

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES

VOLUME 146, ART. 2

PAGES 361-787

CHEMISTRY, PHARMACOLOGY, AND CLINICAL APPLICATIONS
OF PROTEINASE INHIBITORS

Consulting Editor

NATHAN BACK

AUTHORS

N. BACK AND E. F. MAMMEN (*Conference Cochairmen*), C. M. AMBRUS, J. L. AMBRUS, C. J. AMRIS, F. A. ANDERER, L. ANDERSSON, T. ASTRUP, W. H. BACHRACH, L. BALART, M. I. BARNHART, F. K. BELLER, Y. BIRK, B. BLOMBÄCK, M. BLOMBÄCK, G. B. BLUHM, A. R. CASTANEDA, S. COLLEEN, C. C. CRAIGHEAD, M. D. EPSTEIN, H. FRITZ, H. GANS, R. K. GOESSWALD, B. GRANSTRAND, M. GREBERMAN, L. J. GREENE, C. E. GROSSI, E. HABERMANN, H. HAENDLE, U. HAMBERG, M. HILDEN, S. HÖRNLE, S. JOHN, A. J. JOHNSON, J. H. KAY, M. LASKOWSKI, SR., H. B. LASSMAN, H. L. LENON, C. W. LILLEHEI, G. MCHARDY, I. V. MAGOSS, P. MATIS, B. MELANDER, H. MIHARA, I. B. MINK, F. K. MÖRL, I. M. NILSSON, K. R. NISWANDER, J. H. NODINE, S. NORDSTRÖM, S. OKAMOTO, U. OKAMOTO, P. OLSSON, S. OSHIBA, L. L. PHILLIPS, B. PRYTZ, C. QUINTANA, J. V. REDINGTON, J. M. RIDDLE, M. ROCHA E SILVA, L. M. ROUSSELOT, P. D. SCHILD, G. SCHIMERT, W. H. SEEGER, M. SEMAR, F. SICUTERI, L. SKOZA, R. STEGER, L. STUTZMAN, V. SUBRAMANIAN, A. G. THOMPSON, D. A. TICE, I. TRAUTSCHOLD, A. O. TSE, H. K. TSUJI, R. WEISS, E. WERLE, H. WILKENS, C. WOLF, M. W. WOODRUFF, M. H. WORTH, JR., E. ZETTERQVIST

Editor-in-Chief

EDWARD M. WEYER



神戸市生田区梅町6丁目38の2
神戸大学医学部第一生理

NEW YORK
PUBLISHED BY THE ACADEMY

岡本彰祐

June 28, 1968

THE NEW YORK ACADEMY OF SCIENCES
(Founded in 1817)

SCIENTIFIC COUNCIL, 1968

MINORU TSUTSUI, *President*

IRVING J. SELIKOFF, *President-Elect*

ANDRES FERRARI, *Vice-President*

I. B. LASKOWITZ

Recording Secretary

MARGARET MEAD, *Vice-President*

H. CHRISTINE REILLY

Corresponding Secretary

Elected Councilors

JOSEPH F. PAGANO

1966-1968

JOHN deS. COUTINHO

1967-1969

HERMAN COHEN

1968-1970

KENNETH WADE THOMPSON

FRANCIS J. HEYDEN, S.J.

BERT N. LA DU

EDWIN S. SCHANZE, *Acting Executive Director*

SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

BERNARD G. STEINETZ, JR., *Chairman*

LEONARD J. LERNER, *Vice-Chairman*

DIVISION OF ANTHROPOLOGY

ALICE JAMES, *Chairman*

ANTHONY L. LaRUFFA, *Vice-Chairman*

DIVISION OF ENVIRONMENTAL SCIENCES

MORRIS SCHAEFFER, *Chairman*

BERNARD DAVIDOW, *Vice-Chairman*

DIVISION OF INSTRUMENTATION

M. JACK FRUMIN, *Chairman*

WILLIAM GRUEN, *Vice-Chairman*

DIVISION OF MICROBIOLOGY

ALICE E. MOORE, *Chairman*

FRANS C. GOBLE, *Vice-Chairman*

DIVISION OF PSYCHOLOGY

MARVIN A. IVERSON, *Chairman*

EDWARD I. GAVURIN, *Vice-Chairman*

SECTION OF CHEMICAL SCIENCES

GEORGE I. FUJIMOTO, *Chairman*

ANTHONY M. TROZZOLO, *Vice-Chairman*

DIVISION OF BIOCHEMISTRY

PHILIP FEIGELSON, *Chairman*

PHILIP SIEKEVITZ, *Vice-Chairman*

DIVISION OF ORGANOMETALLIC CHEMISTRY

ERNEST I. BECKER, *Chairman*

WOLFRAM R. KROLL, *Vice-Chairman*

DIVISION OF POLYMER SCIENCE

EDMUND H. IMMERGUT, *Chairman*

ARTHUR E. WOODWARD, *Vice-Chairman*

SECTION OF GEOLOGICAL SCIENCES

ROBERT E. KING, *Chairman*

PETER H. MATTSON, *Vice-Chairman*

SECTION OF PHYSICAL SCIENCES

LLOYD MOTZ, *Chairman*

ROBIN O. MOTZ, *Vice-Chairman*

DIVISION OF BIOPHYSICS

IRA PULLMAN, *Chairman*

AARON S. POSNER, *Vice-Chairman*

DIVISION OF ENGINEERING

SIDNEY A. SAVITT, *Chairman*

SIDNEY F. BORG, *Vice-Chairman*

DIVISION OF MATHEMATICS

JOSEPH E. HOULE, *Chairman*

MICHAEL I. AISSSEN, *Vice-Chairman*

SECTION OF PLANETARY SCIENCES

NORMAN L. CANFIELD, *Chairman*

GERALD L. SHAK, *Vice-Chairman*

Past Presidents

N. HENRY MOSS

JACOB FELD

BOARD OF TRUSTEES

J. JOSEPH LYNCH, S.J., *Chairman of the Board*

Class of 1965-1968

GORDON Y. BILLARD

BORIS PREGEL

FREDERICK A. STAHL

Class of 1966-1969

HILARY KOPROWSKI

EDWARD J. BURNS

FREDERICK Y. WISELOGLE

Class of 1967-1970

W. STUART THOMPSON

EDMUND J. BLAKE, JR.

MATTHEW ROSENHAUS

Class of 1968-1971

J. JOSEPH LYNCH, S.J.

MARGARET MEAD

EMERSON DAY

MINORU TSUTSUI, *President of the Academy*

N. HENRY MOSS, *Past President*

JACOB FELD, *Past President*

EDWIN S. SCHANZE, *Acting Executive Director*

The Sections and Divisions hold meetings regularly, one evening each month, during the academic year, October to May, inclusive. All meetings are held at the building of The New York Academy of Sciences, 2 East Sixty-third Street, New York, New York 10021.

Conferences are also held at irregular intervals at times announced by special programs.

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES

VOLUME 146, ART. 2 PAGES 361-787

June 28, 1968

Editor-in-Chief
EDWARD M. WEYER

Managing Editor
MARC KRAUSS

Associate Editors
ARTHUR G. LA MIRANDE AND BEATRICE H. RADIN

**CHEMISTRY, PHARMACOLOGY, AND CLINICAL APPLICATIONS
OF PROTEINASE INHIBITORS***

Consulting Editor
NATHAN BACK

Conference Cochairmen
NATHAN BACK AND EBERHARD F. MAMMEN

CONTENTS

Introduction. *By* N. BACK 363

Part I. Chemistry

- The Chemistry of Proteases. *By* BIRGER BLOMBÄCK 364
- The Mechanism of Formation of a Trypsin-Trypsin Inhibitor Complex. *By* M. LASKOWSKI, SR. 374
- Chemical Studies on Kallikrein Inactivator from Bovine Lung and Parotid Gland. *By* F. A. ANDERER AND S. HÖRNLE 381
- Amino Acid Compositions of Bovine Pancreatic Trypsin Inhibitors. *By* L. J. GREENE 386
- Chemistry and Nutritional Significance of Proteinase Inhibitors from Plant Sources. *By* YEHUDITH BIRK 388
- Chemistry and Biochemistry of Proteinase Inhibitors from Mammalian Tissues. *By* H. FRITZ, I. TRAUTSCHOLD, H. HAENDLE, AND E. WERLE 400
- Synthetic Inhibitors of Fibrinolysis: In Vitro and In Vivo Mode of Action. *By* S. OKAMOTO, S. OSHIBA, H. MIHARA, AND U. OKAMOTO 414
- X Studies on the Mechanism of Action of Inhibitors of the Fibrinolysin System. *By* CLARA M. AMBRUS, JULIAN L. AMBRUS, HOWARD B. LASSMAN, AND IRVING B. MINK 430

Part II. Proteinases in Disease States and Their Inhibition

- Pharmacological Actions of Proteolytic Enzymes (Proteases). *By* M. ROCHA E SILVA 448
- Physiologic, Pharmacologic, and Clinical Aspects of Proteinase Inhibitors. *By* E. WERLE, I. TRAUTSCHOLD, H. HAENDLE, AND H. FRITZ 464
- Inhibitors of Kallikrein and Other Proteinases from Animal Blood. *By* E. HABERMANN 479

* This series of papers is the result of a conference entitled Chemistry, Pharmacology, and Clinical Applications of Proteinase Inhibitors, held by The New York Academy of Sciences on September 12 and 13, 1966. The conference was supported in part by a grant from the National Science Foundation.

Proteinases and Proteinase Inhibitors in Experimental Shock States. By N. BACK, H. WILKENS, AND R. STEGER	491
Plasma Protease and Kinin Release with Special Reference to Plasmin. By ULLA HAMBERG	517
Proteases in Inflammation. By MARION I. BARNHART, CLOTILDE QUINTANA, H. L. LENON, G. B. BLUHM, AND JEANNE M. RIDDLE	527
Proteinase Inhibitors in Experimental and Clinical Pancreatitis. By ALAN G. THOMPSON	540
Pancreatitis - Experimental and Clinical: An Evaluation of Trypsin-Kallikrein Inhibitor. By GORDON MCHARDY, LOUIS BALART, AND CLAUDE C. CRAIGHEAD	548
Proteinase Inhibitors in Human Pancreatitis: Digital Computer Analysis of Clinical Research Data. By JOHN H. NODINE AND MELVYN GREBERMAN	564
A Double-Blind Study of Trasylol® in the Treatment of Pancreatitis. By WILLIAM H. BACHRACH AND PHILIP D. SCHILD	580

Part III. Thrombosis and Fibrinolytic Hemorrhage

Antithrombin as Proteinase Inhibitor. By WALTER H. SEEGER	593
Comparative Studies of Some Antifibrinolytic Agents and Proteinase Inhibitors. By T. ASTRUP	601
Anticoagulant Effects of Trasylol®: In Vitro and In Vivo Studies. By C. J. AMRIS AND M. HILDEN	612
Treatment of Fibrinolytic Hemorrhage with Proteinase Inhibitors: A Preliminary Report. By JULIAN L. AMBRUS, CLARA M. AMBRUS, LEON STUTZMAN, GEORGE SCHIMERT, KENNETH R. NISWANDER, MARVIN W. WOODRUFF, AND IMRE V. MAGOSS	625
Role of Urokinase and Tissue Activator in Sustaining Bleeding and the Management Thereof with EACA and AMCA. By L. ANDERSSON, INGA MARIE NILSSON, S. COLLEEN, B. GRANSTRAND, AND B. MELANDER	642
Comparative Activities of Amino Acid and Polypeptide Inhibitors on Natural and Synthetic Substrates. By L. SKOZA, A. O. TSE, M. SEMAR, AND A. J. JOHNSON	659
Indications and Rationale for the Use of Proteinase Inhibitors in Obstetrics. By FRITZ K. BELLER AND MANFRED D. EPSTEIN	673
Treatment of Subarachnoid and Other Intracranial Hemorrhages with Proteinase Inhibitors. By FEDERIGO SICUTERI	682
Experimental Investigations on the Antithromboplastic and Antifibrinolytic Activity of Trasylol®. By S. NORDSTRÖM, BIRGER BLOMBÄCK, M. BLOMBÄCK, P. OLSSON, AND E. ZETTERQVIST	701
Trasylol® Therapy in the Surgical Patient. By P. MATIS AND F. K. MÖRL	715
Theoretical and Practical (Clinical) Considerations Concerning Proteolytic Enzymes and Their Inhibitors with Particular Reference to Changes in the Plasminogen-Plasmin System Observed During Assisted Circulation in Man. By H. GANS, V. SUBRAMANIAN, S. JOHN, A. R. CASTANEDA, AND C. W. LILLEHEI	721
Coagulation and Fibrinolytic Studies Following Use of Proteinase Inhibitors in Prosthetic Surgery. By LOUISE LANG PHILLIPS, ROBERT WEISS, AND CHARLES WOLF	737
Recognition and Treatment of Postoperative Bleeding Associated with Open-Heart Surgery. By DAVID A. TICE AND MELVIN H. WORTH, JR.	745
Natural Proteinase Inhibitors in Extracorporeal Circulation. By EBERHARD F. MAMMEN	754
The Study of Fibrinolytic and Coagulation Factors During Open-Heart Surgery. By HAROLD K. TSUJI, JOHN V. REDINGTON, JEROME HAROLD KAY, AND RUDOLF K. GOESSWALD	763
Proteinase Inhibitors in Portasystemic Shunts. By CARLO E. GROSSI, BO PRYTZ, AND LOUIS M. ROUSSELOT	778