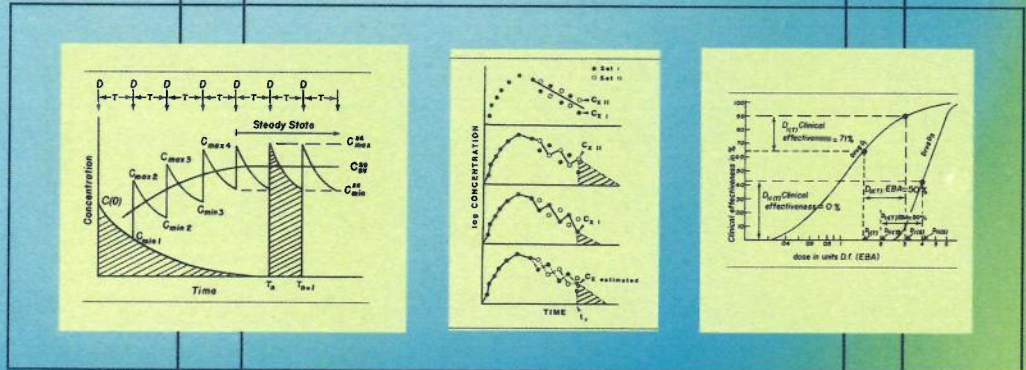


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HANDBOOK of BASIC PHARMACOKINETICS ...INCLUDING CLINICAL APPLICATIONS



SIXTH EDITION



Handbook
of
Basic
Pharmacokinetics

... including Clinical Applications

Sixth Edition

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Appendix

Pharmacokinetic Parameters of Important Drugs

Pharmacokinetic data have become an integral part of the pharmacologic characterization of a drug. Regulatory agencies require determination of pharmacokinetic data in Phase I studies and submission of pharmacokinetic drug data as part of a New Drug Application.

For research and development, pharmacokinetic drug data are used in design of new chemical entities based on structure-activity relationships, and for design of proper dosage forms to result in the desired therapeutic concentrations.

Clinically, pharmacokinetic data are used for the design of dosage regimens in drug-naive patients, for drug monitoring, and for dosage regimen adjustment. Furthermore, pharmacokinetic data give information or indications whether a drug may be excreted in milk (pK_a), whether the half-life may change in renal impairment or advanced age (F_{el}), and whether protein binding may be of clinical importance regarding displacement, hypo- and hyper-albuminemia (if EPB > 80 percent), etc.

Data listed in the appendix have been compiled and extracted from more than a thousand publications. Hence, it is not possible for reasons of space to give a listing of references. The data have been listed as *mean* data. Reports are often conflicting, contradictory, or at least show wide variations among investigators. This, in part, is due to different analytical methods employed for drug assay, different population groups, and different experimental conditions.

Only the elimination half-life ranges are listed for many drugs. This should be indicative that a calculated dosage regimen based on literature mean data may not result in a desired therapeutic concentration and hence, drug monitoring becomes more important. Also, most of the pharmacokinetic data refer to healthy, young adults. However, many physiologic and pathologic conditions may greatly influence the pharmacokinetics of a drug. Again, drug monitoring in such situations may become important.

The following symbols are used:

$t_{1/2}$	= elimination (terminal) half-life
k_{el} or β	= terminal disposition rate constant
V_d	= apparent volume of distribution ($V_{d\beta}$ or $V_{d\text{area}}$)

F_{el}	= fraction of unchanged drug excreted in urine
f	= fraction of drug absorbed = absolute bioavailability. Unless otherwise indicated, f refers to <i>peroral</i> administration.
EPB	= extent of protein binding in plasma
Ther. Range or MEC	= therapeutic range or minimum effective concentration Note: For antimicrobial agents the MEC or MIC (minimum inhibitory concentration) depends on the sensitivity of the microorganism. Hence, a sensitivity test may be more appropriate than a listed mean value.
URA	= usual route of administration. This listing is not exhaustive. Even if not listed, the drug may be used by other routes.
D	= dose size <i>usually</i> employed as maintenance dose. Loading doses are not listed.
τ	= dosing interval for multiple dosing
t_{max}	= time to reach the peak upon extravascular administration
NA	= Not applicable
—	= Data not available
a	= V_d/f
b	= C_{max} or C_{max}^{ss}
c	= C_{min} or C_{min}^{ss}
d	= if required, repeat dose after 2 h
e	= $\mu\text{mol/L}$
f	= poor metabolizer
g	= effective concentration 50% = EC_{50}

Kinetic Parameters of Important Drugs

$t_{1/2}$ (h)
 k_{el} or β (h^{-1})
 V_d (l/kg)
 F
 f
 EPB (%)
 τ (h)
 D (mg/kg)
 t_{max} (h)
 t_{max} (h)

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