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Determination of Total and Free Ceftolozane and Tazobactam in Human Plasma and Interstitial Fluid by HPLC-UV

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Highlights

- Fast and sensitive HPLC-UV method for ceftolozane/tazobactam
- Simultaneous determination of both drugs in plasma and microdialysate
- Both drugs exhibit a negligible plasma protein binding
- Appropriate for pharmacokinetic studies in man

Abstract

Ceftolozane/tazobactam is a new cephalosporin/beta-lactamase inhibitor combination. An HPLC-UV method is described for the determination of total and free ceftolozane and tazobactam in human plasma and in microdialysate of subcutaneous tissue, respectively. Separation was performed using a reversed-phase column with phosphate buffer/acetonitrile as eluent and photometric detection at 260 nm (ceftolozane) or 220 nm (tazobactam). Linearity has been shown down to ceftolozane/tazobactam 0.1/0.05 mg/L in plasma and 0.03/0.015 mg/L in saline, respectively. The plasma protein binding of both drugs as determined by ultrafiltration was less than 10%. Temperature, pH or relative centrifugation force (up to 3000 x g) had no significant impact on the protein binding. The method was applied to the determination of ceftolozane and tazobactam in plasma and interstitial fluid of healthy volunteers following intravenous infusion of ceftolozane/tazobactam 1.0/0.5g.

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