Unit-3
Medicinal Chemistry- II

B.Pharma 5th Sem Notes

Unit: 3

1. **Anti-arrhythmic Drugs:** Quinidine sulphate, Procainamide hydrochloride, Disopyramide phosphate*, Phenytoin sodium, Lidocaine hydrochloride, Tocainide hydrochloride, Mexiletine hydrochloride, Lorcainide hydrochloride, Amiodarone, Sotalol.
2. **Anti-hyperlipidemic agents:** Clofibrate, Lovastatin, Cholesteramine and Cholestipol
3. **Coagulant & Anticoagulants:** Menadione, Acetomenadione, Warfarin*, Anisindione, clopidogrel
4. **Drugs used in Congestive Heart Failure:** Digoxin, Digitoxin, Nesiritide, Bosentan, Tezosentan.

1. **Anti-arrhythmic Drugs:** Quinidine sulphate, Procainamide hydrochloride, Disopyramide phosphate*, Phenytoin sodium, Lidocaine hydrochloride, Tocainide hydrochloride, Mexiletine hydrochloride, Lorcainide hydrochloride, Amiodarone, Sotalol.

Anti-arrhythmic Drugs:

- Anti-arrhythmic drugs are medications used to treat problems with the heart's rhythm.
- They help to control or correct irregular heartbeats, making sure the heartbeats in a regular and normal pattern.
- They work by adjusting the heart's electrical signals to fix or stop irregular heartbeats.
- They are used in Arrhythmic Drugs

Arrhythmia:

- An arrhythmia, also known as dysrhythmia, is an abnormal heartbeat.
- It occurs when the electrical signals that coordinate heartbeats malfunction.
- This can cause the heart to beat too fast, too slow, or irregularly.

Types of Arrhythmia

- **Tachycardia:** Rapid heart rate (over 100 beats per minute).
- **Bradycardia:** Slow heart rate (less than 60 beats per minute).
- **Atrial fibrillation:** Irregular and rapid heartbeat.
- **Ventricular fibrillation:** Rapid, uncoordinated contractions of the heart's lower chambers.

Causes of Arrhythmia

- Heart disease
- High blood pressure
- Thyroid problems
- Electrolyte imbalances
- Certain medications
- Caffeine and alcohol consumption
- Stress

Symptoms of Arrhythmia

- Palpitations
- Chest pain
- Shortness of breath
- Dizziness or lightheadedness
- Fatigue
- Fainting

Diagnosis of Arrhythmia

- Electrocardiogram (ECG)
- Holter monitor
- Event recorder
- Echocardiogram
- Blood tests

Classification of Antiarrhythmic Drugs:

Class I: Sodium Channel Blockers

These drugs interfere with the sodium channels in the heart, affecting the speed at which electrical impulses travel through the heart. They are further subdivided into three subclasses:

- **Class Ia:** Quinidine sulfate, Procainamide hydrochloride, Disopyramide phosphate
- **Class Ib:** Phenytoin sodium, Lidocaine hydrochloride, Mexiletine HCL, Tocainide HCL.
- **Class Ic:** Lorcainide HCL.

Class II: Beta-Blockers

These drugs block the effects of adrenaline and noradrenaline on the heart, slowing down heart rate and reducing the force of contractions. Examples include:

- Propranolol
- Atenolol

- Metoprolol
- Bisoprolol

Class III: Potassium Channel Blockers

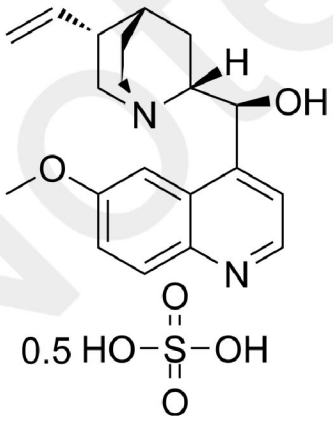
These drugs prolong the duration of the heart's electrical activity, affecting the rate and rhythm. Examples include:

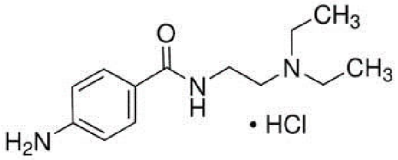
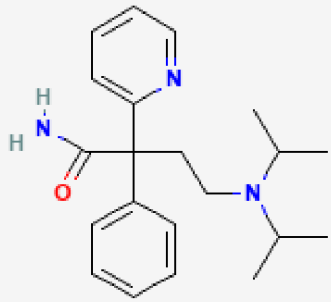
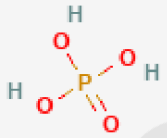
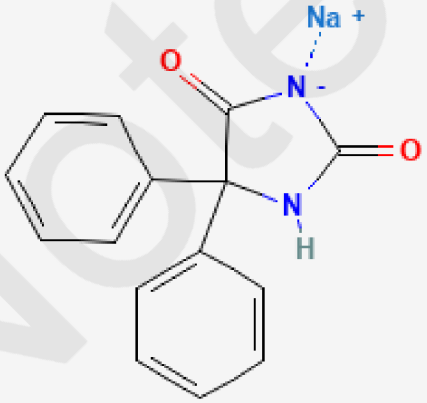
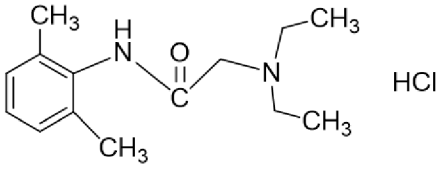
- Amiodarone
- Sotalol
- Dofetilide
- Ibutilide

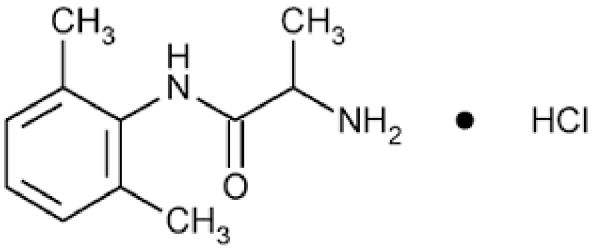
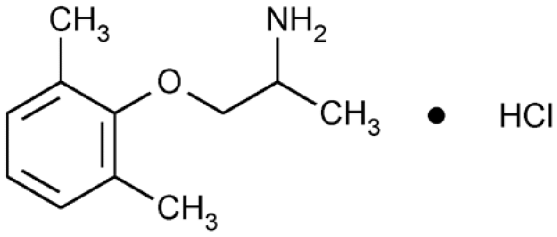
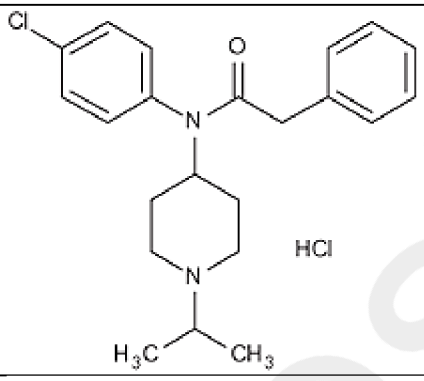
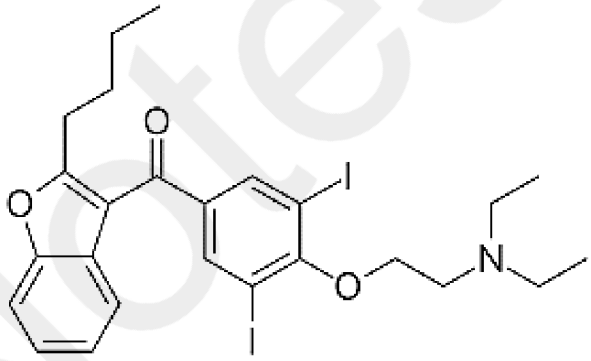
Class IV: Calcium Channel Blockers

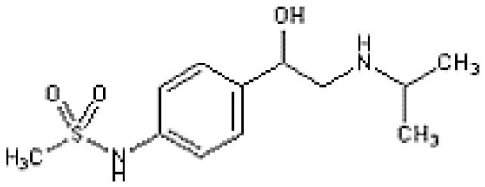
These drugs block calcium channels in the heart, slowing down heart rate and reducing blood pressure. Examples include:

- Verapamil
- Diltiazem

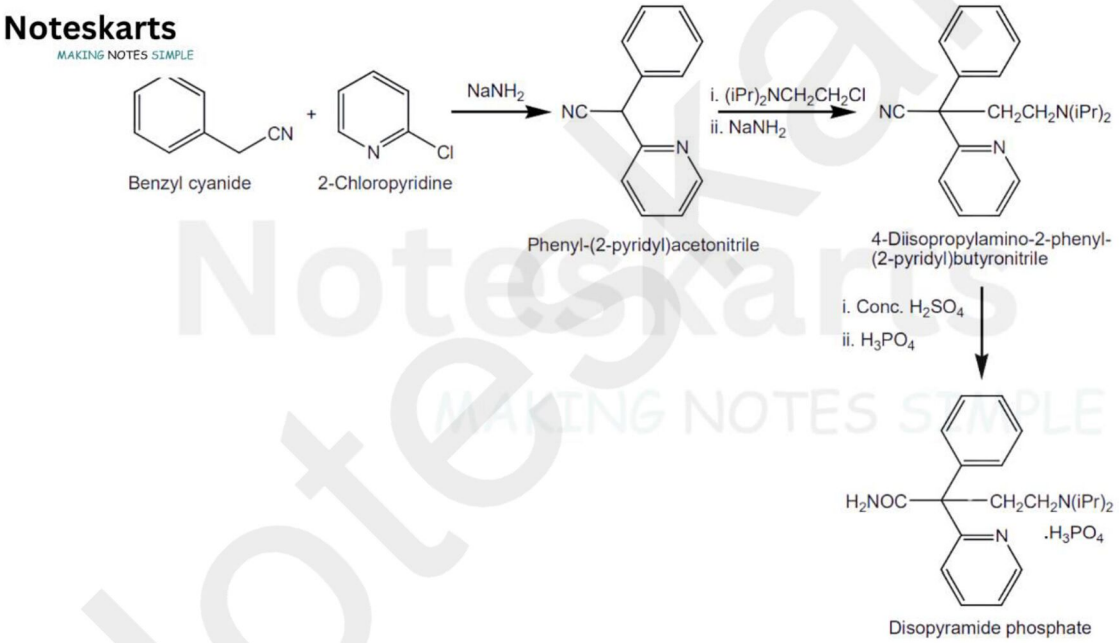
Drug	Structure	Mechanism of Action	Uses
Quinidine Sulphate		Blocks sodium channels (Class Ia antiarrhythmic), prolonging the action potential and refractory period.	Used to treat atrial fibrillation, ventricular arrhythmias.

Procainamide Hydrochloride		Blocks sodium channels (Class Ia antiarrhythmic), prolonging the action potential and refractory period.	Used in the treatment of ventricular tachycardia and atrial arrhythmias.
Disopyramide Phosphate	 	Blocks sodium channels (Class Ia antiarrhythmic), prolonging the action potential and refractory period.	Used for ventricular arrhythmias, especially ventricular tachycardia.
Phenytoin Sodium		Stabilizes neuronal membranes and reduces repetitive firing by blocking sodium channels.	Primarily used as an anticonvulsant; also used for arrhythmias (particularly in digitalis toxicity).
Lidocaine Hydrochloride		Blocks sodium channels (Class Ib antiarrhythmic), shortening the action potential.	Used for ventricular arrhythmias, especially post-myocardial infarction.

Tocainide Hydrochloride		Blocks sodium channels (Class Ib antiarrhythmic), shortening the action potential.	Used for ventricular arrhythmias.
Mexiletine Hydrochloride		Blocks sodium channels (Class Ib antiarrhythmic), shortening the action potential.	Used for chronic ventricular arrhythmias.
Lorcainide Hydrochloride		Blocks sodium channels (Class Ic antiarrhythmic), with minimal effect on the action potential duration.	Used for life-threatening ventricular arrhythmias.
Amiodarone		Blocks potassium channels (Class III antiarrhythmic), prolonging the action potential and refractory period; also affects sodium and calcium channels and has non-competitive alpha- and beta-blocking properties.	Used in the treatment of ventricular and atrial arrhythmias, especially in life-threatening cases.

Sotalol		Non-selective beta-blocker that also prolongs the action potential duration by blocking potassium channels.	Used for ventricular arrhythmias and to maintain sinus rhythm in atrial fibrillation.

Synthesis of Disopyramide phosphate:



Mechanism of Action of Disopyramide Phosphate:

- It targets sodium channels to inhibit conduction.
- It decreases the rate of diastolic depolarization (phase 4) in cells with augmented automaticity, decreases the upstroke velocity (phase 0) and increases the action potential duration of normal cardiac cells, decreases the disparity in refractoriness between infracted and adjacent normally perfused myocardium.
- Disopyramide also has an anticholinergic effect on the heart which accounts for many adverse side effects.

2. Anti-hyperlipidemic agents: Clofibrate, Lovastatin, Cholesteramine and Cholestipol

Anti-hyperlipidemic agents:

- Anti-hyperlipidemic agents, also known as lipid-lowering drugs, are medications used to reduce elevated levels of lipids (fats) in the blood.
- These drugs are primarily used to manage hyperlipidemia, a condition that increases the risk of cardiovascular diseases like heart attack and stroke.

Or

- Antihyperlipidemic agents promote reduction of lipid levels in the blood. Some antihyperlipidemic agents aim to lower the levels of low-density lipoprotein (LDL) cholesterol, some reduce triglyceride levels, and some help raise the high-density lipoprotein (HDL) cholesterol.

Hyperlipidemia:

- **Hyperlipidemia**, also known as high cholesterol, is a condition where there are abnormally high levels of fats (lipids) in the blood.
- These lipids, including cholesterol and triglycerides, can build up in the arteries, leading to a condition called atherosclerosis. This can increase the risk of heart attack, stroke, and other cardiovascular problems.

OR

- Hyperlipidemia (high cholesterol) is an excess of lipids or fats in your blood.
- This can increase your risk of heart attack and stroke because blood can't flow through your arteries easily.
- Adding exercise and healthy foods can lower your cholesterol.

Causes:

- Smoking.
- Drinking a lot of alcohol.

- Eating foods that have a lot of saturated fats or trans fats.
- Sitting too much instead of being active.
- Being stressed.
- Inheriting genes that make your cholesterol levels unhealthy.

Lipids:

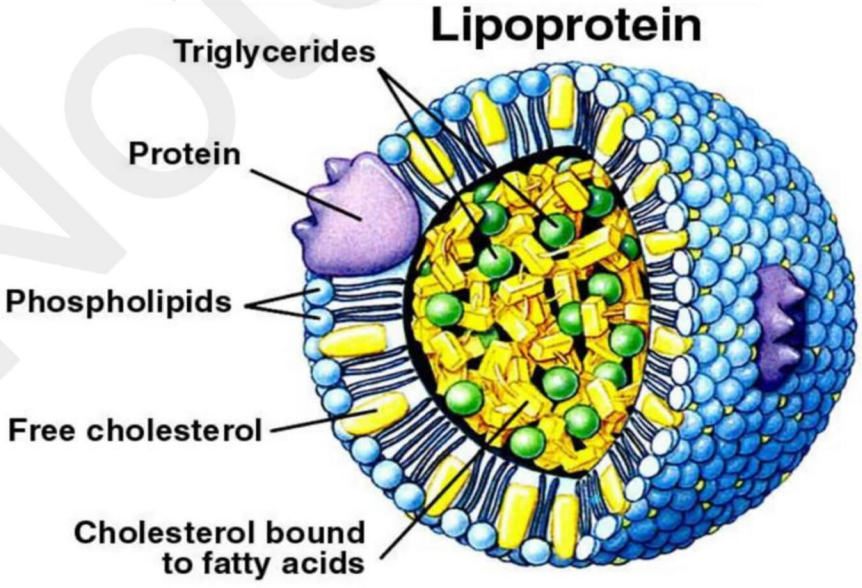
Lipids are organic compounds that contain hydrogen, carbon, and oxygen atoms, which form the framework for the structure and function of living cells.

These are important for our body now these are present in our body in three forms:-

1. **Cholesterol:** Synthesis of bile acid
2. **Triglycerides:** Glycerol + Free fatty acid → Source of energy in body.
3. **Phospholipids:** Major components of cell membrane

These Lipids are insoluble in blood plasma so they have to be transported throughout the body in the form of protein complex which is known as Lipoproteins.

Lipoproteins:



- **Lipoproteins** are complex particles composed of lipids and proteins that transport lipids in the bloodstream.
- The important role in lipid metabolism and distribution throughout the body.

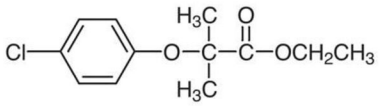
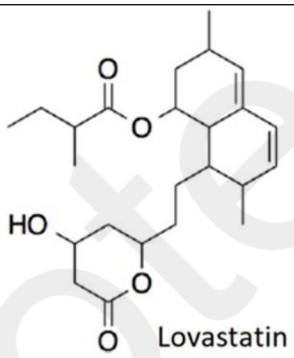
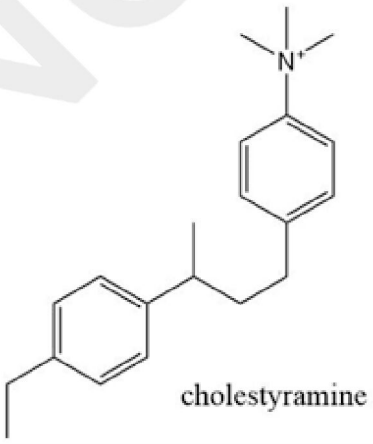
Types of Lipoproteins:

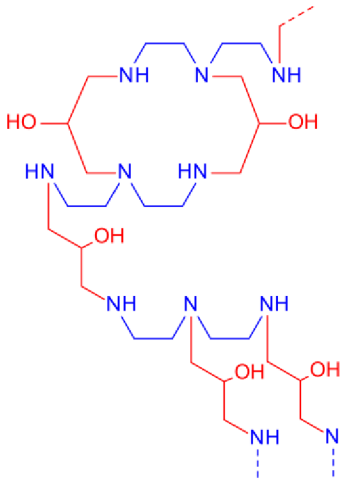
- **Chylomicrons:**
  - Largest and least dense lipoproteins.
  - Transport dietary triglycerides and cholesterol from the intestines to tissues.
- **Very-low-density lipoproteins (VLDL):**
  - Synthesized in the liver and transport endogenous triglycerides to peripheral tissues.
- **Intermediate-density lipoproteins (IDL):**
  - Formed from the breakdown of VLDL.
  - Transport both triglycerides and cholesterol.
- **Low-density lipoproteins (LDL):**
  - Main carrier of cholesterol in the blood.
  - Deliver cholesterol to cells for various functions.
  - High levels of LDL are associated with increased risk of cardiovascular disease.
- **High-density lipoproteins (HDL):**
  - "Good cholesterol" that helps remove excess cholesterol from the bloodstream.
  - Transport cholesterol back to the liver for excretion.

Functions of Lipoproteins:

- **Lipid transport:** Deliver lipids (triglycerides, cholesterol) to tissues for energy, cell membrane synthesis, and hormone production.

- **Cholesterol homeostasis:** Maintain appropriate levels of cholesterol in the blood.
- **Cardiovascular health:** High levels of LDL are associated with increased risk of heart disease, while high levels of HDL are associated with reduced risk.

Drug	Structure	Mechanism of Action	Uses
Clofibrate		Activates peroxisome proliferator-activated receptor alpha (PPAR-α). Increases lipoprotein lipase activity Enhances breakdown of triglycerides	Hyperlipidemia. Hypertriglyceridemia.
Lovastatin		Inhibits HMG-CoA reductase. Reduces cholesterol synthesis in the liver. Increases LDL receptors on hepatocytes	Hypercholesterolemia Prevention of cardiovascular events.
Cholestyramine		Binds bile acids in the intestine. Prevents their reabsorption. Increases conversion of cholesterol to bile acids	Hypercholesterolemia Relief of pruritus due to partial biliary obstruction.

Colestipol		Binds bile acids in the intestine. Prevents their reabsorption. Increases cholesterol catabolism to bile acids	Hypercholesterolemia Adjunct therapy in the management of hyperlipidemia.

Note Area:

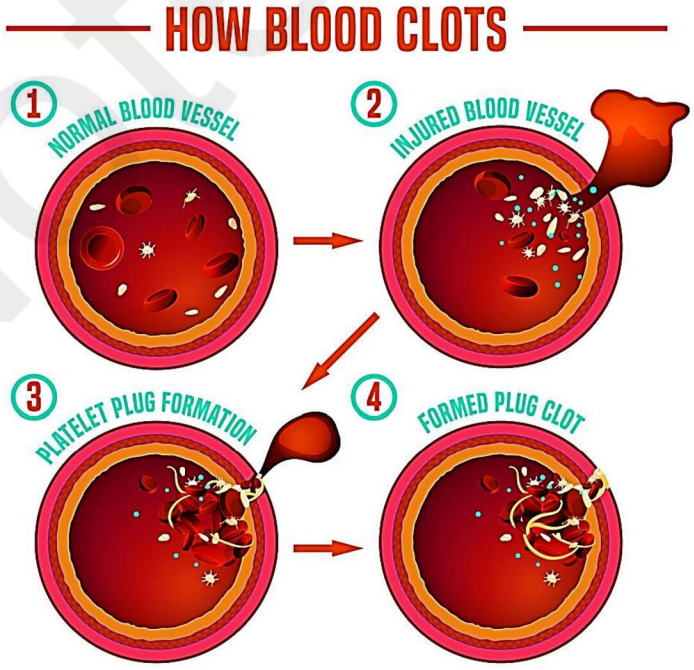
3. Coagulant & Anticoagulants: Menadione, Acetomenadione, Warfarin*, Anisindione, clopidogrel

Coagulant & Anticoagulants:

- **Coagulants** promote blood clotting. They help to form a clot at the site of an injury to stop bleeding.
- **Anticoagulants** prevent blood clotting. They are used to prevent blood clots from forming in blood vessels, which can lead to serious health problems like stroke or heart attack.

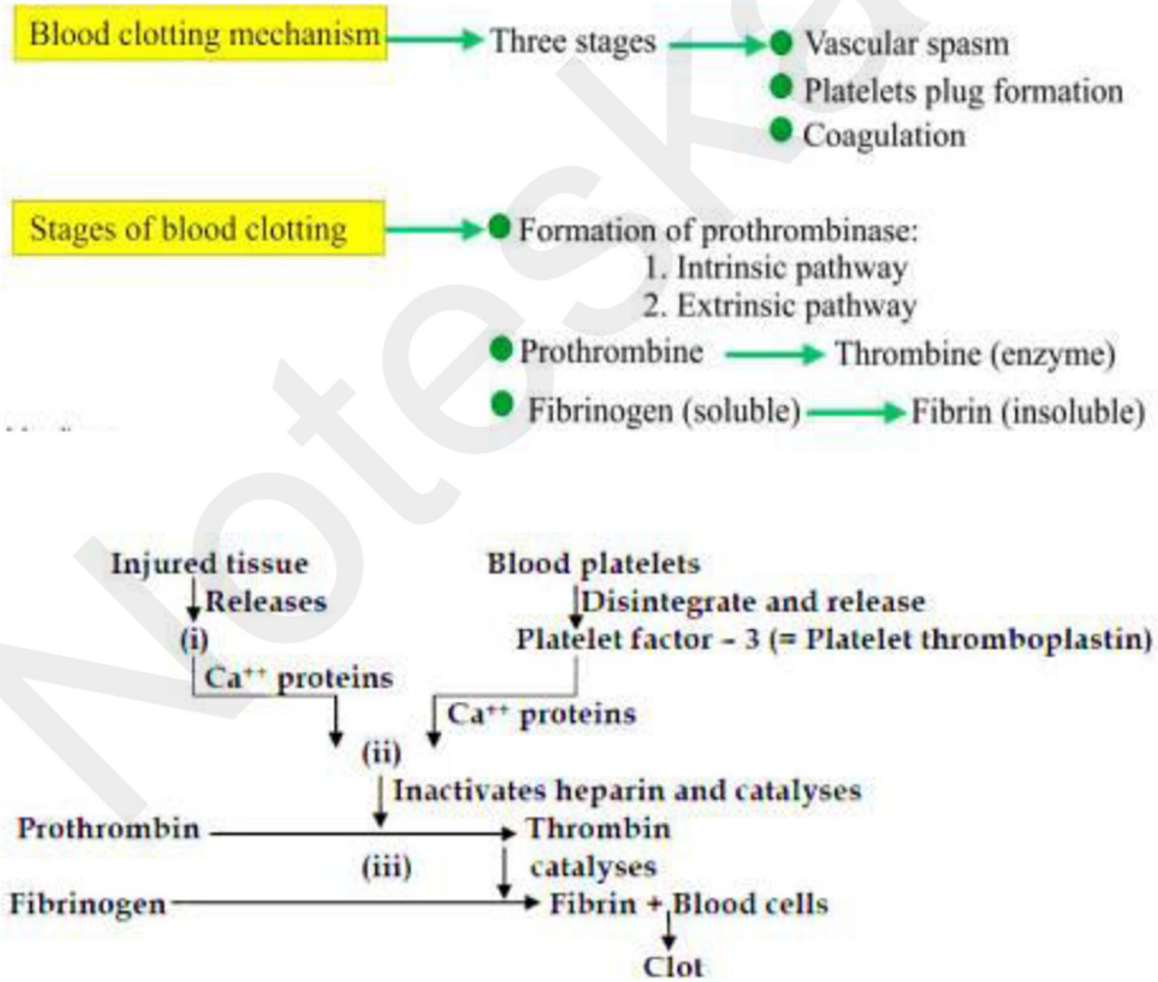
Blood clotting:

- Blood clotting, also known as coagulation, is a process that prevents excessive bleeding when a blood vessel is damaged.
- It involves platelets and proteins in plasma working together to form a clot over the injury.
- The clot creates a strong seal inside the wound, prevents blood from leaking out, and acts as scaffolding for new tissues to grow onto during the healing process.
- The body will usually naturally dissolve the clot after the injury has healed.



Mechanism of Blood Clotting:

1. **Intrinsic pathway:**
   - The intrinsic pathway can be initiated by events that take place within the lumen of blood vessels.
   - This requires only elements (clotting factors, Ca++ platelet surface, etc.) found within or intrinsic to the vascular system.
2. **Extrinsic pathway:**
   - The extrinsic pathway is the other route to coagulation.
   - It requires tissue factor (tissue thromboplastin), a substance that is extrinsic to or not normally cumulating in the vessel.
   - Tissue factor is released when the vessel wall is ruptured.

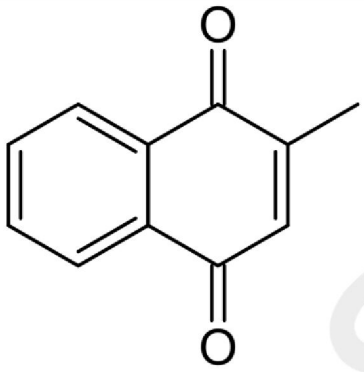
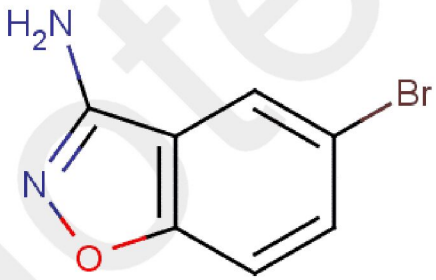


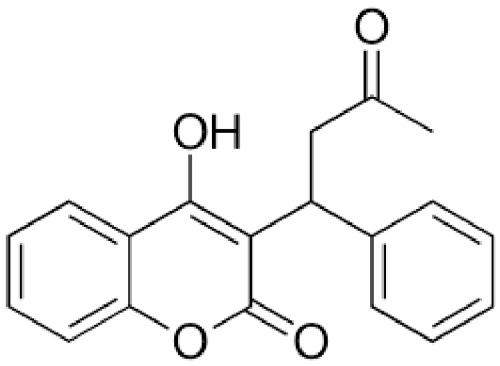
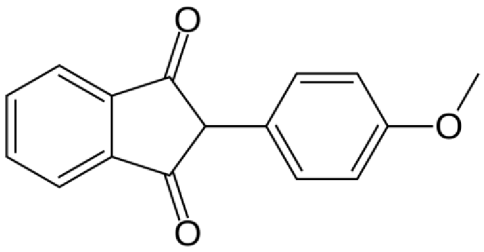
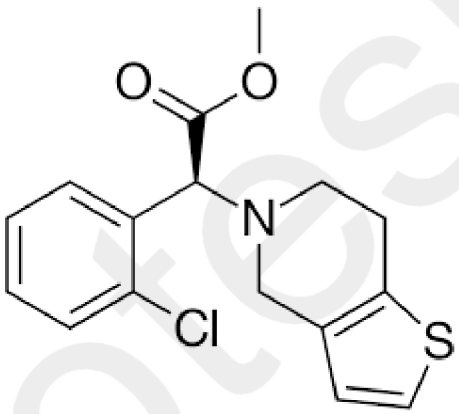
Coagulant:

- Menadione, Acetomenadione

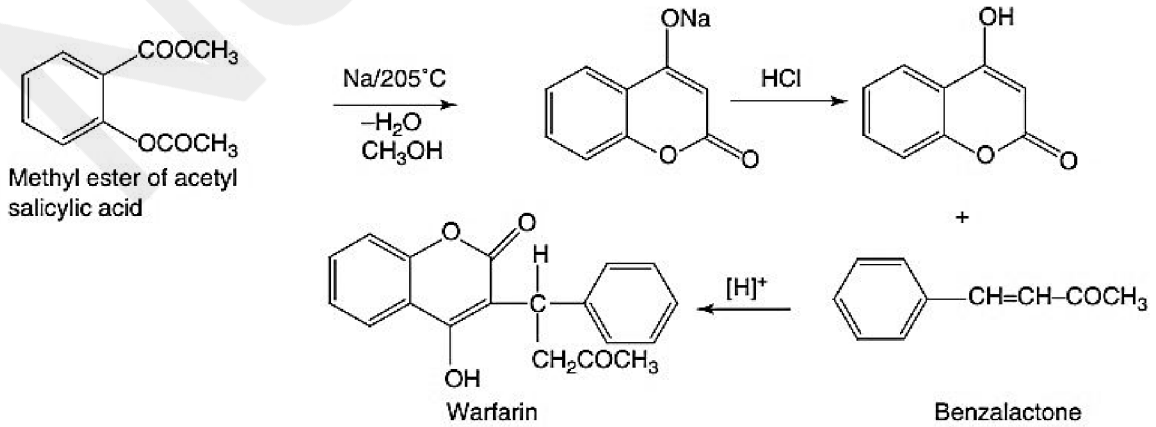
Anticoagulants:

- Warfarin*, Anisindione, clopidogrel.

Drug	Structure	Mechanism of Action	Uses
Menadione		Acts as a precursor to active vitamin K Promotes the synthesis of clotting factors (II, VII, IX, X) in the liver	Hypoprothrombinemia Vitamin K deficiency
Acetomenadione		Similar to menadione; promotes the synthesis of clotting factors Used for vitamin K deficiency	Hypoprothrombinemia Vitamin K deficiency

Warfarin		Inhibits vitamin K epoxide reductase Prevents the activation of vitamin K-dependent clotting factors	Prevention of thrombosis and thromboembolism Atrial fibrillation Venous thromboembolism
Anisindione		Similar to warfarin; inhibits vitamin K epoxide reductase Prevents the activation of clotting factors	Anticoagulant therapy (less commonly used due to side effects)
Clopidogrel		Inhibits the P2Y12 component of ADP receptors on platelet surface Prevents platelet aggregation	Prevention of atherosclerotic events Stroke prevention Post-stent thrombosis prevention

Synthesis of Warfirine:



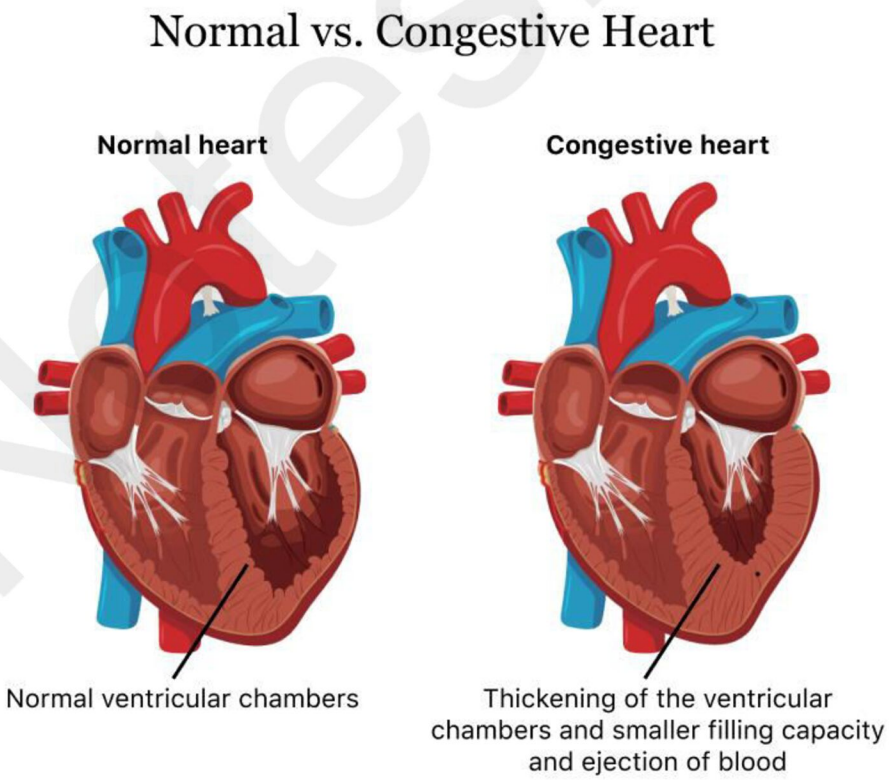
4. Drugs used in Congestive Heart Failure: Digoxin, Digitoxin, Nesiritide, Bosentan, Tezosentan.

Congestive Heart Failure:

- Congestive heart failure (CHF) is a complex clinical syndrome characterized by inefficient myocardial performance, resulting in compromised blood supply to the body.
- CHF results from any disorder that impairs ventricular filling or ejection of blood to the systemic circulation.

Or

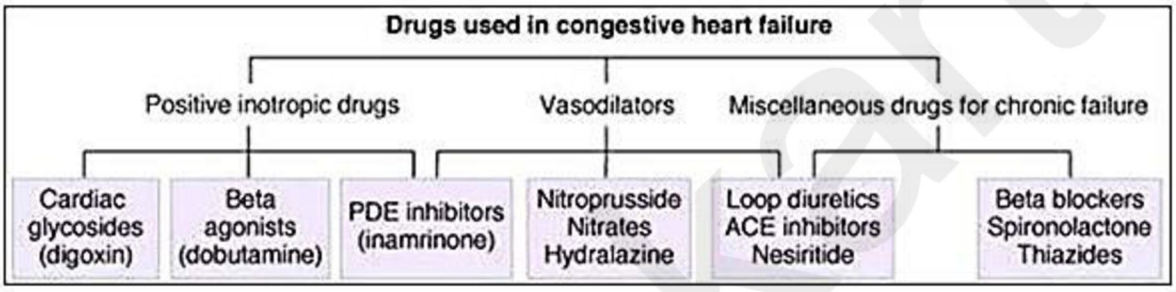
- Congestive heart failure (CHF) is a syndrome that occurs when the heart can't pump enough blood to meet the body's needs.
- This can happen when the heart becomes too weak or stiff, or when there's an impairment in the heart's ability to fill with and pump blood.

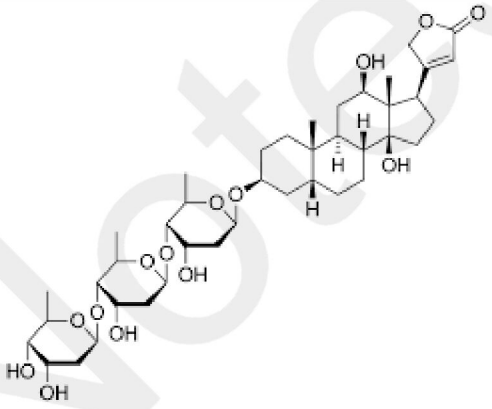


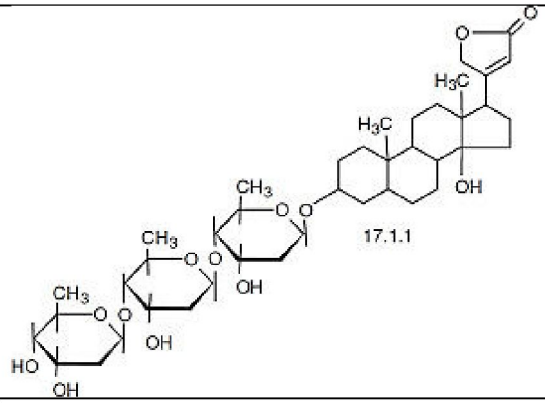
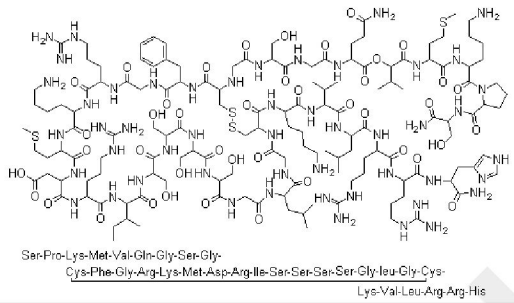
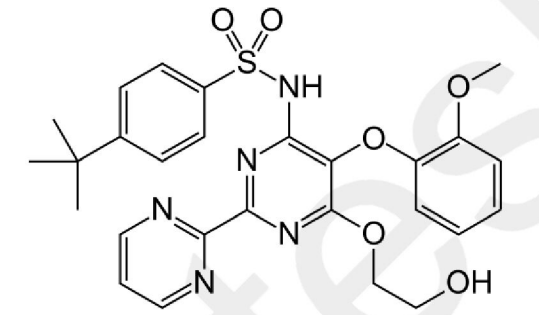
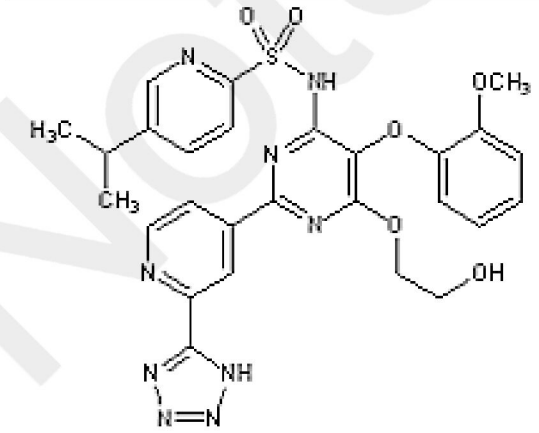
Symptoms:

- Shortness of breath
- Excessive fatigue
- Bilateral leg swelling
- Chest constriction
- Feeling sleepy after eating
- Feeling weak in the legs when walking

Drug used in Congestive Heart Failure:



Drug	Structure	Mechanism of Action	Uses
Digoxin		Inhibits Na+/K+-ATPase pump Increases intracellular calcium concentration Enhances cardiac contractility (positive inotropic effect) Decreases heart rate (negative chronotropic effect)	Heart failure Atrial fibrillation

Digitoxin		Similar to Digoxin; inhibits Na+/K+-ATPase pump Increases intracellular calcium concentration Enhances cardiac contractility	Heart failure Atrial fibrillation
Nesiritide		Binds to guanylate cyclase receptors on vascular smooth muscle Increases intracellular cGMP Promotes vasodilation, natriuresis, and diuresis	Acute decompensated heart failure
Bosentan		Blocks endothelin-1 receptors (ETA and ETB) Reduces vasoconstriction and lowers blood pressure in pulmonary arteries	Pulmonary arterial hypertension (PAH)
Tezosentan		Blocks endothelin-1 receptors (ETA and ETB) Used in the management of acute heart failure	Acute heart failure (investigational)

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