

# Deacon's Challenge

## No 139 - Answer

A patient is given a loading dose of 250 µg of a new drug (MW = 781). After 12 hours, his serum drug concentration is estimated at 1.0 nmol/L. After a further 12 hours, the concentration is re-measured and is estimated at 0.8 nmol/L. Assuming the elimination of this drug follows first-order kinetics, calculate the volume of distribution and the rate constant of elimination.

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The linear form of the integrated first-order rate equation can be used to determine the initial drug concentration ( $C_{p0}$ ) and elimination rate constant ( $K_d$ ):

$$\ln C_{pt} = \ln C_{p0} - K_d t$$

where  $\ln C_{pt}$  is the natural logarithm of the plasma drug concentration at time  $t$ .

As there are two unknowns to determine the easiest approach is to set up two simultaneous equations with a concentration of 1.0 nmol/L at 12 h and 0.8 nmol/L at 24 h:

$$\ln 1.0 = \ln C_{p0} - 12K_d$$

$$\ln 0.8 = \ln C_{p0} - 24K_d$$

working out the natural logarithms:

$$0 = \ln C_{p0} - 12K_d$$

$$-0.223 = \ln C_{p0} - 24K_d$$

Subtraction of the second equation from the first eliminates the  $\ln C_{p0}$  term and since  $-(-0.223) = 0.223$  and  $-12K_d - (-24K_d) = -12K_d + 24K_d = 12K_d$ , this results in:

$$0.223 = 12K_d$$

$$\text{Therefore } K_d = \frac{0.223}{12} = 0.0186 \text{ h}^{-1} \quad (\text{to 3 sig figs})$$

The value of  $\ln C_{p0}$  can be obtained by substitution of this value for  $K_d$  into either of the rate equations. Using the first equation the calculation is:

$$0 = \ln C_{p0} - (12 \times 0.0186)$$

$$\ln C_{p0} = 12 \times 0.0186 = 0.223$$

$$C_{p0} = \text{antilog}_e 0.223 = 1.25 \text{ nmol/L} \quad (\text{to 3 sig figs})$$

An alternative approach would be to plot  $\ln C_{pt}$  against  $t$ , join up and extrapolate the points. The slope would equal to  $-K_d$  and the intercept on the  $\ln C_{pt}$  axis would give  $\ln C_{p0}$ . This would be the preferred approach if there were more than two pairs of data.

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The volume of distribution can be calculated from the value of  $C_{p0}$  and the administered dose:

$$\text{Volume of distribution} = \frac{\text{Dose (nmol)}}{C_{p0} \text{ (nmol/L)}}$$

$$\text{Dose} = 250 \mu\text{g} = 250,000 \text{ ng}$$

$$\text{Dose (nmol)} = \frac{\text{Dose (ng)}}{\text{MW}} = \frac{250,000}{781} = 320 \text{ nmol}$$

$$\text{Volume of distribution} = \frac{320}{1.25} = 256 \text{ L}$$

## Question 140

You have been asked to check the calibration of your laboratory's spectrophotometer. Using a solution of potassium dichromate (50.0 mg/L) in dilute sulphuric acid, you obtain absorption values of 0.523, 0.521, 0.524 and 0.523 at 350 nm. The absorptivity index of potassium dichromate at this wavelength is  $10.7 \pm 0.11 \text{ g}^{-1} \text{ cm}^{-1}$ . Given you have used cuvettes with a pathlength of 1 cm, calculate the probability that the spectrophotometer is correctly calibrated.

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### ACB Trent, Northern & Yorkshire Region Tony Hitch Memorial Lecture & Geoffrey Walker Award

Wednesday 20th March 2013  
Nottingham

Entries are now invited for the 2013 Geoffrey Walker Award.

Trainees in the Trent, Northern & Yorkshire Region are invited to present a 10 minute paper on their clinical or basic research for consideration for the award.

Closing date for entries: 5pm Friday 8th March 2013.

The successful candidate will be awarded a bursary to a national or international meeting.

All speakers receive a £50 book token with the winner receiving a scientific meeting attendance bursary of up to the value of £1000 plus a £100 book token – full details on request.

Full rules and further details from ACB TNY Region Meetings Secretary:  
Mrs Caroline Addison, Tel: 0191-445-3907. Email: caroline.addison@ghnt.nhs.uk