Free Rad. Res., Vol. 23, No. 5, pp. 505–511
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BOOK REVIEWS

Natural Antioxidants in Human Health and Disease
Edited by Balz Frei
Academic Press, San Diego

This attractively-presented book aims to be a comprehensive overview of current scientific knowledge about dietary antioxidant vitamins. According to the back cover 'antioxidant vitamins may be important in preventing not only acute deficiency symptoms but also chronic disorders such as heart disease and certain types of cancer. Specifically, antioxidants may prevent or slow down the progression of cancer, cardiovascular disease, immune system disorders, cataracts, neurological disorders and degeneration due to the ageing process'. Ambitious claims indeed! Is the book then a publicity vehicle for the antioxidant vitamin manufacturers? Most certainly not; the editor is to be congratulated on drawing together an excellent group of talented authors who have, almost without exception, given their topics careful, thorough and critical evaluation.

After a well written introduction by Ames, the book begins with a clear and accurate description of the chemistry of free radicals and related species (Pryor). Kehrer and Smith continue this discussion and expand it to biological systems, and they set out the criteria needed to *prove* that radicals are important in human disease. Shigenaga and Ames discuss the role of 'oxidants' in ageing, with particular reference to mitochondria. I particularly appreciated the tabulations of literature data on oxidative damage. This excellent chapter has only one trivial fault – repeated use of the term 'oxidants' (what a shame after the careful definitions of terms by Pryor and Kehrer/Smith).

The book then turns to antioxidants. Briviba and Sies review non-enzymic antioxidant defences, especially GSH, ascorbate, ubiquinol, vitamin E and carotenoids. Block and Schwarz discuss the relation of ascorbate to cancer in the context of animal and cell culture data, a chapter complemented by that of Fontham on the epidemiological data. The data are carefully reviewed and their limitations discussed. Selenium and carotenoids are given the same thorough treatment. Knekt carefully reviews the often conflicting and confusing data on vitamin E and cancer prevention. Krinsky describes the chemistry and biochemistry of carotenoids, concluding that we do not yet understand the mechanism of carotenoid anti-cancer effects. Garland *et al.* discuss the relation of selenium to human cancer, another confusing field.

Cardiovascular disease is reviewed in Section III of the book. After an excellent chapter on the basic pathology of atherosclerosis (Schwartz and Valente), marred only by the mediocre reproduction of some of the figures, the book turns to LDL oxidation and antioxidants (Keaney and Frei). This chapter is excellent – I particularly enjoyed the table summarising clinical trials of antioxidant protection. The same group then reviews the extensive animal data on the anti-atherosclerotic action of antioxidants (Chapter 12), which leads on naturally to a discussion of epidemiological data, presented clearly and thoroughly by Gaziano *et al.* Janero reviews the potential of antioxidants to prevent myocardial ischaemia/reperfusion injury, and I particularly enjoyed his discussion of injury mechanisms.

The effect of antioxidants on the immune system is a controversial area, not helped

by all the advertising hype about the alleged benefits to the elderly and to AIDS patients. The studies reviewed in chapter 15 clearly point to negative effects of oxidative stress on cells of the immune system, but I was not convinced of the benefits of antioxidant supplementation in this context by any of the studies presented in this chapter. In Chapter 16, Levine *et al.* describe their excellent data on the uptake and fate of ascorbate in neutrophils, which may throw new light on optimal dietary ascorbate intake in humans. On the viral side, Peterhans presents an interesting account of viral 'autotoxicity', ie, many effects of viral infections are caused by the host's attempts to eradicate the virus (which include, of course, increased production of reactive oxygen species). There is an excellent discussion of the pros and cons of antioxidant intervention.

Chapter 18 gives a short discussion of cataract formation and how it is affected by antioxidant intake. Muller (Chapter 19) presents his seminal studies on vitamin E in neurological function and disease, and carefully reviews evidence for oxidative stress in Parkinson's disease, tardive dyskinesia and other human neurological diseases. Finally, Packer *et al.* discuss antioxidants in relation to exercise. The book ends with a good index.

Overall, this is a first rate book. I am pleased to own it and I recommend it to others.

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***In Vitro* Toxicology**
Edited by: Shayne Cox Gad
Raven Press Ltd.: New York, 290pp
ISBN: 0-88167-974-7

This small, attractively produced volume may well turn out to be a bit of a landmark in the field. The editor, who is Director of Toxicology at Synergen, has collected a wide range of contributions from specialists in areas of *in vitro* toxicology, these areas being defined more by organ or tissue than by technique or approach. Thus, most chapters are of the form – **Neurotoxicology *In Vitro*** – or – **Ocular Toxicity Assessment *In Vitro***. These chapters provide varying degrees of methodological, technical information plus discussion of relevant published work in the field. In general, the information is well-referenced.

By way of introduction to these specific chapters the editor has put together, first, an interesting account of some of the history behind the movement to replace *in vivo* with *in vitro* in toxicology, and second, a short but useful chapter on the general principles to be considered in *in vitro* toxicology. This latter chapter contains some interesting tables listing and summarising issues covering concepts such as rationale, limitations and interpretation. I did not find some of these abbreviated points immediately obvious to my relatively uninitiated mind but I certainly gained many insights that I had never formalised in my thinking about such matters. A similar style informs the editor's closing chapter on **Strategy and Tactics for Employment of *in vitro* methods in toxicology**. This is in relation to regulatory agencies in the United States, and doesn't consider European or International Agencies or Regulations, but the general principles are still highly applicable.

Some of the other chapters I personally would highlight for the value of their

content are: **Ocular Toxicity Assessment In Vitro** by J.F. Sina & P.D. Gautheron; **Lethality Testing** by P.J. Guzzie, **In Vitro Assays for Developmental Toxicity** by S.G. Whittaker & E.M. Faustman, **Neurotoxicology *In Vitro*** by P.G. Nelson & D.E. Brenneman; **Primary Hepatocyte Culture as an In Vitro Toxicological system of the Liver** by A.P. Li.; and **In Vitro Assessment of Nephrotoxicity** by J.B. Tarloff & R.S. Goldstein. It may be that the kidney lends itself particularly well to the application of *in vitro* study but I certainly found this last chapter conveyed well the considerable potential of *in vitro* techniques in this field. What I appreciated most in all these chapters, and indeed would have relished more of, was discussion (not just notification) of situations where the *in vitro* model correlated poorly with the *in vivo* situation.

To a reviewer such as myself who is involved more in teaching toxicology than in actively experimenting in the field, this volume was valuable for plugging significant gaps in my knowledge base. However, I feel sure it can also be recommended to experienced practitioners, as well as tutors and advanced students. It is unlikely to be read from cover to cover, but the general chapters, plus a specific chapter of relevance, could be invaluable for a new researcher wishing to gain rapid and informed enlightenment before initiating work in a field new to them. Conceivably, much toil and tribulation could be saved.

A definite must for libraries at institutions where toxicology is part of the syllabus.

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Active Oxygen, Lipid Peroxidation and Antioxidants
Edited by Kunio Yagi
Japan Scientific Society Press: Tokyo
ISBN 4-7622-6738-4, 1993
CRC Press: Boca Raton
ISBN 0-8493-7769-2, 1993
x + 372 pages Y 13,000

The delay in publishing the contributions emanating from the 5th International Congress on Oxygen Radicals (17–22 November 1991), Kyoto, Japan, is probably a major set back for the book.

The 30 chapters in the book consider free radical injury from medical and nutritional points of view. Representative chapters include 'lipid peroxidation in biological membranes: mechanisms and implications (Ernster)', 'lipid peroxides, free radicals, and diseases (Yagi)', 'recent aspects of thiyl and perthiyl free radical chemistry (Asmus)', 'reductive and oxidative decay pathway of semiquinones: the effects of glutathione and superoxide dismutase (Goin *et al.*)', 'superoxide production by neutrophils (Takeshige *et al.*)', 'oxidative stress status measurements in humans and their use in clinical trials (Pryor)', 'superoxide radical anion in some unexpected chain reactions (von Sonntag *et al.*)', 'vitamin E cycle and benefits to health (Packer)', 'macrophages, foam cells, and oxidative stress (Darley-Usmar *et al.*)', and 'suppression of malaria by dietary oxidant stress (Levander *et al.*)'.

Much has been written about the process of lipid peroxidation. In reviewing the mechanisms and biological significance of the process, Ernster reminded us that

research in lipid oxidation began in the 1800s when it was observed that walnut oil exposed to air increases its weight and becomes ill smelling.

Two notable chapters in the book are those by Namiki *et al.* and Okuda *et al.* on food derived antioxidant phenolic compounds. Plant-derived phenolic compounds including flavonoids, are now being considered (in addition to their use in food processing) from the perspective of, antioxidants to promote health and, antioxidants to treat diseases.

In general the book should make an informed contribution to the libraries of researchers with interest in free radical biochemistry.

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Free Radicals, Cardiovascular Dysfunction and Protection Strategies
R C Kukreja and M L Hess
R G Landes Company: Austin, Texas, U S A, 1994

This short book is part of a series from the publisher's *Medical Intelligence Unit*. According to the fly leaf, it was submitted in October 1993 and published in January 1994, a commendable speed. The purpose of the monograph is to provide an overview of the role of free radicals in cardiac ischaemia/reoxygenation injury. It begins with a chapter on the basic biochemistry of reactive oxygen and nitrogen species. This is clearly presented, although I would quibble with some of the statements (eg, "H_2O_2 is very lipophilic", "NO avidly reacts with other molecules", and the apparent suggestion on page 6 that NO and $NO^{\bullet}$ are different species). This is followed by a chapter on mechanisms of oxygen radical generation in myocardium, which clearly sets out the relevance of such radical sources as xanthine oxidase, phagocytes, mitochondria and catecholamines. Some might quarrel with the statement that prostaglandin hydroperoxidase generates $^1O_2$, however. Chapter 4 approaches the important question of how to detect free radicals during ischaemia/reperfusion, covering spin-trapping, ascorbyl radical measurement, salicylate hydroxylation and chemiluminescence. The application of these techniques to the heart is well described; what is missing is any evaluation of their methodological advantages and disadvantages. The diagrams on page 22 are dreadful.

Chapter 5 discusses the damage done to the heart by oxygen radicals (unfortunately, singlet O_2 seems to be included under that category). It is a clear and concise review, as is the following chapter on myocardial stunning.

Chapter 7 reviews the evidence that $NO^{\bullet}$ plays a role in ischaemia/reperfusion. It is clearly written, but has missed out on the latest studies with peroxynitrite (always a problem in a rapidly-moving field). The subject of myocardial protection by antioxidants is nicely summarized in Chapters 8 and 9, although the authors give the unfortunate impression that there are 'specific' $OH^{\bullet}$ scavengers (manitol is 'efficient', allopurinol is 'inefficient') – almost everything reacts at a high rate with $OH^{\bullet}$. I was also surprised to see the amount of space devoted to histidine and, by contrast, not to see a more critical discussion of the SOD protection issue in relation to the problems of assessing infarct size.

Ischaemic preconditioning is the subject of Chapter 10 – this is a very topical issue, and it is well summarized. Chapter 11 deals with heat shock proteins in relation to myocardial protection.

Overall, despite its multiple minor flaws, this is a useful book and can be recommended to newcomers to the field of myocardial ischaemia/reperfusion injury.

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Oxygen and Environmental Stress in Plants (Special issue of the Proceedings of the Royal Society of Edinburgh, volume 102 1994) eds R M M Crawford, G A F Hendry and B A Goodman

In 1993 the first international conference devoted to understanding the role of oxygen in environmental stress in plants was held in St Andrews, Scotland. In recent years there has been a huge upsurge of interest in oxidative damage in animal and bacterial systems, but plants have been somewhat neglected. This conference was therefore timely and welcome. For those unable to attend, the editors of this volume have done an excellent job in drawing together the major papers presented. Wisely, they have avoided book publication and selected a special issue of a journal, thus allowing wider distribution, as well as coverage of the papers in the various databases.

The Volume begins with an excellent overview of the complex relation between O_2 and plants (Hendry and Crawford). It goes on to discuss ozone toxicity (a very valuable and topical set of papers), plant responses to ionizing radiation,antioxidant defences (including their manipulation by transgenic technology), chilling injury, dehydration/rehydration damage (in some ways analogous to ischaemia/reperfusion), photo-oxidative injury and seed ageing. Even allopurinol makes an appearance.

Overall, this is an excellent volume and I recommend it highly. The editors are to be congratulated not only for organising the conference, but also for ensuring that the proceedings will widely read.

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Free Radicals in Aging
B.P. Yu (Ed).
CRC Press: Boca Raton. 1993 pp. 303
ISBN 084934518-9

The role of free radicals in the normal ageing process and in age-related diseases which decrease life expectancy are reviewed in this book by 19 authors, with all but one contributor coming from the United States. Topics discussed within the twelve chapters include two very useful introductions to the basics of free radicals and ageing processes, with more specialised coverage of lipid, carbohydrate, DNA and antioxidant changes resulting from free radical reactions. Further confusion is introduced into antioxidant and free radical terminology, which is already living with a dichotomy of definitions. In chemical terms a 'primary antioxidant' reduces the rate at which new free radical chains are started, in biological terms a 'primary antioxidant' prevents formation of free radicals. Dr Yu introduces the term 'primary antioxidant' to describe the prevention of damage, and in Table 1 incorrectly defines singlet oxygen and lipid peroxides as free radicals. Some of the important age-related diseases of current interest are

reviewed by Denham Harman in chapter 9, and other chapters deal more specifically with exercise, neurodegenerative disorders, cancer and diabetes. The format of presentation, although rather dull, is uniform throughout, and useful references are given in full at the end of each chapter.

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Mitochondria: DNA, Proteins and Disease
Eds. V. Darley Usmar and A.H.V. Schapira
Portland Press Research Monograph V, London, 1994

This is an attractive-looking volume, with its pale-blue and black cover. According to the preface, the editors attempted to produce a book relating mitochondrial biochemistry and genetics to free radicals and "mitochondrial diseases". They have succeeded very well.

The first chapter reviews the role of mitochondria in energy production and the function of the electron transport chain complexes I to V. The structure and function of mitochondrial DNA is discussed in Chapter 2, with an emphasis on mtDNA mutations. Transport of proteins into mitochondria is covered in Chapter 3. Chapter 4 reviews the Krebs cycle and other mitochondrial metabolic pathways, as well as mitochondrial Ca^{2+} uptake. The latter theme is continued in the next chapter, which discusses oxidative stress, Ca^{2+} overload and their effects on mitochondrial function. The discussion of the actions of cyclosporin is especially interesting. Continuing the free radical theme, Chapter 6 reviews changes in mitochondrial function in response to myocardial ischaemia-reperfusion, again emphasizing the role of Ca^{2+}.

The last section of the book is devoted to mitochondrial "defects": those induced experimentally by toxins, including MPTP, dinitrophenol and AZT, and inherited defects, including abnormalities of complexes I, II and III in humans, defects of β-oxidation, and cytochrome oxidase deficiencies.

Overall, this is a useful book which fills a gap in the literature and I recommend it. My only criticism is the poor quality of reproduction of several of the electron micrographs.

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Human Medicinal Agents From Plants
Edited by A. Douglas Kinghorn and Manuel F. Balandrin
ACS Symposium Series 534
American Chemical Society: Washington DC, 1993, pp. xii + 356.
ISBN 08412 2705 5. $89.95.

Human Medicinal Agents From Plants should be viewed as a treatise of excellence by scientists interested in the medicinal properties of plants.

The book contains 22 superb chapters by different authors arranged in four sections: (1) current role and importance of plant-derived natural products in drug discovery

and development (2) anticancer and cancer chemopreventive agents from plants (3) anti-infective and antimicrobial chemotherapeutic agents from plants and (4) promising plant-derived natural products with multiple biological activities.

The book contain camera-ready texts which is an irritating detraction from the appeal of the volume. Nevertheless, this is a very useful and highly readable book.

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