

LETTER TO THE EDITOR

## BIOAVAILABILITY OF AMPICILLIN (ANHYDROUS) AND AMPICILLIN TRIHYDRATE

Sir,

( Received on May 28, 1986 )

Ampicillin can be given orally either as trihydrate or in anhydrous form, anhydrous form having probably a better bioavailability in adults (6) and in children (7). Later studies (2, 3, 5) however, revealed that commercial capsules of two forms of ampicillin exhibit identical bio-availability. MacLeod and co-workers (4) have shown significant difference in biological availability of several commercial brands of ampicillin anhydrous and trihydrate forms marketed in Canada. In view of this, bio-availability of ampicillin from anhydrous form (250 mg capsules, Hindustan Antibiotics Ltd) and trihydrate form (AMPISYN, 250 mg capsules, CIPLA) was studied in human volunteers.

A double-blind, within-subject, cross-over study was carried out in 10 healthy male human volunteers (mean age,  $32.5 \pm 1.4$  yrs; mean body weight,  $56.7 \pm 2.0$  kg). All routine laboratory investigations (SGPT, serum alkaline phosphatase, albumin, bilirubin and creatinine and blood urea) and clinical examination excluded any liver or kidney disease. Informed consent was obtained prior to study from each subject and none of them were allergic to penicillin.

After overnight fasting ampicillin trihydrate or anhydrous preparation (250 mg X 2 capsules) was given randomly at 7 a.m. with 200 ml of water. Nothing was given orally for another 2 hr. Total amount of fluid consumed by subjects during the study period was kept constant. After seven days of wash-out period, the study was repeated with the other formulation i.e. subjects received anhydrous form in the first study were given trihydrate form the vice versa. Blood collection was done at 0, 0.5, 1, 1.5, 2, 3, 4 and 6 hr in sterile tubes. Serum samples were code-labelled and assayed in triplicate on the

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same day of blood collection by microbiological assay method, using *Bacillus subtilis* organism. Ampicillin standards were prepared using subjects' zero-hour sample.

The pharmacokinetic parameters including area under time-serum concentration (AUC), time to reach peak concentration ( $t_p$ ), peak plasma concentration ( $C_{max}$ ) and elimination half-life ( $t_{1/2}$ ) were calculated using standard formulae (1) applicable for single compartment model.

There was no significant difference between the serum concentrations of ampicillin anhydrous and trihydrate formulations (Fig. 1) as assessed from analysis of variance. The AUC,  $t_p$ ,  $C_{max}$  and  $t_{1/2}$  values of two preparations were also not significantly different (comparison by paired 't' test). This suggests that bio-availability of both preparations

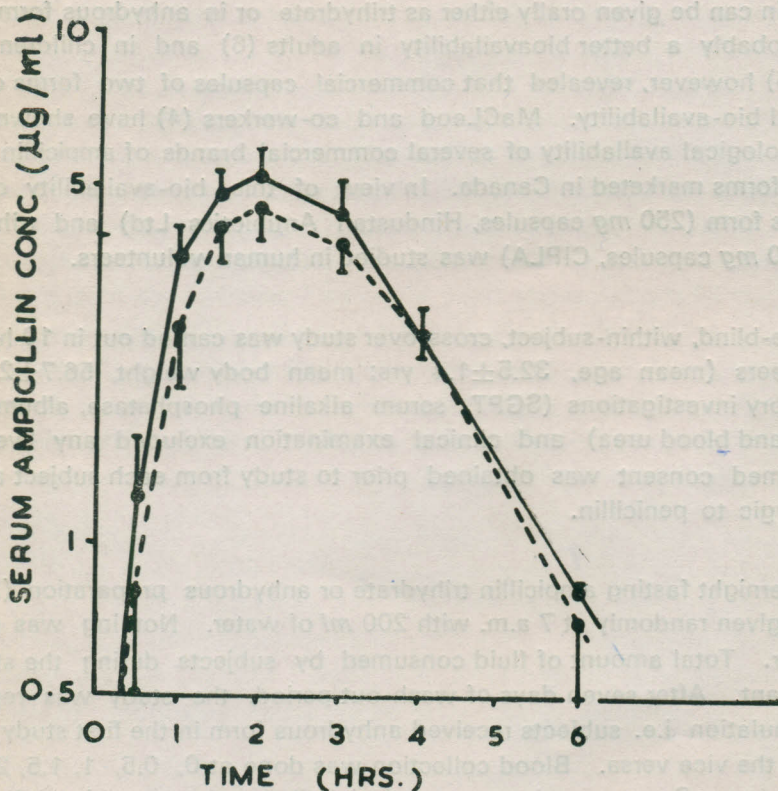


Fig. 1 : Time concentration curves for ampicillin anhydrous (—) and ampicillin trihydrate (---). Values are means ( $\pm$  SEM) from 10 subjects given 500 mg of each drug on empty stomach. AUC ( $\mu\text{g}/\text{h}/\text{ml}$ ),  $t_p$  (hr),  $C_{max}$  ( $\mu\text{g}/\text{ml}$ ) and  $t_{1/2}$  (min) respectively were :  $22.6 \pm 3.0$ ,  $1.59 \pm 0.08$ ,  $7.2 \pm 0.9$  and  $72.4 \pm 4.7$  for anhydrous form and  $21.2 \pm 3.5$ ,  $1.76 \pm 0.16$ ,  $6.6 \pm 0.6$  and  $69.2 \pm 3.9$  for trihydrate. Difference in values for two preparations was not significant.

is comparable and choice between two presentations (as have been used in this study) may have to be made on factors not related to bio-availability. Our results are in agreement with some reports (2, 3, 5) but not all (6, 7). Anhydrous form was introduced since it is not convertible (hydrated) at room/body temperature, has a greater expected thermodynamic (and hence physiological) activity and its solubility increases with rise of temperature and that of trihydrate reduces with rise of temperature. Anhydrous form was reported to have better bio-availability than trihydrate form presumably due to its greater aqueous solubility (6). However, the difference of solubility is only small (10 and 8 mg/l at 37°C, respectively) and their dissolution rate was reported (3) to be identical in acidic medium (like one prevailing in stomach) with which our present findings agree.

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