






Chapter 10. Drugs Used in Congestive Heart Failure

Syllabus:

-  Cardiac glycoside: Digoxin, Digitoxin,
-  Natriuretic peptide: Nesiritide,
-  Endothelin receptor (ET R) Antagonist: Bosentan, Tezosentan.


10.1. CONGESTIVE HEART FAILURE


 CHF refers to the condition wherein heart unable to pump a sufficient amount of blood thus lead to **low cardiac output**. CHF occurs due to systolic and/or diastolic heart failure.

 Heart failure refers when ejection is <40%. Normal Blood Ejection is about 50-70%

$$\text{Ejection Fraction} = \frac{\text{Stroke Vol.}}{\text{End Diastole Volume (EDV)}} = \frac{70}{110} = 0.64$$

$$\text{Ejection (\%)} = 64\%$$

 **Systolic heart failure:** Failure of the systole; left ventricle wall unable to generate adequate wall pressure to overcome the aortic pressure or **Afterload**. Systolic heart failure occurs due to hypertension, ischemic heart diseases and cardiomyopathy.

 **Diastolic heart failure:** Reduction of filling or (EDV) due to chronic hypertension, ventricular hypertrophy, congenital heart disease.

 **Feature of the CHF:**

- ✓ Low CO
- ✓ Tachycardia (due to compensatory action)
- ✓ Oedema and Cardiovascular remodelling (due to activation of RAAS)
- ✓ Shortness of breath
- ✓ Weakness

Pharmacology Lectures:

1. CHF: <https://youtu.be/yA67mQKbs9g>
2. Compensatory Pathways Pathophysiology: <https://youtu.be/E-V9F9jgUVc>
3. Anti CHF Drugs: <https://youtu.be/1WEEqsKEDKc>
4. Digitalis MOA: <https://youtu.be/IJK9sQffW7c>
5. Digitalis Pharmacology: <https://youtu.be/4UKsSUIvAr8>

10.2. ANTI CHF DRUGS

1. Relief of congestive/low output symptoms and restoration of cardiac performance

A. Inotropic Drugs (Enhance the Force of contraction)

- ✓ **Cardiac glycoside:** Digoxin, Digitoxin
- ✓ **PDE inhibitors:** amrinone, milrinone
- ✓ **Beta-1 Agonist:** dobutamine, dopamine

B. Diuretics (Relief from Volume overload): Furosemide, thiazides, K-sparing diuretics

C. RAS Inhibitors (Reduce the volume overload, afterload and preload)

- ✓ **ACE Inhibitors (ACEIs):** Enalapril, captopril, ramipril
- ✓ **Angiotensin Receptor Blockers (ARBs):** Losartan, Telmisartan

D. Vasodilators (Reduce afterload and preload): hydralazine, nitrate, nitroprusside, CCBs

E. Beta Blocker: Metoprolol, bisoprolol, carvedilol, Nebivolol

2. Arrest/reversal of disease progression and prolongation of survival, possible with:

- ✓ *ACE inhibitors/ ARBs,*
- ✓ *β blockers*
- ✓ *Aldosterone antagonist—Spironolactone, eplerenone*


3. Newer Agents:


- ✓ **Natriuretic peptide:** Nesiritide,
- ✓ **Endothelin receptor (ET R) Antagonist:** Bosentan, Tezosentan.


10.3. MEDICINAL CHEMISTRY

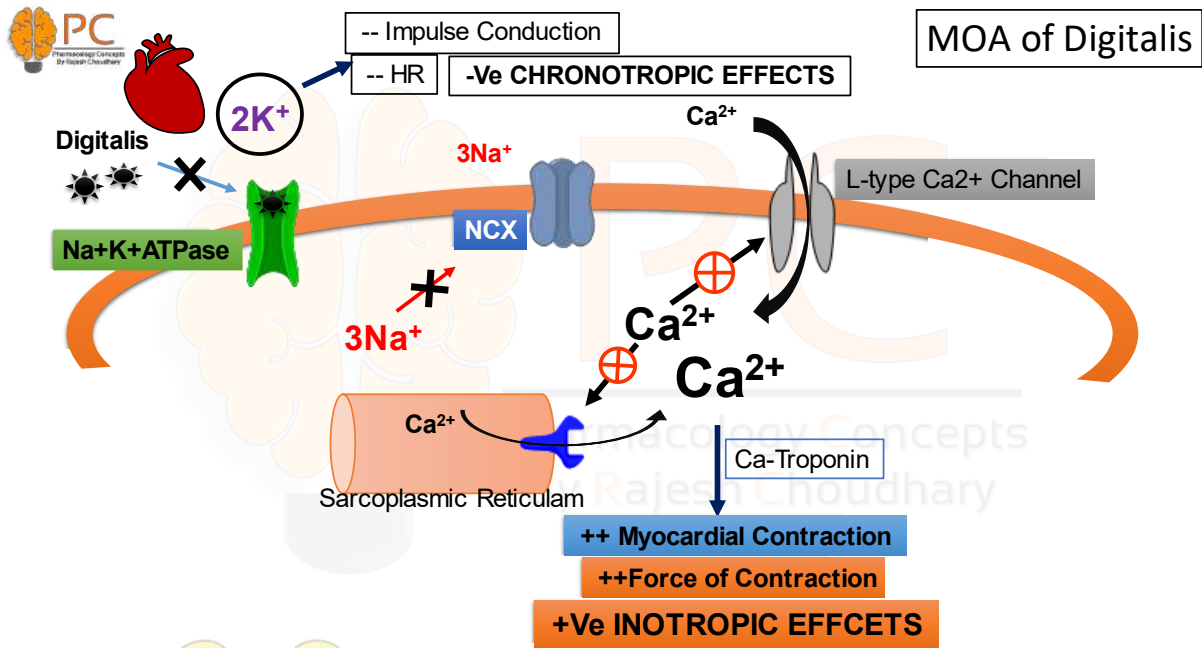
1. Cardiac glycoside:

 **Drugs:** Digoxin, Digitoxin

 **Aglycdn-** Genin (Digitoxigenin and Digoxigenin) **Glycan-** digitoxose

 **+Inotropic Action:** Inhibition of Na⁺K⁺ATpase pump indirectly inhibit NCX which further leads to increasing intracellular Ca²⁺ ion in myocardial tissues

 **-Chronotropic Action:** by hypokalemia and vegal stimulation



PC Uses: CHF, Rapid Atrial Fibrillation

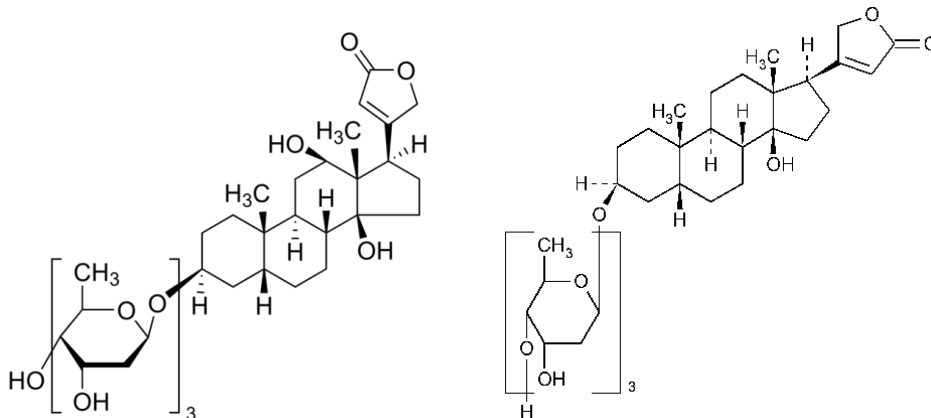
PC Contraindicated In:

- ✓ Arrhythmia
- ✓ Hypokalemic patients
- ✓ Elderly, renal and hepatic dysfunction patient
- ✓ **Wolff Parkinson White Syndrome (arrhythmia)**
- ✓ MI
- ✓ Thyrotoxicity
- ✓ Myxoedema

Pharmacology Concepts
By Rajesh Choudhary




A) Digoxin

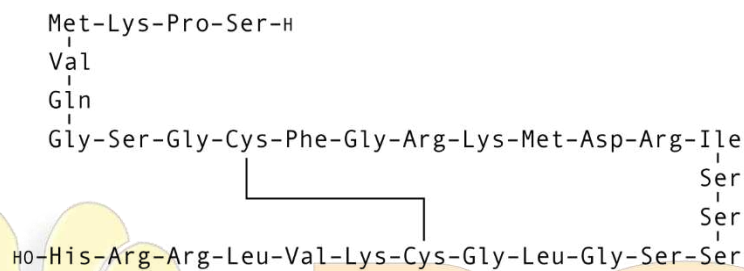
B) Digitoxin






Tridigitoxose-3-tetradecahydrocyclopenta[a]phenanthren-17-yl]-2H-furan-5-one derivatives

2. Natriuretic peptide: Nesiritide

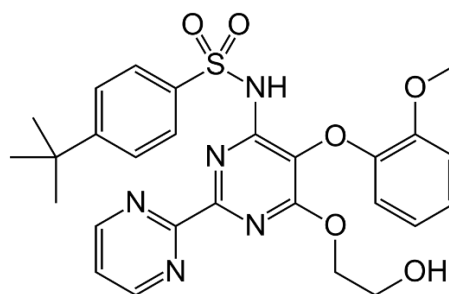
-  It is a recombinant 32-amino acid human B-type natriuretic peptide, a type of hormone released by cardiac muscle cells in the heart ventricles. They show the diuretic effects as well as reduce the blood pressure.
-  **MOA:** act on NP receptors, a guanylyl cyclase enzyme linked receptor and promote the cGMP mediated action.
-  **Uses:** it may be useful in CHF, hypertension.



3. Endothelin Receptor (ET R) Antagonist

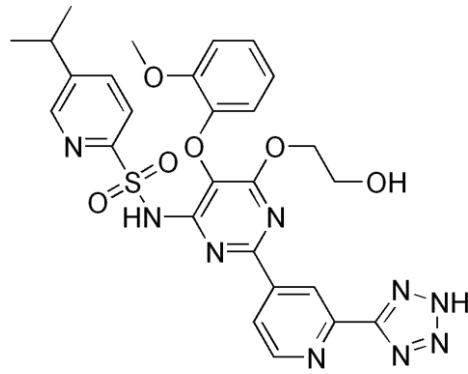
-  **Drugs:** Bosentan, Tezosentan
-  **MOA:** These are the newer class of drug which block the ET receptors which responsible for the vasoconstriction.
-  **Uses:** They may be used in CHF, pulmonary hypertension, and systemic sclerosis

A) Bosentan,

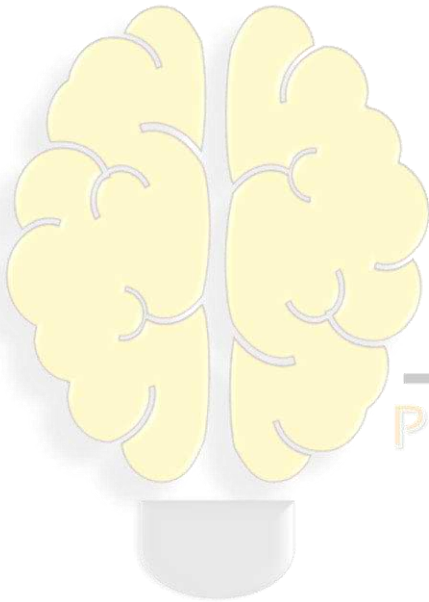


4-tert-butyl-N-[6-(2-hydroxyethoxy)-5-(2-methoxyphenoxy)-2-pyrimidin-2-yl pyrimidin-4-yl] benzene sulfonamide

B) Tezosentan



***N*-[6-(2-hydroxyethoxy)-5-(2-methoxyphenoxy)-2-[2-(2*H*-tetrazol-5-yl) pyridin-4-yl] pyrimidin-4-yl]-5-propan-2-yl pyridine-2-sulfonamide**



PC

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