

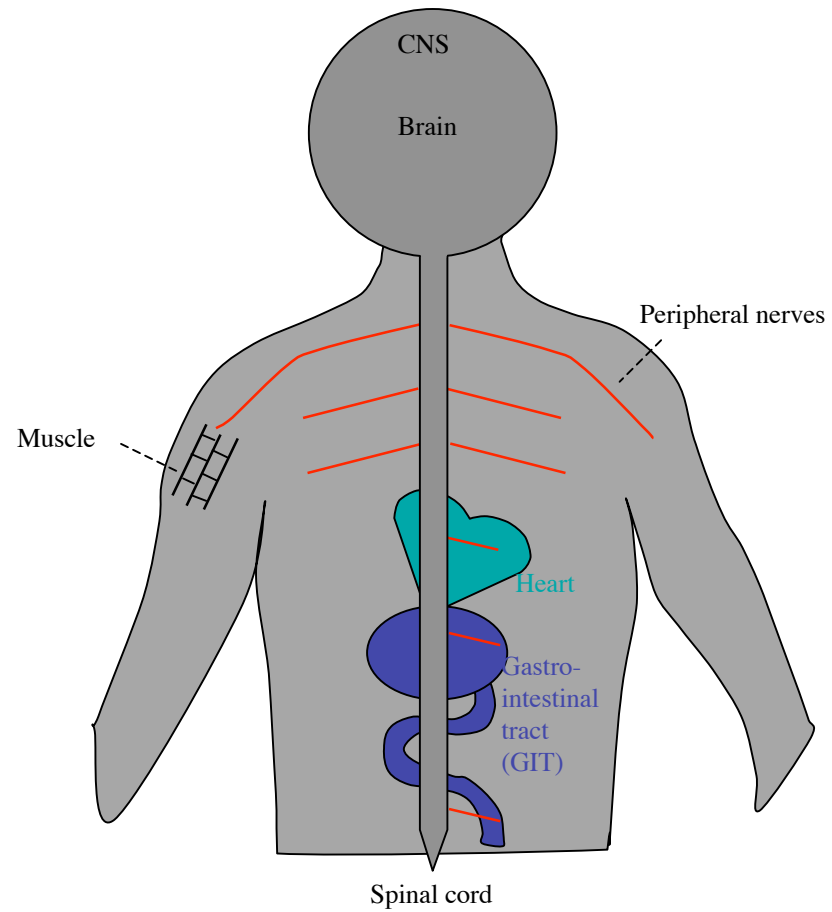
Topic 10-2 Drugs of the Nervous System-Adrenergic

Ch 19,20 Patrick

Part VI- Nervous system -Corey

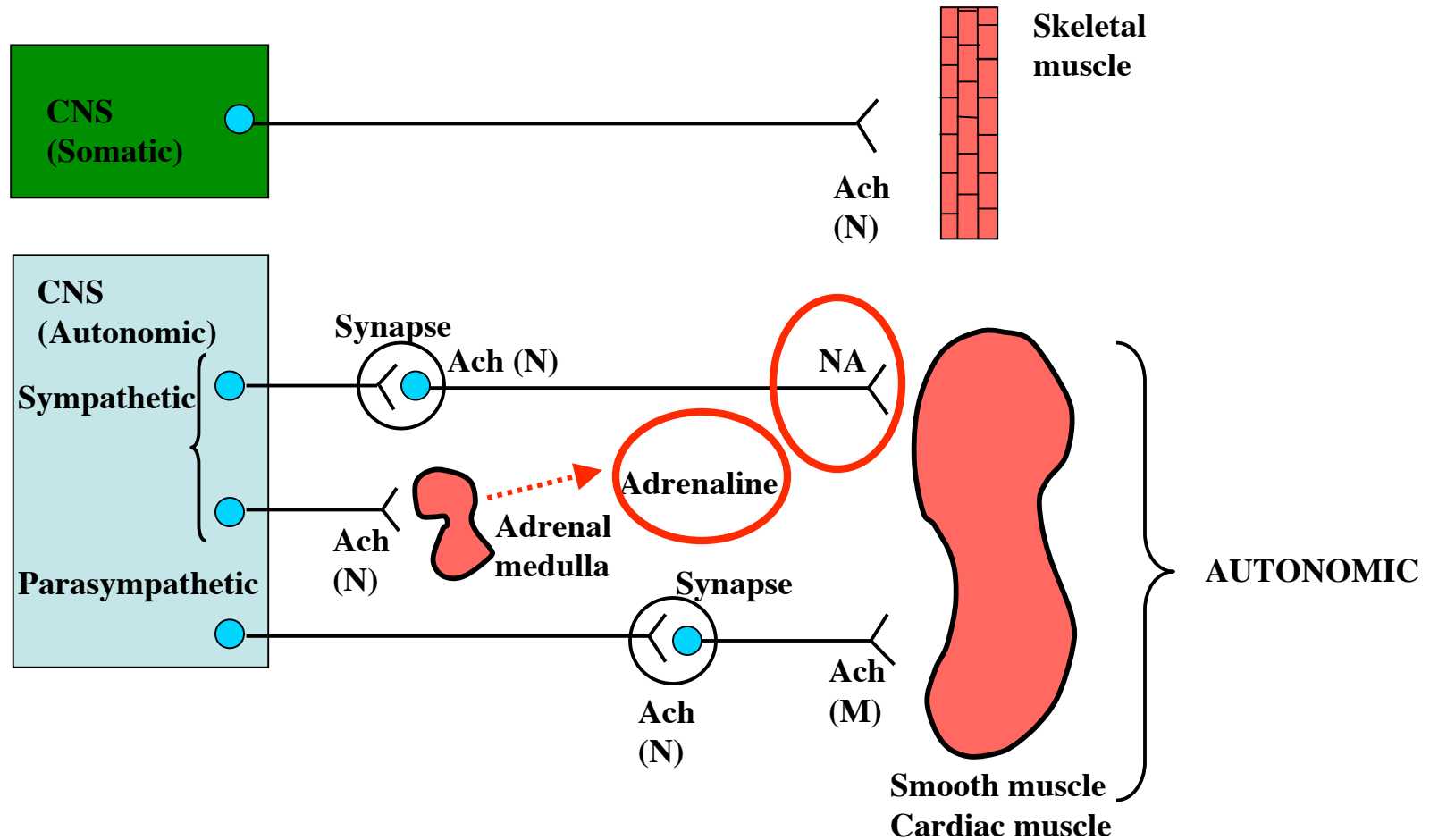
1. Nerve Transmission

Peripheral nervous system

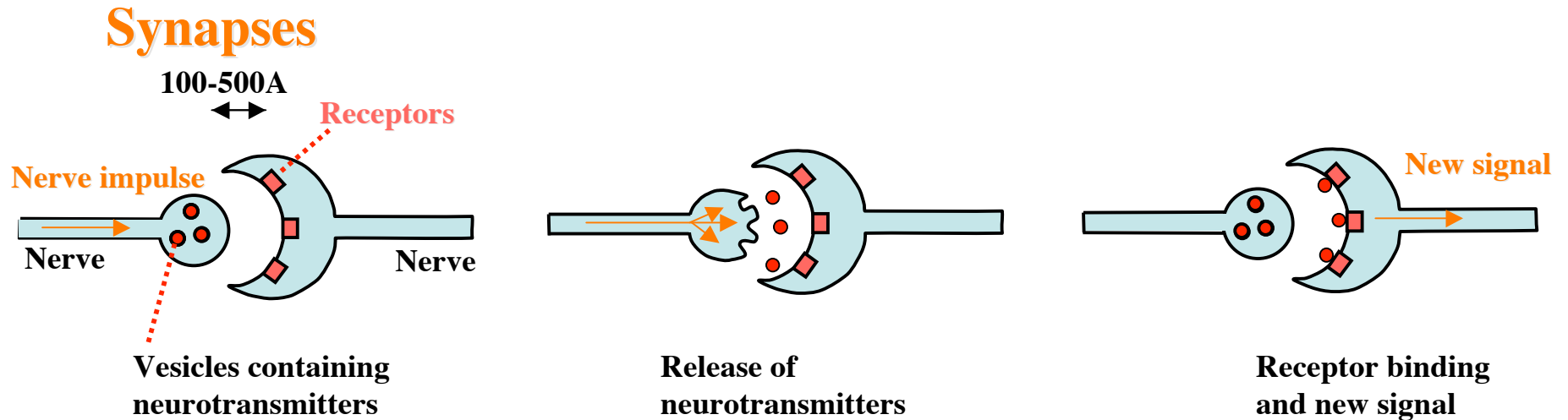


1. Nerve Transmission

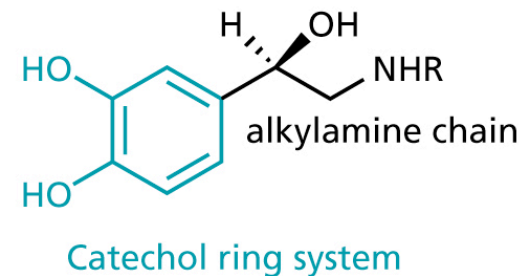
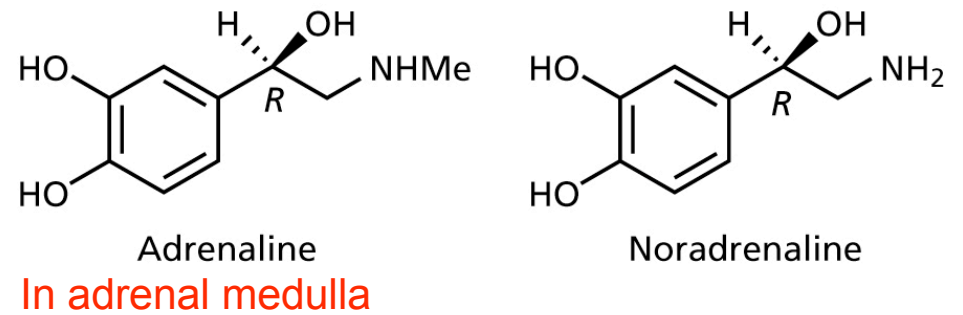
Peripheral nervous system



1. Nerve Transmission



Adrenergic endogenous agonists: catechols



1. Nerve Transmission

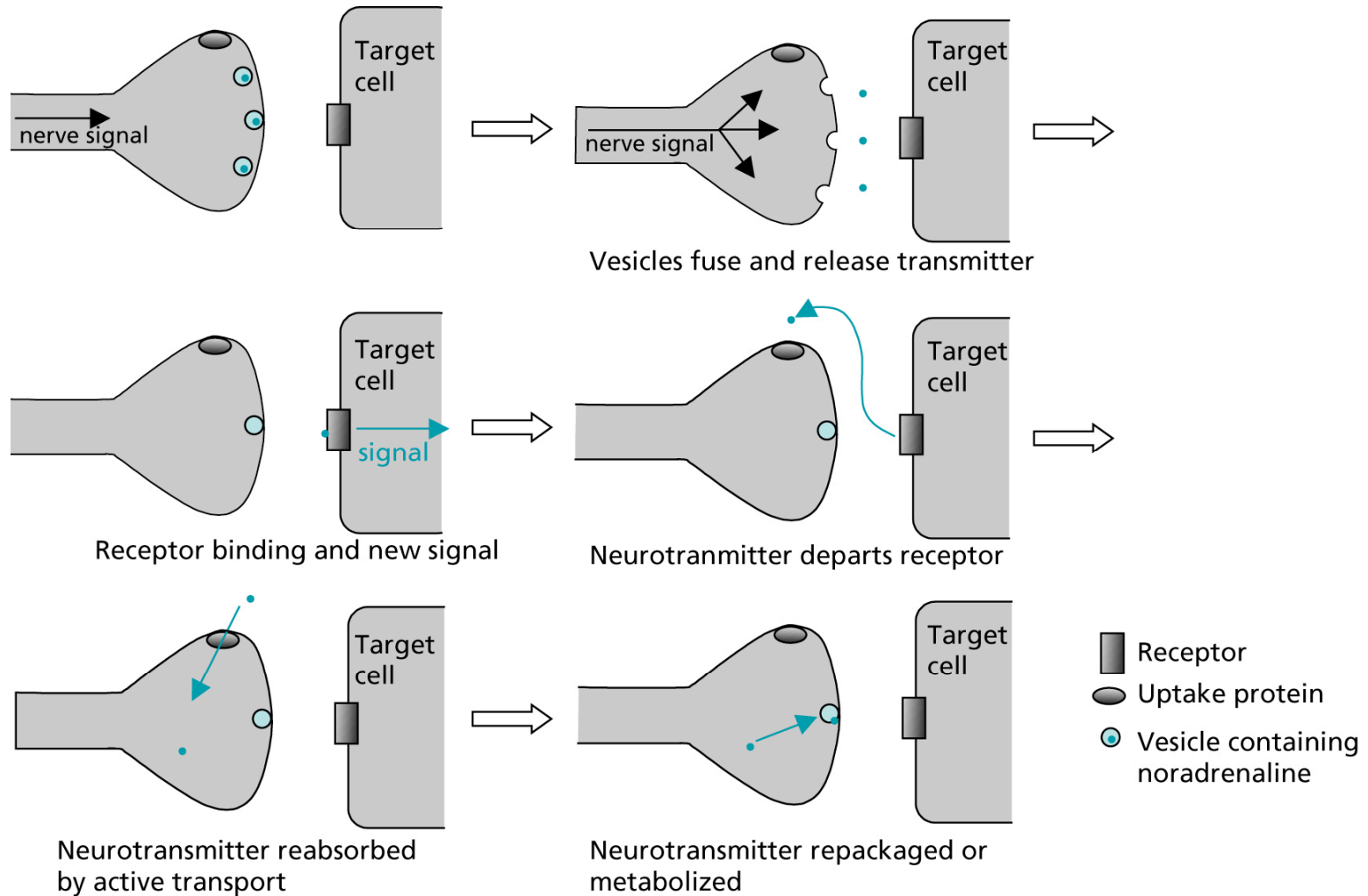
α and β adrenergic G-protein receptors-
many overlapping functions

In *General*:

- β adrenergic receptors
 - Relax smooth muscle (except heart muscle)
 - β 1 blockers slow heart muscle contraction, lowers BP
- α adrenergic receptors
 - Contract smooth muscle(except gut)
 - α 1 agonists -used for vasoconstriction in local anesthesia, α 2 for glaucoma
 - α 1 antagonists relax smooth muscle for hypertension and angina

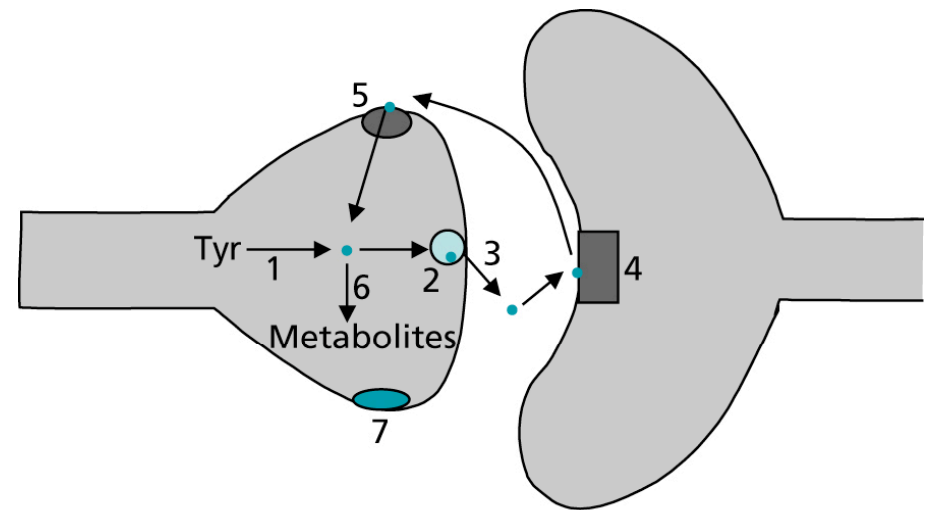
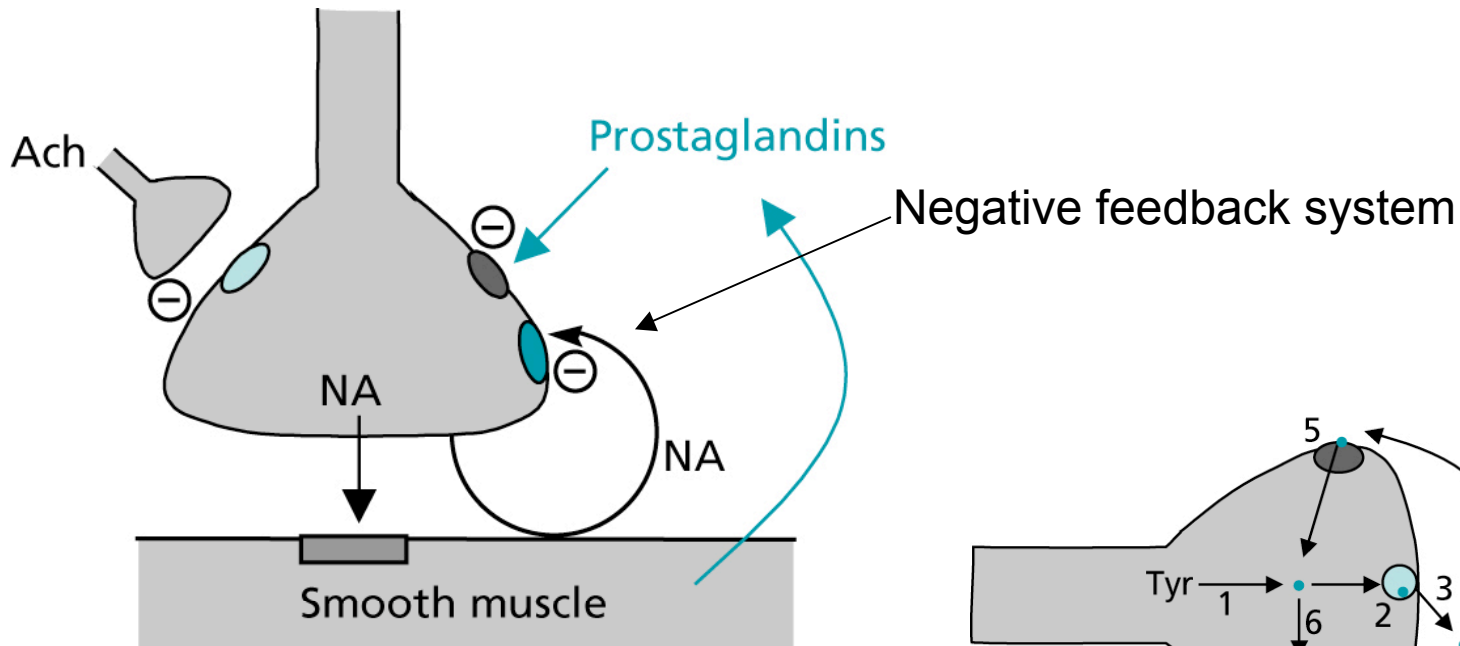
1. Nerve Transmission






α and β adrenergic G-protein receptors-







1. Nerve Transmission

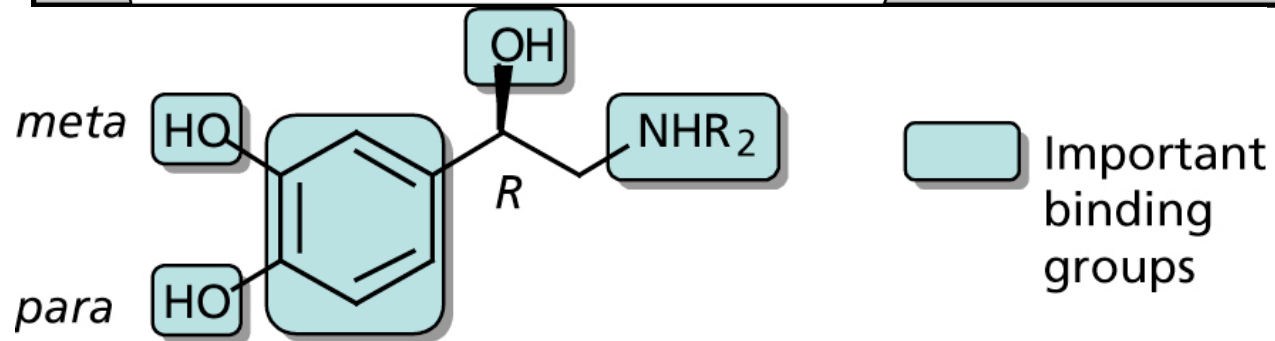
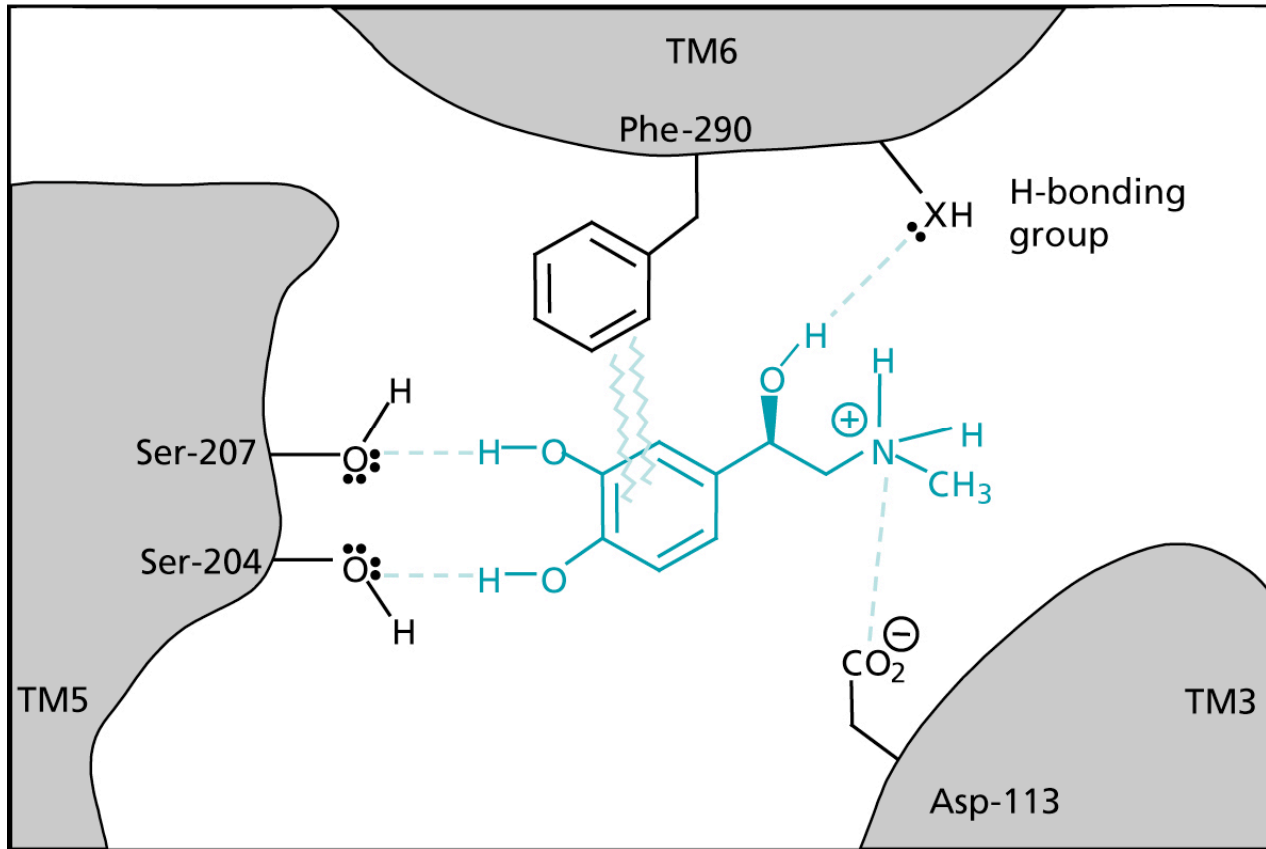
Noradrenalin (norepinephrine) system drug targets



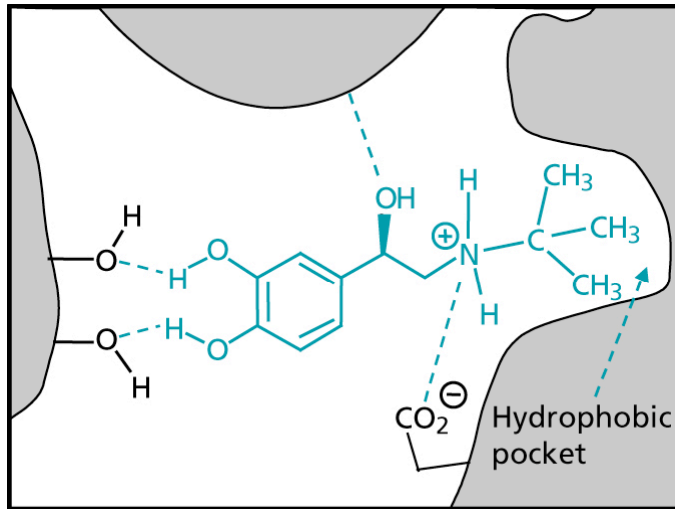
-  Cholinergic receptor
-  Presynaptic adrenergic receptor
-  Prostaglandin receptor
-  Postsynaptic adrenergic receptor
-  ⊖ Activation of receptor reduces noradrenaline release
- NA Noradrenaline

-  Noradrenaline
-  Carrier protein
-  Adrenergic receptor
-  Presynaptic receptor

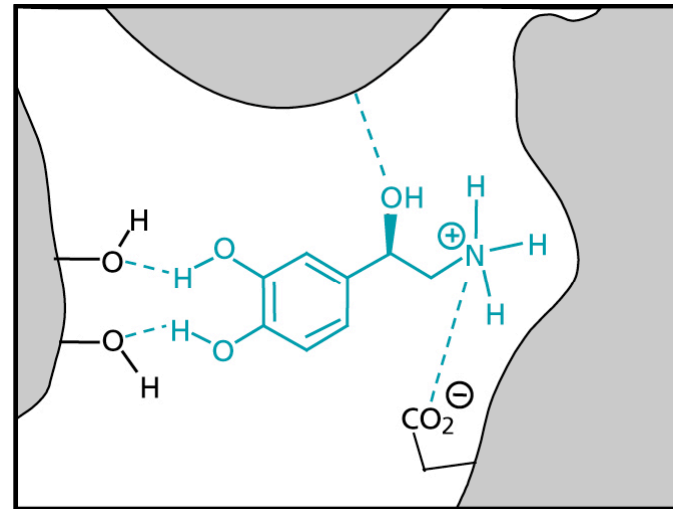
Adrenergic Binding Site



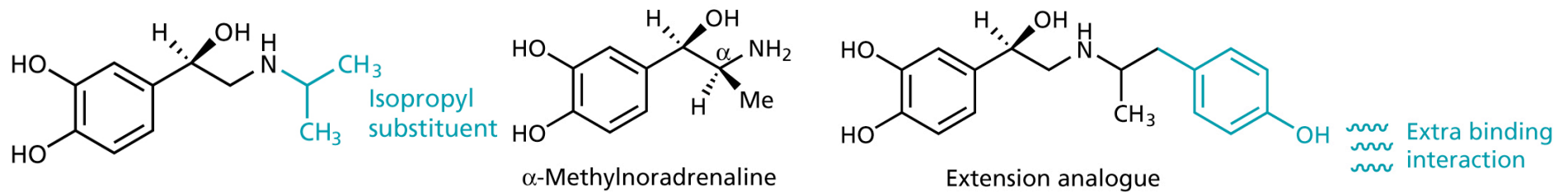
Adrenergic Binding Site: α vs. β



β -Adrenoceptor



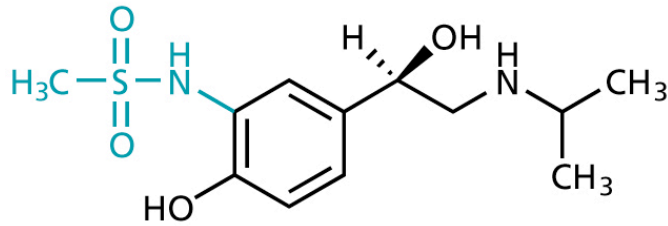
α -Adrenoceptor



Stimulates β , not α due to bulky groups

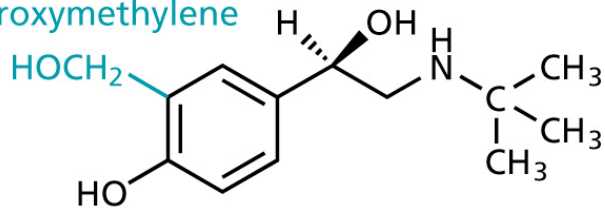
Adrenergic Binding Site: spec. β 2 agonists and asthma

sulfonamide

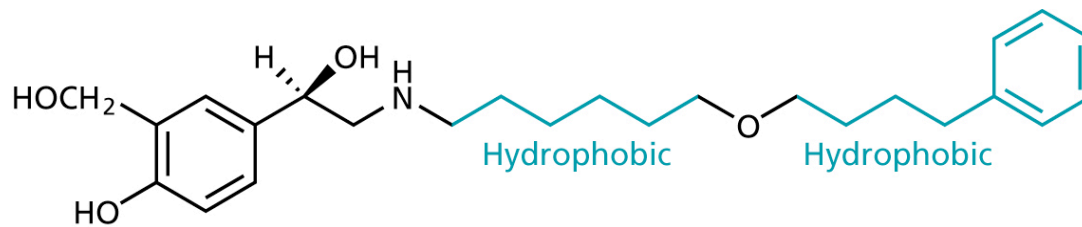
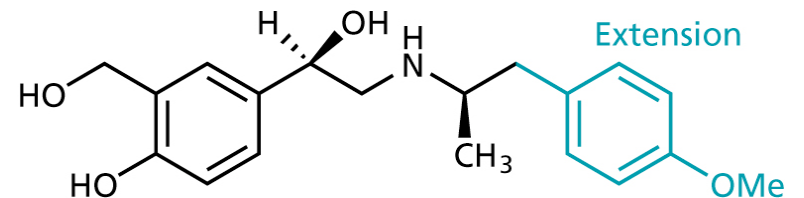


R-Soterenol

hydroxymethylene

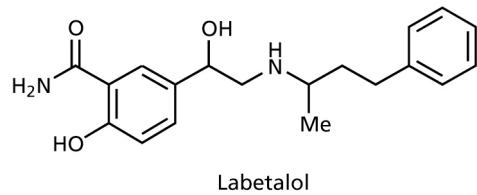
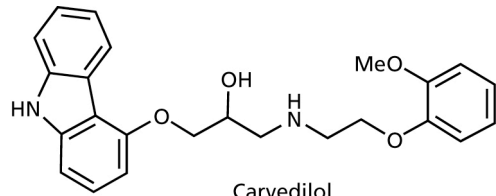


R-Salbutamol

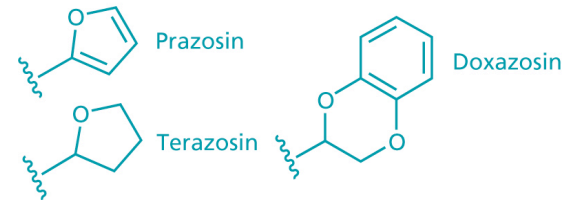
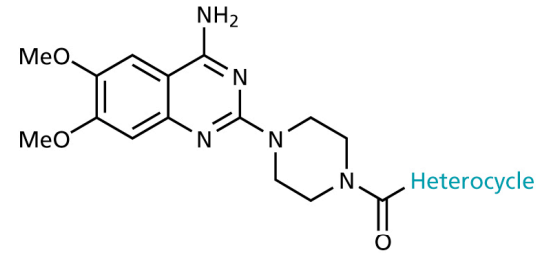


selective β 2 agonists, adrenalin is less specific

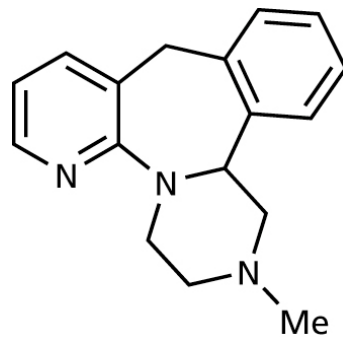
α Adrenergic antagonists:



general α/β for antihypertension

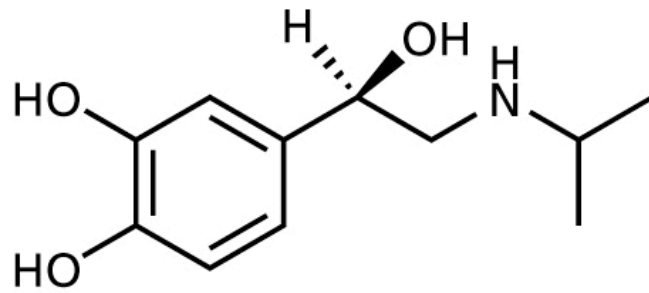


α_1 for urinary tract relaxation prostate enlargement treatment

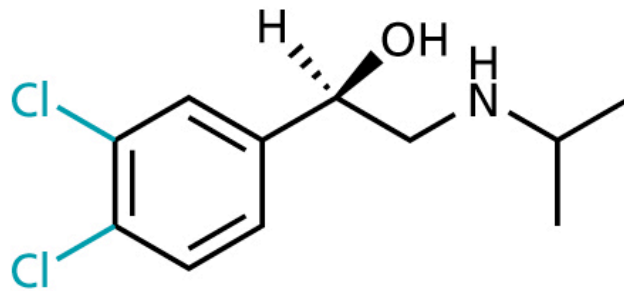


Mirtazepine (Remeron) α_2 blocker for depression-increases serotonin and NA

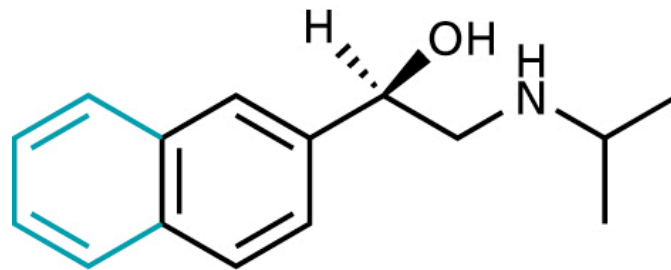
β adrenergic blockers: cardiovascular drugs for BP



Isoprenaline



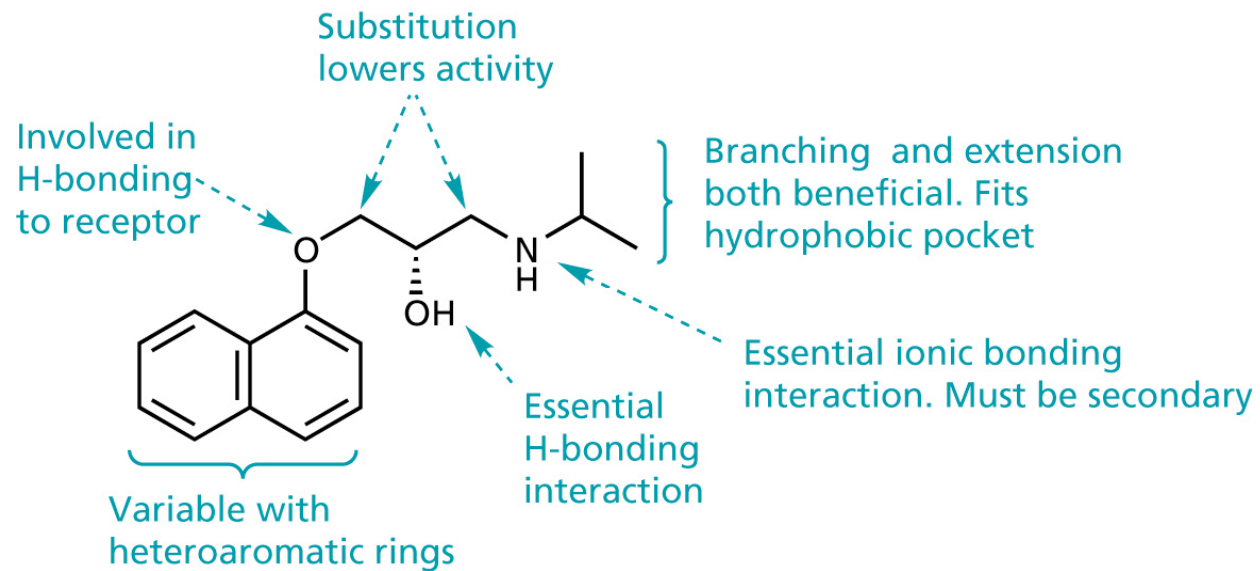
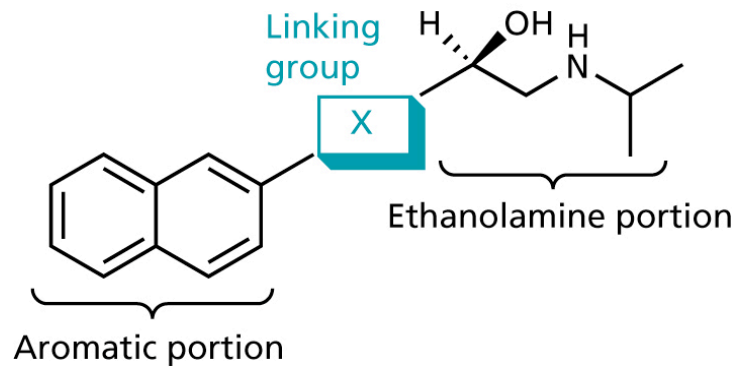
Dichloroisoprenaline



Pronethalol

partial β agonists

specific β adrenergic blockers: cardiovascular drugs for BP

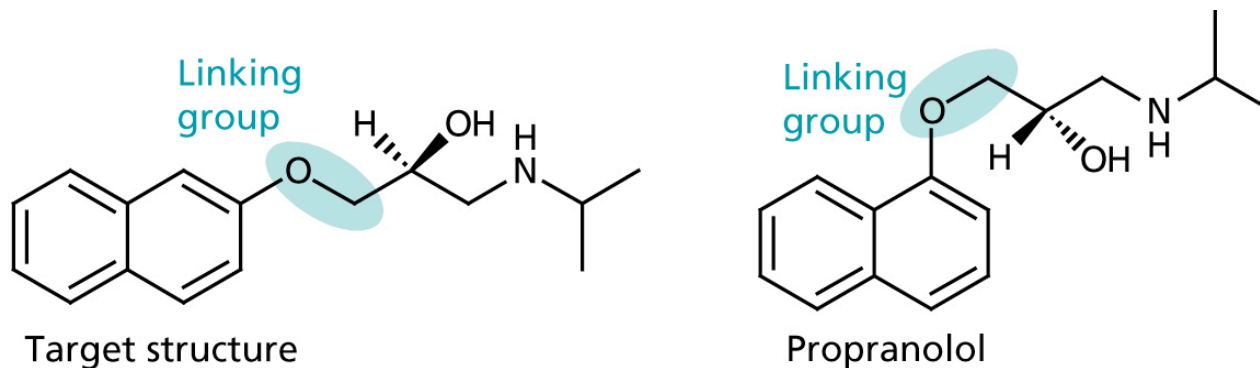


Extra ring converts agonist to antagonist

specific β adrenergic blockers: cardiovascular drugs for BP

β -blockers effects

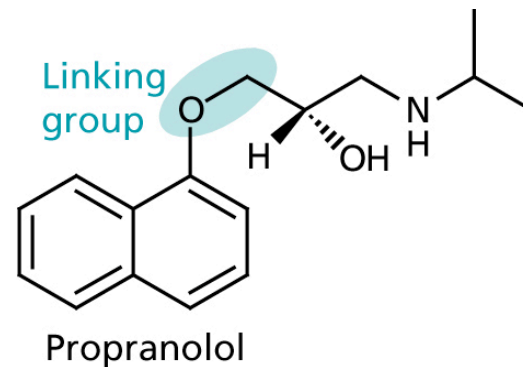
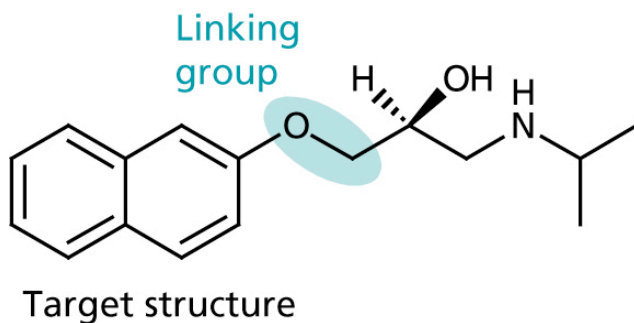
- Reduce cardiac output
- Reduce renin release from kidneys (which produces Angiotensin I and II)
- Reduces general activity of CNS



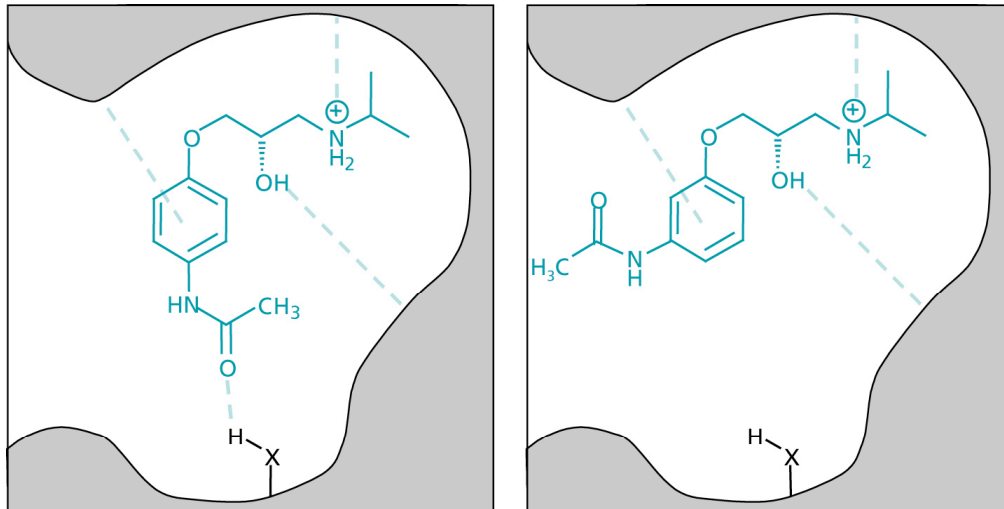
specific β adrenergic blockers: cardiovascular drugs for BP

β -blockers side effects

- Bronchoconstriction due to β_2 blocking
- lethargy
- Dizziness, dreams from bbb passage of hydrophobic propranolol
- Potential heart failure



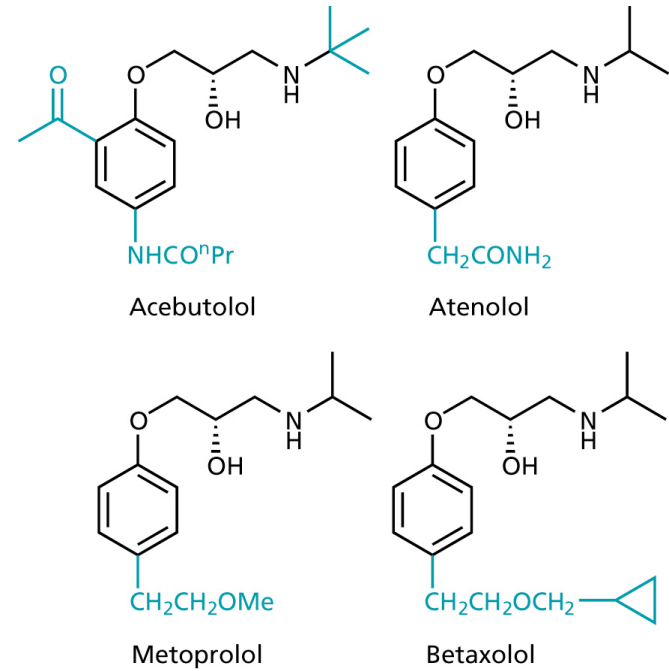
More selective β_1 -blockers- Next generation



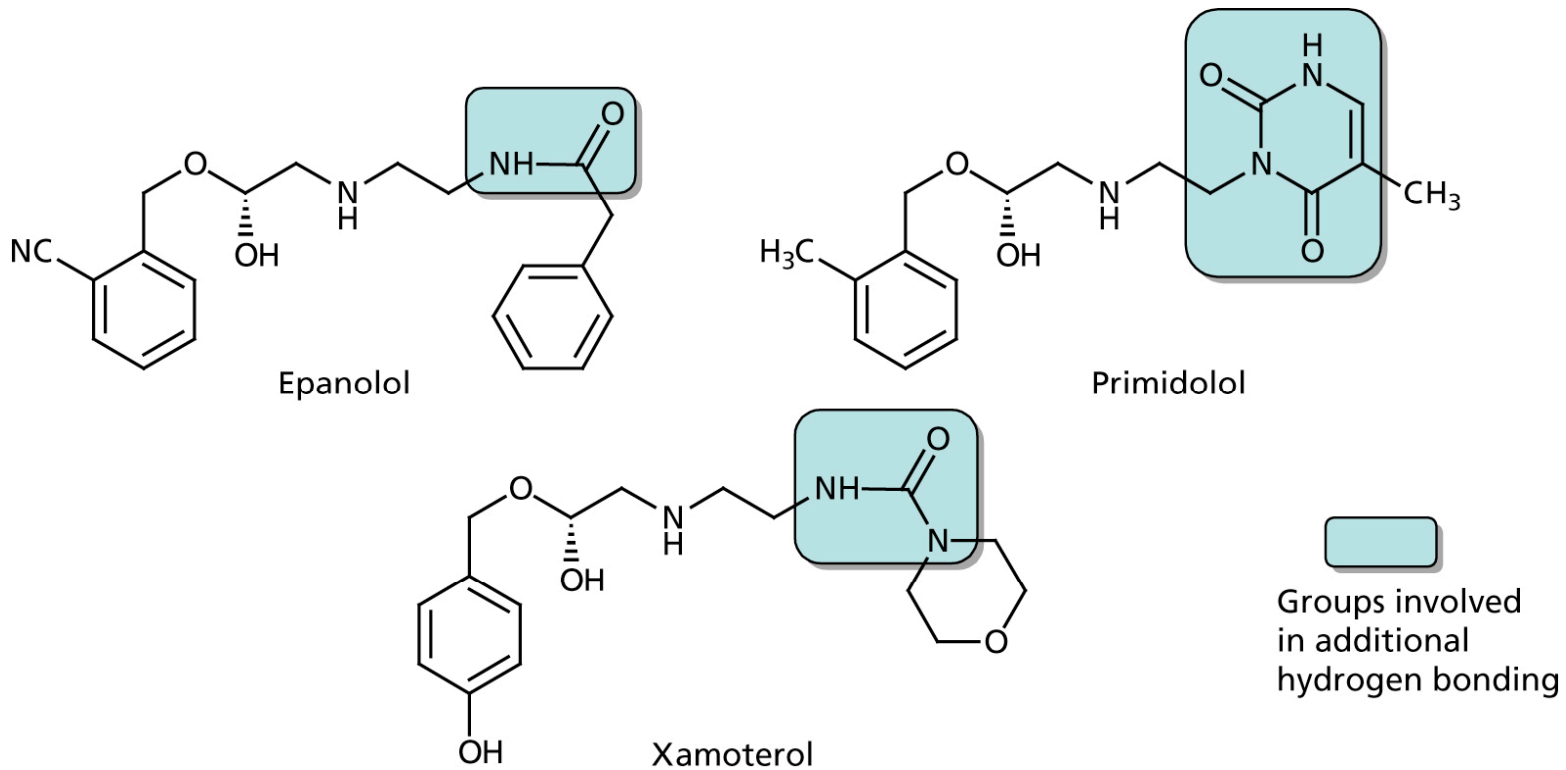
para substitution
Extra H-bonding interaction

meta substitution

β_1 receptor

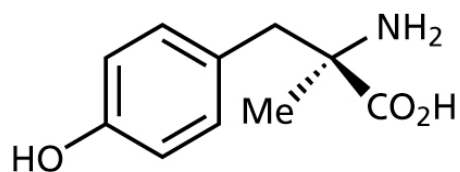
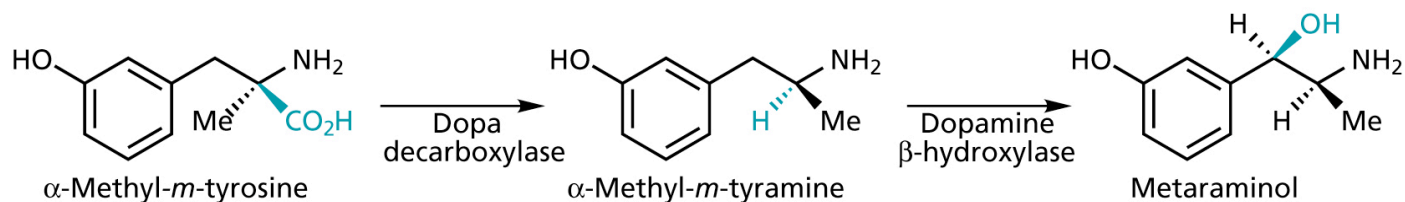
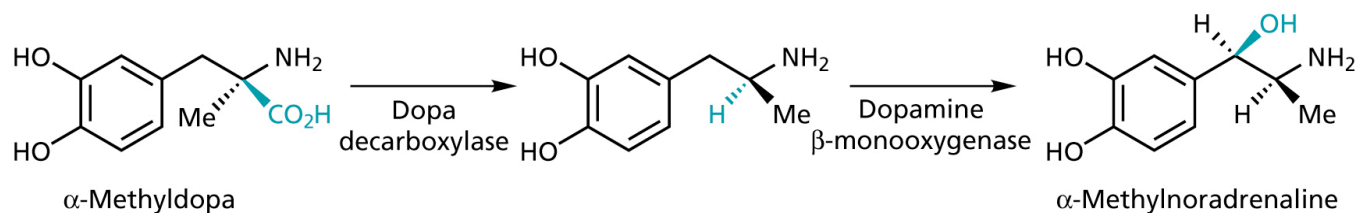


More selective β_1 -blockers-3rd generation !



Other Adrenergic drugs

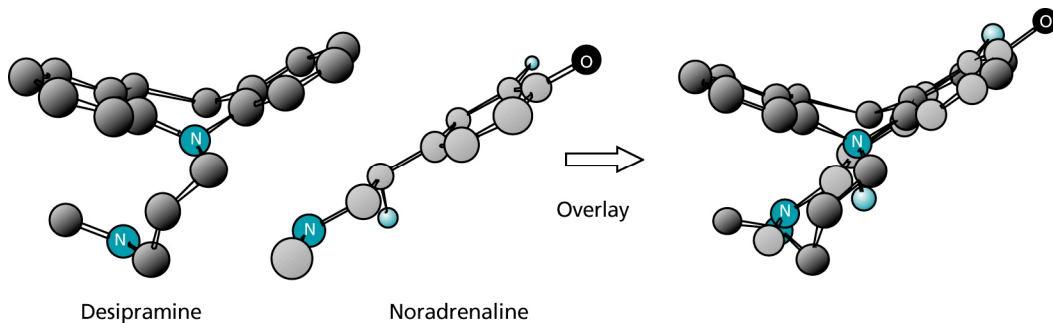
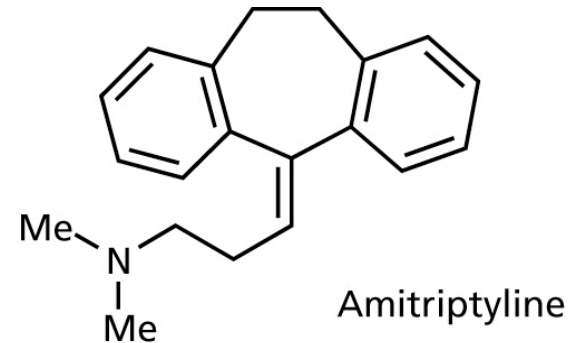
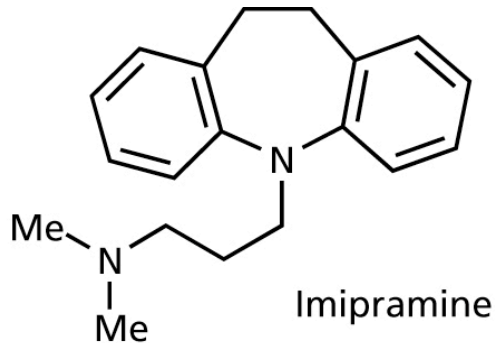
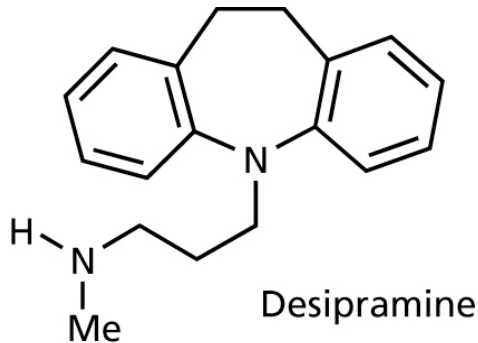
- Biosynthesis “dummies” down regulate adrenergic system



α -methyl tyrosine: a fake amino acid

Other Adrenergic drugs

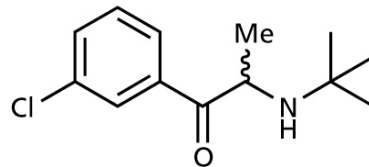
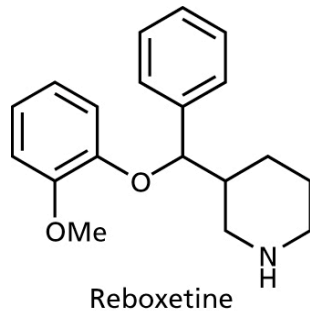
- The tricyclic antidepressants
- NA reuptake inhibitors-desensitize α_2 receptors leading to more serotonin and NA released to get effect.



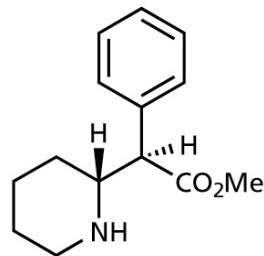
Other Adrenergic drugs

- Newer antidepressants
- Bupropion (Welbutrin) and others inhibit reuptake of both NA and dopamine in CNS.
- Reuptake inhibitors also used for ADHD (ritalin, Strattera)

Edronax

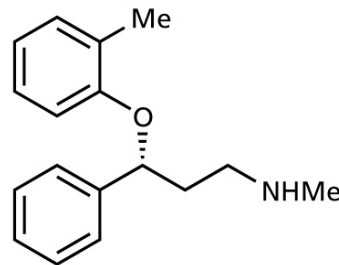


Welbutrin



Methylphenidate

Ritalin



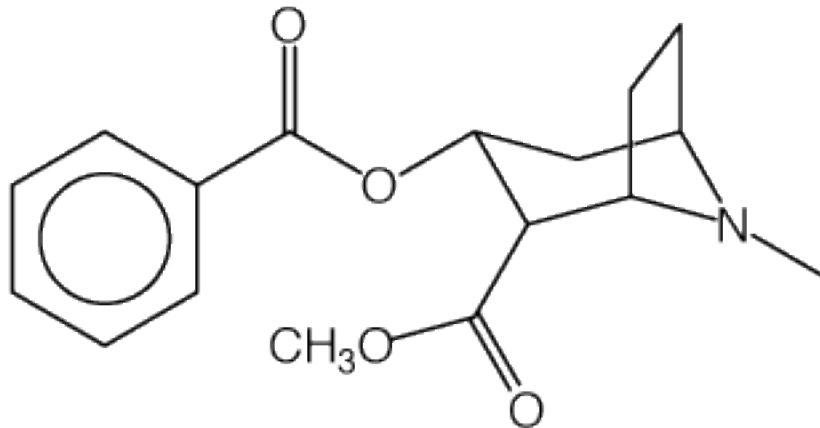
Atomoxetine

Strattera

Other Adrenergic drugs

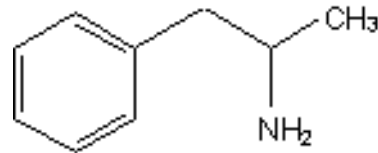
- Cocaine-inhibits NA uptake in peripheral nervous system and dopamine in CNS

cocaine



Other Adrenergic drugs

- Amphetamine-inhibits NA carrier uptake in CNS



Amphetamine

- Monoamine oxidase inhibitors-increase [catecholamine] by stopping breakdown

