Abstract
The blood is a specialized fluid connective tissue or transport system which plays an important part in the maintenance of life. The transport of gases, nutrition, excretion, acid-base equity, body defence, water balance, clotting, regulation of body temperature, blood pressure, ionic balance and as a vehicle are the main functions of the blood. The anaemia, purpura, haemophilia, thrombosis, and clotting related disorders are the major complications of the hemopoietic system. Thrombosis is one of the leading cause of thromboembolic disorders affecting million peoples worldwide. Thromboembolic disorders such as pulmonary emboli, deep vein thrombosis, strokes and heart attacks are the main causes of morbidity and mortality in developed countries. Hence, antithrombotics play a pivotal role as agents for the prevention and treatment of thromboembolic disorders. A current list of various products having antithrombotic activity incorporated and prototype agents discussed. The antithrombotic includes specific antithrombotics agents like aspirin, cloostazol, clopidogrel, prasugrel, epoprostenol, dipyridamole, indomethacin, sulfipyrazone, thromboxane receptor antagonists, thromboxane synthesis inhibitors, ticlopidine, terutroban, abciximab, eptifibatide, tirofiban, and non-specific antithrombotics agents like Ca²⁺ antagonists, ketanserin, nafazatron, α-receptor antagonists, β-blockers. The fibrinolytics like tissue plasminogen activators-streptokinase; urokinase, alteplase, duteplase, anistreplase, reteplase, saruplase, tenecteplase, snake venom, and anticoagulants also equally effective in the treatment of thrombotic disorders are discussed. This article includes general as well as recent pharmacological information on different aspects of antithrombotic, fibrinolytic and anticoagulant drugs that may be useful for their better understanding by users and health care professionals.

Keywords: Thrombosis, Platelets-inhibitors, t-PA, Ticlopidine, Aspirin, Warfarin, Heparin

Introduction
The blood is a specialized fluid connective tissue; play a vital role in maintenance of life by performing various functions. The thrombosis is a major blood disorder and threat to life. It is one of the leading cause of thromboembolic disorders affecting million peoples worldwide. Thromboembolic disorders such as pulmonary emboli, deep vein thrombosis, strokes and heart attacks are the main causes of morbidity and mortality in developed countries (1). Hence, antithrombotics, fibrinolytics and anticoagulants play a pivotal role in prevention and treatment of thromboembolic disorders (2, 3). Basically three factors are responsible for the occurrence of thrombosis—(i) Obstruction of blood flow, (ii) Hypercoagulability and, (iii) Vessel wall injury. Blood coagulation involves complex interaction between the injured vessel wall, platelets and coagulation factors (4). Diseases related to abnormal blood coagulation continues to be the number one cause of death in the world.
mechanism by which blood forms a stable clot has been the subject of much activity over the past 60-70 years (5). The workers in the field have been aided by two main factors, the first is fibrin clot and secondly individuals with inherited isolated deficiencies of single components. In the blood coagulation two separate but merging systems are involved i.e. the extrinsic and intrinsic pathway. The intrinsic pathway is initiated by the activation by Hageman factor (HF Factor XII). It is a plasma protein of approximately 80,000 molecular weight with associated carbohydrate (6). The coagulation cascade includes three fundamental phases-initiations, amplification, and propagation that can be amplified readily to thrombotic events occurring within veins, arteries, arterioles, and cardiac chambers. Intrinsic and extrinsic pathways converge at the point where factor X is converted to factor Xa. Factor X is a two-chain molecule of 50,000 molecular weight and activation involves splitting an arginine-isoleucine bond on the heavy chain, which liberates a peptide and also reveals an active serine site. This site is responsible for conversion of prothrombin to thrombin and then fibrin converted to insoluble fibrin. The process of coagulation occurs via a cascade of sequential reactions requiring several enzymes and other molecules known as coagulation (or clotting) factors. Factor Xa then participates in the final common pathway that results in the fibrin clot by activating prothrombin or factor II to thrombin or factor IIa. Thrombin, the final enzyme in the coagulation cascade or haemostasis, in turn converts soluble fibrinogen into insoluble fibrin monomers (1, 7). Thrombin is a 308 amino acid serine protease that cleaves peptide bonds in selective substrate including fibrinogen. Thrombin also participates in platelet, endothelial cell & leukocyte activation, increasing additional thrombin generation & the required surfaces for inflammatory & thrombotic events (8). Thrombin derives from the clearance of prothrombin after activation of the direct or indirect coagulation cascade. It acts as a catalyst for converting fibrinogen to fibrin, which subsequently cross links to form the mesh that creates a thrombus (9). Apart from its role in the conversion of fibrinogen to fibrin, it also activates factor XIII, accelerates the formation of factor V, which increases thrombin formation, and activates platelets, thereby enhancing platelet aggregation and the release of phospholipids (7). Clotting arises from a complex interaction of various mechanisms, including the activation of the coagulation and fibrinolytic systems, disruption of the vascular endothelium, and the generalised activation of the cellular mechanisms resulting in clotting on the surface of monocytes and platelets in circulation (10). This review focused on antithrombotic, fibrinolytic and anticoagulant agents, and provides general as well as recent pharmacological information that may be useful for their better understanding by users and health care professionals.

Process of blood coagulation: Formation of a blood clot is conversion of a hydrosol into a hydrogel. The blood clot is a semi-gel that retracts on standing. The extrinsic system is activated by damage to the tissue while intrinsic system is activated by blood itself. The clotting of blood involves-activation of prothrombin, conversion of prothrombin into thrombin in the presence of Ca$^{2+}$ and numerous other clotting factors, and finally conversion of fibrinogen to fibrin (clot) by active thrombin.

**Intrinsic system**

**Extrinsic system**

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Drug therapy for thrombosis: The drugs which are used to treat the thrombosis may be classified into three main categories such as (A) antithrombotic or antiplatelet agents, (B) fibrinolytic or thrombolytic agents and (C) anticoagulants:

(A) Antithrombotic or antiplatelet agents: These agents inhibit platelet aggregation by suppressing the formation of thromboxane which promotes platelets aggregation. Platelets initiate clotting by breaking and convert the blood prothrombin into thrombin which is one of the basic substances to for the clot. They are basically useful in arterial thrombosis.

Classification of antithrombotics

<table>
<thead>
<tr>
<th>(I) Specific platelet inhibitors</th>
<th>(1) ADP receptors/ P2Y₁₆ inhibitors</th>
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<tbody>
<tr>
<td>(a) Thienopyridines-Clopidogrel, Prasugrel, Ticlopidine</td>
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<td>(b) Nucleotide/nucleoside analogues-Cangrelor, Einogrel, Ticagrelor</td>
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<td>(2) Glycoprotein IIb/IIIa inhibitors-Abciximab, Eptifibatide, Tirofiban</td>
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<td>(3) COX inhibitors-Aspirin, Alloxiarin, Carbasalate calcium, Indobufen, Triflusal, Indomethacin, Sulfynpyrazone</td>
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<td>(4) Prostaglandins analogues (PGI₂)-Beraprost, Iloprost, Prostacyclin, Epoprostenol, Treprostinil</td>
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<td>(5) Phosphodiesterase inhibitors-Cilostazol, Dipyridamole, Triflusal</td>
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<td>(6) Thromboxane inhibitors-</td>
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<td>(a) Thromboxane receptor antagonists-Terutroban</td>
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<tr>
<td>(b) Thromboxane synthase inhibitors-Dipyridamole, Picotamide</td>
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<td>(7) Miscellaneous agents-Cloricromen, Ditazole</td>
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(B) Fibrinolytic or thrombolytic agents: These agents activate plasminogen to form plasmin, which degrades fibrin and breaks up thrombi by converting insoluble clot to soluble. They are effectively useful in the treatment of myocardial complications, thrombosis and angina pectoris (11).

Classification of fibrinolytics

<table>
<thead>
<tr>
<th>(I) Tissue plasminogen activators</th>
<th>Streptokinase, Urokinase</th>
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<tr>
<td>(II) Recombinant tissue plasminogen activators</td>
<td>Alteplase, Duteplase, Anistreplase, Reteplase, Saruplase, Tenecteplase, Monteplase</td>
</tr>
<tr>
<td>(III) Miscellaneous agents</td>
<td>ASVIN, Ancrod, Fibrinolysis, Brinase</td>
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(C) Anti-coagulant agents: These agents use to inhibit coagulation process of the blood. The coagulation of the blood comprises the formation of fibrin with the involvement of thirteen clotting factors like calcium; several enzymes and various molecules associated with platelets and damaged tissue. The anti-coagulants prevent coagulation by interfering with the clotting factors. They are frequently used to suppress blood clotting in-vitro as well as in-vivo.

Pharmacology of antithrombotics
Pharmacology of Individual Drugs

(A) Antithrombotic or antiplatelet agents:
Ticlopidine is a thienopyridine derivative antiplatelet drug, acts slowly, and takes 3-7 days for peak effect. **Mechanism of action:** ticlopidine act on GPIIb/IIIa fibrinogen receptors which are located on the platelet membrane and inhibits platelet aggregation. **ADME:** onset of action is slow, 3-7 days required to reach maximum effect, converted into an active metabolite. **Dose:** 250mg/BD/with meals. **Adverse effects:** it may cause nausea, vomiting, diarrhoea, abdominal pain, aplastic anaemia, bleeding, haemorrhage, headache, hypercholesterolemia, jaundice, leukopenia, neutropenia, skin rashes, tinnitus and vertigo. **Uses:** it is preferred in the following cases-to prevent restenosis and thrombosis following coronary angioplasty and in prophylaxis of myocardial infarction and stroke, coronary artery diseases, coronary bypass implants, cerebrovascular diseases, venous thrombosis, peripheral vascular diseases, prosthetic heart valves and arteriovenous shunts, acute thrombotic stroke, atrial fibrillation, pulmonary embolism and peripheral arterial occlusion and stable angina pectoris (12).

Epoprostenol (13, 14) is a short acting prostacyclin or PGI₂, useful in treatment of pulmonary hypertension. **Pharmacological actions:** strongly dilate all vascular beds, inhibits platelet aggregation and prevent thrombogenesis and platelet clumping in lungs. **ADME:** administered intravenously as infusion, t½ is 3
minutes. **Dose:** 0.5mg/i.v. infusion. **Adverse effects:** it may cause nausea, vomiting, chest pain, drowsiness, hyperglycaemia, hypotension and tachycardia. **Uses:** it is preferred in the following cases-to inhibit platelet aggregation during haemodialysis, during cardiac bypass surgery and pulmonary hypertension (15).

Dipyridamole (16) is a powerful coronary vasodilator, anti-platelet agent, suppresses platelet aggregation by potentiating PGI2 or inhibiting phosphodiesterase that leads to increase cAMP. It also inhibits thrombus formation in the arterial circulation. **Pharmacological actions:** produces anticoagulant effect, improves blood flow and sinus oxygen saturation by increasing the plasma concentration of adenosine by inhibiting the uptake of adenosine into erythrocytes and other body tissues. **ADME:** administered orally, absorption is highly variable, mainly metabolized in liver. **Interactions:** potentiate the action of aspirin and warfarin. **Contra-indicated in:** aortic stenosis, heart failure, exacerbates migraine, hypotension and myasthenia gravis. **Dose:** 100mg/TDS or QID/orally. **Adverse effects:** it may cause angioedema, blurred vision, diarrhoea, dizziness, dry mouth, GIT effects, headache, hot flushes, hypotension, more bleeding during surgery, myalgia, nausea, precipitates cardiac failure, precipitation of glaucoma, rashes, severe bronchospasm, tachycardia, throbbing headache, thrombocytopenia, urine retention and urticaria. **Uses:** it is preferred in the following cases-angina pectoris (17), thromboembolism, post myocardial infarction, post stroke condition, thrombus formation after cardiac surgery, persistent coronary artery aneurysms, supraventricular and ventricular tachycardia, Wolff-Parkinson white syndrome, ischemic attacks and coronary bypass surgery.

Aspirin (16, 18) is an acetylsalicylic acid, possesses antiplatelet activity and useful in the treatment of thrombosis. **Pharmacological actions:** prevents atheromatous plaques formation in arteries, inhibits PGs synthesis in vessel wall and the release of ADP from platelets. **Mechanism of action:** inhibition of platelet activation, stickiness or aggregation by irreversible inhibition of platelet cyclo-oxygenase and thromboxane synthetase which leads to depletion of prostacyclin (PGI2) and thromboxane (TXA2) which is key platelets activator (19). **Precautions:** asthma, hepatic impairment, peptic ulceration, pregnancy, renal impairment, uncontrolled hypertension. **Contra-indicated in:** peptic ulceration, haemophilia, bleeding disorders, breast feeding and children less than 15 years. **Dose:** 75-300mg/day. **Adverse effects:** it may cause bronchospasm, GIT complications, and haemorrhage. **Uses:** it is preferred in the following cases-thrombus formation after cardiac surgery, persistent coronary artery aneurysms, prophylaxis of stroke, stable angina, myocardial infarction, atrial fibrillation, claudication, eclampsia in pregnancy and diabetic retinopathy.

Clopidogrel (20) is a glycoprotein receptor antagonist, and inhibits platelet aggregation. **Mechanism of action:** suppressed platelet aggregation by inhibition of GPIIb/IIIa receptors. **ADME:** well absorbed after oral administration, platelet aggregation inhibition achieved within 90 minutes, metabolized quickly. **Interactions:** action enhanced by aspirin. **Contra-indicated in:** breast feeding and bleeding. **Dose:** 300mg flowed by 75mg/day/orally. **Adverse effects:** it may cause hemorrhage; GIT upsets CNS disorders, biliary disorders, and hepatic complications. **Uses:** it is preferred in following thromboembolic complications-stroke, myocardial infarction, peripheral arterial disease and unstable angina (21).

Ketanserin (22, 23) is a 5HT2, á-adrenergic and dopaminergic receptor blocker. **Pharmacological actions:** it reduces blood pressure and Inhibits vasoconstriction, bronchoconstriction and platelet aggregation by
blocking the action of serotonin. **ADME:** administered orally, metabolized in liver to an inactive metabolite ketanserinol, $t_{1/2}$ is 10-18 hours, excreted unchanged in urine. **Dose:** 40mg orally/TDS. **Adverse effects:** it may cause nausea, postural hypotension, palpitation, fatigue, dryness of mouth, headache, sedation and dizziness. **Uses:** it is preferred in following cases-aggression, anxiety, carcinoid syndrome, depression, diabetic gastroparesis, dyspepsia, emesis, gastroesophageal reflex disease, hypertension, inflammation, irritable bowel syndrome, migraine, nociception, Parkinsonism, peripheral vascular diseases, schizophrenia and urticaria.

**Abciximab** (24) is a humanized, nonantigenic, potent platelet aggregation inhibitor, Fab fragment of a chimeric monoclonal antibody against GP IIb/IIIa. **Mechanism of action:** it prevents platelet aggregation by blocking glycoprotein IIb/IIIa receptors involved in platelet aggregation. **ADME:** administered as bolus injection followed by slow i.v. infusion, $t_{1/2}$ is 10-30 min, but effect remains for 24 hours. **Dose:** 0.25mg/kg, i.v., 10-60 min before PCI, followed by 10µg/min for 12 hours. **Adverse effects:** it may cause haemorrhage, thrombocytopenia, constipation, ileus and arrhythmias. **Uses:** it is preferred in cases of unstable angina and as adjuvant to coronary thrombosis (25).

**Eptifibatide** (26) is an antiplatelet heptacyclic peptide GP IIb/IIIa receptor antagonists. It is derived from a protein found in the venom of the south eastern pygmy rattlesnake. **ADME:** it is administered as bolus injection initially followed by slow i.v. infusion. It has short half life and excreted in urine. **Contra-indicated in:** thrombocytopenia, renal insufficiency and allergy. **Adverse effects:** it may cause bleeding, thrombocytopenia, hypotension, cardiovascular failure, arrhythmias and severe allergic reactions. **Uses:** it is preferred in cases like unstable angina and as adjuvant to coronary thrombosis (25).

**Terutroban** (27, 28) is a potent, long acting antiplatelet antithrombotic agent, selective antagonist of thromboxane receptors. **Mechanism of action:** it blocks thromboxane induced platelet aggregation and vasoconstriction. **ADME:** it is active orally and $t_{1/2}$ is 6-10 hours. **Uses:** it is effective in animal models of thrombosis, atherosclerosis and diabetic neuropathy and recently undergoing phase-III development for the secondary prevention of acute thrombotic complications of atherosclerosis (29).

**Beraprost** (30) is a prostacyclin (PGI₂) analogue has vasodilatory, antiplatelet and cytoprotective properties. **Pharmacological actions:** it enhances liver enzymes, triglycerides and bilirubin. **Mechanism of action:** it binds to prostacyclin receptors and reduces the release of intracellular calcium and thus cause relaxation of the smooth muscle cells and vasodilation. **ADME:** administrated orally and should be taken with food. **Precautions:** may enhancing bleeding tendency in patients on anticoagulants, antiplatelet or fibrinolytic agents, and menstruating women. **Dose:** 120-180 µg/day. **Contra-indicated in:** patients with haemorrhage and pregnancy. **Interactions:** any drug intensifies bleeding. **Adverse effects:** it may cause headache, hot flushes, nausea, GIT upsets, bleeding tendency and dizziness. **Uses:** it is preferred in cases like thrombosis and atherosclerosis.

**(B) Fibrinolytic or thrombolytic agents :** **Tissue plasminogen activator** (31) is fibrin-selective but does not activate systemic plasminogen. It is synthesized by recombinant technology and is also obtained from cultured human melanoma cells. **Mechanism of action:** it induces fibrinolysis of the formed thrombus by preferentially activating plasminogen bound to fibrin. **Dose:** 100 mg/ i.v./3 hours. **Uses:** it is preferred in the treatment of deep vein thrombosis (32, 33).

**Alteplase** (34) is an enzyme that catalyzes tissue plasminogen to plasin and is commonly used to prevent clot-related myocardial disorders.

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Mechanism of action: it dissolves blood clots by converting plasminogen into plasmin that digests fibrin, fibrinogen, and other proteins. Interactions: Its action accelerates in combination with heparin. Contraindicated in: bleeding, defective homeostasis, trauma, surgical procedures, stroke, acute pericarditis, hypoglycaemia and hyperglycaemia. Dose: 100 mg/ i.v. infusion. Adverse effects: it may cause adverse effects like nausea, vomiting, fever, arrhythmias, allergy, hypotension, intracranial haemorrhage, and GIT bleeding. Uses: it is preferred in cases of angina pectoris, as an anticoagulant, intravascular thrombosis, ischemic diseases, myocardial infarction, pulmonary embolism, and to dissolve thrombi.

Streptase or streptokinase (35) is obtained from α-haemolytic Streptococci group-C. It combines with circulating plasminogen to form an activation complex, which then causes limited proteolysis of other plasminogen molecules to plasmin. Antistreptococcal antibodies present due to the initial dose of streptokinase make a loading dose necessary in the beginning. Mechanism of action: activates the conversion of plasminogen (profibrinolysin) into plasmin (fibrinolysin), which stimulates the conversion of fibrin (insoluble) into fibrin fragments (soluble). Dose: 250,000 units followed by 100,000 units/ hour for 1-3 days/ i.v. Contraindicated in: active internal bleeding, bleeding diathesis, cerebral tumour. If hemostasis is important, pregnancy, previous cerebrovascular accident, recent cranial trauma, surgery within ten days, and uncontrolled hypertension. Adverse effects: it may cause anaphylaxis, bronchospasm, hypersensitivity, fever, hypotension, and arrhythmias. Uses: it is preferred in cases of acute arterial thromboembolism, acute myocardial infarction, acute thrombotic stroke, deep venous thrombosis, local thrombolysis in the anterior chamber of the eye, myocardial infarction, and unstable angina.

Anistreplase (37) or anisoylated plasminogen-streptokinase activator complex is a human plasminogen and streptokinase. The anisoyl group is removed in blood by a hydrolytic deacylation process. Dose: 30 units/ i.v. infusion over 2-5 minutes. Adverse effects: it may cause hypotension and allergy.

Tenecteplase (38) is developed by the recombinant technique and is a mutant of alteplase containing 527 amino acids. It is more fibrin-selective and more resistant to plasminogen activator inhibitor-1. It is given as a single bolus injection of 30-50 mg. It has a longer t1/2 and greater efficacy.

Saruplase (39) is a full-length, human, unglycosylated, single-chain polypeptide containing 411 amino acids, urokinase type plasminogen activator and also known as prourokinase. It is obtained by recombinant technology from E. coli. It is a fibrin-specific fibrinolytic agent and is effectively used for the treatment of thrombotic disorders such as acute myocardial infarction. Dose: 20 mg/ i.v. bolus followed by a 60 mg infusion for 60 minutes. Uses: it is preferred in thrombotic disorders and myocardial infarction.

(C) Anti-coagulant agents: Warfarin (40-42) is a coumarin derivative, structurally similar to...
vitamin-K, used as oral anticoagulating agent because it prevents clot formation. **Mechanism of action:** antagonizes the production and action of vitamin-K, and also inhibiting the reduction of it into active metabolite. **ADME:** well absorbed after oral administration, bound to albumin, metabolized by conjugation and glucuronic acid in liver, t₁/₂ is 36-44 hours, and excreted in urine and stool. **Interactions:** action potentiated by antibiotics, cephalosporins, aspirin, salicylates, phenylbutazone, cotrimoxazole, sulphonamide, phenoxytin, probenecid, moxalactam, carbenicillin, tolbutamide, chloramphenicol, metronidazole, antiplatelet agents, alcohol, cimetidine, anabolic hormones, antimalarials, praziquantel, action inhibited by barbiturates, rifampicin, griseofulvin and oral contraceptives. **Contra-indicated in:** colitis, peptic ulcer, pregnancy, severe hypertension, bacterial endocarditis, renal failure and hepatic disorders. **Uses:** it is preferred in cases like cerebrovascular diseases, defibrination syndrome, myocardial infarction, pulmonary embolism, rheumatic heart diseases, vascular surgery, venous thrombosis and also used as adjunct to antineoplastic chemotherapy.

**Heparin** (45) is a rapid but short acting anticoagulant, obtained from porcine intestine mucosa and bovine lung tissue. It is a mixture of acidic substances, naturally synthesized in body and stored in mast cells and basophils. It is useful in thromboembolic diseases or to prevent further clotting. **Pharmacological actions:** acts as anticoagulant in vitro and in vivo, inhibits platelet aggregation, clear lipemia of plasma by releasing lipoprotein lipase from blood vessels and tissues. **Mechanism of action:** it bound to antithrombin-III and inactivates factor Xa and thrombin. **ADME:** administered i.v. or s.c, metabolized by heparinase in liver and excreted in urine. **Contra-indicated in:** haemophilia, haemorrhage, hypersensitivity, liver disease, neurosurgery, ocular surgeries, peptic ulcer, piles, recent cerebral haemorrhage, sever hypertension, tuberculosis. **Dose:** 5000-15000 units/12 hours. **Adverse effects:** it may cause allergy, alopecia, haemorrhage, haematuria, hyperkalemia, osteoporosis and spontaneous fractures, renal and hepatic dysfunctions, skin necrosis, suppress cell mediated immunity, suppress wound healing and thrombocytopenia. **Uses:** it is preferred in cases like acute peripheral arterial occlusion, myocardial infarction, thrombosis on prosthetic heart valves, to keep blood outside the body in fluid state, to prevent clotting during haemodialysis or bypass surgery, to prevent clotting in open heart surgery, to prevent post operative deep venous thrombosis and pulmonary embolism, unstable angina and venous thrombosis.

**Danaparoid** (43) is a mixture of heparin glycosaminoglycans obtained from porcine intestinal mucosa. **Mechanism of action:** stimulates inhibition of factor Xa by antithrombin. **ADME:** administered subcutaneously or intravenously, t₁/₂ is 24 hours. **Contra-indicated in:** renal failure. **Uses:** it is preferred in cases like deep venous thrombosis and heparin induced thrombocytopenia.

**Dalteparin** (44) is a low molecular weight heparin and having antiplatelet, antithrombotic activities. **Mechanism of action:** inhibition of thrombus and clot formation by blocking clotting factor Xa and IIa. **ADME:** administered subcutaneously, crosses placental barrier and secreted in breast milk, t₁/₂ is about 4.5 hours, excreted out in urine. **Contra-indicated in:** hypersensitivity, benzyl alcohol, severe thrombocytopenia, uncontrolled bleeding and pregnancy. **Adverse effects:** it may cause local irritation and erythema at the site of injection, chills, fever, pain, hematomata, urticaria, thrombocytopenia, hyperkalemia, haemorrhage and asthma. **Uses:** it is preferred in cases like deep vein thrombosis and pulmonary embolism and also used as adjunct to antineoplastic chemotherapy.
Dabigatran etexilate (46, 47) is a prodrug, substrate of P-glycoprotein transporter and use as oral anticoagulant. **Mechanism of action:** it reversibly inhibits the active site of thrombin. **ADME:** administered orally rapidly and completely converted to dabigatran by esterases in plasma and liver. 6% bioavailability reach within 2 hours, \( t_{1/2} \) is 14-17 hours and about 80% of drug as such excreted out through kidneys. **Contra-indicated in:** elderly patients over the age of 75 years due to GIT bleeding. **Interactions:** quinidine reducing the clearance of dabigatran but amiodarone increases dabigatran level upto 50%. **Dose:** 150 mg/BD/orally. **Adverse effects:** it may cause gastrointestinal bleeding. **Uses:** it is preferred in cases like venous thromboembolism, stroke or systemic embolism in patients with atrial fibrillation.

Apixaban (46, 47) is a potent, oral, reversible, direct, highly selective, active drug and use as oral anticoagulant. **Mechanism of action:** it prevents coagulation by blocking thrombin or generation of factor Xa and thrombin activity. It inhibits free and clot-bound factor-Xa, and prothrombinase activity. Activation of factor-X to factor-Xa via the intrinsic and extrinsic pathway plays a central role in the cascade of blood coagulation. It indirectly inhibits platelet aggregation induced by thrombin. **ADME:** administered orally rapidly absorbed, maximum plasma concentration achieved within 3 hours, \( t_{1/2} \) is 8-14 hours and excreted out through kidneys. **Contra-indicated in:** patients receiving azole-antimycotics and HIV protease inhibitors. **Dose:** 2.5 mg/BD/orally. **Adverse effects:** it may cause any type of bleeding. **Uses:** it is preferred in cases like venous thromboembolism following elective hip or knee replacement surgery and stroke in patients with atrial fibrillation.

Hence, antithrombotics play a pivotal role as agents for the prevention and treatment of thromboembolic disorders. The various products having antithrombotic activity include antithrombotics, fibrinolytics and anticoagulants have enlisted in the article. A brief description, pharmacological actions, mechanism of action, ADME, dose, precautions, interactions, contra-indications, adverse effects and therapeutic potential have been described in the present review. This article includes general as well as recent pharmacological information on different aspects of antithrombotic, fibrinolytic and anticoagulant drugs that may be useful for their better understanding by users and health care professionals.

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