

# Essay on pharmacology

Sociology, Population



## Systemic Clearance Extended Calculation

Data: Pharmacokinetic parameters: Fraction unbound ( $f_u$ ), 0.5; Clearance by active secretion ( $CL_{sec}$ ), 2L/h; Fraction reabsorbed (FR), 0.25; Hepatic Extraction Ratio (EH), 0.25.

Q: Total Systemic Clearance ( $CL_{total}$ ) =?

Formula:  $CL_{total} = (F * D) / AUC$  (RMI Pharmacokinetics, 2014)

Where, F = fraction of dose absorbed (mg),  $(1 - FR) * (1 - EH)$  (RMI Pharmacokinetics, 2014)

AUC = area under the curve (mg/L/h),  $(\Delta t / 2) * C_f$  (Summit PK, 2014)

D = single dose (mg),  $Q * AUC * F$  (RMI Pharmacokinetics, 2014)

### Computation:

Step 1: Computation of F

$$F = (1 - FR) * (1 - EH)$$

$$F = (1 - .25) * (1 - .25) = .75 * .75$$

$$F = 0.5625$$

### Step 2: Computation of AUC

$$AUC = (\Delta t / 2) * C_f$$

$$AUC = (1h/2) * (1 + (1 - EH)) = .5 * (1 + (1 - .25)) = .5 * 1.75$$

$$AUC = 0.875 \text{ mg/L/h}$$

### Step 3: Computation of D

$$D = Q * AUC * F$$

$$D = 85 * .875 * .5625$$

$$D = 74.375 \text{ mg}$$

## Step 4: Computation of CL<sub>total</sub>

$$CL_{total} = (F * D) / AUC$$

$$CL_{total} = (.5625 * 74.375) / .875$$

$$CL_{total} = 47.8125 \text{ mg/L/h}$$

## Therapeutic Monitoring Essay

Q1: Identify the circumstances and populations where variability may be most important.

Pharmacokinetic variability may be most important in situations when patients respond optimally to medications in the lower level of the therapeutic range. This condition may be critical in the prophylactic treatment of epilepsy because of the difficulty in closely monitoring outpatient patients, and the medication must exert therapeutic effects without adverse effects (Johannessen & Tomson, 2012: 1061-1062). In prophylactic interventions, dosage adjustments on clinical grounds alone may be difficult due to lack of justifiable signs and symptoms to base the decision to change dosage. Moreover, older antiepileptic drugs, for instance, had been known for their narrow therapeutic range and a pronounced inter-individual pharmacokinetic variability, which can increase adverse effect risks due to unpredictability of patient response. Drug interactions also are another circumstance wherein differences in metabolism may result to variability in pharmacokinetics. The enzyme CYP3A, for instance, can get inhibited by drug interactions resulting to dosage optimization, for instance, in the dosage of immunosuppressive cyclosporine in patients using ketoconazole (Wilkinson, 2005: 2211-2212).

**Q2: Describe the approaches that may be used to control for this variability.**

Shaw et al (2000: 14) observed preferential option towards individualized doze medication guided by plasma studies. In transplant patients, for instance, who receive mycophenolate mofetil (MMF), transplant centers prefer to monitor the presence of mycophenolic acid (MPA) in the plasma as guide in the adjustment of dosages in specific patients.

**Intra-Individual Variability Essay**

Q: Select ONE specific factor (from the categories environmental, genetic OR physiological) that may contribute to intra-individual variability in the activation of CYP2C19, and describe the potential consequences of this variability in terms of patient response and tolerability.

The enzyme CYP2C19 consists of 26 variant alleles (Klaassen, et al., 2008: 387-388). While allele \*1 became known for its involvement in the metabolism of frequently prescribed drugs (e. g. omeprazole, diazepam), alleles \*2 and \*5 are almost exclusively involved with CYP2C19 proteins that have no functional activity. Their presence in certain populations varies significantly. Allele \*2 are present in 30 percent of Asians, a17 percent of African-Americans, and 15 percent of Caucasians. Allele \*3 had been less active in these populations, merely at 5 percent, 0. 4 percent, and 0. 04 percent, respectively. Some alleles are even rarely encountered. These allelic variations describe significant wide variability in their impact to the pharmacokinetics of certain drugs. Omeprazole, for instance, may need higher doses in the treatment of hyperacidity and gastroesophageal reflux disease (GERD) when the strong activity of CYP2C19 results to its shorter

half-life. Moreover, such outcome may require an increase in dosage and frequency of administration in order to obtain the necessary therapeutic effect.

## Reference List

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