الكلية	الصيدلة
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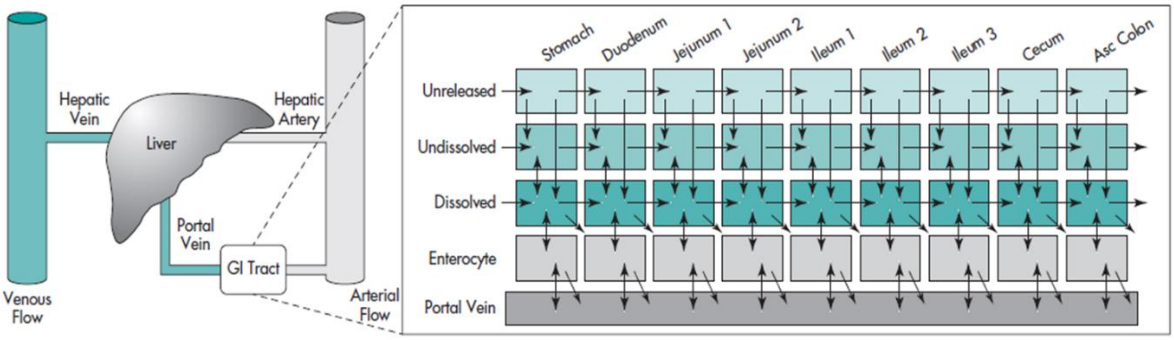
اسم التدريسي	م.م. علي فخري جميل
عنوان المحاضرة باللغة الانجليزية	Determination of PC and pKa
عنوان المحاضرة باللغة العربية	تحديد معامل التقسيم وثابت تأين الحامض
رقم المحاضرة	4
المصادر والمراجع	Laboratory Manual of Biopharmaceutics and Pharmacokinetics, S. B. Bhise, R. J. Dias, S. C. Dhawale, K. K. Mali
	Applied Biopharmaceutics and Pharmacokinetics

محتوى المحاضرة

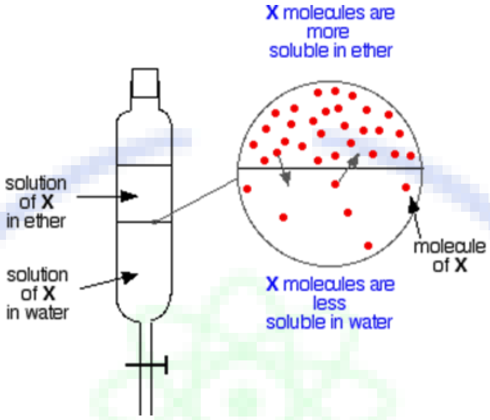
Partition coefficient:

The absorption of several drugs takes place by passive diffusion from GI fluids through the wall of enterocytes going to entering systemic circulation by portal vein.



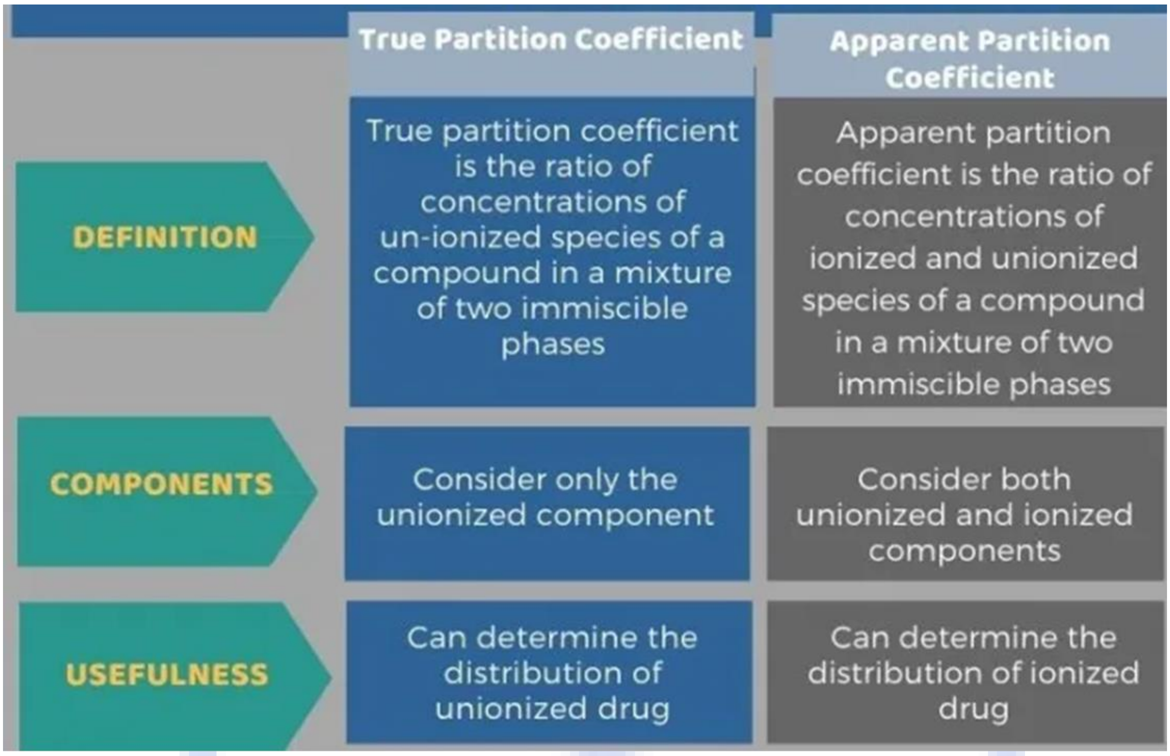
This passive diffusion depends on lipid solubility of the drug (lipophilicity).

PC: is the ratio of the concentration of drug in oil solvent to the concentration of drug in aqueous media, thus giving an idea about how well of the drug will partition between lipids and water.



If the drug has very high or very low PC, it will not be absorbed sufficiently to exert systemic therapeutic concentration.

The absorption process needs sufficient hydrophilicity as well as lipophilicity.



	True Partition Coefficient	Apparent Partition Coefficient
DEFINITION	True partition coefficient is the ratio of concentrations of un-ionized species of a compound in a mixture of two immiscible phases	Apparent partition coefficient is the ratio of concentrations of ionized and unionized species of a compound in a mixture of two immiscible phases
COMPONENTS	Consider only the unionized component	Consider both unionized and ionized components
USEFULNESS	Can determine the distribution of unionized drug	Can determine the distribution of ionized drug

$$PC = \frac{[HA-organic]}{[HA-aqueous]} \qquad PC' = \frac{[HA-organic]}{[HA]+[A^-]}$$

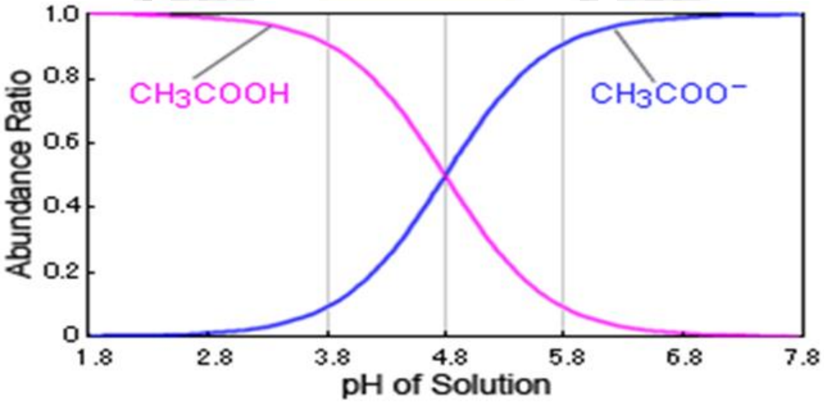
What is the relation of pKa in this process?!

Dissociation constant:

It is a measure of the strength of an acid or a base, calculation of pKa allows the proportion of neutral and charged species at any pH to be estimated, as well as the basic or acidic properties of the compound to be defined.

Lower pKa of acid → stronger acid.

Higher pKa of base → stronger base.



For weak acids,

$$pH = pK_a + \log \frac{\text{ionized drug concentration}}{\text{unionized drug concentration}}$$

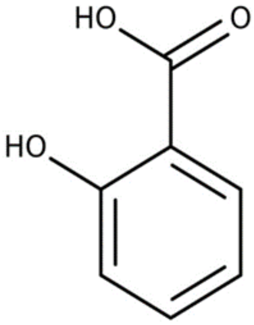
$$\%\ \text{drug ionized} = \frac{10^{\text{pH - pKa}}}{1+10^{\text{pH - pKa}}} \times 100$$

For weak bases,

$$pH = pK_a + \log \frac{\text{unionized drug concentration}}{\text{ionized drug concentration}}$$

$$\%\ \text{drug ionized} = \frac{10^{\text{pKa - pH}}}{1+10^{\text{pKa - pH}}} \times 100$$

Salicylic acid is a relatively polar, poorly aqueous soluble material. The salt form however is quite water soluble. By changing pH of the aqueous buffer, you are able to alter the ratio between the ionized and unionized form of the acid. Since the unionized form is extracted into the organic phase, the fraction extracted will vary with pH of the aqueous solution.



Procedure:

1 .Prepare 100 ml of buffer at pH 2.5.

2 .Weigh accurately 20 mg of Salicylic acid and transfer to 100 ml volumetric flask and adjust volume by buffer of pH 2.5.

Similarly prepare 0.02% solution of Salicylic acid with buffers of pH 2.8, 3.0, 3.5, 3.8, and 4.0.

3. Take 4 ml of the buffer pH of 2.5 containing Salicylic acid stock solution and add 1 ml of the ferric nitrate solution. Allow the color to form and measure the absorbance at 540 nm using spectrophotometer. This is (ABS I).

4. Next, take 5 ml of the buffer pH 2.5 containing Salicylic acid stock solution and add 5 ml of the organic solvent hexane/ethyl acetate. Stopper and shake the test tube for 5 minutes to complete the extraction. Allow the two phases to settle, remove 4ml of the aqueous phase, add 1ml of ferric nitrate solution (0.55% ferric nitrate in 0.4M nitric acid), allow the color to form, and measure the absorbance at 540 nm. This is (ABS II).

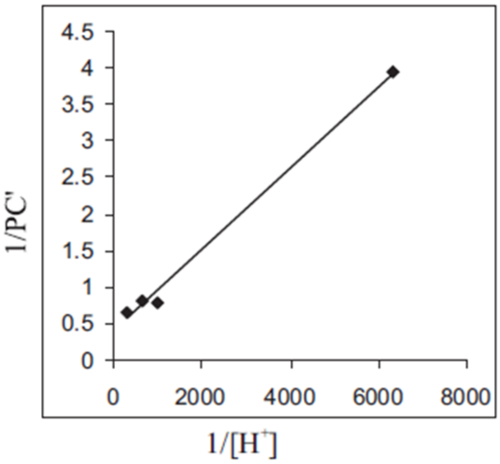
Using the two absorbance readings, calculate the apparent partition coefficient, PC', as:

$$PC' = \frac{[\text{total in organic}]}{[\text{total in aqueous}]} = PC' = \frac{(\text{ABS I} - \text{ABS II})}{\text{ABS I}}$$

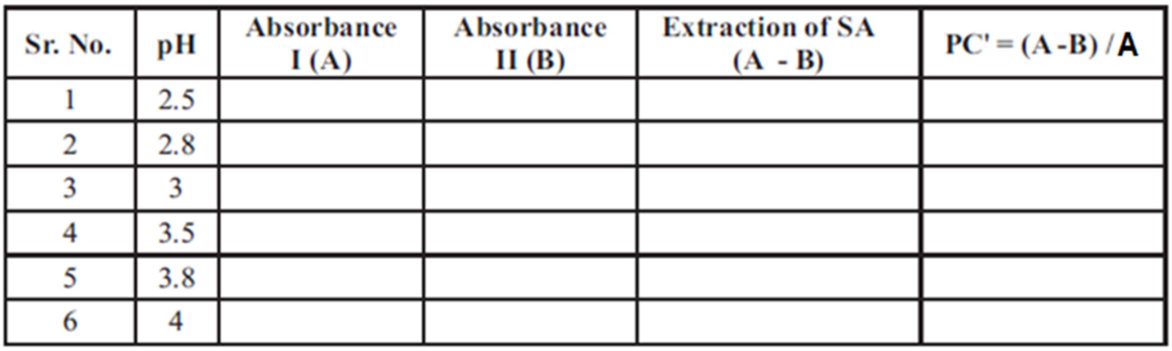
5 .Repeat the experiment with the buffers of pH 2.8, 3.0, 3.5, 3.8, and 4.0. Plot 1/PC' versus 1/[H] and calculate PC, Ka, and pKa.

6 .Calculate H ion concentration with the help of equation, pH= -log [H] .

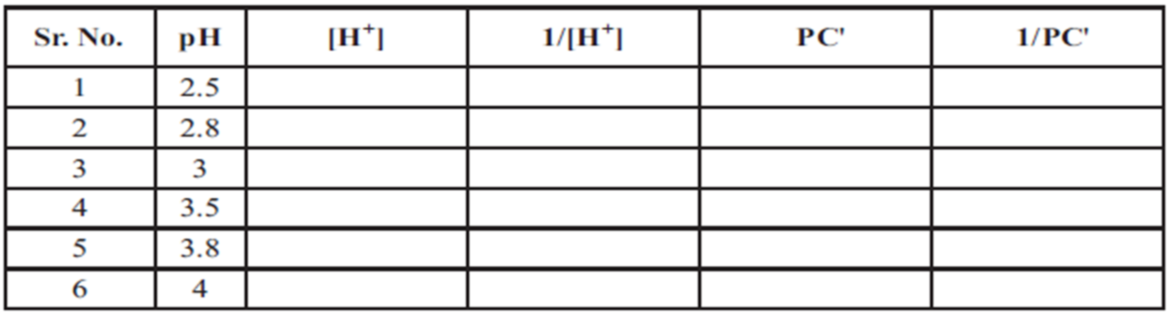
***slope = Ka/PC**
**** intercept = 1/PC**



Observations:



Sr. No.	pH	Absorbance I (A)	Absorbance II (B)	Extraction of SA (A - B)	$PC' = (A-B)/A$
1	2.5				
2	2.8				
3	3				
4	3.5				
5	3.8				
6	4				



Sr. No.	pH	$[H^+]$	$1/[H^+]$	PC'	1/PC'
1	2.5				
2	2.8				
3	3				
4	3.5				
5	3.8				
6	4				

Conclusions:

Determination of pKa: We can calculate the relative amount of unionized (absorbable) and ionized (un-absorbable) forms of the drug and predict the extent of absorption at a given pH of gastro intestinal tract, if pKa of drug is known.

Determination of PC: We can predict the extent of absorption by knowing the lipid solubility because high lipid solubility facilitates the partitioning of the drug in the lipoidal bio-membrane and into the systemic circulation.

The knowledge of value of pKa and PC of particular drug will be useful for designing appropriate dosage form for optimum bioavailability.