DEXTRANS

Current Concepts of Basic Actions and Clinical Applications

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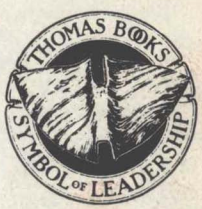

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PREFACE

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.
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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.

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DEXTRANS

Current Concepts of Basic Actions and Clinical Applications

I

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

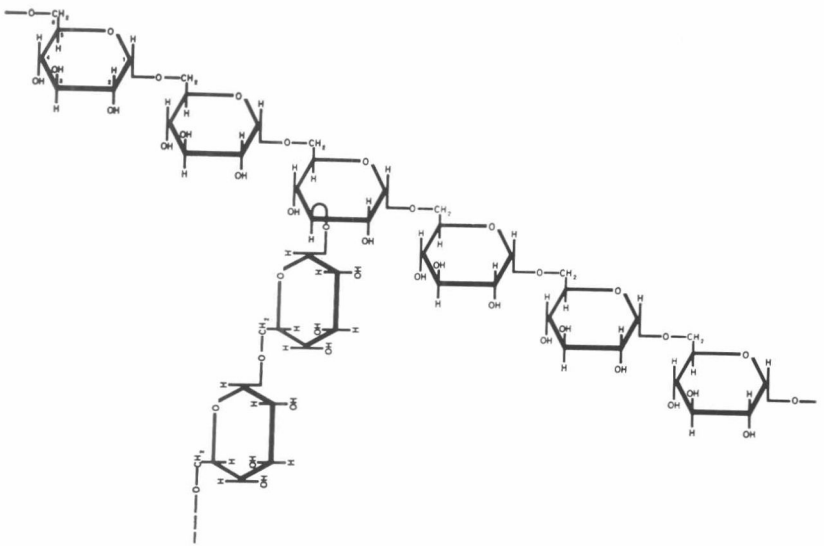

FIGURE I-1. A fraction of the structural formula of dextran molecule.

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).

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

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

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