

# Chapter 9. Coagulants & Anticoagulants

## Syllabus:

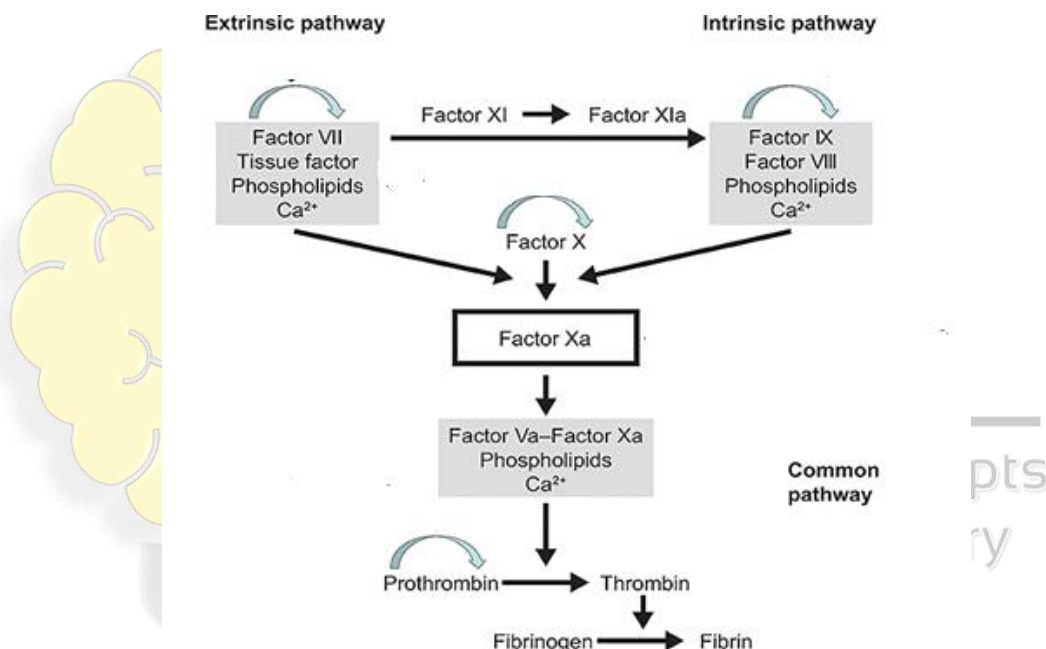
**Coagulant:** Menadione, Acetomenadione

**Anticoagulants:** Warfarin\*, Anisindione, and

**Antiplatelets:** Clopidogrel

## 8.1. COAGULANTS

Coagulants are the agents which promote the haemostasis (arrest the blood loss) and coagulation process and are indicated for haemorrhagic states.



### Pharmacology Lectures:

1. Hemostatic Agents: <https://youtu.be/L5wDP8cj55w>
2. Vit K Pharmacology: <https://youtu.be/1EZ9VptcI5k>

### 8.1.1. Drugs

#### a) Vit K

- K1 (from plants: fat-soluble): Phytonadione (Phylloquinone)
- K3 (synthetic)
- ✓ Fat-soluble: **Menadione, Acetomenadione** Acetomenaphthone

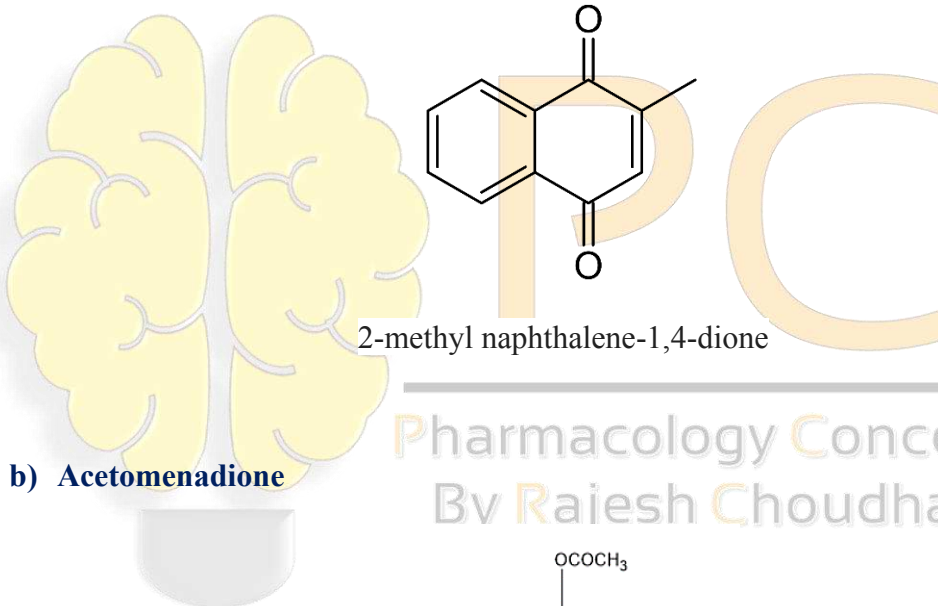
✓ Water-soluble: Menadione sod. bisulfite, Menadione sod. diphosphate

**b) Miscellaneous:** Fibrinogen (human), Antihaemophilic factor, Desmopressin, Adrenochrome monosemicarbazone, Rutin, and Ethamsylate

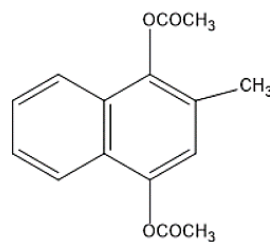
### Vitamin K

- ✓ Vitamin K is essential for synthesis of Factors II, VII, IX and X
- ✓ Function of vitamin K Synthesis of clotting factor II, VII, IX and X and make the  $\gamma$ -carboxylation of these which is essential for the ability  $\text{Ca}^{2+}$  and to get bound to phospholipid surface  $\rightarrow$  further cascade of coagulation.
- ✓ Deficiency of vitamin K Due to liver disease, obstructive jaundice, malabsorption, long term antimicrobial

#### a) Menadione (Vit K3)




#### b) Acetomenadione



**2-Methyl-1,4-naphthalenediol Diacetate**

## 8.2. ANTICOAGULANTS

 The drugs, which inhibit the coagulation process and prolong the coagulation time. They are generally used to prevention and/or treatment of thrombosis, atherosclerosis, embolism, myocardial ischemia, etc.

### 8.2.1. Drugs

#### A. Used in vitro:

- a. Organic acid: Heparin
- b. Organic acid salt: EDTA, Sod. Citrate, sod. oxalate

#### B. Used in vivo:

a. **Perenteral:** Heparin: Heparinoids, Heparan sulfate, Danaparoid, Lepirudin, Ancord

#### b. Oral anti-coagulants:

**Coumarin derivatives:** **Warfarin** (Coumadin), Acenocumarol,

**Indendiones:** Phenindione, **Anisindione**, Diphenadione

- ✓ **Danaparoid** (Heparan sulfate) A heparin of different structure, it may be safer in hypersensitivity to heparin.
- ✓ **Phenindione** Used as oral anticoagulant. It produces serious toxic effects; E.g., rashes, fever, hepatitis, nephropathy, *agranulocytosis* orange urine.

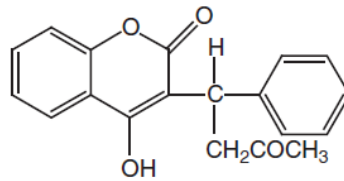
#### Direct thrombin inhibitors (DTIs)

- ✓ **Hirudin and bivalirudin** these are bivalent DTIs that bind at both the catalytic or active site of thrombin as well as at a substrate recognition site → prevents formation of fibrin and clotting of blood.
- ✓ **Argatroban** is a small molecule thrombin inhibitor that is FDA approved for use in patients with heparin-induced thrombocytopenia (HIT) with or without thrombosis and coronary angioplasty in patients with HIT.

#### Pharmacology Lectures:

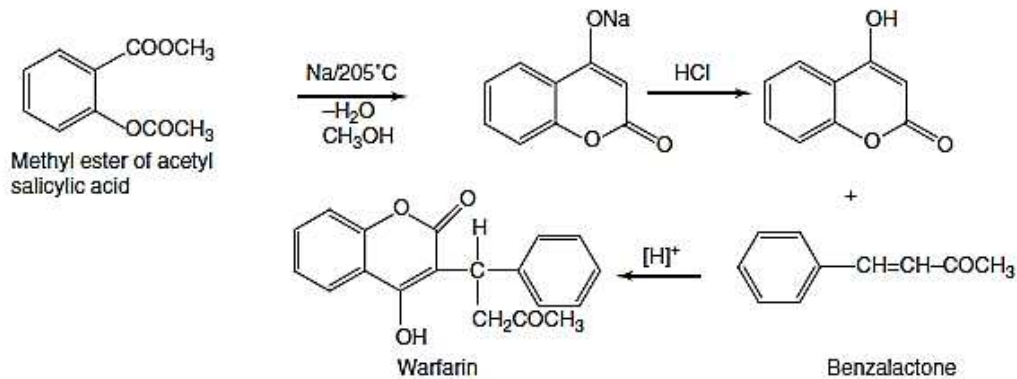
1. Anticoagulants: <https://youtu.be/cklvR0CJcho>
2. Heparin Pharmacology: <https://youtu.be/oXipkNmGI4Y>
3. Warfarin Pharmacology: <https://youtu.be/XCABvpjU4Jo>

### a) Warfarin



**4-hydroxy-3-(3-oxo-1-phenyl butyl)-2H-chromen-2-one**

Synthesis:



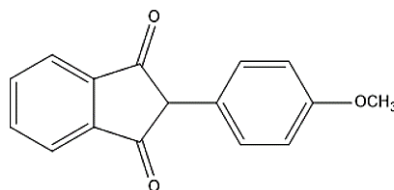
- ✓ The (-) (S) isomer of warfarin is more potent (5-8 times) than (+) (R) enantiomer
- ✓ Commercially Racemic mixture is available for use

**MOA:** Inhibit the Vit K dependent clotting factors (II, VII, IX, X) synthesis.

**Uses:**

- ✓ They are generally used to prevention and/or treatment of thrombosis, atherosclerosis, embolism, myocardial ischemia,
- ✓ Warfarin is a synthetic anticoagulant used in patients undergoing orthopaedic surgery.

### b) Anisindione




**2-(p-methoxy phenyl) indan 1,3-dione**


**MOA:** Inhibit the Vit K dependent clotting factors (II, VII, IX, X) synthesis and also inhibit the anticoagulant proteins C and S

**Uses:**

- ✓ Used as anticoagulant to prevention and/or treatment of thrombosis, atherosclerosis, embolism, myocardial ischemia

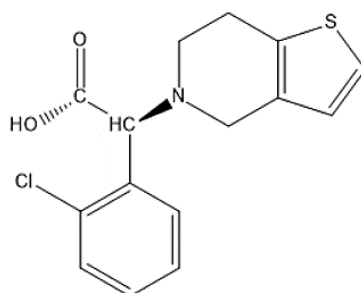
### 8.3. ANTIPLATELET DRUGS

 The drugs, which inhibit the platelet aggregation pathway. They are also used to prevent and/or treatment of myocardial ischemic diseases, atherosclerosis, embolism, etc.

 Drugs: Clopidogrel, aspirin, Dipyridamole, Ticlopidine, etc.

**Pharmacology:** <https://youtu.be/GPN5prZyB6U>

#### a) Clopidogrel



**methyl (2S)-2-(2-chlorophenyl)-2-(6,7-dihydro-4H-thieno[3,2-c] pyridin-5-yl) acetate**

**MOA:** It is an antiplatelet drug which inhibit the platelet aggregation pathway by blocking ADP receptor that is involved in the activation of platelet aggregation.

#### Uses:

- ✓ It is used as an antiplatelet drug to reduce the risk of heart disease and stroke.
- ✓ It is used along with anticoagulants for the prevention of thrombosis, and other MI disease.

Pharmacology Concepts  
By Rajesh Choudhary  
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