COMPARATIVE STUDY OF SERUM TRACE ELEMENTS IN THYROID DYSFUNCTION

THESIS

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By

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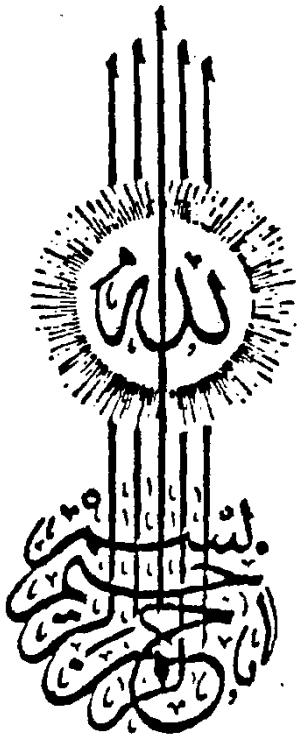
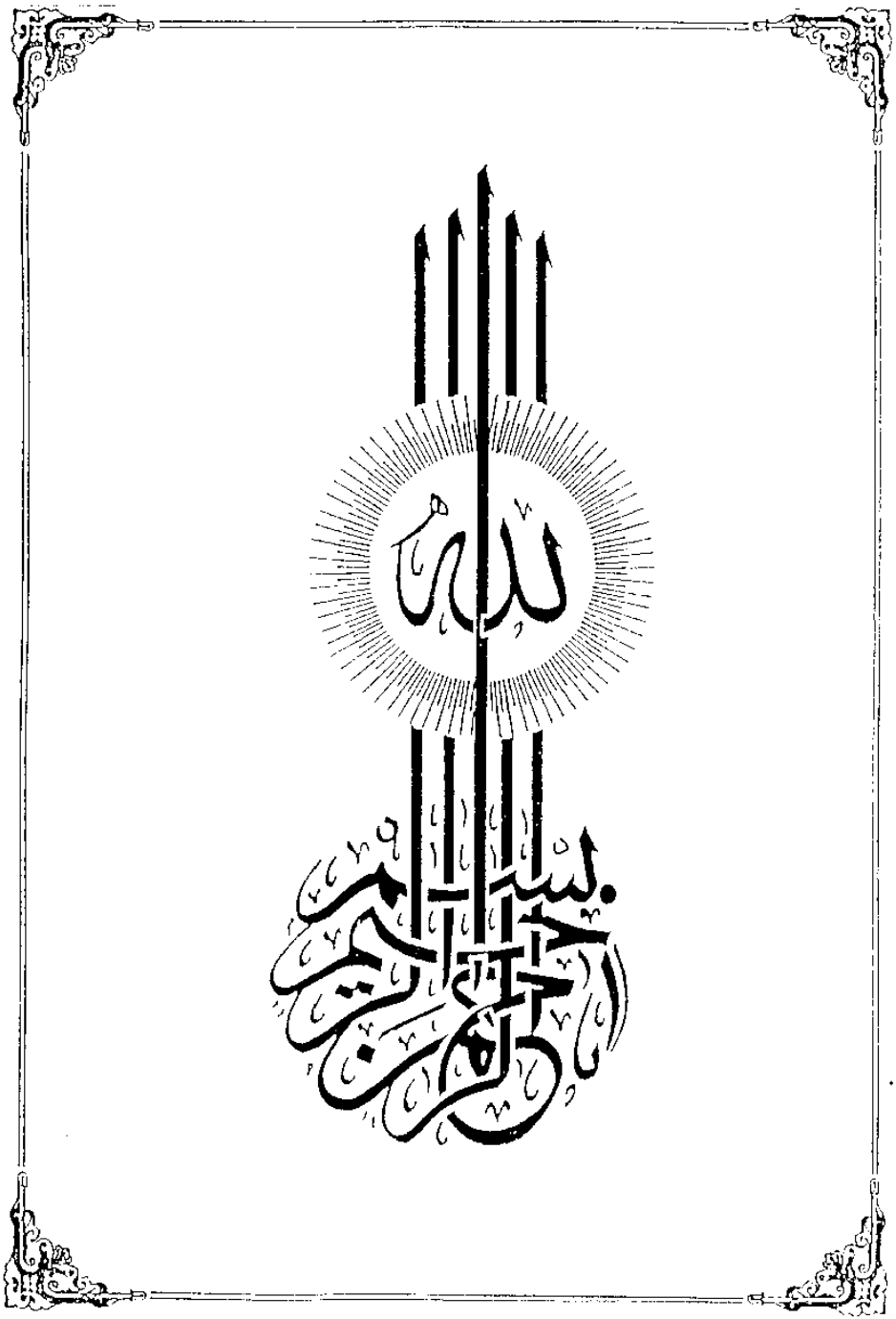


وَقُلِ اعْمَلُوا فَسَيَرَى اللّٰهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ

صَدَقَ اللّٰهُ الْعَظِيمُ



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ABBREVIATIONS

ACTH	=	adreno-corticotrophic hormone.
ADP	=	adenosine diphosphate
cAMP	=	cyclic 3,5 adenosine monophosphate
ATP	=	adenosine triphosphate
BMR	=	basal metabolic rate
EDTA=	=	ethylenédiamine - tetracetic acid.
GI	=	gastro-intistinal
HTS	=	human thyroid stimulator
Ig	=	immunoglobulin
Ibs/in^2	=	I pound per square inch
HTACS	=	human thyroid adenylate cyclase stimulators
hCG	=	human chrionic gonadotropin
hCT	=	human chrionic thyrotropin
MIT	=	monoiodotyrosines
DIT	=	diiodotyrosines
TBG	=	T_4 binding inter - α globulin
TBPA	=	T_4 binding prealbumin
TRH	=	thyrotropin releasin hormone
TSI	=	thyroid stimulating immunoglobulins
TSH	=	thyroid stimulating hormone (thyrotrapin)
RAIU	=	radioactive iodine uptake
RIA	=	radio-immunoassay
TBII	=	TSH-binding inhibitory immunoglobulin

LATS	=	long - acting thyroid stimulators
DNA	=	deoxyribonucleic acid
RNA	=	ribonucleic acid
MTS	=	mouse thyroid stimulator
T_4	=	tetraiodothyronine (thyroxine)
T_3	=	triiodothyronine
MCT	=	Medullary carcinoma
ug	=	microgram
ng	=	nanogram
t	=	test of significance
p	=	probability test
PBI	=	protein bound iodine
rT_3	=	reverse triiodothyronine.

AIM OF THE WORK

Trace elements have been shown to influence hormones at several levels, including hormone secretion and activity, and binding to the target tissue. Moreover, hormones have been shown to influence trace elements metabolism at several levels, including excretion and transport of trace elements.

The aim of the present work is:-

1) To study serum lithium, zinc, copper and magnesium in fifty patients with some thyroid disorders . Aimming to find a new marker of the state of thyroid dysfunction. And:

2) To compare them with serum lithium, zinc, copper and magnesium in twenty normal individuals as a controls.

PART I

INTRODUCTION

BACKGROUND

1. Anatomy of the thyroid gland:

The thyroid gland is one of the largest endocrine organs, it weighs about 15-20 gms. Anatomically it extents from the fifth or the sixth tracheal ring inferiorly to the side of the thyroid cartilage superiorly. It is enclosed in a sheath of pretracheal fascia. The gland consists of two lobes joined by an isthmus. Each lobe is conical in shape and measures about 2.5 cm in both thickness and width at its largest diameter and approximately 4 cm in length.

2. Blood supply:-

Arteries:

The thyroid gland receives ample blood supply from two main arteries, the external corotid and the inferior thyroid arteries from the subclavian arteries. An occasional small artery (thyroidaima) arising from the branchiocephalic trunk or the left common corotid or the aortic arch may all to the blood supply.

Veins:

The venous drainage is mainly through three pairs of veins, the superior and middle thyroid veins ending

in the internal Jugular vein and inferior thyroid veins ending in the innominate vein of the same side or both join the left innominate.

Lymph drainage:

Lymphatic drainage contains higher concentration of newly released radioiodine more than does thyroid venous blood probably in the form of iodoprotein.

Nerve Supply:

It is supplied by branches from the cervical ganglia of the sympathetic trunk and from the cardiac and laryngeal branches of the vagus, therefore it is innervated by both adrenergic and cholinergic nerve fibres.

3. Embryology:-

The human thyroid analage is first recognizable at about one month after conception when the embryo is approximately 3.5-4.0 mm in length (Boyd, 1964).

The ontogeny of thyroid function and its regulation in human fetus is fairly well defined (Fisher, 1974; and Fisher et al., 1975).

Thyroid hormone is essential for life, it maintains metabolic activity and this is reflected in the oxygen

consumption of both isolated tissues and in the intact animal (Ghareeb et al., 1971).

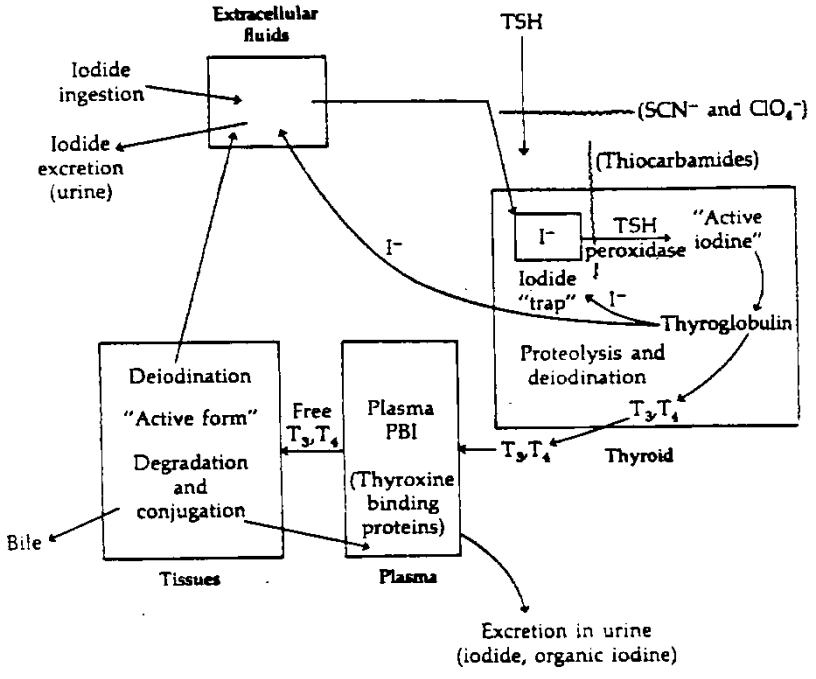


Fig (1) Scheme of the thyroid hormone biosynthesis.

Synthesis of the thyroid hormones:

Thyroid hormone is made up of a iodine and tyrosine. In the thyroid gland, iodine, is actively pumped into the cells against an electrical gradient, since the resting membrane potential is -50 mV (Ganong, 1981). About 120 µg/dL of iodide enter the thyroid gland at normal rates for thyroid hormones synthesis.

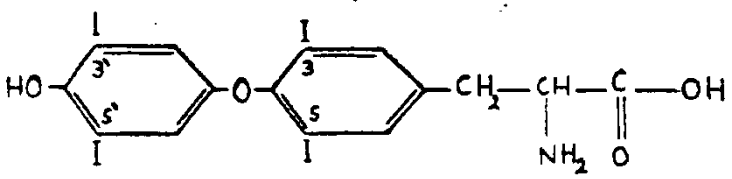
The synthesis of thyroid hormones is related to iodine metabolism Fig. (1).

1) Active transport of iodide into the thyroid constituting what we call iodide trapping.
2) Oxidation of iodide and iodination by perioxidase enzyme and subsequant binding with tyrosine residues to form iodotyrosines.
3) Coupling of iodotyrosines to form the hormonally active iodothyronines, notably T_3 and T_4.

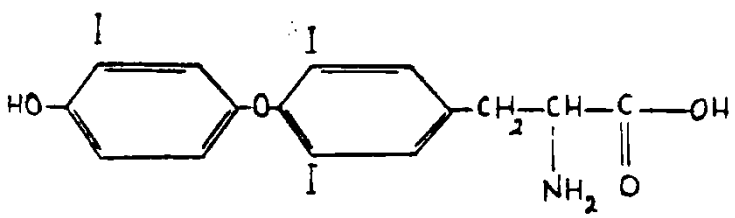
Hormone secretion

The human thyroid secretes about 80 µg of the free thyroxine and up to 8 µg of triiodothyronine/day.

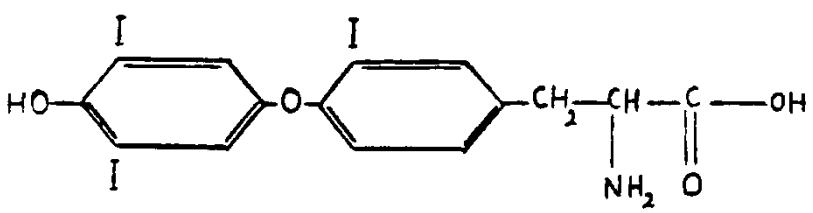
T_3, T_4, diiodotyrosine and monoiodotyrosine Fig.(2) are liberated into cytoplasm and pass into circulation probably by simple diffusion. Iodotyrosine deiodinases acts only on iodinated tyrosine but not thyronines. Normally, iodide liberated there by largely reutilized in the synthesis of thyroid hormones but a small proportion is normally lost into the blood (iodide leak).



3,5,3',5'-Tetraiodothyronine (thyroxine, T_4)



3,5,3' Triiodothyronine (T_3)



3,3',5' Triiodothyronine (Reverse T_3, rT_3)

Fig.(2) Structural formulas of thyroid hormones.

Mode of action of thyroid hormones.

As thyroid hormones enter cells most thyroxine is converted to T_3 in the cytoplasm. T_3 binds to the non-histone proteins in the chromatin and acts on DNA to increase the synthesis of mRNA and rRNA. The synthesized mRNA is translated into proteins presumably acting as enzymes that modifies cell function.

The calorigenic action of thyroid hormone appears to be mediated via an induced protein since it is blocked by inhibitors of protein synthesis (Ganong, 1981).

Metabolism of thyroid hormones:

T_3 and T_4 are deiodinated and deaminated in many tissues. T_4 is mostly converted into T_3, is partially converted into reversed T_3 (rT_3). However, increased amounts of rT_3 are formed from T_4 in early fetal life.

Because T_3 acts more rapidly and more potent than T_4, it has been suggested that T_4 is metabolically inert until it is deiodinated to T_3 i.e. that it is a prohormone (Ganong,1981) Fig. (3).

Approximately 20% of T_3 and T_4 is normally lost in the stools after being conjugated in liver with sulfates