Unit-IV/Part-C

Coagulant & Anticoagulant

Presented By;-

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Specialization:- Pharmaceutical Chemistry

Coagulant & Anticoagulant

Coagulants Coagulants are agents that promote blood clotting by increasing the activity or availability of clotting factors. They are mainly used to treat or prevent bleeding disorders caused by clotting factor deficiencies (e.g., vitamin K deficiency, liver disease, anticoagulant overdose). **Example:** Menadione, Acetomenadione.

Anticoagulants. Anticoagulants are drugs that inhibit the blood coagulation process by preventing the synthesis or function of clotting factors, or by inhibiting platelet aggregation. They are mainly used to prevent and treat thromboembolic disorders. **Examples:** Warfarin, Acenocoumarol, Anisindione.

Table showing Mechanism of Action (MOA) and Uses of the given compounds:

Drug	Mechanism of Action (MOA)	Uses
Menadione (Vitamin K_3)	Synthetic vitamin K analog; promotes γ-carboxylation of clotting factors (II, VII, IX, X), enhancing blood coagulation.	Treatment and prevention of hypoprothrombinemia and vitamin K deficiency-related bleeding.
Acetomenadione (Vitamin K_4)	Similar to vitamin K; acts as a cofactor for the synthesis of clotting factors by activating vitamin K-dependent pathways.	Treatment of vitamin K deficiency and related bleeding disorders.
Warfarin*	Vitamin K antagonist; inhibits vitamin K epoxide reductase (VKORC1) → prevents activation of clotting factors II, VII, IX, and X.	Prophylaxis and treatment of thromboembolic disorders (DVT, PE, atrial fibrillation).
Anisindione	Oral anticoagulant (indandione derivative); inhibits vitamin K–dependent synthesis of clotting factors.	Prevention and treatment of thromboembolic disorders (less common alternative to warfarin).
Clopidogrel	Irreversible $P2Y_{12}$ ADP receptor antagonist on platelets → inhibits platelet aggregation.	Prevention of stroke, myocardial infarction, and vascular events in patients with atherosclerosis or stents.

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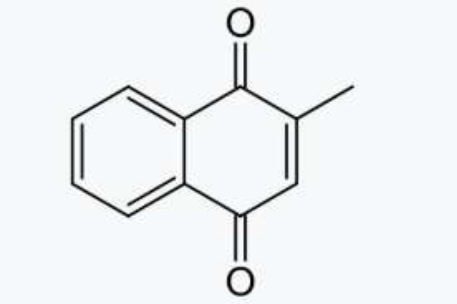
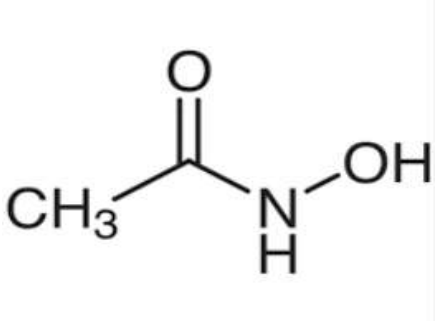
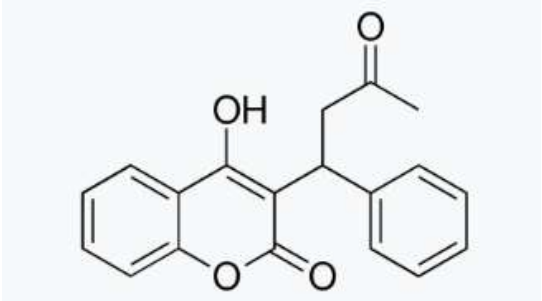


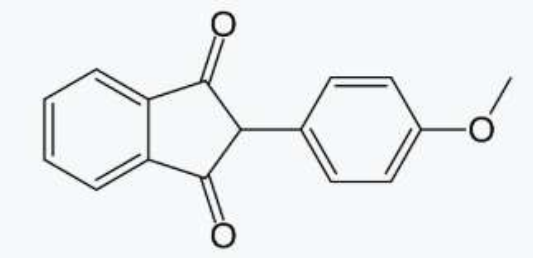
Menadione



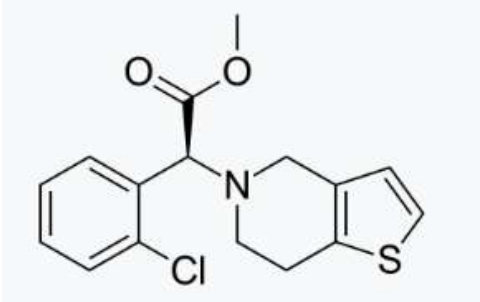
Acetomenadione



Warfarin

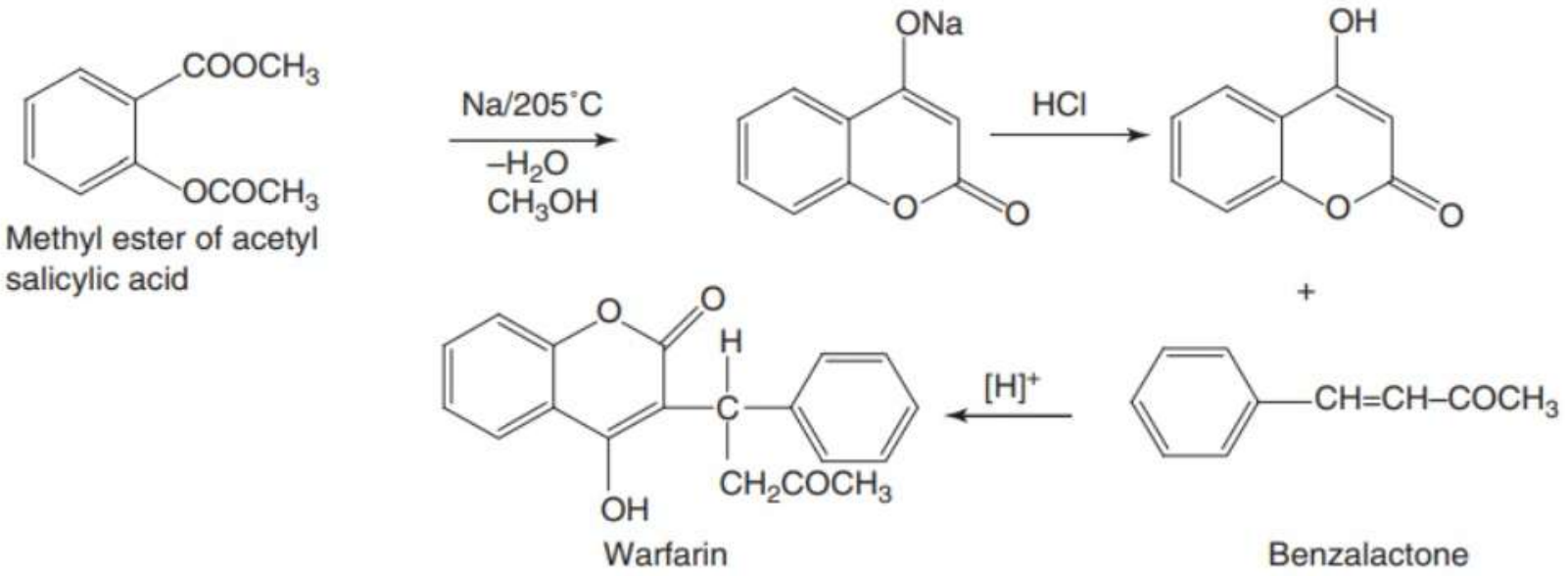


Anisindione

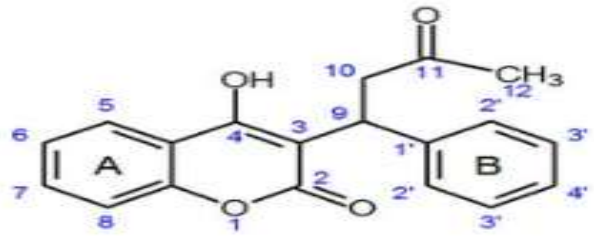


Clopidogrel

Synthesis of Warfarin



SAR OF Warfarin



Warfarin

Structural Feature	Role in Activity
4-Hydroxy group	Essential for anticoagulant activity; mimics vitamin K and allows binding to VKORC1 (vitamin K epoxide reductase).
Benzopyrone ring (aromatic ring)	Maintains planarity necessary for interaction with the enzyme; substitutions on the ring can affect potency.
C3 side chain (3-(α-acetonylbenzyl))	Crucial for activity; variations in length, branching, or substitution affect potency and pharmacokinetics.
Chirality (R- and S-enantiomers)	S-warfarin is 3–5 times more potent than R-warfarin due to stronger VKORC1 binding.
Keto–Enol tautomerism	Enol form is considered active, enabling hydrogen bonding with the enzyme.
7-Position substitution	Hydrophilic substitutions increase water solubility and may modify pharmacokinetics.

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Unit-IV/Part-D

Drugs used in Congestive Heart Failure

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Congestive Heart Failure (CHF)

Congestive Heart Failure (CHF) is a clinical condition in which the heart is unable to pump blood effectively to meet the metabolic demands of the body, leading to congestion (fluid buildup) in the lungs, liver, abdomen, and peripheral tissues.

Table with Mechanism of Action (MOA) and Uses of the given drugs:

Drug	Mechanism of Action (MOA)	Uses
Digoxin	Inhibits Na^+/K^+-ATPase pump → increases intracellular Na^+ → increases Ca^{2+} influx via Na^+/Ca^{2+} exchanger → enhances myocardial contractility (positive inotropic effect).	Treatment of heart failure and atrial fibrillation/flutter (rate control).
Digitoxin	Similar to Digoxin (Na^+/K^+-ATPase inhibition), but longer half-life and more lipophilic.	Heart failure, atrial fibrillation, and supraventricular arrhythmias.
Nesiritide	Recombinant B-type natriuretic peptide (BNP) → activates guanylyl cyclase → increases cGMP → vasodilation and natriuresis.	Acute decompensated heart failure with dyspnea at rest.
Bosentan	Dual endothelin receptor antagonist (ETA and ETB) → reduces endothelin-induced vasoconstriction.	Pulmonary arterial hypertension (PAH).
Tezosentan	Non-selective endothelin receptor antagonist (ETA/ETB blockade) → reduces vasoconstriction and afterload.	Investigational use in acute heart failure and pulmonary hypertension.

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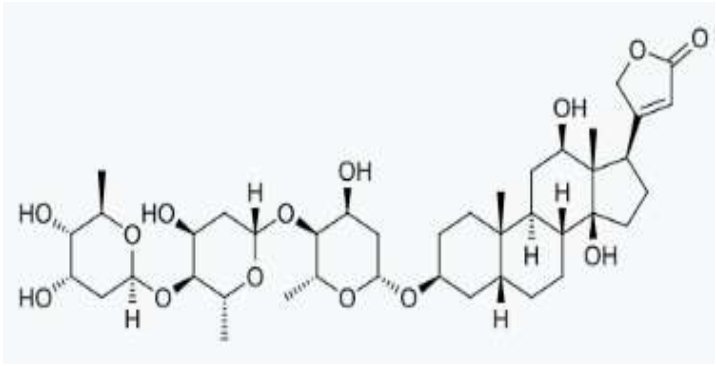
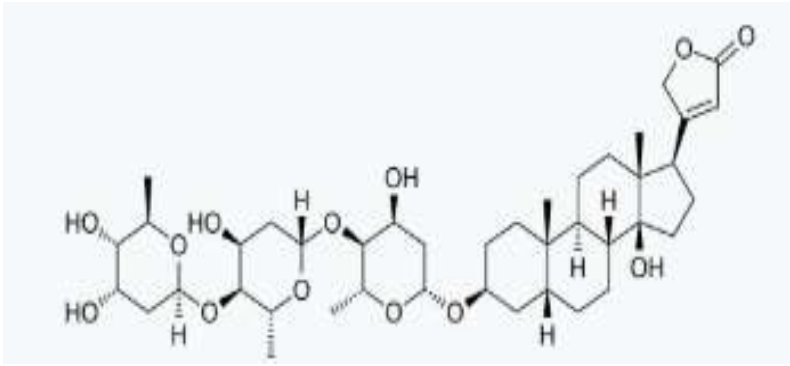
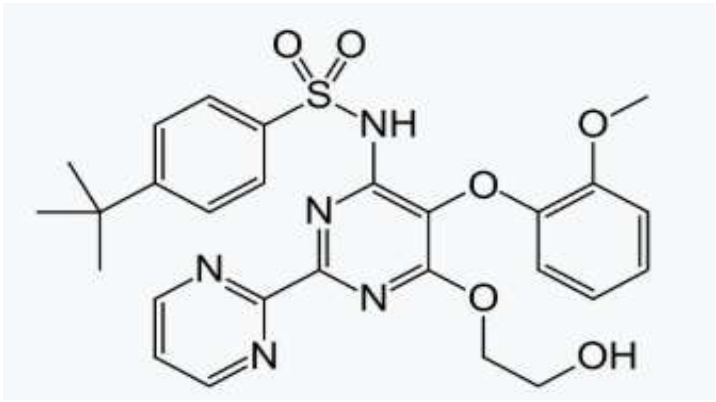


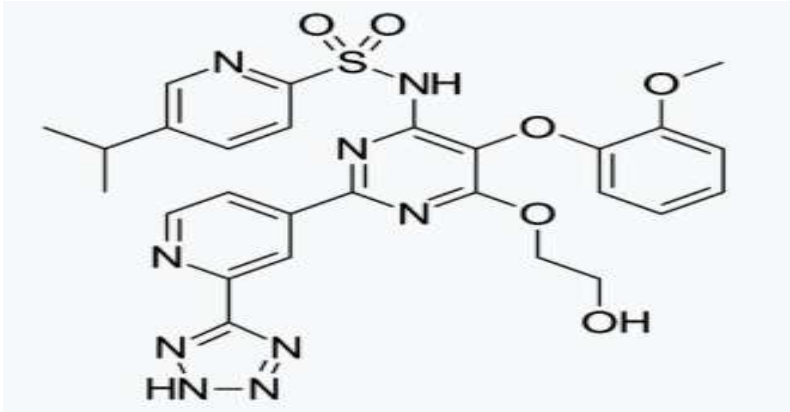
Digoxin



Digitoxin



Nesiritide



Tezosentan

Thank you

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