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](https://youtu.be/L5wDP8cj55w)
2. Vit K Pharmacology: [https://youtu.be/1E79VptcI5k](https://youtu.be/1E79VptcI5k)

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 γ–carboxylation of these which is essential for the ability Ca2+ and to get bound to phospholipid surface → further cascade of coagulation.
✓ Deficiency of vitamin K Due to liver disease, obstructive jaundice, malabsorption, long term antimicrobial

a) Menadione (Vit K3)

![Menadione](image)

2-methyl naphthalene-1,4-dione

b) Acetomenadione

![Acetomenadione](image)

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:
   b. Oral anti-coagulants:
      - **Coumarin derivetives:** 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 effecs; 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 cotting 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](https://youtu.be/cklVR0CJcho)
2. Heparin Pharmacology: [https://youtu.be/oXipkNmGl4Y](https://youtu.be/oXipkNmGl4Y)
a) Warfarin

![Chemical structure of 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

![Chemical structure of 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/GPN5prZvB6U](https://youtu.be/GPN5prZvB6U)

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.