

BOOK REVIEWS

THE PHARMACOLOGY OF BENZOPYRONE DERIVATIVES AND RELATED COMPOUNDS

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The benzopyrones are a remarkable group of compounds, which include the flavonoids and the coumarins. They are of particular interest to lymphologists since a number of very differing members of the group have recently been shown to reduce lymphedema and even elephantiasis. These drugs are also of general interest since high-protein edemas that frequently accompany many disease processes promote reduced tissue oxygenation, function and healing and long-term chronic inflammation and intense fibrosis. While the benzopyrones have many diverse properties they each appear capable of reducing high-protein edema and thereby alleviating these sequelae.

Because of the similarities of their properties, these compounds including the flavonoids and coumarins are now united under the rubric of "benzopyrones." Apart from an effect on high-protein edema, benzopyrones also share the common property of vitamin P-like action, i.e., supplying an essential factor to minimize excess blood capillary permeability.

Prof. Gabor is justifiably renowned for pioneering work on many of the benzopyrones, both for original investigation of their pharmacology and for superb overviews of the subject. These reviews have been of great assistance to other workers and it is clear that the latest book will be of equal value. The text is divided into three parts.

Part One is devoted to the pharma-

cokinetics of the benzopyrones and closely related substances with similar properties. This is a valuable collection of data which has not been compiled before in such detail. It will be of inestimable value for those trying to design appropriate doses and schedules. There is one issue of potential disagreement--conventional concerns about steady blood drug levels may be unnecessary in considering treatment of high-protein edema. Because benzopyrones appear to reduce edema by increasing proteolysis by macrophages and this macrophage response persists for many days to weeks after dosage has ceased, a steady blood drug level may not be required for therapeutic response. Therefore, pharmacokinetics need to address the issue of how much of the drug reaches macrophages, a near-impossible task, except indirectly by observing the drug effect on tissue swelling. There is also the possibility that the "inactivated" glycosides of the benzopyrones in the bloodstream may not, in fact, remain inactive but are converted back to an active form in the tissues!

Part Two discusses the broad effects of benzopyrones on a wide variety of enzyme systems. Nonetheless, they all exert a common effect on specific systems, as, for example, proteolysis by macrophages. This area of the book is extremely valuable for providing insight into these properties.

Part Three discusses new results of the pharmacological effects of the benzopyrones and related compounds. The therapeutic uses of these drugs are remarkably broad including inflammation, various high-protein edemas, and disorders involving the central and vegetative nervous systems, smooth muscle, cardiovascular system, respiratory system, and gastrointestinal tract. When one considers

that benzopyrones as a group are of remarkably low toxicity, with few side effects as well as demonstrable therapeutic value, it is evident that they should be used much more widely than is currently the case. In a way, it seems a pity that this useful group of drugs remains so little known and so seldom used. Prof. Gabor's book should help remedy this situation.

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HIGH-PROTEIN OEDEMAS AND THE BENZO-PYRONES

Authors: J.R. Casley-Smith and Judith R. Casley-Smith

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The Casley-Smiths have provided a summary of the anatomy and physiology of the microcirculation and lymphatics, and the pathology, patho-physiology and epidemiology of edemas, especially high-protein edemas. These are all covered well in the first four chapters. Then, after six chapters on benzo-pyrones, the eleventh and final chapter reviews applied physiology of various methods of treatment of high-protein edemas.

The structure, history and sources of benzo-pyrones are presented followed by a chapter on their actions in animals. It is alleged that there is reduction of excess fibrosis in high-protein edemas, and reduction of other aspects of inflammatory reaction. A listing of actions in a paragraph in a summary of chapters seems to depict benzo-pyrones as a panacea for almost all oncologic and vascular disorders. "The benzo-pyrones also stabilize the interstitial tissue, reduce its permeability if this is elevated, and improve wound healing." Other actions of the benzo-pyrones are mentioned more briefly: as an anti-spasmodic for smooth muscle (in general, and of blood and lymphatic vessels); preventing the

aggregation of blood components; against hepatic poisons; preventing the desquamation of blood endothelial cells; acting as a vitamin P factor; as bacteriocidal, anti-viral and anti-helminthic agents; and as an antipyretic. "The benzo-pyrones also tend to increase immunologic defense mechanisms and to have many anticarcinogenic actions."

The attempts to explain the method of action of the benzo-pyrones suggest that the principal actions lie in the areas of increased proteolysis and effects on the stabilization of vascular membranes.

The chapter dealing with human trials continues to extol the numerous alleged benefits of the benzo-pyrones. Cited are improvements in lymphedema and the associated symptoms and complications; ophthalmologic pathology; Meniere's disease; chronic venous insufficiency and varicose conditions associated with pregnancy, hemorrhoids and micro-varices of the vocal cords; pancreatitis; hepatitis; cirrhosis; tuberculosis; pulmonary fibrosis and allergic conditions. Of special interest are the references to increased tolerance to ionizing irradiation and improved immunological capacity. These include improvement in carcinomas, melanomas and Kaposi's sarcoma and trials in AIDS. Side effects and toxicity are considered negligible.

In the dedication, due credit is given to Professor Mihaly Földi, "who was the parent of many of the concepts." The concluding sentence of the preface states, "They (benzo-pyrones) often cannot cure the underlying disease; but they can do much to reduce the disability caused by its consequent edema, to prevent the sequelae of this, and to accelerate healing."

In view of today's concerns with immunologic deficiency, even if many of the possible beneficial effects of the benzo-pyrones are not conclusive, reference to this book can stimulate thoughts which may lead to profitable future investigations and clinical trials.

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