**Quantitative Pharmacology**

**– An Introduction to Integrative Pharmacokinetic-Pharmacodynamic Analysis**

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It is with great excitement that I hold a brand new book on pharmacokinetics –pharmacodynamics in my hands. This has occurred a number of times before in my professional life and my question is always: How will these authors explain the stuff and how will they make the readers interested? Will there be some new approaches? Even more so when you know the authors as extremely competent in the area and also with a high reputation as teachers. The new book by Johan Gabrielsson and Stephan Hjorth has the wise and very timely title *Quantitative Pharmacology,* further specified as an *Introduction to Integrative Pharmacokinetic Pharmacodynamic Analysis*. The authors explain convincingly why it is now time to apply the integrative approach in this area which I find refreshing.

The journey of the drug through the body in its strict sense is known as pharmacokinetics and the drug effects, are collected under the term pharmacodynamics . The drug molecules have to reach a site of action where they interact with some target structures to produce the response. This principle is epitomized in the introductory graph below showing the integrated 3D plot with time as an independent variable and its relation to drug concentration and response as well as the relationship between concentration and response.



Failure to exploit and understand integrated effects of PK and PD is a driver for the author team and is rooted in their experiences from pharmaceutical drug development. Insight in experimental design and how to analyze and interpret results will prove to be also of great economical importance. Mistakes here could even kill a promising drug candidate of which pharmacokinetic properties do not seem favorable. Three compounds are stated as examples; felodipine, omeprazole and quetiapine with quite or rather low bioavailability and short half lives in man. However, they were all successful in oral dosage forms since they have long pharmacodynamic half life. – This approach indicates the primary reader target group for the book, but it can undoubtedly also benefit senior students and workers in the pharmacological and clinical pharmacological areas. Hence, it is recommended that readers should have some prior familiarity with PK and PD before starting the book.

The structure of the content is to present kinetic phenomena from a “pharmacodynamic point of view” which is a refreshing and useful approach. Other standard items like the influence and treatment of protein binding are conventionally explained. I felt stimulated by collecting one set of phenomena under the subtitle “Principles of Dose, Time and Flow Dependencies.

One highlight is the chapter on “Time delays between plasma concentrations and response”. The authors review how a delay is observed e.g. as hysteresis and a number of reasons for such a delay. Strategies taken to evaluate the observations e.g. the introduction of an effect compartment or the application of mechanism based turnover models that have gained increased popularity in recent years. This means that accepted mathematical expressions e.g. for enzyme inhibition or receptor interaction may be used in the context to fit and interpret observational data to model parameters.

The concept of biomarkers is increasingly stressed in this area of research. Some quantity has to be measured to make the work meaningful and a discussion persist about the properties of biomarkers, their relevance, distribution, precision, etc. A useful 7-step grading of biomarkers reaching from the fundamental type 0 genetic and phenotypic markers up to type 6 which characterizes clinical states is presented.

The book is ended by a thoughtful and accurate chapter on why, how and when interspecies scaling shall be applied.

I consider the book by Gabrielsson and Hjorth to be very useful for in depth studies by scientists working with drug development and experimentalists in clinical pharmacology. It combines the analysis of effects versus time patterns with kinetic corollaries in a most comprehensive way. Moreover, it is a book of great graphical beauty exceptionally styled with a cover painted by one of the authors.

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