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Book Reviews

Reactive Oxygen and Oxidative Stress: A New Route for Tackling Disease?
Scrip Report, anonymous, 1994
PJP Publications, UK.

Scrip reports publish a wide range of pharmaceutical therapeutic market reports, in depth profiles of companies, financial analyses etc. They appear to be aimed at companies, especially given the price of £395 for 123 pages held together by a plastic spiral binder. The purpose of the present report is presumably to provide a company/investor briefing about the therapeutic potential of antioxidants.

The report begins with a brief but clear executive summary, well-written on the whole but slightly out of date with respect to ALS (also true of the longer discussion on pages 32/33; the defects in SOD are only in the familial form of the disease, and loss of enzyme activity *per se* is unlikely to be responsible for tissue damage), stroke (xanthine oxidase is probably not very important in humans) and the status of N-acetylcysteine in AIDS treatment. Chapter 1 describes reactive oxygen species and antioxidants in more detail: it is generally well done but the misprints (e.g. on page 4) would be confusing to the non-expert ($O_2^{\cdot}$ for $O_2^{\cdot -}$, $ROOH^{\cdot}$ for ROOH etc). One minor irritation to this reviewer was the use of diagrams (pages 9, 15, 22, 42) from 4 of my own publications without seeking my permission: of course, the publishers are the copyright holders but it is a usual courtesy to ask the authors as well. In fact, they missed the updates of Table 1.4 in my more recent papers. The section on regulation of antioxidant enzymes (page 17) is weak: no mention of ARE's, for example. It is also erroneous (page 17) to state that CuZnSOD is largely peroxisomal - the JBC paper describing this has since been rebutted.

Chapter 2 describes diseases in which oxidative stress-induced damage is thought to be important. The data are well summarized on the whole, although the discussion of myocardial xanthine oxidase on page 24 is confused (the enzyme is present in rat and dog heart, little in *human* heart), the Ames *et al.* figures (page 26) have since been revised, I am not sure what 'oxidized alpha-trypsin gas (!!)' is (page 29) and peroxynitrite is *not* a radical (page 29).

Chapter 3 discusses methods for detecting free radicals. Again, it is well written, although I thought that the section on 'detection of DNA damage' should have mentioned 8-hydroxydeoxyguanosine, now the most commonly-measured product.

Chapter 4 gives an interesting account of 'nutriceuticals' but Table 4.1 could have been updated. Chapter 5 attempts to assess the therapeutics market for diseases involving oxidative stress, showing that it is potentially enormous. I enjoyed this chapter, although perhaps the lazaroids could have been given more prominence in the stroke section, as being closest to market. Guanine is confused with guanidine on page 68.

Chapter 6 nicely reviews potential therapeutic agents, with useful tables of 'compounds and

companies' and 'dropped products'. However, I was surprised that lipoic acid (Asta Medica) was not mentioned. The report ends with lists of free radical research groups in Universities and details of companies in the field. The UK list is good but several European and US research groups are missing: Lester Packer (Berkeley, California) is placed in Switzerland! It might also have been helpful to give full postal addresses and FAX numbers.

Overall, I enjoyed this report and I am sure that some companies will find it worth the money (about £3.20 per page of text). The multiple irritating errors detract from the overall quality of the product, however.

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Non-Steroidal Anti-inflammatory Drugs: Mechanism and Clinical Uses
Edited by Alan J. Lewis and Daniel E. Furst
(Second edition) xii + 461 pages
Marcel Dekker: New York, 1994
ISBN 0 8247-8856-7

Nonsteroidal antiinflammatory drugs (NSAIDs) are among the most frequently used prescription and over-the-counter (OTC) drugs in the musculoskeletal and joint disorders therapeutic category of the pharmaceutical market. *Non-Steroidal Antiinflammatory Drugs: Mechanism and Clinical Uses* contains 24 pertinent chapters arranged in four sections: clinical applications of non-steroidal antiinflammatory drugs; toxicity of non steroidal antiinflammatory drugs; new anti-inflammatory drugs and analgesics; and future developments.

NSAIDS share a common mechanism in that they interfere with the activity of cyclo-oxygenase, reducing prostaglandins formation compared with the slow acting anti-inflammatory drugs (SAADS) which affect the cellular aspects of inflammation. The book is educative in many respects. It discusses among other issues, the clinical uses of NSAIDs in the treatment of arthritides and their potential benefits in the treatment of migraine, adult respiratory distress syndrome and stroke, OTC strategies, safety and clinical toxicity aspects, the genetic basis of rheumatic disease, and the factors regulating cartilage and bone regeneration.

This is very useful source book and is highly recommended to all those with an active interest in inflammatory diseases and their treatment.

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Bioinorganic Chemistry: An Inorganic Perspective of Life
Edited by Dimitris P. Kessissoglou
NATO ASI (Advanced Science Institutes), Series C: Mathematical and Physical Sciences Volume 459: 1995
Kluwer Academic Publishers: Dordrecht
ISBN 0 7923 3380 2 xx + 415 pages

The stated aims of ASI include dissemination of advanced scientific and technological knowledge with a view to strengthening links between scientific communities. *Bioinorganic Chemistry: Inorganic Perspective of Life* is a proceeding of a NATO ASI meeting of the same title held in Rhodes Island, Greece, 5 June 1994.

The book contains 29 well written and pertinent chapters arranged in three sections: **metalloenzymes**: (methane monooxygenase (S.L. Lippard), the coordination chemistry of iron in biological transport and storage: iron removal in vivo (K.N. Raymond and J.R. Telford), on the mechanism of epoxidation and hydroxylation catalysed by iron porphyrins: evidence for non-intersecting reaction pathways (J.T. Groves and Z.Gross), self assembly, catalysis

and electron transfer with metalloporphyrins in phospholipid membranes (R.M. Kim, G.D. Fate, J.E. Gonzales, J. Lahiri, S.B. Ungashe and J.T. Groves), mechanistic studies on the behaviour of binuclear Fe enzymes ribonucleotide reductase and purple acid phosphatase (M.A.S. Aquino, J.-Y. Han, J.C. Swarts and A.G. Sykes), structure and reactivity of the blue copper proteins (P. Kyritsis, C. Dennison and A.G. Sykes), copper-zinc superoxide dismutase: mechanistic and biological studies (J.S. Valentine, L.M. Ellerby, J.A. Graden, C.R. Nishida and E.B. Gralla), NMR of paramagnetic molecules: a contribution to the understanding of enzymatic mechanisms (I. Bertini and M.S. Viezzoli), magnetic and EPR studies of superoxide dismutases: electronic structure of the active sites for the copper-zinc SOD, its cobalt substituted derivative and the iron (III) SOD from *E. Coli* (I. Morgenstern-Badarau), mechanism of action of thiamin enzymes: role of metal ions (N. Hadjiliadis, K. Dodi and M. Louloudi); **metal-DNA interaction** platinum anticancer drugs (S.J. Lippard), NMR spectroscopic structure determination of metal ion-oligonucleotide complexes: the results of sequence-selective binding studies (E. Sletten and N.A. Froystein), metal-nucleobase chemistry: coordination, reactivity and base pairing (B. Lippert), DNA cleavage by cationic metalloporpyrins (B. Meunier, G. Pratviel and J. Bernadou), the role of metal irons in biological systems and medicine (J. Anastassopoulou and T. Theophanides), thermodynamics and kinetics of competing redox processes during DNA cleavage: reactivity-based selectivity (C.C. Cheng, G.A. Neyhart, T.W. Welch, J.G. Goll and H.H. Thorp); **modelling active sites**: Mo/ S chemistry and its importance in enzymatic catalysis (D. Coucouvanis), use of *de novo* designed peptides for the study of metalloproteins and enzymes (G. Diekmann, S. Heilman, D. McRorie, W. DeGrado and V.L. Pecoraro), modelling the chemistry and properties of multinuclear manganese enzymes (V.L. Pecoraro, A. Gelasco and M.J. Baldwin), manganese-proteins and enzymes and relevant trinuclear synthetic complexes, and molybdenum-copper antagonism (D.P. Kessissoglou), catalytic oxidation of pollutants by ligninase models based on metalloporphyrins and metallophthalocyanines (B. Meunier and A. Sorokin), nickel coordination chemistry with oxothiolate ligands and its relevance to hydrogenase enzymes (J.H. Chou, C. Varotsis and M.G. Kanatzidis), artificial batteries with lanthanide porphyrins (A.G. Coutsoleos), novel transition metal heteropolymetalate and derivatives: structural chemistry, biological and catalytic relevance, and, purple acid phosphatases and catechol oxidase and their model compounds: crystal structure studies of purple acid phosphates from red kidney beans (B. Krebs).

The significance of much of the work done in the biomedical area of free radicals accrued from the discovery of the enzyme superoxide dismutase by McCord and Fridovich in 1969. Valentine *et al.* discuss the mechanistic and biological studies of Cu-Zn SOD and the association of this enzyme with Lou Gehrig's disease, amyrotropic lateral sclerosis. Anastassopoulu and Theophanides discuss the role of metal ions in biological systems and medicine aptly reminding the reader that the subject of inorganic chemistry is not 'dead chemistry'. The more you read the book the more appreciative the wealth of information it contains becomes. In general, this is a useful source book for scientist working in the area of inorganic biochemistry and related areas of free radical research.

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Regulatory Toxicology

Edited by C.P. Chengelis, J.F. Holson and S.C. Gad
Raven Press: New York, 1995, pp. ix + 251
ISBN 0 781 701 910, $109.50

The stated objective and coverage of the book was to present 'a clear and practical guide to the

government (and, where applicable, nongovernment) regulations that govern why and how toxicology/safety testing is done, and how the results of such testing are reported and used in regulating the entry and use of products in the market place'. The editors largely succeeded in this endeavour.

Regulatory Toxicology contains ten scintillating, well written and uniformly educative chapters contributed by authors from the United States of America. Issues such as 'human health products: drugs and medical devices', 'food additives', 'animal health products', 'consumer products: cosmetics and topical over-the-counter drug products', 'consumer products: nonpersonal care products', 'agricultural chemicals: the Federal Insecticide Fungicide and Rodenticide Act and a review of the European Community regulatory process', 'regulation of new and existing chemicals: the toxic substances control act and similar worldwide chemical control laws', 'hazard communication and exposure limits: labelling and other workplace and transportation requirements for industrial chemicals under the Occupational Safety and Health Authority and the Department of Transport, and similar authorities around the world' and 'oversight regulations', are sufficiently discussed for the reader to grasp the concept under consideration.

Regulatory Toxicology is enthusiastically readable and would be of value in addition, to environmental health professionals. One would have wished a more global coverage.

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Oxidative Stress and Aging

Edited by R.G. Cutler, L. Packer, J. Bertram and A. Mori
Birkhauser Verlag AG, 1995
ISBN 3-7643-5039-3. £79, $124

This book is a product of the first International Conference on Oxidative Stress and Aging held in Hawaii in 1994 which addressed the molecular and cellular aspects of aging as related to oxidative stress.

A Figure depicting the current thinking of antioxidants, free radicals and reactive oxygen species is followed by introductory remarks on 'oxidative stress, antioxidants, aging and disease (Packer)' and 'longevity determinant genes, cellular dysdifferentiation and oxidative stress (Cutler)'. 34 well written articles contributed by participants at the meeting are then presented grouped into the following topics: 'oxidative stress and cellular senescence', 'genetic stability and damage: DNA repair', 'genetics and lifespan', 'proteins and lipid oxidation', 'mitochondria', 'aging related disease and cancer', 'aging related disease neurodegeneration', 'nutrition' and 'nitric oxide'.

This is certainly one of the best books in recent years dealing with aging in the context of oxidative stress. The body of evidence suggesting that oxidative stress plays a role in the pathology of human diseases has provoked interest in the evaluation of 'natural' and 'synthetic' compounds as potential antioxidant prophylactics. The article by Tomita *et al.*, page 355 on tea antioxidants, gives a respectable account of the assessment of tea antioxidant compounds in minimising oxidation of low density lipoproteins.

Notable articles such as 'oxidative stress and apoptosis' (Slater and Orrenius), 'DNA damage and epigenetic mechanism of aging' (Holliday), 'Parkinson disease, dopamine and free radicals' (Ogawa and Mori), 'free radicals in the pathogenesis of diabetes and its complications' (Gries, Kolb and Koschinsky), 'mitochondria, free radicals, neurodegeneration and aging' (Schapira), 'oxidative stress in neurobiology: an important role for iron' (Gutteridge), and 'dietary vitamin E in oxidative stress and aging' (Meydani), combine to make the book a worthwhile addition to any research library.

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Neurotoxicology: Approaches and Methods
Edited by L.W. Chang and W. Slikker Jr.
Academic Press, San Diego
ISBN 0-12-16 8055-X. $149.95 (£100 approx.)

This attractive book, written by a selection of excellent authors, aims to review current approaches and methods in the testing of agents for neurotoxicity (defined in the Introduction as 'any adverse effect on the structure and function of the nervous system'). The book is part of a trilogy, being preceded by *Principles of Neurotoxicology* and *Handbook of Neurotoxicology*.

The present volume begins with a section devoted to neuromorphological and neuropathological approaches: histopathology, histochemistry, labelling of neurones, enzyme histochemistry, electron microscopy and quantitative morphometry. Most chapters have valuable appendices detailing composition of reagents and other useful practical information. My only criticism of Section I is the poor reproduction of many of the photographs, particularly unfortunate in a section devoted to morphology/histology. Particularly bad examples are those on pages 6, 16, 47, 55, 74 and 77. A few glossy plates and colour prints would not have been amiss here.

Part II of the book is devoted to neurophysiological techniques: measurement of ion channel function, synaptic transmission, hippocampal neurophysiology and sensory-evoked potentials. Part III covers the essentials of neurobehavioural toxicology: behavioural screening tests, evaluation of sensory motor and cognitive functions, and the use of drug discrimination learning behaviour. Examples are given from lead-induced learning impairments and polychlorinated biphenyl-induced neurotoxicity. There are also chapters on the role of excitatory amino acids and serotonergic systems in behavioural neurotoxicity. Glutamate receptor-mediated neurotoxicity is also discussed in Chapter 26 in part IV: somewhat of an overlap.

Part IV of the book is devoted to 'neurochemical and biomolecular approaches'. It covers such topics as HPLC analysis of brain amino acids and catecholamines, measurement of Ca^{2+} uptake by injured neuronal tissue, nucleic acid hybridization techniques, microdialysis, cell volume measurements, electron probe X-ray microanalysis, axonal transport and assessment of cell energy status and mitochondrial metabolism.

Part V discusses the various *in vitro* models that can be used, including neuronal and glial cell cultures (both single cell-types and combinations, e.g. Schwann cell-neuronal interactions), brain slices, cell suspension techniques, and patch clamp.

The last section of the book is devoted to clinical neurotoxicology. After a chapter on basic principles, listing the major neurological syndromes produced by neurotoxic agents, the book moves on to more specific considerations of agrochemicals, organic solvents, metals, gases (such as CO), drug abuse (including ethanol), antineoplastic agents, MPTP and domoic acid. The clinical recognition of neurotoxic syndromes is reviewed in Chapters 44, 46 and 47. Chapter 45 approaches the thorny problem of exposure assessment. The applications of evoked potential testing and neuroimaging (again, poor reproduction spoils the CT scans on pages 760 and 761) are also presented.

Part VII continues the theme of risk assessment and the use of biomarkers, and also extends these concepts to developmental neurotoxicology. Clearly this is an area in which much more research is needed. The book ends with an adequate index.

Overall, this is a very useful volume: my only criticism is poor quality reproduction of photographs. I am pleased to have it on my bookshelf and I recommend it to others.

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Radical Chemistry
by M.J. Perkins
Ellis Horwood Series in Organic Chemistry, Ellis Horwood Limited 1994 pp. 182
ISBN 0 13 3209202.

This concise book is written as a self study with chemists in mind, but has much of value for the interested non-chemist. It is written in a style which reflects a scientific career involved throughout with research in the radical field. The author slips easily from a brief historical background into descriptions of reaction types and patterns of reactivity which form the basis of modern developments discussed in the second half of the book.

The book consists of ten chapters written with a definite clarity which makes even the more sophisticated science easy to follow. Readers involved in biological studies will find the chapter on electron spin resonance (ESR) spectroscopy particularly informative as it teaches in empirical rather than theoretical terms the types of information which may be deduced from ESR spectra. This chapter is approached from a largely phenomenological standpoint, but does assume some basic knowledge of NMR spectroscopy.

The book goes a long way to dispel old ideas of radicals as invariably being highly reactive and unselective chemical intermediates. It shows how an understanding of radical chemistry has been put on to a quantitative footing, and how, in recent years, this has led to remarkable control of high yielding synthetic procedures – which now often include efficient stereochemical control. This approach is of particular value to the organic chemist, for whom efficient synthetic methodology assumed a position of pre-eminence during the 1970's and 1980's.

Selectivity is also important in biological systems, for instance in lipid autoxidation. This topic is introduced in a "special topics" chapter, but is developed further in a long concluding chapter which deals specifically with radicals in biology. This begins with an introduction to oxidising species, including methods of production of hydroxyl, the damage it can inflict, and the enzyme systems which, in healthy tissues, prevent this. Other topics introduced in this wide-ranging chapter, include modes of operation of selected enzyme systems, addressed at a molecular level, as well as the biological applications of spin trapping (introduced in the chapter on ESR), and spin labelling. There is unfortunately one omission in this final chapter, in that the mechanism for P450 which is presented in some detail was later retracted by Bowry and Ingold, but appeared too late for inclusion in this book.

Apart from that, this camera ready book prepared by the author is remarkably free from trivial errors. There is ample coverage of many topics dealing with free radicals in this short book but the purist might be dismayed that the only discussion of biradicals is found in an abstract reporting of enediyne antibiotics. There is also no coverage of gas phase systems.

However, in the main this book is very easy to follow with perfect balance between text and illustration. The readers may wish to test their knowledge gained from this book by attempting to answer the problems the author has set at the end of the book (references to the original reports are given to help). Also included is a bibliography and guide to further reading.

Finally, this book is reasonably priced at £15.00 and its size makes it easy to carry as a reference copy. I enjoyed reading this excellent book and recommend it highly to all those interested in developing an understanding of the importance of free radicals in modern science.

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Immunopharmacology of Free Radical Species
Edited by D. Blake and P.G. Winyard
Academic Press, London, pp. 301
ISBN 0121035204. £45.00.

This book is a specialised contribution to the series 'The Handbook of Immunopharmacology' edited

by Clive Page, and as the title suggests specifically highlights current research in which reactive oxygen species are important. Thirty-five scientists, predominantly from the UK, contribute seventeen chapters under the joint editorship of two well-known researchers in the field of free radicals and inflammation, namely Professor Blake and Doctor Winyard. A useful introductory chapter is provided on methods available for the detection and measurement of reactive oxygen species in biological systems, followed by more organ-specific contributions covering cardiovascular, CNS, renal, joint, eye, gastric, muscle and pancreatic diseases. Damage at the molecular level is also considered in detail for DNA and lipids, but not for proteins. Aspects of environmental pollution are considered, with a concluding chapter discussing therapeutic intervention strategies.

The publication style allows a great deal of information to be compacted into the book, and at the same time produces a clear, and pleasing format for reading and reference. Full references are given after each chapter, increasing the book's usefulness for research purposes. At £45.00 the book is excellent value for the specialist researcher, and is highly recommended by the reviewer.

John M.C. Gutteridge