Determination of pharmacokinetic parameters for urinary excretion of sulphafurazole under normal and controlled alkaline urine conditions

Pharmacokinetic parameters for sulphafurazole have been calculated from urinary excretion evidence (Nelson & O'Reilly, 1960) and blood concentration figures (Bünger, Diller & others, 1961) under normal urine conditions, and under controlled acid and alkaline urine conditions from blood concentration estimations (Dettli & Spring, 1966). In our experiments the drug was administered under both normal urine conditions and after an alkali load so as to eliminate diurnal fluctuations in the urinary pH over a period of 48 h and thus examine the effect of these urine conditions on the rate and other constants involved in the urinary excretion of sulphafurazole. The kinetic data was obtained by using the model and differential equations described by Nelson & O'Reilly (1960).

The drug was administered in the form of compressed tablets of which a representative sample was found to contain 101·50% of label claim. Alkaline urine conditions were maintained by ingesting approximately 4 g of sodium bicarbonate 1·5 h before the tablets were taken, followed by 4 g at 3 hourly intervals. One g of drug was administered on a fasting stomach to three healthy male subjects, and no ingestion of food was allowed until at least 2 h after the tablets had been taken. Urine samples were collected hourly for the first 6 h, and thereafter at increasing intervals up to 48 h. Treating the zero-hour sample as a blank, the specimens were assayed for free and total sulphafurazole by the Bratton & Marshall (1939) method. All hydrolysable conjugates were regarded as acetylated drug.

The computed rate and other constants involved in the acetylation and excretion of sulphafurazole are listed in Table 1. F, A and T are the percentages of free, acetylated, and total sulphafurazole respectively, excreted in 48 h. PA is the percentage acetylation, based on the total amount of drug excreted. The theoretical curves, defined by the equations quoted, for subject A are given in Figs 1 and 2. The experimental values are in close agreement with those computed from the equations. This is evident from the fact that most of the experimental data points lie on the computed curves.

As was to be expected, the controlled alkaline urine conditions have a marked effect on the elimination of sulphafurazole. The elimination half-life is reduced from a mean 6·3 h under normal urine conditions to a mean 4·4 h under alkaline urine conditions. The former figure is practically the same as the 6·4 h calculated from the data of Nelson & O'Reilly (1960) for four subjects over a 72 h excretion

Table 1. *Parameters for urinary excretion of sulphafurazole under normal and controlled alkaline urine conditions by human test subjects*

| Parameter | Normal urine conditions | | | Alkaline urine conditions | | |
| | Subject* | | | Subject* | | |
	A (33–64)	B (34–82)	L (31–77)	A (33–64)	B (34–82)	L (31–77)
k_1 (h^{-1}) ..	0·0382	0·0395	0·0394	0·0388	0·0481	0·0376
k_2 (h^{-1}) ..	0·0925	0·1914	0·1152	0·0953	0·1710	0·1257
k_3 (h^{-1}) ..	0·0695	0·0729	0·0699	0·1134	0·1173	0·1173
K (h^{-1}) ..	0·1077	0·1124	0·1093	0·1522	0·1654	0·1549
F (%) † ..	50·85	51·51	59·18	63·82	62·04	73·74
A (%) ..	26·53	27·64	32·47	21·21	25·42	23·35
T (%) ..	77·39	79·15	91·65	85·03	87·46	97·09
PA (%) ..	34·28	34·92	35·43	24·94	29·06	24·05
t50 (h) ..	6·43	6·16	6·34	4·55	4·19	4·47

* Within parentheses following the subject's initial are shown respectively, age, and weight in kg.
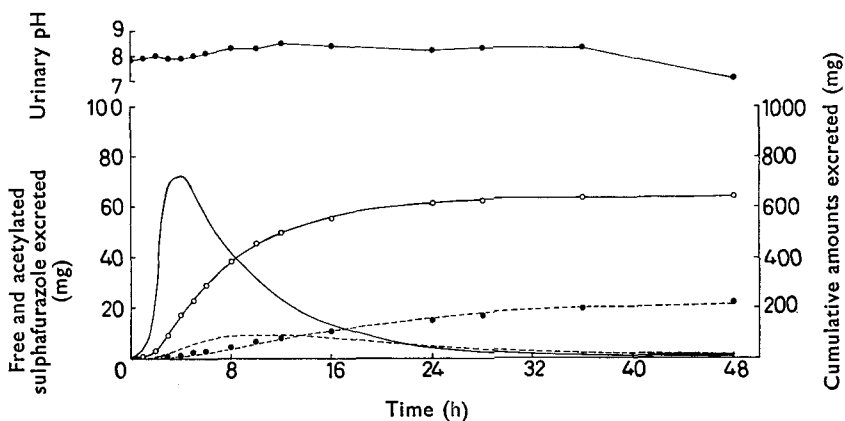† For definition see text above.

FIG. 1. Computed curves and experimental data points (○, ●) for urinary excretion of sulpha-furazole for subject A under controlled alkaline urine conditions. ——— Free drug. —○— Free drug (cumulative). – – – Acetylated drug. – – ● – – Acetylated drug (cumulative).
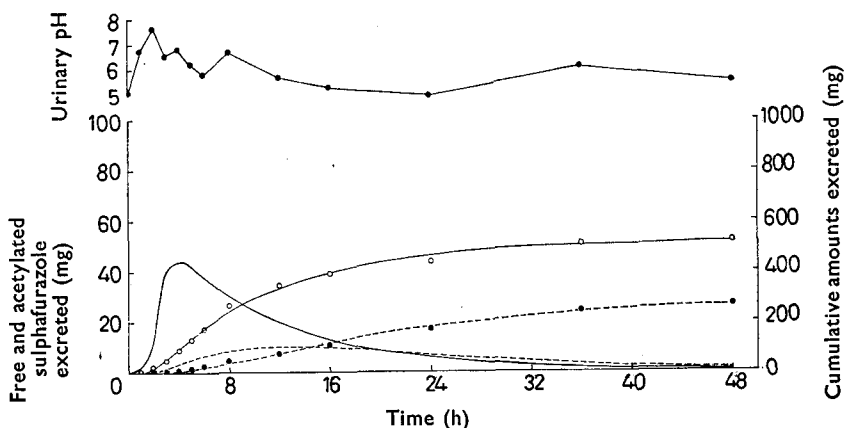

FIG. 2. Computed curves and experimental data points (○, ●) for urinary excretion of sulpha-furazole for subject A under normal urine conditions. ——— Free drug. —○— Free drug (cumulative). – – – Acetylated drug. – – ● – – Acetylated drug (cumulative).

period. These elimination half-life periods also correlate well with both the 4·7 h at a urinary pH of 8 and the 9·5 h at a urinary pH of 5 that were found by Dettli & Spring (1966) from blood level data, and the average of 6·1 h under normal urine conditions that was found by Bünger, Diller & others (1961) also from blood level data. Similarly the percentage of drug acetylated is reduced from an average of 34·9 to 26·0% while the percentage of total drug excreted is increased from a mean 82·7% under normal urine conditions to a mean 89·9% under alkaline urine conditions.

Department of Pharmaceutics,   A. P. GOOSSENS
Potchefstroom University for C.H.E.,   M. C. B. VAN OUDTSHOORN
Potchefstroom, South Africa.
October 16, 1969