

### III Determination of Partition coefficient of any two drugs

**Aim:** To determine 1-octanol/water partition coefficients of ofloxacin, norfloxacin, lomefloxacin, ciprofloxacin, pefloxacin and piperidic acid from 293.15 K to 323.15 K by shake-flask method.

#### References

1. Zhang C, Yan W. Determination and Correlation of 1-Octanol / Water Partition Coefficients for Six Quinolones from 293.15 K to 323.15 K. *Chem Res Chinese Univ.* 2010;26 (4):636-639.
2. Congliang Z, Yan W, Fuan W. Determination and temperature dependence of n-octanol/water partition coefficients for seven sulfonamides from (298.15 to 333.15) K. *Bull Korean Chem Soc.* 2007;28(7): 1183-1186. doi:10.5012/bkcs.2007.28.7.1183.

#### Principle

If a solute / drug is added to two immiscible liquids such as oil (organic phase) and water (aqueous phase) in contact with each other, the solute / drug distributes itself between the two liquids and an equilibrium is set up between the solute molecules in oil and solute molecules in water. The ratio of the concentration of the solute in the two liquids is known as distribution coefficient or partition coefficient.

$$\text{Partition Coefficient} = \frac{[\text{Concentration of drug in oil or organic phase}]}{[\text{Concentration of drug in water or aqueous phase}]}$$

Partition Coefficient of a drug is a measure of how well a substance distributes or partitions between a lipid (oil) and water. High partition coefficient means more tendency to distribute in lipids and less partition coefficient means less tendency to distribute. Partition Coefficient in the range of 1 to 2 is supposed to predict passive absorption of drug across lipidic membranes. High partition coefficient usually do not result in more absorption as high lipid solubility and less water solubility may cause precipitation of drug in the intestinal fluid. For optimum absorption, a drug should have sufficient aqueous solubility to dissolve in the intestinal fluid at the absorption site and lipid solubility high enough to facilitate partitioning of the drug in the lipoidal membrane into blood vessels.

#### Requirements

##### Chemicals

1. Quinolones: ofloxacin, norfloxacin, lomefloxacin, ciprofloxacin, pefloxacin and piperidic acid.
2. Double distilled Water

##### Apparatus

1. Mechanical shaker, water bath, glass flasks
2. UV absorbance, mass balance etc.

##### Procedure

1. 1-Octanol/water partition coefficient was measured by a shake-flask method. Both the solvents were mutually saturated before performing the experiments.
2. Solutions of about  $5 \times 10^{-5}$  mol/L quinolones were prepared in aqueous buffer solutions.
3. Then 10.0 mL of 1-octanol was added to 10.0 mL of the aqueous quinolone solution in glass flasks.

4. The mixtures were then stirred in a mechanical shaker for 1 h. Samples were left in water bath and kept at the appropriate temperature ( $\pm 0.02$  K) for at least 72 h.
5. After that, the aqueous phases were isolated and the concentrations were determined by measuring the UV absorbance.
6. The partition coefficients were calculated by mass balance. All the partitioning experiments were performed in at least triplicate. 1-Octanol/water partition coefficients of ciprofloxacin and sulfamethazine listed in Table 1 were measured, respectively, to complete the data reported in the literature [1, 2].

**Table 1 Measurement and reference values for 1-octanol/ water partition coefficients (lgKow) of some substances at 298.15 K**

Substance	lgKow exp	lgKow ref
Ciprofloxacin	1.0825	1.0800

$$K_{ow} = c_o / c_w$$

where,  $K_{ow}$  is 1-octanol/water partition coefficient of quinolone,

$c_o$  is the concentration of quinolone in 1-octanol phase at equilibrium,

$c_w$  is the concentration of quinolone in aqueous phase at equilibrium.

$K_{ow}$  is actually the phase equilibrium constant for quinolone partitioned in 1-octanol phase and aqueous phase saturated with each other at some temperature.

#### Observation and result

Substance	' $c_o$ ' concentration of quinolone in 1-octanol phase	' $c_w$ ' concentration of quinolone in aqueous phase	Partition coefficient $K_{ow}$
Ciprofloxacin			

$$\log p(K) = C_1 / C_2$$

Where,  $K$  = Partition co-efficient,

$C_1$  &  $C_2$  = Concentration of solute in two immiscible liquids.

#### Conclusions

The results show that 1-octanol/water partition coefficient of each quinolone increases with the increase of temperature. Based on the fluid phase equilibrium theory, the thermodynamic relationship of 1-octanol/water partition coefficient depending on the temperature was proposed, and the changes of enthalpy, entropy, and Gibbs free energy for quinolones partitioning in 1-octanol/water were determined, respectively.