

gressively increase, then reach a maximum or asymptotic value. When the individual values are expressed as percentages of the maximum or asymptotic value, the results are per cent absorbed values to various times. Theoretically, the maximum or asymptotic value of the right-hand side of Eq. 5 is $K \cdot \int_{t=0}^{t=\infty} C \cdot dt$ and of Eq. 6 is $(A_e)_\infty$, where $\int_{t=0}^{t=\infty} C \cdot dt$ is the area under the blood level time plot from $t = 0$ to $t = \infty$, and $(A_e)_\infty$ is the amount of unchanged drug excreted in the urine in infinite time. The methods are independent of the values of V and f since these values cancel out when the percentages are calculated. The per cent absorbed value so calculated is the cumulative amount absorbed to time T expressed as a percentage of the total amount of drug which is absorbed (not as a percentage of the dose).

When the cumulative percentages absorbed are plotted against time, the resulting plots may contain linear segments; the slope of such a linear segment is the absorption rate in per cent/hour. If the plot is curved, or contains curved and linear segments, it may often be resolved to yield the components of the rate $d\%A_T/dt$. In this way the model which applies to a particular set of blood level or urinary excretion data can be determined accurately. The method may also be applied to problems in chemical kinetics involving consecutive and/or simultaneous first-order and zero-order reactions.

The process of obtaining the per cent absorbed-time plots from blood level data has been automated in two ways. In the first method, the blood level data are plotted on suitable graph paper and the points joined with a smooth line using a special conducting ink. Using a curve-

follower, an analog computer was programmed to perform the operations dictated by Eq. 5 and to plot the result on another piece of graph paper. The asymptotic value is estimated from the plot, the values of A_T/V are obtained from the plot, and then expressed as a percentage of the asymptotic value. In the second method, the blood level-time values are fed to a suitably programmed digital computer. The computer calculates the cumulative areas, using the trapezoidal rule, then performs the necessary operations shown in Eq. 5. The print-out contains the values T , C_T , $\int_{t=0}^{t=T} C \cdot dt$, and $\left[C_T + K \cdot \int_{t=0}^{t=T} C \cdot dt \right]$. The latter are then expressed as percentages of the asymptotic or maximum value of the same function to yield the cumulative per cent absorbed values.

Per cent absorbed-time plots derived from *in vivo* data are the optimum data to correlate with per cent released time plots derived from *in vitro* testing.

Future publications will illustrate applications of these methods in detail.

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Book Notices

Recent Advances In Pharmacology. 3rd ed. By J. M. ROBSON and R. S. STACEY. Little Brown and Co., 34 Beacon St., Boston 6, Mass., 1962. x + 406 pp. 15 X 23.5 cm.

The reader of this book will find several areas of recent progress in pharmacology discussed in some detail through the efforts of the authors and nine contributors. The chapter on pharmacologically active substances in the central nervous system requires 38 pages. One-third of the chapter is devoted to catechol amines and 5-hydroxytryptamine;

5-hydroxytryptamine is later treated in a separate chapter of 30 pages and the catechol amines in another of 25 pages. Other chapters deal with psychotropic drugs, pharmacologically active polypeptides, hypoglycaemic agents and diabetes mellitus, diuretics and electrolyte balance, newer steroids, cholesterol, hypotensive drugs, bacterial chemotherapy, new drugs in the treatment of tropical diseases, and hypnotics, anticonvulsants, analgesics, and antitussives. References to pertinent literature follow each chapter.