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Fibrinolytic Bacterial Enzymes with Thrombolytic Activity

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*This book is dedicated with profound
gratitude to the world's mother, Egypt*



Preface

Stress, high blood pressure, smoking, pollution, fast foods, overweight, excessive travelling, surgery, and less movement are common features in our modern life. These features are risky for blood clotting disorders. According to WHO, over 29% of the total mortalities worldwide are due to thrombosis. By the year 2020 cardiovascular diseases (CVDs) may cause an estimated 25 million deaths per year, thus antithrombotic therapy is of great interest.

The available thrombolytic agents such as urokinase are highly expensive, unavailable for commoners, highly antigenic, unspecific, liable, pyretogenic, and hemorrhagenic. Therefore, the production of fibrinolytic enzymes, which was in effect the rapid dissolution of thrombi within the vascular tree, without the last named detriments by microorganisms is considered one of the most influential subjects and is my aim in this book.

The first part of this book throws light on the mechanism of thrombus formation and all thrombolytic medications regimens, focusing on the fibrinolytic enzymes as a new and future promising therapy. The book also throws light on the microbial and non microbial sources of these enzymes, with great scope on the production of these enzymes in vitro from microorganisms, different protocols of enzyme purification and the physical and biochemical characters of these enzymes.

In fact the use of fibrinolytic enzymes in the treatment of thrombi passed with two important stations. The first was with streptokinase and staphylokinase that dissolve thrombi indirectly by activation of endogenous plasmin to degrade fibrin. The second was started in 1987 with the discovery of nattokinase which is able to degrade fibrin directly and efficiently without the previous drawbacks. I think the future research will make great efforts to find other plasmin-like enzymes like nattokinase and increase the enzyme efficacy and fibrin specificity, focusing on developing effective targeted thrombolytic agents by incorporation with thrombus-specific polypeptide or monoclonal antibody.

It is my intent that researchers, pathologists, clinical laboratory scientists, and other physicians serving as laboratory directors will find this book helpful to understand and carry out their responsibilities. Another intent is that residents and fellows will find this book to be a useful tool for learning the basics of assessing of

clot lysis abilities of fibrinolytic enzymes and for studying the hemostasis screening tests. I would like to acknowledge my wife, Dr Asmaa, and my children. Their patience and understanding gave me the time and inspiration to research and write this book.

Essam Kotb

Glossary

3,4-DCI	3,4-dichloroisocoumarin
ACE	Angiotensin converting enzyme
AMMP	Armillaria mellea metalloprotease
AOT	Bis(2-ethylhexyl)sodium sulfosuccinate
APSAC	Acylated plasminogen–streptokinase activator complex
APTT	Activated partial thromboplastin time
BAEE	Na-benzoyl-L-arginine ethyl ester
BHI	Brain–heart infusion
BKII	Bacillokinase II
BT	Bleeding Time
CBC	Complete blood count
CCD	Central composite design
CDM	Chemically defined media
CLNE	Na-CBZ-lysine-p-nitrophenyl ester
CU	Plasmin unit
CVDs	Cardiovascular diseases
D	D domain of fibrinogen
DBCLT	Dilute blood clot lysis time
DEAE	Diethylaminoethyl
DFP	Diisopropylfluorophosphate
DIC	Disseminated intravascular coagulation
DIP	Di-isopropyl fluorophosphates
DJ	Doen-Jang, a traditional Korean fermented food
DSC	Differential scanning calorimetry
E	E domain of fibrinogen
ECLT	Euglobulin clot lysis time
EDTA	Ethylenediaminetetraacetic acid
EFA	Euglobulin fibrinolytic activity
ELISA	Enzyme-linked immunosorbent assay
EMS	Ethyl methane sulfonate
FDPs	Fibrin degradation products

FFD	Fractional factorial design
Fibrin	Insoluble fibrin
Fibrins	Soluble fibrin
FT-IR	Fourier transform infrared
FU	Fibrin unit
HIT	Heparin-induced thrombocytopen
HMWK	High-molecular-weight kininogen
HPLC	High performance liquid chromatography
IgG	Immunoglobulin type G
INR	International normalizing ratio
IP	Intraperitoneal injection
IPTG	Isopropyl- β -D-thiogalactopyranoside
ITP	Idiopathic thrombocytopenic purpura
IV	Intravenous injection
LB	Luria-Bertani medium
NMR	Nuclear magnetic resonance
NPGB	p-nitrophenyl-p-guanidinobenzoate
PAI-1	Plasminogen activator inhibitor-1
Pas	Plasminogen activators
PEG	Polyethylene glycol
PK	Prekallikrein
PMSF	Phenylmethylsulfonyl fluoride
PSLT	Plasma streptokinase lysis test
PT	Prothrombin time
PTT	Partial-thromboplastin time
Rpm	Rotation per minute
SAK	Staphylokinase
SALT	Streptokinase activated lysis time
SBP	Systolic blood pressure
SGE	Group E streptococci
SK	Streptokinase
SLE	Systemic lupus erythematosus
SMCE	Soybean milk coagulating enzyme
SSF	Solid-state fermentation
SVs	Snake venoms
TAME	Na-tosyl-L-arginine methyl ester
TF	Tissue factor
TLCK	Tosyl-L-lysine chloromethyl ketone
t-PA	Tissue-plasminogen activator
TT	Thrombin time
TTP	Thrombotic thrombocytopenic purpura
U	International unit
UK	Urokinase
VTE	Venous thromboembolism
vWD	Von Willebrand's disease

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