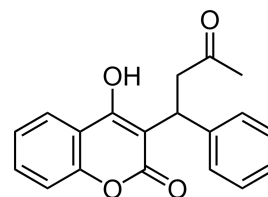
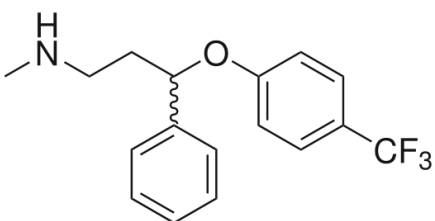
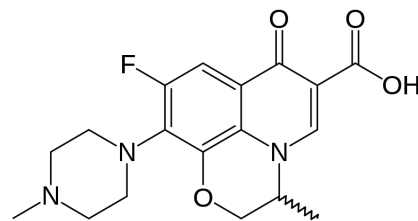
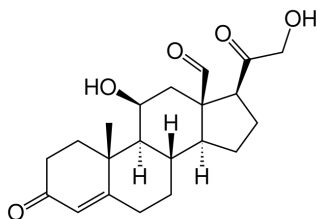
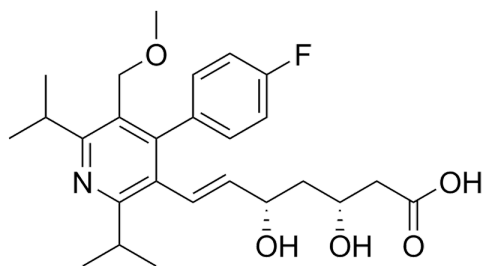
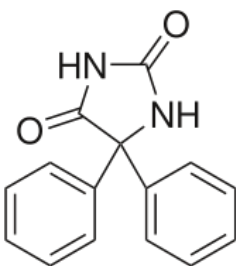
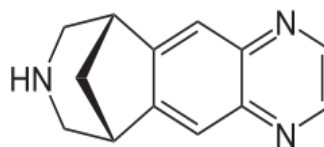
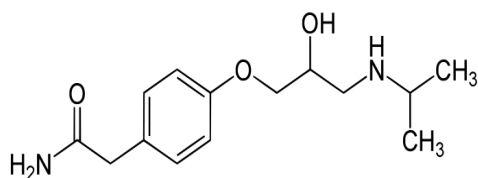
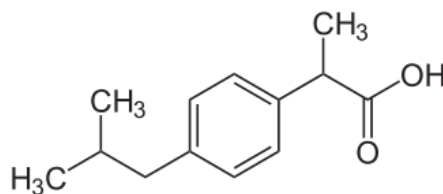
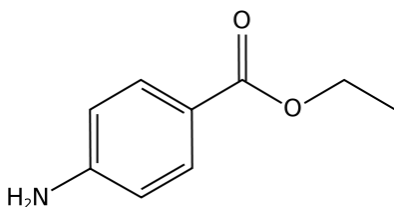


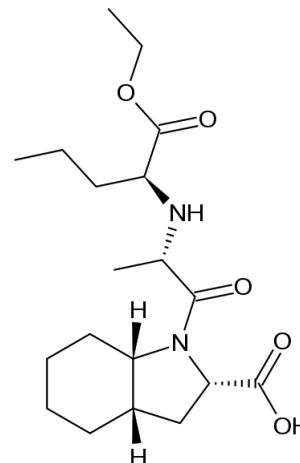
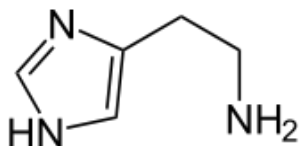
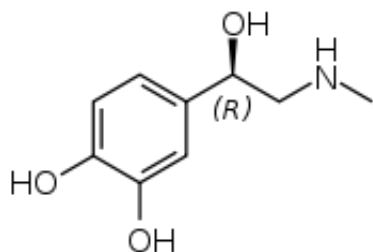
MEDCEM 562

Problem Set 1

pKa, lipophilicity, stereochemistry

1. Examine the drug structures and identify groups with pKa values between 2 and 12. For each group in each structure indicate the predominant ionization state at pH 3, pH 7 and pH 11.





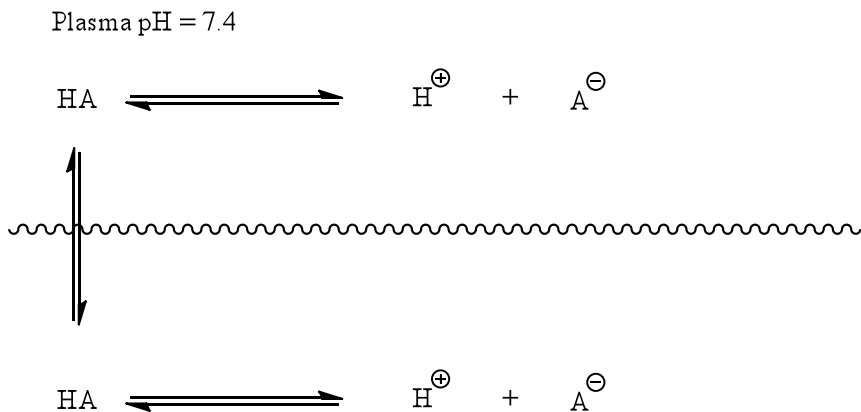
2. Calculate the D and Log D values of the following drugs.

	Phenytoin; pKa = 8.3 ; cLogP = 2.47				Ibuprofen; pKa = 5.2 ; cLogP = 3.5			
pH	4.2		7.4		4.2		7.4	
Species	HA	A ⁻	HA	A ⁻	HA	A ⁻	HA	A ⁻
Octanol								
Water								
D								
Log D								
Log P	2.47		2.47		3.5		3.5	

	Fluoxetine; pKa = 8.7 ; cLogP = 3.9				Benzocaine; pKa = 2.5 ; cLogP = 1.86			
pH	4.2		7.4		4.2		7.4	
Species	BH ⁺	B	BH ⁺	B	BH ⁺	B	BH ⁺	B
Octanol								
Water								
D								
Log D								
Log P	3.9		3.9		1.86		1.86	

3. We have a drug with a pKa of 5.4.

- a) What is the ratio of ionized and unionized form of the drug in each compartment below (intestine and plasma if the drug is acidic and the system is at equilibrium? What is the ratio of total drug in each compartment?
- b) What is the ratio of ionized and unionized form of the drug in each compartment below if the drug is basic and the system is at equilibrium? What is the ratio of total drug in each compartment?



4. Stereoisomers:

Identify the stereocenters in the following compounds and draw or otherwise indicate the (S) configuration in each case.

