DESCRIPTION

Closing a gap in the scientific literature, this first comprehensive introduction to the topic is based on current best practice in one of the largest pharmaceutical companies worldwide. The first chapters trace the development of our understanding of drug metabolite toxicity, covering basic concepts and techniques in the process, while the second part details chemical toxicophores that are prone to reactive metabolite formation. This section also reviews the various drug-metabolizing enzymes that can participate in catalyzing reactive metabolite formation, including a discussion of the structure-toxicity relationships for drugs. Two chapters are dedicated to the currently hot topics of herbal constituents and IADRs.

The next part covers current strategies and approaches to evaluate the reactive metabolite potential of new drug candidates, both by predictive and by bioanalytical methods. There then follows an in-depth analysis of the toxicological potential of the top 200 prescription drugs, illustrating the power and the limits of the toxicophore concept, backed by numerous case studies. Finally, a risk-benefit approach to managing the toxicity risk of reactive metabolite-prone drugs is presented.

Since the authors carefully develop the knowledge needed, from fundamental considerations to current industry standards, no degree in pharmacology is required to read this book, making it perfect for medicinal chemists without in-depth pharmacology training.
ABOUT THE AUTHOR

Amit Kalgutkar received his academic degrees from the University of Bombay (India) and from Virginia Polytechnic Institute (USA). Joining Pfizer in 1999, he is currently a Research Fellow in the Pharmacokinetics, Dynamics and Metabolism Department at Pfizer (Groton Laboratories). He is also an adjunct faculty member in the Department of Biomedical and Pharmaceutical Sciences, University of Rhode Island.

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Scott Obach received his Ph.D. in biochemistry from Brandeis University and was a post-doctoral fellow at the New York State Department of Health Research Labs. He joined Pfizer in 1992, where he is currently a Senior Research Fellow in the Pharmacokinetics, Dynamics, and Drug Metabolism Department at Pfizer in Groton (USA). In addition, Dr. Obach is on the editorial boards of Drug Metabolism and Disposition, Chemical Research in Toxicology, Xenobiotica, and Drug Metabolism and Pharmacokinetics.

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Dennis Smith has worked in the pharmaceutical industry for 32 years after gaining his Ph.D from the University of Manchester (UK). For 20 years he was at Pfizer Global Research and Development, Sandwich where he was Vice President-Pharmacokinetics, Dynamics and Metabolism. During this time he has helped in the Discovery and Development of eight marketed NCEs. He has authored over 130 publications including three books.

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