



**This work is  
Dedicated  
To my Dear Family**

فارس

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## Contents

	Page
<b>I. Introduction and Aim of the essay.</b>	1
<b>II. Review of Literatures:</b>	
<b>A) Renin</b>	
1. Biosynthesis	5
2. Purification of Renin	11
3. Prorenin and Activators	13
4. Tissue Renin	16
5. Renin Release	18
6. Renin Assay	23
<b>B) Angiotensins:</b>	
1. Angiotensins Synthesis	27
2. Angiotensins Assays	37
<b>C) Renin-Angiotensin system and Hypertension:</b>	
1. Essential Hypertension.	39
a. Low renin essential hypertension	41
b. High renin essential hypertension	42
c. Normal renin essential hypertension	43
2. Secondary Hypertension	46
a. Renovascular Hypertension	46
b. Renal Parenchymal diseases	49
c. Estrogen induced hypertension	52
d. Pregnancy induced hypertension (Preeclampsia)	53
e. Hypertension associated with cushing's syndrome	54

f. Hypertension due to coarctation of the aorta	55
3. Malignant Phase of Hypertension.	57
D) Renin. Angiotensin System And Diabetes Mellitus:	58
1. Diagnosis and classification of diabetes mellitus	58
2. Renin-angiotensin system in diabetes with nephropathy.	63
3. Plasma renin activity in diabetes with neuropathy	65
III. Summary	71
IV. References	74
V. Arabic summary	

## LIST OF ABBREVIATIONS

1) Angiotensin I	AI
2) Angiotensin II	AII
3) Angiotensin III	AIII
4) Angiotensin converting enzyme	A.C.E.
5) Converting enzyme assay	C.E.A.
6) Cushing's syndrome	C.S.
7) High renin essential hypertension	H.R.E.N.
8) Impaired glucose tolerance	I.G.T.
9) Juvenile onset diabetes mellitus	J.O.D.M.
10) Juxtaglomerular	J.G.
11) Juxtaglomerular index	J.G.I.
12) Low renin essential hypertension	L.R.E.H.
13) Maturity onset diabetes mellitus	M.O.D.D.
14) Maturity onset diabetes of young	M.O.D.Y.
15) Pancreatic islet cell antibodies	P.I.C.A.
16) Plasma renin activity	P.R.A.
17) Plasma renin concentration	P.R.C.
18) Pregnancy induced hypertension	P.I.H.
19) Prostaglandin synthesis	P.G.S.
20) Renin-angiotensin system	R.A. system
21) Vasoactive intestinal peptide	V.I.P.

## LIST OF THE FIGURES

	Page
1. Juxtaglomerular apparatus and its relationship to the glomerulus and renal tubule.....	6
2. Anatomic relations of the granular J.G. cells .....	8
3. The fine structure and innervation of the J.G. apparatus....	10
4. Factors participating in acid activation of inactive renin and their interactions.....	15
5. Pathways regulating renin release .....	19
6. Reactions initiated by renin resulting in the formation of AI and AII .....	28
7. Biochemistry of the renin angiotensin system .....	29
8. Negative feed back control of renin secretion .....	34
9. The renin angiotensin aldosterone system for blood pressure and for sodium volume homeostasis.....	40

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# INTRODUCTION

## INTRODUCTION

The renin-angiotensin system has always been regarded as a blood pressure regulating system of renal origin (Lee, 1969). Some studies have demonstrated that renin biosynthesis can occur in several organs (Yu, et al., 1972) and that angiotensin II (AII) can be formed locally in the tissues (Boucher, et al., 1974).

The renin-angiotensin system regulates sodium balance, fluid volume and blood pressure. Renin is secreted in response to decreased blood volume as in haemorrhages, sodium depletion, fluid transudation and decreased arterial pressure. In these conditions the kidney's perfusion is reduced and it secretes renin into the blood stream (Laragh and Sealy, 1981).

Renin is a proteolytic enzyme that is synthesized stored and secreted mainly by the preglomerular epitheloid cells of the juxta glomerular "J.G." apparatus in the kidney.

The circulating half life of renin in normal subject is 15 minutes (Douglas, 1985). It acts on renin substrate (angiotensinogen) which is produced in the liver and is widely distributed in the blood and other extracellular fluids leading to the formation of Angiotensin I (AI). A converting enzyme (Kininase II) acts on AI to yield AII mainly in the lungs (Keeton and Campbell, 1984). Renin is inactivated in the liver and in plasma by proteolytic enzymes and excreted in urine and bile (Peart, 1975).

AII, in addition of its vasopressor action stimulates aldosterone secretion. Aldosterone causes sodium and water retention, expanding extracellular fluid volume and shutting off the stimulus that increased renin secretion (Ganong, 1985).

AII is rapidly broken down by a group of enzymes called angiotensinases. They are present in tissue as well as in plasma (Ledingham, 1974).

All the metabolic products of AII are devoid of physiologic activity with the exception of the (Angiotensin III). It is one third to one half as potent vasoconstrictor as AII but has an equal stimulatory effect on aldosterone synthesis (Blair-west, et al., 1981).

The renin angiotensin system in diabetics has been studied some years ago. Low plasma renin has been reported in patients with long term diabetes mellitus complicated by nephropathy (Christlieb et al., 1976 and Tomita et al., 1982) and neuropathy (Fernaudez-Cruz, 1981 and Nakamaru et al., 1983). Where as Drury et al (1982) reported high levels in diabetes with retinopathy.

The mechanism for hyporeninemia in diabetes mellitus have not been clarified. In uncomplicated long-standing diabetes mellitus, plasma renin activity (PRA) has been reported to be low (De Chatel et al., 1977 and Weidman et al., 1980) normal (Campbell, 1976 and Berreto Piccoli, 1981)

or possibly elevated (Gossain, 1975 and Burden and Thurston, 1976). Because the hyperkalemia can be symptomatic and life threatening and because the syndrome of hyporeninemic hypoaldosteronism can be recognized and is potentially treatable, we considered that more studies of R.A. system are relevant and important in diabetic patients.

## **AIM OF THE WORK**

The aim of this essay is to review the physiology, biochemistry and pathological states of the renin-angiotensin system and its relation to hypertension and diabetes mellitus.

**RENIN**

## A. RENIN

### 1. Biosynthesis

Renin is a glycoprotein, an acid protease enzyme with high substrate specificity. It produces the decapeptide AI from angiotensinogen (Douglas, 1985). Renin is synthesized, stored and secreted by the granular juxtaglomerular "JG" cells which are differentiated smooth-muscle cells that are usually found in the media of the renal afferent arteriole just adjacent to the glomerulus (Keeton and Campbell, 1984).

#### Morphology of Juxtaglomerular apparatus:

Nephron has a region known as the 'JG' apparatus or complex which is made up of three morphologic structures :

- (a) Juxta glomerular cells (granular, epitheloid, myoepithelial or glomus cells).
- (b) Macula densa
- (c) Lacis cells (agranular cells or pseudo-Meissnerian afibrillar cells of goormaghtigh) (Keeton and Campbell, 1984) Fig. 1.

#### (a) The granular epitheloid or (JG cells)

They are myoepithelial cells located in the media of the distal part of the afferent arterioles of the glomeruli. They are occasionally observed in the efferent arterioles near the glomerulus (Marcantin, 1983). Myofibrils, which are characteristic of vascular smooth muscle cells, are observed in the granular JG cells. The granules found in these cells are relatively homogeneous and dense and are membrane-bound. The granular JG cells have well developed endoplasmic reticulum and golgi membranes,