

Testa B & Jenner P. *Drug metabolism: chemical and biochemical aspects*.

New York: Dekker, 1976. 500 p.

[School of Pharmacy, University of Lausanne, Switzerland and Department of Neurology, Institute of Psychiatry and King's College Hospital Medical School, London, England]

As explicit in its title, this book presents drug metabolism from two vantage points. Its systematic approach based on metabolic pathways and biological factors has heuristic value probably accounting for its success. [The *SCI*® indicates that this book has been cited in over 385 publications.]

## The Coming of Age of Drug Metabolism

Bernard Testa  
Ecole de Pharmacie  
Université de Lausanne  
Institut de Chimie Thérapeutique  
CH-1005 Lausanne  
Switzerland  
and  
Peter Jenner  
Pharmacology Group  
Biomedical Sciences Division  
King's College  
London SW3 6LX  
England

March 6, 1990

This book was conceived in explicit form in May 1973, but its implicit unfolding should be traced to the date of our first encounter two and a half years earlier. At that time, our doctoral exams still a very fresh memory, we were both starting a hopefully independent scientific career as postdoctoral fellows under the airborne and benevolent guidance of Professor Arnold H. Beckett. It was thus pure chance that brought us together in Chelsea College and allowed us to work for two years in the same laboratory (the infamous B25), a converted courtyard where ether was evaporated in the open by the gallon and green plants would not survive for more than a fortnight despite our loving care and the pale light that would filter through a translucent ceiling on sunny days. Fortunately for Testa, the Swiss National Science Foundation and the Royal Society, whose common grant supported him, were aware only of the invigorating intellectual climate of the place.

Our research projects both dealt with stereochemical aspects of drug metabolism and drug action, and these rapidly became the main topic of

our beer-time conversations. Our effective collaboration began with a conformational study of nicotine<sup>1</sup> and continued with a much more ambitious work, namely, a systematic and extensive review of the influence of stereochemical factors on drug metabolism.<sup>2</sup> Dr. Frederick J. Di Carlo, the editor of the just-founded *Drug Metabolism Reviews*, deserves our warmest gratitude for trusting two inexperienced postdocs and helping them with advice and encouragement.

By that time our casual postdoctoral period was over, and we had both taken up new academic rôles—one as an assistant professor in Lausanne, the other as a lecturer in London. Despite distance and duties, our collaboration continued to thrive, but the idea of writing a book on drug metabolism, when first conceived, seemed too formidable a challenge. Even worse, the danger was genuine that the time and energy necessary for such an undertaking would be diverted from research on whose success our future careers depended. On the other hand, there was a real need for a book encompassing the chemistry, biochemistry, and biology of drug metabolism in a methodical and comprehensive manner. Much progress had been made since the publication of the classic textbook by R.T. Williams.<sup>3</sup> New pathways had been discovered, biochemical mechanisms were beginning to make sense in a number of cases, some structure-metabolism relationships had become apparent, and a wealth of data had been published on the factors, both endogenous and exogenous, regulating or affecting drug metabolism. Again, Di Carlo offered advice, encouragement, and essential help in recommending us to a publisher. That Fred wrote the foreword in that inimitable style of his is only a fit tribute to his trust, distinction, and friendship.

The book commanded attention as soon as it was published, confirming that it was indeed filling a void. Part of its interest, we have reasons to believe, lies in a presentation that is based on functional groups and metabolic pathways rather than on classes of substrates. The heuristic value of such a presentation is evident as it renders the student capable of educated guesses on the metabolism of other or novel drugs. Interestingly, the book has provided the ground material for an expert system<sup>4</sup> capable of drawing, in a more or less systematic manner, a metabolic tree for a practically unlimited number of chemicals.

Fourteen years have now passed since the publication of this book, 14 years of extraordinary advances in the mature science of xenobiotic metabolism. This, however, is another story!

1. Testa B & Jenner P. Circular dichroic determination of the preferred conformation of nicotine and related chiral alkaloids in aqueous solution. *Mol. Pharmacol.* 9:10-6, 1973. (Cited 10 times.)
2. Jenner P & Testa B. The influence of stereochemical factors on drug disposition. *Drug Metab. Rev.* 2:117-84, 1973. (Cited 95 times.)
3. Williams R T. *Detoxication mechanisms*. London: Chapman & Hall, 1959. 796 p. (Cited 1,545 times.)
4. Darvas F. Predicting metabolic pathways by logic programming. *J. Mol. Graphics* 6:80-6, 1988.