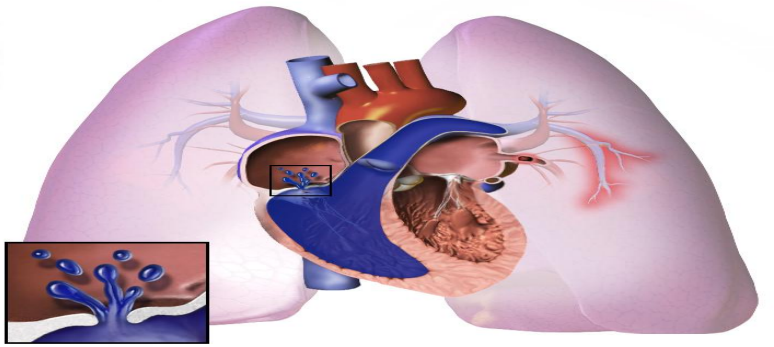
Drugs used in Congestive Heart Failure



By

Mangesh A. Mapari

Congestive Heart Failure (CHF)

- When a heart fails to pump blood in a quantity sufficient to fulfil the body requirements, a condition of Congestive Heart Failure (CHF) occurs, which is also known as a Heart Failure (HF).
- Change in electrophysiology of heart.

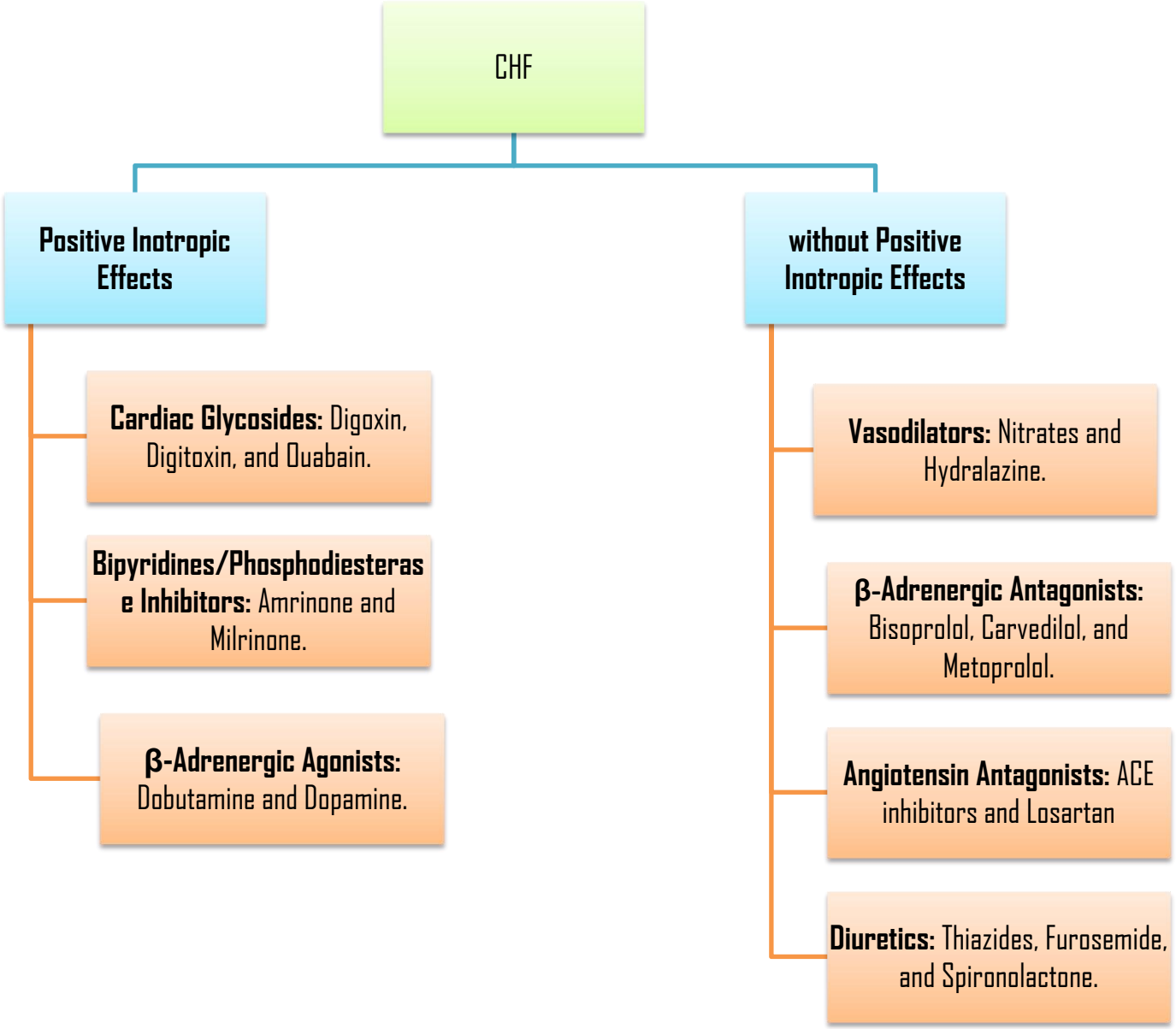
✓ Narrowing of the arteries, supplying blood to the heart muscles,

✓ The patient suffered in the past with myocardial infarction or heart attack with the injured tissue that obstructs the normal functioning of heart,

✓ Any congenital heart defects,

✓ Endocarditis (infection in heart valve) or myocarditis (infection of heart muscles)

Classification

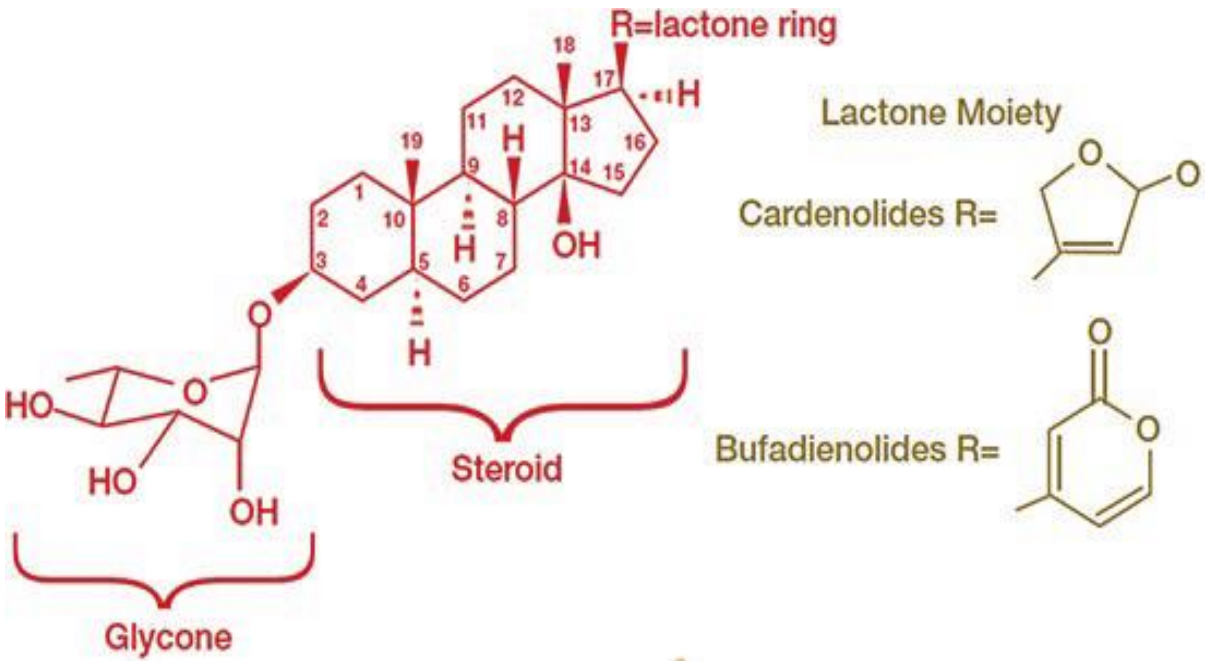


Cardiac Glycosides

- Cardiac glycosides are derived from the foxglove plant (*Digitalis purpurea*).
- **William Withering** described the therapeutic benefits of digitalis in **1785**.
- Primarily, digitalis was used for treating dropsy, an old word for oedema. Further investigations established that digitalis was most helpful for oedema caused by weakened heart (i.e., heart failure).

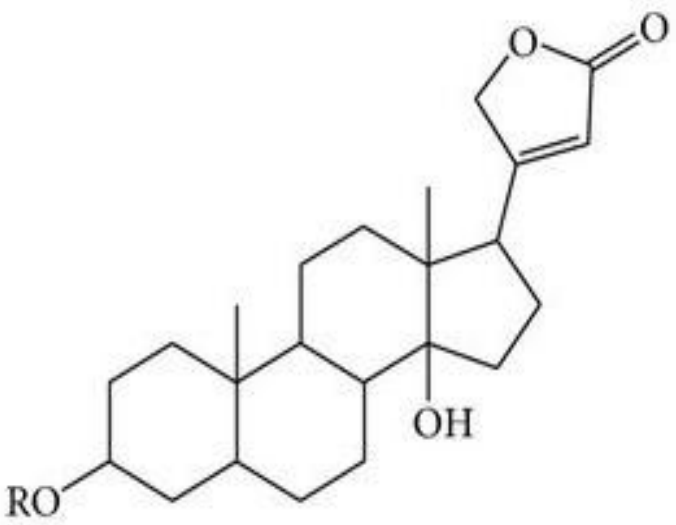
Structures of Cardiac Glycosides

- The sugar which is known as glycone and
- The nonsugar which consists of steroid and lactone ring known as aglycone moieties

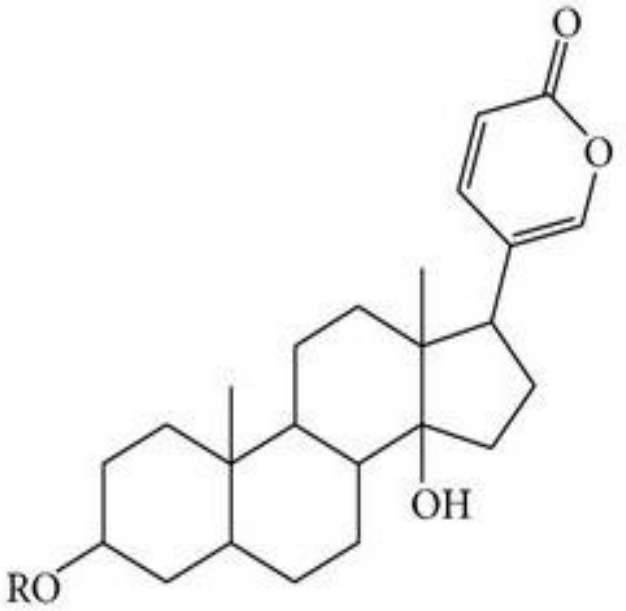


Cardiac glycosides are categorised into

Cardenolides and Bufadienolides

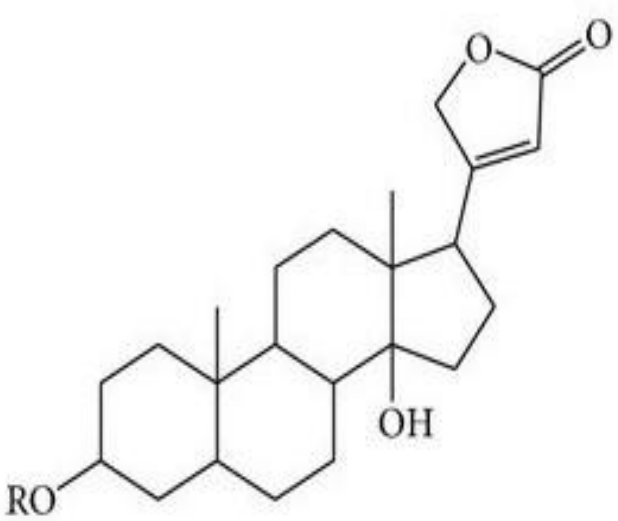


Cardenolide



Bufadienolide

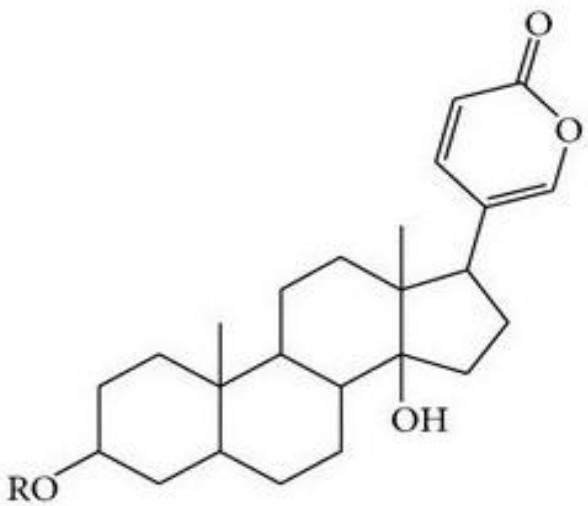
Cardenolides



Cardenolide

- A cardenolide is a type of steroid.
- Cardenolides (cardiac glycosides derived fr om plants) have a 5 - membered α,β-unsaturated lactone ring. OR
- CG having the lactone 2-furanone is known as cardenolides.

Bufadienolides

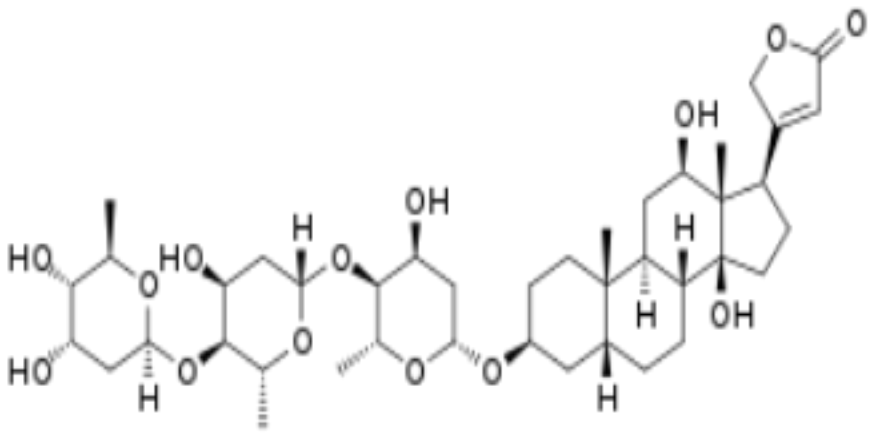


Bufadienolide

- Bufadienolides (cardiac glycosides derived from animals) have a 6 - membered lactone ring with two conjugated double bonds (generally referred to as α-pyrone). OR
- Those having the lactone 2-pyrone are known as bufadienolides
- Bufadienolides are present in the secretions from the skin of toad species, thus, are referred to as toad poison.

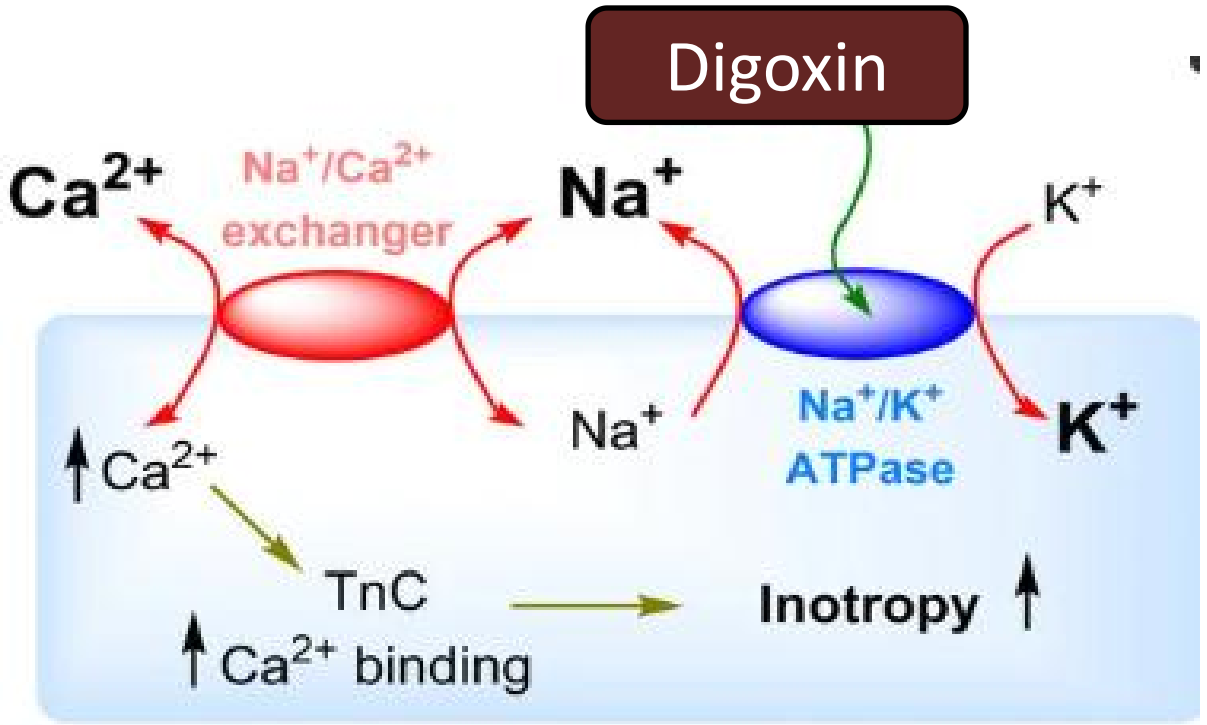
Digoxin

Digoxin is a purified **Cardinolide** cardiac glycoside, derived from the leaves of **digitalis** plant.



Digoxin

Mechanism of Action



Digoxin
Mechanism of Action

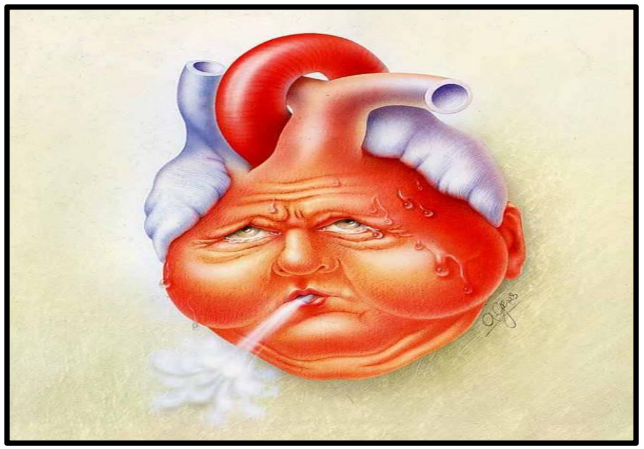
- Digoxin inhibits the Na +-K+-ATPase membrane pump and increases the intracellular Na+ ions.
- The sodium calcium exchanger tries to extrude the Na+ ions and pumps in more Ca2+ ions, thereby increasing the intracellular concentrations of Ca2+ ions.

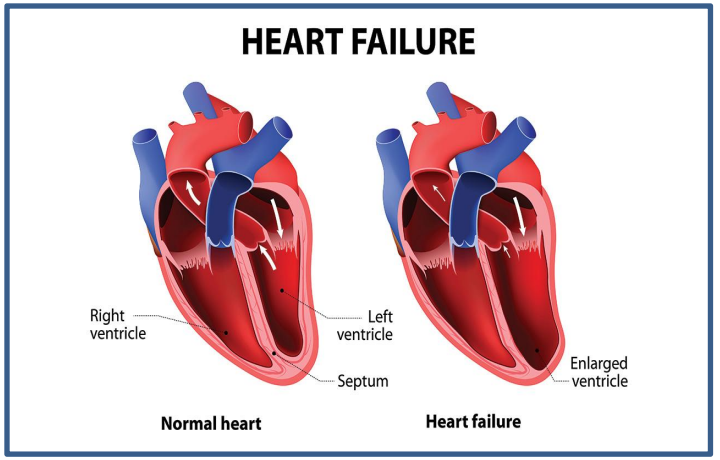
Digoxin
Mechanism of Action

- This promotes the activation of contractile proteins (e.g., actin and myosin).
- Digoxin also acts on the electrical activity of the heart, increases the slope of phase 4 depolarisation, shortens the action po tential duration, and decreases the maximal diastolic potential.

Digoxin
Uses

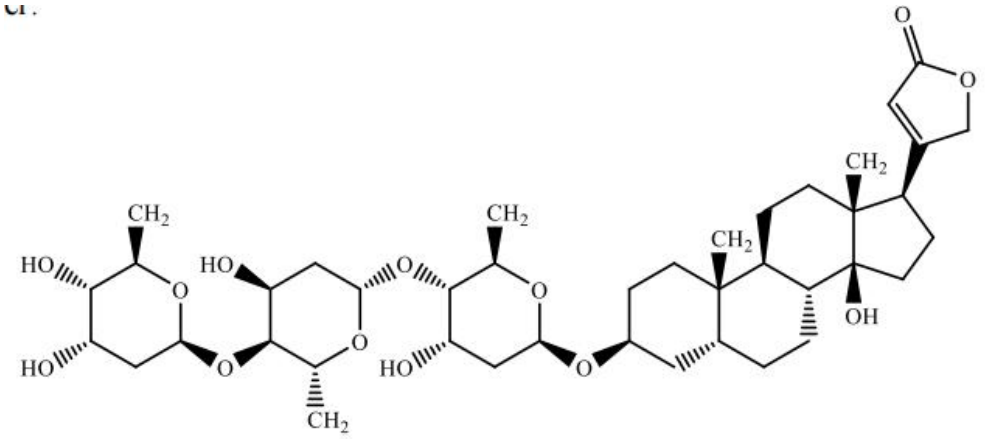
- It is used for treating and managing congestive cardiac insufficiency, heart failure, and arrhythmias.
- It is also used to treat a certain type of irregular heartbeat (chronic atrial fibrillation)





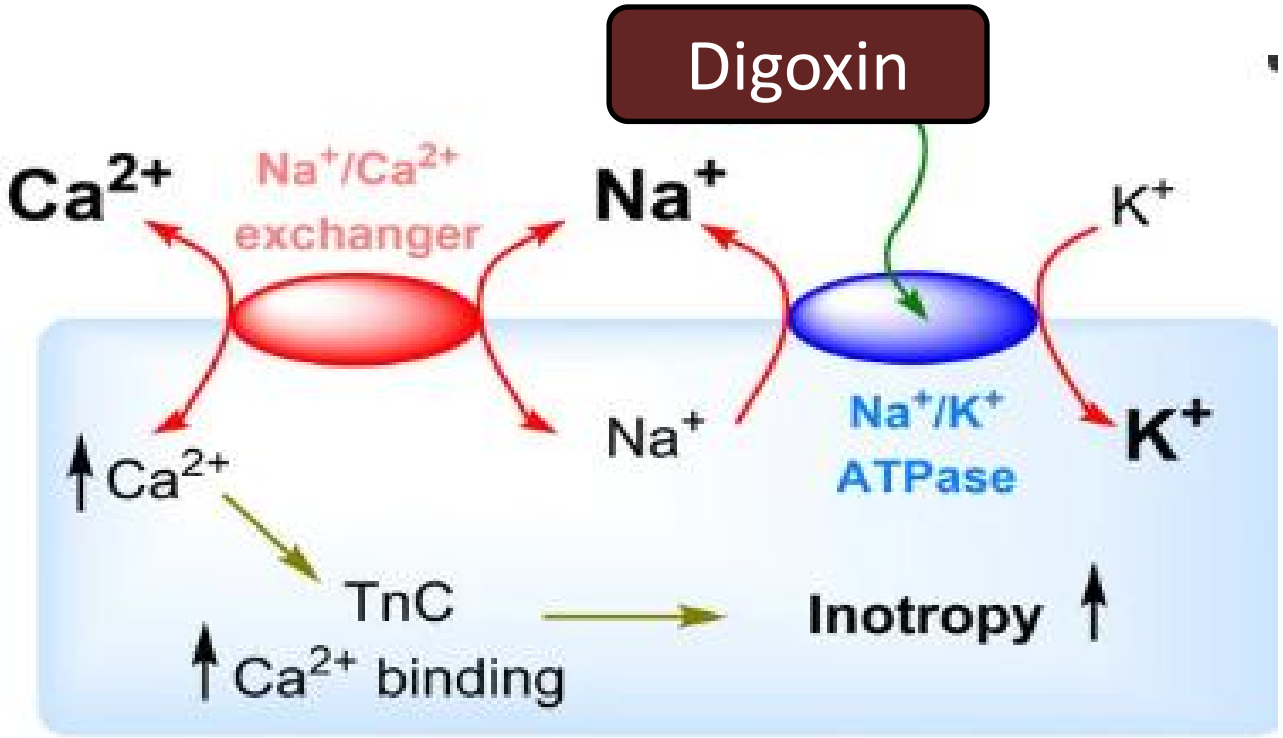
Digitoxin

- Digitoxin is a cardiac glycoside which is occasionally used in place of digoxin.
- Its half -life is longer than digoxin, and toxic effects similar to digoxin lasts longer.



Digitoxin

Mechanism of Action



Digitoxin

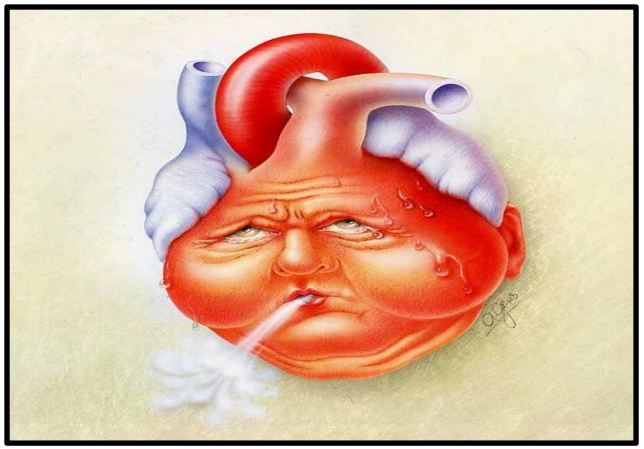
Mechanism of Action

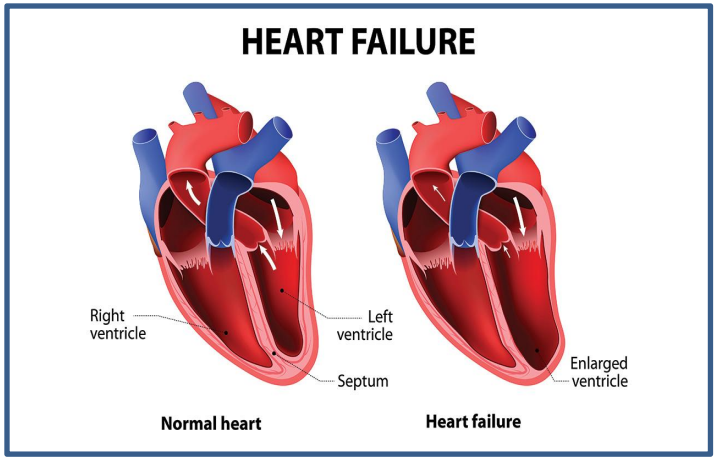
- Digitoxin inhibits the Na+-K+-ATPase membrane pump and increases the intracellular concentration of Na+ and Ca2+ ions.
- This increased intracellular concentration of Ca2+ ions activate the contractile proteins (e.g., actin and myosin).
- Digitoxin also acts on the electrical a ctivity of the heart, increases the slope of phase 4 depolarisation, shortens the action po tential duration, and decreases the maximal diastolic potential.

Digitoxin

Uses

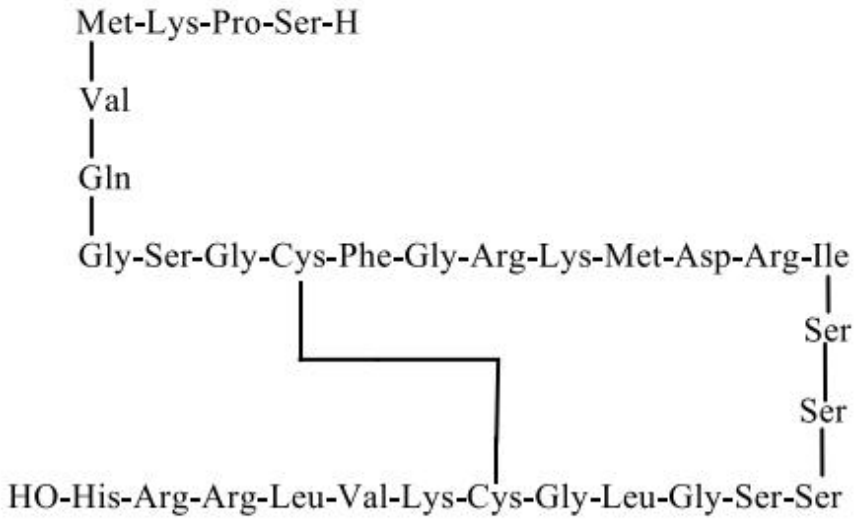
- It is used for treating and managing congestive cardiac insufficiency, heart failure, and arrhythmias.



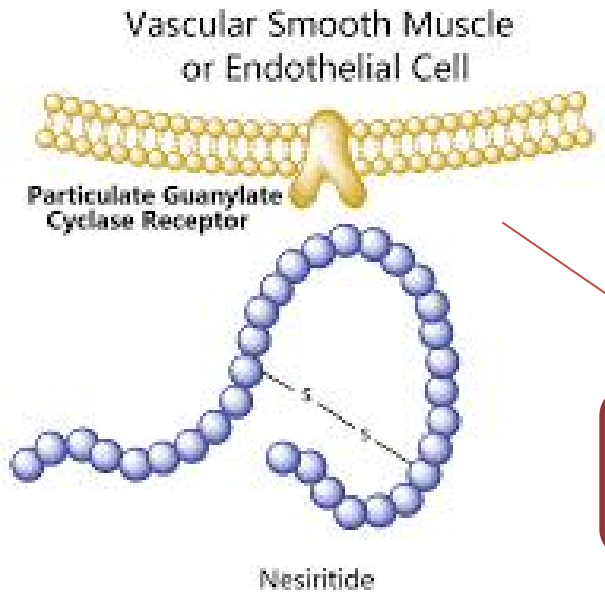


Nesiritide

- Nesiritide is the recombinant form of **32** amino acid human B -type natriuretic peptide.
- It is obtained by ventricular myocardium.



Nesiritide
MOA



Guanosine 3'5'-cyclic monophosphate (cGMP)

Smooth muscle cell relaxation

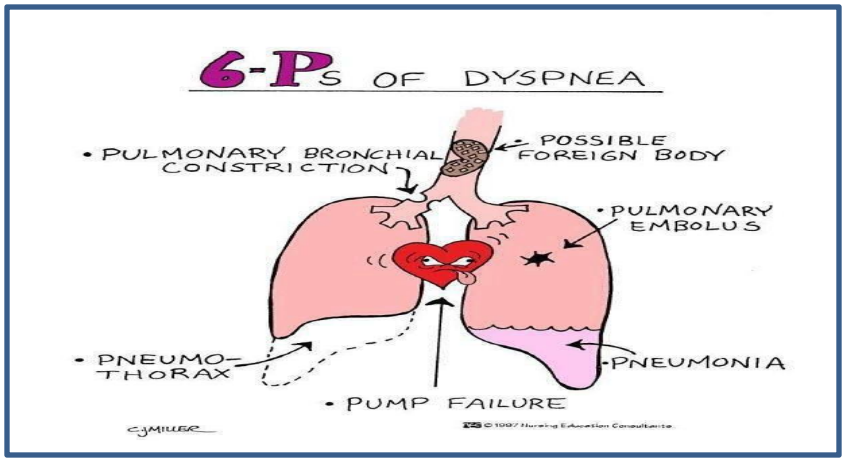
Nesiritide
Mechanism of Action

- Nesiritide is a Natriuretic Peptide (BNP) binds to the particulate **guanylate cyclase receptor** of vascular smooth muscles and endothelial cells.
- This increases the intracellular concentration of **guanosine 3'5' - cyclic monophosphate** (cGMP)and smooth muscle cell relaxation.
- The cGMP serves as a second messenger to dilate veins and arteries. Nesiritide relax es isolated human arterial and venous tissue preparations pre -contracted with either endothelin -1 or phenylephrine (α-adrenergic agonist).

Nesiritide

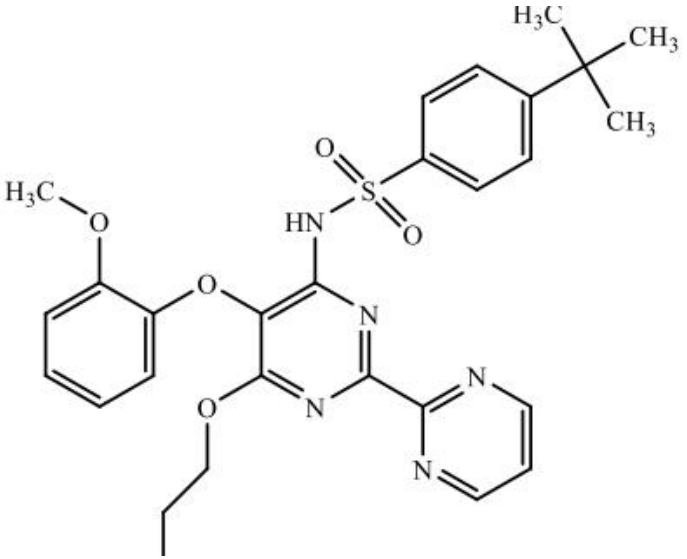
Uses

- It is used for treating acute decompensated **congestive heart failure** in patients having with dyspnoea at rest or with minimum activity, such as talking, eating ,and bathing.



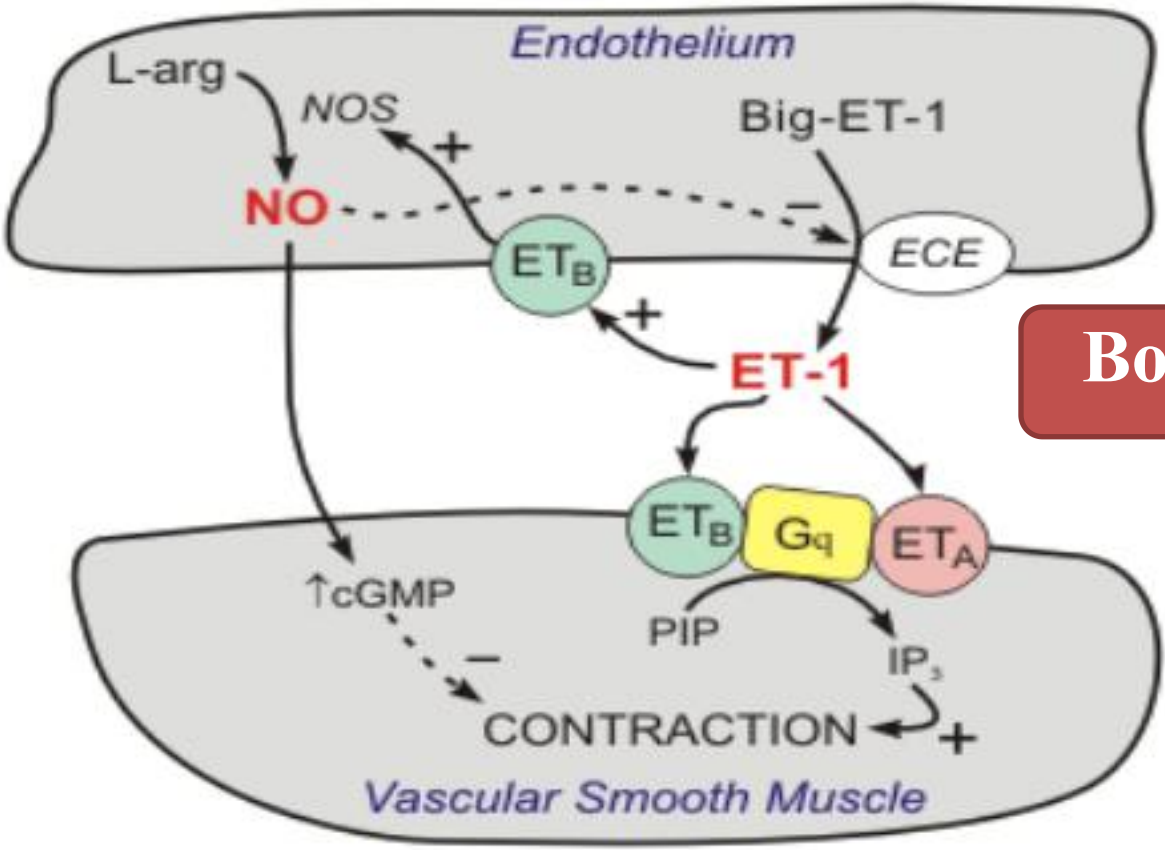
Bosentan

- Bosentan is a **pyrimidines** derivatives
- Bosentan is a endothelin receptor antagonist.
- It is essential ly used for treating Pulmonary Artery Hypertension (PAH).



Bosentan

MOA

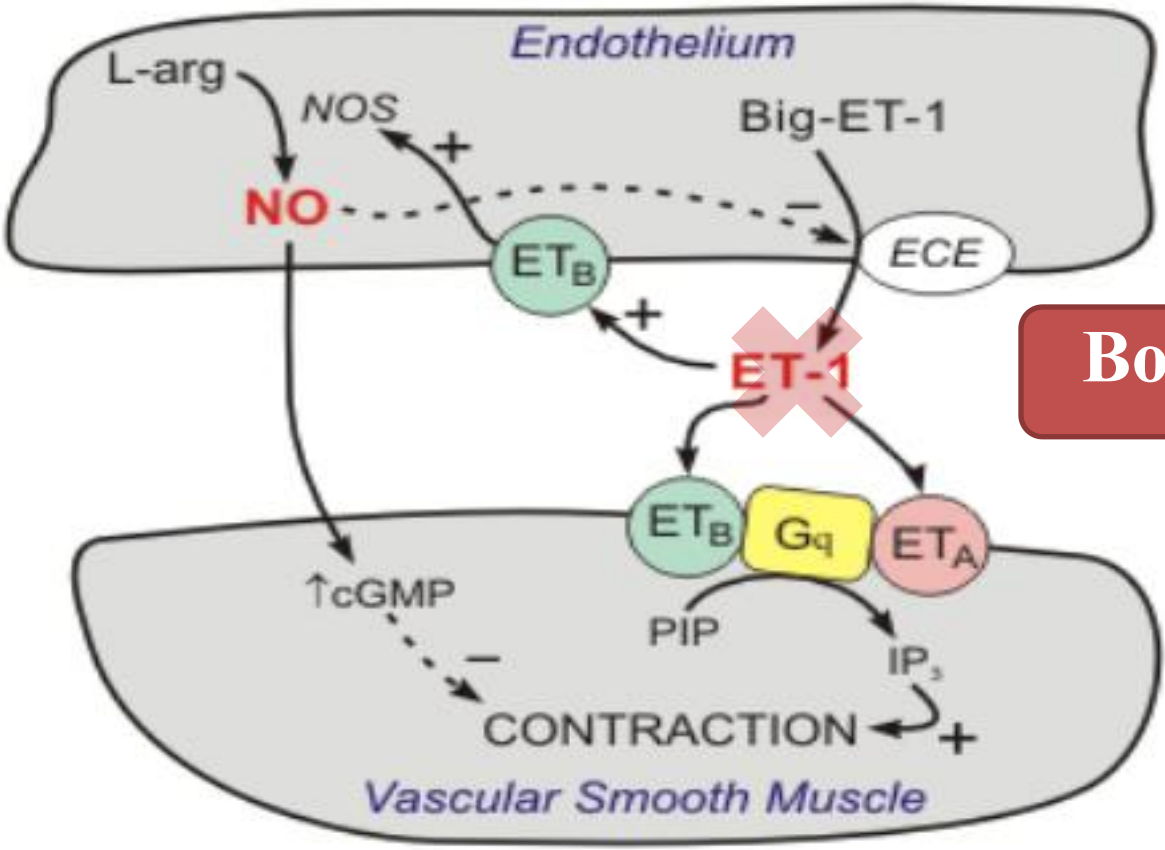


Bosentan

Endothelin-1 (ET-1)

Bosentan

MOA



Endothelin-1 (ET-1)

Bosentan

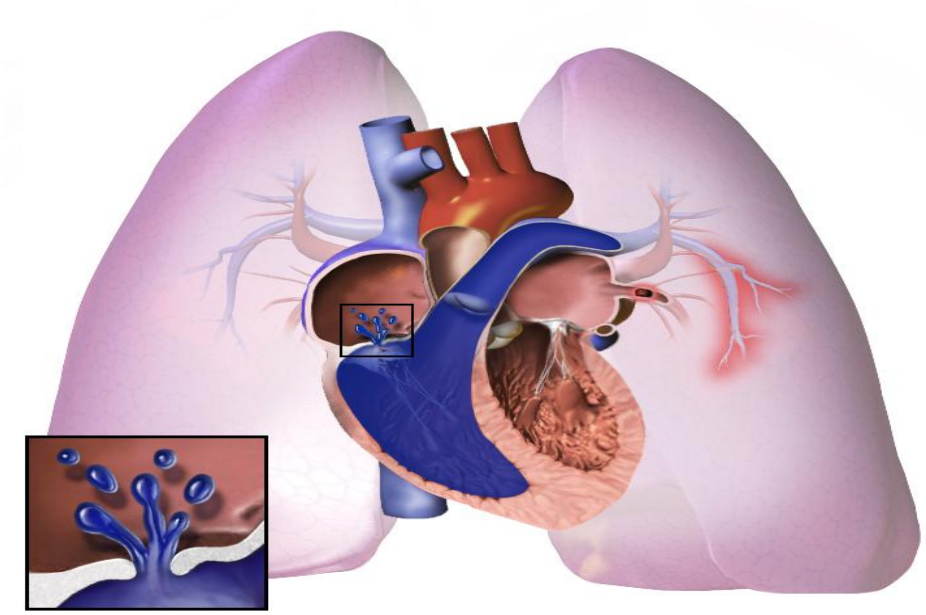
MOA

- Endothelin-1 (ET -1) is a neurohormone. It produces its effects by binding to **ET_A and ET_B** receptors in the endothelium and vascular smooth muscles.
- The levels of ET-1 in plasma and lung tissue increase in patients having pulmonary arterial hypertension .
- Bosentan is a specific and **competitive antagonist** of endothelin ET_A and ET_B receptor, having a comparatively high affinity for ET_A receptors.

Bosentan

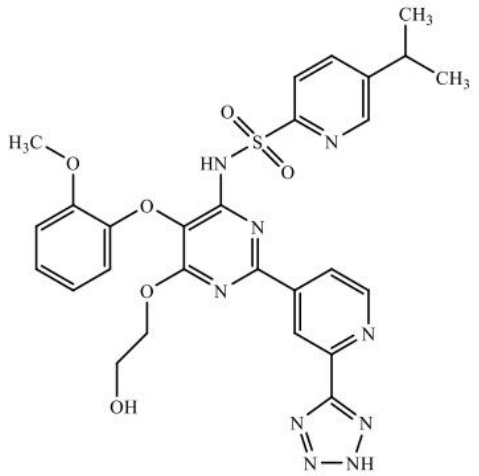
Uses

- It is used for treating **pulmonary arterial hypertension**.



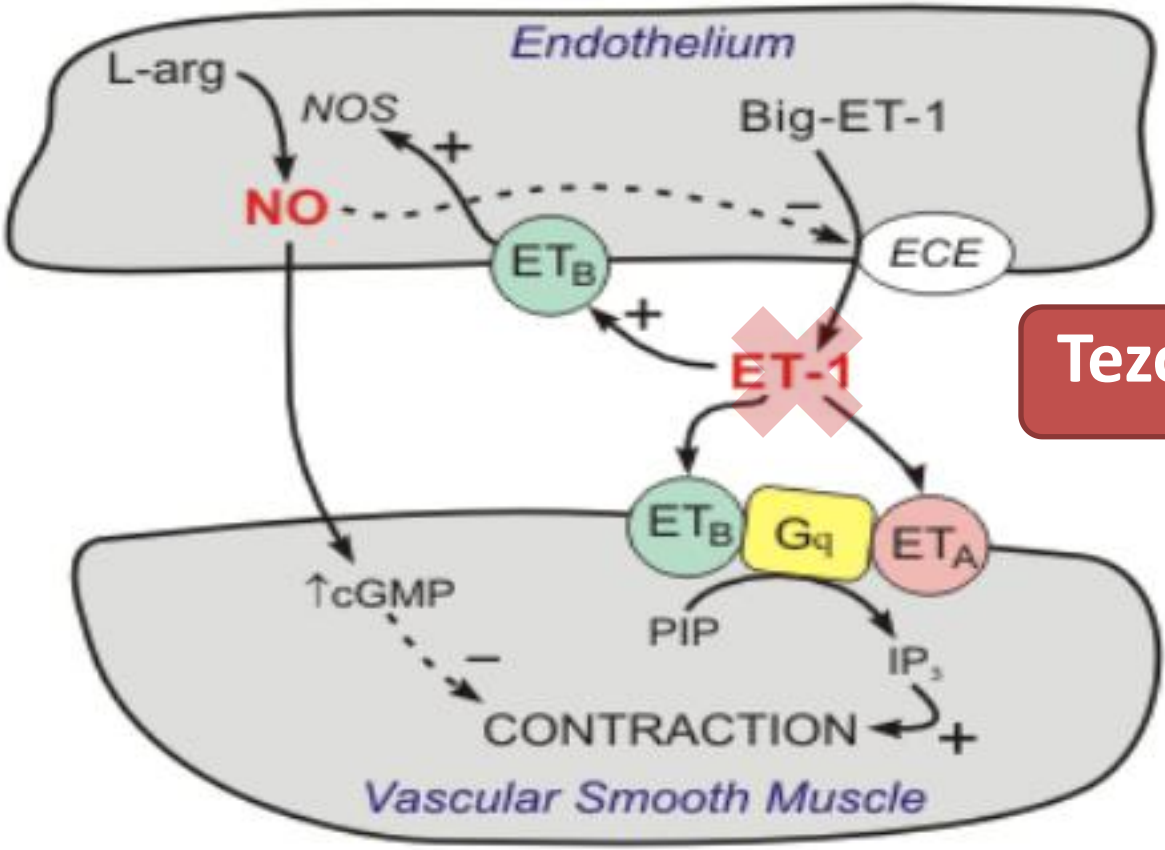
Tezosentan

- Tezosentan is an antagonist of **endothelin ET_A** and **ET_B** receptors.
- It acts as a vasodilator.
- It is designed to be used intravenously in patients with acute heart failure.



Tezosentan

MOA



Tezosentan

Endothelin-1 (ET-1)

Tezosentan

Mechanism of Action

- Tezosentan relaxes the smooth muscle s in blood vessels, and dilates them.
- This dilation of arterial (resistance) vessels reduces systemic vascular resistance, and ultimately leads to fall in arterial blood pressure.
- Dilation of venous (capacitance) vessels decreases venous blood pressure.

Tezosentan

Uses

- It is designed to be used intravenously in patients with acute heart failure.