

	( Acetylsalicylic Acid ) Aspirin	ADP pathway inhibitors Ticlopidine & Clopidogrel	Phosphodiesterase inhibitors e.g. dipyridamol	Glycoprotein IIb/ IIIa receptor inhibitors eg: Abciximab , Tirofiban
MOA	<ol style="list-style-type: none"> <li>1. <b>Irreversible inhibition of cyclooxygenase enzyme via acetylation.</b></li> <li>2. <b>Small dose inhibits thromboxane synthesis in platelets (TXA2)</b> But not prostacyclin (PGI2) synthesis in endothelium (larger dose).</li> </ol>	<p>Inhibits the binding of ADP to its platelet receptor by irreversibly modifying the platelet ADP receptor.</p> <p>ps: ( <b>Monitoring of blood count every month is essential</b>)</p>	Phosphodiesterase inhibitor thus ↑ cAMP in the blood platelets → inhibition of platelet aggregation.	<ul style="list-style-type: none"> <li>• <b>Is a receptor for fibronectin, fibrinogen, vitronectin and von Willebrand factor.</b> <b>Abciximab</b></li> <li>• a monoclonal antibody that inhibits glycoprotein IIb/ IIIa receptor.</li> <li>• It inhibits all the pathways of platelet activation (Final common pathway).</li> <li>• Tirofiban</li> <li>• inhibits glycoprotein IIb/ IIIa receptor at site that interacts with Arginine-Glycine-Aspartic sequence of fibrinogen (by occupancy of the receptor) fibrinogen like mimetic agent.</li> <li>• Non peptide drug.</li> </ul>
PK		<ul style="list-style-type: none"> <li>- Given orally.</li> <li>- Extensively bound to plasma proteins.</li> <li>- Metabolized in the liver to give active metabolites.</li> <li>- Slow onset of action (3 - 5 days).</li> <li>- is taken twice ( 250 mg twice daily ).</li> </ul>		<ul style="list-style-type: none"> <li>• <b>Abciximab</b></li> </ul> <p>-Given I.V. infusion</p> <p>- adjuncts to heparin and aspirin for prevention of cardiac ischemic complications.</p> <ul style="list-style-type: none"> <li>• <b>Tirofiban</b></li> </ul> <p>-Excreted unchanged by the kidney.</p>
USE	<b>Prophylaxis of myocardial infarction</b>		<ul style="list-style-type: none"> <li>• Taken orally.</li> <li>• <b>Primary prophylaxis in patients with prosthetic heart valves ( in combination with warfarin ).</b></li> <li>• As prophylactic therapy to treat angina pectoris in combination with aspirin .</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Tirofiban</b></li> </ul> <p>-Acute coronary syndromes to decrease incidence of thrombotic complications</p>
Side effects	<ol style="list-style-type: none"> <li>1. <b>Peptic Ulcer.</b></li> <li>2. <b>Increased incidence of GIT bleeding</b></li> </ol>	<b>Sever neutropenia</b> , Bleeding (Prolong bleeding time) , CYT P450 <b>inhibitors</b> , G.I.T : Diarrhoea, Nausea,Dyspepsia. Allergic Reactions.	<p>Disadvantages : Headache</p> <p>Advantage : No excess risk of bleeding</p>	

	Streptokinase	Anistreplase ( APSAC )	Urokinase	Tissue Plasminogen Activators ( t - PA ) Alteplase
MOA	acts indirectly by forming plasminogen-streptokinase complex which converts inactive plasminogen into active plasmin.	-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 <i>prodrug</i> , de-acylated in circulation into the active plasminogen-streptokinase complex (acts directly to convert plasminogen into plasmin).	-Human enzyme synthesized by the kidney, obtained from either urine or cultures of human embryonic kidney cells. - acts directly converting plasminogen to active plasmin.	Alteplase ( Single Chain ). - Reteplase ( Deleted Form ). - Tenecteplase • All are recombinant human t - PA. • Synthesis by recombinant DNA technology.
PK	-It is the least expensive. - T 1/2 = half an hour. - I.V. Infusion (250,000U then 100,000U/h for 24-72 h).		-given by intravenous infusion - Dose 300,000U over 10 min then 300,000U/h for 12h.	Alteplase very short half life (5 min.) (60 mg i.v. bolus + 40 mg infusion over 2 h). Reteplase (two I.V. bolus of 10 U ).
Side effects	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).	Advantages Longer duration of action ( $T_{1/2}$ is <u>70-120 min</u> ). 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	Disadvantages 1. Expensive. 2. Systemic lysis. Advantages 1. Not antigenic. 2. No Hypotension	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).