The mechanism of ectonuncleotidase upregulation by aspirin is unknown. Since previous results using isolated renal glomeruli or aorta fragments in-vitro show similar nucleotidase enhancement induced by other prostacyclin-inhibiting drugs (e.g. minoxidil) as well as by cAMP-increasing drugs (e.g. caffeine, isoprenaline), we feel that this effect may be mediated by the adenylyl cyclase system (Cheung et al 1991). Interestingly, both in-vitro as well as following aspirin administration in-vivo, these effects of aspirin could be observed already after a 30-min incubation period, or intraperitoneal injection, respectively.

Although Crutchley et al (1980) studied ADPase and aspirin in bovine lung endothelial cells in-vitro, their data do not contradict our present results obtained in human endothelial cell cultures. Those authors concluded that 1 mM aspirin had no inhibiting effect on the metabolism of ADP by endothelial cells. In contrast, instead of a reduction of the ectoenzyme activity, a slight enhancement of nucleotide conversion was shown, even after a short incubation period (15 min) with aspirin. Thus, from their data it also appears that aspirin is able to induce increased conversion of the added nucleotides suggesting upregulation of ectoenzyme activity.

From the present results we conclude that one of the antithrombotic mechanisms of aspirin may involve enhancement of ecto ATP-diphosphohydrolase activity of cultured human endothelial cells. This novel aspect of aspirin action may increase our understanding of this intriguing drug.

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Book Review

Ophthalmic Drug Delivery Systems
(Drugs and the Pharmaceutical Sciences/58)
Edited by Ashim K. Mitra
Published 1993 Marcel Dekker, Inc., New York
536 pages
ISBN 0 8247 8806 0 $165.00

This is volume 58 of the very successful series, under the general editorship of James Swarbrick, which has covered every conceivable area of the pharmaceutical sciences and yet still expands. This volume deals with delivery of drugs to the eye, and is a timely volume given the increasing interest in routes of delivery which offer an alternative to the oral route for the systemic delivery of biological agents, particularly those compounds which have properties which disallow oral absorption. The ocular route has been explored for the delivery of insulin, among other proteins and peptides (dealt with in two chapters), and thus requires serious consideration as a route of drug entry, which is achieved mainly via the capillary blood supply of the conjunctival sac. However, the eye is an important organ with other functions and the first chapter deals with both a review of ocular drug delivery and iatrogenic ocular states arising from topical delivery of drugs and vehicles. The remaining 20 chapters take the reader logically through ocular anatomy and physiology, precorneal, corneal and post-corneal factors in drug delivery in a section entitled Fundamental Considerations. Transport Models are dealt with in five chapters in part II, dealing with ocular pharmacokinetics and pharmacodynamics, cell culture systems, and animal studies inter alia. Disease states such as bacterial and viral keratitis, conjunctivitis and corneal trauma obviously impact on drug delivery. The chapter on disease state models deals with animal models and not mathematical models of these conditions. Traditional delivery systems are dealt with in a lone chapter in Part III. Part IV introduces advanced delivery and attacks such approaches as mucoadhesion, ocular inserts, nanoparticles and liposomes as vehicles. Chemical delivery systems derived from drugs with modified structures to enhance delivery has a separate chapter in Part V.

Ocular iontophoresis, the new ophthalmic delivery systems known as NODS and ocular penetration enhancers are included under novel delivery systems, but quibbles about advanced and novel are probably pointless. Non-corneal delivery by the non-routine routes of intracameral, intravitreal and retinal delivery are also reviewed and there is a complementary chapter on the use of systemic medication for ophthalmic diseases.

The cost of each volume in the series is high for the UK market (and no doubt many others); this volume is no exception, but the cost is worthwhile given the wide range and detail of the information which is brought together. Most of the names that one would expect to see appear in the list of authors including such luminaries as Kenneth Himmelstein, Joseph Robinson, Vince Lee, Ronald Schoenwald, Jörg Kreuter and Ian Kellaway. One might ask who such volumes are aimed at. Obviously companies which are developing ophthalmic products and postgraduate researchers involved with ophthalmic delivery would need a copy close at hand, but such weighty compendia almost contain too much information and certainly cannot be read from cover to cover if one wishes to do anything original oneself. Academic libraries in Schools of Pharmacy should have such volumes on their shelves for all students to dip into, and one would hope that departments of ophthalmology would have sufficient interest in the future possibilities of the ophthalmic route that they too would purchase. The shear volume of material, even in what might seem a narrow field as the one covered in this book, is such that the primary purpose of such tomes is to collect and connect and scrutinize the literature and sift ideas. Ashim Mitra is to be congratulated on bringing the book to fruition and logically arranging the chapters to provide excellent coverage of the field.

A. T. FLORENCE
THE SCHOOL OF PHARMACY, LONDON, UK

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Book Review

Liposomes: From Physics to Applications
By D. D. Lasic
Published 1993 Elsevier Science Publishers B.V., Amsterdam
580 pages
ISBN 0 444 89548 5 Dfl.475·00 US $271·50

As the title suggests this book attempts to cover the subject of liposomes from the physics of bond angles in fatty acids through to commercial-scale production and use in cosmetics. This panoply is covered in four parts incorporating twenty four chapters and eight appendices totalling over 500 pages, which reflects the spread of liposomal research into a wide variety of scientific fields. The four parts cover a general introduction to liposomes, application of liposomes in basic sciences, in pharmacology and medicine, and other miscellaneous areas. The general introduction covers the chemistry and physics of lipids and lipid aggregates, preparation and mechanisms of liposome formation and methods of characterization. Basic physicochemical data is provided on the most common phospholipids used in liposome formation along with newer synthetic and polymerizable surfactants. The physical properties of these amphiphiles and how this affects their ability to form vesicular structures is discussed and all the common methods of liposome preparation are presented in detail. However, the chapter on characterization methods is relatively short in comparison with the preceding chapters. Liposomes in basic science is covered by chapters on application in theoretical sciences, biophysics, evolution, chemistry and protein reconstitution. The chemistry chapter includes the use of liposomal systems in photosynthetic studies, catalysis, and in separation and purification techniques. Some of these sections are relatively small but do provide a basic insight into the subject. The largest part of the book concerns itself with the application of liposomes in pharmacology and medicine and covers subjects such as drug delivery, treatment of cancer and infectious diseases, use as immunoadjuvants, topical routes of administration and site-specific drug delivery. The drug delivery chapter for example contains information on the toxicology of liposomes, their stability in biological fluids and the development of Stealth systems. This latter subject recurs in the chapter on cancer therapy; however, there is little repetition of content since the topic is approached this time from the disease. The final part covers a variety of applications including cosmetics, genetic engineering, diagnostics, food and industrial manufacturing. This latter chapter presents the problems associated with manufacture and the need to achieve a sterile, stable and pharmaceutically acceptable product. It concludes by describing the techniques that companies have used to overcome these difficulties and the liposomal products that are currently available.

For the newcomer to liposomal research the book undoubtedly provides a comprehensive introduction to liposomes and the techniques and science associated with this research field. The more experienced individual will find something of interest in its content, but also as a useful reference source. The appendices, for example, contain information on size of phospholipid head groups and bilayer thickness, whilst the main text provides data on fatty acid compositions of phosphatidylcholine. Each chapter is well illustrated with figures and photographs, normally of a high quality, which enhance the text, but it is slightly disappointing that there was not a greater use of colour. Each part has a separate reference section which is relatively up to date and in some instances provides further reading sources. It is difficult to find omissions in content rather the reverse, for example, a periodic table and list of physical constants is included which seems excessive. It is unfortunate that the proposed cost is high and likely to restrict distribution to libraries, which is a pity as the book would be a useful tool for a new research student. The general content is covered by other published textbooks in this area; however, overall this is a well presented text that largely succeeds in fulfilling its title's promise and presents a useful addition to liposomal literature.

G. W. HALBERT
UNIVERSITY OF STRATHCLYDE, UK

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Book Review

Side Effect of Drugs Annual 16
Edited by M. N. G. Dukes and J. K. Aronson
Published 1993 Elsevier Science Publishers B.V., Amsterdam
xiv + 500 pages
ISBN 0 444 89657 0 US $185.75, Dfl.325.00

In 1952 Meyler's 'personal experiences, some of which have been most disconcerting' led him to offer a book called Side Effects of Drugs (known in the sequels, and in the trade, as SED) 'on the harmful effects which can arise from the indiscriminate use of drugs'. The English edition, 268 pages including the index, cost 30/-. It included important monographs on the adverse effects of mercurials, the arsphenamines and bromine. This was the progenitor of 12 editions of SED, and more recently 16 editions of SEDA, the Side Effects of Drugs Annual, the last of which is reviewed here. It is 12·3 times longer than Meyler's first slim volume, and about 60 times more expensive. The Annual sets out 'to provide a critical and up-to-date account of new information relating to adverse drug reactions...'

SEDA-16 succeeds better in some of its intended tasks than others. The book cover is labelled 1992, though it was actually published in 1993, and the references to many of the 51 chapters are predominantly from 1990 and 1991. It therefore lags behind a publication like Reactions, which appears several times each year. The Annual claims to review 'all reports presenting significant new information on adverse reactions to drugs from July 1991 to December 1992', but this is not so, and those who rely on it for this will be misled.

It also carries the burden of its long line of forebears, which are often referred to. This makes the possession of SED-12 and SEDA-15 almost indispensable for readers of SEDA-16.

Even within SEDA-16 there is some overlap between one section and another. For example, BCG treatment of bladder tumours is dealt with both in Dittman's chapter on immunobiological preparations and in the chapter on immunomodulating agents; and two different chapters tackle priapism associated with papaverine injection into the penis.

However, with these provisos, SED-16 is a tour-de-force of collation and analysis. It contains more references to the non-English literature than the two other major books in the field, D'Arcy and Griffin (Iatrogenic Disease, Oxford 1986) and Davies (Textbook of Adverse Drug Reactions, Oxford 1991) perhaps because its authors are a cosmopolitan band. This foreign flavour also touches on the drugs discussed. For example, few English doctors will have met Wobe-Mugos. This is 'an enzyme preparation manufactured in Germany, and not generally recognized by drug regulatory agencies', perhaps because of its peculiar composition, which includes a hydrolysate of calf thymus. I would certainly have missed the article by de Smet et al entitled 'Acute circulatoire shock na toepassing van het niet-reguliere enzympreparaat Wobe-Mugos' if it had not been for SEDA-16.

I might also have missed a critical account of the Pisa syndrome, in which the authors, like the patients treated with antipsychotic drugs, bend over backwards. As they say, the uncontrolled study prevents firm conclusions.

The newer drugs receive due attention. Botulinum toxin, erythropoietin and the fluoroquinolones, for example, are dealt with well: they are not indexed in D'Arcy and Griffin.

The 17 reviews which spice the text are an interesting addition. Among others, the trenchant contribution on the politics of antibiotic prescribing, the warnings on dental anaesthesia, and the description of the adverse effects of germanium, were worthwhile essays in the form of editorials, rather than meta-analyses or formal reviews.

Perhaps meta-analyses will come in the future, for SED and SEDA will undoubtedly continue to help drug information pharmacists and clinical pharmacologists, and through them all prescribers and patients. Whilst it is sad to read that M. N. G. Dukes, the present distinguished editor, is to lay down his pen, we should be pleased that J. K. Aronson, of Oxford Textbook of Clinical Pharmacology fame, is to take over.

R. E. FERNER
WEST MIDLANDS CENTRE FOR ADVERSE DRUG REACTION REPORTING, BIRMINGHAM, UK

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Book Review

Enzymes of Molecular Biology
(Methods in Molecular Biology/16)
Edited by Michael M. Burrell
Published 1993 Humana Press Inc., Totowa, NJ
384 pages
ISBN 0 89603 234 5 $59.50

Nothing beats learning at Nelly's knee. Particularly if Nelly has made the buffer solutions and set up the apparatus. Six months slog at the bench developing a technique can often be saved by a short 'hands on' visit to a laboratory where the technique is up and running. To replace Nelly, there have appeared on the market whole series of experimental guides. This is Number 16 in a series entitled 'Methods in Molecular Biology', and deals specifically with the properties of the enzymes used in gene technology and other molecular biological techniques. In his introduction, Michael Burrell makes the very valid point that protocols devised for one enzyme under a particular set of conditions may not be optimal for another enzyme, or when conditions change. This volume, therefore, seeks not only to give guidance on materials, buffers and protocols, but also to give information on the nature and requirements of the various enzymes. It is to be treated as a companion volume to the others in the series, and seeks to minimize the time spent in literature-searching to discover how best to make reactions work efficiently. The enzymes covered are nucleases, including nearly 100 pages on, and over 250 detailed listings of, restriction endonucleases, DNA polymerases and ligases, reverse transcriptase, methyl transferases, RNAases and proteinases, carboxy- and aminopeptidases, alkaline phosphatases and polynucleotide kinases. The book contains much that is lucid and reliable. If time is money, it is cheaper than visiting Nelly, and saves the rail fare too!

R. J. PINNEY
THE SCHOOL OF PHARMACY, LONDON, UK