STUDY OF POSSIBLE ROLE OF CALCITONIN IN THE PATHOGENESIS OF REFLUX OESOPHAGITIS

THESIS

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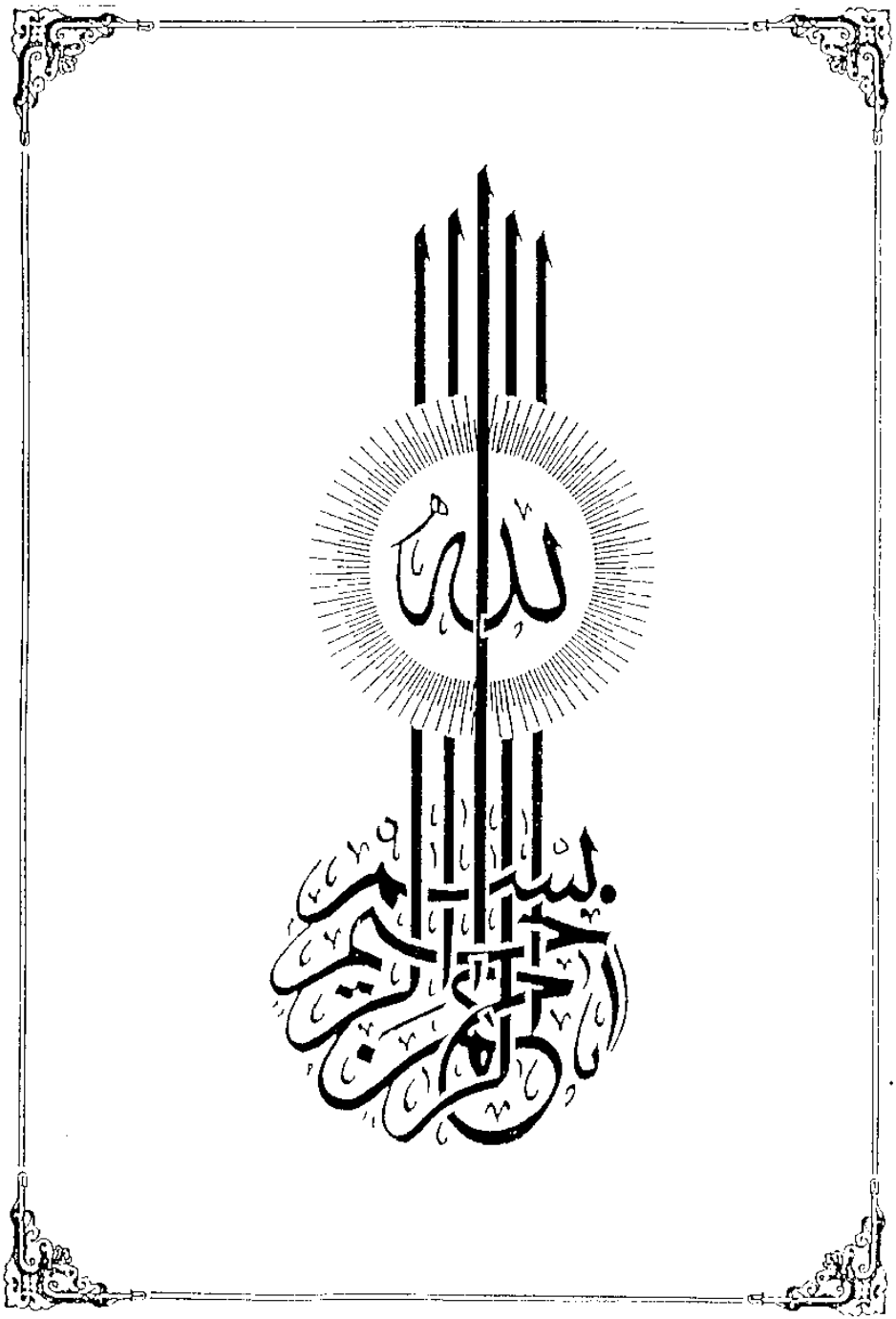

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List of Abbreviations

APUD	:	Amine content, amine precursor uptake, and amino-acid decarboxylase
Ca	:	Calcium
CT	:	Calcitonin
D.U	:	Duodenal ulcer
G.E	:	Gastroesophageal
GERD	:	Gastroesophageal reflux disease
H.P.Z	:	High pressure zone
L.E.S	:	Lower esophageal sphincter
PEG	:	Poly Ethylene Glycerol
PNE	:	Pulmonary neuroendocrine cells
PO_4	:	Phosphorus
PTH	:	Parathormone hormone
RASH	:	Reflux associated squamous hyperplasia
V.I.P	:	Vaso active intestinal peptides

Introduction and Aim of the Work

INTRODUCTION

Gastroesophageal reflux disease refers to the varied clinical manifestations of reflux of gastric and duodenal contents into oesophagus **[Pope, 1988]**. It is one of the most common problems occurring in clinical practice.

It is mainly due to oesophageal sphincter motility disorder with decreased clearance of gastric secretion from the oesophagus. The tone of lower oesophageal sphincter can be modulated by medications and hormones **[Nelson , 1984]**.

Motility disorder due to multifactors and aetiologies play a major role in the pathogenesis of reflux oesophagitis via the effect on lower oesophageal sphincter tone.

Calcitonin may play a role in motility either through its C.N.S. effect on motility or via its influence on calcium level which is associated with hyperacidity **[Barreras, 1973]**.

The role of calcitonin hormone was not previously explored in this aspect.

AIM OF THE WORK

Is to find out any aetiological relationship between serum calcitonin level and reflux oesophagitis.

Review of Literature

CALCITONIN

Until calcitonin was discovered, it was believed that parathormone (PTH), a hormone of the parathyroid glands, was alone responsible for maintaining calcium homeostasis. More than 35 years were to elapse before the functional antagonist of parathormone, namely calcitonin or thyrocalcitonin, was discovered.

In 1961, **Copp et al.** observed that on the infusion of the thyroid-parathyroid apparatus of the dog with hypercalcaemic blood there much more pronounced systemic hypocalcaemia than after these organs had been removed. They therefore summrise that an elevated calcium level causes the release of a hypocalcaemic factor or hormone from the thyroid-parathyroid apparatus. They considered the parathyroid gland to be the site of origin but this assumption proved to be incorrect. The authors proposed the name calcitonin for the new hormone, signifying that, like PTH, it participated in regulating the tone or concentration of calcium in the blood.

Calcitonin is biosynthesized and secreted by the ultimobranchial (parafollicular "C") cells **[Arnaud and Koble, 1986]**, of the thyroid which is the main source of hormone.

The cells are members of the APUD cell series. The term APUD is derived from initial letters of three most reliable characteristics, Amine content, amine Precursor Uptake, and amino-acid Decarboxylase. The series includes the medullary carcinoma, branchial and intestinal carcinoids and pheochromocytomas. The common origin also explains why C cell tumour can excrete ACTH and carcinoid cells, on occasion, produce calcitonin **[Arnaud, 1985 and Loeb, 1985]**. In man, calcitonin is also present in the parathyroid and thymus as well as in the thyroid **[Thomas and Delvin, 1982]**.

Another extrathyroidal sites for calcitonin production have been demonstrated in the adrenal, and recently it has been suggested that calcitonin like material is synthesized in the pars intermedia of the pituitary gland **[Kanis, 1985]**. Moreover, calcitonin and calcitonin receptors had been demonstrated in many extrathyroid tissues including the male genital tract. Calcitonin immunoreactivity has also been found in human seminal fluid, and an inhibitory effect of salmon calcitonin on human sperm motility in vitro was recently reported with identification of calcitonin receptors in human spermatozoa **[Sivestroni et al., 1987]**. There was also evidence for cigarettes smoking induced-calcitonin secretion from the lungs of man, possibly from the immunoreactive calcitonin (ICT) containing pulmonary neuroendocrine (PNE) cells **[Tabassian et al., 1988]**. In the human, there is more calcitonin within the lungs than in the thyroid gland **[Becker et al., 1979]**.

Calcitonin could be isolated from a total of 8 different species in pure form and its structure was elucidated in 7 of them Five of them were produced synthetically, and three of them, namely human, procine and salmon calcitonin are available with the natural sequence of amino acids for therapeutic purposes **[Doepfner, 1983]**.

Chemistry:

A common feature of all calcitonins is a sequence of 32 amino acids with a ring closure invariably at the N-terminal with 2 cystines in position 1 and 7.

Comparison of the various sequences shows that at the N-terminal there are only 7 amino acids and at the C-terminal only 2 amino acids occurring at the same place in all known structures. The other sequence, on the other hand, displays notable species differences. If common structural features are sought. There are relatively great similarities to be found in 3 groups:

1- Human and rat: 30 amino acids in common.

2- Procine, bovine and ovine: 28 amino acids in common.

3- Salmon and eel: 29 amino acids in common .

Surprisingly enough, however, it can be shown, for example, that salmon