Deacon's Challenge No. 87 Answer

A 44-year old woman, who suffered a miscarriage of pregnancy four days previously, was found to have a serum β-HCG concentration of 578 IU/L. Given that the half-life of β-HCG at more than 48-hours after termination of pregnancy is 56 hours, in how many days time would you expect her serum β-HCG concentration to reach a level of 5 IU/L?

MRCPath, Autumn 2007

The integrated from of the first-order rate equation is:

$$\ln Cp_t = \ln Cp_0 - k_d.t$$

Where Cp_t = β-HCG concentration at time t = 5 IU/L

Cp_0 = initial β-HCG concentration = 578 IU/L

t = time for β-HCG to fall to 5 IU/L = ?

k_d = elimination rate constant = ?

k_d is not given but it is related to the half-life ($t_{1/2}$):

$$k_d = \frac{0.693}{t_{1/2}} = \frac{0.693}{56} = 0.0124\ h^{-1}\ (3\ sig\ figs)$$

Substituting these values and solving for t:

$$\ln 5 = \ln 578 - 0.0124.t$$

$$1.609 = 6.360 - 0.0124.t$$

$$0.0124.t = 6.360 - 1.609 = 4.751$$

$$t = \frac{4.751}{0.0124} = 383\ h\ (3\ sig\ figs)$$

Dividing by 24 to convert from hours to days:

$$t = \frac{383}{24} = \textbf{15 days 23 hours}$$

Another approach is to calculate the number of half-lives (N) which must pass to achieve the desired β-HCG concentration using the expression:

$$\ln (Cp_t/Cp_0) = -0.693\ N$$

then multiplying this value by the half-life. ■

Question 88

Drug A is routinely used in the treatment of patients with rheumatoid arthritis. It is metabolised *in vivo* to its active metabolite B by the enzyme PP. The possibility of introducing drug C into the treatment regimen is being investigated but there are some concerns that drug C may inhibit the metabolism of drug A. In order to investigate the effect of drug C on the metabolism of drug A the effect of varying the concentration of drug A on the activity of the enzyme PP was investigated in both the presence and absence of drug C. The method for measuring the activity of PP is:

- 0.5 mL substrate (drug A)
- 1 mL Reagent 1 (contains the enzyme PP)
- 2 mL Reagent 2 (contains a second enzyme which converts B into a coloured end-product)
- 0.5 mL of buffer OR buffer containing drug C at a concentration of 50 mmol/L

The rate of formation of the coloured end-product was measured by following the increase in absorption at 505 nm.

The double reciprocal plots (1/[S] versus 1/v) were linear. In the absence of drug C the Km of the enzyme was found to be 80 µmol/L and the Vmax 200 µmol/min/L. In the presence of inhibitor the apparent Km was 280 µmol/L with an apparent Vmax of 195 µmol/min/L.

a) What is the most likely mode of inhibition?

b) Calculate the inhibitor constant.

Based on MRCPath practical, Autumn 2003