Clinical Significance of Angiopoietins in Different Pathological Conditions

Essay Submitted for Partial Fulfillment of Master Degree in Clinical and Chemical Pathology

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.List of Abbreviations

CONTENTS

	Page
.List of Tables	iv
.List of Figures	v
.Introduction and Aim of The Essay	1
.Review of Literature	4
CHAPTER I:	
ANGIOGENIC FACTORS	4
A. Introduction to Angiogenesis	4
B. Steps of Angiogenesis	5
1. Vessel Destabilization	5
2. Proliferation and Migration	5
3. Vessel Maturation	6
C. Angiogenic Factors and Their Inhibitors	7
1. Factors Affecting Endothelial Proliferation	
and Migration	9
2. Factor Affecting the Basement Membrane	
and Extra-Cellular Matrix (ECM)	27

CONTENTS (cont.)

	Page
CHAPTER II:	
ANGIOPOIETINS	36
A. Structural Characterization of Angiopoietins	36
1. Angiopoietin 1 (Ang1)	36
2. Angiopoietin 2 (Ang2)	38
3. Angiopoietin 3 (Ang3) and Angiopoietin 4	
(Ang4)	39
B. Receptors of Angiopoietins	42
1. The Tie Receptor Family	42
2. Integrins	52
C. Physiological Role of Angiopoietins	54
1. Angiopoietins as Angiogenic and	
Lymphangiogenic Factors	54
2. Role of Angiopoietins in Wound Healing	57
3. Angiopoietins in Menstrual Cycle and	
Pregnancy	60
D. Clinical Significance of Angiopoietins in	
Pathological conditions	61
1. Angiopoietins and Diabetic Retinopathy	61
2. Angiopoietins and Rheumatoid Arthritis	63

CONTENTS (cont.)

	Page
3. Angiopoietins and Tumors	66
E. Methods of Assay of Angiopoietins and Their	
Tie Receptors	71
1. Sampling	71
2. Reference Range	72
3. Analytical Methods	72
. Summary and Conclusion	79
.Recommendations	84
. References	85
. Arabic Summary	

LIST of ABBREVIATIONS

aFGF : Acidic fibroblast growth factor

Angs : Angiopoietins

AM : Adrenomedullin

bFGF : Basic fibroblast growth factor

DNA : Deoxy ribonucleic acid

E8.5 : Embryonic day 8.5

ECM : Extra-cellular matrix

EDTA : Ethylene Diamine tetra acetic acid

EGF : Epidermal growth factor

ELISA : Enzyme linked immunosorbent assay

eNOS : Endothelial nitric oxide synthase

Eph : Ephrin

FGF : Fibroblast growth factor

Flk-1 : Fetal liver kinase

Flt-1 : Fms-like tyrosine kinase 1

HGF : Hepatocyte growth factor

HSPG : Heparan sulfate proteoglycans

IHC: Immunohistochemistry

Ig : Immunoglobulin

IL: Interleukin

ILMA : Immunoluminometric assay

LIST of ABBREVIATIONS (Cont.)

ISH : In situ hybridization

IRMA : Immunoradiometric assay

KDR : Kinase domain region

mAbs : Monoclonal antibodies

MMPs : Matrix metallo-proteinases

mRNA : Messenger ribonucleic acid

ND : Not determined

NGF : Nerve growth factor

NPY : Neuropeptide Y

PAMP : Proadrenomedullin N-terminal 20 peptide

PDGF : Platelet derived growth factor

PI3-K : Phosphatidylinositol 3' kinase

PIGF : Placental growth factor

RA : Rheumatoid arthritis

RGD : Arginine glycine aspartic acid

RTK : Receptor tyrosine kinase

RT-PCR: Reverse transcriptase polymerase chain

reaction

SMC : Smooth muscle cells

Tek : Tunica endothelial kinase

TF : Tissue factor

LIST of ABBREVIATIONS (Cont.)

Tie : Tyrosine kinase with immunoglobulin and

epidermal growth factor homology domain

TP : Thymidine phosphorylase

tPA : Tissue type plasminogen activator

uPA : Urokinase type plasminogen activator

VEGF : Vascular endothelial growth factor

LIST of TABLES

	Page
Table (1): Angiogenic Factors and Their Inhibitors.	7
Table (2): Characteristic Features of Angiopoietin.	41

LIST of FIGURES

	Page
Figure (1): VEGF family and their receptors	9
Figure (2): Schematic presentation of fibrinolytic	
system	31
Figure (3): Structural organization of Tie receptors	43
Figure (4) : Schematic presentation of Ang1/Tie2	
signaling	46
Figure (5): Mechanism of angiogenesis in RA	64
Figure (6): Tie2 dependent and Tie2 independent	
signaling of Angs in endothelial and	
non endothelial cells	69

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INTRODUCTION and and of THE ESSAY

INTRODUCTION

The formation of functional vasculature is a complex process requiring spatial and temporal coordination of multiple, receptors, intracellular signaling pathways, regulatory factors and angiogenic factors (*Saito et al.*, 2003).

Angiopoietins (Angs) are promising angiogenic protein growth factors which include four members namely Ang1, Ang2, Ang3 and Ang4. Angiopoietins exert their action through binding to a specific tyrosine kinase receptor named Tie receptor (*Eklund and Oslen, 2006*). Ang1 has been shown to promote the integrity of blood vessels through inhibition of vascular inflammation and suppression of vascular leakage (*Shyu, 2006*). Meanwhile, Ang2 exhibits a context dependent behaviour; in the absence of VEGF, Ang2 promotes vessel destabilization and regression, while in the presence of VEGF, Ang2 stimulates sprouting of new blood vessels (*Haninec et al., 2006*). The effect of Ang3 and Ang4 have been less characterised but they also show

context dependent actions as antagonistic and agonistic ligands respectively (*Eklund and Oslen, 2006*).

The angiopoietin family also plays a crucial role in the pathogenesis of different pathological conditions including, diabetic retinopathy (*Peters et al.*, 2007), arthritis (*Clavel et al.*, 2007) and carcinomas (*Caine et al.*, 2007).

AIM of THE ESSAY

The aim of the present study is to highlight the different members of angiopoietin family, their structure, mechanisms of action with special emphasis on their role in the pathogenesis of different pathological conditions.