

22.1.3.1. Heparin

Heparin is a strong anticoagulant agent which is naturally found in human blood cells (mainly in basophils or mast cells). It is synthesised in the liver and lungs of domestic animals. It is synthetically available as heparin sodium and the low- and high-molecular weight heparins (fractionated heparins). It is a potent organic acid and commercially obtained from bovine lung and porcine intestinal mucosa.

Molecular Formula: $C_{26}H_{42}N_2O_{37}S_5$

IUPAC Nomenclature: 6-[6-[6-[5-acetamido-4,6-dihydroxy-2-(sulfooxymethyl)oxan-3-yl]oxy-2-carboxy-4-hydroxy-5-sulfooxyoxan-3-yl]oxy-2-(hydroxymethyl)-5-(sulfoamino)-4-sulfooxyoxan-3-yl]oxy-3,4-dihydroxy-5-sulfooxyoxane-2-carboxylic acid

Chemistry: Heparin is a polysulphuric ester of mucoitin, i.e., it is highly sulphated anionic mucopolysaccharide. Its molecular skeleton is made up of acetylated D-glucosamine and D-glucuronic acid. Its molecular weight is variable. Heparins and heparinoids (heparin derivatives for removing inflammation) having low molecular weights are also anticoagulants.

Properties: Heparin occurs as a white or pale-coloured amorphous, solid powder with no odour. It is soluble in water; and insoluble in alcohol, acetone, benzene, chloroform, and ether.

Uses: Unfractionated heparin is prescribed for prophylaxis, for treating venous thrombosis and its extension, for preventing post-operative deep venous thrombosis and pulmonary embolism, and for preventing clotting during arterial and cardiac surgery. It is used in cardiology for preventing embolism in patients having atrial fibrillation and as an adjunct in anti-thrombin treatment in patients having unstable angina. Moreover, it is used for preventing clotting while dialysis and surgical procedures, and for preventing *in vitro* coagulation of blood transfusions and in blood samples taken for laboratory procedures.

Stability and Storage Conditions: Heparin is hygroscopic in nature and remains stable at pH 7-8 for minimum 7 years. It should be stored in sealed containers at temperatures not above 25°C. After opening the container it can be stored for up to 28 days at 25°C.

Types of Pharmaceutical Formulation: Injections.

Brand Names: Hepalean, Lovenox, Fragmin, and Innohep.

22.1.3.2. Thrombin

Thrombin is a serine protease which converts fibrinogen into fibrin and plays an important role in haemostasis and thrombosis. Thrombin also stimulates platelets and clotting factors V, VIII, and XI for enhancing haemostasis.

Molecular Formula: $C_{54}H_{84}N_{16}O_{18}$

Properties: Thrombin is a thermolabile, cream coloured powder which solubilises in saline water and gives a cloudy, pale yellow coloured solution.

Uses: Thrombin activates platelets and factors V, VIII, and XI to enhance haemostasis. It is useful in inflammation and wound healing, and is a potent mitogenic factor.

Stability and Storage Conditions: Thrombin gets affected by air (oxygen), heat, and light, thus should be stored in nitrogen-filled glass containers which are sealed to protect it from microbes and moisture. The containers may contain suitable bactericide and are kept away from light at a temperature between 2-8°C.

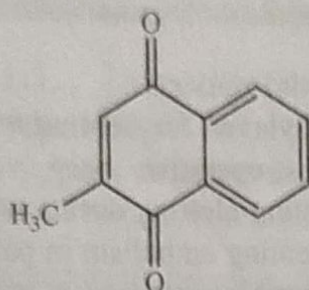
Types of Pharmaceutical Formulations: Topical solution, pump spray, syringe spray, and gel foam.

Brand Names: Thrombin-JMI, Evithrom, Thrombi-Pad, and Thrombostat.

22.1.3.3. Menadione

Menadione is a synthetic naphthoquinone with no isoprenoid side chain and biological activity. It can be converted to pharmacologically active vitamin K₂ (menaquinone) by undergoing *in vivo* alkylation. It can act as a precursor for various forms of vitamin K, but it is not used as a nutritional supplement.

Chemical Structure



Menadione

Molecular Formula: C₁₁H₈O₂

IUPAC Nomenclature: 2-methyl-1,4-dihydronaphthalene-1,4-dione

Properties: Menadione occurs as bright yellow coloured solid crystals with a very slight acrid odour and a bitter taste. It is highly soluble in water and cold alcohol; soluble in ethyl ether, benzene, chloroform, and sulphuric acid; and faintly soluble in ethanol, acetic acid, and ligroin.

Uses: Menadione helps in blood clotting and bone calcification.

Stability and Storage Conditions: Alcoholic solutions of menadione are neutral to litmus test, and remains stable up to 120°C. But it can be destroyed by reducing agents and alkali solutions, and should be protected from light.

Types of Pharmaceutical Formulations: Injections and tablets.

Brand Names: Kapilin, Injek, and K nat.

22.1.3.4. Bishydroxy Coumarin

Bishydroxy coumarin (or Dicoumarol) is an oral anticoagulant which affects the metabolism of vitamin K.

Molecular Formula: C₁₉H₁₂O₆

IUPAC Nomenclature: 4-hydroxy-3-((4-hydroxy-2-oxochromen-3-yl)methyl)chromen-2-one

Properties: Bishydroxy coumarin occurs as a solid white or creamy white coloured crystalline powder with a faint, pleasing odour and a slightly bitter taste. It is almost insoluble in water, ether, and alcohol.

Uses: Bishydroxy coumarin is used as an efficient vitamin K depleter. It is also used as an inhibitor of reductases in biochemical experiments, and for decreasing blood clotting. It is frequently used with heparin to treat deep vein thrombosis.

Stability and Storage Conditions: Bishydroxy coumarin should be stored in well-closed containers away from heat and moisture, as it decomposes on heating.

Types of Pharmaceutical Formulations: Tablets and injections.

Brand Names: Coumadin, Miradon, and Sintrom.

22.1.3.5. Warfarin Sodium

Warfarin sodium is an anticoagulant which inhibits the synthesis of coagulation factors dependent on vitamin K.

Molecular Formula: $C_{19}H_{15}NaO_4$

IUPAC Nomenclature: sodium 2-oxo-3-(3-oxo-1-phenylbutyl)chromen-4-olate

Properties: Warfarin sodium occurs as a white coloured crystalline powder with a slightly bitter taste. It is highly soluble in water; readily soluble in alcohol; and very little soluble in chloroform.

Uses: Warfarin is used for prophylaxis, and for treating venous thrombosis, pulmonary embolism and atrial fibrillation with embolisation. It is also used as an aid in the prophylaxis of systemic embolism after myocardial infarction.

Stability and Storage Conditions: Warfarin sodium loses its colour when exposed to light and air, thus should be stored away from light, moisture, and high temperature. It should not be frozen and should be stored at temperatures between 20-25°C.

Types of Pharmaceutical Formulations: Powder for injection and tablets.

Brand Names: Coumadin, Panwarfin, and Athrombin.