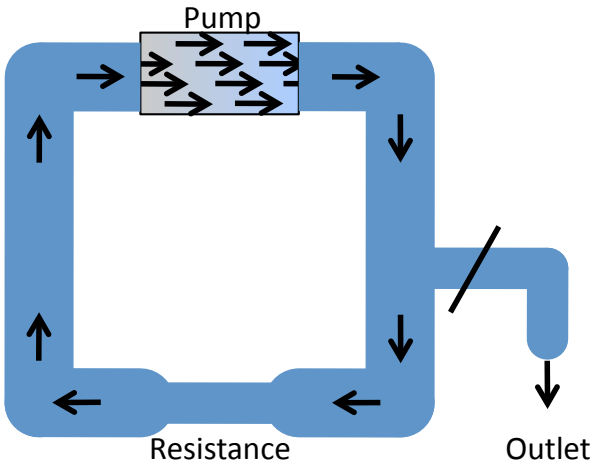
Task

Discussion

Discussion

Principal Drug Classes for Treating Systemic Hypertension

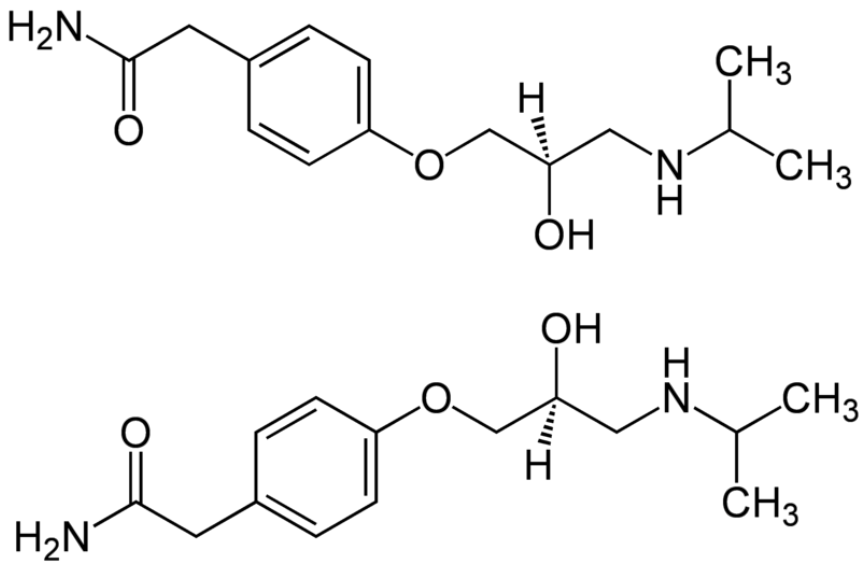
- Drugs that affect the sympathetic nervous system
  - β-blockers
  - α-blockers
- Centrally-acting drugs
  - α_2-agonsts / imidazoline receptor agonists
- Drugs that affect the renin-angiotensin-aldosterone system
  - ACE inhibitors
  - Angiotensin receptor antagonists
- Diuretics
  - Thiazide diuretics
  - Loop diuretics
  - Potassium-sparing diurtetics



Discussion

β_1-Adrenoceptor Antagonists

- Block effects of noradrenalin on β_1-adrenoceptors
- β_1-adrenoceptors found mainly in the heart
  - Antagonism decreases heart rate and heart contractile strength
- Reduction in cardiac output
  - Decrease in systemic BP
- Example: Atenolol

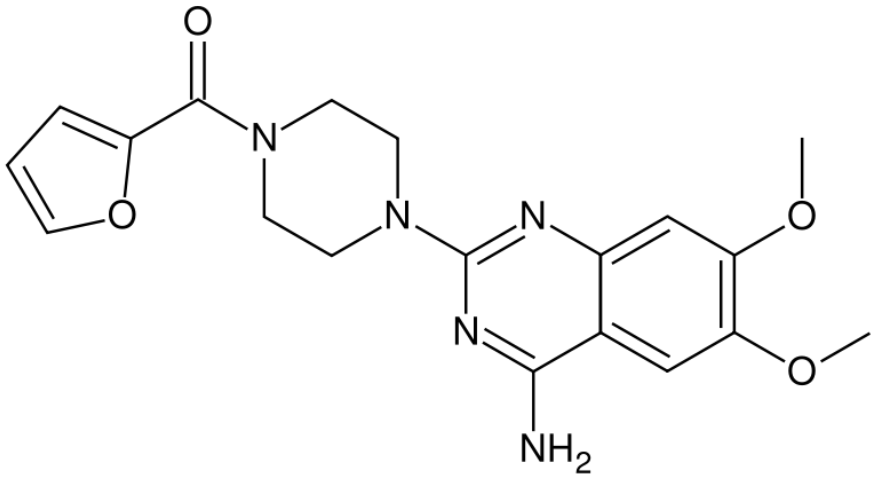


Atenolol

Discussion

α_1-Adrenoceptor Antagonists

- Stimulates α_1-adrenoceptors
- α_1-adrenoceptors found mainly in smooth muscle of blood vessels
- Antagonism decreases signals for vasoconstriction
  - Result in vasodilation
- Increase in vasodilation decreases systemic BP.
- Example: Prazosin

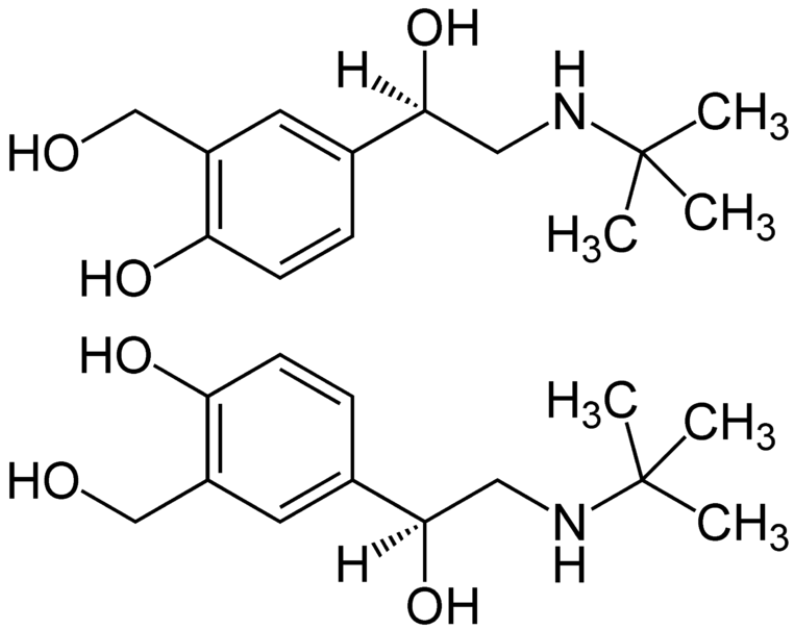


Prazosin

Discussion

β_2-Adrenoceptor Agonist

- Active at β_2-adrenoceptors
- β_2-adrenoceptors found mainly in bronchi and GI tract
- Agonism causes vasodilation in smooth muscle
- Increased perfusion of organs
- Opening of airways (bronchiodilation)
- Minor effect on systemic BP.
- Example: Salbutamol



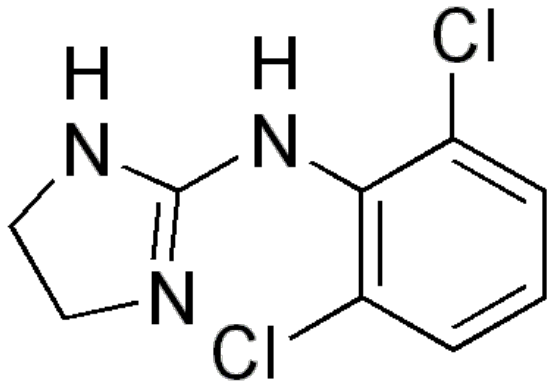
Salbutamol

- *Note*: At present there are no common β_2-adrenoceptor agonist used for treating hypertension

Discussion

α_2-Adrenoceptor Agonists

- Stimulates central α_2-adrenoreceptors
- α_2-adrenoreceptors found in the CNS
- Decreases cardiac output
- Decreases peripheral vascular resistance
- Example: Clonidine



Clonidine

- *Note*: α_2-adrenoreceptors found in the presynaptic neurons and agonism here reduces neuronal release of noradrenalin

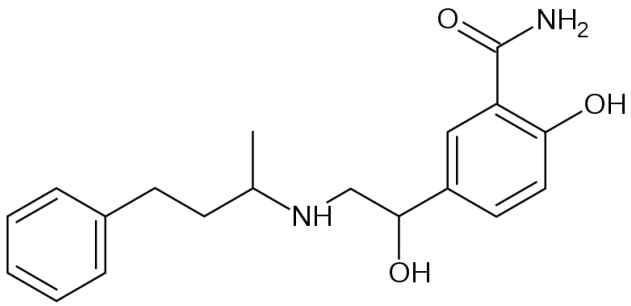
Discussion

Mixed Action Adrenoceptor Blockers

- Some drugs interact with more than one type/ subtype of adrenoceptor activity/affinity

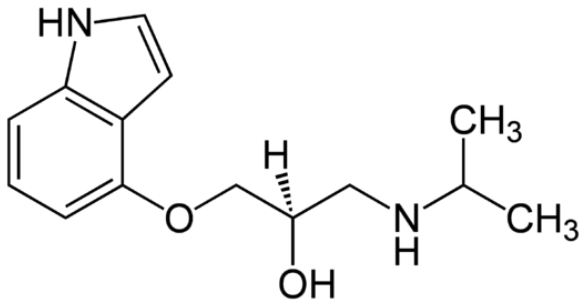
- The actions of these drugs are a combination of α-/β- agonists/antagonist

- Examples: Labelatol
  - β_1-antagonist / α_1-antagonist



Labelatol

- Examples: Pindolol
  - β1-antagonist / β_2-agonist



Pindolol

Discussion

ACE Inhibitors

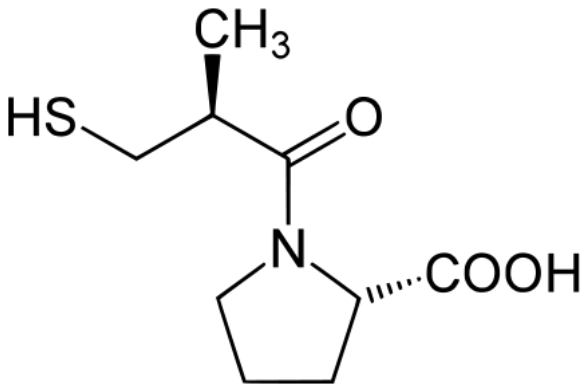
- A circulating peptide – bradykinin – is a potent vasodilator

- In addition to cleavage of angiotensin I, ACE also degrades bradykinin
  - Vasodilatory effect reduced

- Angiotensin converting enzyme (ACE) is responsible for:
  - Cleavage of angiotensin I to angiotensin II
  - Degradation of bradykinin

- ACE inhibitors act to reduce blood pressure
  - By inhibiting the action of ACE
  - Reducing circulating angiontensin II
    - (and related multiple effects e.g. aldosterone)
  - Increasing circuating bradykinin

- Example: Captopril



Captopril

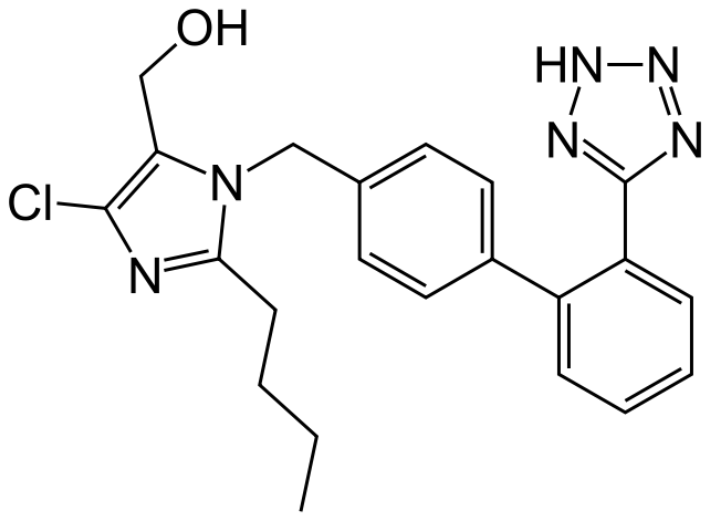
Discussion

AT Inhibitors

- Angiotensin II receptor type 1 (AT_1R) inhibitors
  - Reduce response to circulating angiotensin II
  - Reduced AT-related changes in target organs

- Antagonism of multiple AT-related effects
  - Reduced aldosterone secretion
  - Vasodilation
  - Reduced sympathetic tone

- Example: Losartan

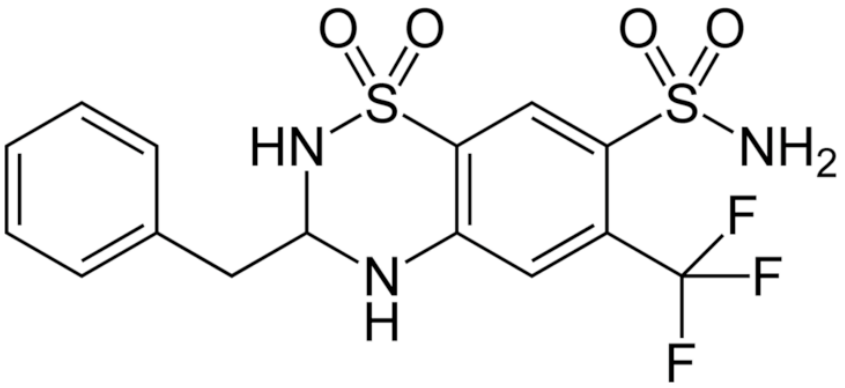


Losartan

Discussion

Thiazide Diuretics

- Inhibit the Na+ / Cl- cotransporter in the distal convoluted tubule (kidney)
  - Prevents reabsorption of H_2O



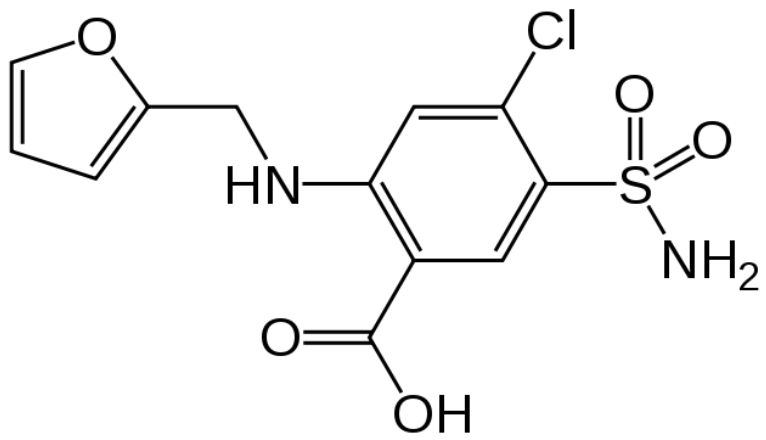
Bendroflumethiazide

Discussion

Loop Diuretics

- Loop diuretics inhibit the reabsorption of Na^+ and Cl^-
  - Inhibit the Na^+/Cl^- cotransporter
  - In the kidney (ascending limb of the loop of Henle)
  - Compete for the Cl- binding site in the transporter

- Reduced reabsorption of Na+ and Cl-
  - Reduces reabsorption of H_2O



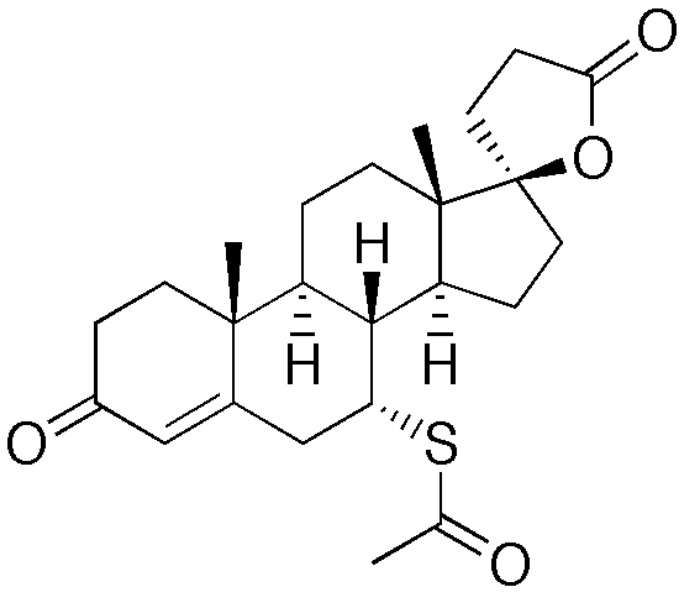
Furosemide

Discussion

Potassium-Sparing Diuretics

- The potassium-sparing diuretics are competitive antagonists that either:
  - Competes with aldosterone for intracellular cytoplasmic receptor sites
  - Reduces expression of $Na^+/K^+/2Cl^-$ transport proteins
  - Reduces reabsorption of Na^+, Cl^-
  - Reduces excretion of K^+
  - Reduces reabsorption of H_2O

- Example: Spirolactone



Spirolactone

- *Note*: Alternatively, some of these diuretics may act by blocking Na^+ channels directly.