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Book reviews

Herbal and Traditional Medicine. Molecular Aspects of Health.
Edited by Lester Packer, Choon Nam Ong and Barry Halliwell
Marcel Dekker, New York, 2004-12-31. ISBN: 0-8247-5436-0, 941 pages

This book is wonderful. Like on a treasure hunt, you can find answers to most questions that you might have on the topic of herbal and traditional medicine: Positive, negative, scientific, anecdotal, ranging from botany and nutrition to medicine and society. Not to forget a rigorous assessment of the issue of toxicity and risk, coupled with a look into future development.

How could this come about? Three colleagues came together on the occasion of a visit by Lester Packer to the National University of Singapore as a distinguished visiting Professor at the Medical School's Department of Biochemistry, where Barry Halliwell (Co-Editor-in-Chief of this Journal) holds a chair, and Choon Nam Ong is at the Department of Community, Occupational and Family Medicine. This fortunate combination of editors made for the requirement of particular sensitivity at the fingertips to identify topics and individuals for an up-to-date and cutting-edge representation of the field.

What's in the book? It highlights traditional and herbal medicines with emphasis both on the molecular basis of their biological activity and their health effects. It is timely because there is now unprecedented interest throughout the world in bringing to light the molecular basis of the biological activity of traditional remedies used for centuries and in some cases for thousands of years. Many of these traditional medicines are derived from plants and herbs (phytomedicines) or from products that are often readily available as herbal supplements. Western and traditional medicine is now at a crossroads, and the future holds great promise.

While the list of herbal remedies is staggering, with thousands of them described with origins in the Chinese and Indian subcontinent, Singapore, Malaysia, Japan, Korea, and tribal cultures in all continents throughout the world, for most of the traditional medicines the active principles and basic mechanisms of action are not well known.

The editors decided to review and critically evaluate the issues involved in the wider use of traditional and herbal products for health maintenance and treatment of disease: The drawbacks in their continuing and further use, issues regarding their chemistry and methods of preparation, the proper design to conduct clinical trials to evaluate their efficacy, their potential adverse effects, the challenges that lie ahead in combining traditional and Western medicines, and their role in national health care and public policy issues.

The book has 42 chapters and an extensive Subject Index. So, it is easy to find information, from (purported) *aphrodisiac* properties (four pages!) to *zhi shi* (from *citrus aurantium*) and its role in herb–drug interactions. I'd like to refer, in particular, to a chapter by Barry Halliwell, entitled "Traditional Chinese Medicine: Problems and Drawbacks", where in a nutshell interesting problems for the future are carved out: (1) the product is toxic, (2) the product is not what it is supposed to be, (3) the product may have deteriorated or become contaminated, (4) the product may have been deliberately adulterated, (5) the products may produce harm by interactions with each other or with pharmaceuticals taken concurrently, and (6) the way forward. And the future seems to be bright: There are oligonucleotide chips utilized in authentication, and there are technologies to put the concept on a molecular basis as well as an assessment of efficacy in clinical trials.

The predominant part of the book, however, is simply a delight to find up-to-date information on many interesting plant and herb medicines. Just to name some of them: Tea, ginkgo, ginger, shiitake mushrooms, cruciferous vegetables, chrysanthemum, rosemary, crataegus, resveratrol, ginseng, licorice, tongkat ali, ephedra, echinacae, St. John's wort, curcumin, and many others.

Ninety (90!) authors contributed chapters, and this combined expertise makes for the high standard of the book. It will attract students and teachers, and the range is from botany and chemistry to biology and medicine, as well as nutrition, food industry and agriculture and public health policy.

Helmut Sies

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Carotenoids and Retinoids-Molecular Aspects and Health
(Lester Packer, Ute Obermüller-Jevic, Klaus Kraemer, Helmut Sies, Editors)
AOCS Press, Champaign, IL, USA, 2005, 350 pages, $ 113
ISBN 1-893997-83-9

A roundtable discussion on the safety of β-carotene and a workshop "Carotenoids and Retinoids: Molecular Aspects and Health" were held at the the annual Oxygen Club of California conference in Santa Barbara, CA, in March 2004. The chapters in this book represent an account of the information presented at the workshop together with several additional invited contributions to cover relevant topics. The book commences with comprehensive chapters on Vitamin A, and retinoids as well as oxidative degradation of carotenoids. Other chapter address Raman detection of carotenoids in human tissues and the role of carotenoids and retinoids in cellular gap junctional communication and in eye health. The effects of β-carotene cleavage products on mitochondria and nucleus are discussed. Several chapter focus on the role of lycopene and other phytochemicals in cancer prevention and their beneficial properties in cardiovascular health. The human epidemiological evidence for the association of carotenoids and human health is summarized and evaluated.

Chapter 1 (S.M.O'Byrne, W.S.Blaner) defines retinoids, retinoid-binding proteins, their transcriptional activity and oxidation in a thorough and in-depth manner.

In Chapter 2 (A.C.Ross) the functions and physiologic requirements for Vitamin A across the life cycle are explored. These are well elaborated from childhood to adulthood and aging. The Retinol Activity Equivalent, a unit of bioactivity, is defined.

The role of Vitamin A in signal transduction is described in Chapter 3 (B.Hoyos, U.Hammerling). The various forms of modified Retinol (Vitamin A) are lucidly distinguished, e.g. retinoic acid, dihydroxy-retinol, retinal, hydroxy-retro-retinol and anhydror-etinol, and the search for retinol targets outside the nucleus is reported in a gripping way. The binding of retinol to serine/threonine kinases is discussed in detail, its function as a promoter of redox pathways and biological mediator is emphasized. This catalyst role of retinol, however, is not well understood. It may be doubted whether the redox properties of alpha-tocopherol serve as as a proper model since the hydroxyl groups of retinol and alpha-tocopherol are totally different in a chemical sense.

Chapter 4 (F.Khachik) deals with the comparatively small number of 34 carotenoids and metabolites detected in humans. Special stress is laid upon lutein and zeaxanthin and their oxidative metabolites in human eyes. Under controlled conditions, the chemical oxidation of carotenoids such as lutein and lycopene can yield the same metabolites as those observed in humans.

In Chapter 5 (W.Stahl, H.Sies) the modulation of the direct exchange of signals between neighboring cells, triggering gap junctional intercellular communication (GJIC), by carotenoids and their cleavage products is thoroughly investigated. It was found that stimulation of GJIC is not restricted to compounds with provitamin A activity. Data indicate that the presence of four conjugated double bonds in the side chain provides optimal activity and that a number of other vitamins, micronutrients and signaling molecules also affect GJIC.

The importance and benefit of Resonance Raman Scattering (RRS) is impressively explained in Chapter 6 (W.Gellermann, J.A.Zidichouski, C.R.Smidt, P.S.Bernstein). It is a highly specific, sensitive and precise noninvasive optical method for rapid assessment of macular and dermal carotenoid content in large populations. In addition there is an excellent correlation of dermal to serum levels. It is remarkable that different conjugation lengths allow some carotenoids to be measured independently of other carotenoids (e.g. lycopene and β-carotene).

In Chapter 7 (R.A.Bone, J.T.Landrum) the function of the macular carotenoids is discussed in detail together with their spatial distribution, stereoisomerism and possible interconversion. The age-related macular degeneration (AMD) is well explained and a reasonable model is presented how the carotenoids may interfere with these degenerative processes. Methods for *in vivo* measurements of macular pigment are reviewed as has been done in Chapter 6.

The question whether β-carotene cleavage products (BCCP) are able to attack mitochondria and the nucleus are answered in Chapter 8 (W.Siems, I.Wiswedel, A.Alija, N.Bresgen, P.Eckl, C.D.Langhans, O.Sommerburg). The data provide evidence that BCCP deplete mitochondrial sulfhydryl groups possibly by direct reactions of aldehydes with mitochondrial SH-groups. An increase in oxidative stress is induced in mitochondria. The studies also revealed prominent genotoxic effects of BCCP.

Chapter 9 (O.Sommerburg, C.D.Langhans, C.Salerno, C.Crifo, W.Siems) addresses the negative effects seen in smokers after intake of relatively high doses of supplemented β-carotene. It might be possible that the prooxidative effects seen in heavy smokers are also the result of an increased oxidative stress due to the large pool of stimulated neutrophils in the lung tissue of smokers.

Recent evidence shows that lycopene exerts protective effects against smoke-induced lung carcinogenesis, and the reason for that is traced back in Chapter 10 (X.D.Wang) to upregulating the insulin-like growth factor (IGF-1) binding protein IGFBP-3.

Gap junctional communication (GJC) has been discussed in Chapter 5 and is also dealt with in Chapter 11 (L.M.Hix, A.L.Vine, S.F.Lockwood, J.S.Bertram). The emphasis is on the mechanisms of upregulated connexin-43 expressions by retinoids and carotenoids. Retinoids appear to act via interactions with retinoic acid nuclear receptors, whereas there is evidence that carotenoids may activate peroxisome proliferator-activated receptors. A novel astaxanthin derivative is described, which can upregulate connexin 43 when delivered in aqueous vehicle.

Lycopene and the risk of cardiovascular disease is discussed in Chapter 12 (L.Petr, J.W.Erdman). Epidemiology as well as tomato and lycopene supplementation trials suggest a role of lycopene in preventing cardiovascular disease.

Chapter 13 (K.J.Yeum, G.Aldini, E.J.Johnson, R.M.Russel, N.I.Krisnky) addresses the effects of high fruit and vegetable diet (feeding and depleting) on oxidizability in human serum. It was found that carotenoids either are the direct determinants of oxidizability in human serum or that they are serving as a marker for other dietary factors.

Continued examination of the mechanisms of synthetic retinoid-induced apoptosis should provide further clues to support the notion that the mitochondria are important targets for both cancer chemoprevention and therapy, and this is thoroughly discussed in Chapter 14 (N.Hail, R.Lotan).

The state of knowledge about the molecular components of the vitamin A biosynthetic pathway is reviewed in Chapter 15 (J.v.Lintig), with special emphasis on the discussion of carotene oxygenases, regulation of the pathway, the role of provitamin A as an essential precursor and centric vs. eccentric cleavage.

Chapter 16 (Y.Sharoni, R.Agbaria, H.Amir, A.Ben-Dor, N.Dubi, Y.Giat, K.Hirsh, G.Izumchenko, M.Khanin, E.Kirilov, A.Nahum, M.Steiner, Y.Walfisch, S.Walfisch, M.Danilenko, J.Levy) discusses that carotenoids modulate the basic mechanisms of cell proliferation, growth factor signaling, gap junctional intercellular communication (see Chapters 5 and 11) and produce changes in the expression of many proteins participating in these processes. These all can form the basis for the beneficial effects of carotenoids on human health and disease prevention. The evidence presented suggests also a synergistic action of low concentrations of various carotenoids and other micronutrients, which modulate a network of transcription systems.

The important problem of malnutrition and Vitamin A deficiency in developing countries is addressed in Chapter 17 (M.v.Lieshout, C.E.West). Bioavailability, bioconversion and bioefficacy are emphasized. The efficacious supply of a nutrient is defined. Strategies are suggested: increasing the efficacious supply of vitamin A and reducing the body's vitamin A demand, e.g. by controlling infection. Food-based approaches like fortification, biofortification and nutrification are also mentioned.

Lycopene is the major carotenoid detected in the human prostate gland and the lycopene-prostate cancer link is a topical discussion in Chapter 18 (U.C.Obermüller-Jevic, L.Parker). Among carotenoids only lycopene is inversely related to the risk of prostate cancer. Lycopene may inhibit the increase of PSA in blood and tumor development. There is clear evidence to support that lycopene is a promising nutrient in prostate health.

Chapter 19 (K.Kraemer, G.Krennrich, U.Obermüller-Jevic, P.P.Hoppe) attempts to go into the matter of a relationship across studies between β-carotene dose and blood response, which is unknown as a rule. The influences of multiple-unit dosing, beadlet formulation and cosupplementation with other micronutrients are evaluated.

New horizons in carotenoid research in Chapter 20 (H.Sies, W.Stahl) encompass many aspects in health issues: prevention of macular degeneration, cancer and cardiovascular disease by carotenoids, orientation in cellular membranes, carotenoid binding and metabolizing proteins, optimal dietary intake, long-term supplementation, retinoic acid pathways, cooperative activity with other micronutrients, induction of phase I and phase II metabolic enzymes, gap junctional communication, UV-protection, Vitamin A deficiency, focus on more and other carotenoids, analysis of cleavage products.

Chapter 21 (J.M.Gaziano, H.D.Sessoa) reviews critically the proposed biological mechanisms, by which carotenoids may be associated with heart and vascular diseases.

The final Chapter 22 (N.I.Krinsky) subsumes important questions under the aspect "safety": Is β-carotene from supplements safe? Which population groups are likely to benefit from supplemental β-carotene? Can a safe upper level be established for β-carotene? These and other questions are answered, elucidated or commented.

The book is well written and presented in unobjectionable format with instructive figures and tables. It contains a most comprehensive depiction of the vital and indispensable functions of retinoids and carotenoids with regard to topical health issues. The book is recommended to all interested in natural products, phytochemicals, micronutrients and nutrition.

Hans-Dieter Martin