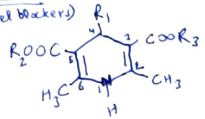
SAR of Anti-Anginal Agents

SAR of Dihydropyridines:

(Calcium channel blockers)



- 1,4-dihydropyridine skeleton
  - A secondary nitrogen in dihydropyridine ring
  - An aromatic or heteroaromatic C_4-substituent

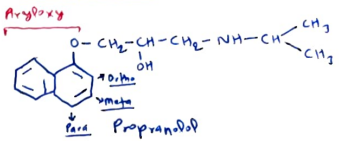
→ Essential for activity

- Substitution at 'N' or oxidation or reduction of ring → ↓se activity
- Phenyl substitution at 4th position → Optimum activity
- Substituted Phenyl activity → Ortho > Meta > Para
  - Unsubstituted Phenyl → ↓sed activity
- Ester group at 3rd & 5th position → Optimizer activity
- Steric hindrance in ortho position → required to fix the dihydropyridine in favourable condition/conformation.
- When Ester at C_3 & C_5 are nonidentical → C_4 become chiral & Stereoselectivity is observed.
  - S-enantiomers found to be more effective

SAR of Nitrate:

- The number of nitrate groups determines the Potency of organic nitrates for Guanylate cyclase activation
- ↑se nitric group → ↑ses potency
- ↑se lipophillicity → No major effect over activation of drug.

SAR of β-blocker:



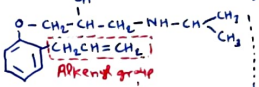
Propranolol

- Substitution (modification) is possible on –
  1. Aromatic ring (Phenyl ring)
  2. Carbon chain
  3. Amino chain

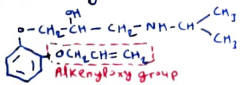
1- Aromatic ring: * Most derivatives have substituted "Phenyl ring" in the place of "Naphthyl ring"

* At ortho position
  - Alkenyl group
  - Alkenyloxy group

→ ↑se activity



Alprenolol



Oxprenolol

is

A hydrocarbon group formed when a hydrogen atom is removed from an alkene group

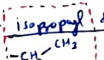
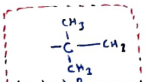
* Addition of –OH group in phenyl ring → ↓se activity
* Naphthyl /or Substituted Naphthyl → Non selective (eg: Propranolol)

Phenyl ring → selective (eg: Atenolol, Betaxolol, Bisoprolol, Metoprolol, Esmolol etc.)

2- Carbon chain:

* $-OCH_2$ group b/w Aromatic ring & Ethanolamine side chain → K/a Aryloxy propanolamines → ↑ses the activity
* 'H' in the place of '$-OCH_2$' → K/a Arylethanolamines → Non selective

3- Amino group:

* If isopropyl () & t-butyl group () present on amino group
  - Provides nucleophilicity to the Amino group
  - ↑ses the binding affinity with receptor
  - ↑ses the activity (eg: Atenolol, Timolol)