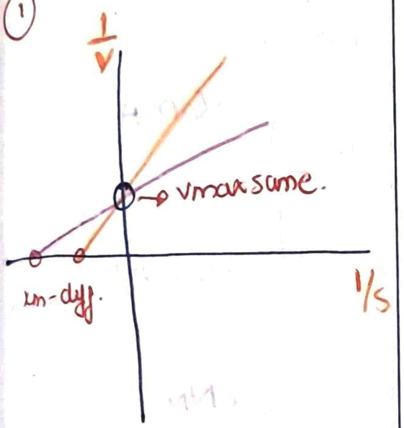
Line-weaver Burke plot

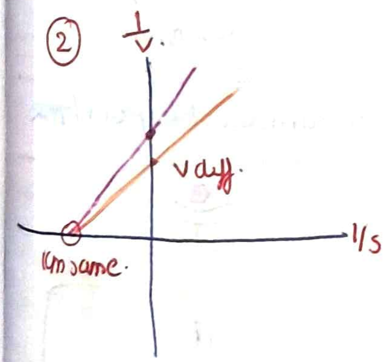
aka Double reciprocal plot

①



⇒ Competative

②



⇒ Non competative.

Short cut

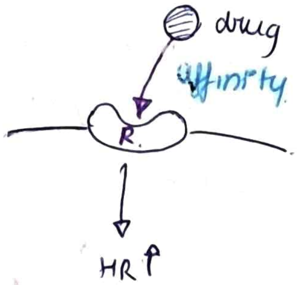
If meeting on 1/V

→ competative.

• If meeting on 1/S.

→ Non competative.

Receptors



receptor – is something that is used to receive drug.

affinity → ability of drug to bind to receptors.

Intrinsic activity → ability of drug to produce action after binding to receptors

• affinity is must for every drug to bind to receptors.

• but their intrinsic activity are different

• Based on Intrinsic activity

Drugs are →

① Agonist

② partial agonist.

③ Inverse agonist.

④ Antagonist

They all have high affinity

★★★ Impt★

NOTE: If low affinity is written in MCQ, it will never be the answer.

Agonist → maximum intrinsic activity, – max stimulation

simply → receptors normal work.

eg. Icon pattern, with agonist max efficacy (↑HR)

partial agonist → Submaximum intrinsic activity.

It stimulates ✓ but not to max capacity (↑HR)

Inverse agonist →

→ negative / opposite intrinsic activity

(↓HR)

Antagonist → It produces No action

↓

neither stimulate / decreases.

⇒ It's function is just blocking

⇒ It just hinders others action

⇒ It doesn't do it's own action ✗

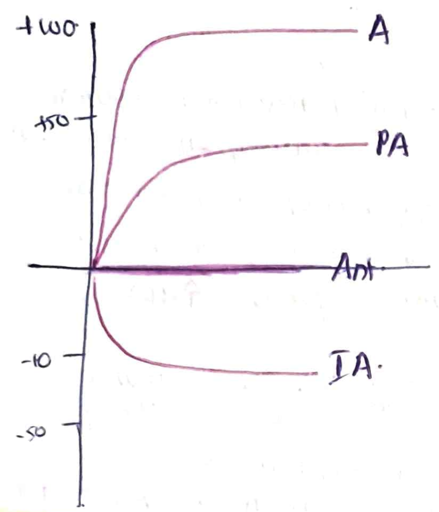
• agonist → high affinity ✓ max action ✓.

• partial agonist → high affinity ✓ → submax action.

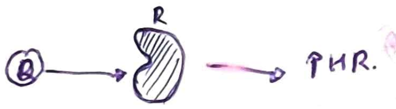
• inverse agonist → high affinity ✓ opposite action (–ve) action.

• antagonist → high affinity ✓ no action.

GRAPH



Receptors (?)



- when drug binds to R, a signal is produced.
- which turned into action → tachycardia
- signal is converted to action.

"Signal transduction" mechanism

- Drug does not tell Receptors WHAT to do!
- receptors where always present, so they already have a way of working.
- dyy drugs just tell them നിനക്ക് കാര്യം വെച്ചു, but ഒറ്റി വെച്ചു, ഇങ്ങനെ cheyy, like that!

Receptors → "WHAT" to do.

Drug → How much to do the "WHAT".

Thats, why, we classified drugs & receptors Based on.

- drugs → Intrinsic activity
- receptors → Signal transduction mechanism.

Receptors based on.

- → Inotropic
- → Enzymatic
- → GPCR.

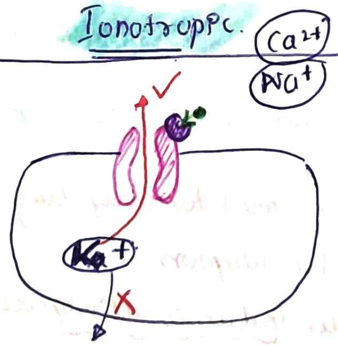
- Since the action is quick, they are seen in impt areas where quick action is needed?
  - → CNS
  - → Nerves.

CNS
- → GABA
- → glutamate
  - → NMDA
  - → AMPA

Nerves
- → N_N
- → N_M

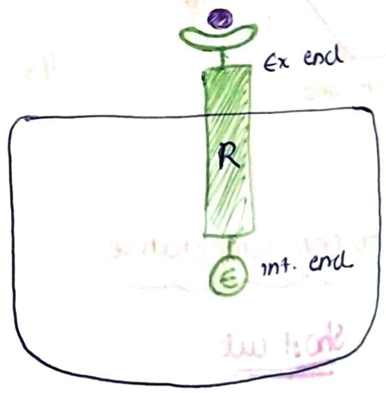
$5HT_3$ → 3rd receptors of Serotonin

Ionotropic



- Since ions are polar, they cannot diffuse directly through membrane
- they can only cross through ion channels.
- If receptor is associated with such ion channels → it is called Ionotropic receptor.
- Binding of Drug to (IR) quickly opens ion channel.
- Fastest acting receptor!

Enzymatic Receptors / ~~ER~~



It has 2 ends
- Extracellular end → drug binds
- Intracellular end → Enzyme.

- Enzyme → most cases → tyrosine kinase.

AKA → tyrosine kinase receptor. TKR.

(others, also ok?)

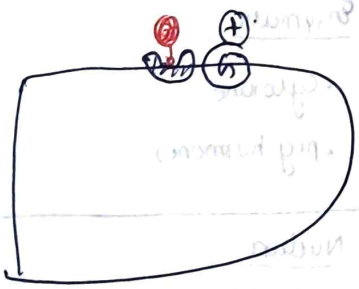
Use : Drug, even without entering inside cell, can produce action inside, by the Enzyme.

Who all act by Enzymatic Receptors?

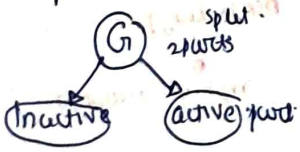
① all cytokines → IL, TNF α, IFN

② Hormones
- P – prolactin
- I – Insulin
- Gr – growth hormone

GPCR
AKA
- Heptahelical
- Serpentine receptors
- Metabotropic receptor. Controls metabolism.

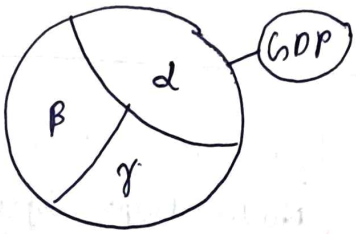


- drug binds to receptor.
- receptor activates G protein.
- G splits into 2 parts.



G-protein

=) GDP/GTP binding part.



- GDP → joins all 3 parts.
- Drug → receptor → GDP → GTP.

* α-GTP → does work by 3 way.
* β γ × no function

① Adenylate cyclase.

α-GTP → will activate adenylate cyclase.

ATP → cAMP.

cAMP – different actions in different organs.
- Heart - stimulate
- most others → Inhibition.

i.e, stimulate β_1.

cAMP ↑

heart rate ↑

adrenaline but β_2.

cAMP ↑

Bronchodilation.

② Ca^{2+}.

PIP_2 – membrane protein

IP_3 + DAG.

Ca^{2+} ↑

adrenaline.

α receptor.

α-GTP.

Enzyme ①

PIP_2 → PI_3

Ca^{2+}

vasoconstriction

BP ↑

③ Ion channels

- α-GTP

open ion channels.

GPCRs work by either:

- ↑ cAMP
- ↑ Ca^{2+}
- Open ion channels.

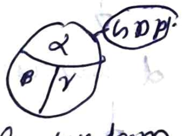
Gs → stimulate Adenyl cy → ↑ cAMP.

Gi → ⊖ AC = ↓ cAMP.

Gq → PIP_2 → IP_3 + DAG
↑ Ca^{2+}

GTPase enzyme present in α component — GTP → GDP.

α + GDP →



Inactive form.

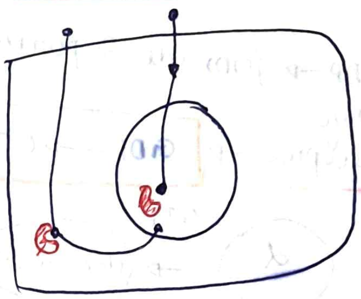
~~Impt points to remember.~~

- Drug binds to Receptor ✓ not to G protein
- Stabilizing is GDP not GTP.
- GDP is on α.
- Active Component - α.
  - Gs — ↑ cAMP
  - Gi — ↓ cAMP.
  - Gq — ↑ Ca^{2+}

Examples

- lot of drugs act through GPCRs

Intracellular Receptors/
Nuclear Receptor Superfamily



- cytoplasmic / nuclear receptors
- only lipid soluble drugs can act on Intracellular receptors.
- Both cytoplasmic as well as nuclear receptor forms, and then ultimately binds to DNA →
- nuclear receptor & Nuclear receptor super family are not the same thing, ✗

cytoplasmic

- Corticosteroids (C D)
- Vit D.

Nuclear receptor

sex

- Vit A (S A T)
- T_3, T_4

(watch DOON Saturday)

Vit D receptor
↓
not nuclear receptor ✗
is nuclear receptor superfamily ✓

Which drug act via nuclear receptor?

- Aldosterone] cytoplasmic
- Vit D]
- Thyroxine ✓
- All of these. ✗

But all act via Nuclear mechanism

~~Nucleotide~~ I

IDO

CNS → GABA
glutamate NMDA. AMPA

- Nm NN
- $5HT_3$

Enzymatic

- cytokine
- pig hormones.

Nuclear.
SAT CD

remaining: GPCR

Benzodiazepine
↓
Orphan receptor.

Pharmacodynamics.

- what drug does to body.

PD
- action of drug
- mechanism of action of drug.

- Mechanism of action of Drugs.

① physical: just physical presence is enough eg: charcoal in OP poisoning.

② Chemical → drug act by simple chemical reactions
eg: antacids → neutralize by binding.
protamine in heparin overdose.

③ Enzymes (basic) (acid) → most drugs act by inhibiting. Enzymes catalyzing reactions.

④ receptors → bind to receptors. next chapter.

Enzyme Inhibitors.

- most of drugs are Enzyme Inhibitors.
- why not stimulators?
  cause Enzymes are already working at maximal capacity.
  - It's difficult to ↑ working.
  - can easily inhibit Enzyme, though

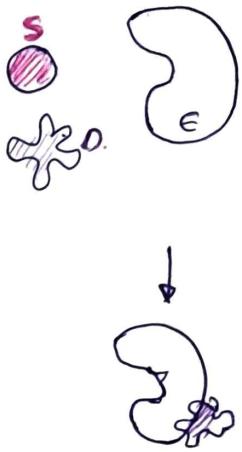
Enzyme Inhibitors
- Competitive
- Non-competitive

Competitive Inhibition.

- Drug & substrate have similar structure. / so they compete with each other for binding to active site.
- binding of drug can be reversed by ↑ substrate concentration.
  ↓
  Surmountability.

Competitive Inhibition.
- ✱ same structure.
- ✱ sam site.
- ✱ Surmountability

Non-Competitive Inhibition.



- diff structure
- binds to allosteric site.
  ↓
  Induce change in activesite
  ↓
  Substrate can't bind.
- permanent / unsurmountable.

Non-Competative
- ✱ different str.
- ✱ diff site (allosteric)
- ✱ unsurmountable.

	Comp	Non-comp.	
Km	↑ ↑	no change.	Km - S con to get half vmax how ↓↓ much S needed so that ½ of enzyme does work ↓↓ ½ Vmax.
Vmax.	no change.	↓ ↓	• Vmax - maxno. of enzymes