MEDICINAL CHEMISTRY-II

UNIT 3 NOTES

- Anti Arrhythmic Drugs
- Anti Hyperlipidemic Drugs
- Coagulant & Anticoagulant
- Congestive Heart Failure

IMPERFECT PHARMACY

NOTES AVAILABLE AT :

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ANTI - ARRHYTHMIC AGENTS

- Anti - Arrythmic Agents are medications used to treat Arrythmias. which are abnormal heart beats that can be too fast, too slow or irregular.
- These drugs work by modifying the electrical activity of the Heart to restore or maintain a normal rythm.

ARRYTHMIA

- Arrythmia refers to an abnormality in the rythm of heart's electrical activity, which can cause the heart to beat too fast, too slow or irregularly
- Generally Arrythmias are harmless. However long term may result into a weak or damaged heart.

CARDIAC ELECTROPHYSIOLOGY

- Deviation from normal pattern of cardiac rythm of heart is known as Arrythmia.
- The resting membrane potential of cardiac cell as about -90 mV.
- It is determined mainly by Sodium, Potassium, Calcium & Chloride Ions.
- Normally K^+ is more in intracellular fluid while Na^+ is more in Extracellular fluid.

ELECTROPHYSIOLOGY OF HEART

- Electrophysiology of heart refers to the study of electrical processes that govern the function of the heart, particularly how the generates and conduct electrical impulses
- These electrical impulses coordinate the contraction of the heart muscles, ensuring proper blood flow.
- It consit of 5 Phases :

① Phase 0
② Phase 1
③ Phase 2
④ Phase 3
⑤ Phase 4

~~Phase~~

Phase 0

- The phase is characterized by a rapid upstroke in membrane potential.
- It is caused by sudden opening of voltage gated sodium (Na^+) channels, leading to a large influx of Na^+ ions
- The cell membrane potential becomes more positive, moving around -90 mV to + 30 mV.
- This triggers muscle contraction.

Phase 1

- Na^+ channels closes, and there is a transient outward flow of potassium ions (K^+) through k^+ channels
- This creates a little, small dip in membrane potential.
- This phase is known as Initial or Partial Repolarization.

Phase 2

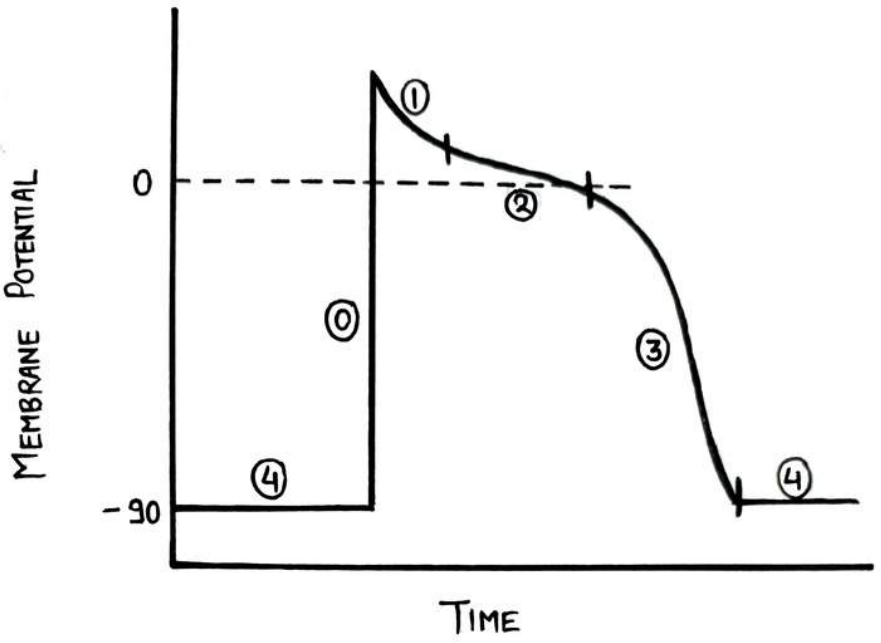
- It is known as Plateau Phase.
- Ca^{2+} channels, allowing Ca^{2+} to enter the cell slowly, while K^+ continues to exit.
- L-type Ca^{2+} channels open, while some K^+ channels remain open.
- The inflow of Ca^{2+} balances the outflow of K^+, causing the membrane potential to remain relatively stable.
- This Plateau phase prolongs the action potential, ensuring sustained contraction of heart muscle necessary for effective pumping.

Phase 3

- Ca^{2+} channels close, while K^+ continues to leave the cell.
- K^+ channels dominate as Ca^{2+} channels close.
- The membrane potential returns to its resting state due to continued efflux of K^+.
- The cell repolarizes, preparing for next cycle of depolarization.

Phase 4

- The cell remains at its resting membrane potential until it is depolarize again by a new stimulus.
- K^+ channels maintain the resting membrane potential by allowing K^+ to flow out, while (Na^+/K^+ ATPase) actively maintain ion gradients.
- The cell is in its resting state at round -90 mV, awaiting the next depolarization phase.



Phases Of Action Potential

Types

Generally it is of 4 types :

- Bradycardia
- Tachycardia
- Atrial Fibrillation
- Ventricular Fibrillation

Causes

- Electrolyte Imbalances (potassium, Calcium)
- Coronary Artery Disease
- High Blood Pressure
- Stress
- Thyroid Disorders.
- Medications

Symptoms

- Palpitations (Feeling of Fast or Irregular Heartbeat)
- Dizziness
- Shortness of Breath
- Chest Pain
- Fatigue

CLASSIFICATION OF ANTIARRYTHMIC AGENTS

Anti- Arrythmic Agents can be classified as follows :

① Class I (Na^+ Channel Blockers)

- IA (Moderate) : Quinidine Sulphate, Procainamide HCl, Disopyramide HCl*
- IB (Weak) : Lidocaine HCl, Phenytoin Sodium, Tocainide HCl, Mexiletine HCl
- IC (Strong) : Lorcainide HCl

② Class II (β Blockers)

③ Class III (K^+ Channel Blockers)

- Amiodarone
- Sotalol

④ Class IV (Ca^{2+} Blockers)

① CLASS I (SODIUM CHANNEL BLOCKERS)

- Sodium Channel Blockers are a class of Antiarrythmic Agents used to manage various cardiac arrythmias.
- They work by inhibiting the influx of sodium ions during depolarization phase of cardiac action potential which stabilizes the cardiac membrane & reduces excitability.

Mechanism Of Action

They work by blocking Na^+ channels & slows down the rate of depolarization, which can prolong the refractory period & prevent abnormal electrical activity.

Classes

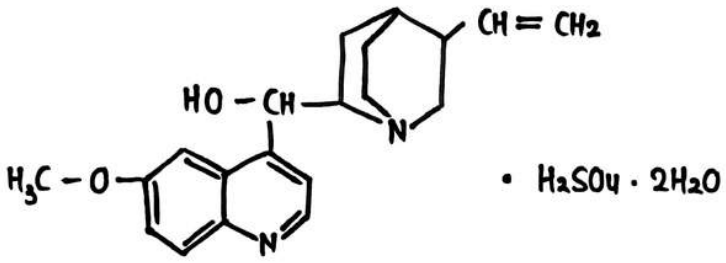
ⓐ Class IA :
- They are intermediate sodium channel blockers
- They block Na^+ as well as k^+ channels & prolongs the action potential.
- Example : ① Quinidine Sulphate
  ② Procainamide HCl
  ③ Disopyramide Phosphate *

ⓑ Class IB :
- They are weak sodium channel blockers.
- They & shorten action potential duration.
- Example : ① Phenytoin Sodium
  ② Lidocaine HCl
  ③ Tocainide HCl
  ④ Mexiletine HCl

© **Class IC** :
- They are strong sodium channel blockers.
- They slows conduction with minimal effect on action potential duration.
- Example : Lorcainide HCl

DRUGS

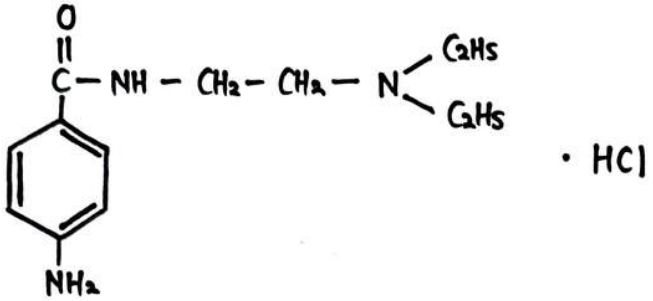
① QUINIDINE SULPHATE



• $H_2SO_4 \cdot 2H_2O$

Uses
- Atrial & Ventricular Arrythmias.
- It is also used to treat malaria.

② PROCAINAMIDE HYDROCHLORIDE

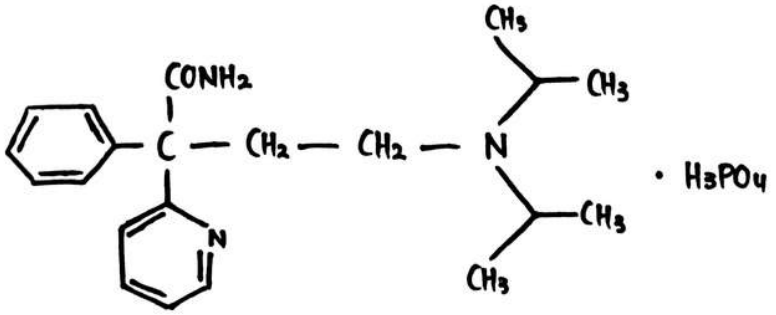


Uses

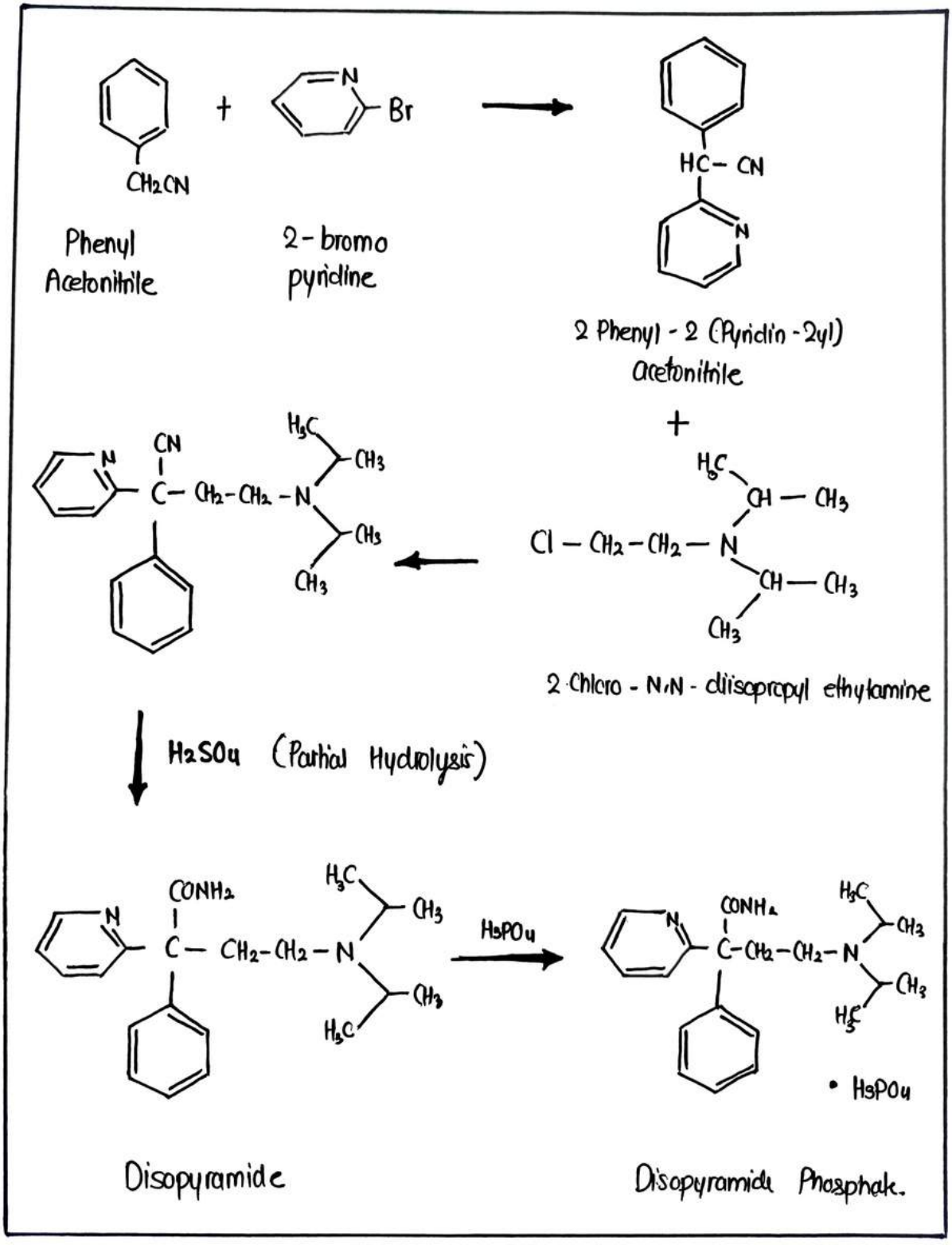
- Ventricular Arrythmias.
- Atrial fibrillation.

③ DISOPYRAMIDE PHOSPHATE *

Disopyramide phosphate is an antiarrythmic agent primarily used to treat certain types of irregular heartbeat, particularly ventricular arrythmias.



Synthesis



MOA

They blocks sodium channels belonging to class IA drugs & prolonging the action potential & refractory period.

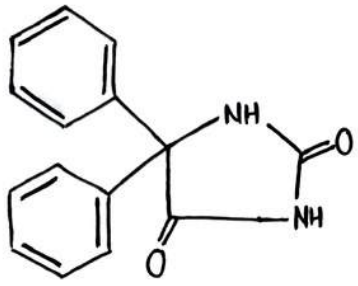
Chemical Properties

It is white or almost white powder, soluble in water, sparingly soluble in alcohol.

Uses

Ventricular Arrythmia

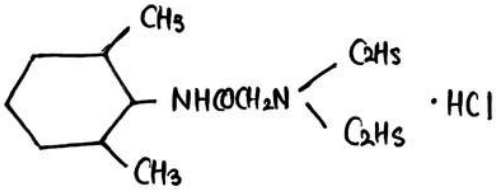
④ PHENYTOIN SODIUM



Uses

- Treatment of certain seizures
- Arrythmia

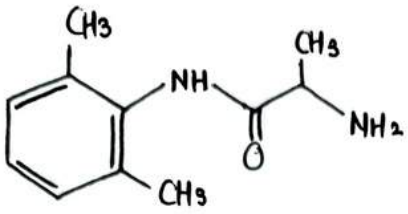
⑤ LIDOCAINE HCl



Uses

- Ventricular Arrythmia
- Local Anaesthetic Agent

⑥ TOCAINIDE HCl

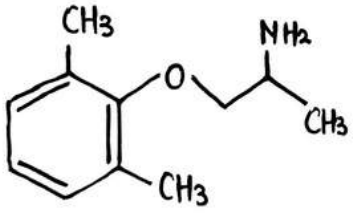


• HCl

Uses

Treatment of Ventricular Arrythmia

⑦ MEXILETIN HCl

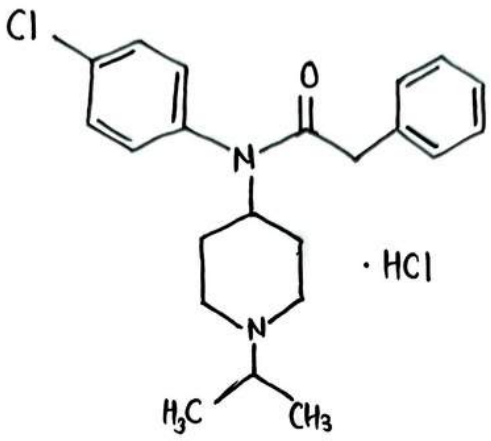


• HCl

Uses

Chronic Ventricular Arrythmia

⑧ LORCAINIDE HCl



Uses

Life-threatning Ventricular Arrythmias

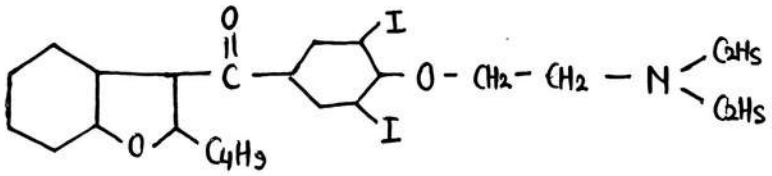
② CLASS - III (K^+ CHANNEL BLOCKER)

Potassium Channel blockers are class of antiarrhythmic drugs that primarily work by prolonging repolarization phase of cardiac action potential.

MOA

- Potassium Channel Blockers inhibits the outward potassium flow during repolarization phase of cardiac action potential.
- By blocking K^+ channels, they delay repolarization, thereby prolonging action potential.

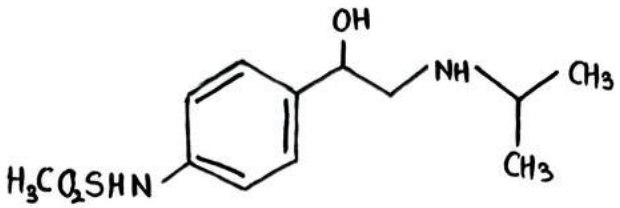
① AMIODARONE



Uses

- Life-threatening ventricular arrythmia.

② SOTALOL



Uses

- Ventricular Arrythmias
- Atrial Fibrillation

ANTI - HYPERLIPIDEMIC DRUGS

- Anti - Hyperlipidemic agents are medications designed to lower lipid levels in the blood, particularly Cholesterol & Triglycerides.
- They help manage conditions like, Hyperlipidemia, which is associated with an increased risk of cardiovascular disease

HYPERLIPIDEMIA

- Hyperlipidemia is a medical condition characterized by abnormally high levels of lipid in blood, which include cholesterol & triglycerides.
- These elevated lipid levels can increase the risk of developing cardiovascular diseases such as coronary artery disease, stroke & peripheral artery disease.

Types Of Lipid Involved

- Cholesterol
  - Low Density Lipoprotein
  - High Density Lipoprotein
- Triglycerides

Symptoms

It itself has no specific symptoms, However long term elevated lipid levels can lead to development of atherosclerosis which can cause :

- Chest Pain
- Heart Attack / Stroke etc.

Classification of Anti-Hyperlipidemic Agents

① HMG Co-A Reductase Inhibitors

- Lovastatin

② Bile Acid Sequestrants (Resins)

- Cholesteramine
- Cholestipol

③ Lipoprotein Lipase Activator (Fibrates)

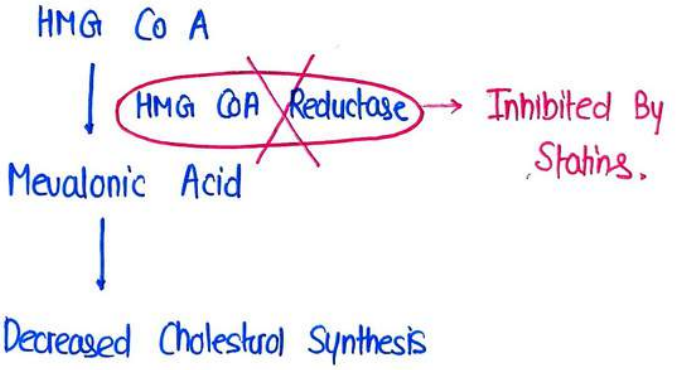
- Clofibrate

HMG CoA Reductase Inhibitors

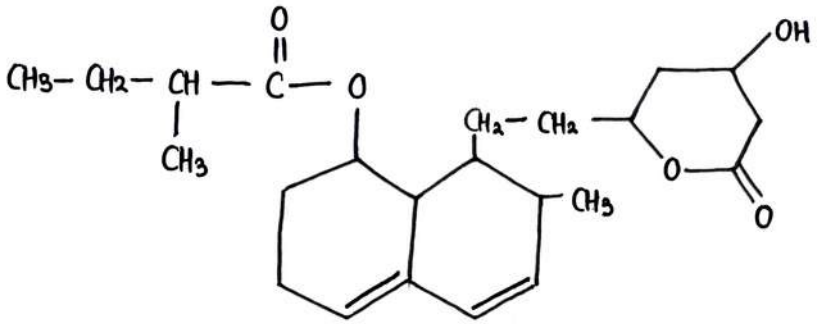
HMG Co-A reductase inhibitors, commonly known as Statins, are class of drugs that reduce cholesterol levels by inhibiting HMG Co-A reductase enzyme.

Mechanism Of Action

- HMG - CoA reductase is an enzyme responsible for converting HMG - CoA into mevalonate, an early & essential precursors in cholesterol biosynthesis pathway.
- Statins act as competitive inhibitors of HMG Co-A reductase, effectively lowering production of cholesterol in liver.
- This inhibition leads to a decrease in intracellular cholesterol levels, which triggers an upregulation of LDL Receptors on hepatocyte surfaces.
- These receptors increase the uptake of LDL cholesterol from blood thereby reducing LDL levels.
- They shows maximum activity in midnight.



① LOVASTATIN



Chemical Properties

- It is a white or almost white crystalline powder
- It is soluble in water & sparingly soluble in alcohol.

Uses

- Coronary Artery disease
- Hyperchlestrolemia.

BILE ACID SEQUESTRANTS

Bile Acid sequestrants are a class of medications that used to lower cholesterol levels.

Mechanism of Action

- They work by binding to bile acids in the intestine.
- This binding forms an insoluble complex that prevents the reabsorption of bile acids into blood stream.
- As a result, the liver must convert more cholesterol into bile acids to replace those lost, leading to decrease LDL levels.

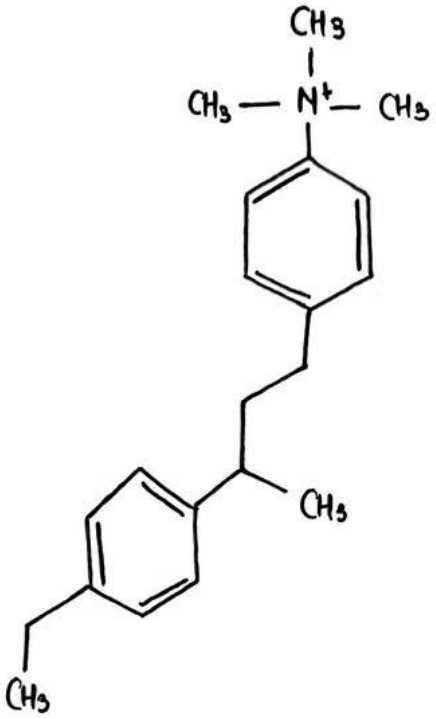
Common Drugs

- Cholestyramine
- Colestipol
- Colesevelam

SIDE EFFECTS

- Constipation
- Bloating
- Interference with absorbtion of fat soluble vitamins (A, D, E, k)

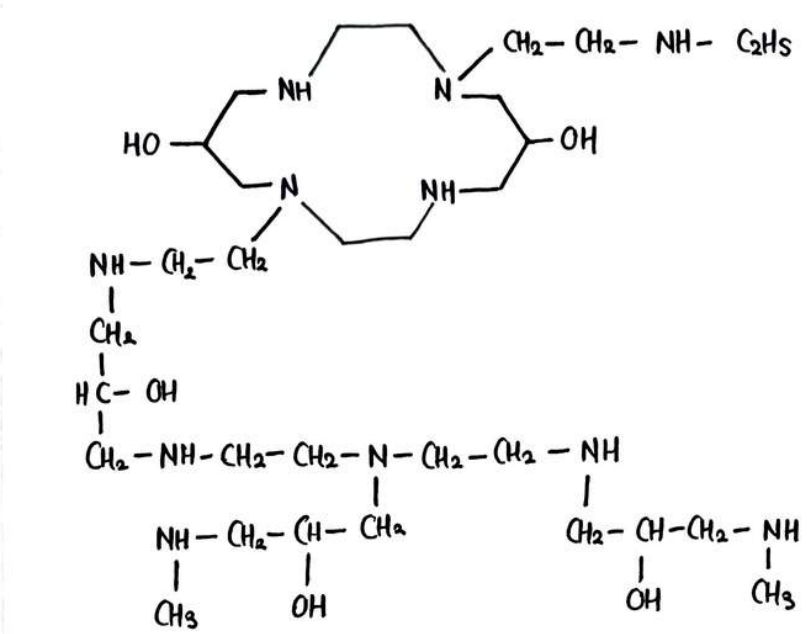
① CHOLESTYRAMINE



Uses

- Hypercholestrolemia
- Hypertriglyceridemia

② COLESTIPOL



Uses

- Hypercholesterolemia
- Hyperlipidemia

LIPOPROTEIN LIPASE ACTIVATOR

Lipoprotein Lipase Activators are a class of agents designed to enhance the activity of LPL, which plays a key role in lipid metabolism.

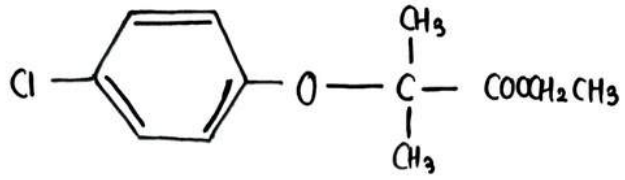
Mechanism Of Action

- Lipoprotein Lipase Activators enhance the enzyme's activity, leading to increased hydrolysis of triglycerides in lipoproteins (like chylomicrons & VLDL) into free fatty acids & glycerol.
- By facilitating the breakdown of triglycerides, these agents promote the clearance of triglyceride-rich lipoproteins from the bloodstream, thereby reducing overall triglyceride levels.

SIDE EFFECTS

- Gastrointestinal Disturbances
- Allergic Reactions

① CLOFIBRATE



Uses

- Hyperlipidemia
- Hypertriglyceridemia

HAEMOSTASIS

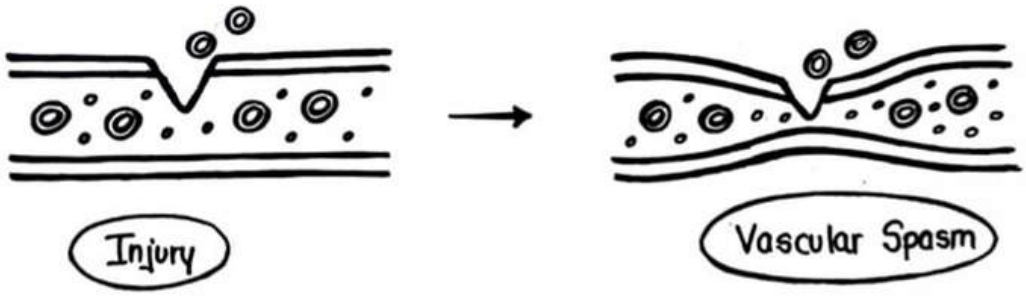
- Haemostasis is also known as 'Blood Clotting' or 'Blood Coagulation'
- It is a fast series of action for the body to stop bleeding & loss of blood.
- Haemostasis occurs when blood is present outside the blood vessel.
- Haemostasis simply stands for prevention of blood loss from a broken blood vessel.
- It requires various clotting factors and chemicals released by platelets and injured tissues.

Steps of Haemostasis

- Vascular Spasm / Vasoconstriction
- Platelets Plug formation
- Blood Clotting

Vascular Spasm

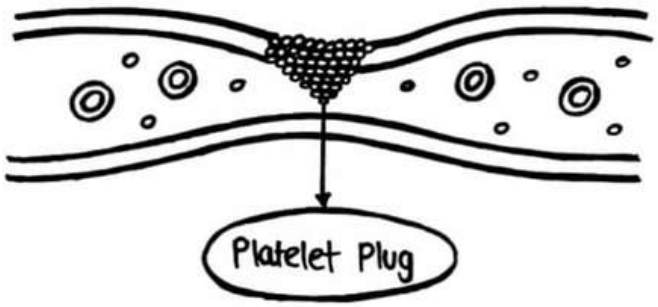
- It is also known as vasoconstriction.
- It is the blood vessel's first response towards injury.
- As the name indicates in this step blood vessel gets contracted.
- The constriction of blood vessels reduces the amount of blood & limits the blood loss.
- It is a temporary response.
- It is most effective in smaller blood vessels.



Platelet Plug Formation

- Platelets plays an important role in haemostasis process.
- In this step platelets stick together to form a plug that temporary seals the breakage in the walls of the blood vessels.
- The platelet plug formation is activated by a factor called Von Willebrand Factor (VWF)
- Platelets in the blood vessels attached with collagen fibres & become much more stickier.

- After that they release some chemical messengers such as ADP, Serotonine, Thromboxane A_2. This phase is called platelet release reaction.
- ADP cause more platelets to stick over vessels.
- Serotonine and thromboxane A_2 Enhances vascular spasm and platelet plug formation.



Blood Clotting

- It is the main and final process of blood clotting.
- It is the process by which blood clot forms.
- It is a complex procedure of enzymatic reactions in the presence of various clotting factors which results in the formation of clot over the injured blood vessels.

- It can be divided into three pathways :

① Intrinsic Pathway
② Extrinsic Pathway
③ Common Pathway

Clotting Factors

NUMBER	FACTOR NAME
I	Fibrinogen
II	Prothrombin
III	Tissue Factor (Thromboplastin)
IV	Calcium Ions
V	Proaccelerin / Labile Factor
VII	Proconvertin / Stable Factor
VIII	Antihaemophilic Factor A
IX	Christmas Factor / Antihaemophilic Factor B
X	Stuart Factor / Prower Factor
XI	Plasma Thromboplastin / Antihaemophilic Factor C
XII	Hageman Factor
XIII	Fibrin stabilizing Factor

- Clotting factors always written in roman numbers.
- Factor VI is not in the existence

Intrinsic Pathway

- This is a complex pathway & occurs slowly.
- This pathway occurs due to blood trauma.
- In this pathway when blood vessel gets injured, then endothelial tissue inside blood vessel also gets damaged and blood comes in direct contact with collagen fibres of connective tissue present around the endothelial tissue.
- Now damage to the endothelial tissue cause damage to platelets which results in the release of phospholipids by platelets.

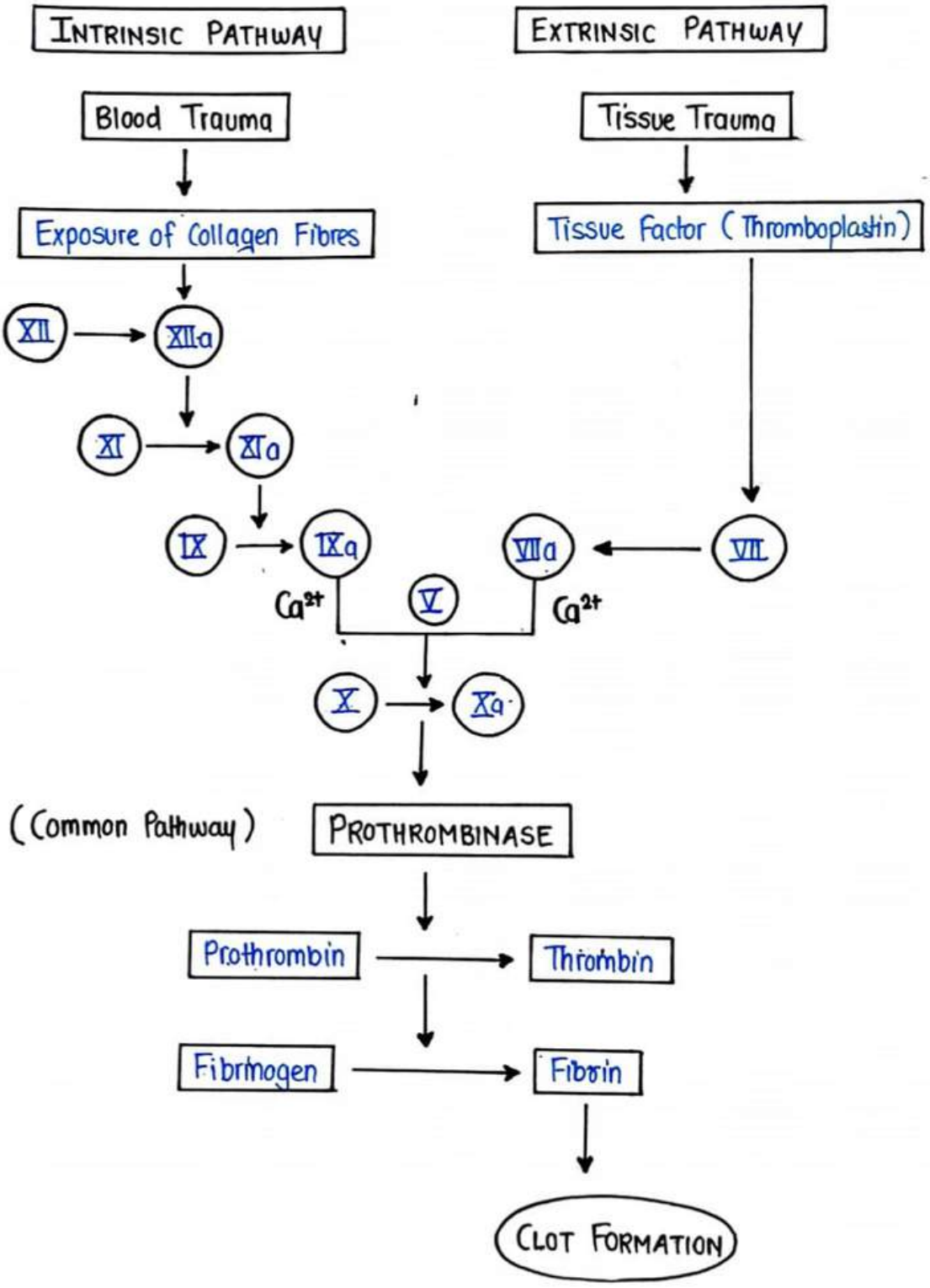
- Now all these events activates clotting factor XII which ultimately activates factor X in the presence of Ca^{2+} ions.
- Once factor X is activated, it combines with factor V & activate enzyme Prothrombinase.

Extrinsic Pathway

- It is a simple pathway & occurs rapidly
- This pathway occurs due to tissue trauma.
- In this pathway tissue factor (Thromboplastin) activates factor VII which ultimately activates factor X in the presence of Ca^{2+} ions.
- Once factor X is activated, it combines with factor V & activates enzyme Prothrombinase.

Common Pathway

- In common pathway enzyme prothrombinase converts Prothrombin into Thrombin.
- In final stage thrombin converts Fibrinogen into Fibrins in the presence of Ca^{2+} that forms clot over the damaged blood vessels.



COAGULANTS

- Coagulants are pharmacological agents that promote the process of Blood Coagulation, which is essential for stopping bleeding.
- Coagulation is a complex physiological mechanism where liquid blood transforms into a solid clot to prevent excessive blood loss during injuries.
- Coagulants act by enhancing or initiating this process & they are used in clinical settings to manage bleeding disorders & conditions where blood clotting is impaired.

Classification Of Coagulants

They can be classified into two main categories :

① Vitamin K

- K_1 (from plants) - • Phytonadione (Phylloquinone)
- K_3 (Synthetic) - • Menadione
  • Acetomenaphthone
  • Menadione Sodium diphosphate

② Miscellaneous

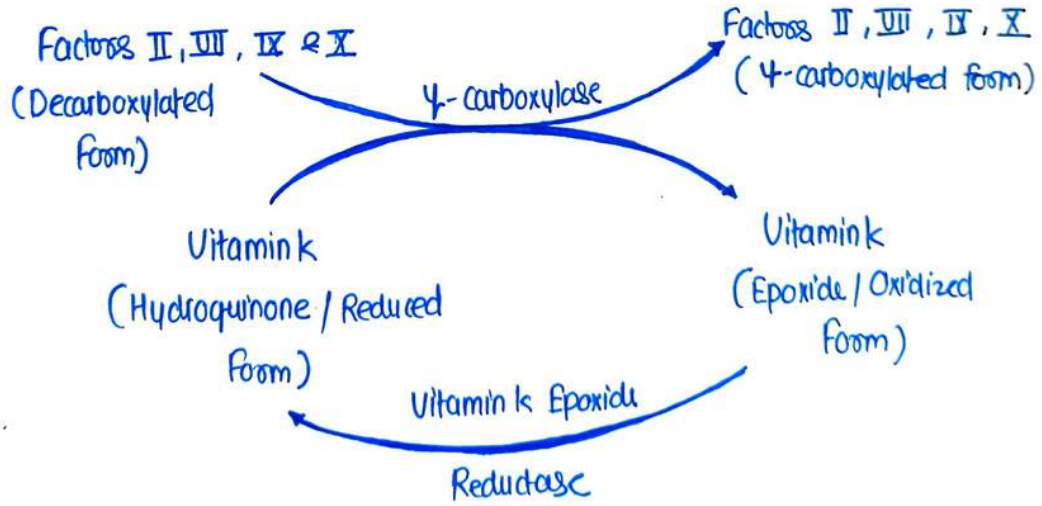
- Fibrinogen
- Antihaemophilic factor
- Desmopressin
- Adrenochrome Monosemicarbazone
- Rutin
- Ethamsylate.

Vitamin k

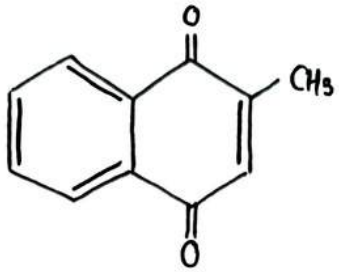
- Vitamin k plays a crucial role in pharmacology as a coagulant because it is essential for synthesis of certain proteins required for blood clotting.
- These proteins known as clotting factors, includes factor II, VII, IX & X as well as protein C & S which regulate clotting.

Mechanism of Action

- Vitamin k is absorbed from intestine & transported to liver
- Vitamin k is then converted to its reduced form by the enzyme Vitamin k epoxide reductase.
- Reduced vitamin k serves as a cofactor for gamma-glutamyl carboxylase which is essential for functionalization / activation of proteins like prothrombin (factor II) & factors VII, IX & X.



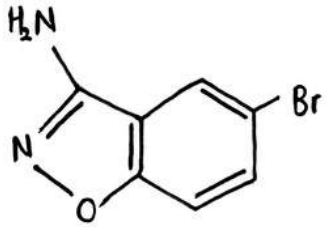
① MENADIONE



Uses

- Hypoprothrombinemia
- Vitamin K Deficiency

② ACETOMENADIONE



Uses

- Hypothrombinemia
- Vitamin K Deficiency

ANTICOAGULANTS

- Anticoagulants are drugs that inhibit blood coagulation, preventing the formation of harmful clots inside blood vessels.
- They are the agents that decreases coagulation ability of blood.
- They do not dissolve the already form clots, but are used to ~~formation~~ prevent the formation of new clots.

CLASSIFICATION OF ANTICOAGULANTS

Anticoagulants can be mainly classified into two types

① Parenteral Anticoagulants
② Oral Anticoagulants.

Oral Anticoagulants

- Vitamin K Antagonist
  - Warfarin
  - Anisindione
- Factor Xa Inhibitor
- Direct Thrombin Inhibitor

② ORAL ANTICOAGULANTS

- These are anticoagulants taken orally & help prevent the formation of blood clots in the body.
- These drugs are often prescribed to individuals at risk of developing clots that could lead to serious conditions like
- Deep Vein Thrombosis, Pulmonary Embolism, Stroke or Heart Attacks
- They are mainly divided into 3 classes :

① Vitamin k Antagonist
② Direct Factor Xa Inhibitor
③ Oral Direct Thrombin Inhibitor

① Vitamin k Antagonist

- Vitamin k antagonist is a type of medication that inhibits the action of vitamin k, which is essential for synthesis of certain blood clotting factors.
- Warfarin is most popular oral anticoagulant.

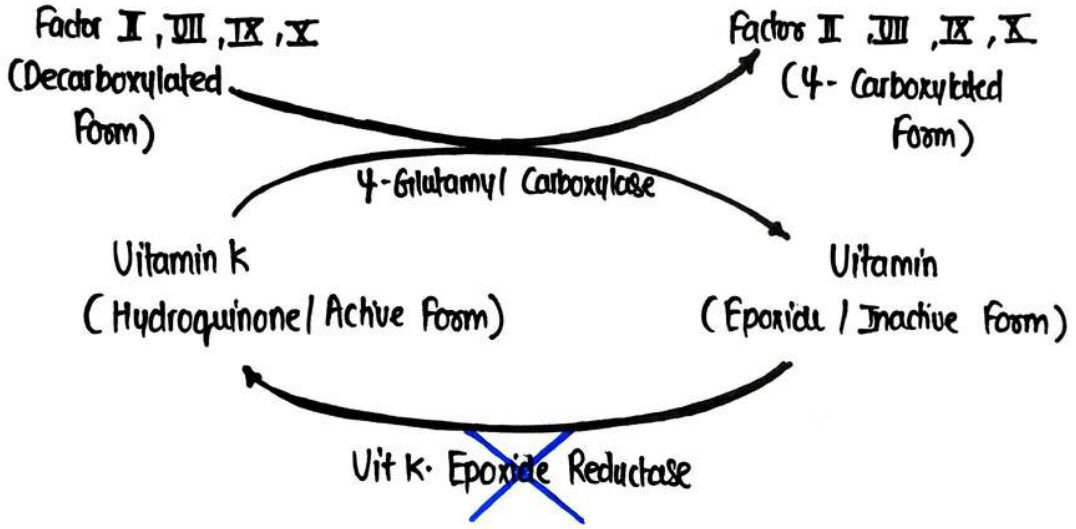
WARFARIN

- Warfarin is the most popular oral anticoagulant & used only in vivo.
- It contains 4 Hydroxycoumarine ring.
- It is a coumarin derivative & belongs to the class of Vitamin k Antagonist.

Mechanism Of Action

- Warfarin acts by inhibiting the enzyme vitamin k epoxide reductase which is necessary to recycle vitamin k into its active form.
- Active vitamin k is essential for synthesis of certain vitamin k dependent clotting factors such as

① Factor II
② Factor VII
③ Factor IX
④ Factor X

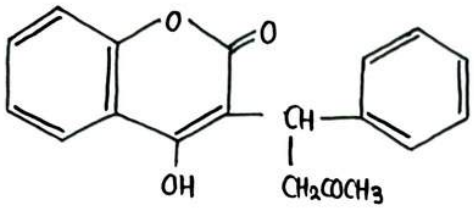


Blocked By Warfarin

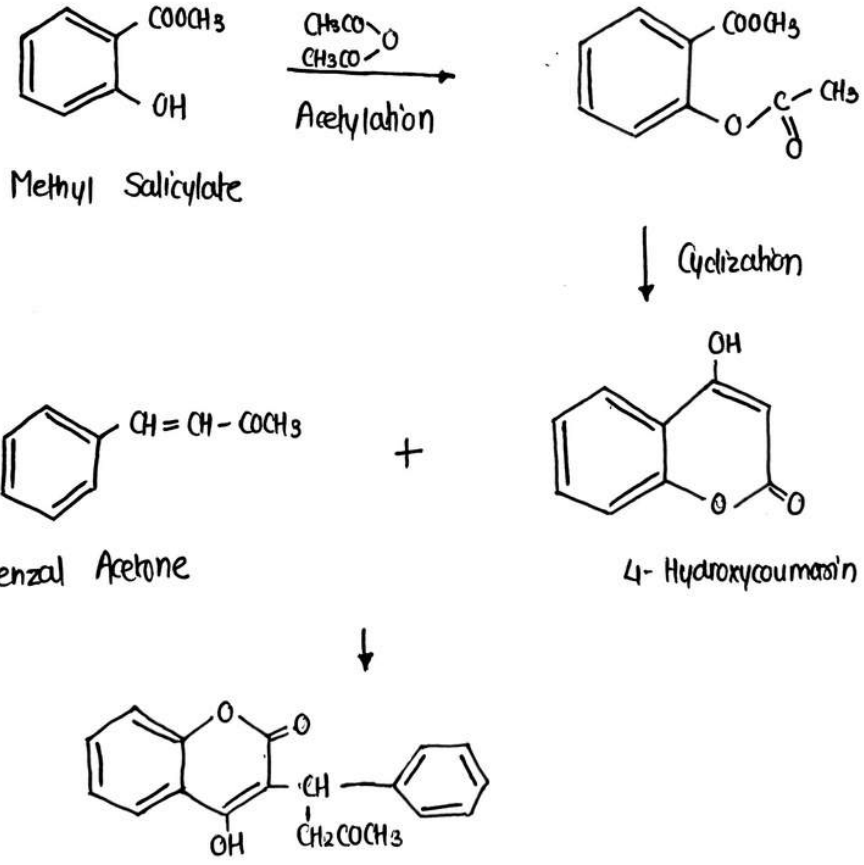
Pharmacokinetics

- **Absorption** : Warfarin is well absorbed from Gastrointestinal Tract.
- **Distribution** : Warfarin is highly bound to plasma proteins, hence its highly distributed in body.
- **Metabolism** : It is primarily metabolized by liver's cytochrome P450 enzyme system.
- **Half Life** : Half Life ranges from 20-60 hours.
- **Excretion** : Warfarin and its metabolites are excreted via urine.

STRUCTURE



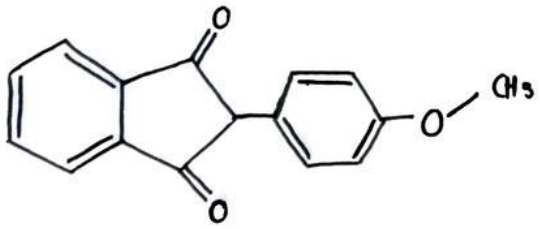
Synthesis



Uses

- Prevention of Thrombosis & Thromboembolism
- Atrial fibrillation, Venous Thromboembolism.

② ANISINDIONE



Uses

- Anticoagulant
- Venous Thrombosis
- Pulmonary Embolism

ANTIPLATELET DRUGS

- Antiplatelet Drugs are medications that inhibit platelet aggregation preventing the formation of blood clots.
- They work by interfering with various pathways involved in platelet activation and aggregation.
- These drugs are commonly used to reduce the risk of cardiovascular events, such as heart attacks and strokes etc.

Mechanism Of Platelet Aggregation

- Platelet aggregation is an important step in hemostasis.
- It involves clumping together of platelets ~~plug~~ to form a platelet plug, which helps in sealing wound & initiating blood clotting.
- It involves following steps:

① Vascular Injury & Endothelial Cell Disruption

- When blood vessels are injured, endothelial cells lining the blood vessels are damaged, exposing the underlying collagen and other extracellular matrix components like **von Willebrand factor** to the bloodstream.

② Platelet Adhesion

- Von Wibrand factor binds to exposed collagen at the site of injury.
- Platelet in the circulating blood binds to vWF via glycoprotein Ib receptors on their surface
- This allows platelets to stick to damaged site.

③ Platelet Activation

- Once adhered, platelet gets activated & release granules containing substances like ADP, Thromboxane A2, Serotonin etc.
- ADP binds to P2Y12 receptors on platelets, enhancing aggregation.
- Thromboxane A2 is a potent vasoconstrictor and platlet activator that promotes further platelet requirment & activation.

④ Platelet Aggregation

- Platelet activation leads to conformational change in Glycoprotein IIb/IIIa receptors on surface of platelets, enabling them to find fibrinogen.
- Fibrinogen acts as a bridge between Gp IIb/IIIa receptors on adjacent platelets, allowing them to stick togethers, forming a platelet plug.

③ P2Y12 Receptor Blocker

P2Y12 receptor blockers are crucial antiplatelet medications used primarily in cardiovascular disease management.

Mechanism of Action

- P2Y12 is a g-protein coupled receptor activated by ADP.
- P2Y12 blockers prevent ADP from binding to the receptor, inhibiting platelet activation and aggregation, thus reducing the risk of thrombus formation.

Examples

- Clopidogrel
- Prasugrel
- Ticlopidine
- Ticagrelor

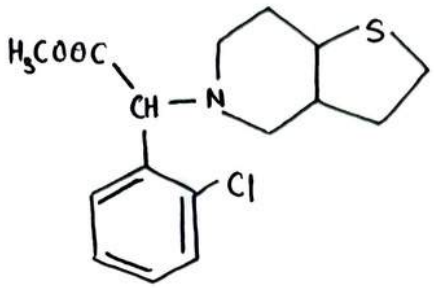
Clinical Uses

- Thromboembolic Prevention
- Dual Antiplatelet Therapy

Side Effects

- Bleeding Risks
- Gastrointestinal Disturbances

① CLOPIDOGREL



Uses

- Prevention of Thrombosis
- Atherosclerosis

CONGESTIVE HEART FAILURE

- Congestive Heart Failure is defined as failure of heart capacity to pump sufficient blood that required for proper functioning of body.
- The term CHF used for chronic form of Heart Failure.
- Heart Failure leads the blood to move through body & heart at slower rate.
- CHF is the end result of various forms of serious heart disease.
- It can be further classified into 3 types :

① Left Sided Heart Failure
② Right Sided Heart Failure
③ Both Sided Heart Failure

TYPES OF CHF

Congestive Heart Failure is of mainly two types :

① Systolic Heart Failure
② Diastolic Heart Failure

SYSTOLIC HEART FAILURE

- In systolic heart failure Heart muscles becomes too weak & enlarged & fails to contract properly.
- In systolic heart failure.
  - Stroke Volume ↓
  - Cardiac Output ↓
  - Ejection Factor ↓

Diastolic Heart Failure

- In diastolic heart failure Heart muscles becomes stiff, thick & enlarged hence the ventricles fails to fill properly.
- In Diastolic Heart Failure :
  - Preload ↓
  - Cardia Output ↓
  - Stroke Volume ↓

Etiology / Causes

- Ischemic Heart Disease / Coronary Artery Disease
- Hypertension
- High Sodium Diet
- Diabetes
- Overweight
- Smoking
- Alcohol
- Myocarditis
- Arrythemia

PATHOGENESIS

Failure of Heart is frequently seen in elderly patients suffering from Hypertension, Angina pectoris etc. Following factors can be responsible for Heart Failure.

① Intrinsic Pump Failure

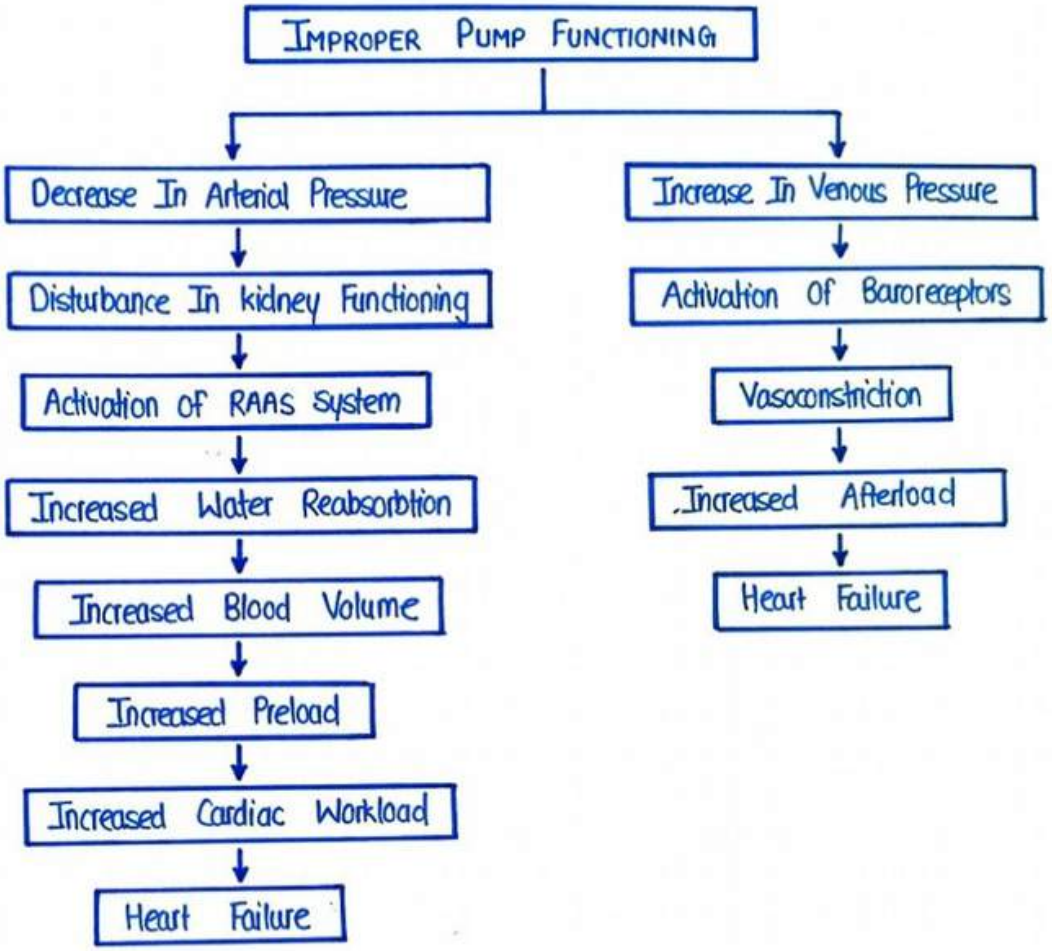
- The most common & most important cause of Heart Failure is weakening of ventricular muscle due to various diseases that leads to failure of efficient pumping of blood by heart.
- It can be occur due to :
  - Ischemic Heart Disease
  - Myocarditis
  - Beriberi Disorder
  - Various kidney Diseases

② Increased Workload On Heart

- An increase in the workload on Heart can also be a major cause of Heart Failure.
- It can be occur due to :
  - Increased Pressure Load
  - Increased Volume Load

③ Improper Pump Functioning

Improper pump functioning can leads to heart failure through following mechanism.



SIGN & SYMPTOMS

- Chest Pain
- Fatigue
- Irregular Heartbeat
- Headache
- Blurred Vision
- Cough
- Shortness of Breath
- Swelling

COMPLICATIONS

- kidney Damage
- Lungs Disorders
- Heart Attack
- Liver Damage
- Heart Valve Problems

TREATMENT / MANAGEMENT

① Non Pharmacological :

- Exercise
- No Smoking
- Healthy Diet / Proper Lifestyle

② Pharmacological :

- β Blockers
- ACE Inhibitors
- Diuretics / Vasodilators

DRUGS USED IN TREATMENT OF CHF

Digoxin
Digitoxin
Nesiritide
} → Cardiac Glycosides

Bosentan
Tezosentan
} → Endothelin Receptor Antagonist

CARDIAC GLYCOSIDES

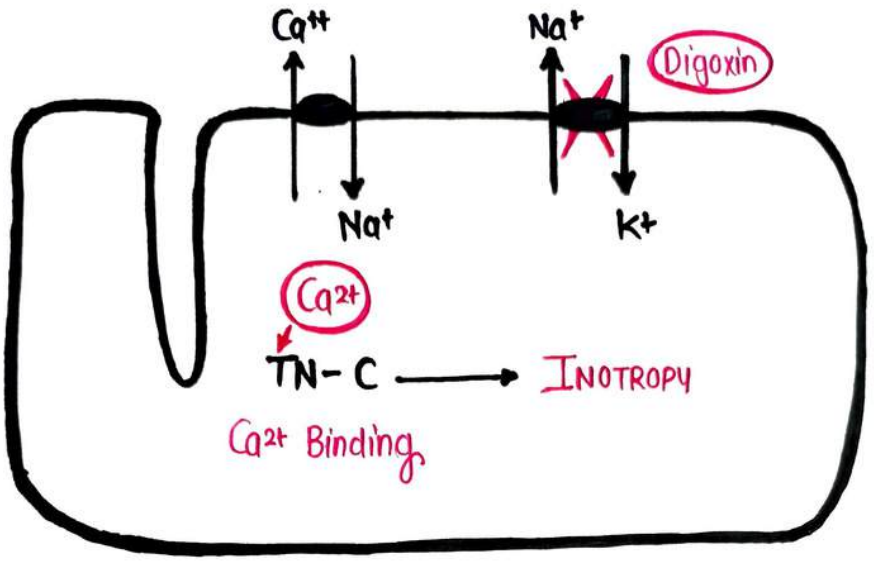
- Cardiac Glycosides are class of medications that are used to treat heart failure, particularly congestive heart failure (CHF).
- They work by increasing force of heart's contraction & slowing heart rate.
- This improves heart's efficiency and helps relieve symptoms of Heart failure.
- Digoxin is most well known and effective cardiac Glycoside.

DIGOXIN

- Digoxin is a cardiac glycoside commonly used in the treatment of congestive heart failure.
- Its mechanism of action in CHF primarily revolves around its positive inotropic effect, meaning it increases the force of heart contractions.

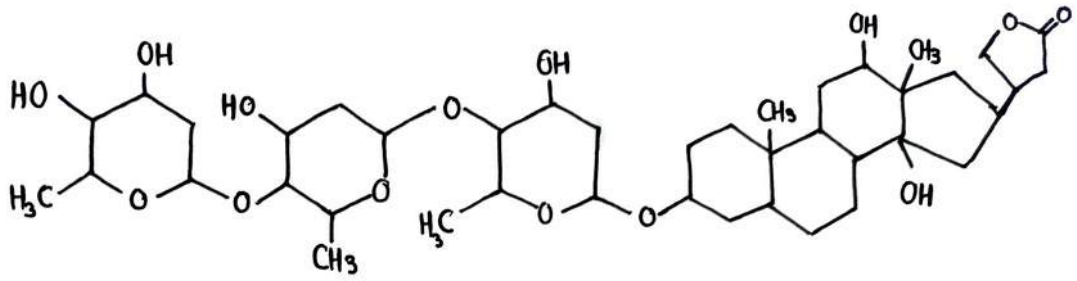
Mechanism Of Action

- Digoxin inhibits the Na^+/K^+ ATPase pump, which is located in the membranes of cardiac myocytes.
- By inhibiting this pump, digoxin increases the intracellular concentration of sodium.
- The increased intracellular sodium indirectly affects Na^+/Ca^{2+} exchanger, which pumps calcium out in exchange for sodium.
- Due to inhibition of Na^+/K^+ ATPase pump, the Na^+/Ca^{2+} exchanger become less effective, reducing calcium efflux.
- As a result more calcium remains inside the cell.



- The increased intracellular calcium allows for more calcium to be available during each heartbeat.
- During cardiac contraction, this extra calcium is released, leading to stronger contractions of the heart muscle.
- The increased contractility helps improve the heart's pumping efficiency.
- Digoxin also slows down conduction through AV node, which helps to control Heart Rate.

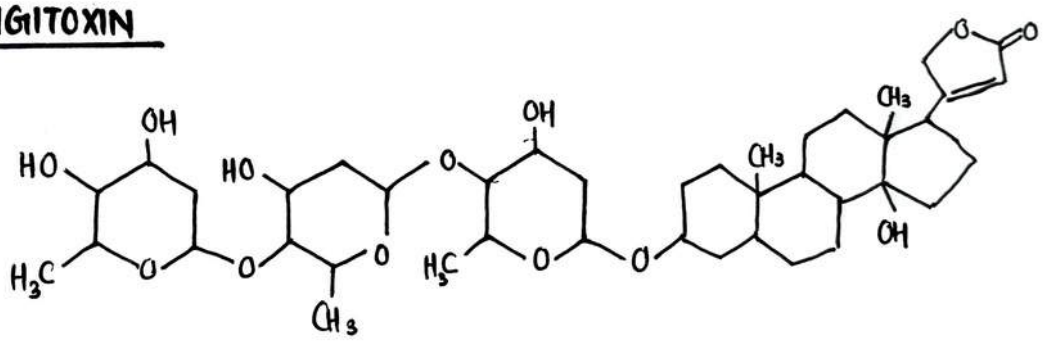
① DIGOXIN



Uses

- Heart failure
- Atrial fibrillation

② DIGITOXIN



Uses

- Heart failure
- Atrial fibrillation

③ NESIRITIDE

Nesiritide is a recombinant form of B- type natriuretic peptide (BNP), which is naturally produced by ventricles of heart in response to increased cardiac wall stress.

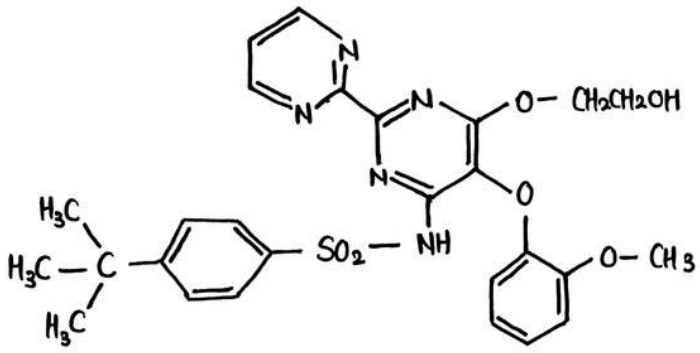
MOA

- Nesiritide activates guanylate cyclase receptors on vascular smooth muscle, leading to an increase in cGMP. Elevated cGMP causes relaxation of smooth muscle, resulting in vasodilation of both arteries & veins, which reduces both preload & afterload on heart.
- It also promotes diuresis decreasing fluid overload.

Uses

- Congestive Heart failure.

④ BOSENTAN



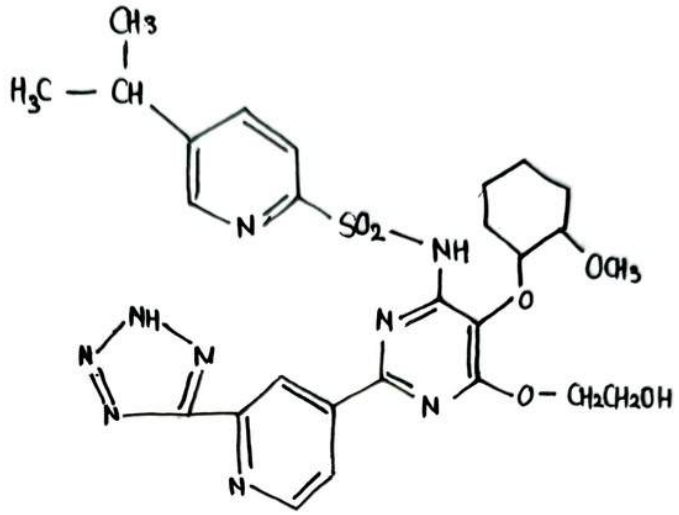
MOA

- Bosentan is a dual endothelin receptor antagonists, which works by blocking the effect of Endothelin-1, a potent vasoconstrictor peptide.
- Endothelin-1 act by binding of ETA & ETB receptors.
- When Endothelin-1 binds to these receptors it causes vasoconstriction
- Bosentan selectively blocks both ETA & ETB receptors & inhibits vasoconstriction.

Uses

- CHF
- Hypertension.

⑤ TEZOSENTAN



MOA

Same as Bosentan

Uses

Acute heart Failure.

THANK YOU

FOR CHOOSING IMPERFECT PHARMACY AS YOUR STUDY PARTNER

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