Lecture : Pharmaceuticals

stage : second

Section : Anesthesia techniques

College : Al-Mamoun University

Course : second

Dr.Sarmad.M.hashim

Drug used in CVS

- Anticoagulants
- Antiplatelet agents and dual antiplatelet therapy
- ACE inhibitors
- Angiotensin II receptor blockers
- Angiotensin receptor-neprilysin inhibitors
- Beta blockers
- Calcium channel blockers
- Cholesterol-lowering medications
- Digitalis preparations
- Diuretics
- Vasodilators

Anticoagulants

- Anticoagulants are a family of medications that stop your blood from clotting too easily. They can break down existing clots or prevent clots from forming in the first place. These medications can help stop life-threatening conditions like strokes, heart attacks and pulmonary embolisms, all of which can happen because of blood clots.

Why would I need to take these medications?

- When blood clots work like they’re supposed مفترض to, they form at the site of an injury that needs repair and they stay put. However, when clots don't stay in one place or form in your bloodstream, they can be extremely dangerous. If a clot is too large, it can get stuck in a smaller blood vessel. If that smaller blood vessel is in a critical location, it can block blood flow that one of your organs needs to survive.

Why would I need to take these medications? Indication of anticoagulant

- Blockages from blood clots can cause the following deadly events:
- Stroke. Blood clots are particularly dangerous if they travel up to your brain, where they can easily get stuck in the smaller blood vessels
- Pulmonary embolism (PE). This occurs when a blood clot gets stuck and blocks an artery in your lungs. If the blockage is severe enough, a pulmonary embolism can be deadly

Why would I need to take these medications? Indication of anticoagulant

- Heart attack (myocardial infarction). These occur when arteries that supply blood to your heart become blocked. These can also be deadly.

Work of anticoagulant

- The anticoagulant drugs inhibit either the action of the coagulation factors (for example, heparin)
- or interfere with the synthesis of the coagulation factors (for example, vitamin K antagonists such as warfarin).

Type of anticoagulant

- Heparin
- Warfarin

Heparin

- Heparin is an anticoagulant drug that prevents the formation of new clots as well as the expansion of clots that already exist.
- Heparin occurs naturally in the body and is produced by basophils and mast cells.
- Heparin does not break down clots directly, but enhances the body's natural clot lysis mechanisms
- Heparin is a medication that inhibits clotting by activating your body's anti-clotting processes. One of the anticlotting processes uses a type of blood protein called antithrombin.

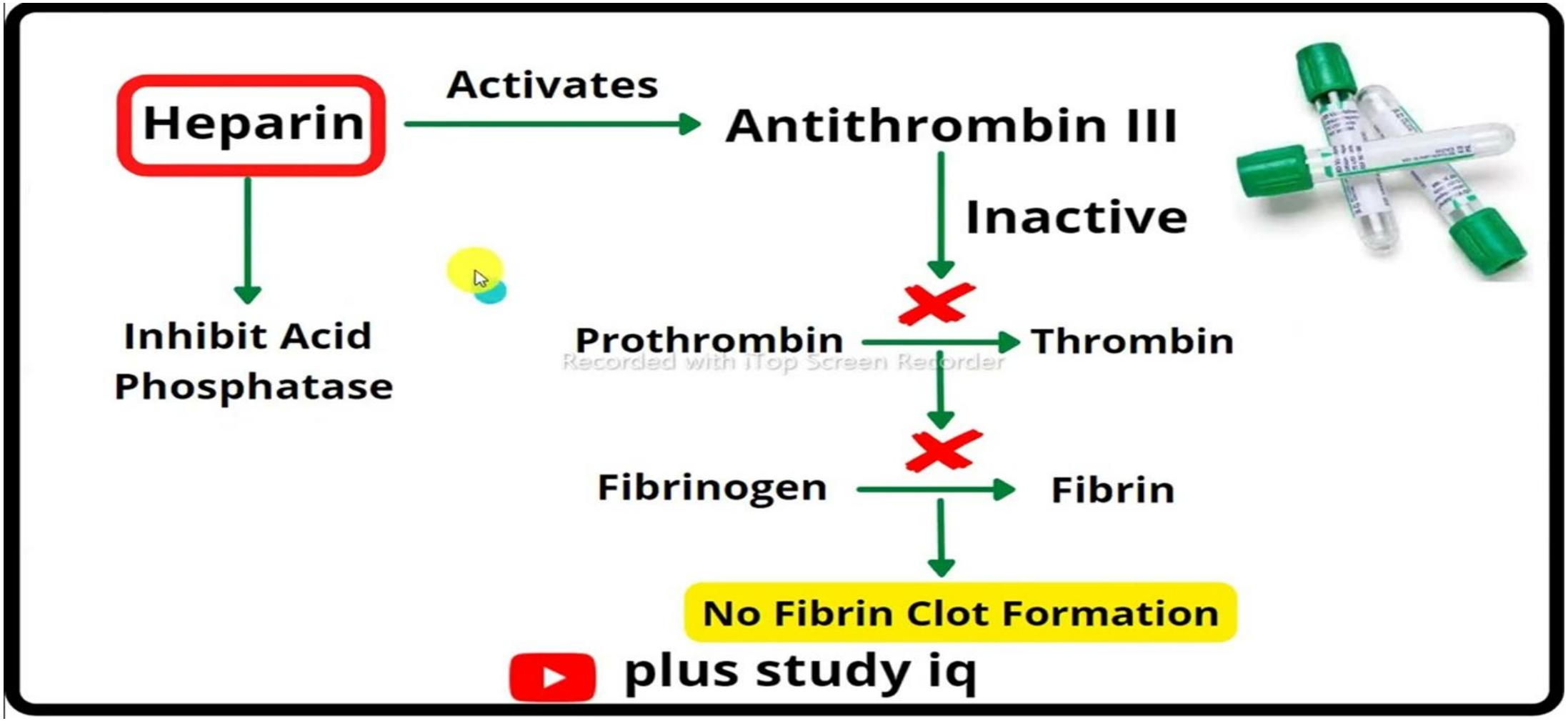
Heparin

- Heparin works by activating antithrombin, and antithrombin prevents other coagulation process elements from functioning effectively. Finally lead to prevent clotting .
- The first heparin production protocols used canine or bovine livers as a source. Later, mainly porcine mucosa and bovine lungs were used

Mechanism of action of heparin

- Under normal circumstances, ant-thrombin III (ATIII) inactivates thrombin (factor IIa) and factor Xa.
- This process occurs at a slow rate. Administered heparin binds reversibly to ATIII and leads to almost sudden inactivation of factors IIa and Xa
- The heparin-ATIII complex can also inactivate factors IX, XI, XII and plasmin inhibition clotting factor lead to stop process of clotting.

Mechanism of action of heparin



Therapeutic use of heparin

1) Treatment acute deep vein thrombosis and pulmonary embolism (DVT or PE).
2) Clinically use to prevent post-operative venous thrombosis.
3) In pregnant , to treat venous thrombo-embolism , because not enter placenta.

Pharmakentaic

- **Absorption:** Heparin is not absorbed through the gastrointestinal tract and is therefore administered via a parenteral route. Peak plasma concentration and the onset of action are achieved immediately after intravenous administration.
- **Volume of distribution :**The volume of distribution is 0.07 L/kg
- **Protein binding:** Heparin is highly bound to antithrombin, fibrinogens, globulins, serum proteases, and lipoproteins
- **Metabolism:** Heparin does not undergo enzymatic degradation

Route of administration

- Heparin is supplied parenterally, either by IV infusion or by subcutaneous (SC) injection, as it is poorly absorbed orally due to its size and polyanionic charge.

Side effect of heparin

1) bleeding from the gums when brushing teeth
2) blood in the urine
3) Thrombocytopenia : circulating blood contains an abnormally low number of platelets.
4) coughing up blood

Warfarin

- Warfarin is a vitamin K antagonist used to treat venous thromboembolism, pulmonary embolism, thromboembolism with atrial fibrillation, thromboembolism with cardiac valve replacement, and thromboembolic events post myocardial infarction

Indicated

- 1) Prophylaxis and treatment of venous thromboembolism and related pulmonary embolism.
- 2) Prophylaxis and treatment of thromboembolism associated with atrial fibrillation.
- 3) Prophylaxis and treatment of thromboembolism associated with cardiac valve replacement.
- 4) Use as adjunct therapy to reduce mortality, recurrent myocardial infarction, and thromboembolic events post myocardial infarction.

Mechanism of action Of warfarin

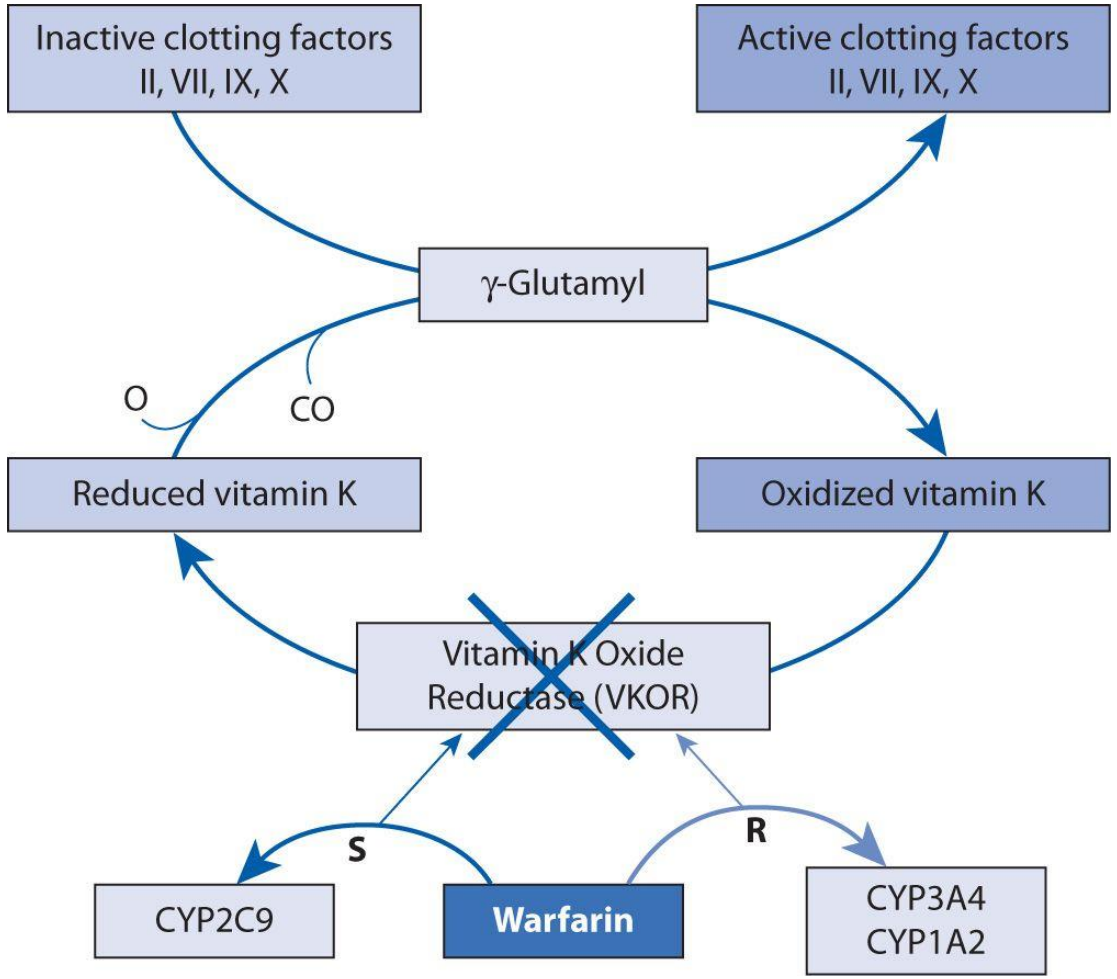
- warfarin is a [vitamin K] antagonist which acts to inhibit the production of vitamin K by vitamin K epoxide reductase
- The reduced form of vitamin K, vitamin KH_2 is a cofactor used in the γ-carboxylation of coagulation factors VII, IX, X, and thrombin
- Uncarboxylated factors VII, IX, X, and because thrombin is biologically inactive, it functions to stop the coagulation cascade.
- Warfarin binds to vitamin K epoxide reductase complex subunit 1 and irreversibly inhibits the enzyme thereby stopping the recycling of vitamin K by preventing the conversion of vitamin K epoxide to vitamin K_1

Mechanism of action Of warfarin

Mechanism of action

1. Inhibit **Vitamin K epoxide reductase**
2. Depletion of the reduced form of vitamin K (which is a cofactor of gamma carboxylation of vitamin K-dependent coagulation factors)
3. Without gamma caroxylation, the vitamin K-dependent factors (**factor II, VIII, IX, X**) cannot function
4. Clot-forming pathway is less effective, thus anticoagulant effect

Mechanism of action Of warfarin



Pharmakentic

- **Absorption:** Completely absorbed from the GI tract. The mean Tmax for warfarin sodium tablets is 4 hours.
- **Volume of distribution Vd:** of 0.14 L/kg. Warfarin has a distrubution phase lasting 6-12 hours. It is known to cross the placenta and achieves fetal serum concentrations similar to maternal concentrations.
- **Protein binding:** 99% bound primarily to albumin.

Pharmakentic

- **Metabolism:** The major metabolic pathway is oxidation to various hydroxywarfarins, comprising 80-85% of the total metabolites. CYP2C9 is the major enzyme catalyzing the 6- and 7-hydroxylation of S-warfarin while 4'-hydroxylation occurs through CYP2C18 with minor contributions from CYP2C19.
- **Route of elimination:** The elimination of warfarin is almost entirely by metabolism with a small amount excreted unchanged.Label,17,9 80% of the total dose is excreted in the urine with the remaining 20% appearing in the feces.

Route of administration

- warfarin comes as a tablet to take by mouth. It is usually taken once a day with or without food.
- Intravenous warfarin provides an alternative administration route for patients who cannot receive the oral formulation and cannot be administered subcutaneous low-molecular-weight heparins due to adverse effects.

Side effect of warfarin

- Bleeding from a cut or the nose or gums that lasts more than 5 or 10 minutes when applying pressure.
- Vaginal bleeding
- Coughing up blood.
- Dizziness or weakness.
- Severe stomach pain.
- Vomiting of blood or material that looks like coffee grounds.
- Stools that are black or bloody.

THROMBOLYTIC DRUGS

- Include Streptokinase & Alteplase.
- - Streptokinase : one of the first agents that activate a systemic fibrinolytic state that can lead to bleeding problems.
- - Alteplase : acts more locally on the thrombotic fibrin to produce fibrinolysis.

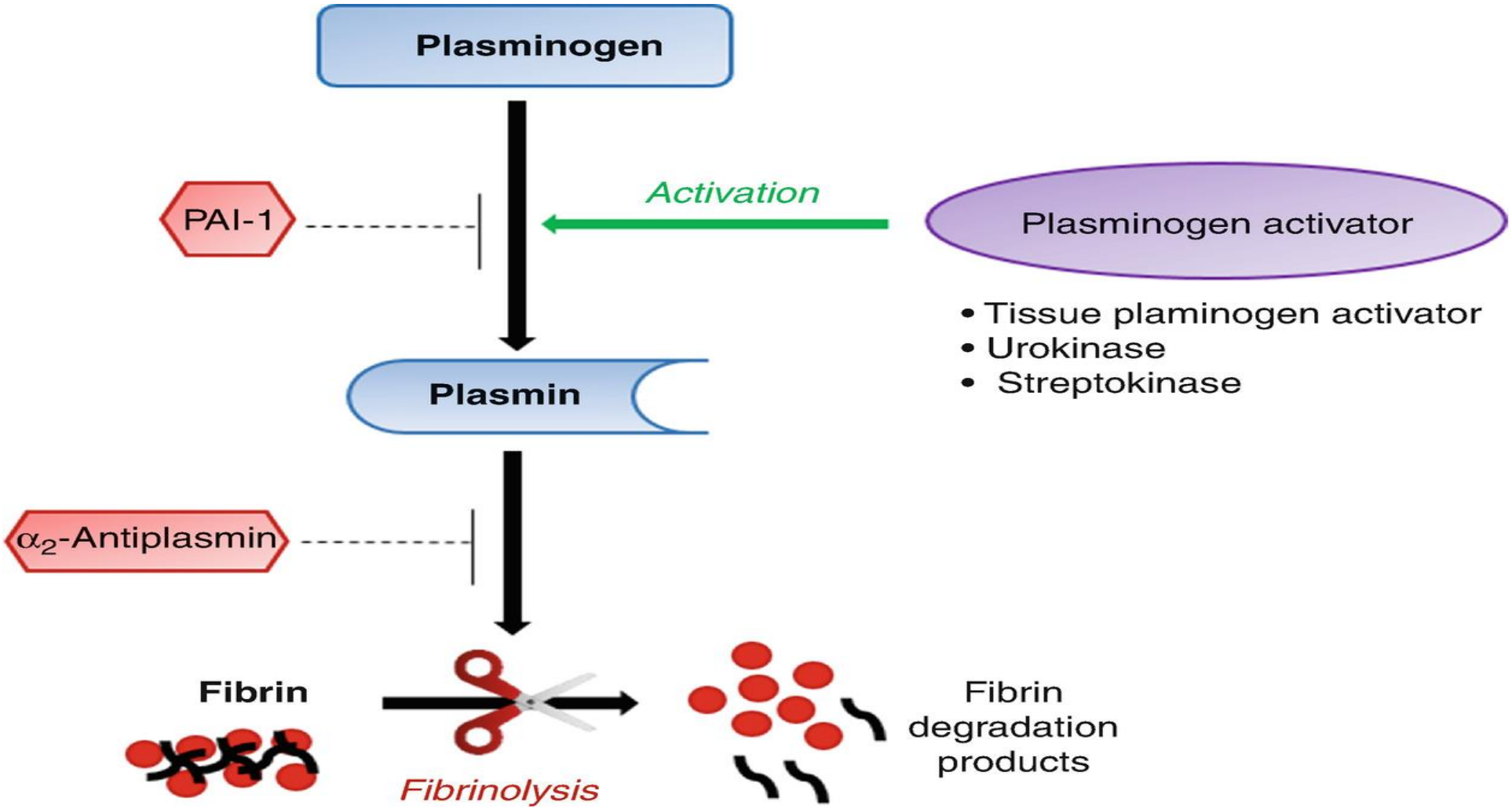
Overview

- Streptokinase is used to dissolve blood clots that have formed in the blood vessels. It is used immediately after symptoms of a heart attack occur to improve patient survival. This medicine may also be used to treat blood clots in the lungs (pulmonary embolism) and in the legs (deep venous thrombosis)
- Alteplase is a fibrinolytic agent; it also is referred to as tissue plasminogen activator (tPA). Alteplase converts plasminogen to the proteolytic enzyme plasmin, which lyses fibrin as well as fibrinoge

Mechanism of action of Streptokinase

- Plasminogen is an inactive molecule that becomes activated to plasmin when the Arg/Val bond is cleaved. Plasmin breaks down fibrin clots created by the blood clotting cascade. Streptokinase forms a highly specific 1:1 enzymatic complex with plasminogen which converts inactive plasminogen molecules into active plasmin. Plasmin degrades fibrin clots as well as fibrinogen and other plasma proteins. This in turn leads to the degradation of blood clots

Mechanism of action of Streptokinase



Therapeutic use of Streptokinase

- myocardial infarction
- pulmonary embolism
- deep vein thrombosis
- arterial thrombosis or emolism
- occlusion of arteriovenous cannulae

Pharmakentic

- clearance by sites in the liver
- having short biological half-life (i.e. 15 to 30 min)
- Duration of action 4 – 12 hours

- **Not :** The time required for 50 % of the drug concetrition to leave the body.

Route of administration streptokinase

- Systemic administration: A single dose of 1.5 million IU streptokinase should be infused intravenously over one hou

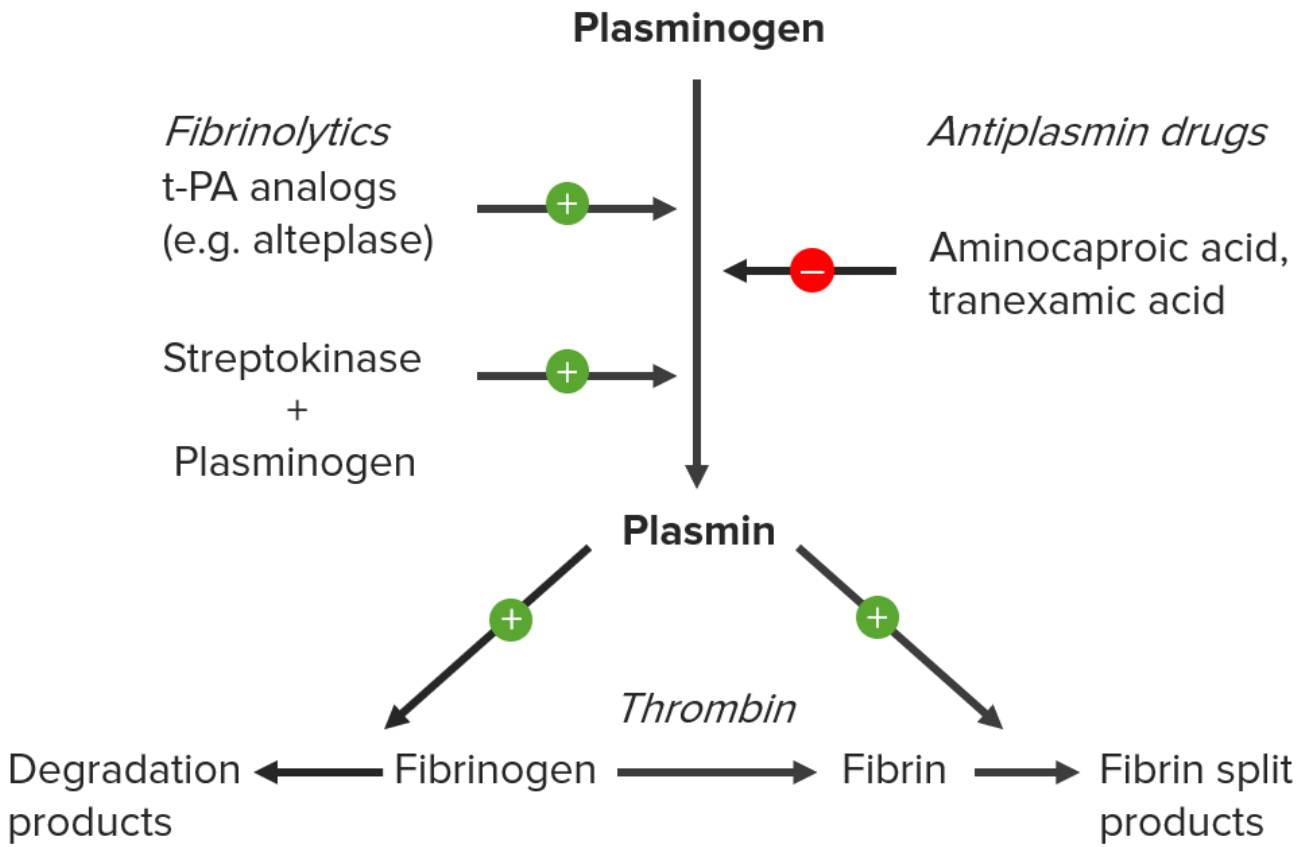
Side effect of streptokinase

- allergic reactions.
- hypotension.
- bleeding.

Mechanism of action of alteplase

- Alteplase is a fibrinolytic agent; it also is referred to as tissue plasminogen activator (tPA). Alteplase converts plasminogen to the proteolytic enzyme plasmin, which lyses fibrin as well as fibrinogen

Mechanism of action of alteplase



Therapeutic uses of alteplase

- n acute ischemic stroke,
- pulmonary embolism,
- acute myocardial infarction
- deep vein thrombosis
- and occluded catheters thrombosis .

Pharmakentic of alteplase

- Intravenous alteplase is cleared primarily by the liver with an initial half-life of fewer than 5 minutes and a terminal half-life of 72 minutes.

Route adminstration of alteplase

- Alteplase may be administered intra-venously (IV) by infusion directly into a vein through a peripheral or central venous catheter.
- or it may be given through an endovascular mircrocatheter delivery system positioned in an artery to directly infuse alteplase into the clot.

Side effect of alteplase

- bleeding, angioedema, anaphylaxis, and fever