Wroclaw Medical University

Calculating the pH of a solutions
Strong and weak acids and bases

Dr inż. Jolanta Lis-Kuberka **jolanta.lis-kuberka@umed.wroc.pl**

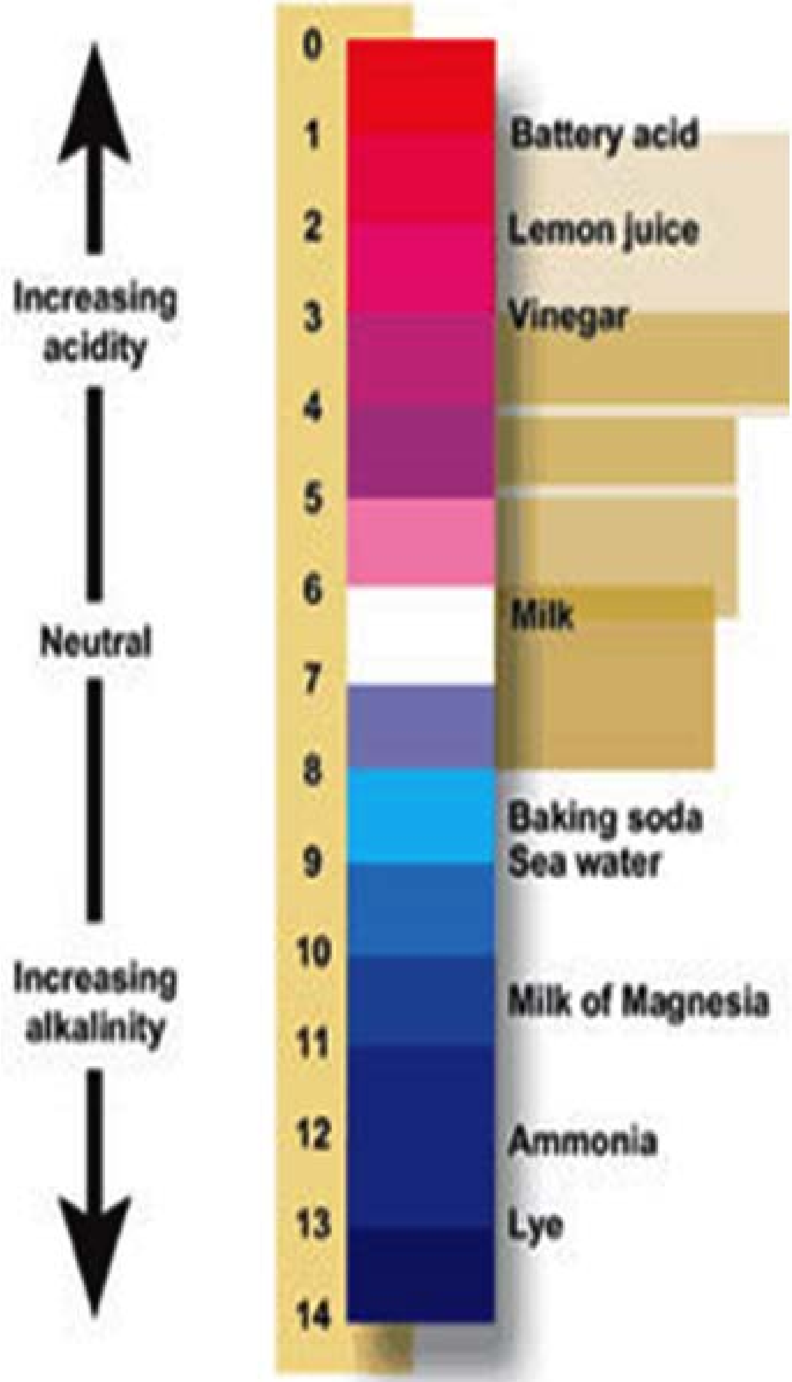
Wroclaw, 01.04.2020

pH Scale

pH is a measure of the concentration of hydrogen ions in a solution. Strong acids like hydrochloric acid at the sort of concentrations you normally use in the lab have a pH around 0 to 1. The lower the pH, the higher the concentration of hydrogen ions in the solution.

The mathematical definition of pH is a bit less intuitive but in general more useful. It says that the pH is equal to to the **negative logarithmic value of the Hydrogen ion (H^+) concentration**, or

$$pH = -\log [H^+]$$



Example 1

$$pH = -\log[H^+]$$
$$[H^+] = \text{antilog}(-pH)$$

- Find the pH of a 0.0025 M HCl solution.

$$pH = -\log(0.0025) = -(-2.60) = 2.60$$

- What is the hydronium ion concentration in a solution that has a pH of 8.34?

$$8.34 = -\log[H_3O^+]$$
$$-8.34 = \log[H_3O^+]$$
$$[H_3O^+] = 10^{-8.34} = 4.57 \times 10^{-9}\ M$$

Example 2

$$pOH = -\log[OH^-]$$
$$[OH^-] = \text{antilog}(-pOH)$$

- What is the pOH of a solution that has a hydroxide ion concentration of 4.82×10^{-5} M?

$$pOH = -\log[4.82 \times 10^{-5}] = -(-4.32) = 4.32$$

- What is the hydroxide ion concentration in a solution has a pOH of 5.70?

$$5.70 = -\log[OH^-]$$
$$-5.70 = \log[OH^-]$$
$$[OH^-] = 10^{-5.70} = 2.00 \times 10^{-6} \text{ M}$$

Example 3

$$pH + pOH = 14$$

- A solution has a pOH of 11.76. What is the pH of this solution?

$$pH = 14 - pOH = 14 - 11.76 = 2.24$$

Strong Acids *vs* Weak Acids

Strong Acids	Weak Acids
Strong acids are molecules that completely dissociate into their ions when it is in water	Weak acids are molecules that partially dissociate into ions in aqueous solution
pH of a strong acid solution is very low	pH of a weak acid solution is about 3-5
Acid dissociation constant is a higher value	Acid dissociation constant is a lower value
Release all the H+ ions to the solution	Do not release all H+ ions

Visit www.pediaa.com

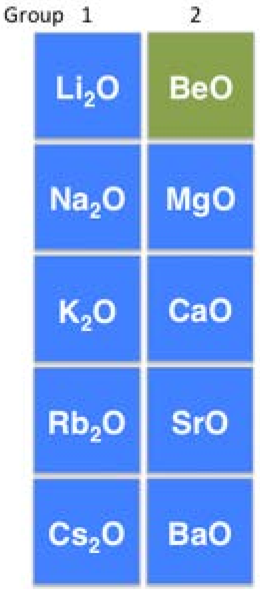
Strong Bases *vs* Weak Bases

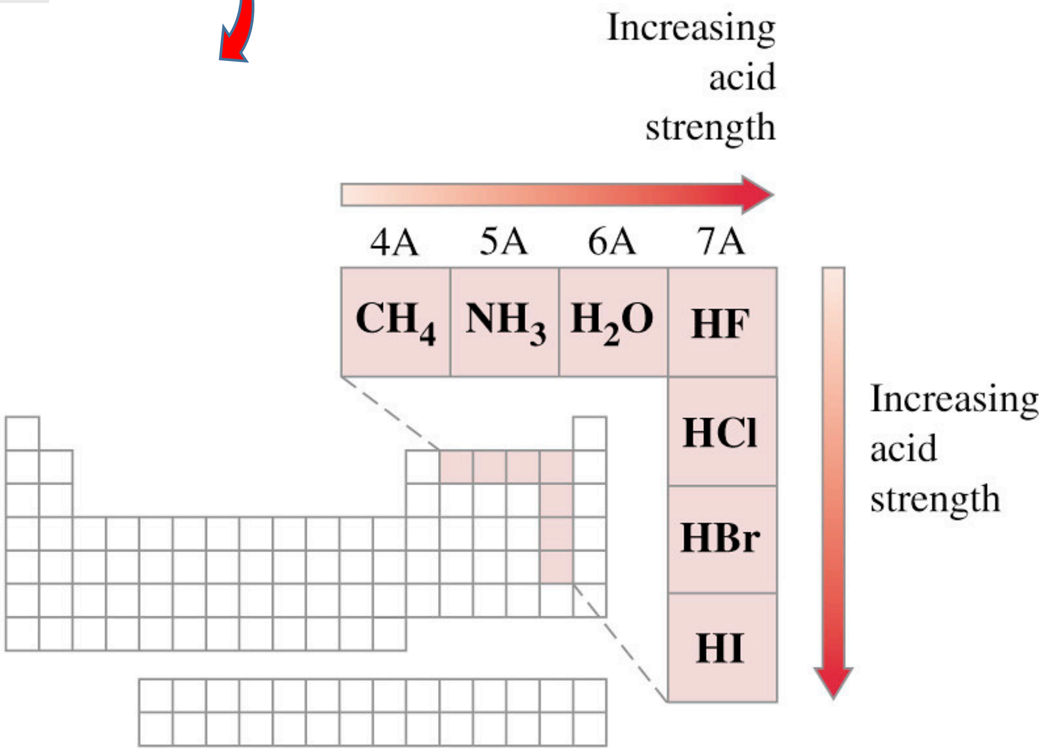
Strong Bases	Weak Bases
A strong base is a compound that can completely dissociate into its cation and hydroxyl ion in aqueous solution	A weak base is a compound that partially dissociates into its hydroxyl ion and the cation creating an equilibrium condition
Dissociate into ions almost 100%	Partially dissociate into ions
Indicated by a pH value closer to 14	Indicated by a pH value greater than 7 but lower than 14
Highly reactive	Less reactive
pKb value is almost 0	pKb value is high

Visit www.pediaa.com

Strong Acids & Strong Bases

Bases	Acids
Li(OH)	HCl
Na(OH)	HBr
K(OH)	HI
Rb(OH)	HNO_3
Cs(OH)	H_2SO_4
$Mg(OH)_2$	$HClO_3$
$Ca(OH)_2$	$HClO_4$
$Sr(OH)_2$	
$Ba(OH)_2$	





Increasing acid strength (↑) | Increasing base strength (↓)

perchloric acid	$HClO_4$	Undergo complete acid ionization in water	Do not undergo base ionization in water	ClO_4^-	perchlorate ion
sulfuric acid	H_2SO_4			HSO_4^-	hydrogen sulfate ion
hydrogen iodide	HI			I^-	iodide ion
hydrogen bromide	HBr			Br^-	bromide ion
hydrogen chloride	HCl			Cl^-	chloride ion
nitric acid	HNO_3			NO_3^-	nitrate ion
hydronium ion	H_3O^+			H_2O	water
hydrogen sulfate ion	HSO_4^-			SO_4^{2-}	sulfate ion
phosphoric acid	H_3PO_4			$H_2PO_4^-$	dihydrogen phosphate ion
hydrogen fluoride	HF			F^-	fluoride ion
nitrous acid	HNO_2			NO_2^-	nitrite ion
acetic acid	CH_3CO_2H			$CH_3CO_2^-$	acetate ion
carbonic acid	H_2CO_3			HCO_3^-	hydrogen carbonate ion
hydrogen sulfide	H_2S			HS^-	hydrogen sulfide ion
ammonium ion	NH_4^+			HN_3	ammonia
hydrogen cyanide	HCN			CN^-	cyanide ion
hydrogen carbonate ion	HCO_3^-			CO_3^{2-}	carbonate ion
water	H_2O			OH^-	hydroxide ion
hydrogen sulfide ion	HS^-	Do not undergo acid ionization in water	Undergo complete base ionization in water	S^{2-}	sulfide ion
ethanol	C_2H_5OH			$C_2H_5O^-$	ethoxide ion
ammonia	NH_3			NH_2^-	amide ion
hydrogen	H_2			H^-	hydride ion
methane	CH_4			CH_3^-	methide ion

Example 4

Write the balanced chemical equation for the dissociation of $Ca(OH)_2$ and indicate whether it proceeds 100% to products or not.

Solution

This is an ionic compound of Ca^{2+} ions and OH^{-} ions.

When an ionic compound dissolves, it separates into its constituent ions:

$$Ca(OH)_2 \rightarrow Ca^{2+}(aq) + 2OH^{-}(aq)$$

Because $Ca(OH)_2$ is in 2nd group of the periodic table,
this reaction proceeds 100% to products.

Example 5

Write the balanced chemical equation for the dissociation of H_2SO_4 and indicate whether it proceeds 100% to products or not.

Solution

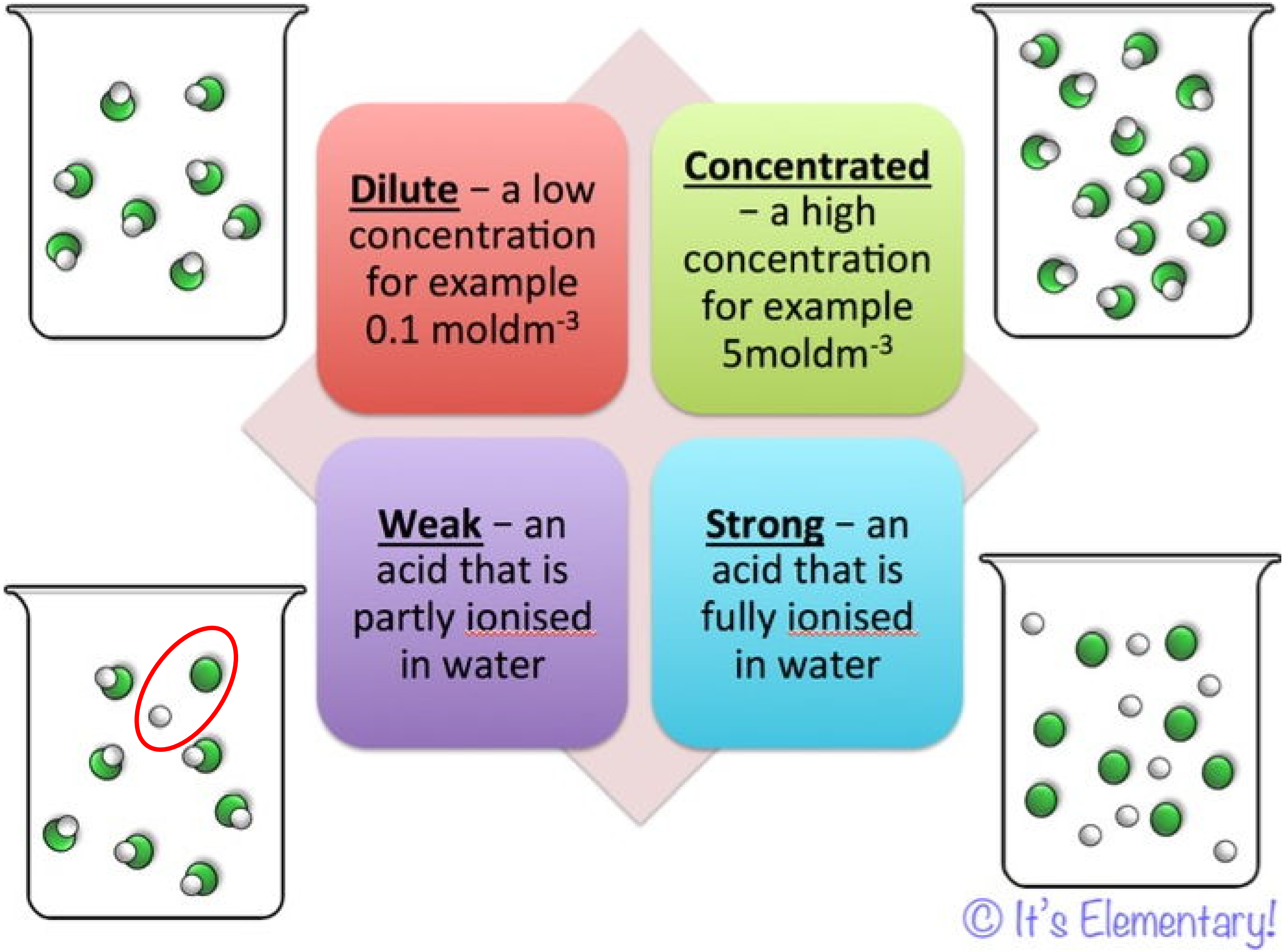
This is an ionic compound of H^+ , $HSO_4{}^-$ ions and $SO_4{}^{2-}$ ions.

When an ionic compound dissolves, it separates into its constituent ions:

$H_2SO_4 \rightarrow H^{+(}aq) + HSO_4{}^-(aq)$

$H_2SO_4 \rightarrow H^{+(}aq) + SO_4{}^{2-}(aq)$

Because H_2SO_4 is strong acid, this reaction proceeds 100% to products.


Dilute – a low concentration for example 0.1 moldm-3
Concentrated – a high concentration for example 5moldm-3
Weak – an acid that is partly ionised in water
Strong – an acid that is fully ionised in water
© It's Elementary!

pKa and Dissociation Equilibrium

When an acid dissociates, it releases a proton to make the solution acidic, but weak acids have both a dissociated state (A^-) and undissociated state (AH) that coexist according to the following dissociation equilibrium equation.

$$AH \leftrightarrow A^-(aq) + H^+(aq)$$

The concentration ratio of both sides is constant given fixed analytical conditions and is referred to as the acid dissociation constant (Ka). Ka is defined by the following equation.

$$K_a = \frac{[A^-][H^+]}{[AH]}$$

Based on this equation, **Ka expresses how easily the acid releases a proton** (in other words, its strength as an acid). In addition, the equation shows how the dissociation state of weak acids vary according to the $[H^+]$ level in the solution. Carboxylic acids (containing -COOH), such as acetic and lactic acids, normally have a Ka constant of about 10^{-3} to 10^{-6}. Consequently, expressing acidity in terms of the Ka constant alone can be inconvenient and not very intuitive. Therefore, pKa was introduced as an index to express the acidity of weak acids, where pKa is defined as follows.

$$pK_a = -log_{10}K_a$$

For example, the Ka constant for acetic acid (CH_3COOH) is 0.0000158 (= $10^{-4.8}$), but the pKa constant is 4.8, which is a simpler expression. **In addition, the smaller the pKa value, the stronger the acid**. For example, the pKa value of lactic acid is about 3.8, so that means lactic acid is a stronger acid than acetic acid.

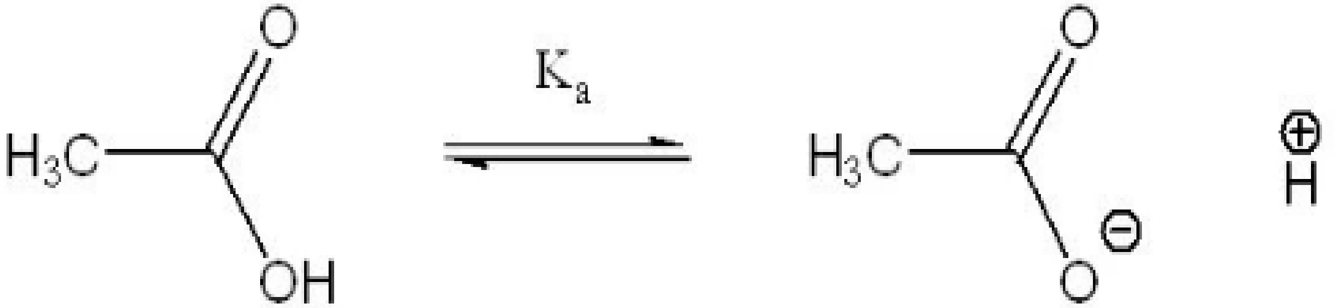
Short pKa table

Functional group	*Example*	*pKa*	*conj. base*
Hydrochloric acid	HCl	–8	Cl^{-}
Carboxylic acids	$H_3C\text{–}C(=O)OH$	5	$H_3C\text{–}C(=O)O^{-}$
Protonated amines	$NH_4^{+}\ Cl^{-}$	10	NH_3
Water	$HO\text{–}H$	14	^{-}OH
Alkyne	$H_3C\text{–}C{\equiv}C\text{–}H$	25	$R\text{–}C{\equiv}C^{-}$
Amine	NH_3	~35	$^{-}NH_2$
Alkane	CH_4	~50	$^{-}CH_3$

Stronger acid ↓ Weaker acid

Stronger base ↑ Weaker base

Example 6



$$K_a = \frac{[CH_3COO^-][H^+]}{[CH_3COOH]}$$

K_a for CH_3CO_2H is approximately 10^{-5}

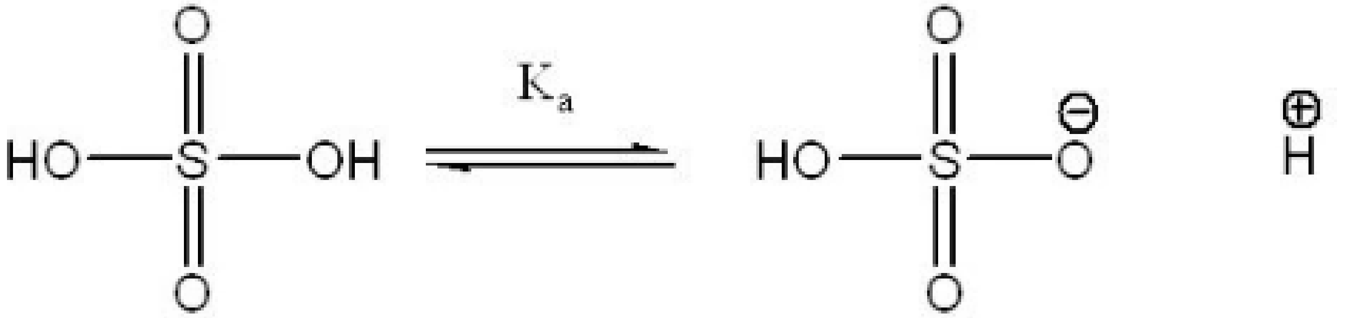
$$K_a = \frac{1}{10^5}$$

i.e. only 1 molecule in 100,000 is DISSOCIATED (ionised).

$-\log_{10}K_a = pK_a$

So pKa for acetic acid is 5

Example 7



$$K_a = \frac{[HSO_4^-][H^+]}{[H_2SO_4]}$$

K_a for H_2SO_4 is approximately 10^5 $\quad K_a = \frac{10^5}{1}$

i.e. 100,000 molecules are DISSOCIATED (ionised) for every one undissociated.

The pKa of H_2SO_4 is therefore -5

Example 8

$$K_a = \frac{[PhCH_2NH_2][H^+]}{[PhCH_2NH_3^+]}$$

K_a for $PhCH_2NH_3^+$ is approximately 10^{-9} (pKa = 9)

$$K_a = \frac{1}{10^9}$$

i.e. only 1 molecule in 1,000,000,000 is DISSOCIATED (UNIONISED).

A weak conjugate acid does not easily donate its proton
(1 molecule in 1,000,000,000 donates a proton)

Therefore a strong base willingly accepts a proton
(1,000,000,000 molecules accept a proton for every one)

pKa is a different term than pH

pH is simply a measure of the $[H^+]$ concentration in a given solution

pH = 1 ....the environment is acidic

pK_a = 1 DOES NOT mean an acidic molecule

pH = 14 ....the environment is basic

pK_a = 1 DOES NOT mean a basic molecule

pKa *vs* pH

pKa	pH
pKa is the negative value of the logarithmic of Ka	pH is the logarithmic value of the inverse of H+ concentration
Indicates whether an acid is a strong acid or a weak acid	Indicates whether a system is acidic or alkaline
Gives details of the dissociation of an acid in aqueous solution	Gives details about the concentration of H+ ions in a system
If the pKa of an acid is high, it is a weak acid; if the pKa of an acid is low, it is a strong acid	If the pH of a system is high, the system is alkaline; if the pH is low, that system is acidic
Depends on the concentration of acid, conjugate base and H+	Depends on the H+ concentration

Factors affecting the strength of the acid

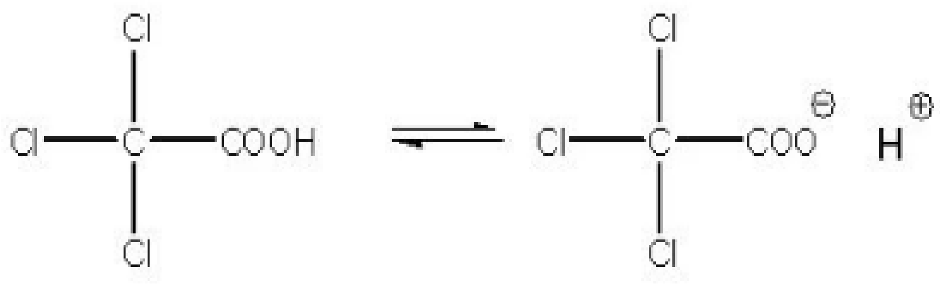
- **The more stable conjugate base (anion) formed, the stronger the acid will be**

- **So any factor will stabilize the anion will increase the acidity of the group, such as resonance and induction stabilization**

- **Stable negative charge results from lowering the electron density on the atom**

Which one is the stronger acid?

Considering Ka values relates ratio of products to reactants

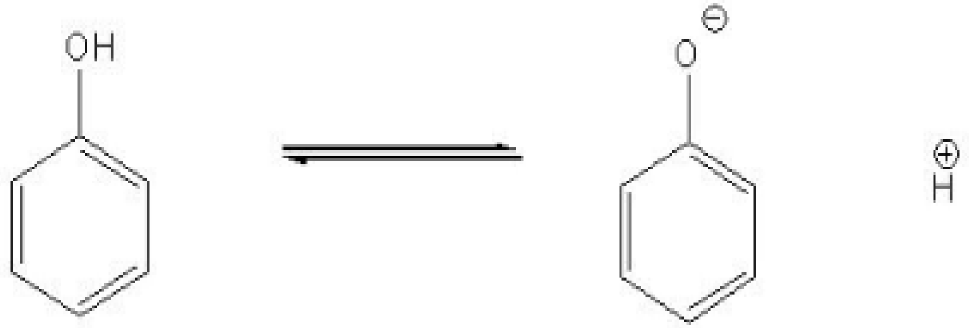


pKa = 0.9

$Ka = 10^{-0.9}$

$$K_a = \frac{[Cl_3COO^-][H^+]}{[Cl_3COOH]}$$

$$K_a = \frac{1}{10^{0.9}}$$



pKa = 10.0

$Ka = 10^{-10}$

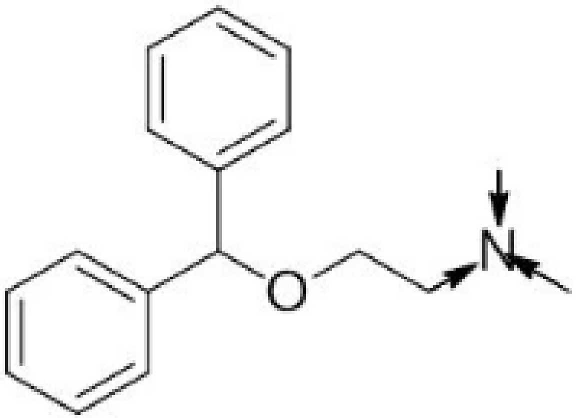
$$K_a = \frac{[PhO^-][H^+]}{[PhOH]}$$

$$K_a = \frac{1}{10^{10}}$$

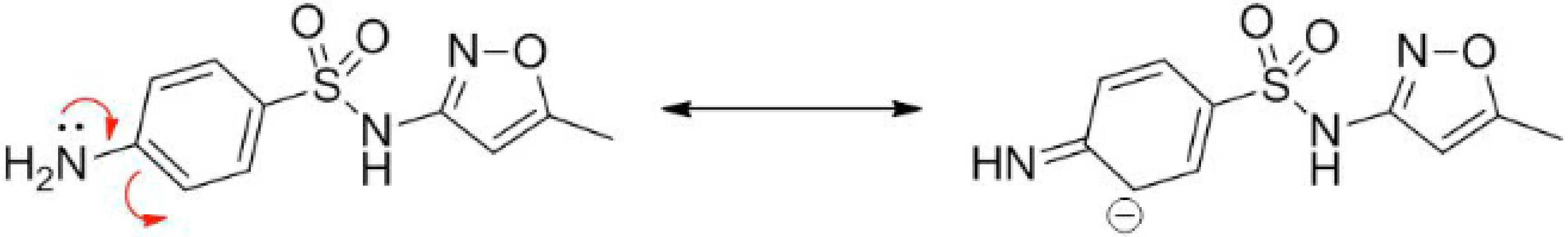
Phenols are weaker acids than acetates

Factors affecting the strength of the base

- If the atom has an available lone pair of electrons, it can act as a base....
- The availability of these electrons will determine the strength of the base
- As a result of that, aromatic amino group is much weaker base than aliphatic one

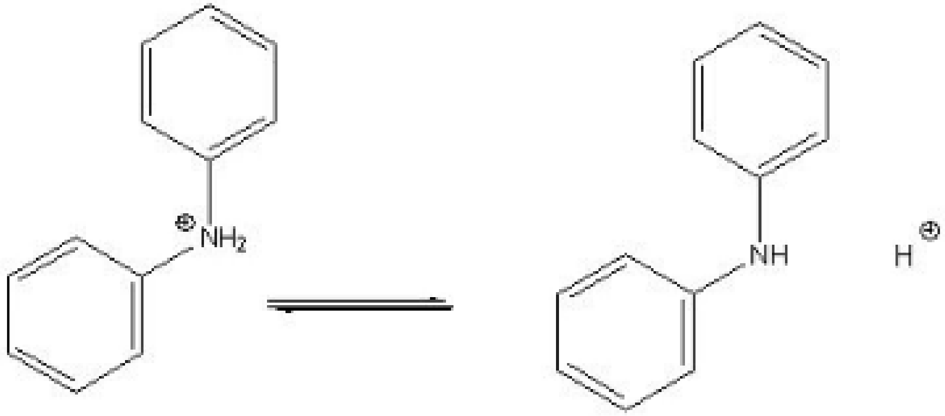


tertiary amine: methyl groups compared to phenyl group are better donating groups by induction
(more available lone pair of electrons)



the lone pair of electrons are not available....delocalized through the phenyl group
(stable by resonance)

Which one is the stronger base?



pKa = 0.5

Ka = $10^{-0.5}$

$$K_a = \frac{[Ph_2NH][H^+]}{[Ph_2NH_2^+]}$$

$$K_a = \frac{1}{10^{0.5}}$$

pKa = 9.0

Ka = 10^{-9}

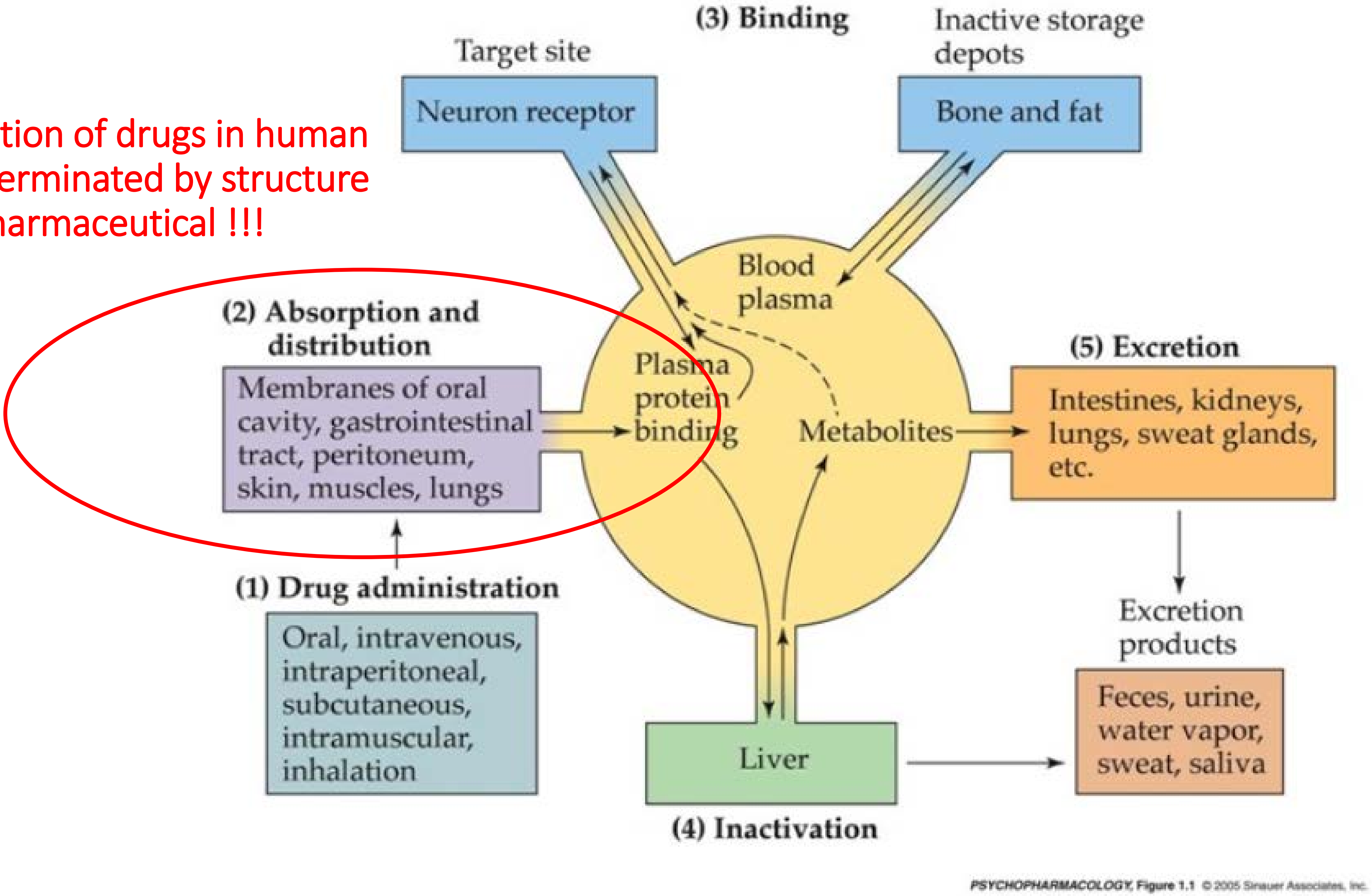
$$K_a = \frac{[PhCH_2NH_2][H^+]}{[PhCH_2NH_3^+]}$$

$$K_a = \frac{1}{10^{9}}$$

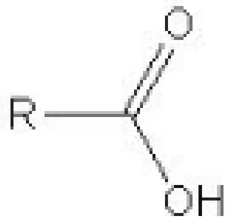
Aromatic amines are weaker bases than aliphatic amines

Ionization and dissociation of drug

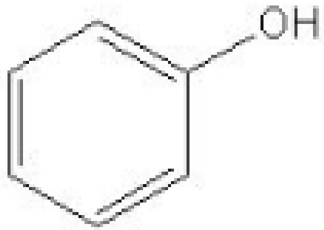
The absorption of drugs in human body is determinated by structure of pharmaceutical !!!



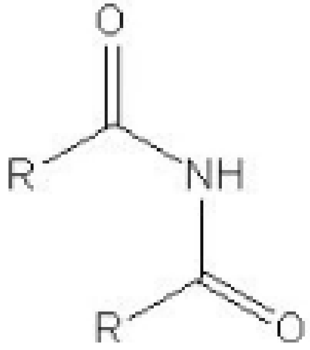
Common acidic functional groups in pharmaceutical chemistry and their pKa values



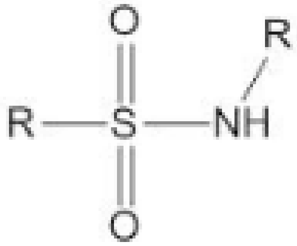
4-5



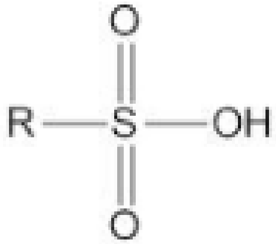
9.9



8-10

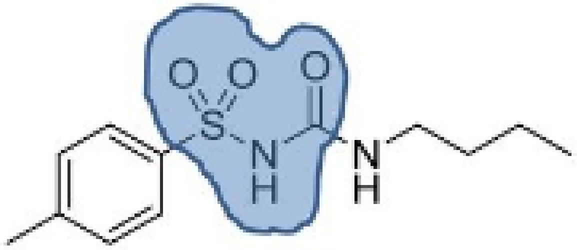


10

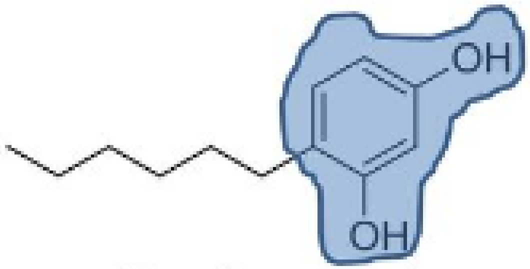


<2

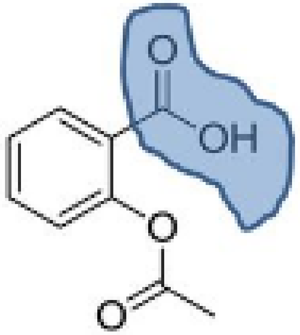
Examples of acidic drugs



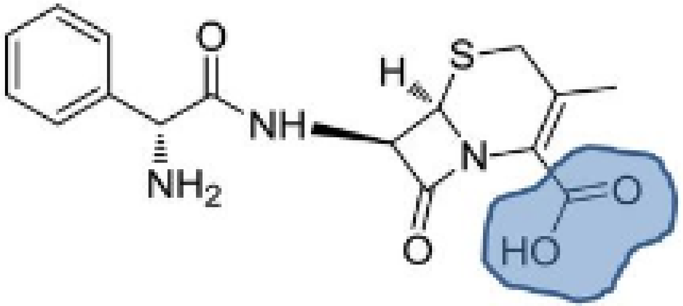
Tolbutamide
hypoglycemic agent



4-hexylresorcinol
topical anesthetic

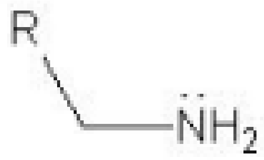


Aspirin
NSAID

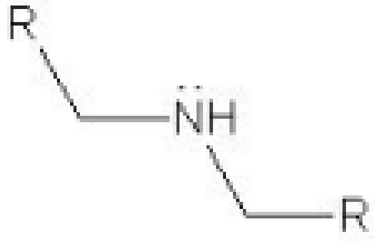


Cephalexin
Antibacterial agent

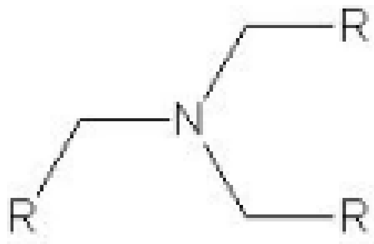
Common basic functional groups in pharmaceutical chemistry and their pKa values



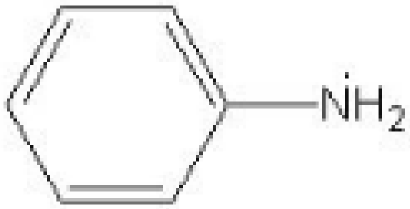
10.0



10.6-11.0

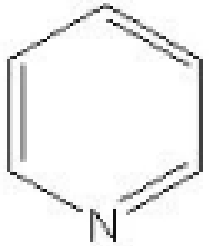


9.8-10.8



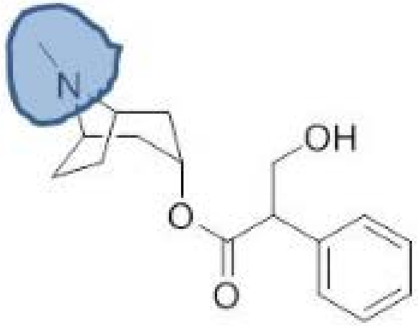
4.6

6.5

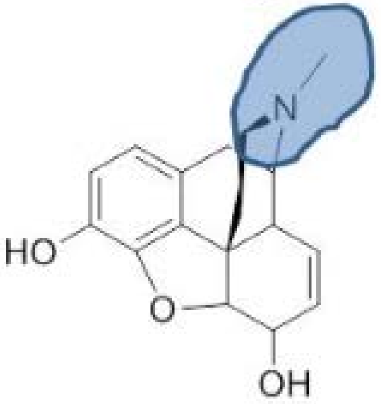


5.2

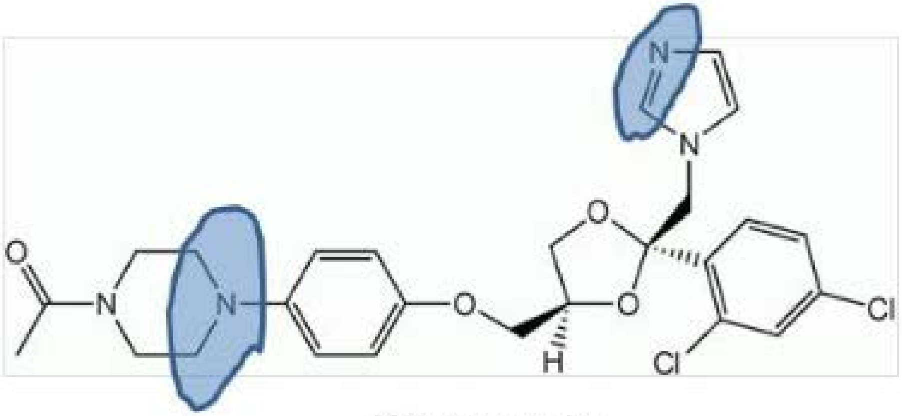
Examples of basic drugs



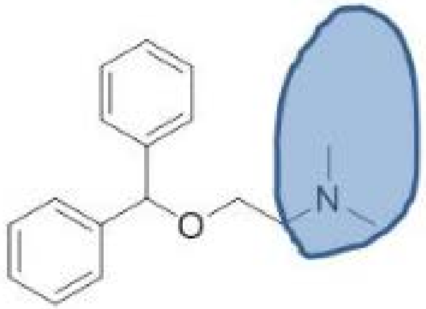
Atropine
Anticholinergic agent



Morphine
opioid analgesic

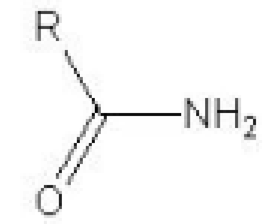


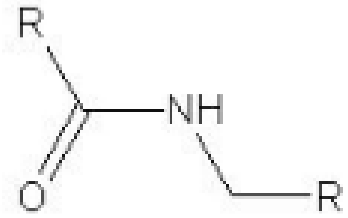
Ketoconazole
Antifungal agent

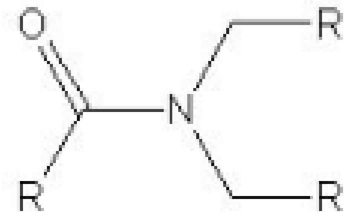


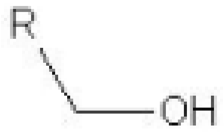
Diphenhydramine
Antihistaminic agent

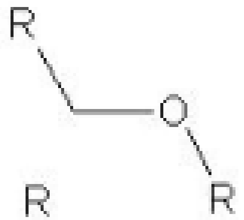
Common neutral functional groups in pharmaceutical chemistry

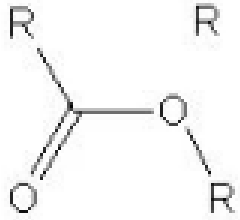


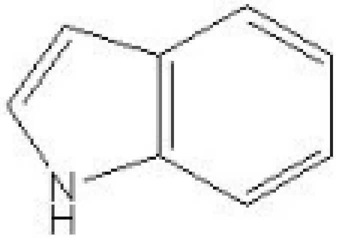












Basic drugs increasingly ionized

Bases	pH	Acids
Weak		*Strong*
	2	Penicillin G (pK_a 2.8)
Diazepam (pK_a 3.3)	3	Probenecid (pK_a 3.4)
		Aspirin (pK_a 3.5)
Chlordiazepoxide (pK_a 4.8)	4	Furosemide (pK_a 4.7)
	5	Warfarin (pK_a 5.1)
		Sulfamethoxazole (pK_a 5.8)
Triamterene (pK_a 6.2)	6	Cimetidine (pK_a 6.8)
Trimethoprim (pK_a 7.2)		
Ergometrine (pK_a 7.3)		
Physiological pH	7.4	**Physiological pH**
Etidocaine (pK_a 7.7)		Thiopental (pK_a 7.5)
Lidocaine (pK_a 7.9)		Phenobarbital (pK_a 7.5)
Morphine (pK_a 8.0)	8	Phenytoin (pK_a 8.3)
Cocaine (pK_a 8.4)		
Propranolol (pK_a 9.5)	9	Chlorthalidone (pK_a 9.4)
Atropine (pK_a 9.7)		
Amphetamine (pK_a 9.8)		
Amantadine (pK_a 10.8)	10	
Lorazepam (pK_a 11.5)	11	Ascorbic acid (pK_a 11.6)
Neostigmine (pK_a 12)	12	
Strong		*Weak*

Acidic drug increasingly ionized

Importance of environmental pH & drug pKa

- Degree of ionization (polarity) depends on the pKa of drug (and pH of body fluid)

- pKa: value of drug pH when the concentration of ionized and non-ionized drug form is equal

- If pKa of a drug is equal to pH of the media, then … „50% of the drug are ionized & 50% are non-ionized"

What is the importance of studying the pKa values for Acidic and Basic drugs ???

- Only the unionised form of a drug can partition across biological membranes (providing the unionized form is lipophilic)
- The ionised form tends to be more water soluble (required for drug administration and distribution in plasma)

Plasma	7.35 – 7.45
Buccal cavity	6.2 – 7.2
Stomach	1.0 – 3.0
Duodenum	4.8 – 8.2
Jejunum & ileum	7.5 – 8.0
Colon	7.0 – 7.5

The Human Digestive System

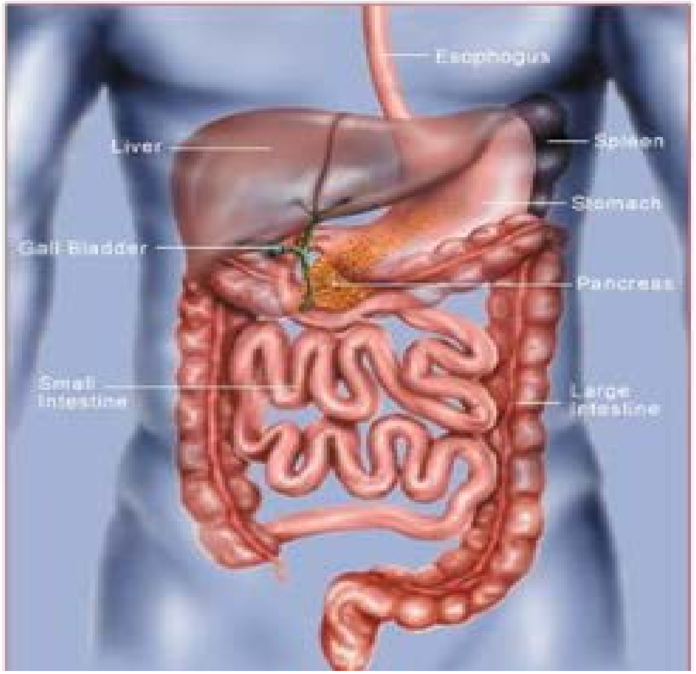


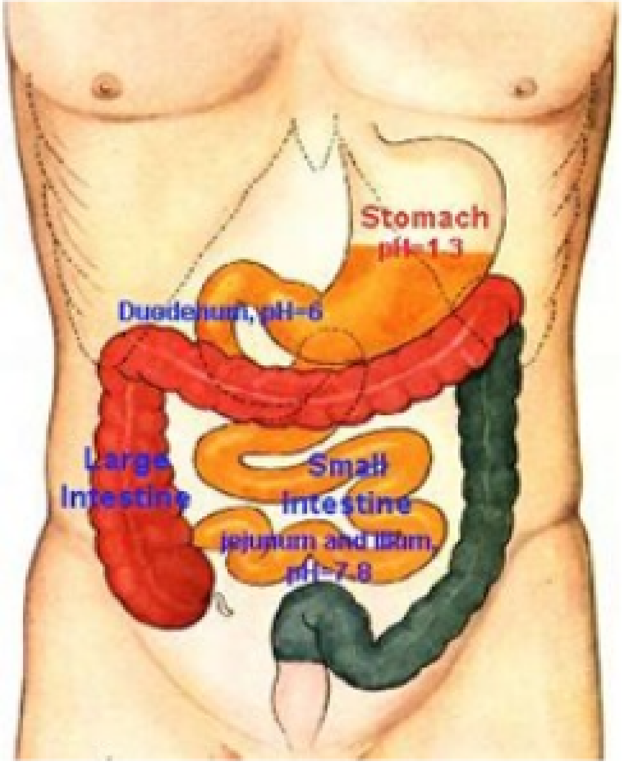
TABLE 1.2 pH of Body Fluids

Fluid	pH
Stomach fluid	1.0–3.0
Small intestine	5.0–6.6
Blood	7.35–7.45
Kidney urine	4.5–7.5
Saliva	6.2–7.2
CSF	7.3–7.4

Absorption after ingestion is effected by pH gradient between the drug and absorbing surface.

In the **stomach** , which is highly acidic, acidic drugs are absorbed while basic drugs tend to accumulate.

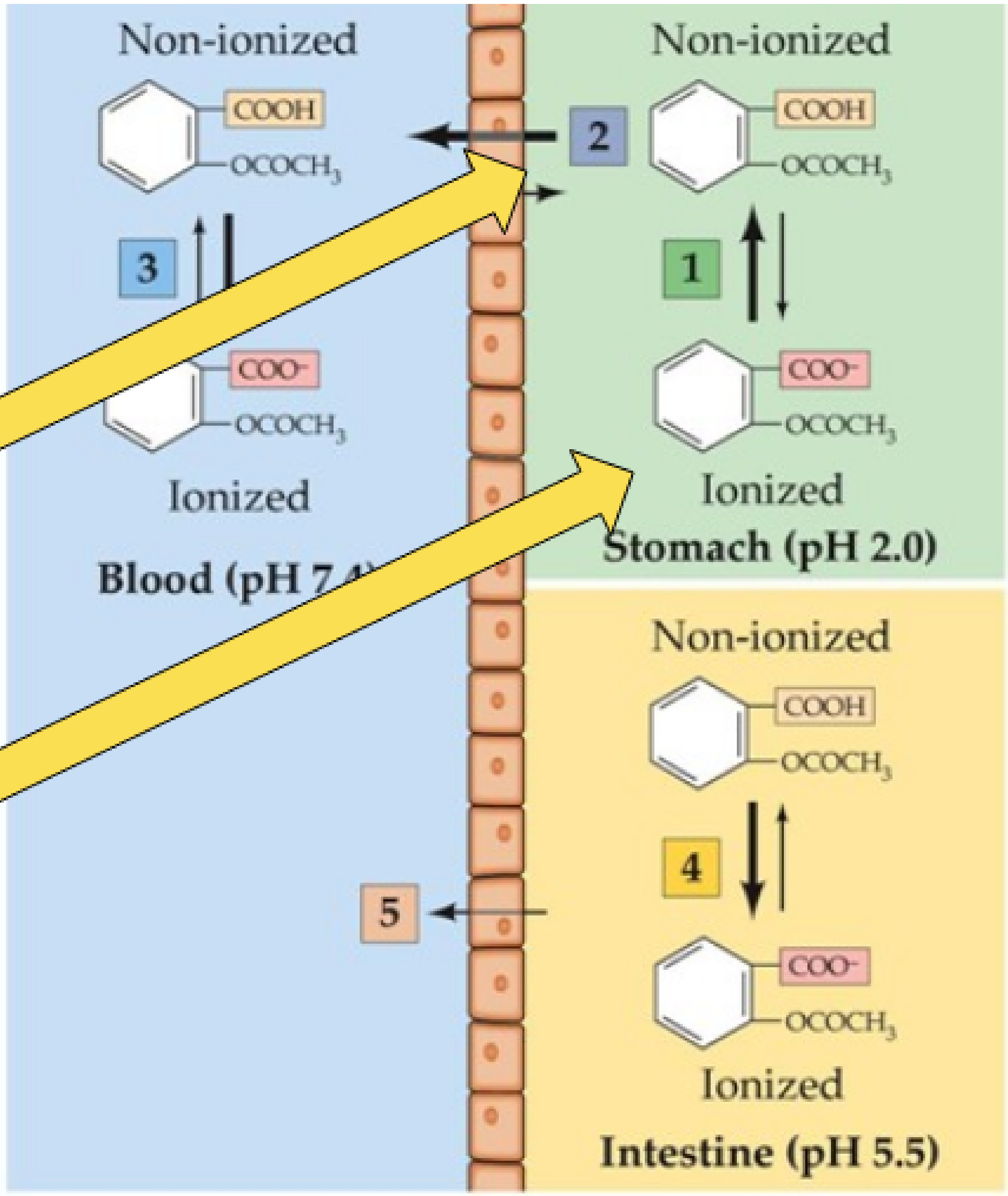
In the **intestine** , which is only slightly acidic, basic drugs are better absorbed than acidic drugs.



Effect of ionization on drug absorption

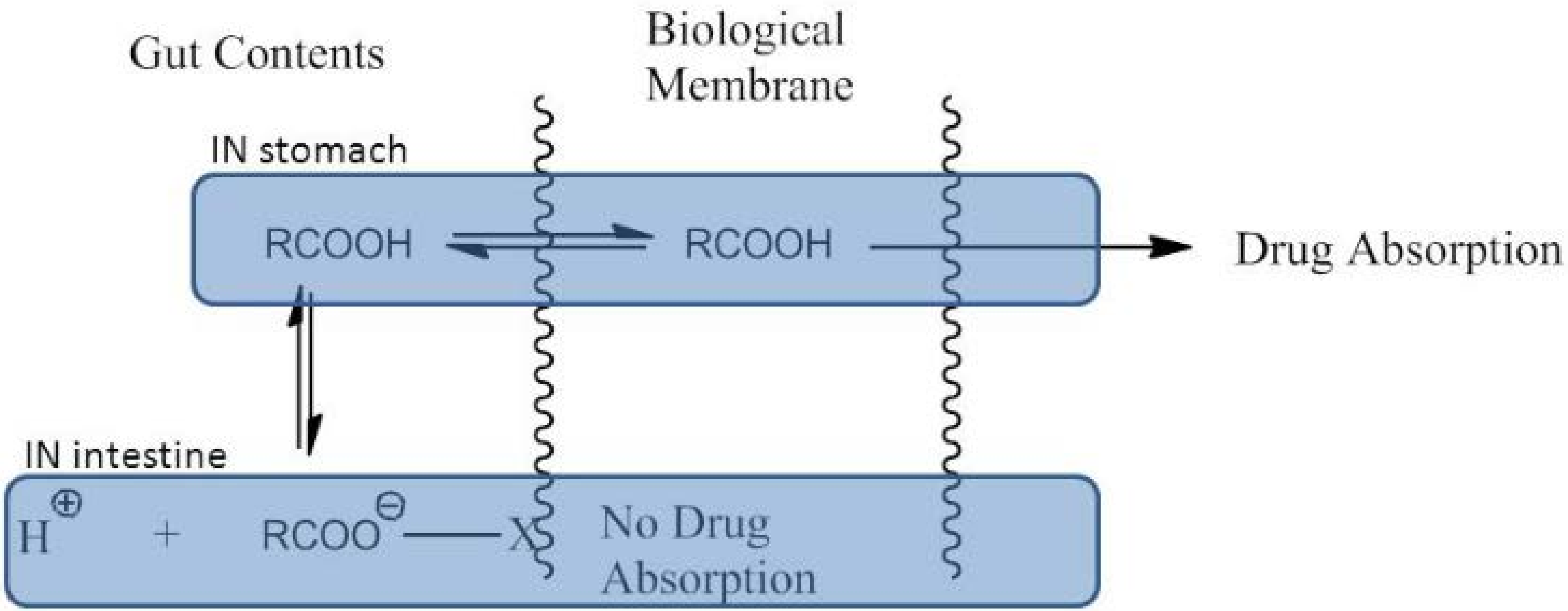
Non-ionized drugs can easily pass through membranes

Ionized drugs can not easily pass through membranes

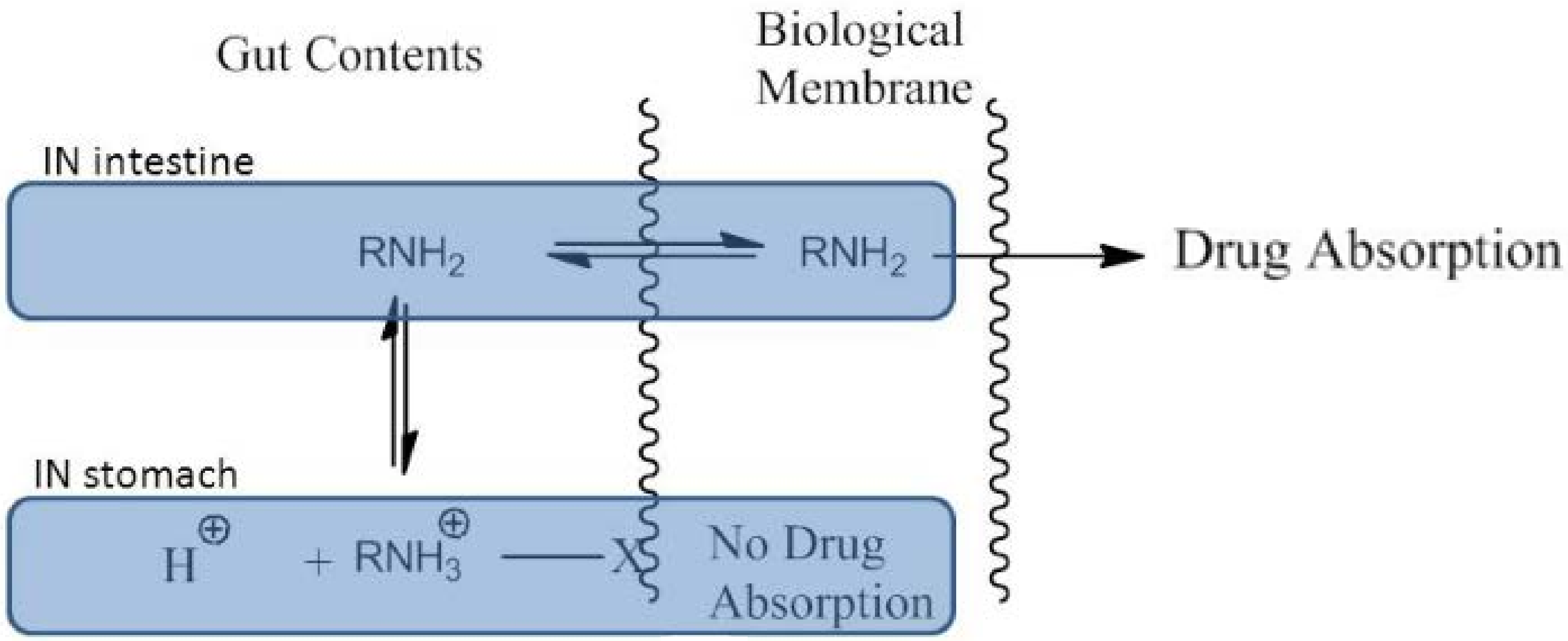


PARTITIONING OF ACIDS AND BASE

For acidic drugs, with a pKa of 4.0, the ionization state will be as follows



For basic drugs, the ionization state will be as follows



Remember the followings !!!

For ACIDS:

1. A high pKa means the species is predominantly unionised, is a bad proton donor, and a weak acid
2. A low pKa means the species is predominantly ionised, is a good proton donor, and a strong acid

pH < pKa by 2 units, 99% unionised
pH > pKa by 2 units, 99% ionised

For BASES:

1. A high pKa means the species is predominantly ionised, is a good proton acceptor, and a strong base
2. A low pKa means the species is predominantly unionised, is a bad proton acceptor, and a weak base

pH < pKa by 2 units, 99% ionised
pH > pKa by 2 units, 99% unionised

Unionized = mimic lipid → ↑ ABSORPTION ↓EXCRETION

Ionized = mimic water → ↓ABSORPTION ↑EXCRETION

Acidic drugs in basic solution → ↑EXCRETION

Basic drugs in acidic solution → ↑EXCRETION

} ↓ABSORPTION

Acidic drugs in acidic solution → ↓EXCRETION

Basic drugs in basicsolution → ↓EXCRETION

} ↑ABSORPTION

Ionization and lipophility

When the drug become ionized, this will increase its water solubility becease there will be a better solvation by ionic-dipole interaction between ionized drug and water molecule.

So, once the drug get ionized, are more polar.

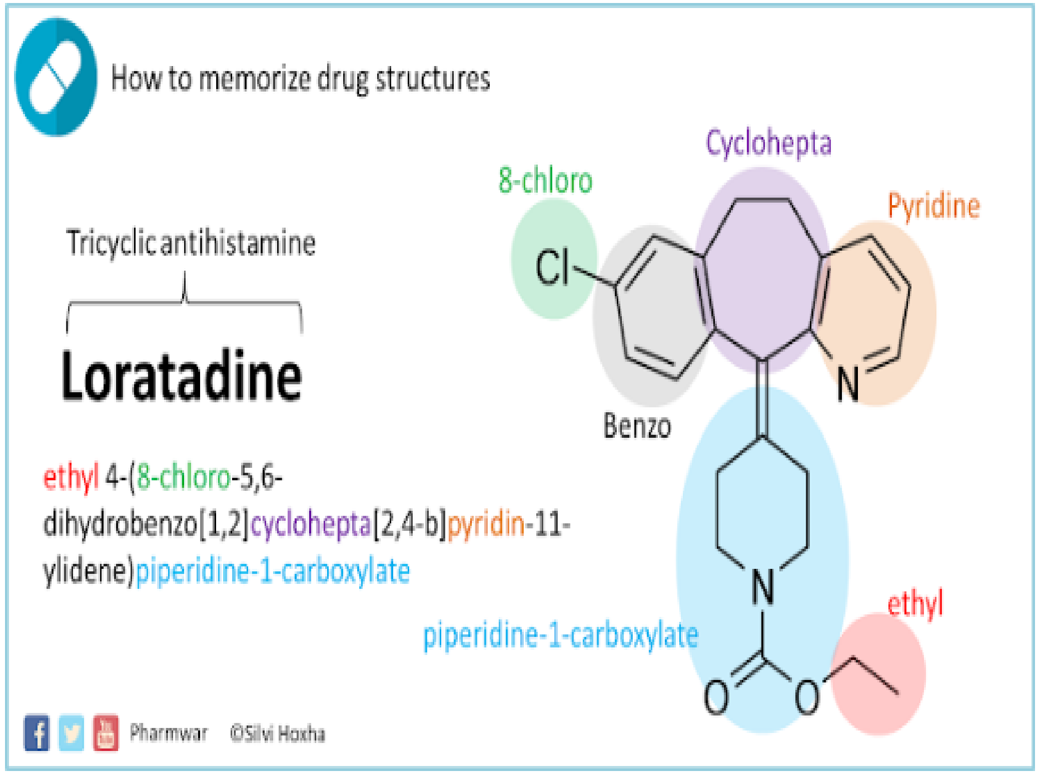
Because most drugs are ionizable at different body pH ranges, the % ionization must be taken into consideration when we are about to synthesize or develop certain drug.

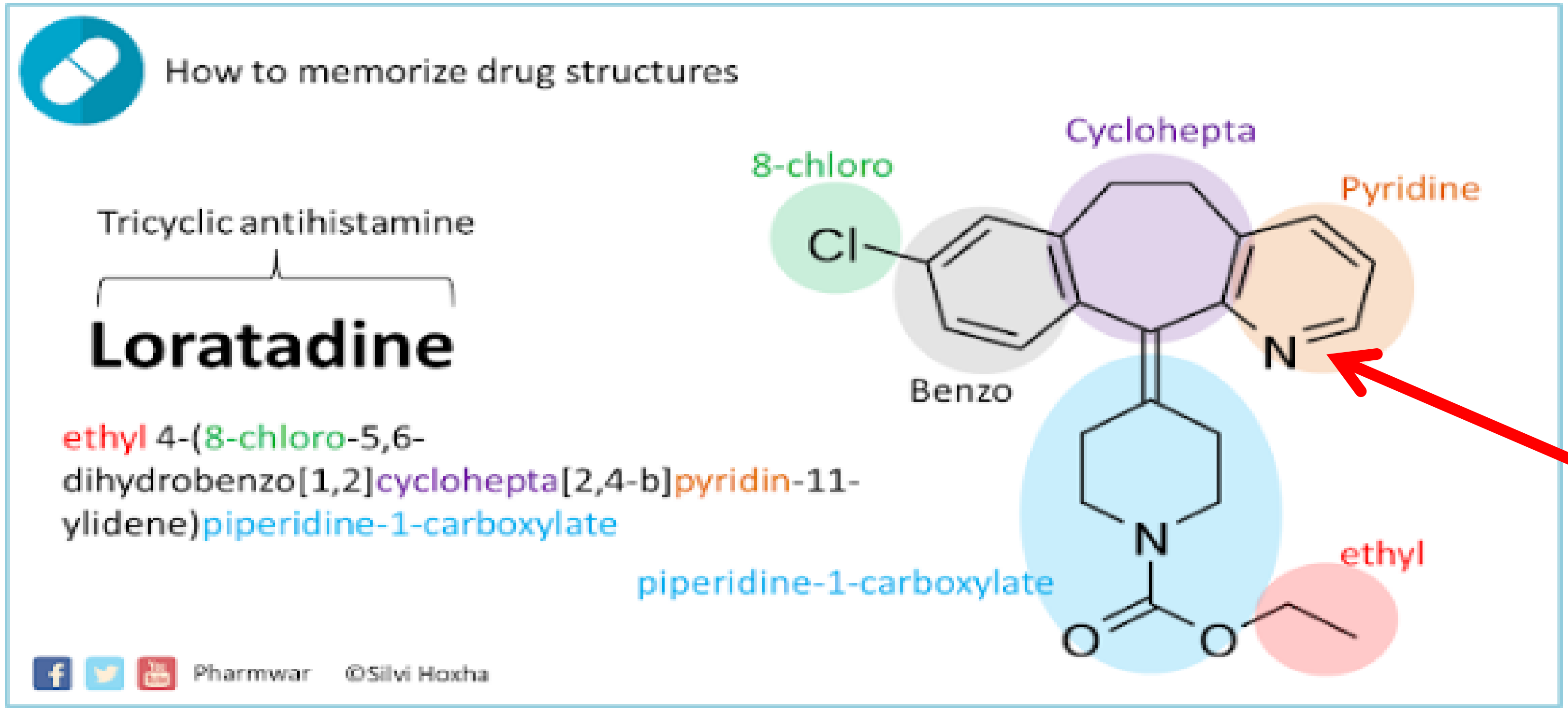
Lipophilicity will determine from where the drug will be absorbed and what tissue will reach.

Practice question

Loratadine is an orally available drug, it has a pKa of 5, answer the followings according to its structure:

- Is it basic, acidic or neutral compound?
- Where do you think loratadine will be absorbed (in stomach ph=2 or in intestine ph=8)





Weak base
pKa=5

In stomach pH=2 so:
pH < pKa
more than 99% ionised

In intestine pH=8 so:
pH > pKa
more than 99% unionised

<u>It will be better absorbed from intestinal membrane not from stomach</u>

FINAL SLIDE

Thank you for your attention

This presentation has been prepared for educational purposes as part of the Medicinal Chemistry course for Students of Faculty Medicine Wroclaw Medicine University.