A simple high performance liquid chromatography (HPLC) assay for aciclovir and ganciclovir in serum

J Antimicrob Chemother 1996; 38: 739–740

Sir,

Aciclovir and ganciclovir are clinically important antiviral agents derived from purine nucleosides. Aciclovir is available in oral and iv formulations. The peak serum aciclovir concentration is approximately 8.8 mg/L following a 5 mg/kg iv dose. After a single 200 mg oral dose the peak serum aciclovir concentration would be in the range 0.35–1.0 mg/L. However, aciclovir has unpredictable oral bioavailability. Typically, dosages of 800 mg five times a day are required to ensure inhibitory serum concentrations against varicella-zoster virus. Although aciclovir appears to be free from serious toxicity, there have been reports of neurotoxicity and nephrotoxicity in immunocompromised patient groups (Feldman, Rodman & Gregory, 1988; Krieble et al., 1993).

Ganciclovir is associated with serious toxic side effects, such as haematological toxicity and is generally reserved for the treatment of viral infection in immunocompromised patient groups (Faulds & Heal, 1990). Until recently it was available only as an iv preparation. A peak serum concentration of 7.0 mg/L has been reported after a 5.5 mg/kg iv dose. The new oral formulation is for use in HIV patients. Little is known of the pharmacokinetics of the drug in this patient group and it is possible that drug absorption may be impaired by co-existant gastro-intestinal disease. The assay of these agents could ensure adequate serum concentrations and dosage optimisation and the avoidance of toxicity.

We have developed a simple, isocratic HPLC assay for these antivirals. The stationary phase was Techsphere 5 C8 in a stainless steel column, 10 cm x 4 mm (HPLC Technology; Macclesfield, UK). The mobile phase was 1% ortho-phosphoric acid containing 10g/L octane sulphonic acid and the flow rate was 1 mL/min. Detection was by uv absorbance (lambda max 254 nm: Model 441 detector, Waters Associates, Watford, UK). Serum samples were mixed 50:50 with 7% perchloric acid, allowed to stand for 5 min and centrifuged at 25 000g for 5 min. Twenty μL of the supernatant was injected.

A chromatogram with the separated aciclovir and ganciclovir peaks is shown in the Figure. The reproducibility of the assay, expressed as the % coefficient of variation (%CV), was investigated by the repeat assay (n = 6) of serum containing 5 mg/L of aciclovir and ganciclovir. For both drugs the %CV was less than 10. The detection limit, defined as the aciclovir or ganciclovir concentration equivalent to a peak three times the height of the base-line noise, was 0.5 and 0.3 mg/L respectively. Linearity and serum recovery were investigated by assaying a series of spiked aqueous and serum specimens with 0, 5, 10, 25, 50 and 100 mg/L aciclovir or ganciclovir. The correlation between drug concentration and peak height was good for the aqueous and serum aciclovir samples (r = 0.994 and 0.999, respectively) and for the aqueous and serum ganciclovir samples (r = 0.999 and 0.999, respectively). Percentage serum recovery (serum peak height/aqueous peak height x 100) was 100% for both antivirals at each drug concentration. The accuracy of the assay was investigated by the assay of serum samples containing 1.3, 4.8 or 9.1 mg/L of aciclovir and 1.5, 5.6 or 8.4 mg/L ganciclovir. The accuracy, expressed as the percentage error ((measured concentration – target concentration)/target concentration x 100) was 0% for the 1.3 mg/L aciclovir sample, 0% for the 4.8 mg/L aciclovir sample and 3.2% for the aciclovir 9.1 mg/L sample. For ganciclovir the percentage errors were 6.7% for ganciclovir 1.5 mg/L, 1.8% for ganciclovir 5.6 mg/L and 1.1% for ganciclovir 8.4 mg/L. The assay was specific, there being no interference from 16 commonly used antibiotics and other unknown drugs present in sera from patients (with normal and impaired renal function).

Published HPLC methods for aciclovir and ganciclovir involve complex, time consuming sample preparation techniques (Smith &...
Sir,

In the past Corynebacterium species, apart from Corynebacterium diphtheriae, have rarely been involved in clinical infections. However, in the last few years many species have been involved as opportunistic pathogens in compromised patients, but in only two species has the pathogenic potential been well established: Corynebacterium jeikeium and Corynebacterium urealyticum. The first is the causative agent of serious infections such as septicaemia, generally in patients who are immunocompromised and/or with medical devices. C. urealyticum is an important urinary tract pathogen (Coyle & Lipsky, 1990). These species are the most resistant to antibiotics among the coryneforms usually isolated from clinical specimens (Soriano, Zapardiel & Nieto, 1995).

Ciprofloxacin and other fluoroquinolones have been considered suitable treatments for...