

viruses have been associated with development of chronic infection which lead to autoimmune diseases either by persistent or latent viral antigen or molecular mimicry. Modulation of apoptosis may play a role in pathogenesis of arthritis associated with infection of adenovirus, baculovirus, HIV and influenza virus. Inhibition of apoptosis is associated with persistent infection, latency enhancement of viral production whereas promotion of apoptosis facilitates virus spread and release. Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting synovial tissue in multiple joints. There is a strong evidence to suggest a role of CD<sub>4</sub><sup>+</sup> T cells as well as of activated macrophages and fibroblasts like synovocytes which destroy articular structure in chronic RA disease. Inadequate apoptosis appears to play a significant role in the increased cellularity in the synovial tissue. Interventions aimed at enhancing apoptosis in the synovium are emerging as potentially effective forms of treatment. Osteoarthritis (OA) is the most frequent musculoskeletal disorder, especially in the aging population. There is reduction in chondrocyte cell number due to apoptosis involving a number of multiple molecular pathways. The pathogenesis of systemic lupus erythematosus (SLE) is multifactorial and multigenetic. Chronic inflammation associated with it is thought to be due to loss of self-tolerance and apoptosis defects. Fas and Fas ligand regulate NF $\kappa$ B, kinases, phosphatases, bcl-2 family members, interleukin 1- $\beta$  converting enzyme (ICE) and FLICE (FADD-like ICE) family members which may be dysregulated in patients with SLE. There is strong evidence for involvement of apoptosis in acute renal failure but it is not clear whether it is involved in disease progress or the repair process or both. Thus a direct connection of apoptosis with numerous disease states has been established and the number of examples will probably increase as more apoptosis and disease regulation genes are identified, and their biochemical activities established. Opportunities for novel therapy may then become apparent.

I trust that both experienced and new researchers alike will read this book as a primer on what is new and possible in apoptosis and immune system. This book will serve as a useful resource material and guide for biochemists/researchers who wish to understand the role of

apoptosis, particularly in immune/inflammatory disease. The number of references to the primary literature is fairly large, i.e. more than 850. It covers a small number of topics in depth and with relevant detail. In summary this book will find an appreciable but limited audience.

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**Proton Pump Inhibitors: Milestones in Drug Therapy.** L. Olbe (ed.). Birkhäuser Publication. 1999. 264 pp. Price: SFr 188/DM 238.

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Innovation has become the industrial religion of the new millennium. Healthcare business sees it as the key to increasing profits and market share. For more than 100 years it has been known that gastric acid secretion is not the only but an essential causative factor in the pathogenesis of acid-related diseases. Thus reduction of acid secretion became a major therapeutic goal. For quite sometime, surgical procedures (gastric resection and vagotomy) were used as effective interventions in the management of peptic ulcer diseases. The introduction of potent inhibitors of acid secretion, that is the H<sub>2</sub> receptor blocking agent cimetidine and its analogues in the late seventies and the even more potent proton pump inhibitor omeprazole and its analogues in the late eighties have revolutionized therapy. Around the world, the rhetoric of innovation has replaced the redundant products or surgical approaches in the management of peptic ulcer disorders.

This new monograph series – *Milestones in Drug Therapy* – highlights new therapeutic developments of proton pump inhibitors, which have provided significant steps forward in the fight against

peptic acid disease. Each book in this series generally deals with an individual drug or drug class, which has altered the approach to therapy. Experts in the field place emphasis on the scientific background to the discoveries and the development of the therapy, with an overview of the current state of knowledge of the drugs. The series is aimed at a broad readership, covering biochemistry, pharmacology and clinical aspects, as well as revealing the personal stories behind these milestone developments.

This book *Proton Pump Inhibitors* presents the story starting from the initial observation of classical experiments to the launch of four proton pump inhibitors in six chapters namely: the discovery and development of the proton pump inhibitor; mechanism of action; the pharmacology of proton pump inhibitors; pharmaceutical considerations; clinical experience with proton pump inhibitors and socio-economic impact of acid-related diseases. Modern drug discovery mostly relies on identification and characterization of potential targets by genome research, molecular biology, combinatorial chemistry and automated screening. But the first chapter takes the reader back by thirty-three years and gives narration how director Ivan Östholm initiated an innovative research project in the gastrointestinal field at Astra Hässle using classical screening methods. It is worthwhile for all researchers engaged in drug discovery research to read the development of the first proton pump inhibitor – omeprazole – starting from a chemical structure with an observed antisecretory effect but also severe toxic effects that had to be eliminated. As always, the basic and the applied research operate hand in hand to optimize the delicate balance between efficacy and safety of a new drug.

The second chapter starts with the landmark paper of William Prout presented at the Royal Society Meeting on 11 December 1823, stating that 'On the Nature of Acid and Saline Matters Usually Existing in the Stomach of Animals'. He was the first to identify the hydrochloric acid in the gastric juice of many species and was able to quantify the free and total acid. Further, work on acid secretion in isolated frog mucosae in the 1960s paved way to identify the molecular target involved in acid production. This chapter gives a detailed biochemical description of the gastric H<sup>+</sup>, K<sup>+</sup> ATPase

and its gastric acid secretion inhibition potentials. The third chapter gives greater details of animal pharmacology and clinical studies pertaining to proton pump inhibitors. Overviews compare omeprazole and other proton pump inhibitors and discuss their pharmacology, including the mechanism of action, the effect on *Helicobacter pylori* infection and the consequences of profound inhibition of gastric acid secretion. The fourth chapter deals with physicochemical properties of omeprazole, lansoprazole, pantoprazole and rabeprazole; oral formulation principles, dosages; influence of food and antacids; parenteral dosage forms and pharmaceuticals delivery system for other routes of administration of proton pump inhibitors.

The clinical experience with proton pump inhibitors in acid-related diseases is reviewed in the fifth chapter with focus on gastro-esophageal reflux disease, peptic ulcer diseases including *Helicobacter pylori*, non-steroidal anti-inflammatory drugs associated ulcers and Zollinger-Ellison syndrome. Socio-economic impact including aspects that concern both the individual and society are dealt with in the last chapter. Here the authors provide some background of concepts like prevalence and incidence of acid-related disorders, emphasizing the important aspect of quality of life, direct and indirect cost (pharmacoeconomic) associated with acid-related disorders and its total socio-economic impact.

Overall this book gives information about the problem faced in launching a tailor-made drug for a specific target; the dramatic changes in the outcome of results in the treatment of peptic ulcer disease and its impact on pharmacoeconomics. It is written by eminently qualified scientists from industry, academics and clinicians. This volume is intended not only for those active in research into proton pump inhibitors but also for those with an interest in peptic ulcer disorders.

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**Geology of Rajasthan: Status and Perspective.** P. Kataria (ed.). Department of Geology, M. L. Sukhadia University, Udaipur, 1999. pp. 250. Price: Rs 400.

Rajasthan State constitutes the bulk of Aravalli Craton which preserves a fascinating geological record from 3500 million years ago to the present. Rajasthan is geologically well known for its Proterozoic rocks of the Aravalli mountains which throw light on the operation of plate tectonics in the distant past. It has a singular and complete example of acid magmatism in the Malani Igneous Suite. A wide array of Quaternary formations provide valuable evidence of neotectonics, and throw new light on the lost Vedic river Sarasvati. The Thar Desert presents a unique example for the study of desert geology. Rajasthan has major lead-zinc (and copper) deposits and a host of useful industrial minerals including the famous Makrana marbles and alluring gemstones. It is not surprising that such an attractive geological tapestry has spawned several new edited volumes on the geology of the region. For example, the Geological Society of India has published two Memoirs (No. 7, 1988 and No. 31, 1995), besides a textbook on *Rajasthan Geology* by S. Sinha-Roy and others in 1998. B. S. Paliwal edited a volume on the Indian Precambrian (1998), a large part of which is devoted to Rajasthan geology. The present volume which represents the proceedings of the seminar with the same title is brought out to felicitate the distinguished Professor A. B. Roy on his retirement from the University of Rajasthan (now called M. L. Sukhadia University). It contains nine thematic as well as review papers contributed by specialists in their respective fields.

The volume begins with a comprehensive update on the regional geology of Rajasthan by A. B. Roy and P. Kataria, which provides a balanced appraisal with emphasis on the stratigraphic classification proposed by A. B. Roy and his associates. B. Sreenivas and coworkers describe geochemical changes across one of the major hiatuses in earth history at the Archaean-Proterozoic boundary/transition about 2500 million years ago. They confirm the widely documented change in the earth's record, viz. decrease in the abundance of Cr, Ni, Sc in the Proterozoic rocks compared to the Archaean, from the Aravalli rocks of Rajasthan. S. Sinha-Roy deals with his favourite

subject of Precambrian plate tectonics as applied to Rajasthan, with emphasis on Rakhabdev and Phulad ophiolites marking two major sutures between tectonic blocks at 1500 and 1100 Ma respectively. S. K. Bhushan describes two major felsic magmatic events in Rajasthan, namely, the Erinpura and Abu granites (800–900 Ma) formed by anatexis during collision, and the Malani volcanic and plutonic suite (730–750 Ma) formed by rift tectonics related to 'hot spot' activity. D. S. Chauhan describes the evolution of the largest sedimentary basin (Marwar basin) formed in Neoproterozoic to Cambrian time. Anil Bhandari provides an excellent overview of the Phanerozoic stratigraphy of the major sedimentary basins of western Rajasthan, viz. Jaisalmer, Bikaner-Nagaur and Barmer. He makes a brief mention of possible hydrocarbon resources and lignite in these basins. Amal Kar traces the evolution of landforms carved by aeolian and fluvial processes in the Quaternary, with special emphasis on the development of Thar Desert with its dunes and saline depressions (ranns) like Mitha or saline lakes like Sambhar.

Mihir Deb gives a succinct account of classification and genesis of the metallic mineral resources of Rajasthan, prominent among them being the well-known deposits of zinc and lead at Agucha, Zawar and others. There are also other potential deposits of copper, gold, silver, tin, tungsten and uranium in Rajasthan. The book has the concluding paper on the industrial minerals and decorative stones of Rajasthan by M. K. Pandya and others. The important minerals in this category are phosphorite, soapstone, asbestos, gypsum, salt, ochre, limestone, graphite, wollastonite, fluorite, calcite, etc. The marbles of Rajasthan are famous the world over. Rajasthan is also well known for its precious stones like garnet.

This volume encompasses all aspects of Rajasthan geology leaving out groundwater resources and geoenvironmental problems. This book is printed and bound well, although the reproduction of figures could have been better. The volume is a very valuable addition to our knowledge of Rajasthan geology and is useful for teachers, students and professional geologists.

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