PHA 5127
Case study #2

1. Buproprion (R_x Wellbutrin) has the following pharmacokinetic properties:

- Absorption: Nearly complete and rapid absorption from the intestinal tract.
- Distribution: Readily crosses the blood-brain barrier and placenta as well as into other organs and tissues. Protein binding is 85%.
- Metabolism: Extensively and exclusively metabolized by the liver. Four metabolites are produced, with possible lesser therapeutic activity than the parent drug. Intrinsic clearance (enzymatic activity) = 2180 L/hr.
- Elimination: Half-life is 14 hours. Systemic clearance is 1.14 L/hr/kg of body weight.

A) What is the calculated hepatic clearance of buproprion in Jerry B., (age 50, weight 62 kg, height 5'9", with normal hepatic blood flow of 1500 ml/min and normal hepatic function.)?
B) What is Jerry B.'s oral bioavailability (F_h)?

2. Predict the changes in Cl_h given the following scenarios:

Parameter	Direction of change	effect on Cl_h for a low E drug	effect on Cl_h for a high E drug
fraction of unbound drug	decreases		
intrinsic clearance	increases		
hepatic blood flow	decreases		

3. The USPDI monograph for fluvoxamine (R_x Luvox) gives the following pharmacokinetic information:

- Absorption: The absolute bioavailability of fluvoxamine is low.
- Distribution: The apparent volume of distribution is 25 L/kg.
- Protein binding: High (~80%)
- Metabolism: Extensively metabolized in the liver. All metabolites are inactive.
- Half-life: 15.6 hours

A) What is the calculated hepatic clearance of fluvoxamine for Sally T.(age 25, weight 70 kg, liver blood flow of 1500 ml/min)?
B) Is fluvoxamine a high or low clearance drug?
C) What is the extraction ratio of fluvoxamine in Sally T.?
D) What is the oral bioavailability (F_h)?