THROMBOPOIETIN: PHYSIOLOGICAL AND BIOLOGICAL PROPERTIES

Essay
Submitted for partial fulfillment of master degree in CLINICAL and CHEMICAL PATHOLOGY

BY
Salwa Abd El Latif Shendy
(MB., B.Ch 1991)

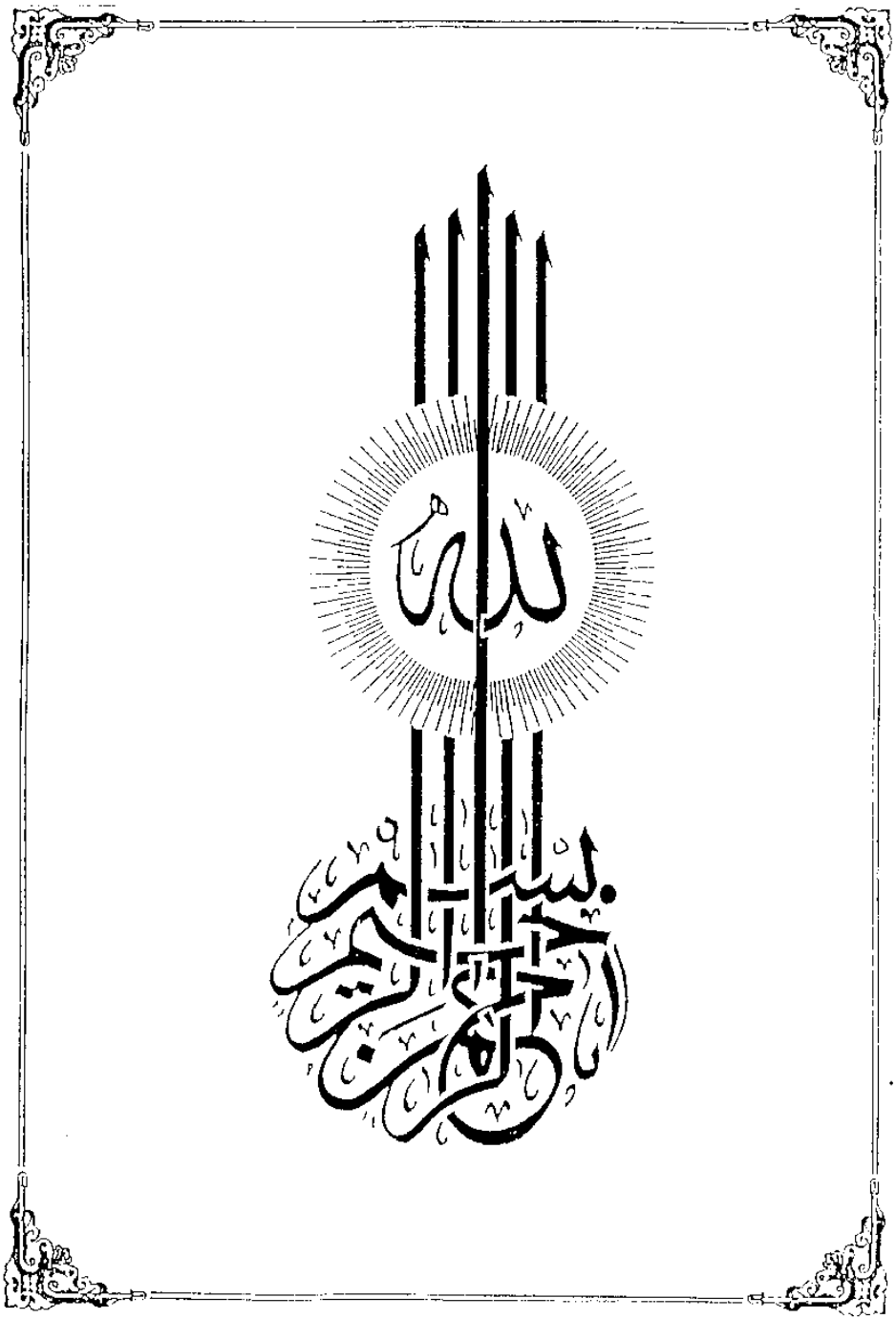
Under Supervision of

Prof. Dr. Nadia M.A. Mowafy
Professor of Clinical & Chemical Pathology
Faculty of Medicine, Ain Shams University

Dr. Hoda Mohamed El Gendi
Lecturer of Clinical & Chemical Pathology
Faculty of Medicine, Ain Shams University

Dr. Iman Mohamed Amin Omar
Lecturer of Clinical & Chemical Pathology
Faculty of Medicine, Ain Shams University

Ain Shams University
1997



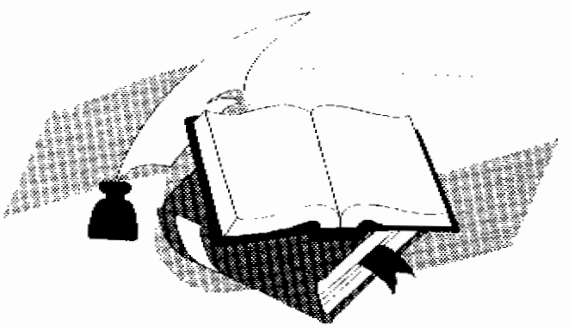
Acknowledgment

First and foremost, I feel indebted to god the most kind and most merciful for helping and guiding me to the right path.

I wish to express my sincere appreciation and deepset gratitude to Prof. Dr. Nadia M.A.Mowafy, Professor of Clinical & Chemical Pathology, Faculty of Medicine, Ain Shams University, for her precious guidance, comments, and valuable suggestion through out this work.

I am also deeply indebted to Dr. Hoda Mohamed El Gendi, Lecturer of Clinical & Chemical Pathology, Faculty of Medicine, Ain Shams University, for her supervision, sincere advice continous encouragement through out this work.

I would like to express my sincere grtitude and thanks to Dr. Iman M. A. Omar, Lecturer of Clinical & Chemical Pathology, Faculty of Medicine, Ain Shams University, for her kind supervision, encouragement and energetic help through out this work.



To my Dears.....

Parents ....

Husband .....

Daughters.....

Table of contents:

Abbreviations

AA	Aplastic Anaemia
AchE	Acetyle choline - estrase.
ALL	Acute lymphoblastic leukaemia
AMM	Agnogenic myeloid metaplasia
ATP	Adenosin triphosphate
BFU-E	Burst forming unit erythrocyte
BM	Bone marrow
BPA	Burst promoting activity
BTG	Beta Thromboglobin
CAMT	Congenital amegakaryocytic thrombocytopenia
CFU-GEMM	Colony forming unit granulocyte erythrocyte macrophage megakaryocyte
CFU-Meg	Colong forming unit - megakaryocyte
CMS	Colony megakaryocyte stem cell
CTAP	Connective tissue activating peptides
DMS	Demarcation membrane system
ELISA	Enzyme linked immunosorbant assay
EPO	Erythropoietin
ET	Essential Thrombocytosis
FACS	Flourscine activated cell sorting
FBS	Fetal bovin serum
GPA	Glycophorine A
GP	Glycoprotein
HEL	Human erythroleukemia cell line
IMP	Intera membranous particle
IL	Interleukin
KD	Kilo dalton
LIF	Leukaemia inhibitory factor

MK	Megakaryocyte
Mega - CSA	Megakaryocyte colony stimulating activity
MGDF	Megakaryocyte growth and development factor
ML	Myeloproliferative ligand
MpL	Myeloproliferative leukaemia ligand
MPU	Mean platelet volume
PEG-rHu-MGDF	Pegylated recombinant human megakaryocyte growth and development factor
PF4	Platelet factor-4
PPF	Proplatelet formation
PVSG	Polycythemia vera specific group
RT	Reactive thrombocytosis
RT-PCR	Reverse transcriptase polymerase chain reaction
SCF	Stem cell factor
S-MpL	Soluble form of MpL
TPO	Thrombopoietin
vWF	von Willebrand factor

Introduction and Aim of the work

Aim of the work

The aim of this review is to present available data for the physiological and biological properties of thrombopoietin, its measurment in blood, its involvement in the pathogenesis of thrombocytopenic and Thrombocythaemic disorders and its therapeutic uses.

Review of Literature

Megakayocyte progenitors have been shown to adhere to thrombospondin. Morover, ***MK*** may adhere to marrow stromal fibroblasts expressing the membrane-bound form of kit ligand ***[Stem cell factor (SCF)].*** The ashesive properties of ***MK*** may prove to be important in the delivery of platelet to the circulation ***(Avraham, et al., 1992).***

Cytoplasmic maturation :

As polyploid progresses, cytoplasmic maturation occurs, but, do not appear to be inextricably linked. ***(Herker, et al., 1969).*** It can be defined to include the synthesis of protein and other biochemical constituents of platelets with attended cytoplasmic volume expansion, the synthesis and packing of specific organelles, and the production of the demarcation membrane system ***(DMS)*** which will ultimately constitute the membrane of the platelets. This system appears to be involved in delimiting areas beleived to represent platelet territories ***(Farnklin, et al., 1984, Williams, et al., 1982)***

As in other cells, the cell specific proteins are synthesized by ribosomes on the rough endoplasmic reticulum and then packaged via the golgi zone into granules ***(Jones, 1960).*** Megakaryocyte granules contain B-thromboglobulin , ***Pf4,*** thrombospondlin, fibronectin, ***vWF***, and P-selectin. In addition, the granules of ***MK*** and platelets have been shown to contains several plasma proteins, such as fibrinogen,