormones exert a stimulating effect on intestinal sugar and fluid absorption [3 – 6]. A survey of available literature reveals that there is a dearth of information on the mechanisms of thyroid hormone actions on the gut. The catecholamines have been found to have synergistic actions with thyroid hormones in a number of organs such as the brain [7] and adipose tissue [8]. Other studies have shown that the actions of thyroid hormones in these organs are Jediated by catecholamines. [4]. The present study was designed to investigate the role of catecholamines in the increased intestinal glucose absorption by thyroxine.

Materials and methods

Animals:

Adult male albino rats of the Wistar strain (120-160g) were obtained from the small animal house, College of Medicine, University of Ibadan, Nigeria and were divided into three groups. Animals in the first group were sham operated by making a small incision on the neck under light ether anaesthesia, exposing the thyroid gland under aseptic conditions. These animals were used as euthyroid (ET) controls. A second group was surgically thyroidectomised (Thx) under ether anaesthesia with care taken to spare the parathyroid. The last group (TH↑) was sham operated and thereafter received a daily dose of thyroxine (Levothyroxine

Correspondence: Dr. S.B. Olaleye, Department of Physiology, College of Medicine, University of Ibadan, Ibadan,Nigeria. Email. olaleye_ui@hotmail.com

sodium, Evans medical Ltd, England) (10ug/kg/day, p.o.). Water and food were allowed *ad libitum*. The animals were weighed on weekly basis. Thyroid status was confirmed by the radioimmunoassay assays five weeks postoperative for Serum tri-iodothyronine (T_3) and Serum thyroxine (T_4). Basal oxygen consumption was also determined in each group of animals as previously described by Bolarinwa and Olaleye [9]

Five weeks post-operative, intestinal glucose absorption was studied in the three groups using both in *vivo* and in *vitro* techniques as follows:

Intestinal absorption in vivo

Surgical preparation of animal: The method of Levinson and Englert [10] was essentially followed. After an overnight fast, each animal was anaesthetized using urethane (0.6ml of 25% W/V of urethane per 100g body weight). The trachea was exposed and cannulated. A midline incision was then made into the abdominal wall. The intestine was gently pushed out without much massage and two intestinal segments (15-20 cm long) were identified for consistency, it was always ensured that the first segment was just distal to the ligament of Treitz while the other was just proximal to the ileocecal junction. The segments were opened at both ends and washed by syringe irrigation with Kreb's bicarbonate solution, the excess fluid being removed by gently forcing air under low pressure through the segments. The unopened end of each segment was then ligated. Each segment was thereafter filled with 4ml of the Kreb's bicarbonate solution containing 5.6mM glucose and 2g/l polyethylene glycol (PEG) after which the ends were ligated. The segments were replaced in the abdominal cavity, which was closed with a clamp. The temperature of each animal was maintained with a heating lamp.

Collection of samples: Each study lasted one hour. At the end of which the two segments were removed from each animal. Each segment was drained of its contents and then weighed. The samples were then analyzed for glucose

Effect of drugs: Six animals were studied in each group without injecting any drug prior to ligation of the segments. Another set of six (6) animals in each group were studied for the effect of the following drugs in equal volumes of 0.2ml): Normal saline (0.2ml), Adrenaline (0.1mg/kg), Noradrenaline (0.1mg/kg), Adrenaline (0.1mg/kg) + Prazocin (0.05mg/kg), Adrenaline (0.1mg/kg) + propanolol (0.05mg/kg).

Calculation of net glucose absorption: Glucose absorption per hour was calculated as the measured disappearance of glucose per hour from the intestinal lumen as follows:

$$\text{Glucose absorption (mMl/hr/gm wet tissue)} = \frac{[\text{Sugar initial}] - [\text{Sugar final}]}{(\text{PEG ratio}) \times \text{tissue wt.}}$$

In vitro intestinal transport

Preparation of sac: The everted intestinal sac technique originally described by Wilson and Wiseman [11] was used. After an overnight fast, animals were killed by ether anaesthesia. The abdomen was opened and the whole of the small intestine taken out and flushed with Krebs's bicarbonate solution. Polyethylene tubing, closed at one end, was inserted and tied at one end of the intestinal loop. Through this, the gut was everted and placed in Krebs's bicarbonate solution. Four segments (5-8cm) were prepared for each animal, one of the ends being tied with a thread and the other ends encircled by a ligature of thread. 0.5ml of Krebs's bicarbonate solution and a bubble of 95% 5% O_2/CO_2 mixture was introduced into each sac through a syringe and the loose ligature tied. The sac was then placed in the test tube containing 10ml of Krebs's bicarbonate solution kept at 37°C and aerated continuously.

After 30 minutes of incubation, the sacs were removed and the contents emptied for the determination of glucose and sodium concentrations.

Effect of drugs: Sacs were prepared as described above but in addition to 0.5ml of Krebs's bicarbonate solution, saline solution containing 0, 10^{-6}M, 10^{-5}M and 10^{-4}M of Adrenaline, in the presence or absence of propranolol and prazocin were added in volumes of 0.1ml

Calculation of net glucose fluxes: Glucose fluxes were calculated by the following measurements according to the method of Varma and Banerjeee [12] as modified by Adeniyi and Olowookorun [13] as follows:

GGU -Gut Glucose Uptake = MGT –SGT

Where,

GGU = Gut Glucose Uptake
SGT = Serosal Glucose Transfer =SF – I
MGT = Mucosal Glucose Transfer =I - MF
I = Initial concentration of glucose in Krebs's solution
SF = Final concentration of glucose in serosal fluid
MF = Final concentration of glucose in mucosal fluid

Glucose estimation:- this was determined by the glucose oxidase method of Trinder [14]

Results

In vivo studies

Body weight changes and thyroid hormone levels

Significant reductions in the growth rate were observed in both the thyroidectomised and thyroxine treated rats from week 3. There were also significant reductions in the percentage weight gain in thyroidectomised (29.05 ± 4.13; $p = 0.00095$) and thyroxine treated rats (36.02 ± 5.60; $p = 0.0032$) when compared with the sham-operated controls (57.00 ± 5.61) as shown in Table 1. The initial, final and percentage change in basal oxygen consumption in the animal groups are also shown in Table 1.

Table 1: Thyroid function in rats before and five weeks after thyroidectomy and/or thyroxine treatment

Group	Body weight (g)			Oxygen consumption (ng/g/hr)			Thyroid hormones*	
	Initial	Final	%change	Initial	Final	% change	T_3	T_4
ET	82.64 ± 2.25	129.65 ± 6.15	57.00 ± 0.04	0.76 ± 0.04	0.79±0.05	+3.95	3.85 ± 0.18	3.78 ± 0.96
Thx	85.14 ± 3.24	109.87 ± 5.42	29.05 ± 4.13**	0.78 ± 0.04	0.47 ± 0.03**	-39.74	0. 97 ± 0.08	1.05 ± 0.07*
Thx + T4	83.42 ± 2.74	116.16 ± 4.15	39.25 ± 5.60**	0.78 ± 0.04	1.05 ± 0.08**	+34.62	3.65 ± 0.35	4.25 ± 0.71
TH↑	80.43 ± 4.15	109.40 ± 7.96	36.02 ± 5.60**	0.76 ± 0.05	2.98 ± 0.23**	+292.10	13.45 ± 1.02	11.50±1.08**

*$P < 0.005$; **$P < 0.001$;

Blood samples of rats from each group were collected 5 weeks after thyroxine treatment and/or thyroidectomy and the samples analysed for serum T3 and T4 using the IMMUNOCHEM™ R.I.A. Kit.

Table 2: Basal glucose absorption (*in-vivo*) in euthyroid (ET), untrteated hypothyroid (Thx) thyroxine treated hypothyroid (Thx + T4) and hyperthyroid (TH ↑) rats. Values are mean ± S.E.M of 16 animals in each group

Group	PEG ratioa	Conc. of glucose in fluid before incubation (mM)	Conc. of glucose in fluid after incubation (mM)	Net weight of intestinal portion used (g)	Net absorption (mM/g/hr)
ET	0.968 ± 0.003	5.58 ± 0.02	4.63 ± 0.09	0.72 ± 0.02	1.34 ± 0.15
Thx	0.955 ± 0.002	5.58 ± 0.02	4.87 ± 0.10	0.70 ± 0.02	0.92 ± 0.10*
Thx + T4	0.970 ± 0.003	5.58 ± 0.02	4.52 ± 0.10	0.71 ± 0.02	1.13 ± 0.12
Th↑	0.973 ± 0.004	5.58 ± 0.02	4.11 ± 0.13	0.76 ± 0.02	1.97 ± 0.19**

*$P<0.05$; **$P<0.02$;

PEG ratio were not significantly affected in all the test groups. Thus, the ratio was neglected in the final computation of the net glucose absorption.

To determine whether the observed changes in body weight and oxygen consumption were due to altered levels of thyroid hormones, serum T_3 and T_4 concentrations were measured in pooled blood samples of ET, Thx, Thx + T_4, and TH↑ rats by RIA technique. The results (Table 1) show that chronic thyroxine treatment in rats for 35 days increased T_3 and T_4 levels. There were also significant changes in the thyroid hormone levels of the Thx animals when compared with the control.

Glucose absorption from ligated intestinal segments- effects of thyroxine and thyroidectomy.

The effects of thyroid hormone on basal glucose absorption from the ileal and jejunal segments of the intestine of rat are presented in Table 2. The basal rate of glucose absorption in euthyroid rats was 1.34 ± 0.15mM/g/hr. Glucose absorption was significantly reduced by thyroidectomy (0.92 ± 0.10mM/g/h; $P<0.05$) while chronic thyroxine treatment increased absorption of glucose (1.97 ± 0.19mM/g/h; $P<0.02$)

Intestinal glucose absorption in response to catecholamines in altered thyroid states.

(a) Adrenaline: In a preliminary investigation, test-dose experiment using 0.05mg /kg, 0.1mg/kg, 0.5mg/kg and 1.0mg/kg was carried out in rats. The result revealed that an optimum dose of 0.5mg/kg was adequate for the study. This dose was thus considered for the catecholamines used.

Table 3 shows the effect of i.v. administration of adrenaline (ADR) before the onset of incubation. ADR significantly increased intestinal glucose absorption in all the four treatment groups. The magnitude of the increases (c.f. basal values) however differs as follows: ET- 71.64% ($t = 3.97$; $P< 0.001$), Thx .39% ($t=2.62$; $P<0.02$), Thx±T_4 - 69.03% ($t=4.06$; $p<0.001$) TH↑ -86.80% ($t=6.53$; $P<0.001$).

(b) Noradrenaline: -the increase in glucose absorption in the euthyroid rats in response to 0.5mg/kg noradrenaline was not significant when compared with the basal value ($t = 1.69$; $P > 0.05$). Significant increases in response to N.A. were however recorded in the other groups of rats as follows: Thx - 46.74% ($t=2.76$; $P<0.02$), Thx± T_4 - 34.21% ($t = 2.06$; $P<0.05$); TH↑ - 38.50% ($t = 2.46$; $P<0.05$). The results are presented in Table 3

Antagonistic potency of phentolamine and propranolol on glucose absorption in response to adrenaline.

The effect of administration of non-selective alpha adrenoceptor antagonist, phentolamine prior to adrena-

line is shown in Fig. 1. Phentolamine did not significantly alter the response of adrenaline in the ET, Thx±T_4 and TH↑ rats. However, the same dose of phentolamine significantly reduced the response of adrenaline to glucose absorption (from 42.3% increase in those with adrenaline alone, to 19.57% in those given phentolamine with adrenaline).

Table 3: Effects of Adrenaline and Noradrenaline on *in-vivo* intestinal glucose absorption compared in rats with normal and altered thyroid states.

Group	Basal glucose absorption (mM/g/hr)	Absorption in response to Adrenaline (0.5mg/kg)	Noradrenaline (0.5mg/kg)
ET	1.34 ± 0.15	2.30 ± 0.19 (71.64)	1.70 ± 0.15 (26.87)
Thx	0.92 ± 0.10*	1.31 ± 0.10 (42.39)	1.35 ± 0.11 (46.74)
Thx + T4	1.13 ± 0.12	1.91 ± 0.15 (69.03)	1.53 ± 0.16 (34.21)
Th↑	1.97 ± 0.19**	3.68 ± 0.18 (86.80)	2.63 ± 0.19 (38.50)

N.B. Values in parenthesis represent percentage changes in absorption over basal

hypothyroid rats was not significantly different from the response observed for adrenaline alone (42.39% to 28.26%; t = 1.02, P>0.10).

In vitro studies

Basal uptake of glucose in the isolated everted intestinal sac- Effect of chronic thyroxine treatment and thyroidectomy.

The uptake of glucose by isolated sacs of intestine from ET, Thx, Thx±T_4 and TH↑ rats are shown in Table 4. The basal glucose uptake in euthyroid control was 0.51 ± 0.13 mM/g/hr. In the untreated hypothyroid and hyperthyroid rats, glucose uptake was significantly reduced as both procedures caused a negative glucose uptake.

Effect of incubation of isolated intestinal sac with graded concentrations of adrenaline on glucose uptake.

The dose-response relationships for the effect of adrenaline on net gut glucose uptake are shown in fig. 2. The dose response curve for everted sacs from thyroidectomised rats was shifted to the right of the curve for the sacs from normal (euthyroid) rats. On the other hand, the curve for the hyperthyroid rats was shifted to the left of the normal curve. The dose of adrenaline which produced 50% of the maximum absorption was 7.5 x 10^{-3} ug/ml for the hyperthyroid rats, 2.0 x 10^{-1} for the euthyroid and 7.0 x 10^{-1} ug/ml for the hypothyroid animals.

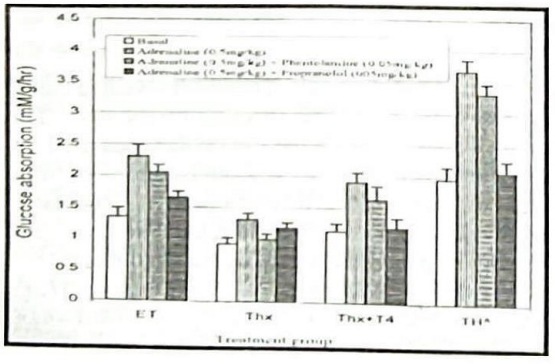

Fig.1: Effect of Phentolamine and Propranolol on glucose absorption in response to adrenaline in normal (ET), untreated hypothyroid (Thx), thyroxine - treated hypothyroid (Thx + T4) and hyperthyroid (TH^) rats.
**P < 0.05; **P< 0.001 (versus adrenaline alone)*
[a]P < 0.05), [b]P < 0.01, [c]P<0.001 (versus adrenaline alone)

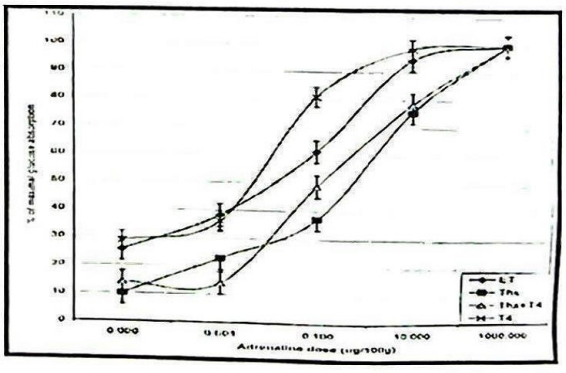

Fig. 2: Glucose absorption in response to graded doses of adrenaline in Euthyroid (ET), untreated hypothyroid (Thx), thyroxine-treated hypothyroid (Thx +T_4) and hyperthyroid (T_4) rats

Propranolol significantly reduced the response to adrenaline in the euthyroid (71.64% to 23.88%, t = 3.04, P<0.001) and hyperthyroid rats (86.80% to 5.58%; t = 6.27; P<0.001). However, the effect observed for the same dose of propranolol on adrenaline induced response in untreated

Adrenaline increased the absorption of glucose (mucosal glucose transfer) by the intestine. Although the adrenaline also increased the serosal glucose transfer (which is equivalent to the liberation of glucose in the bloodstream in an *in vivo* situation) the magnitude of each increment was low compared with the mucosal transfers.

Table 4: Glucose absorption by the isolated intestinal sac of euthyroid (ET), untreated hypothyroid (Thx) thyroxine treated hypothyroid (Thx + T4) and hyperthyroid (TH ↑) rats.

Group	Initial glucose cone (mM)	final glucose conc (mM) Serosa l fluid	Mucosa l fluid	Net gut weight (g)	S.G..T	M.G.T	G..G..U
ET	5.45 ± 0.06	6.07 ± 0.14	4.59 ± 0.09	0.48 ± 0.09	1.29 ± 0.02	1.79 ± 0.23	0.51 ± 0.13
Thx	5.45 ± 0.06	4.54 ± 0.24	6.87 ± 0.19	0.48 ± 0.01	-1.96 ± 0.50	-2.96 ± 0.35	-1.30 ± 0.38**
Thx + T4	5.45 ± 0.06	4.43 ± 0.10	6.49 ± 0.23	0.42 ± 0.02	-2.46 ± 0.31	-2.44 ± 0.51	0.08 ± 0.48
Th	5.45 ± 0.06	3.98 ± 0.15	6.98 ± 0.17	0.46 ± 0.02	-3.11 ± 0.28	-3.35 ± 0.40	-0.35 ± 0.49**

S.G.T. - *Serosal Glucose Transfer*
M.G.T. - *Mucosal Glucose Transfer*
G.G U. - *Gut Glucose Uptake*
***P < 0.001*

Discussion

In the present study, the effects of altered thyroid hormone activity on the functional sensitivity of the gastrointestinal tract to catecholamines were investigated. This was accomplished by daily injections of moderate doses of thyroxine and thyroidectomy under light ether anaesthesia.

The thyroxine dose of 50μg/100g used falls within the range used previously to produce hyperthyroid conditions in experimental rats. Doses ranging from 10μg/kg [15] to 75ug/kg [16] have been used successfully to produce hyperthyroid conditions and also to reverse the effects of thyroidectomy. The choice of 50μg was based on the recommendation of 50μg/100g as a moderate dose in experiment to test the hormonal effects on gastrointestinal functions [17]. Furthermore, the duration and route of administration agree with the report of Bolarinwa and Olaleye [9] to produce hyperthyroid rats. Although, hyperthyroidism had been induced by single injection of thyroxine for shorter periods of 1 and 4 days [14] the use of long term treatment with thyroxine in this work is justified by the fact that daily injections of thyroxine will maintain the level of circulating hormone at the desired level. The half–life of a tracer dose of thyroxine is 18 to 24 hours [18] and large doses are excreted in bile relatively faster [19]. Since the metabolic effect of a single large dose of thyroxine does not become evident until 12 hours and is not maximal until after several days [20] long term administration of thyroxine will summate to give a smooth level of the hormone.

From the results of the thyroid function tests, there can be little doubt that the animals were either hypothyroid, or hyperthyroid at the time of the experiments. The T_3 and T_4 blood levels were in a pathophysiologic range and confirms the results of the indirect test such as basal oxygen consumption and body weight changes.

The result of both *in vitro* and *in vivo* methods used in the study of intestinal glucose absorption in the present work is in harmony with previous findings. The findings that thyroxine increased the rate of intestinal absorption of glucose by the perfused intestine of the frog [21], drew attention to the possible role of endocrine glands in intestinal absorption. Subsequently works by Althausen and Weaver [22], Adeniyi and Olowookorun [5] and Olaleye *et al*, [6] agreed that intestinal absorption of glucose is increased in hyperthyroid states.

The exact mechanism of thyroxine on intestinal absorption has not been fully established. However changes in morphology of the intestinal tract have been proposed [23]. In addition, there is evidence that the secretion metabolism and clearance of peptide hormones which affect glucose metabolism such as insulin, and somatotropin and gastrin are abnormal in hyperthyroidism [24,25].

There has been very few studies on the role of catecholamines on intestinal absorption of glucose. In this study, it is evident that catecholamines stimulate glucose absorption in both the intact and isolated tissues. In an attempt to classify adrenergic receptors involved in regulating intestinal absorption, Barry and other workers [26] suggested that the α-adrenergic receptors mediate inhibition of glucose absorption. As a follow-up to this assertion, the present study suggests that the stimulatory effect of catecholamines appear to be mainly via the β-adrenergic receptors. This is evidenced by the fact that in the normal rats the non-selective β-blocker, propranolol significantly blocked the stimulatory effect of adrenaline on glucose absorption, whereas the alpha-blocker, phentolamine had little or no effect. The order of stimulation by the three agonists tested is also in support of a β-receptor mediation going by Alquist's original classification of adrenoceptors using the order of catecholamine action [27]. A recent finding that adrenaline-mediated uptake of glucose from the canine gut is via the β-adrenoceptors [28, 29] supports this view.

The present study provides strong evidence in support of the concept that the various actions of the

thyroid hormones on the gastrointestinal tract may be explained on the basis of changes in the sensitivity of the gut adrenoceptors to catecholamines. The stimulation of glucose absorption by the adrenergic agonists were significantly greater in the hyperthyroid than the hypothyroid animals. In many cases, the thyroidectomised rats failed to respond to the catecholamines.

The observations in the present study would have been easier to explain on the basis of changes in the sympathetic nerve activity, since the latter releases the catecholamines. However, the inability to observe significant alteration in sympathetic nerve activity when thyroid states are changed rules out this possibility. There is no evidence so far that the sympathetic nervous system or the adrenal medulla are overactive in hyperthyroidism or inactive in hypothyroidism respectively [30].

Aumann and Young [31] originally proposed the concept of differential sensitivity of adrenergic receptors in altered thyroid states in terms of inhibitory and excitatory responses. They compared the inhibitory effect of adrenaline on intestinal smooth muscle with the excitatory effect of adrenaline on the heart rate and noted that thyroid feeding greatly increased the magnitude of the cardioaccelerator response to adrenaline but did not affect intestinal inhibition. They concluded that thyroid hormone affected excitatory processes but not inhibitory ones. This concept of differential sensitivity has been subsequently restated in terms of alpha and beta receptors changes and have been used to explain several published observations, including the adrenergic regulation of lipolysis in altered states [8]; hypergastrinemia of hyperthyroidism [25]; the role of thyroid hormones in mammary [32], nervous [33] and cardiovascular [34] functions. All these studies agreed that β-adrenergic receptor responses increase in hyperthyroidism and decrease in hypothyroidism. On the other hand, the role of α-adrenergic receptors is not fully agreed upon. While some workers believed that the sensitivity of α-receptors is increased in the hypothyroid condition [35. 36], others maintained that the sensitivity of α-receptors remain unchanged even in the face of altered thyroid status [37]. Such characterization has hitherto not been investigated for the thyroid hormone effects on gastrointestinal functions.

The results of the study appear to agree with the concept that thyroid hormones increase the sensitivity of β-receptors to catecholamine and decreased that of the α-receptors. Based on this hypothesis, the gastrointestinal effects observed in the thyroidectomised and thyroxine-treated hormone is further evidenced by the results of the *in-vitro* studies. In the isolated stomach preparation devoid of the catecholamines, no significant changes in gastric secretion were observed in either the hyperthyroid or hypothyroid animals. Furthermore, in the studies on glucose absorption in the isolated everted sacs, the absence of circulating catecholamines greatly impaired the regulatory role of thyroxine on glucose absorption. As a result, the responses observed in the *in-vivo* study could not be established in the *in-vitro* preparations, hence the negative glucose uptake observed in the isolated intestines of both thyroidectomised and thyroxine treated rats.

Conclusions

The results obtained in this study show that changes in glucose absorption in response to thyroid hormones are dependent, at least in part, on the presence of circulating catecholamines. Although the levels of circulating catecholamines remain unchanged in the face of altered thyroid status as reported by earlier workers, the present finding provides evidence that a mechanism, based on inverse changes in alpha and beta adrenergic receptors responses in altered thyroid status may be involved.

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