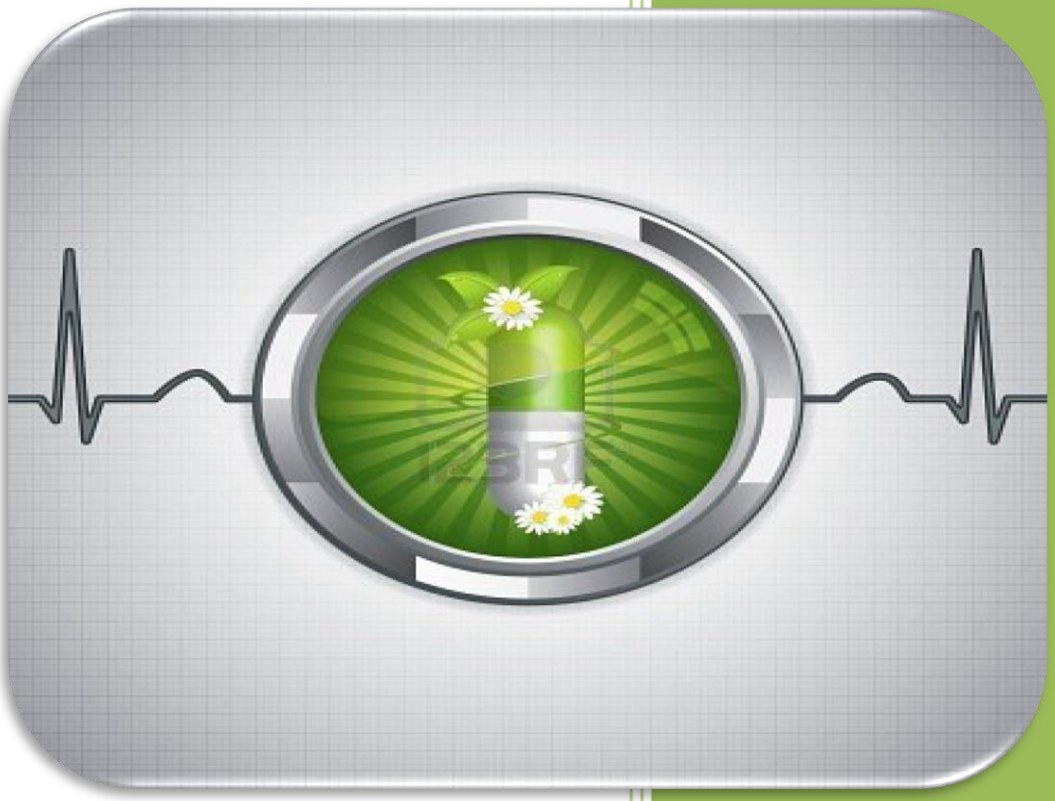
Pharmacology team

Fibrinolytic Drugs

Fibrinolyic drugs

1. Streptokinase.
2. Anistreplase.
3. Urokinase
4. Tissue plasminogen activators (t -PA).



Definition:

Drugs that cause lysis of already formed thrombus in clinical settings where ischemia may be fatal so blood flow can be restored to prevent further damage and assist healing.

Uses of fibrinolytic drugs :

1. **Acute myocardial infarction.**
2. **Acute thrombotic stroke.**
3. **Peripheral artery occlusion " Blockade".**
4. **Pulmonary embolism.**
5. **Deep venous thrombosis.**

Contraindications to Thrombolytics :

- **Cerebrovascular disease**
- **Recent head trauma or cranial tumor**
- **Active internal bleeding**
- **Major surgery within two weeks**
- **Active peptic ulcer**
- **Pregnancy**
- **Uncontrolled hypertension**

	MOA	PK	Side effects
Streptokinase	1. protein produced by B- hemolytic streptococci 2. Acts indirectly by forming plasminogen-streptokinase complex which converts inactive plasminogen into active plasmin.	-It is the least expensive. - T 1/2 = half an hour. - I.V. Infusion	1. Bleeding due to *activation of circulating plasminogen* 2. Hypersensitivity due to antigenicity (rash, fever, allergic reaction). 3. Hypotension. 4. not used in patients with streptococcal infections (have antistreptococcal antibodies and may develop fever, allergic reactions and resistance upon treatment with streptokinase).
Anistreplase (APSAC)	-Anisoylated plasminogen-streptokinase activator complex - Is a complex of purified human plasminogen + bacterial streptokinase that rendered inactive by introducing anisoyl group at its active site. - It is a *prodrug, de-acylated in circulation into the active plasminogen-streptokinase complex (acts directly to convert plasminogen into plasmin).*		Advantages Longer duration of action (T1/2 is 70-120 min). Given as a bolus I.V. (30 U over 3 - 5 min.). Disadvantages (less than streptokinase alone). 1. Expensive. 2. Antigenic. 3. Allergic reactions. 4. Bleeding due to minimal fibrin specificity
Urokinase	-Human enzyme synthesized by the kidney, obtained from either urine or cultures of human embryonic kidney cells. - acts directly converting plasminogen to active plasmin.	-given by intravenous infusion - Dose 300,000U over 10 min then 300,000U/h for 12h.	Disadvantages 1. Expensive. 2. Systemic lysis. Advantages 1. Not antigenic. 2. No Hypotension

Tissue Plasminogen Activators (t - PA) Alteplase	Alteplase (Single Chain). - Reteplase (Deleted Form). - Tenecteplase • All are recombinant human t - PA. • Synthesis by recombinant DNA technology.	Alteplase very short half life (5 min.) Is delivered by an initial IV bolus injection,followed by two IV infusions (60 mg i.v. bolus +40 mg infusion over 2 h).	Advantages 1. Clot specific (fibrin specific). • activate fibrin-bound plasminogen rather than free plasminogen in blood. 2. Limited systemic fibrinolysis. 3. Non–antigenic (Can be used in patients with antistreptococcal antibodies).

the process of taking a gene from one organism and inserting it into the DNA of another; called also gene splicing

Antiplasmin (Antifibrinolytics)

Inhibit plasminogen activation and thus inhibit fibrinolysis and promote clot stabilization.

Uses

- **Antidote for fibrinolytics.**
- **Adjunctive therapy in hemophilia.**

Aminocaproic Acid & tranexamic acid

- **Given orally**
- **It competitively inhibits conversion of plasminogenin to plasmin**

Aprotinin

- **It acts by inhibiting plasmin. (inhibit the action of plasmin)**
- **Can be taken orally or I.V.**

Questions:

A)Which one of these drugs acting indirectly:

1)Streptokinase.

2)Anistreplase.

3)Urokinase.

B)All of these drugs are fibrinolytic drugs except:

1)Alteplase.

2)Aprotinin.

3) Anistreplase.

C)Which one of the following is the major side effect of all fibrinolytic drugs:

1)Antigenic.

2)Hypotension.

3) Bleeding.

Answers:

- **A) 1**
- **B) 2**
- **C) 3**