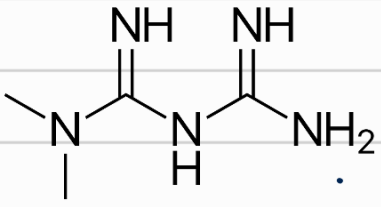
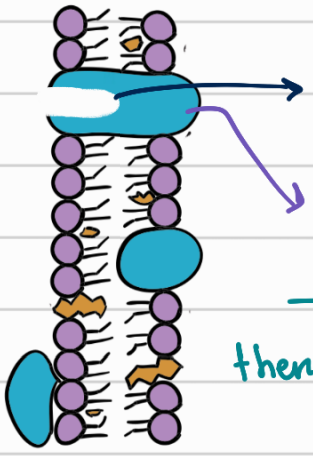
LO3 - How Structure affects the Absorption of Drugs.

week02

* Absorption of metformin is through Complexation w/ mucin → which is a -vely charged protein that transferrs metformin to the blood.



Metformin (+vely Charged through GI)



→ it forms a Complex then enters the blood.

→ This mechanism is called "Ion Complexation"

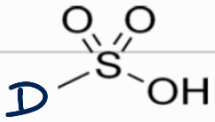
☆ it explains the Absorption of +vely charged compounds.

Functional Groups Categories:-

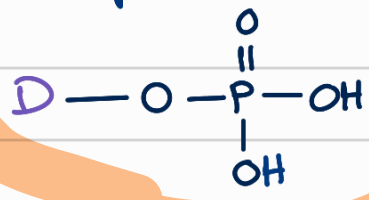
★ Strong acidic groups:-

- strength of the acid is determined by the stability of its Conj base, the more the Conj base is stable, the more the strength of the acid.

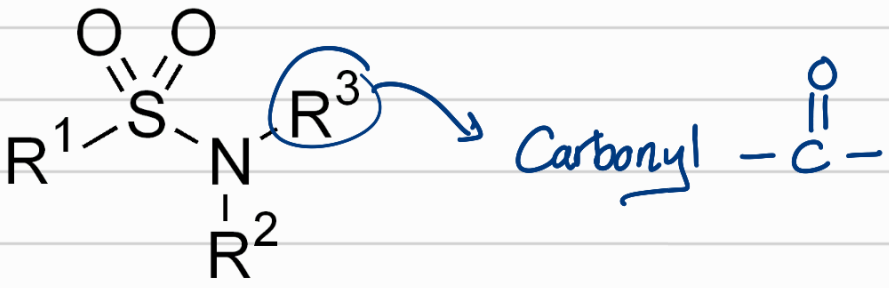
1) Sulfonic Acid



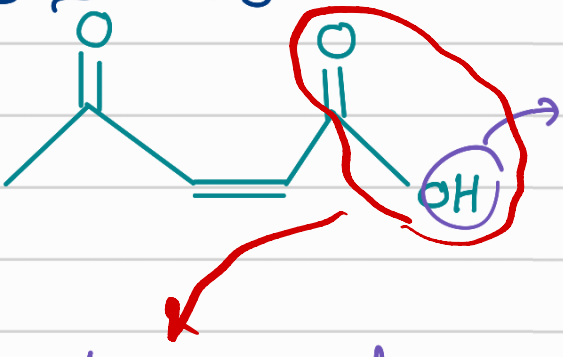
2) Phosphoric acid:



3) Sulfonamide, if one of the R groups is Carbonyl



4) highly Conjugated Systems

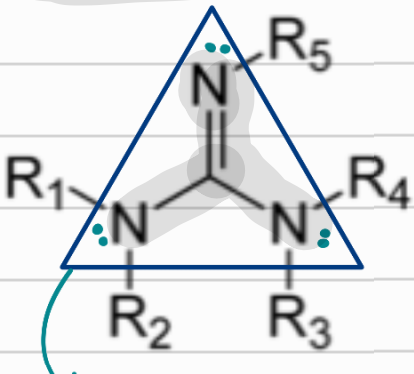


→ Conj. system if H+ is lost

* Carboxylic acid moiety (with no conjugated system, i.e. alone), is Considered moderate acid.
* strong acidic drugs don't get absorbed, thus they're usually given for local GI use.

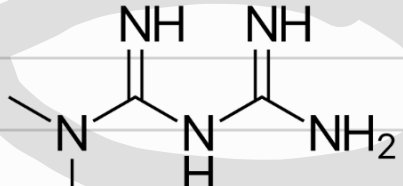
★ Strong Basic Groups:-

1) Guanidine : it's ionized through GI tract (pka > 12) → always ionized
⇒ So absorption is pH independent

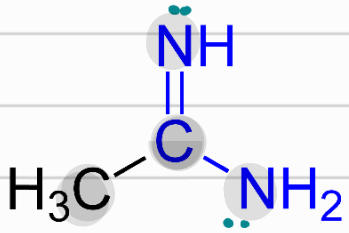


Guanidine

e.g: (drugs Contain Guanidine)
→ Metformin

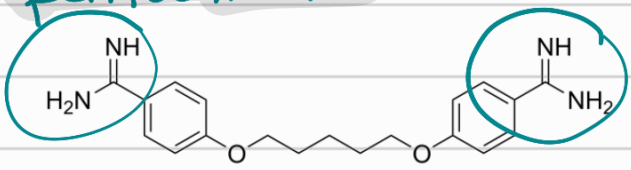


2) Amidine:



e.g: (Drugs Contain Amidine)

pentamidine

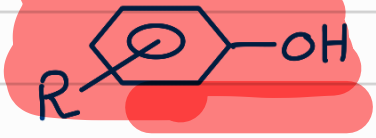


Drug pH	Basic pH independent	Acidic pH independent
Absorption	Could be absorbed	not absorbed
ionization	ionized through GI (pka > 12)	ionized through GI (pka < 2)

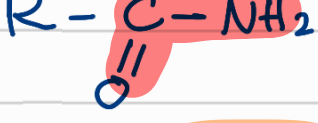
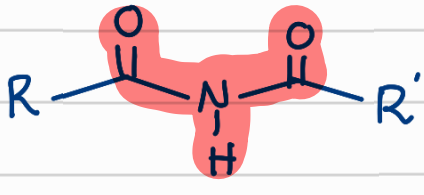
★ Weak Acidic Groups :-

1) Alcohols & phenols :

R-OH

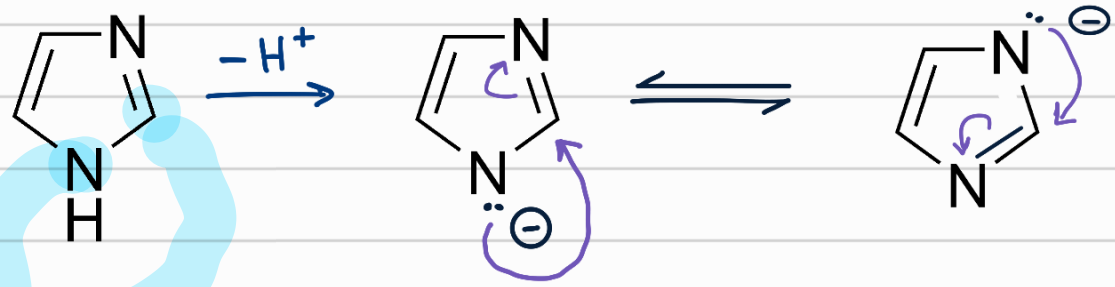


pka > 12, unionized at physiological pH. 7.4

2) Amide  & Imide 

* Imide is stronger than amide, but it's still weak
* Both amide & Imide pka > 10 so they're unionized @ physiological pH

3) Imidazole (can behave as an acid)



* Both N & C are low electronegative atoms, so they don't favor having negative charge.
  * in this situation, the Conj base has low stability, so the acid is very weak.

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e.g: order these acidic compounds according to their strength (1 stands for strongest).

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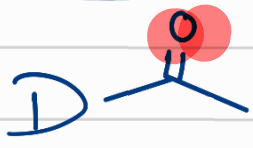


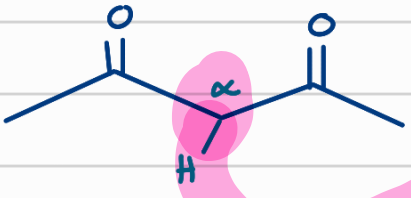
① Most stable conj. base (resonance → charge is distributed between 2 Oxygen).

لأضعف

③ Weakest Acid (least stable Conj. base)

بالوسط

② it is weaker than the carboxylic acid b/c charge is partially held on Nitrogen, which is a low electronegative atom that doesn't favor negative charge.



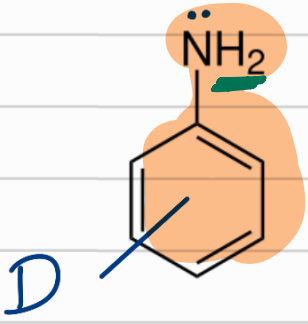
α - carbon is acidic (moderate acid) charge is partially held on the Carbon which is a low electronegative atom that doesn't favor negative charge.

Weak Basic Drugs 8-

1) Amines — D – $\ddot{N}H_2$

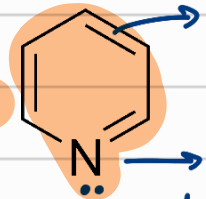
*N is sp3 hybridized, so the lone pair are available for Donation.

2) Anilline



→ here electrons are busy w/ resonance, so the lone pair are less available → weaker base

3) Pyridine

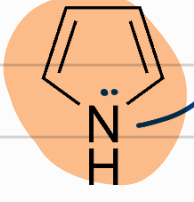


→ pi bond are perpendicular to the plane (in y-axis)

→ sp2 hybridized

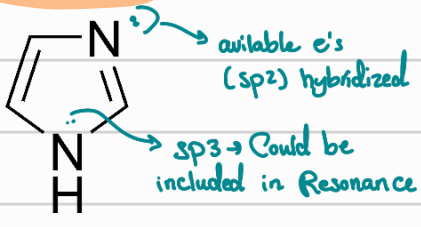
↳ Whereas this lone pair is out of the plane so it's available for resonance (in x-axis)

4) Pyrrole



Nitrogen is sp3 hybridized, so they're included in the resonance → weaker than pyridine

5) Imidazole



*stronger than pyrrole but weaker than pyridine