# Bioavailability of cephalexin after intramuscular injection of its lysine salt

The sodium salt of cephalexin is poorly absorbed after intramuscular injection (Gower, Dash & O'Callaghan, 1973; Solberg, Schreiner & others, 1973; Nicholas, Meyers & Hirschman, 1973); similar observations (Mischler, Sugerman & others, 1974) have been made with the related compound, cephradin.

During an investigation of other soluble salts of cephalexin which might facilitate absorption of cephalexin from muscle tissue, it was found that some basic amino acid salts had the desired properties. Preliminary experiments in groups of 4 rabbits (3–4 kg, fasted overnight) showed that the L-lysine salt of cephalexin (≡20 mg $kg^{-1}$ of cephalexin) gave higher peak plasma concentrations of drug and greater cumulative urinary excretion of drug than did cephalexin monohydrate (≡20 mg $kg^{-1}$) used orally (Fig. 1). Thus, good absorption from the lysine salt used intramuscularly is indicated, and a more detailed study of the two products in man by the two routes was therefore carried out.

Healthy volunteers, fasted overnight, were given the lysine salt of cephalexin (Ultralexin) by deep intramuscular injection in the gluteal muscle (≡1 g cephalexin in 21 volunteers and ≡2 g cephalexin in 10 volunteers); also cephalexin monohydrate (≡1 g cephalexin), contained in two gelatin capsules, was given orally to six volunteers. Urine was voided before drug administration and then collected during 8 h; samples of venous blood were also collected at intervals. The serum and urine samples were stored at −20° before assay by the agar diffusion method using *Sarcina lutea* (ATCC 9341) (sensitivity limit 0·3 μg $ml^{-1}$). The serum half-lives were calculated from the mean serum concentration by linear regression analysis by the method of least squares.

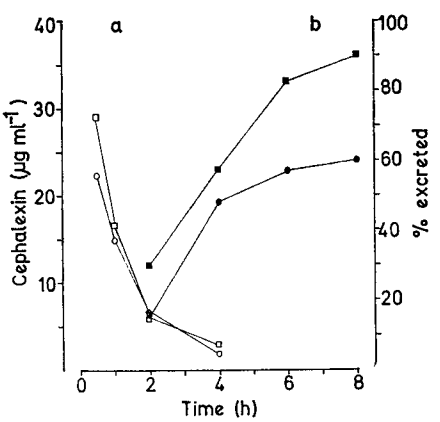


FIG. 1

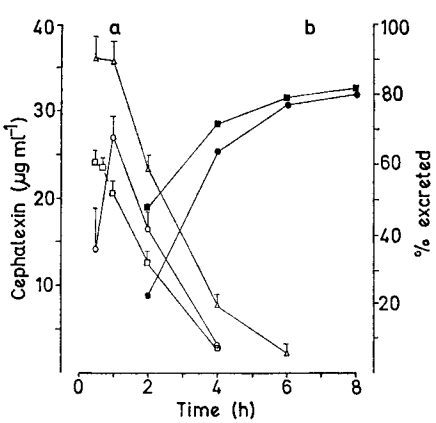


FIG. 2

FIG. 1a. Mean serum concentrations (μg $ml^{-1}$) of cephalexin in rabbits after oral administration of the monohydrate (○) and after intramuscular administration of the lysine salt (□).

b. Urinary excretion of cephalexin in rats, expressed as a percentage of the dose given, after oral administration of the monohydrate (●) and after intramuscular injection of the lysine salt (■).

FIG. 2a. Mean serum concentrations of cephalexin (μg $ml^{-1}$) in human volunteers after oral administration as the monohydrate, equivalent to 1 g of cephalexin ○, after intramuscular administration of the lysine salt, equivalent to 1 g of cephalexin □ and equivalent to 2 g of cephalexin △. Standard error of means indicated by vertical bars.

b. Cumulative urinary excretion of cephalexin (expressed as a percentage of the dose given) after oral administration of the monohydrate, equivalent to 1 g cephalexin ●, and after intramuscular administration of the lysine salt, equivalent to 1 g of cephalexin ■.

Cephalexin (≡1 g) by the oral route gave mean peak drug serum concentrations of 27·0 $\mu$g ml$^{-1}$ at 60 min (Fig. 2), i.e. within the range 21·8–31·6 $\mu$g ml$^{-1}$ at 60 min as previously reported (Naumann & Fedder, 1969; Gower & others, 1973; Nicholas & others, 1973; Solberg & others, 1973); the half life of the drug (51·3 min) is also within the reported range (49–66 min). Intramuscular injection of cephalexin (≡1 g) as the lysine salt gave the mean peak serum concentration of drug (24·1 $\mu$g ml$^{-1}$) after 30 min; this declined rapidly, until after 4 h, little antibiotic remained in the serum, the drug half-life being 63·8 min, i.e. much shorter than that reported (99–124 min) following intramuscular injection of the sodium salt of cephalexin. The amount of drug excreted in the urine during the first 2 h after intramuscular injection of the lysine salt was significantly higher ($P < 0.01$) than after oral administration of cephalexin monohydrate.

When the dose of lysine salt was increased (≡2 g cephalexin), the mean peak serum concentration increased (36 $\mu$g ml$^{-1}$ in 30 min) and the apparent half-life of cephalexin in serum (i.e. 72·9 min) was not enhanced greatly. On the other hand, Gower & others (1973) showed that the sodium salt of cephalexin given intramuscularly was poorly mobilised and that, when the dose was increased from 250 mg to 1 g, the rate of absorption was retarded and the mean serum concentration, in contrast to that following cephalexin administered orally, did not increase in proportion to the dose.

It is concluded that, in contrast to the sodium salt, the lysine salt of cephalexin was well absorbed after intramuscular injection; probably the greater solubility of the latter and the better buffering capacity of lysine accounts for this difference of systemic distribution of the drug from the two salts in muscle tissue.

Local intolerance to the injection of the lysine salt of cephalexin was not observed. This well absorbed form of the antibiotic will allow parenteral as well as oral administration of the same antibiotic in accord with current medical practise in many countries.

We thank Mr. J. M. Jauregui and Miss F. Niubo for technical assistance and Dr. Bakke and Dr. Roberts for helpful discussions.

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April 18, 1975

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