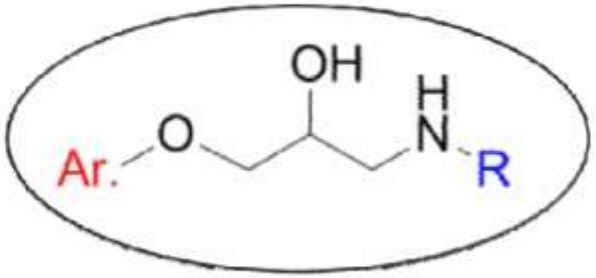
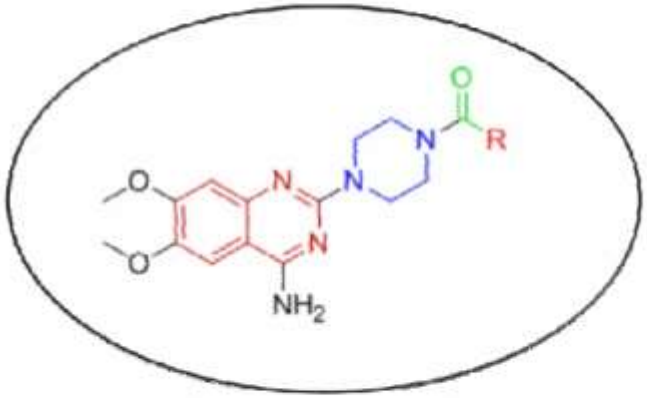


SympathoLytics



Amit Z Chaudhari

INTRO

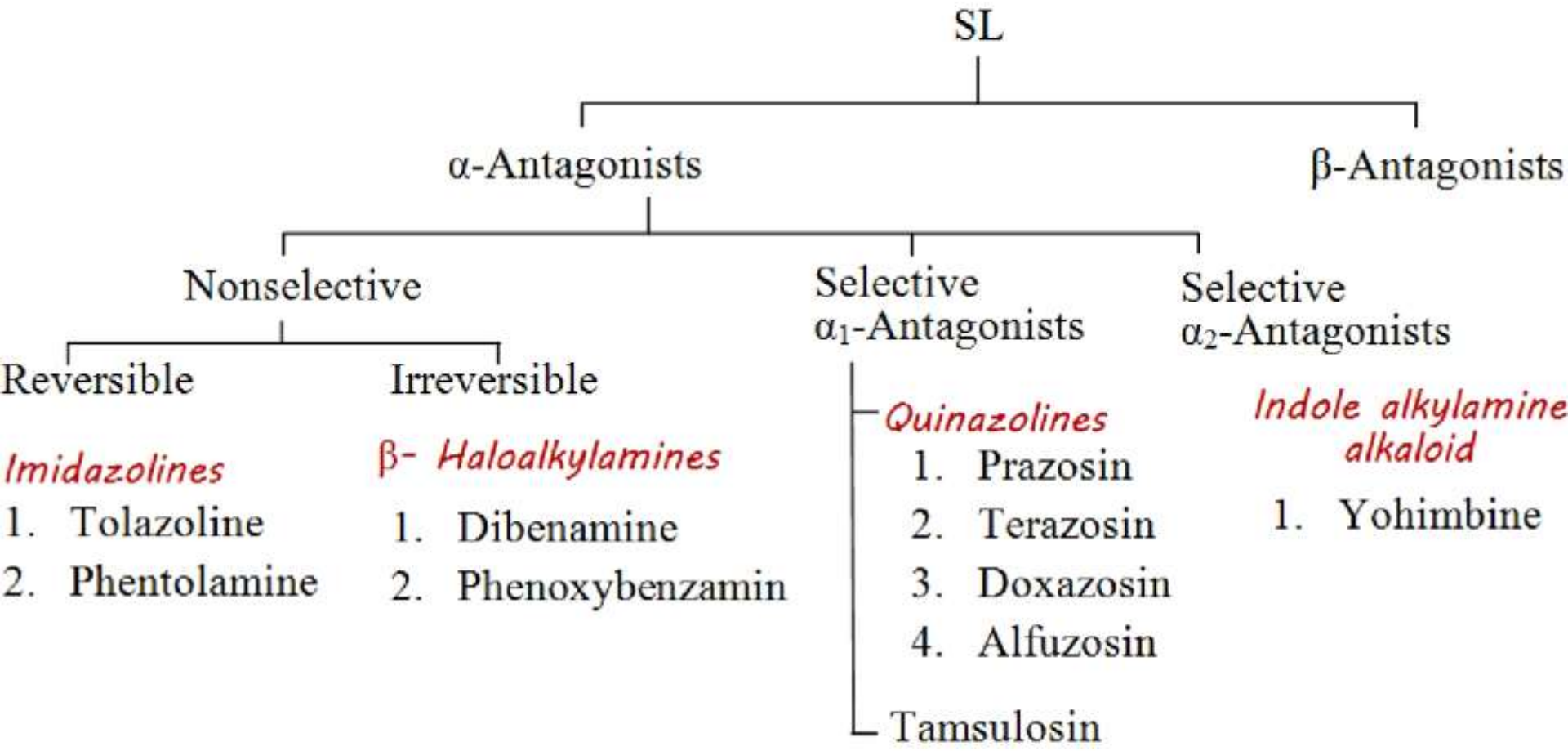
Defination:

- Compounds that that decrease sympathetic activity
- that blocks the interaction of Norepinephrine (and other Adr. agonist) with receptor

Synonym: *antiadrenergics , adrenergic-blocking agents ,*

or adrenergic-blockers

CLASSIFICATION



CLASSIFICATION

β-Antagonists

Nonselective
(First Generation)

1. Propranolol
2. *Nadolol*
3. *Pindolol*
4. *Penbutolol*
5. *Carteolol*
6. *Timolol*
7. *Levobunolol*
8. *Sotalol*
9. *Metipranolol*

Selective β_1-Antagonists
(Second Generation)
(Cardioselective β-blockers)

1. Acebutolol
2. Atenolol
3. Betaxolol
4. Bisoprolol
5. Esmolol
6. Metoprolol

Mixed α/β-antagonist
(Third Generation)

1. Labetalol
2. Carvedilol

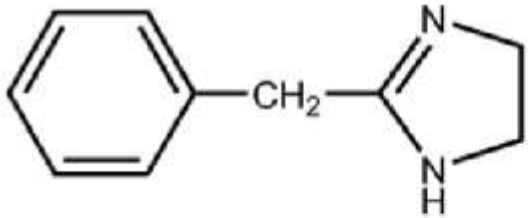
α-Antagonists

Imidazolines

- Similar to the imidazoline α_1-agonists, but does not have the lipophilic substituents required for agonist activity.
- $\alpha_1 > \alpha_2$-blocking activity

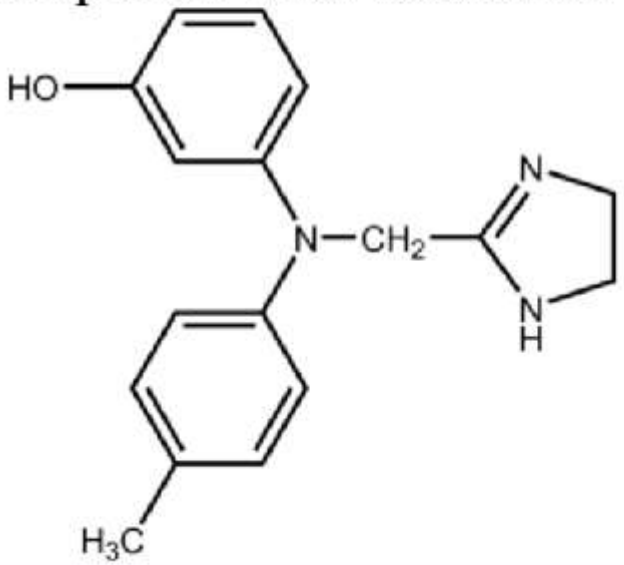
Use: treating the symptoms of pheochromocytoma

(1) Tolazoline



(2) phentolamine

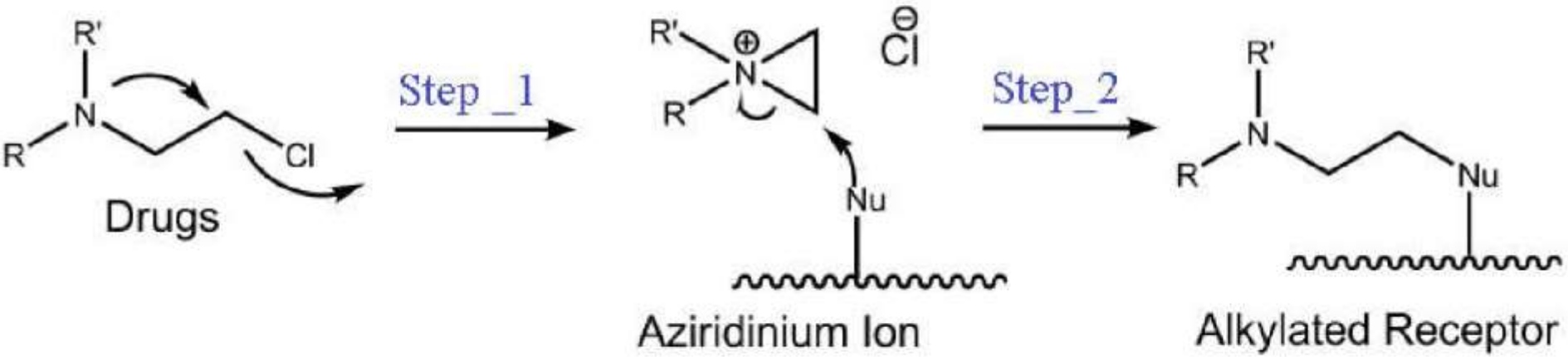
- More potent than Tolazoline



β- Haloalkylamines

M/A

- Step _1: the formation of an intermediate aziridinium ion (ethylene iminium ion)
- Step_2: The positively charged aziridinium ion electrophile then reacts with a nucleophilic group on the α –receptor



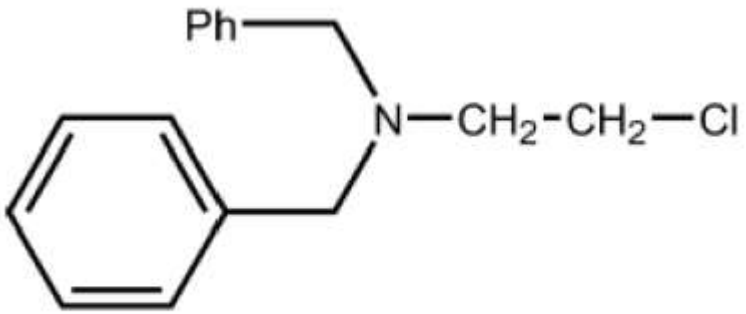
β- Haloalkylamines

- nonselective drugs alkylate not only α –receptor but also other biomolecules leading to their toxicity.
- Long DOA , single dose of drug may last 3 to 4 days

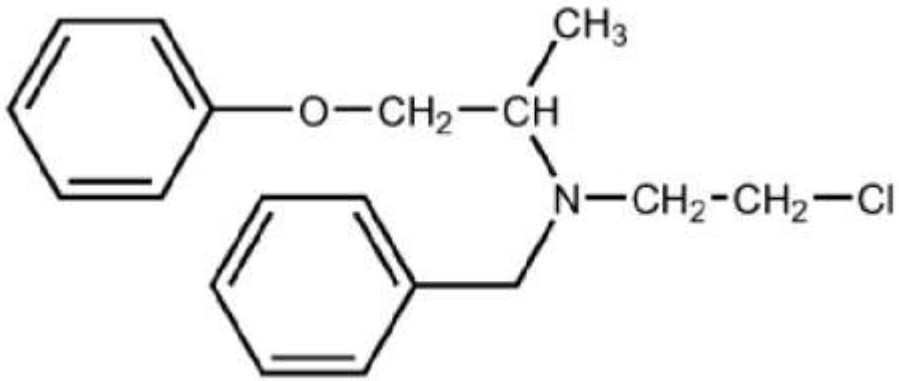
Use : limited use ,
in pheochromocytoma

(1) Dibenamine

- Not used currently

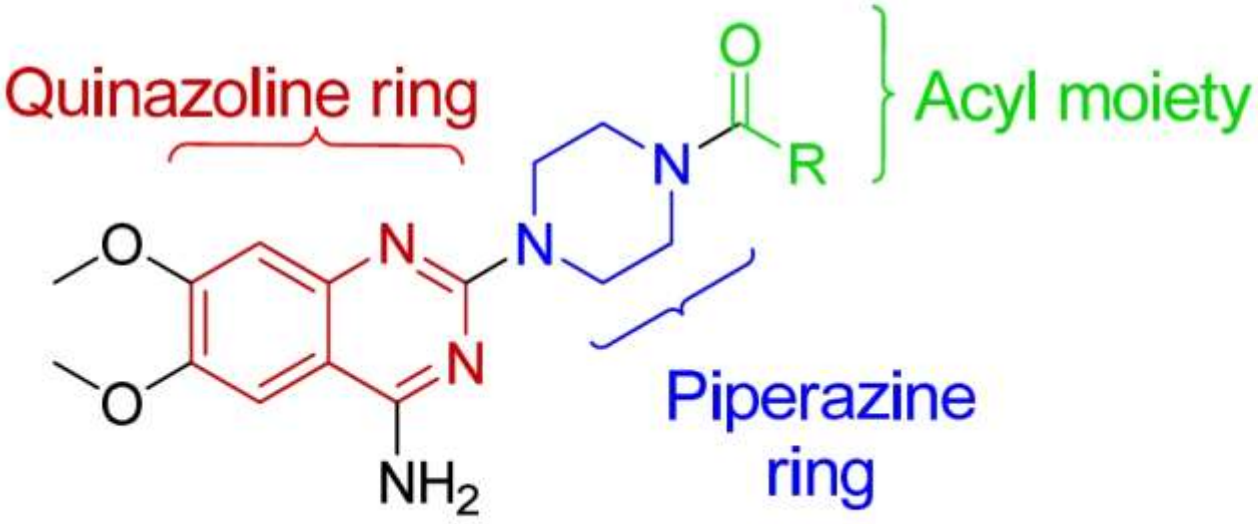


(2) Phenoxybenzamine



Quinazoline

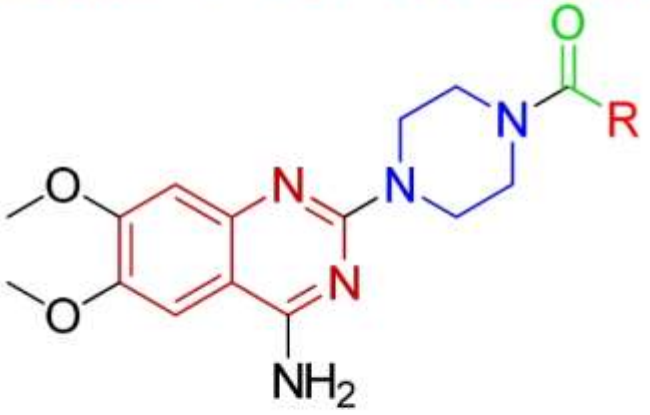
- Selective α_1-Antagonists
- Structurally, these agents consist of three components:
- the quinazolines ring, → 4-amino group important for α_1-receptor affinity
- The piperazine ring
- the acyl moiety → effect on the pharmacokinetic properties



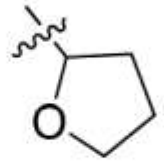
α-Antagonists

Quinazoline

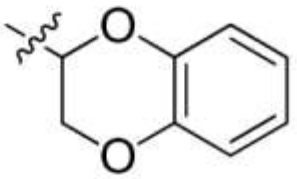
(1) Prazosin , (2) Terazosin , (3) doxazosin



Prazosin :



Terazosin :



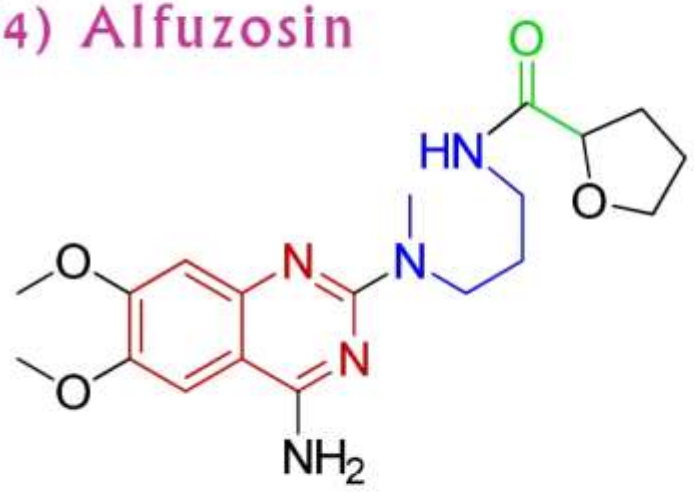
Doxazosin :

- Action : dilate both arterioles and veins (without ↑ heart rate) and are thus Use : in the treatment of hypertension.
- α_{1A}-Antagonism → relaxes the prostatic and urethral smooth muscle → treatment of BPH (benign prostatic hyperplasia)

α-Antagonists

Quinazoline

(4) Alfuzosin



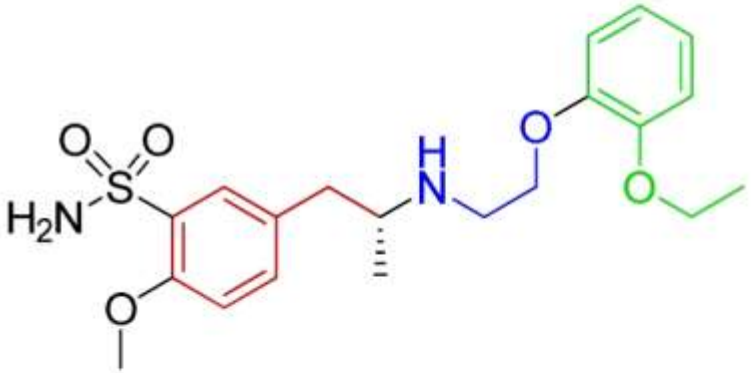
Open piperazine ring analogue of Quinazoline

more selective for the subtype of α_{1A} - receptor

- Action : α_{1A}-Antagonism → relaxes the prostatic and urethral smooth muscle → treatment of BPH (benign prostatic hyperplasia)
- first-line drug for BPH with fewer cardiovascular side effects

α-Antagonists

(5) Tamsulosin

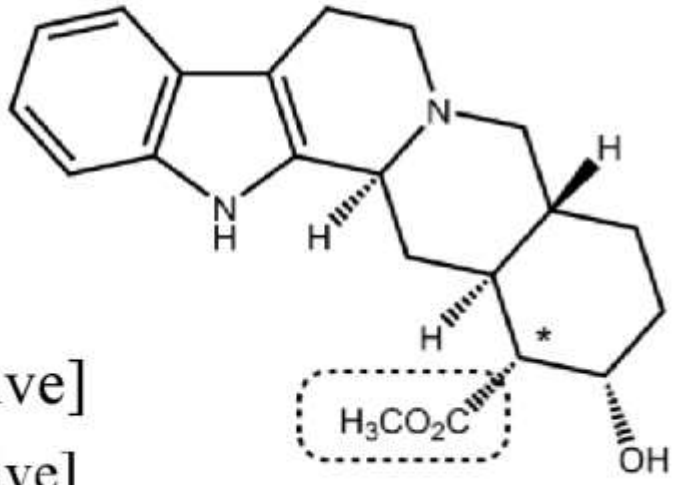


Nonquinazoline benzensulfonamide

- Action: most selective α_{1A}-Antagonist→ treatment of BPH
- first-line drug for BPH with little cardiovascular side effects

Indole alkylamine alkaloid

Yohimbine



- B.S. = *Pausinystalia yohimbe* and in *Rauwolfia root*
- Structure resembles that of reserpine.

(19 *R*) isomer = Yohimbine [α_2 selective]

(19 *S*) isomer = Corynanthine [α_1 selective]

- Action: blockade of α_2-receptors in the CNS → increases heart rate and blood pressure
- used to increase peripheral b.p.. It is also used to dilate the pupil of the eye