Current Concepts of Basic Actions and Clinical Applications

Compiled and Edited by

JOHN R. DERRICK, M.D.

Professor and Chief
Division of Thoracic
and Cardiovascular Surgery
University of Texas Medical Branch
Galveston, Texas

M. MASON GUEST, Ph.D.

Professor and Chairman
Department of Physiology
University of Texas Medical Branch
Galveston, Texas

CONTRIBUTORS

Benjamin Alexander Marion I. Barnhart Walter L. Bloom Ted P. Bond Richard W. Brown John R. Derrick Lars-Erik Gelin John Gilroy Magnus I. Gregersen M. Mason Guest Robert M. Hardaway Lerner B. Hinshaw Harry Hint Paul M. James, Jr. Robert D. Langdell Per H. Langsjoen

William H. Lee Richard Lillehei William G. Manax. J. Sterling Meyer John A. Moncrief Eric Ponder Raymond C. Read Thomas K. Shires



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CONTRIBUTORS

BENJAMIN ALEXANDER, M.D.

Senior Investigator New York Blood Center New York, New York

MARION I. BARNHART, Ph.D.

Wayne State University School of Medicine Detroit, Michigan

WALTER L. BLOOM, M.D.

Assistant to the Vice President for Academic Affairs and Professor of Applied Biology Georgia Institute of Technology Atlanta, Georgia

TED P. BOND, M.A.

Research Assistant Professor Department of Physiology University of Texas Medical Branch Galveston, Texas

RICHARD W. BROWN

Clinical Associate
Division of Thoracic and Cardiovascular Surgery
University of Texas Medical Branch
Galveston, Texas

JOHN R. DERRICK, M.D.

Professor and Chief Division of Thoracic and Cardiovascular Surgery University of Texas Medical Branch Galveston, Texas vi Dextrans

LARS-ERIK GELIN, M.D.

Professor, Department of Surgery University of Gothenburg Gothenburg, Sweden

JOHN GILROY

Professor and Chairman
Department of Neurology
Wayne State University School of Medicine
Detroit, Michigan

Magnus I. Gregersen, Ph.D.*

Dalton Professor of Physiology Laboratory of Hemorheology College of Physicians and Surgeons Columbia University New York, New York

M. MASON GUEST, Ph.D.

Professor and Chairman Department of Physiology University of Texas Medical Branch Galveston, Texas

ROBERT M. HARDAWAY

Col. MC USA 97th General Hospital Frankfurt, Germany

LERNER B. HINSHAW, Ph.D.

Professor, Department of Physiology University of Oklahoma School of Medicine Oklahoma City, Oklahoma

HARRY HINT, M.D.

Assistant Director of Research Pharmacia, A. B. Uppsala, Sweden

^{*} deceased

PAUL M. JAMES, JR., M.D.

Director, Residency and Internship Program Hahnemann Medical College and Hospital Philadelphia, Pennsylvania

ROBERT D. LANGDELL, M.D.

Professor of Pathology University of North Carolina School of Medicine Chapel Hill, North Carolina

PER H. LANGSJOEN, M.D.

Chief of Cardiology Scott and White Clinic Temple, Texas

WILLIAM H. LEE, M.D.

Chairman, Division of Thoracic Surgery Medical College of South Carolina Charleston, South Carolina

RICHARD LILLEHEI, M.D.

Professor of Surgery University of Minnesota Medical School Minneapolis, Minnesota

WILLIAM G. MANAX, M.D.

Assistant Professor of Surgery University of Minnesota Medical School Minneapolis, Minnesota

J. STERLING MEYER

Professor and Chairman Department of Neurology Baylor College of Medicine Houston, Texas

JOHN A. MONCRIEF, M.D.

Director, United States Army Surgical Research Unit Brook Army Medical Center Fort Sam Houston, Texas viii Dextrans

ERIC PONDER, M.D.

Investigator Institute de Pathologie Gellulaire Kremlin-Bicêtre Paris, France

RAYMOND C. READ, M.D.

Chief of Surgical Service Veterans Administration Hospital Little Rock, Arkansas

THOMAS K. SHIRES

Veterans Administration Hospital Department of Urology University of Oklahoma Medical Center Oklahoma City, Oklahoma

PREFACE

DURING the past two decades, numerous research and clinical reports about the benefits—and hazards—of dextrans in cardiovascular and related disease have appeared in the literature. Many questions still remain unanswered about these agents, but the consensus is that they do have therapeutic value for some conditions.

Because of the widespread interest and unanswered questions, it seemed obvious that a symposium, at which experiences, ideas, and opinions could be exchanged by authorities knowledgeable about dextrans, would be valuable. Such a symposium would also provide a way to disseminate currently available knowledge, both research and clinical, to a large segment of the medical population. Therefore, several interested organizations elected to sponsor the First International Symposium on Dextrans which was held in Galveston, Texas, on May 19 and 20, 1968.

This volume is made up of discussions given at that symposium. Those interested in the subject of dextrans will find this book most informative, both as to what is now known and as to what questions are under investigation.

JOHN R. DERRICK, M.D. M. MASON GUEST, PH.D.

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SINCERE appreciation is expressed to Abbott Laboratories for their generous educational grant in support of the First International Symposium on Dextrans.

Co-sponsors of the symposium were the Texas Heart Association, the Council on Circulation of the American Heart Association, The University of Texas Medical Branch Postgraduate Education Division, the University of Minnesota Medical School, and the Biomedical Division of the Georgia Institute of Technology.

The Editors and the Sponsors wish to thank all of those persons who helped to make the symposium a success.

The opening remarks were made by Doctor Truman Blocker who had over a decade previously helped to stimulate interest in the first conference concerning the Dextrans.

Special notice should be taken of Pharmacia Laboratories who assisted with the cost of editing and compiling the manuscript.

CONTENTS

	Page
Contributors	v
Preface	ix
Acknowledgements	xi
Chapter	
I. Relationships Between the Chemical and Physico- chemical Properties of Dextran and its Pharmaco- logical Effects Harry Hint	3
II. Effects of Artificial Expander Agents on Blood Viscosity Magnus I. Gregersen	27
III. Hypervolemia and Hemodilution in Certain Effects of Low Molecular Weight Dextran *Raymond C. Read	39
IV. Interaction of Dextrans with Serum Proteins, and Their Interaction with Red Cells and Platelets Eric Ponder	54
V. Effect of Dextran on Renal Hemodynamics Lerner B. Hinshaw and Thomas K. Shires	62
VI. Dextrans in Organ Transplantation William G. Manax	73
VII. Specificity of Sharply Cut Dextran Fraction to Inhibit Thrombus Propagation John A. Moncrief	77
DISCUSSION—William H. Lee	82

V	1	ч	7
Λ	1	١	

Dextrans

VIII. COATING ACTION OF DEXTRANS Walter L. Bloom	86
IX. Effects of Dextran and Other Macromolecules on Coagulation and Hemostasis Benjamin Alexander	93
X. Adsorption of Radioactive Dextran on Red Cells Robert D. Langdell	130
XI. Rheological Effects of Dextran Lars-Erik Gelin	137
XII. Effects of Dextran on Microcirculatory Flow M. Mason Guest and Ted P. Bond	154
XIII. PLATELET FUNCTION IN ACUTE STROKE PATIENTS TREATED WITH RHEOMACRODEX Marion I. Barnhart, John Gilroy and J. Sterling Meyer	162
XIV. Dextrans in Shock: Experimental and Clinical Observations *Richard Lillehei	180
XV. Dextrans in Battle Casualties: Benefits and Hazards Paul M. James, Jr	186
XVI. Dextrans in Ischemic States John R. Derrick and Richard W. Brown	194
XVII. CLINICAL EXPERIENCE WITH LOW MOLECULAR WEIGHT DEXTRAN IN ISCHEMIC PROBLEMS Per H. Langsjoen	203
XVIII. Summary M. Mason Guest	209
Index	211

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RELATIONSHIPS BETWEEN THE CHEMICAL AND PHYSICOCHEMICAL PROPERTIES OF DEXTRAN AND ITS PHARMACOLOGICAL EFFECTS

HARRY HINT

THE structural formula of dextran is shown in Figure I-1. This material was considered initially to be devoid of pharmacological effects apart from those concerned with its plasma volume expanding activity.

However, it is now known that dextran has several distinct pharmacological effects. These may be divided into two categories: effects which are determined by the physicochemical properties of

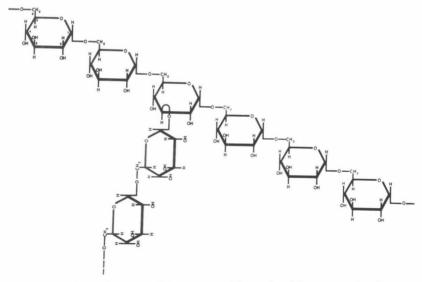


FIGURE I-1. A fraction of the structural formula of dextran molecule.

4 Dextrans

dextran solutions used and effects which are specific to dextran molecules.

Three different pharmacological effects of dextran are of definite clinical interest: plasma volume expansion, flow improvement, and antithrombotic effect. Dextran also lowers plasma lipid levels. This may also be of clinical interest.

EFFECTS DETERMINED BY PHYSICOCHEMICAL PROPERTIES

Plasma volume expansion and flow improvement by dextran depend on the physicochemical properties of the solutions used. The principal factors that determine the physicochemical properties of dextran solutions are a) the molecular size, b) the molecular size distribution, and c) the final concentration of dextran in solution. Since properties such as colloid osmotic pressure, colloid osmotic effects, water-retaining capacity, viscosity, the effects of dextran on red cell aggregation and transport of dextran through capillary membranes may be varied profoundly by varying the physicochemical properties of dextran solutions, it is obvious that a study of the physicochemical properties of dextran solutions in relation to the molecular weight and concentration of dextran forms a basis for understanding the pharmacological effects of dextran.

The purpose of this paper is, therefore, to summarize some elementary facts, based mainly on the experimental data from our Research Department in Uppsala.

The relationships between the colloid concentration and colloid osmotic pressure (c.o.p.) for a dextran fraction comparable to clinical dextran (Macrodex®) and for normal plasma are presented in Figure I-2 and equations (1), (2), and (3).

$$\pi = \frac{RT}{M} C \tag{1}$$

$$\pi = \frac{RT}{M} C + AC^2$$
 (2)

$$\frac{\pi}{C} = \frac{RT}{M} + AC \tag{3}$$