Liposome Technology

Volume I

Preparation of Liposomes

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PREFACE

Targeting of drugs through carrier systems that would, ideally, ignore the normal part of the body and home to diseased areas in need of treatment, has been for the most part of this century only a little more credible than the philosophers' stone. Recently, however, parallel but separate developments have began to transform drug targeting from a striking intellectual concept to a powerful exact science. First, a wide array of biological molecules are now recognized to possess ligands with specific affinity for respective receptors on the cell's surface. Second, the technical breakthrough in the production of monoclonal antibodies has made available in large quantities immunoglobulins that are highly specific for individual antigens. Such molecules form the basis of the modern approach to receptor (including cell surface antigens in a wider sense) mediated drug delivery. Further, they are being instrumental to a third development namely, the emergence of sophisticated artificial carriers exemplified by liposomes.

Liposomes are unusually versatile, notably in size, surface charge, lipid composition, the plethora of pharmacologically active molecules they can accommodate in both the aqueous and lipid phase and permeability to entrapped molecules. This not only has led to a number of ingenious techniques for the preparation of liposomes with practical advantages, it has also helped to adjust the system to a multitude of uses in cell biology, pharmacology, immunology, genetic engineering, and therapeutic and preventive medicine. A significant advance has also been made by our ability to control the fate of liposomes and the effect of their contents in vivo. This was achieved through knowledge of factors in the body that influence liposomal behavior. Modification of the structure of liposomes in a variety of ways enables us to harness such behavior to suit particular needs. The drug-carrier potential of liposomes has now acquired a new important dimension through the use of targeted molecules. Receptor-recognizing antibodies, glycoproteins, and glycolipids anchored onto the surface of liposomes are able to mediate uptake of the liposomal moiety and its drug contents by target cells. There are clear indications that targeting of liposomes can occur in vivo, at least for cells to which the carrier has immediate access.

Although the role of liposomes in drug targeting has been discussed extensively in several reviews and books, there has been no comprehensive coverage of related methodology. This book constitutes the first attempt to put together all aspects of liposome technology as applied to medical sciences. Contributors were encouraged to place emphasis on methodology as experienced in their own laboratory and in certain cases, the same methodologies are described by more than one laboratory. This was a deliberate policy: several aspects of liposome technology are still not an exact science and personal experience coming from more than one source was thought likely to help everyone, especially those who have just entered the field. A typical chapter includes (1) an introductory section directly relevant to the author's subject with concise coverage of relevant literature; (2) a detailed methodology section presenting experiences from the author's laboratory and a few examples of actual application of the method presented; (3) a critical discussion to enable the reader to appreciate the advantages and disadvantages of the method and compare it with those developed by other workers. The fifty chapters contributed have been distributed logically into three volumes. Volume I deals directly with methods for the preparation of liposomes and auxiliary techniques. Volume II describes procedures for the entrapment of a number of drugs, including genetic material, into selected types of liposomes. These two volumes contain virtually all methods available for efficient drug entrapment in the presence or, preferably, absence of organic solvents. Finally, Volume III is devoted to the growing variety of techniques yielding targeted liposomes and to approaches of studying liposomal behavior in the biological milieu both in vitro and in vivo.

It has been a pleasure for me to edit this book and to come into close contact with the thoughts and experiences of so many liposomologists. It is hoped that in view of the great

and ever increasing number of workers in the field and the significance that liposomes have attained in a wide spectrum of disciplines, this multi-authored book in liposome technology will serve a useful purpose. I take this opportunity to thank all authors for their enthusiastic response to my invitation to contribute. I am also grateful to Mrs. M. Moriarty for editorial assistance and to CRC Press, Inc. personnel for their valuable help and truly professional cooperation.

Gregory Gregoriadis
June 1983

THE EDITOR

Gregory Gregoriadis, Ph.D., is a senior member of staff at the Medical Research Council's Clinical Research Centre, Harrow, Middlesex, England. He received his first degree in Chemistry from the University of Athens and his M.Sc. and Ph.D. in Biochemistry from McGill University. He has carried out research in as diverse fields as the metabolism of trace metals and the interaction of plasma glycoproteins with hepatic receptors. Since 1970 he has worked, published, and lectured extensively on the targeting of drugs via liposomes. Dr. Gregoriadis' interest in drug targeting is reflected in his founding in 1978 the Gordon Research Conference Series on "Drug Carriers in Biology and Medicine" of which he was the first Chairman and in 1981 the NATO Advanced Studies Institute Series "Targeting of Drugs" of which he is the Director. He has also been the editor of *Drug Carriers in Biology and Medicine* and the senior editor of *Liposomes in Biological Systems* and *Targeting of Drugs*.

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