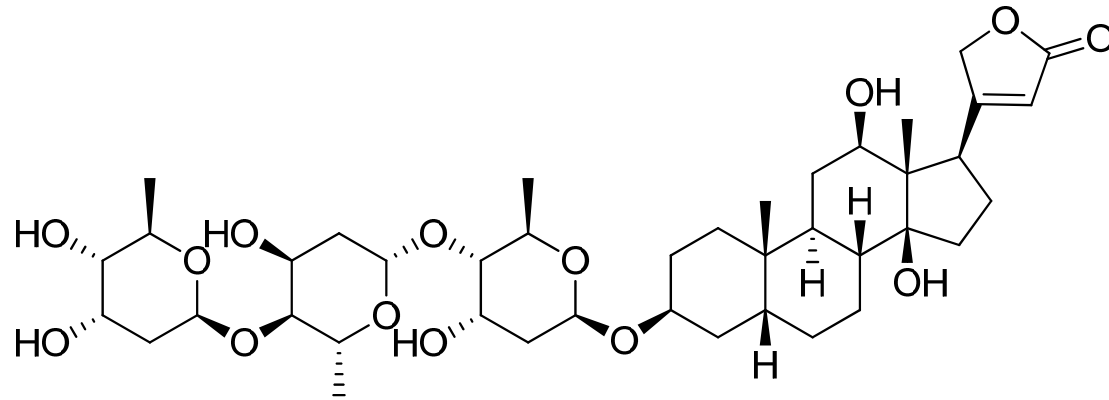


Digoxin

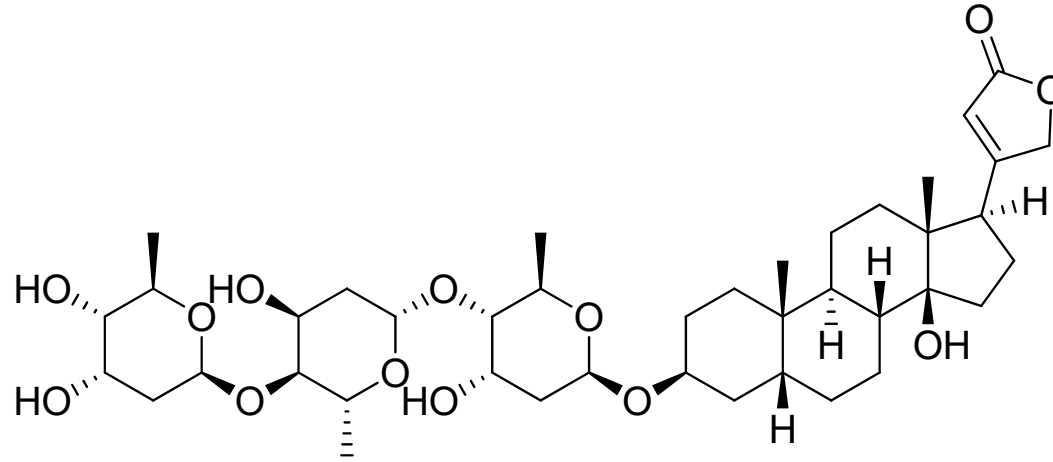


MOA: Digoxin exerts hemodynamic, electrophysiologic, and neurohormonal effects on the cardiovascular system. It reversibly inhibits the Na-K ATPase enzyme, leading to various beneficial effects. The Na-K ATPase enzyme functions to maintain the intracellular environment by regulating the entry and exit of sodium, potassium, and calcium (indirectly). Na-K ATPase is also known as the *sodium pump*. The inhibition of the sodium pump by digoxin increases intracellular sodium and increases the calcium level in the myocardial cells, causing an increased contractile force of the heart. This improves the left ventricular ejection fraction (EF), an important measure of cardiac function.

Uses: Digoxin is indicated in the following conditions:

- 1) For the treatment of mild to moderate heart failure in adult patients.
- 2) To increase myocardial contraction in children diagnosed with heart failure.
- 3) To maintain control ventricular rate in adult patients diagnosed with chronic atrial fibrillation.

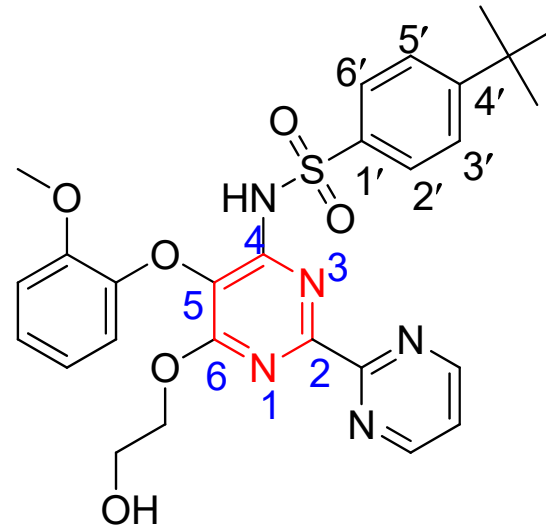
Digitoxin



MOA: Digitoxin inhibits the Na-K-ATPase membrane pump, resulting in an increase in intracellular sodium and calcium concentrations. Increased intracellular concentrations of calcium may promote activation of contractile proteins (e.g., actin, myosin). Digitoxin also acts on the electrical activity of the heart, increasing the slope of phase 4 depolarization, shortening the action potential duration, and decreasing the maximal diastolic potential.

Uses: For the treatment and management of congestive cardiac insufficiency, arrhythmias and heart failure.

Bosentan

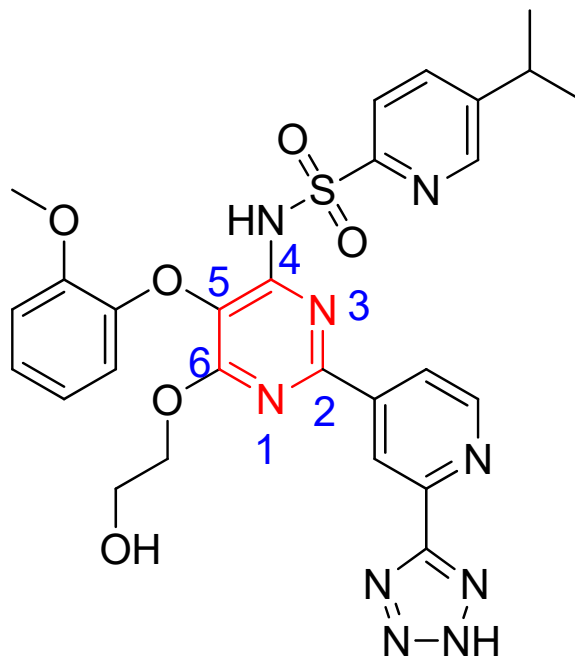


IUPAC: 4'-tert-butyl-N-[6-(2-hydroxyethoxy)-5-(2-methoxyphenoxy)-2-(pyrimidin-2-yl)pyrimidin-4-yl]benzene-1-sulfonamide

MOA: Endothelin-1 (ET-1) is a neurohormone, the effects of which are mediated by binding to ET_A and ET_B receptors in the endothelium and vascular smooth muscle. It displays a slightly higher affinity towards ET_A receptors than ET_B receptors. ET-1 concentrations are elevated in plasma and lung tissue of patients with pulmonary arterial hypertension, suggesting a pathogenic role for ET-1 in this disease. Bosentan is a specific and competitive antagonist at endothelin receptor types ET_A and ET_B .

Uses: Used in the treatment of pulmonary arterial hypertension (PAH), to improve exercise ability and to decrease the rate of clinical worsening.

Tezosentan



IUPAC: N-[6-(2-hydroxyethoxy)-5-(2-methoxyphenoxy)-2-[2-(2H-1,2,3,4-tetrazol-5-yl)pyridin-4-yl]pyrimidin-4-yl]-5-(propan-2-yl)pyridine-2-sulfonamide

MOA: Tezosentan is a non-selective ET_A and ET_B receptor antagonist. It acts as a vasodilator and was designed as a therapy for patients with acute heart failure.

Nesiritide

Nesiritide is a 32 amino acid recombinant human B-type natriuretic peptide. Nesiritide is a medication used to treat acutely decompensated congestive heart failure with dyspnea at rest or with minimal exertion (such as talk, eating or bathing).

MOA: It binds to the particulate guanylate cyclase receptor of vascular smooth muscle and endothelial cells, leading to increased intracellular concentrations of guanosine 3'5'-cyclic monophosphate (cGMP) and smooth muscle cell relaxation. Cyclic GMP serves as a second messenger to dilate veins and arteries. Nesiritide has been shown to relax isolated human arterial and venous tissue preparations that were precontracted with either endothelin-1 or the alpha-adrenergic agonist, phenylephrine.

Uses: For the intravenous treatment of patients with acutely decompensated congestive heart failure who have dyspnea at rest or with minimal activity.