PHI 5127 Dose Optimization I

Homework III (10 points)

Due on Friday, 09/25/2009

Do not forget the units of the results. 0.1 points will be deducted for each time an answer is provided without the appropriate unit.

1) TRUE (T) or FALSE (F) (3 points, 0.5 each)

For a one compartment body model, K_e can be calculated as \( \frac{C_0}{AUC_{\infty}} \)

T  F

Clearance and volume of distribution are independent

T  F

A drug with a high volume of distribution always possesses a high clearance.

T  F

If, for a given drug, \( Q_H << f_u \times CL_{int} \), the drug is considered to be a high extraction drug

T  F

Metabolites are always less active than their parent compounds

T  F

Enzyme induction affects the hepatic clearance of low extraction drug

T  F

2) 10 mg Dexamethasone were administered to 50-year old patient (70 kg) through an IV bolus injection. The following plasma concentrations (Cp) were measured. (Hint: A semi-log plot of the concentration vs. time profile will yield a straight line for a one-compartment body model) (3 points)

<table>
<thead>
<tr>
<th>time(h)</th>
<th>Cp (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.133</td>
</tr>
<tr>
<td>2</td>
<td>0.101</td>
</tr>
<tr>
<td>4</td>
<td>0.059</td>
</tr>
<tr>
<td>6</td>
<td>0.034</td>
</tr>
<tr>
<td>8</td>
<td>0.020</td>
</tr>
<tr>
<td>10</td>
<td>0.012</td>
</tr>
<tr>
<td>12</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Determine k_e, C_0, VD, CL, AUC_{\infty}, and C5 (plasma concentration at t = 5h)
3) Assume an intrinsic clearance of i) 80000 L/min and ii) 0.08 L/min. The plasma protein binding and liver blood flow are 50% and 80 L/min, respectively, for both situations. (4 points)

a) Calculate the hepatic clearance for both situations

b) Calculate the hepatic clearance when the plasma protein binding is 1%.