# RESULTS

## STABILITY

Stability of ceftriaxone as a dry powder form of both ROCEPHIN and CEF-3 preparations were satisfactory throughout 90 days at room (26-30°C), refrigerated (0-4°C) and freezing (-11°C) temperatures (Table 7 ). The stability profiles of these two different preparations were quite similar (Fig. 5). However, after reconstitution with 1% lidocaine solution, the amount of ceftriaxone in both preparations decreased significantly at room temperature; the amount of ceftriaxone at day 1 after reconstitution was 97.9 $\pm$ 1.0 and 99.2 $\pm$ 15.5 % , comparing to 51.6 $\pm$ 3.6 (p=0.002) and 43.7 $\pm$ 1.9 % (p=0.0005) after 30 days for ROCEPHIN and CEF-3, respectively (Table 8), but there was no further decrease in the amount of ceftriaxone at day 90. We also observed a colour change of the reconstituted solution of ceftriaxone of both preparations, from clear to reddish-orange colour, within the first 24 hr at room temperature but neither at refrigerated nor freezing temperature, or as the powder form. The stability of both preparations after reconstitution were quite stable at refrigerated and freezing throughout 90 days. The amount of ceftriaxone in ROCEPHIN appeared to increase significantly at day 9 and 90 when kept at refrigerated and at days 9, 30 and 90 when kept at freezing while it was increased significantly at day 30 for CEF-3 at freezing temperature. The stability profiles of ROCEPHIN and CEF-3 after reconstitution are illustrated in Fig. 6 .

Table 7. Stability of ceftriaxone powder after storage in different temperatures

| Time (day) | % initial amount of ceftriaxone after storage at different temperatures compared to the amount of ceftriaxone at day 0. mean (SD) | | | | | |
|---|---|---|---|---|---|---|
| | Room temperature (26-30°C) | | Refigerated (0-4°C) | | Freezing (-11°C) | |
| | ROCEPHIN | CEF-3 | ROCEPHIN | CEF-3 | ROCEPHIN | CEF-3 |
| 1 | 106.0 (24.1) | 81.7 (11) | 101.7 (33.4) | 88.0 (13.7) | 95.7 (1.3) | 89.0 (19.7) |
| 4 | 113.1 (6.7) | 94.0 (11.2) | 94.7 (13.2) | 81.7 (13.5) | 103.2 (30.9) | 91.5 (16.9) |
| 9 | 101.3 (15.4) | 86.0 (16.2) | 100.4 (7.9) | 94.3 (5.6) | 105.6 (8.1) | 89.2 (3.8) |
| 30 | 96.9 (15.9) | 94.3 (19.5) | 110.7 (11.0) | 104.1 (8.0) | 102.5 (7.0) | 111.9 (3.2) |
| 90 | 96.0 (7.8) | 99.0 (5.3) | 104.6 (5.3) | 80.9 (9.1) | 103.9 (4.3) | 98.1 (7.6) |

n=3

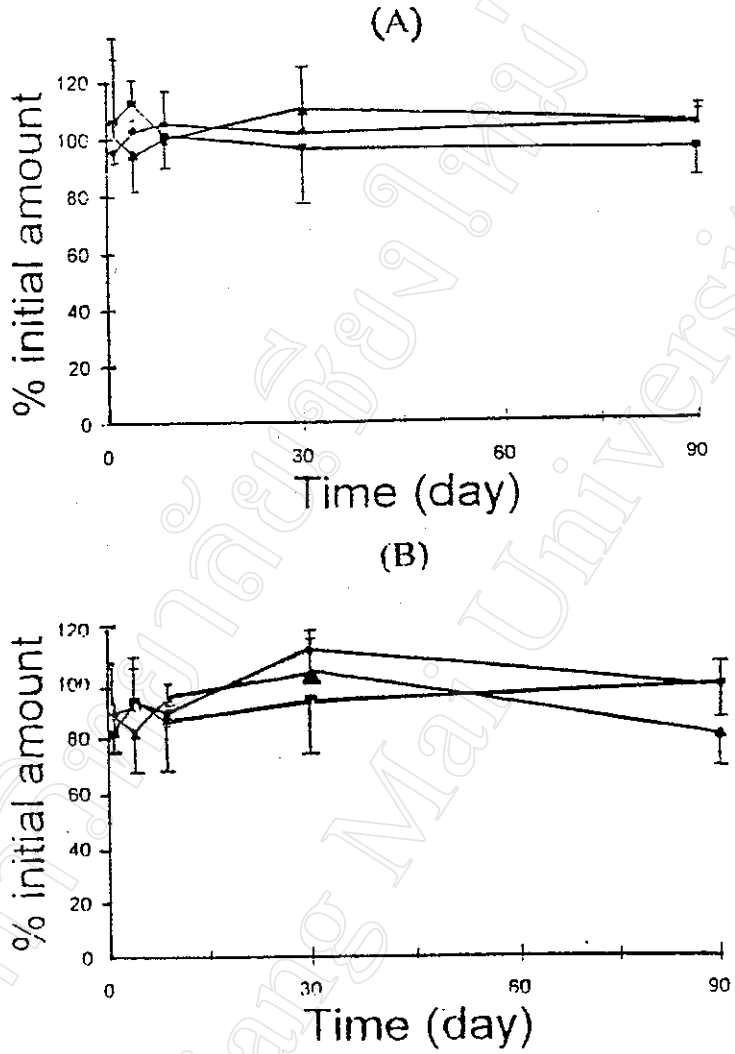


Figure 5. Stability of ceftriaxone in ROCEPHIN (A) and CEF-3 (B) powder at room temperature (■), 0-4° C (▲) and -11° C (●). Data are expressed as mean ± SD.

Table 8. Stability of ceftriaxone solutions after storage in different temperatures

| Time (day) | % initial amount of ceftriaxone after storage in different temperatures compared to the amount of ceftriaxone at day 0. Mean (SD) | | | | | |
|---|---|---|---|---|---|---|
| | Room temperature (26-30°C) | | Refigerated (0-4°C) | | Freezing (-11°C) | |
| | ROCEPHIN | CEF-3 | ROCEPHIN | CEF-3 | ROCEPHIN | CEF-3 |
| 1 | 97.9 (1.0) | 99.2 (15.5) | 105.0 (6.5) | 103.2 (3.3) | 100.4 (8.8) | 99.0 (0.56) |
| 4 | 83.8* (3.2) | 77.3 * (0.8) | 105.2 (7.3) | 99.4 (2.1) | 105.3 (5.7) | 88.6 (4.8) |
| 9 | 69.2 * (2.4) | 62.6* (3.4) | 106.2* (2.1) | 107.0 (7.0) | 108.2 * (1.9) | 98.6 (4.0) |
| 30 | 51.6 * (3.6) | 43.7* (1.9) | 108.6 (5.7) | 90.4 (9.5) | 111.5 * (1.4) | 110.0 * (4.7) |
| 90 | 46.3* (0.45) | 43.0* (0.55) | 115.8 * (5.8) | 88.4 (11.8) | 107.1 * (1.5) | 92.8 (6.5) |

* $p \angle 0.05$ VS day 0

n=3

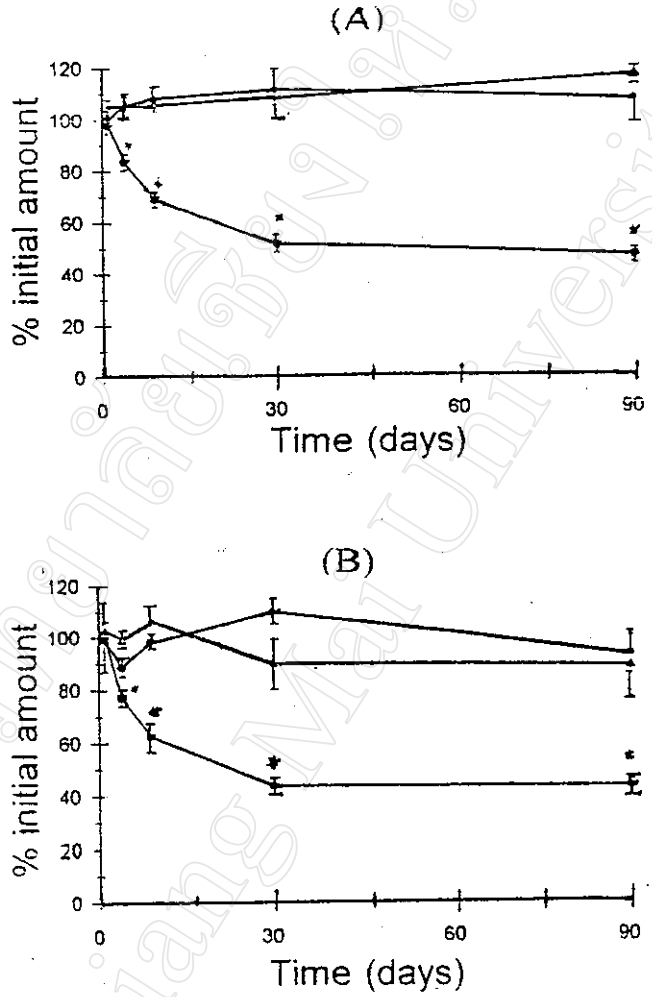


Figure 6. Stability of ceftriaxone in ROCEPHIN (A) and CEF-3 (B) solution at room temperature (■), 0-4° C (▲) and -11° C (●). Data are expressed as mean ± SD. ( $* p < 0.05$ )

PHARMACOKINETICS

Twenty healthy volunteers were recruited in the study. The median age was 24.5 yr. Nine subjects received the 250 mg dose and eleven subjects received the 1,000 mg dose of ceftriaxone.

The mean plasma concentrations of ceftriaxone at various time points observed in 9 subjects after intramuscular administration of 250 mg of ROCEPHIN and CEF-3 are shown in Table 9 and the plasma concentration-time curves are shown in Fig 7. The pharmacokinetic parameters obtained from the plasma ceftriaxone concentration-time curves are shown in Table 10 . The $C_{max}$ was slightly lower for ROCEPHIN with the mean value of $31.2 \pm 6.4$ ug/mL, comparing to $34.3 \pm 4.8$ ug/mL for CEF-3 ($p=0.01$). The $V_d$ was slightly higher for ROCEPHIN with the mean value of $7.4 \pm 3.1$ L, comparing to $6.4 \pm 2.3$ L for CEF-3 ($P=0.048$). There was no statistical difference in other pharmacokinetic parameters, including $T_{max}$, $AUC_{0-24}$, $t_{1/2}$, $V_d$ , CL, $K_e$ and $K_a$(Table 10).

The mean plasma concentrations of ceftriaxone at various time points observed in 11 subjects after intramuscular administration of 1,000 mg of ROCEPHIN and CEF-3 are shown in Table 11, and the plasma concentration-time curves are shown in Fig 7. The pharmacokinetic parameters obtained from the plasma ceftriaxone concentration-time curves are shown in Table 12. There was no statistical difference in any pharmacokinetic parameters after 1,000 mg intramuscular administration of CEF-3 comparing to ROCEPHIN.

Since there were no statistical differences in the interested pharmacokinetic values of either ROCEPHIN or CEF-3, except for the $C_{max}$ and $V_d$ after the 250 mg dosage, the pharmacokinetic data of the

same intramuscular dosage of both preparations were combined to compare any difference in their pharmacokinetic values. For comparison of the $C_{max}$ and $V_d$ after the 250 mg and 1000 mg dosages, we then used only the ROCEPHIN data, and the pharmacokinetic values of ceftriaxone after the two different intramuscular dosages are shown in Table 13. The apparent $C_{max}$ observed after the 1,000 mg dosage was 13.8% less than that predicted if the linear pharmacokinetics of the 250 mg dose were assumed. The $T_{max}$ value of the 1,000 mg dosage was significantly higher than the 250 mg dosage of ceftriaxone (2.1 $\pm$ 0.8 vs 1.5 $\pm$ 0.5 hr, p=0.04). The ratios of $C_{max}$ and AUC between the 1000 and 250 mg dosages were approximately 3.52:1 (109.8 $\pm$ 20.1 : 31.2 $\pm$ 6.4 ug/mL) and 3.1:1 (1231.3 $\pm$ 214.1 : 396.2 $\pm$ 74.6 ug.hr/mL), respectively. Comparing the 1,000 mg to the 250 mg dosages, significantly shorter $t_{1/2}$ ( 6.1 $\pm$ 1.5 vs 7.3 $\pm$ 0.87 hr, p=0.04 ), lower $K_a$ (1.5 $\pm$ 0.68 vs 2.6 $\pm$ 1.1 $hr^{-1}$, p=0.01) and higher $CL_p$ (0.84 $\pm$ 0.15 vs 0.66$\pm$ 0.04 L/hr, p=0.009 ) and $K_e$ values (0.13 $\pm$ 0.04 vs 0.10 $\pm$ 0.01 $hr^{-1}$, p=0.047 ) were observed, respectively.

The relative bioavailability ($F_{rel}$) of CEF-3 for intramuscular preparation in comparison to the innovator ROCEPHIN preparation, were 1.04 $\pm$ 0.22 for the 250 mg dosage and 1.0$\pm$ 0.15 for the 1,000 mg dosage (Table 10 and 12 ).

Table 9. Plasma concentrations of ceftriaxone over time after an intramuscular administration of 250 mg of ROCEPHIN and CEF-3.

| Time after dose (hr) | Mean plasma ceftriaxone concentrations (ug/mL) (n=9) | |
|---|---|---|
| | ROCEPHIN | CEF-3 |
| 0 | 0 | 0 |
| 0.25 | 15.3 ± 4.6[a] | 17.6 ± 5.8 |
| 0.5 | 22.8 ± 7.0 | 26.5 ± 5.1 |
| 0.75 | 27.7 ± 7.7 | 29.8 ± 5.2 |
| 1 | 30.5 ± 5.7 | 33.7 ± 7.0 |
| 2 | 29.8 ± 6.0 | 31.6 ± 7.0 |
| 3 | 28.6 ± 6.4 | 32.2 ± 6.3 |
| 4 | 25.5 ± 6.9 | 28.6 ± 5.6 |
| 6 | 20.9 ± 5.0 | 21.2 ± 3.0 |
| 8 | 17.8 ± 3.6 | 18.1 ± 2.9 |
| 24 | 5.3 ± 1.3 | 5.2 ±1.5 |

a mean ± SD

Table 10. Pharmacokinetic parameters of ceftriaxone after an intramuscular administration of 250 mg of ROCEPHIN and CEF-3 .

| Pharmacokinetic parameters | ROCEPHIN | CEF-3 | P- value |
|---|---|---|---|
| $C_{max}$ (ug/mL) | 31.2 ± 6.4 [a] | 34.3± 4.8 | 0.01 * |
| $T_{max}$ ( hr) | 1.5 ± 0.7 | 1.4 ± 0.6 | 0.52 |
| $t_{1/2}$ (hr) | 7.7 ± 1.2 | 7.0 ±1.1 | 0.19 |
| $V_d$ (L) | 7.4 ± 3.1 | 6.4 ± 2.3 | 0.048 * |
| $CL_p$(L/hr) | 0.67 ± 0.17 | 0.65 ± 0.11 | 0.69 |
| $K_e(hr^{-1})$ | 0.09 ± 0.01 | 0.10 ± 0.02 | 0.15 |
| $K_a$ ($hr^{-1}$) | 2.5 ± 1.0 | 2.7 ± 1.4 | 0.62 |
| AUC (ug.hr/mL ) | 394.2 ± 89.7 | 398.2 ± 59.4 | 0.89 |
| $F_{rel}$ | 1.04 ± 0.22 | | |

a mean ± SD

* statistically significant

Table 11. Plasma concentrations of ceftriaxone over time after an intramuscular administration of 1,000 mg of ROCEPHIN and CEF-3.

| Time after dose (hr) | Mean plasma ceftriaxone concentration (ug/mL) (n=11) | |
|---|---|---|
| | ROCEPHIN | CEF-3 |
| 0 | 0 | 0 |
| 0.25 | 34.8 ± 20.3[a] | 37.1 ± 22.8 |
| 0.5 | 63.8 ± 23.3 | 62.4 ± 24.8 |
| 0.75 | 85.8 ± 26.3 | 84.8 ± 30.6 |
| 1 | 98.0 ± 25.9 | 96.8 ± 27.5 |
| 2 | 108.9 ± 18.2 | 108.8 ± 22.7 |
| 3 | 104.0 ± 17.8 | 102.7 ± 26.4 |
| 4 | 92.5 ± 14.3 | 93.5 ± 18.1 |
| 6 | 78.1 ± 14.3 | 76.3 ± 10.7 |
| 8 | 57.0 ± 12.0 | 63.7 ± 7.3 |
| 24 | 13.4 ± 3.7 | 15.1 ± 3.6 |

a mean ± S.D.

Table 12. Pharmacokinetic parameters of ceftriaxone after an intramuscular administration of 1,000 mg of ROCEPHIN and CEF-3 .

| Pharmacokinetic parameters | ROCEPHIN | CEF-3 | P- value |
|---|---|---|---|
| $C_{max}$ (ug/mL) | 110.1 ± 18.0 [a] | 109.5 ± 22.1 | 0.69 |
| $T_{max}$ ( hr) | 2.0 ± 0.7 | 2.1 ± 0.9 | 0.65 |
| $t_{1/2}$ (hr) | 5.7 ± 1.4 | 6.5 ±2.1 | 0.19 |
| $V_d$ (L) | 7.0 ± 1.3 | 7.3 ± 2.2 | 0.53 |
| $CL_p$(L/hr) | 0.89 ± 0.2 | 0.87 ± 0.15 | 0.068 |
| $K_e(hr^{-1})$ | 0.13 ± 0.03 | 0.12 ± 0.06 | 0.61 |
| $K_a$ ($hr^{-1}$) | 1.5 ± 0.7 | 1.6 ± 0.8 | 0.60 |
| AUC (ug.hr/mL ) | 1176.1± 223.7 | 1286.4± 204.4 | 0.07 |
| $F_{rel}$ | 1.0 ± 0.15 | | |

a mean ± SD

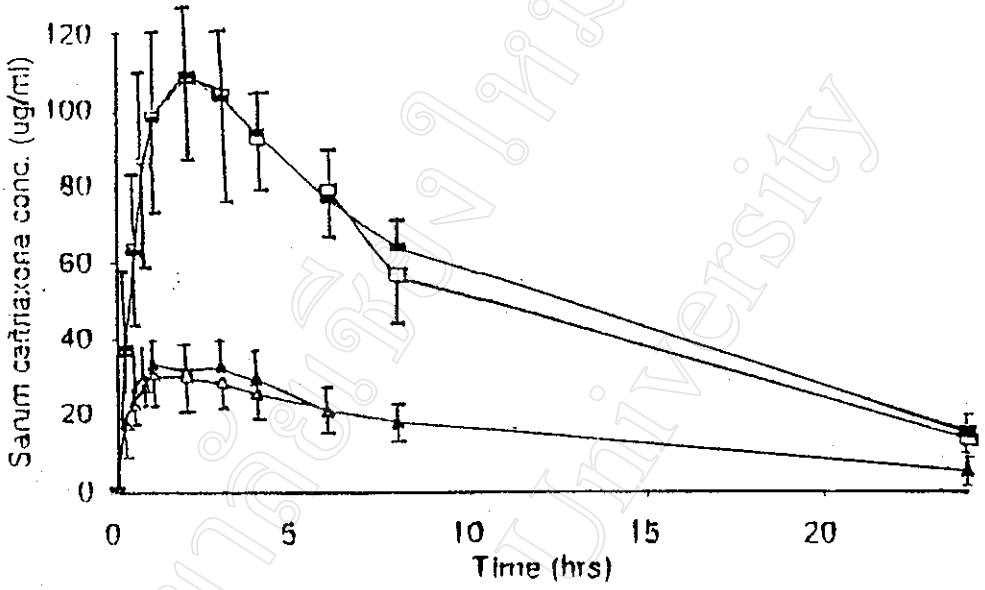


Figure 7. Comparison of the mean plasma concentration-time curves after single 250 ( Δ, ▲ ) and 1,000 mg ( □ , ■ ) intramuscular dosages of ROCEPHIN and CEF-3. Data represent mean ± SD.

Table 13. Comparison of pharmacokinetic parameters of ceftriaxone after single intramuscular doses of 250 (n=18) and 1,000 mg (n=22) of ceftriaxone .

| Pharmacokinetic parameters | ceftriaxone 250 mg | ceftriaxone 1000 mg | P- value |
|---|---|---|---|
| $C_{max}$ (ug/mL)* | 31.2 ± 6.4 [a] | 109.8 ± 20.1 | <0.0001 |
| $T_{max}$ ( hr) | 1.5 ± 0.5 | 2.1 ± 0.8 | 0.04 |
| AUC (ug.hr/mL ) | 396.2 ± 74.6 | 1231.3±214.1 | <0.0001 |
| $t_{1/2}$ (hr) | 7.3 ± 0.87 | 6.1 ±1.5 | 0.04 |
| $V_d$ (L)* | 7.4 ± 1.2 | 7.2 ± 1.6 | 0.84 |
| $CL_p$(L/hr) | 0.66 ± 0.04 | 0.84 ± 0.15 | 0.009 |
| $K_e(hr^{-1})$ | 0.10 ± 0.01 | 0.13 ± 0.04 | 0.047 |
| $K_a$ ($hr^{-1}$) | 2.6 ± 1.1 | 1.5 ± 0.68 | 0.01 |

a Mean ± SD

* The mean value for the 250 mg dosage was the data of the innovator preparation only.

URINARY EXCRETION

Urinary concentrations of an unchanged form of ceftriaxone after intramuscular administration of 250 or 1,000 mg dosages of ROCEPHIN and CEF-3 are shown in Table 14 and 15. There was no difference in the amount of ceftriaxone excreted in the urine over time when the same dose of different preparations were compared. The cumulative renal excretion of ceftriaxone after 250 mg dose of ROCEPHIN and CEF-3 were 51.3 $\pm$ 12.4 and 57.3 $\pm$ 5.3%, respectively, comparing to 47.4 $\pm$ 10.8 and 46.1$\pm$ 13.8% after 1,000 mg dosage. The average renal clearance of ceftriaxone estimated during each interval are shown in Table 16 and there were significant differences in the renal clearance values observed during 8-12 ($p=0.001$) and 12-24 ($p=0.007$) comparing to during 0-2 hr after the 1000 mg dose. The average renal clearance of ceftriaxone of each interval was plotted as a function of time at midpoint of each collection interval (Fig. 8) and urinary excretion rate compared to the plasma concentration-time profile (Fig.9). The peak urinary excretion of ceftriaxone occurred between 2-4 hr after 250 and 1,000 mg intramuscular dosages and appeared to be paralleled to the plasma concentration-time profiles. A significantly high correlation was observed between the plasma concentration of ceftriaxone and rate of urinary excretion ($r=0.917$) (Fig.10). The renal clearance over 24 hr after 250 and 1,000 mg of ceftriaxone administration were not significantly different (0.37$\pm$ 0.06 and 0.39 $\pm$ 0.1 L/hr , respectively, $p=0.4$) (Table 17 ).

Since there was no statistical difference in the percentage of dose excreted in the urine and renal clearance of ceftriaxone after

ROCEPHIN and CEF-3 administration, the pharmacokinetic data obtained after the same intramuscular dosage of the two preparations were combined to compare any difference in the pharmacokinetic values when different drugs were administered (Table 18 ). These pharmacokinetic values of ceftriaxone estimated from the urinary ceftriaxone time-concentration profiles were similar to those estimated from the ceftriaxone plasma concentration-time profiles (Table 19 ).

Table 14. Urinary excretion of ceftriaxone over 24 hours after single 250 mg intramuscular administration.

| Time (hr) | Urinary ceftriaxone concentration (ug/mL) | | Amount of ceftriaxone excreted in the urine (mg)* | | % Dose excreted in the urine | | Cumulative % dose excreted | |
|---|---|---|---|---|---|---|---|---|
| | Rocephin | Cef-3 | Rocephin | Cef-3 | Rocephin | Cef-3 | Rocephin | Cef-3 |
| 0-2 | 204.0 ±69.3 | 126.5 ±105.0 | 22.1 ± 10.1 | 26.8 ±10.3 | 8.8 ± 4.0 | 10.7 ± 4.1 | 8.8 ± 4.0 | 10.7 ± 4.1 |
| 2-4 | 140.6 ±99.4 | 202.9 ± 7.0 | 18.9 ± 4.7 | 31.7 ± 7.9 | 7.6 ± 1.9 | 12.7 ± 3.2 | 16.4 ± 5.7 | 23.4 ± 2.7 |
| 4-8 | 257.1 ±162.9 | 165.0 ±108.4 | 35.0 ± 11.4 | 34.7 ±10.5 | 14.0 ± 4.6 | 13.9 ± 4.2 | 30.4 ± 9.2 | 37.3 ± 2.9 |
| 8-12 | 143.5 ±79.6 | 112.8 ± 42.9 | 23.0 ± 11.9 | 21.8 ± 3.7 | 9.2 ± 4.8 | 8.7 ± 1.5 | 39.6 ± 11.3 | 46.0 ± 3.2 |
| 12-24 | 63.1 ± 24.0 | 72.8 ± 29.8 | 29.2 ± 15.8 | 28.2 ± 9.1 | 11.7 ± 6.3 | 11.3 ± 2.4 | 51.3 ± 12.4 | 57.3 ± 5.3 |

* Calculated from the urinary concentration of ceftriaxone(mg/mL) x volume of urine (mL).
Data represent mean ± SD.

Table 15. Urinary excretion of ceftriaxone over 24 hours after single 1,000 mg intramuscular administration.

| Time (hr) | Urinary ceftriaxone concentration (ug/mL) | | Amount of ceftriaxone excreted in the urine (mg)* | | % Dose excreted in the urine | | Cumulative % dose excreted | |
|---|---|---|---|---|---|---|---|---|
| | Rocephin | Cef-3 | Rocephin | Cef-3 | Rocephin | Cef-3 | Rocephin | Cef-3 |
| 0-2 | 1065.2 ±915.9 | 1045.1 ±1099.1 | 95.8 ±31.2 | 97.1 ±52.2 | 9.6 ±3.1 | 9.7 ±5.2 | 9.6 ± 3.1 | 9.7 ± 5.2 |
| 2-4 | 1227.4 ±650.1 | 1914.8 ±921.7 | 108.6 ±17.0 | 98.0 ±35.1 | 10.8 ±1.7 | 9.8 ±3.5 | 20.4 ± 4.1 | 19.5 ± 6.6 |
| 4-8 | 847.8 ±439.7 | 1173.1 ± 878.4 | 147.2 ±12.6 | 103.0 ±47.8 | 14 .7 ±1.3 | 10.3 ±4.8 | 35.1 ± 4.6 | 29.8 ± 9.2 |
| 8-12 | 315.6 ±226.7 | 590.6 ±449.5 | 53.8 ± 28.7 | 80.5 ±27.9 | 5.4 ±2.9 | 8.0 ±2.8 | 40.5 ± 7.3 | 37.8 ± 12.0 |
| 12-24 | 14.0 ± 130.0 | 256.5 ± 164.0 | 68.7 ± 39.5 | 82.7 ± 19.2 | 6.9 ±3.9 | 8.3 ±1.9 | 47.4 ± 10.8 | 46.1 ± 13.8 |

* Calculated from the urinary concentration of ceftriaxone (mg/mL) x volume of urine (mL)
Data represent mean ± SD.

Table 16. Renal clearance of ceftriaxone after single intramuscular administration of 250 and 1,000 mg dose of ceftriaxone.

| Time (hr) | Renal clearance of ceftriaxone (L/hr) | | | | | |
|---|---|---|---|---|---|---|
| | 250 mg | | | 1000 mg | | |
| | ROCEPHIN | CEF-3 | average | ROCEPHIN | CEF-3 | average |
| 0-2 | 0.45 ± 0.14 [a] | 0.48 ± 0.15 | 0.47 ± 0.0 | 0.54 ± 0.15 | 0.54 ± 0.17 | 0.54 ± 0.14 |
| 2-4 | 0.39 ± 0.14 | 0.55 ± 0.25 | 0.47 ± 0.19 | 0.54 ± 0.08 | 0.45 ± 0.18 | 0.50 ± 0.10 |
| 4-8 | 0.42 ± 0.12 | 0.43 ± 0.20 | 0.42 ± 0.16 | 0.50 ± 0.02 | 0.31 ± 0.16 | 0.40 ± 0.07 |
| 8-12 | 0.40 ± 0.20 | 0.38 ± 0.11 | 0.39 ± 0.06 | 0.28 ± 0.14 * | 0.37 ± 0.14* | 0.33 ± 0.14 * |
| 12-24 | 0.27 ± 0.18 | 0.30 ± 0.09 | 0.28 ± 0.11 | 0.21 ± 0.10 * | 0.24 ± 0.08 * | 0.23 ± 0.08 * |

a mean ± SD

* $p < 0.05$ comparing to 0-2 hr.

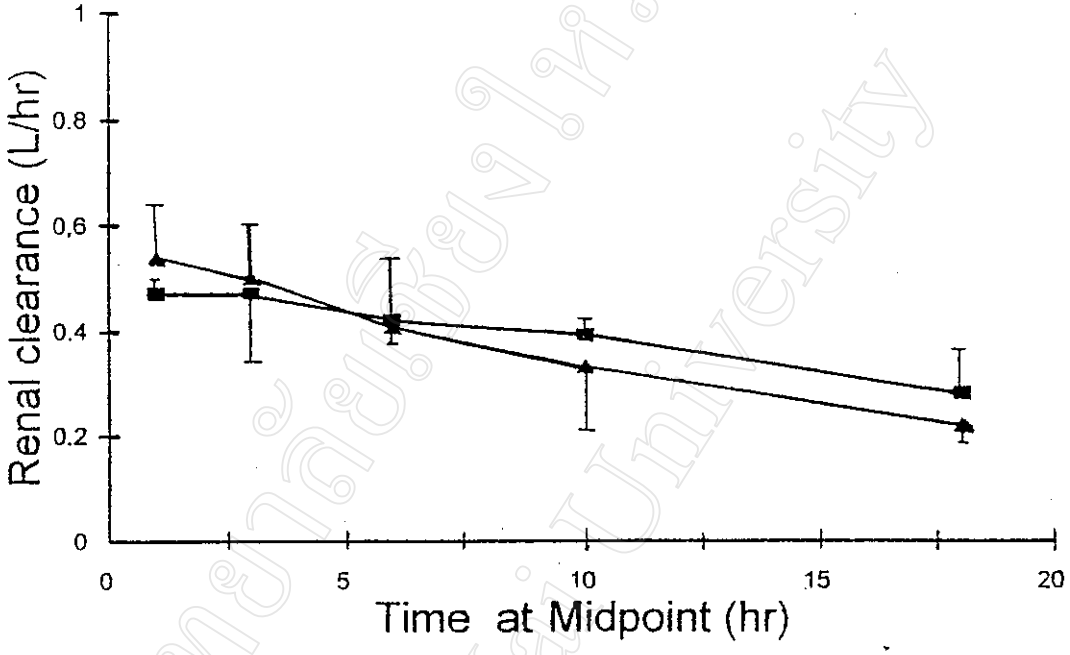


Figure 8. Average renal clearance of ceftriaxone after single 250 (■) and 1,000 mg (▲) of ceftriaxone intramuscular administration. Data are expressed as mean ± SD.

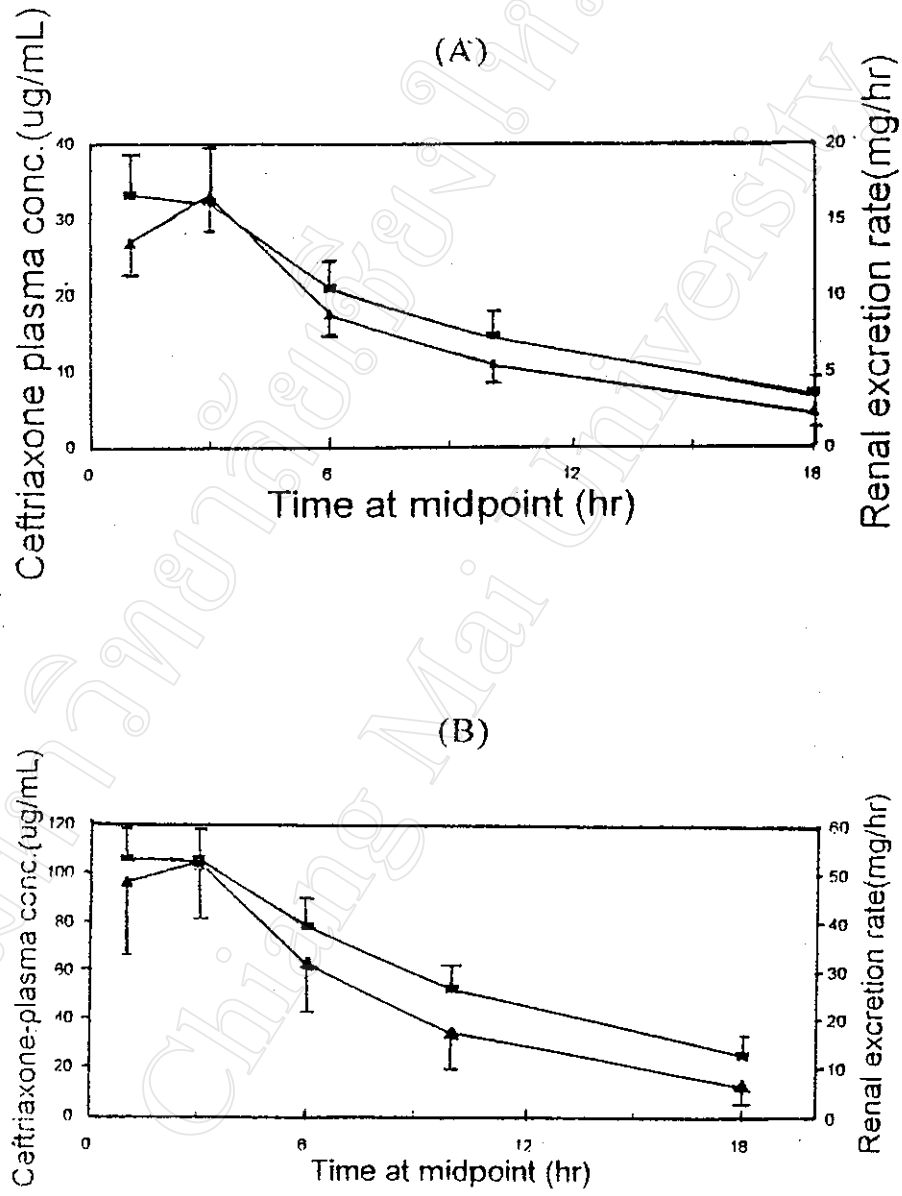


Figure 9. Comparison of the plasma concentration-time profile ( ■ ) and the average renal excretion rate ( ▲ ) of ceftriaxone over time after single 250 mg ( A ) and 1000 mg ( B ) of ceftriaxone intramuscular administration. Data represent mean ± SD.

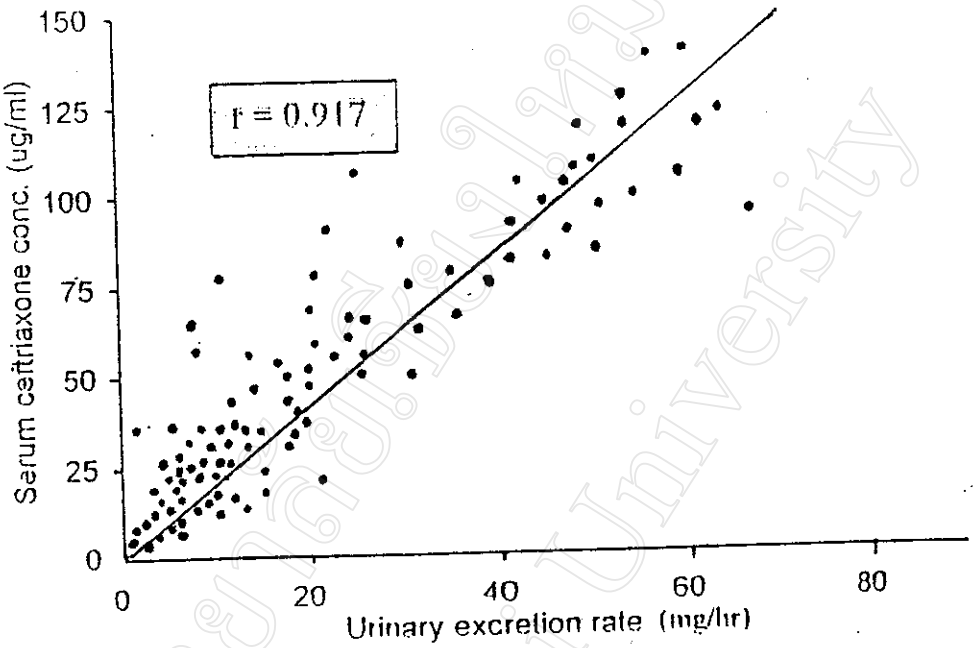


Figure 10. Correlation between the plasma concentrations and renal excretion rate of ceftriaxone after 250 and 1000 mg of ceftriaxone intramuscular administration (r=0.917, n=100).

Table 17. Renal clearance over 24 hr after single intramuscular administration of 250 and 1,000 mg dosage of ceftriaxone.

| Dose of ceftriaxone (mg) | Renal clearance (L/hr) mean ± SD | | | P-value |
|---|---|---|---|---|
| | ROCEPHIN | CEF-3 | average | |
| 250 | 0.36 ± 0.05 | 0.38 ± 0.10 | 0.37 ± 0.06 | 0.09 |
| 1000 | 0.42 ± 0.08 | 0.36 ± 0.12 | 0.39 ± 0.10[a] | 0.71 |

a p=0.4 vs 250 mg dosage

Table 18. Pharmacokinetic parameters calculated from the urinary excretion after single intramuscular administration of 250 and 1,000 mg of ceftriaxone.

| Pharmacokinetic parameters | 250 mg dosage | 1,000 mg dosage | P-value |
|---|---|---|---|
| $K_e$ ($hr^{-1}$) | 0.12 ± 0.03[a] | 0.14 ± 0.07 | 0.70 |
| $t_{1/2}$(hr) | 6.60 ± 2.50 | 5.10 ± 0.92 | 0.10 |
| $K_r$ ($hr^{-1}$) | 0.09 ± 0.04 | 0.09 ± 0.03 | 0.60 |
| $K_{nr}$ ($hr^{-1}$) | 0.03 ± 0.03 | 0.05 ± 0.03 | 0.13 |
| $f_e$ | 0.60 ± 0.08 | 0.50 ± 0.15 | 0.54 |

a mean ± SD

Table 19. Comparison of the $t_{1/2}$ and $K_e$ calculated from the plasma concentrations and urinary excretion of ceftriaxone after intramuscular administration.

| Pharmacokinetics parameters | 250 mg dose (n=5) | | 1,000 mg dose (n=5) | |
|---|---|---|---|---|
| | serum | urinary excretion | serum | urinary excretion |
| $K_e$ ($hr^{-1}$) | 0.10 ± 0.008[a] | 0.12 ± 0.03 | 0.13 ± 0.05 | 0.14 ± 0.07 |
| $t_{1/2}$(hr) | 7.4 ± 0.58 | 6.6 ± 2.5 | 6.2 ±1.7 | 5.1 ± 0.92 |

a mean ± SD