POLYMER SCIENCE AND TECHNOLOGY

Volume 7

POLYMER SCIENCE AND TECHNOLOGY
Volume 7

BIOMEDICAL APPLICATIONS OF POLYMERS

Edited by
Harry P. Gregor

Department of Chemical Engineering
and Applied Chemistry
School of Engineering and Applied Science
Columbia University
New York, New York

PLENUM PRESS · NEW YORK AND LONDON

Library of Congress Cataloging in Publication Data

Main entry under title:

Biomedical applications of polymers.

(Polymer science and technology; v. 7)
"A symposium held by the American Chemical Society, Division of Organic Coatings and Plastics Chemistry, in Chicago, Illinois, in August, 1973."
Includes bibliographical references and index.
1. Polymers in medicine–Congresses. 2. Biomedical materials–Congresses. I. Gregor, Harry P. II. American Chemical Society. Division of Organic Coatings and Plastics Chemistry. III. Series. [DNLM: 1. Biomedical Engineering–Congresses. 2. Polymers–Congresses. QT34 A514b 1973]
R857.P6B56 610'.28 75-6846
ISBN 0-306-36407-7

Proceedings of a symposium held by the American Chemical Society,
Division of Organic Coatings and Plastics Chemistry,
in Chicago, Illinois, in August, 1973.

A Division of Plenum Publishing Corporation
227 West 17th Street, New York, N.Y. 10011

United Kingdom edition published by Plenum Press, London
A Division of Plenum Publishing Company, Ltd.
Davis House (4th Floor), 8 Scrubs Lane, Harlesden, London, NW10 6SE, England

Printed in the United States of America

POLYMER SCIENCE AND TECHNOLOGY
Volume 7

BIOMEDICAL APPLICATIONS OF POLYMERS

POLYMER SCIENCE AND TECHNOLOGY

Volume 1 • STRUCTURE AND PROPERTIES OF POLYMER FILMS
Edited by Robert W. Lenz and Richard S. Stein • 1972

Volume 2 • WATER-SOLUBLE POLYMERS
Edited by N. M. Bikales • 1973

Volume 3 • POLYMERS AND ECOLOGICAL PROBLEMS
Edited by James Guillet • 1973

Volume 4 • RECENT ADVANCES IN POLYMER BLENDS, GRAFTS, AND BLOCKS
Edited by L. H. Sperling • 1974

Volume 5 • ADVANCES IN POLYMER FRICTION AND WEAR (Parts A and B)
Edited by Lieng-Huang Lee • 1974

Volume 6 • PERMEABILITY OF PLASTIC FILMS AND COATINGS
TO GASES, VAPORS, AND LIQUIDS
Edited by Harold B. Hopfenberg • 1974

Volume 7 • BIOMEDICAL APPLICATIONS OF POLYMERS
Edited by Harry P. Gregor • 1975

This volume is dedicated to

Maurice B. Visscher, M. D.

Professor Emeritus of Physiology, The Medical School,
University of Minnesota, a pioneer in interdisciplinary
studies which now constitute the field of Bioengineering

Foreword

The intense integration of physical and biological science that has developed in the last several decades has led to major problems in the wise use of available knowledge, both conceptual and factual. In the last century, before the separation of the physical and biological sciences became distinct, all the knowledge recognizable as bearing on a biological problem was relatively small and one man, albeit often an exceptional one, could contribute importantly to the advance of that knowledge.

Now the recognizable knowledge pertaining to living systems is much larger, our questions are correspondingly more complex, and our goals are set higher. As many of the papers in this symposium show, we aim beyond analyzing injury and disease toward the synthetic goals of imitating arrested or inadequate life processes and reconstructing maimed organisms. Such activity supposes adequate knowledge of the natural functions to be replaced, and, because artificial materials are seldom indistinguishable from their natural archetypes, the prosthetic attempt raises a host of new questions about the reactions between artificial and living materials in intimate contact.

Among problems of this sort are: thromboresistance, the quality by which an artificial surface avoids activating clotting enzymes or allowing cells to stick or be activated for thrombus formation; tissue compatibility; maintenance of chemical and mechanical integrity of artificial materials in contact with body fluids; and absence of tissue irritation. All of these desiderata have been considered here, some from several points of view.

I am especially familiar with the thromboresistance problem, which has turned out to be surprisingly difficult, at the level both of its amelioration and of its understanding. Duplicating the passivity of vascular endothelium to blood seemed at first to be an easy task. It soon became clear that understanding of the endothelial-blood symbiosis was complex and inadequate to the specification or development of artificial thromboresistant materials. Supposed solutions to the problem fell short of what was desired. Some of these attempts raised their own problems whose analysis represented a diversion of effort from the main goal, but others placed fundamental problems in a new light. Thus, some work on thromboresistance (including much of that reported here) contributed not only to the improvement of thromboresistant materials but also to a better understanding of the mechanism of thrombosis in vivo and various coagulopathies. The synthetic goal stimulated analysis of normal and abnormal function, and it brought new disciplines into contact with a fundamental biological problem.

Chemistry has played a special role in sustaining some contact between medical and biological science and physical science. Sight was never lost of the fundamental chemical nature of life processes. Biochemistry was one of the earliest, most heavily populated of the bio-something sciences. Still, the exchange of knowledge and overlap of education between the industrially oriented and the biochemically oriented chemist was seriously limited. A major conceptual difference resulted insofar as the former group was concerned primarily with synthesis while the latter was largely concerned with the analysis of pre-existing, highly complex systems.

A number of presentations here deal with model systems whose utility may reach to both an understanding of natural processes and a basis for exploiting natural processes for new purposes or for replacing them to compensate for disease or injury. The synergistic effect of contiguous efforts at synthesis and analysis is great even when final benefits are not completely responsive to original goals.

This timely symposium, therefore, strikes me as rich, not only for its specific content and its testimony of solid technical progress, but also because it shows a new confluence of thought between the analyzers of natural

chemical processes and materials and the synthesizers of artificial chemical processes and materials which augment, replace, and emulate nature. The range of problems considered here precludes a full-faceted, definitive treatment of any one, but it shows a healthy catholicity of thought and some surprising commonality of approach to diverse problems of creating compatible and synergistic juxtapositions of artificial and living materials.

E. F. Leonard

Columbia University
December, 1974

Contents

THE HYDRATION OF PHOSPHOLIPID FILMS AND ITS RELATIONSHIP TO PHOSPHOLIPID STRUCTURE

J. H. Hasty* and G. L. Jendrasiak

Biophysics Division and
Program in Bioengineering
University of Illinois
Urbana, Illinois 61801

Little work has been done on the hydration of lipids and its concomitant effect on their electrical conductivity. Since the membrane-water interface is thought to play an important part in membrane permeability, such studies may have biological relevance. The nature of the water bound by the lipids might be expected to play some part in the structure of the membrane interface region in membranes containing these lipids. Elworthy (1,2) has obtained the adsorption isotherms for certain phospholipids, whereas Jendrasiak (3) has investigated the hydration and concomitant electrical conductivity of egg phosphatidylcholine. The purpose of the work reported in this paper is to determine the adsorption isotherms for egg phosphatidylcholine (PC), egg phosphatidylethanolamine (PE), and bovine phosphatidylserine (PS), in both their lyso and diacyl forms. The effect of complexation of PC with cholesterol and the effect of varying the number of double bonds in the hydrocarbon chains are also studied. In this way, it is hoped to obtain some idea as to the relative contribution to hydration of these lipids by the hydrocarbon chains and polar head groups, respectively. Also, the effect of varying the nature of the polar head group on lipid hydration can be studied. The effect of the hydration on electrical conductivity of the lipids is also studied. The complete study will be published (4).

*Kendall Research Center, Barrington, Ill., 60010

MATERIALS AND METHODS

Lipid films were cast, from the appropriate lipid dissolved in chloroform, on thin teflon strips. After removal of the solvent the films were placed in a Cahn G-2 electrobalance operating in the "remote weighing" mode. The entire assembly was separated from the balance controls and placed in a chamber where both the relative vapor pressure (P/Po) and temperature (22 ± 0.]5°C) were controlled. The controlled humidities were obtained by means of saturated salt solutions. The electrical conductivities of the films were measured using films cast on quartz and an electrometer circuit.

RESULTS AND DISCUSSION

From Fig. 1 it can be seen that egg PC, in its diacyl form, exhibits, according to Brunauer's (5) classification scheme, a type II or IV isotherm. Type II isotherms are frequently encountered and represent multilayer physical adsorption by non-porous solids or microporous solids. From the inflection points of such a plot, the amount of water necessary for the formation of an adsorbed monolayer can be obtained: We judge this value to be near 2.0 water molecules adsorbed per lipid molecule. Our scanning electron micrographs do reveal some structure in the egg PC films which might represent a certain degree of porosity.

Egg PE and bovine PS, in their diacyl forms display type III or V isotherms. Such isotherms are indicative of no rapid initial uptake of water vapor and occur when the forces of adsorption in the first monolayer are relatively small.

All of the phospholipids, in their lyso form display type III (or V) isotherms, again suggesting no rapid initial uptake of water, as seen in Fig. 2.

Type IV and V isotherms exhibit saturation which apparently reflects capillary condensation.

Since the isotherms for the diacyl and lyso form of PC differ in shape, it appears that removal of a hydrocarbon chain in PC does have a significant effect on the water adsorption characteristics. In the case of PE, on the other hand, the isotherms for the lipid in both the

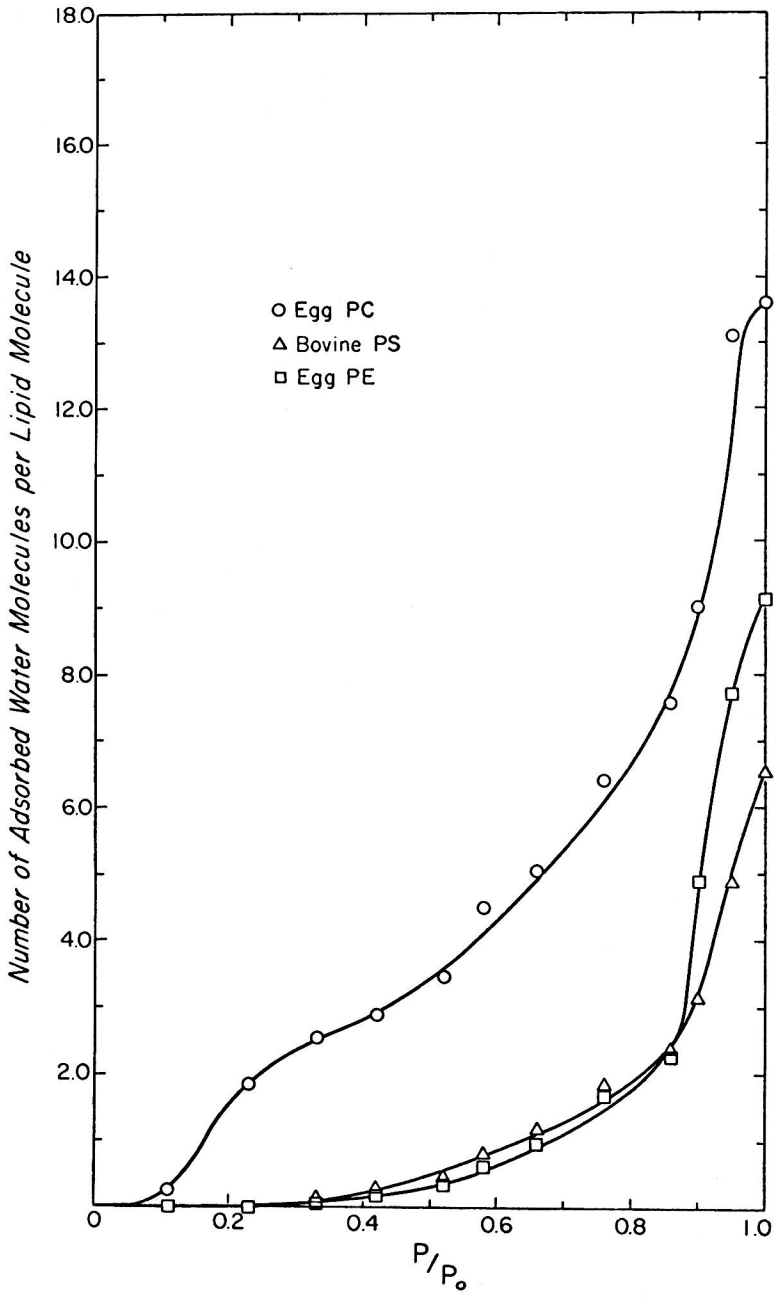
Number of Adsorbed Water Molecules per Lipid Molecule
18.0
16.0
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0
0.2
0.4
0.6
0.8
1.0
P/Po
O Egg PC
Δ Bovine PS
□ Egg PE

Fig. 1

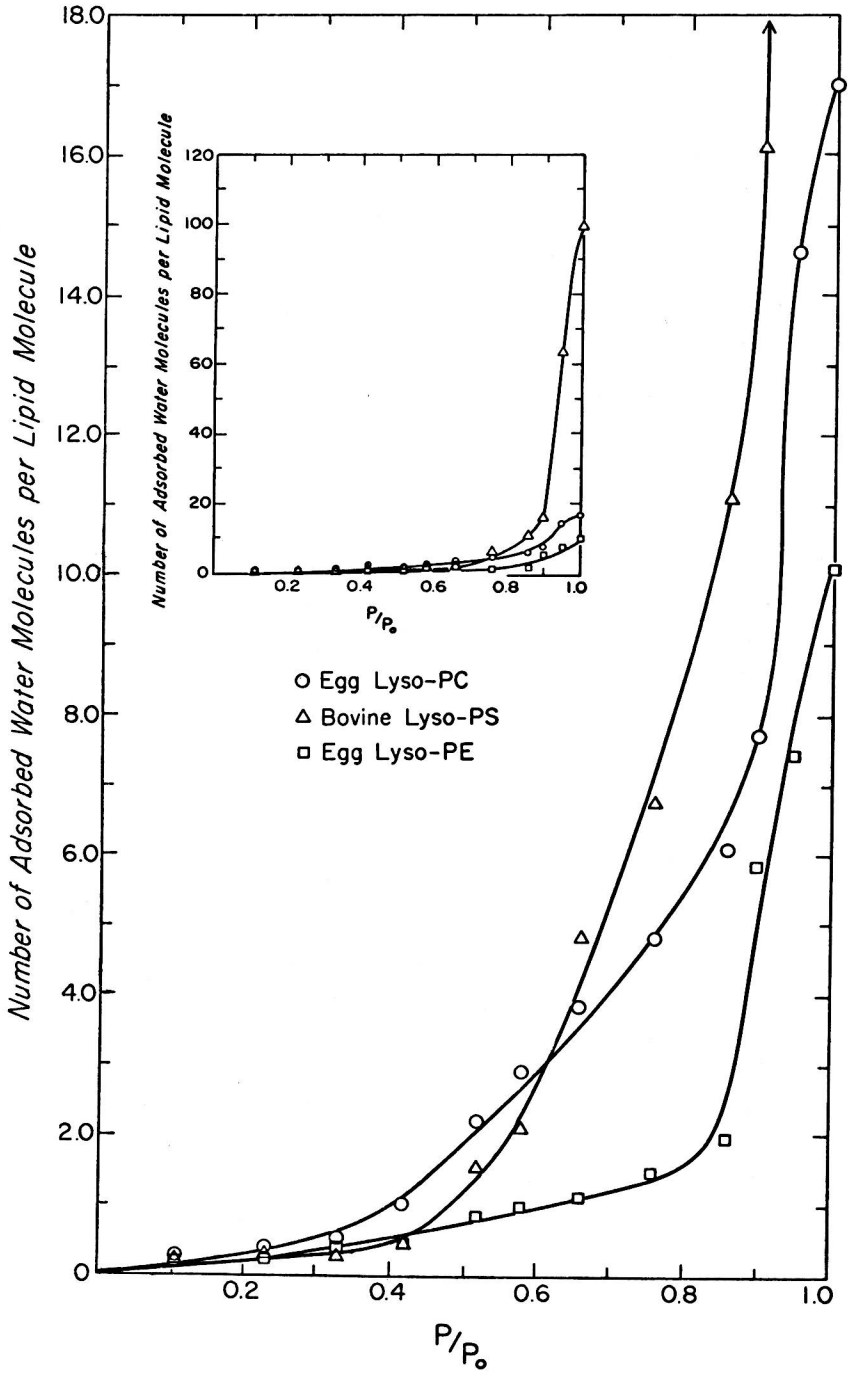
Number of Adsorbed Water Molecules per Lipid Molecule
P/P₀
Egg Lyso-PC
Bovine Lyso-PS
Egg Lyso-PE
Number of Adsorbed Water Molecules per Lipid Molecule
P/P₀

Fig. 2

diacyl and lyso forms are almost identical; this suggests that the polar head group plays the dominant role in the water adsorption behavior of this lipid. The lyso form of PS adsorbs more water than does the diacyl form at all vapor pressures. Particularly striking is the fact that lyso-PS adsorbs some one hundred molecules of water per molecule of lipid at a vapor pressure of 1.0, whereas for the diacyl form of PS, the figure is closer to six. This suggests that the removal of a hydrocarbon chain has a very strong influence on the water adsorption of PS. This deviation of the lyso-PS isotherm from the diacyl PS isotherm does not become apparent until the lyso-PS has adsorbed about one water molecule per two molecules of lipid. It may well be that at this amount of water, the polar head group of the serine is ionized and the sample micellizes with ionic regions in between the micelles.

The effect of the complexation of cholesterol with egg PC (1:1,mole:mole) is shown in Fig. 3. The isotherm displayed by the complex is a type II (or IV) suggesting that the cholesterol molecule has no strong effect on the configuration of the polar head group of PC. The amount of water adsorbed per PC molecule is increased, over the entire vapor pressure range, from the corresponding values with no cholesterol present. Since the cholesterol itself adsorbs a negligible amount of water compared to PC, the increase may be due to some effect on the PC by the cholesterol. We postulate that the effect is due to an increase in the size of the cavity occupied by the PC head group, allowing more water to enter the cavity. It has been found by other methods that complexing cholesterol to PC increases the water bound to PC; our results support such a conclusion.

Fig. 4 illustrates the effect of increasing the number of double bonds in the hydrocarbon chains of diacyl PC, on the water adsorption characteristics of the lipid. Increasing unsaturation increases the amount of water adsorbed at all vapor pressures. There is some question as to whether the increase in water adsorption with unsaturation arises because of double bonds in both hydrocarbon chains, or in only one of the hydrocarbon chains. From Fig. 4, one can see that the basic character of the isotherm is established by the polar headgroup with the hydrocarbon chains having a strong modulating effect on the isotherms. All of the isotherms remain type II (or IV), suggesting that the head group

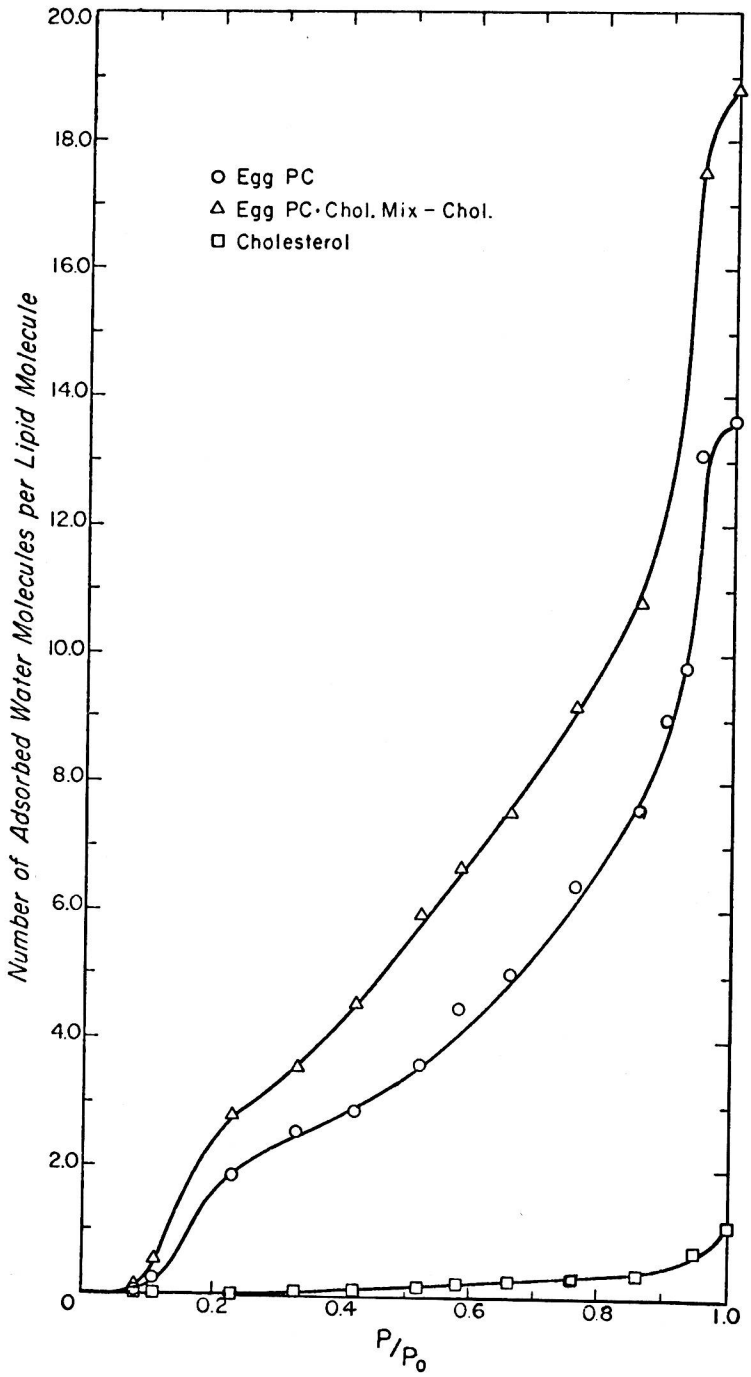

Fig. 3