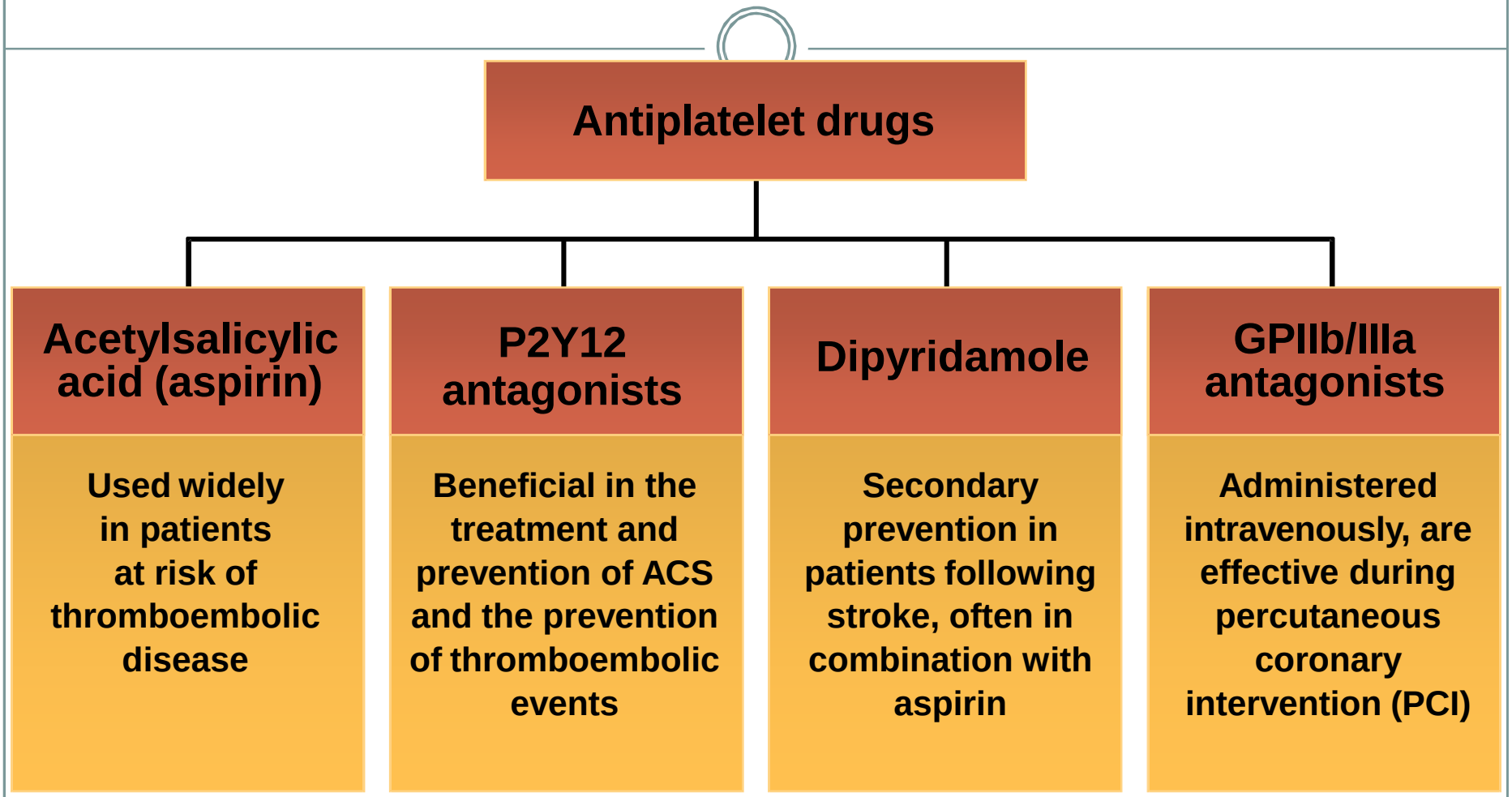
PharmD IIIrd Yr

PHARMACOLOGY-II

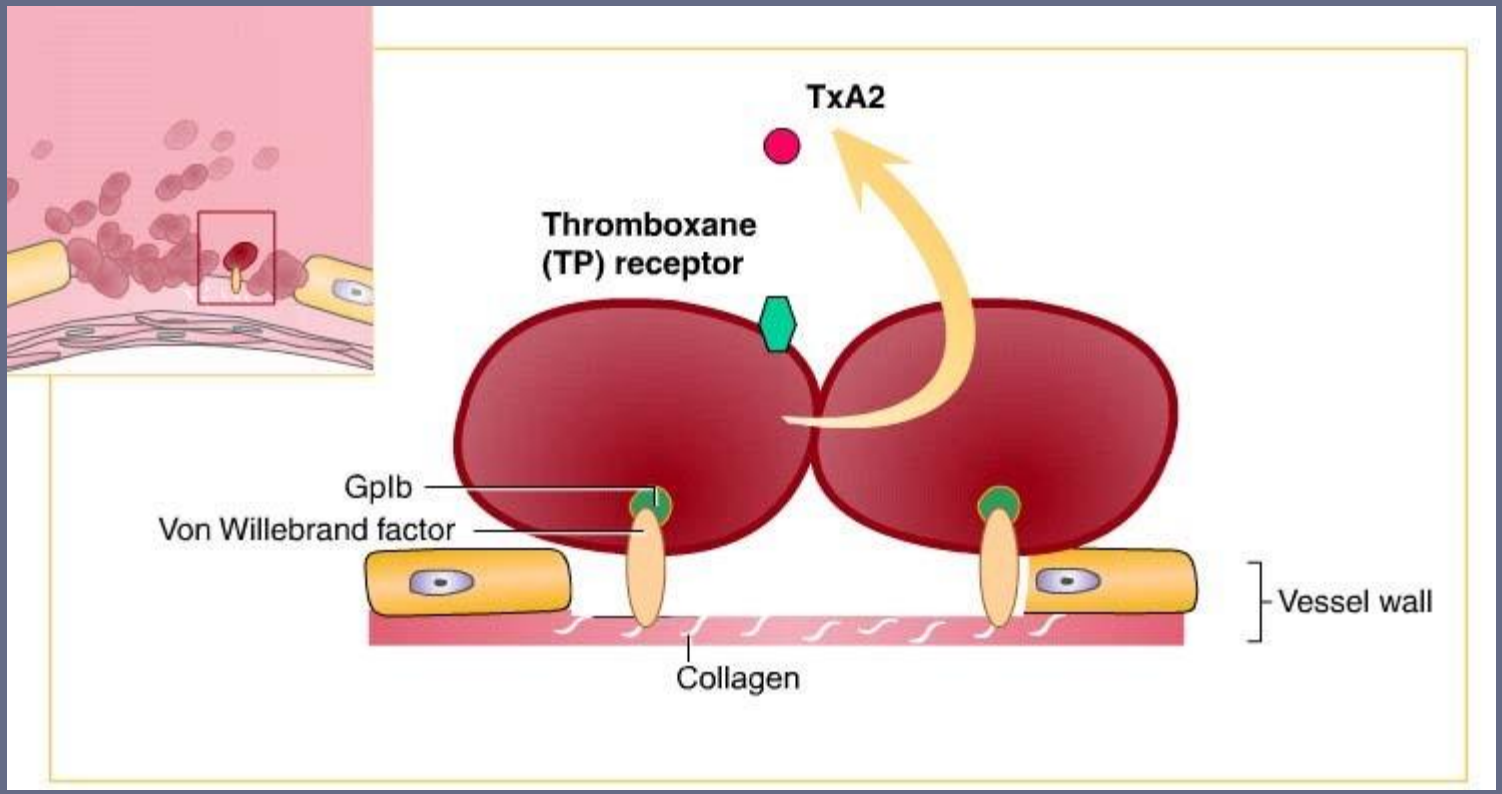
Antiplatelet drugs

-By Rupam Swain

Antiplatelet drugs



Acetylsalicylic acid – mechanism of action



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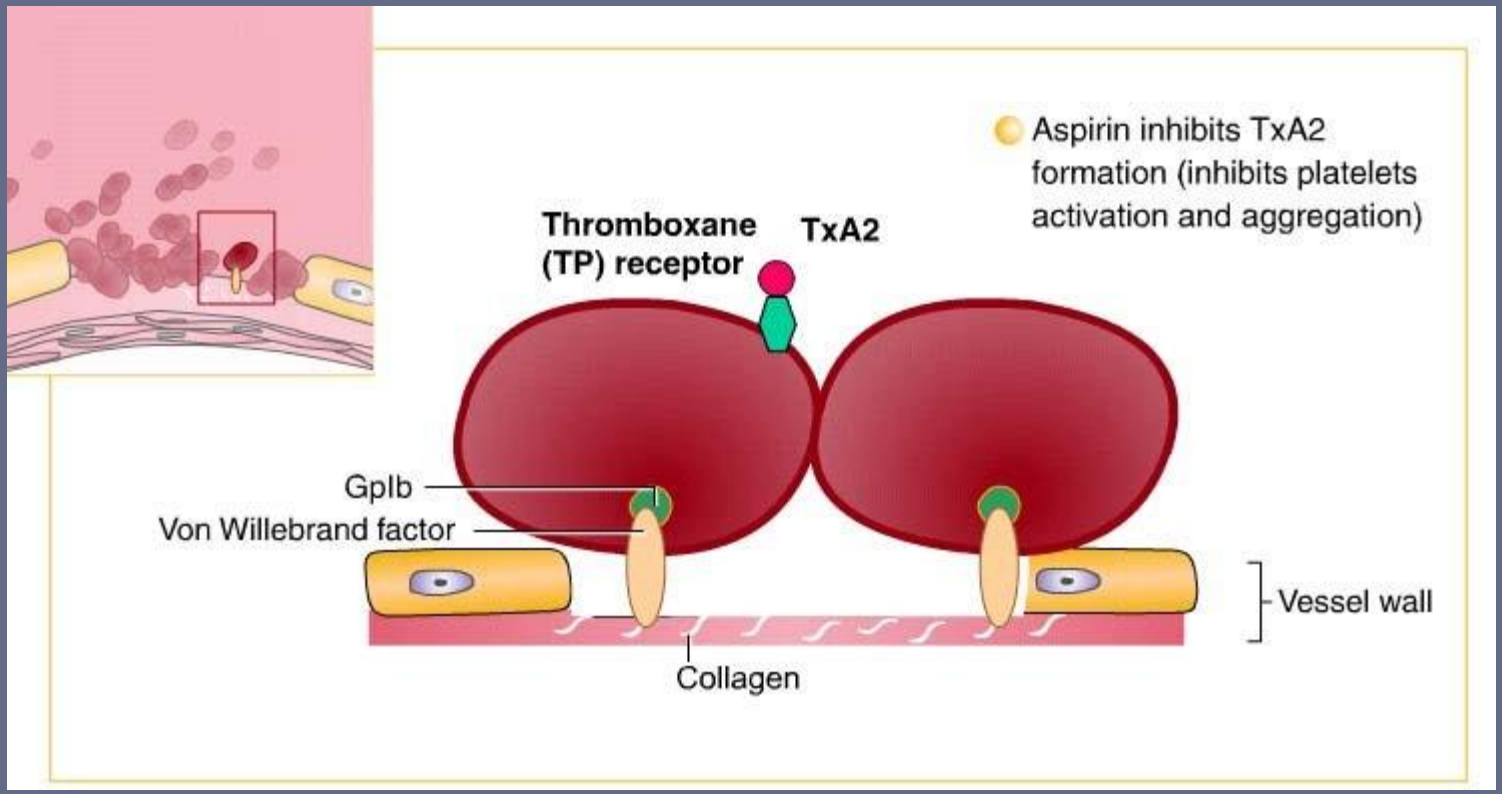

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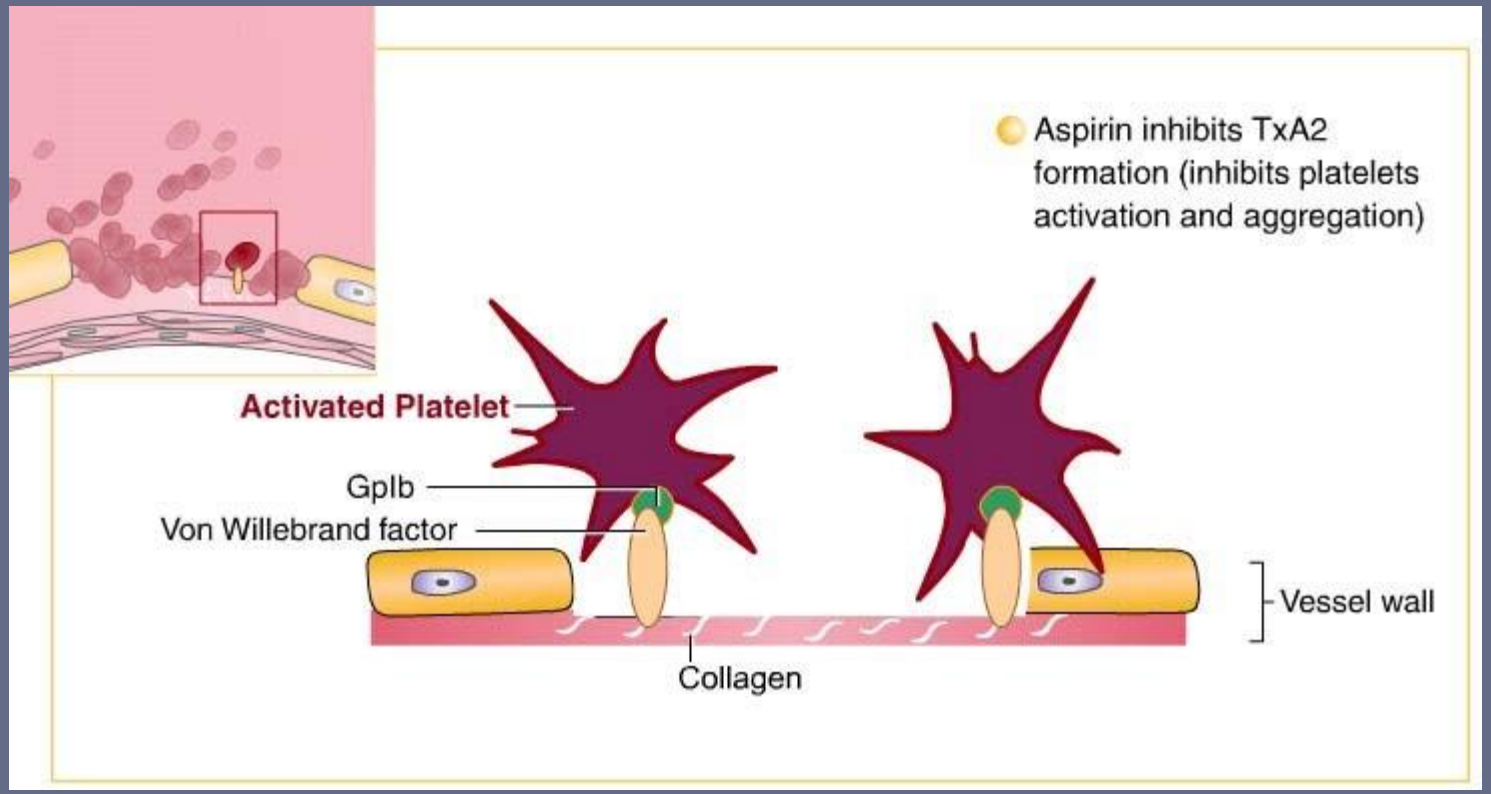

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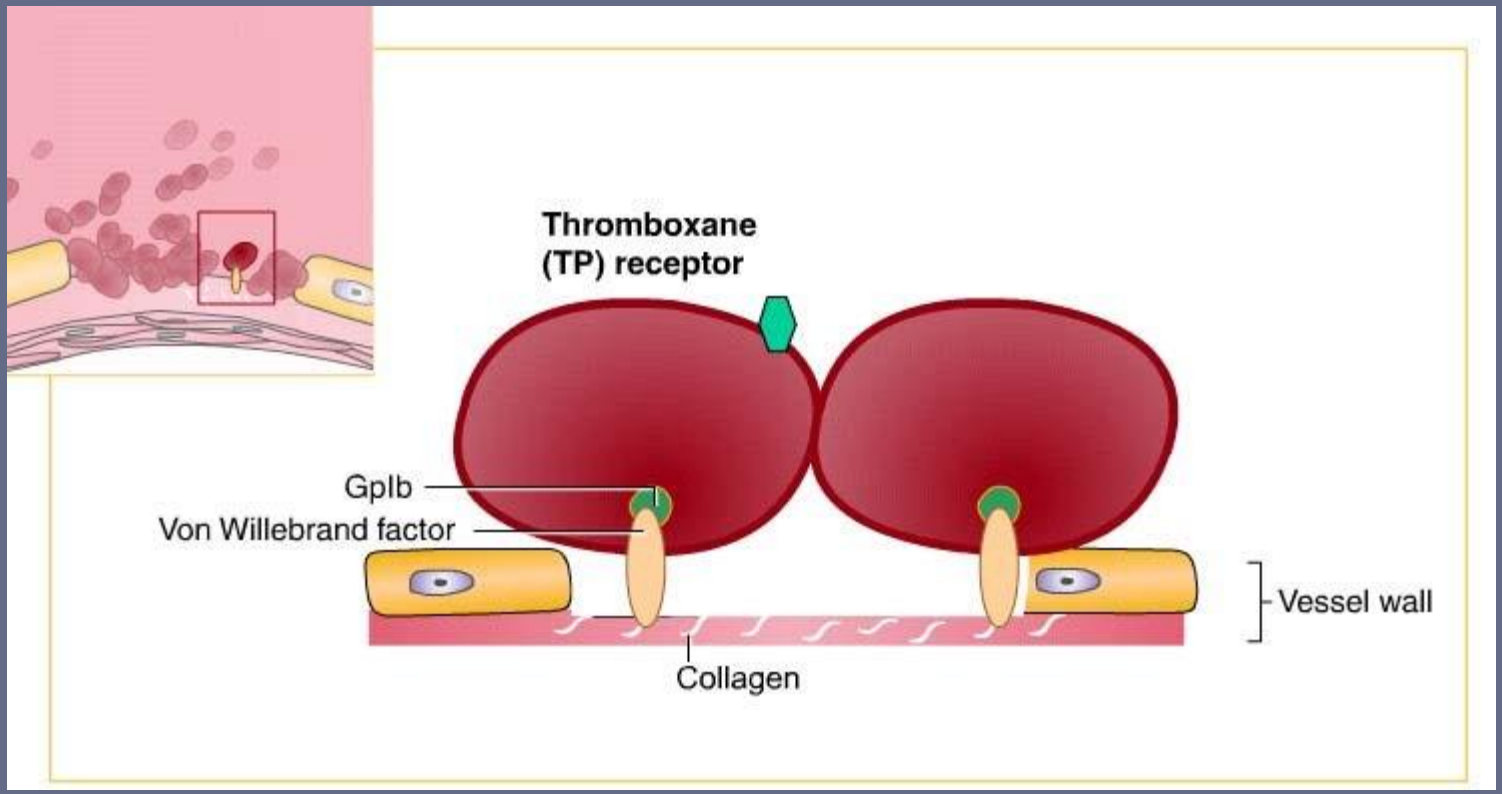

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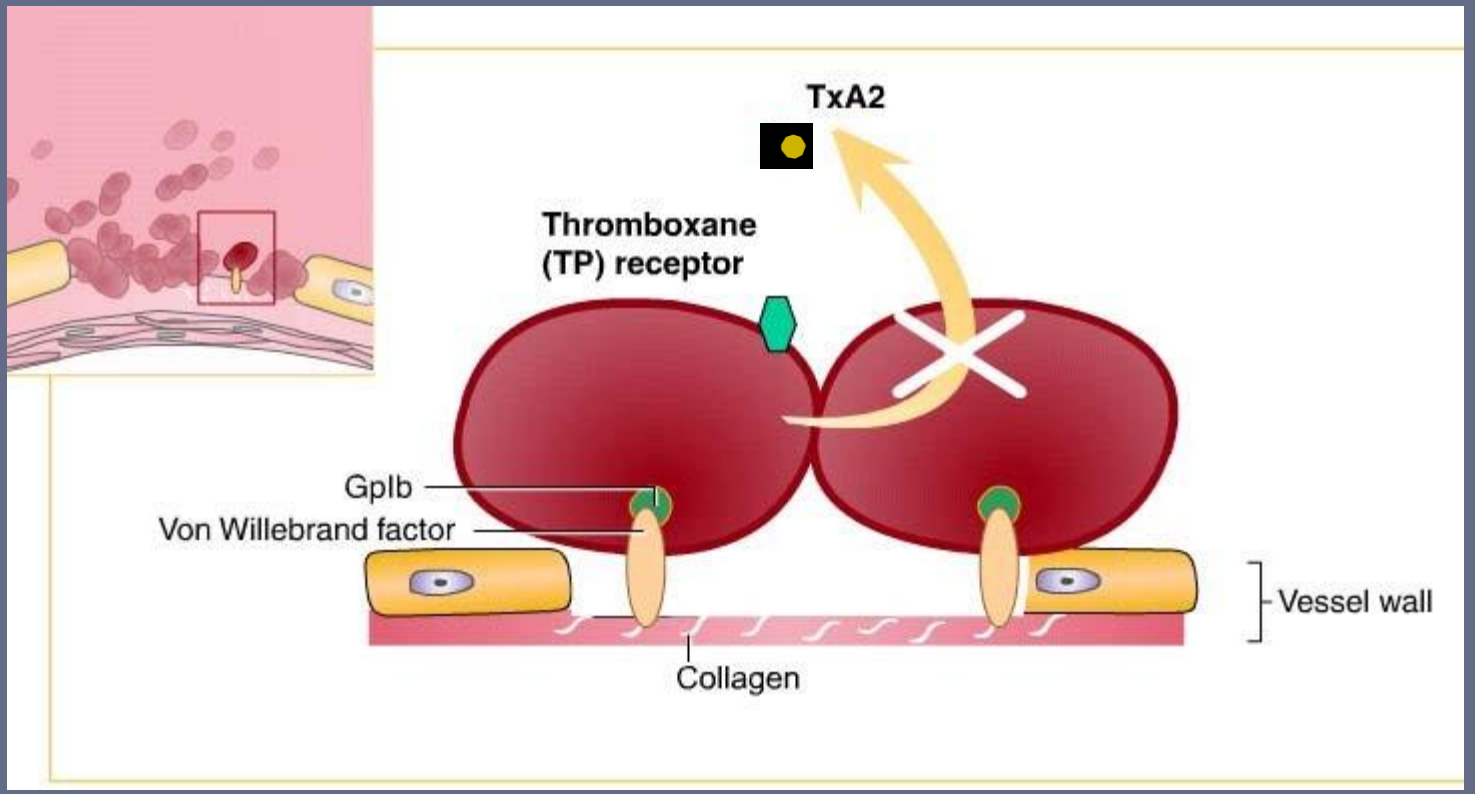


Acetylsalicylic acid – pharmacokinetics

- Rapid absorption of aspirin occurs in the stomach and upper intestine, with the peak plasma concentration being achieved 15-20 minutes after administration
- The peak inhibitory effect on platelet aggregation is apparent approximately one hour post-administration
- Aspirin produces the irreversible inhibition of the enzyme cyclo-oxygenase and therefore causes irreversible inhibition of platelets for the rest of their lifespan (7 days)

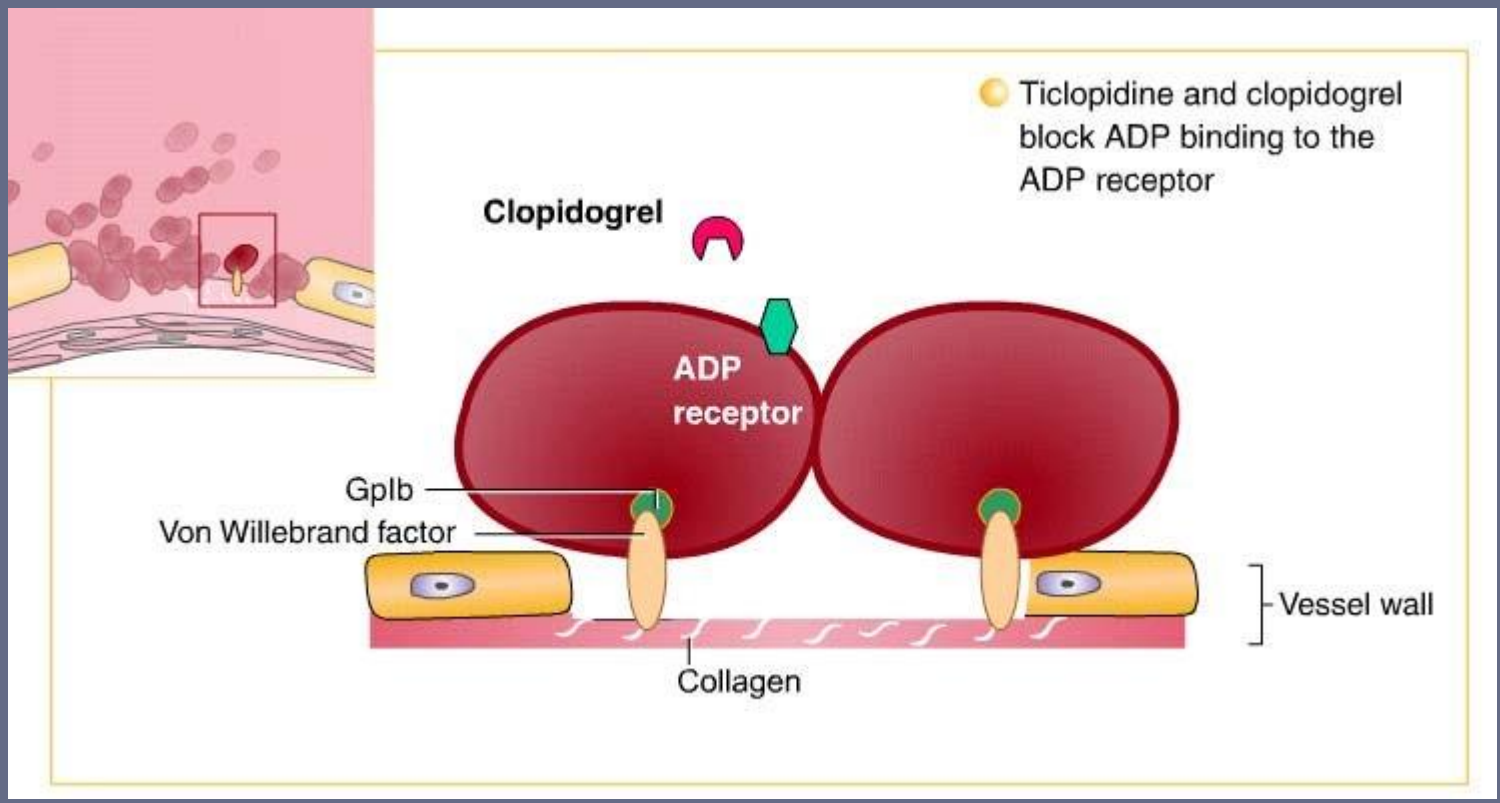
Acetylsalicylic acid – major use

- Secondary prevention of transient ischaemic attack (TIA), ischaemic stroke and myocardial infarction
- Prevention of ischaemic events in patients with angina pectoris
- Prevention of coronary artery bypass graft (CABG) occlusion

Acetylsalicylic acid – major drawbacks

- Risk of gastrointestinal adverse events (ulceration and bleeding)
- Allergic reactions
- Is not a very effective antithrombotic drug but is widely used because of its ease of use
- Lack of response in some patients (aspirin resistance)
- The irreversible platelet inhibition

ADP-receptor antagonists – mechanism of action



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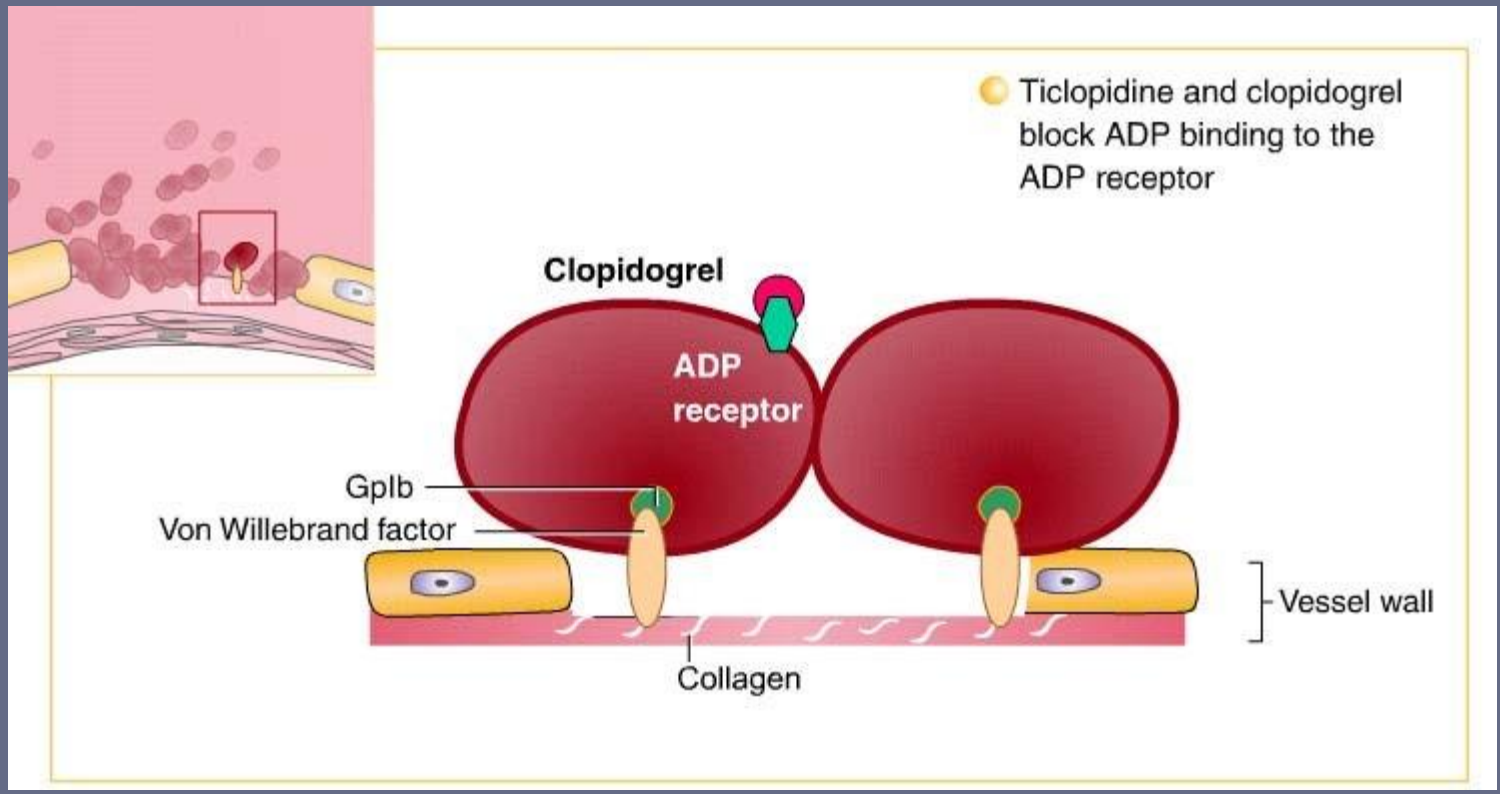
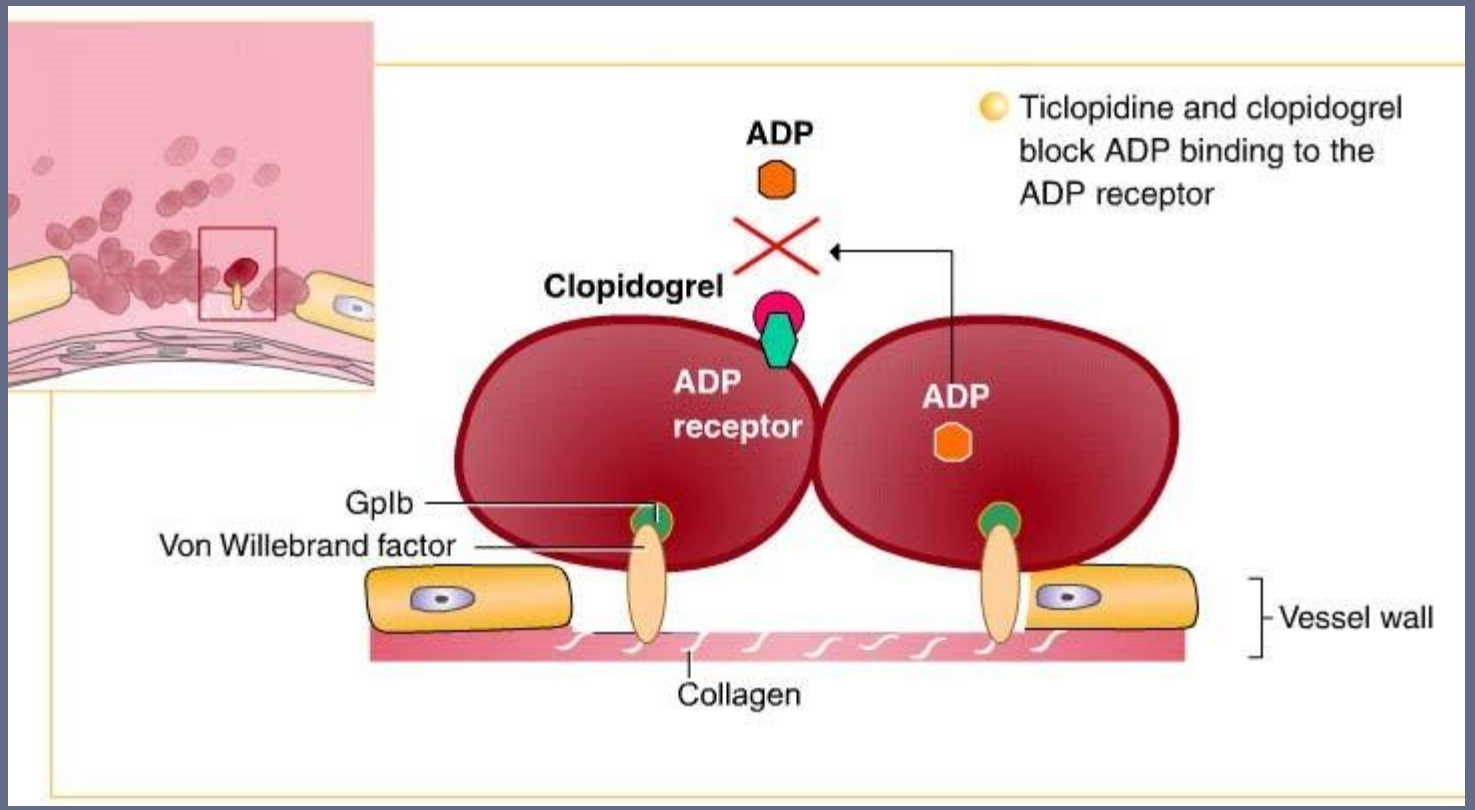
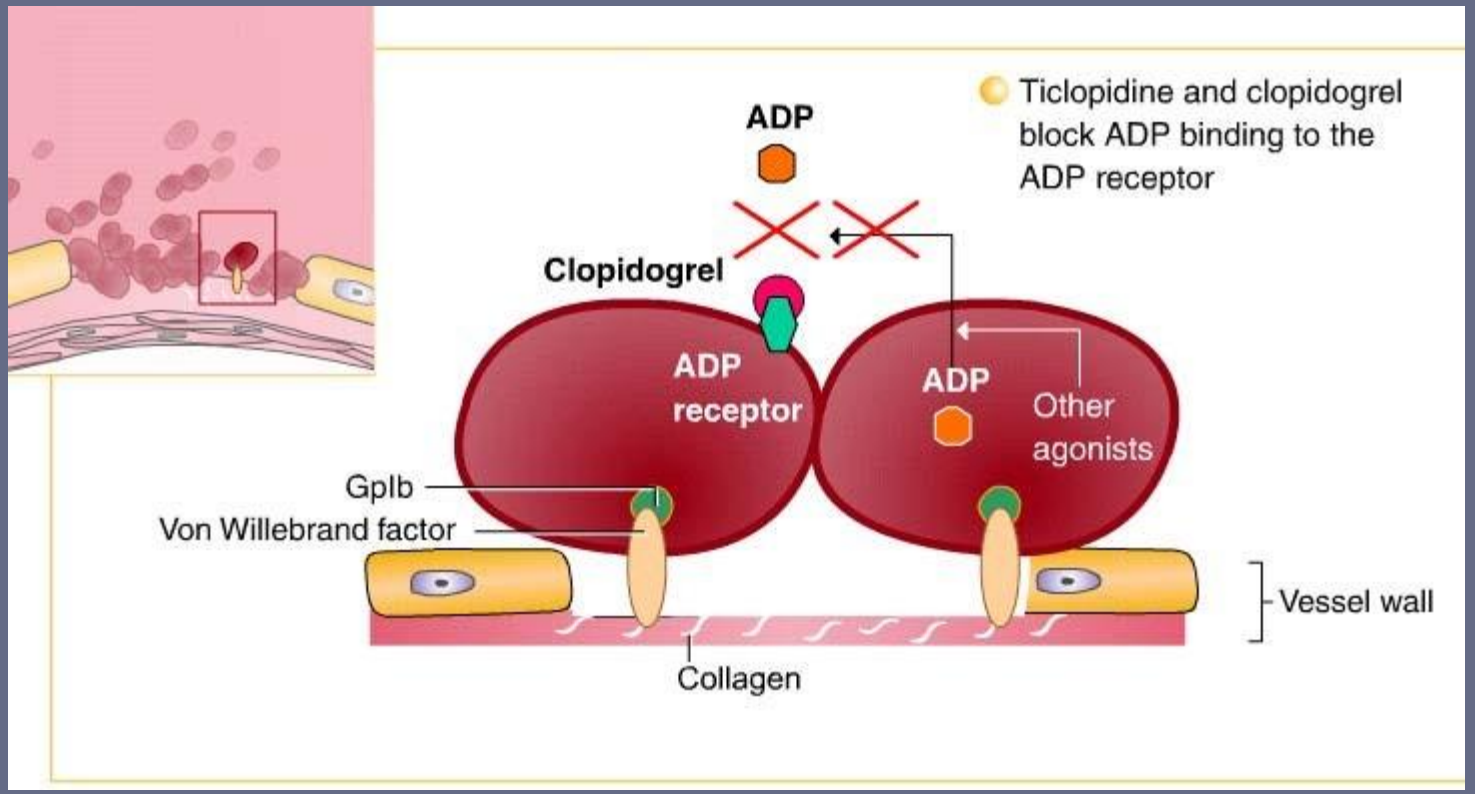


ADP-receptor antagonists – mechanism of action



ADP-receptor antagonists – mechanism of action



ADP-receptor antagonists – pharmacokinetics

- Both currently available ADP-receptor antagonists are thienopyridines that can be administered orally, and absorption is approximately 80-90%
- Thienopyridines are prodrugs that must be activated in the liver

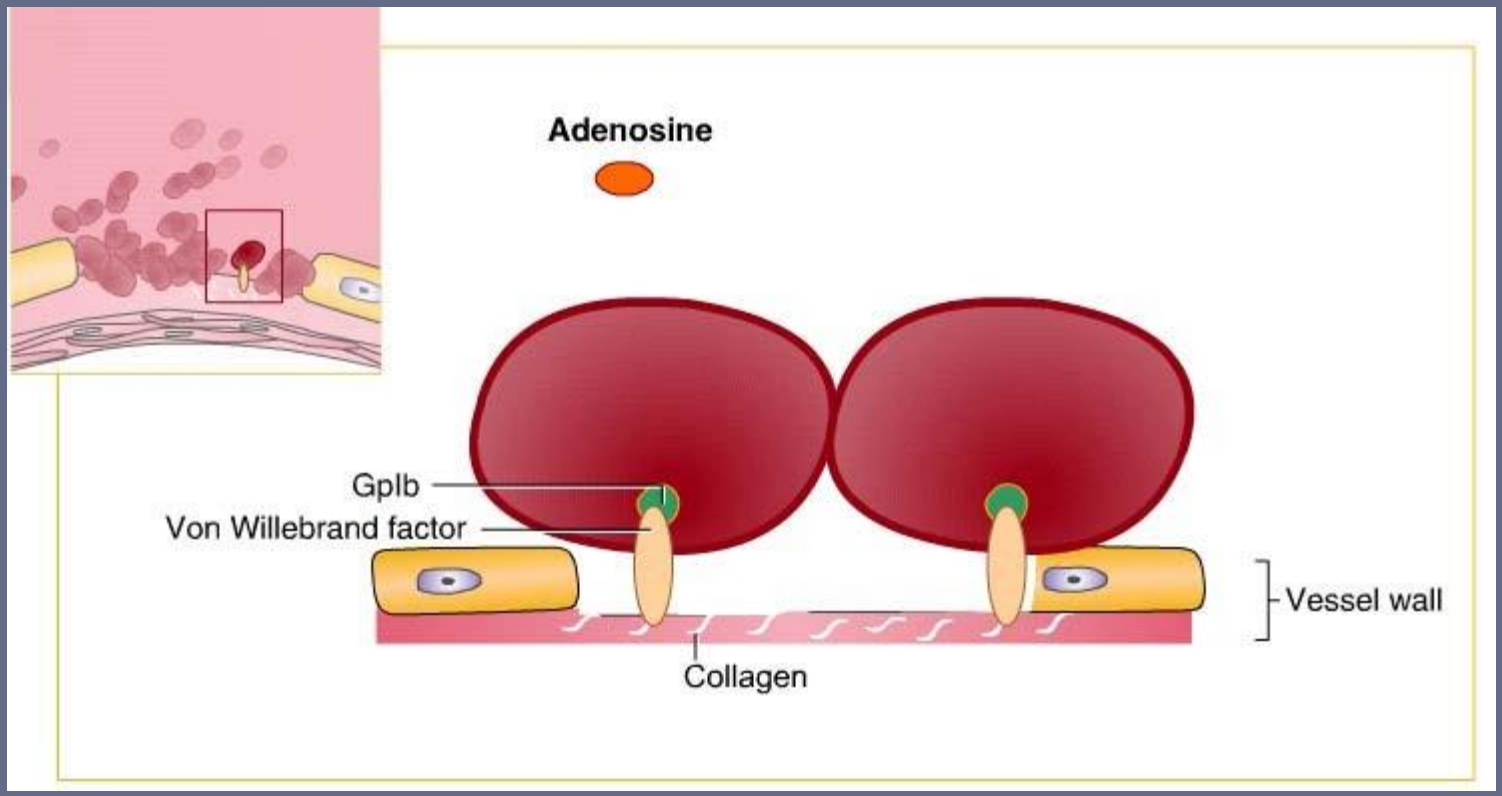
ADP-receptor antagonists – major use

- Secondary prevention of ischaemic complications after myocardial infarction, ischaemic stroke and established peripheral arterial disease
- Secondary prevention of ischaemic complications in patients with acute coronary syndrome (ACS) without ST-segment elevation

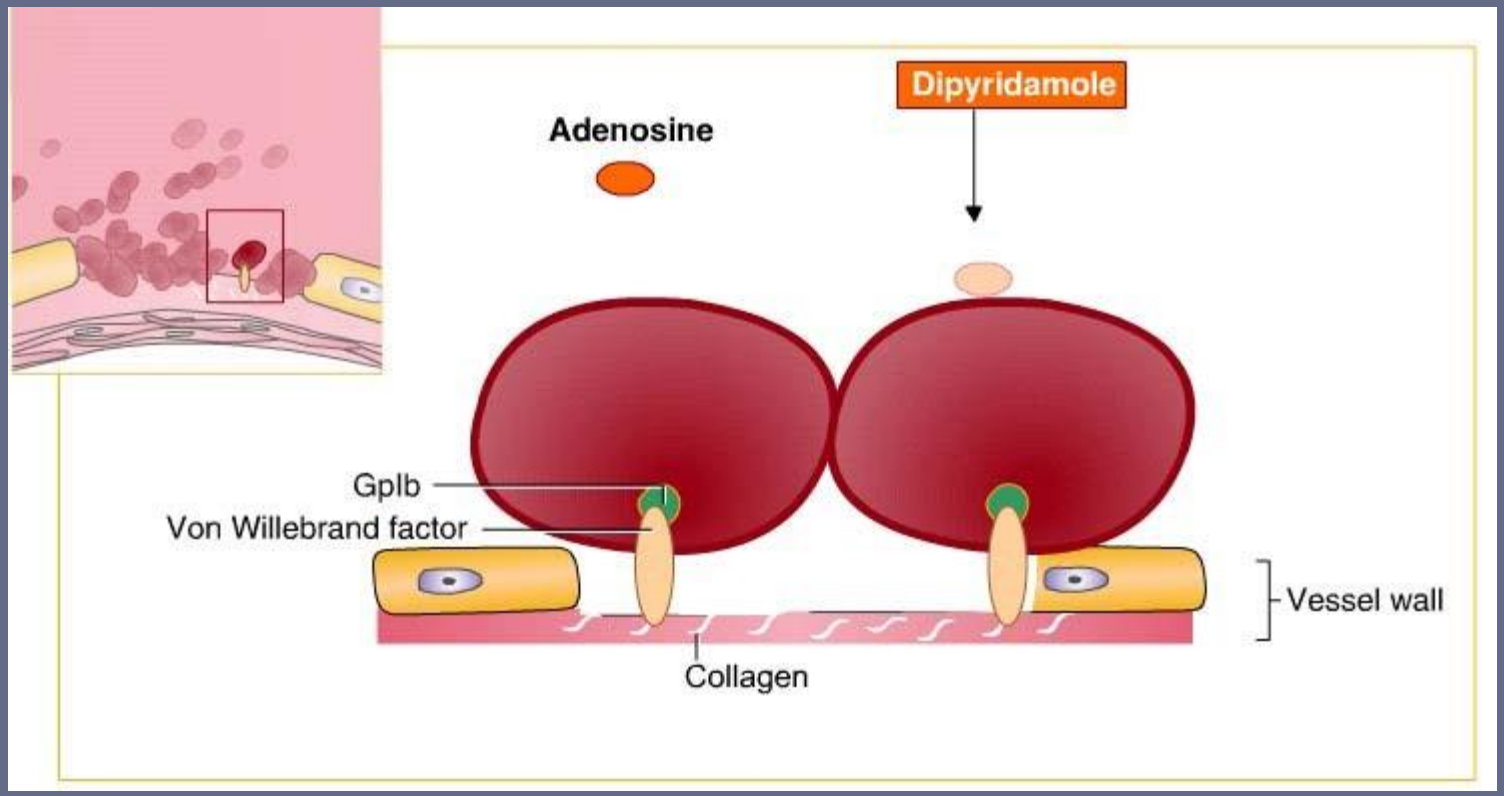
ADP-receptor antagonists – major drawbacks

- Clopidogrel is only slightly more effective than aspirin
- As with aspirin, clopidogrel binds irreversibly to platelets
- In some patients there is resistance to clopidogrel treatment

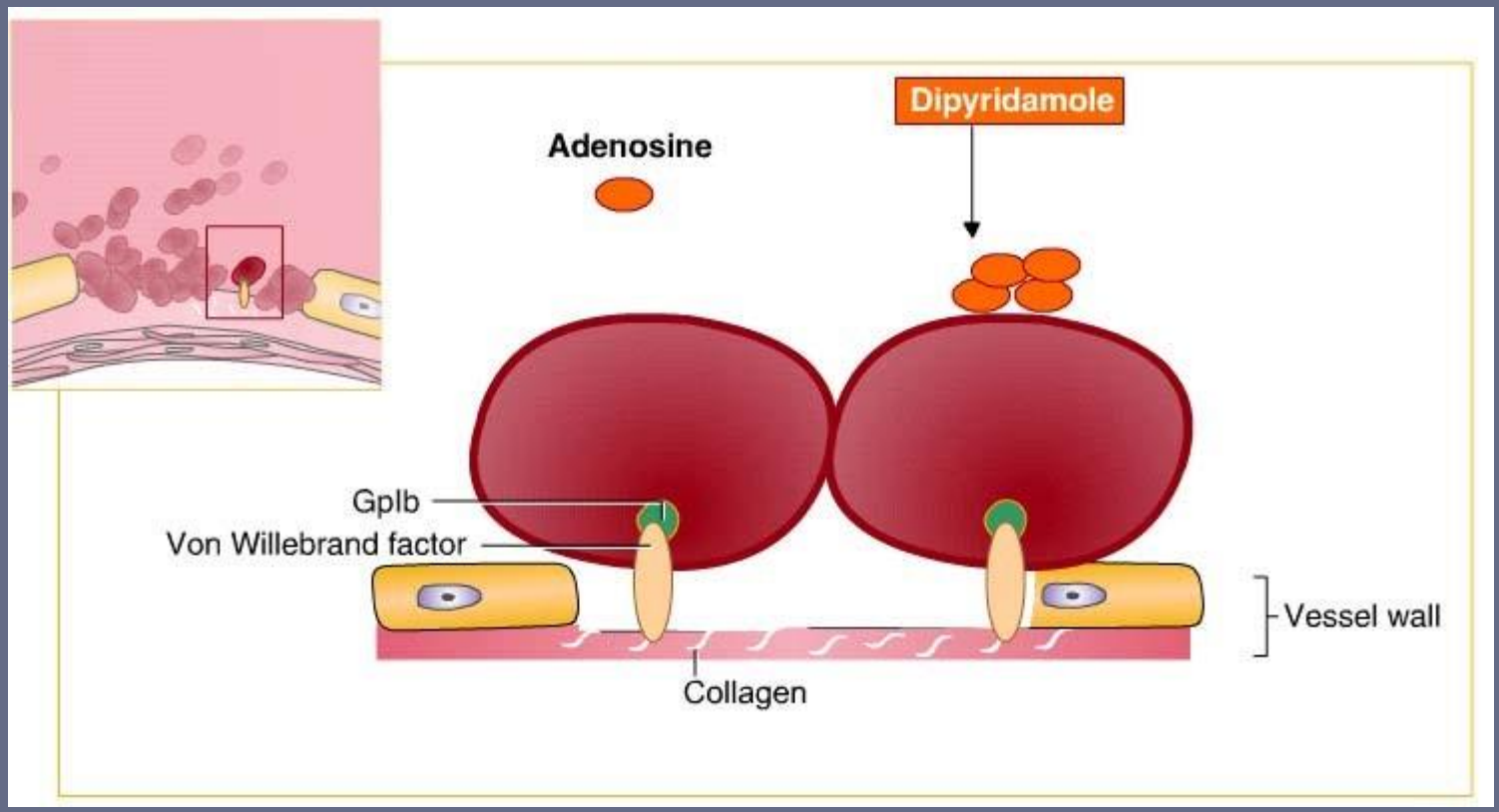
Dipyridamole – mechanism of action



Dipyridamole – mechanism of action



Dipyridamole – mechanism of action



Dipyridamole – pharmacokinetics

- Incompletely absorbed from the gastrointestinal tract with peak plasma concentration occuring about 75 minutes after oral administration
- More than 90% bound to plasma proteins
- A terminal half-life of 10 to 12 hours
- Metabolised in the liver
- Mainly excreted as glucuronides in the bile; a small amount is excreted in the urine

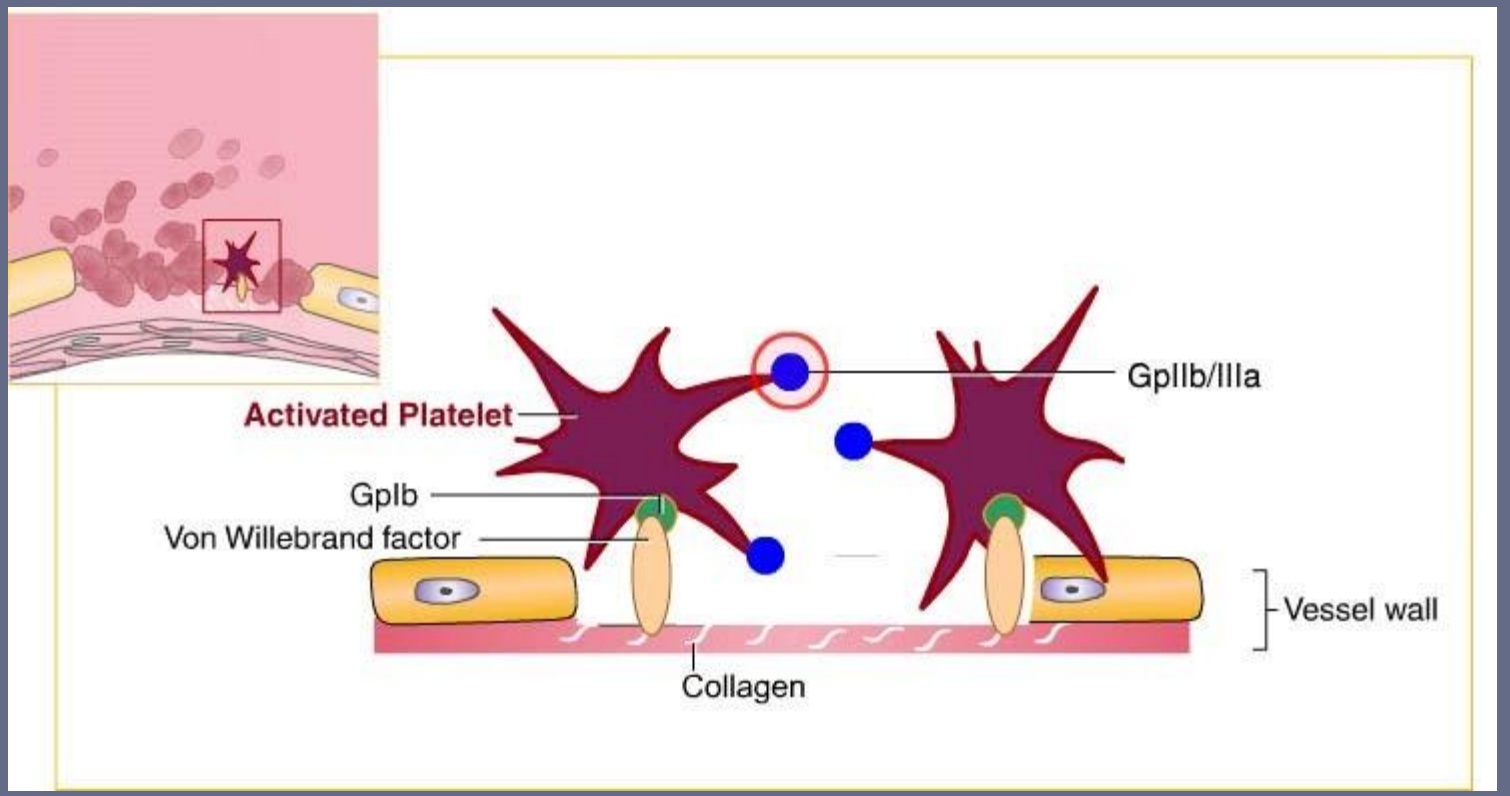
Dipyridamole – major use

- Secondary prevention of ischaemic complications after transient ischaemic attack (TIA) or ischaemic stroke (in combination with aspirin)

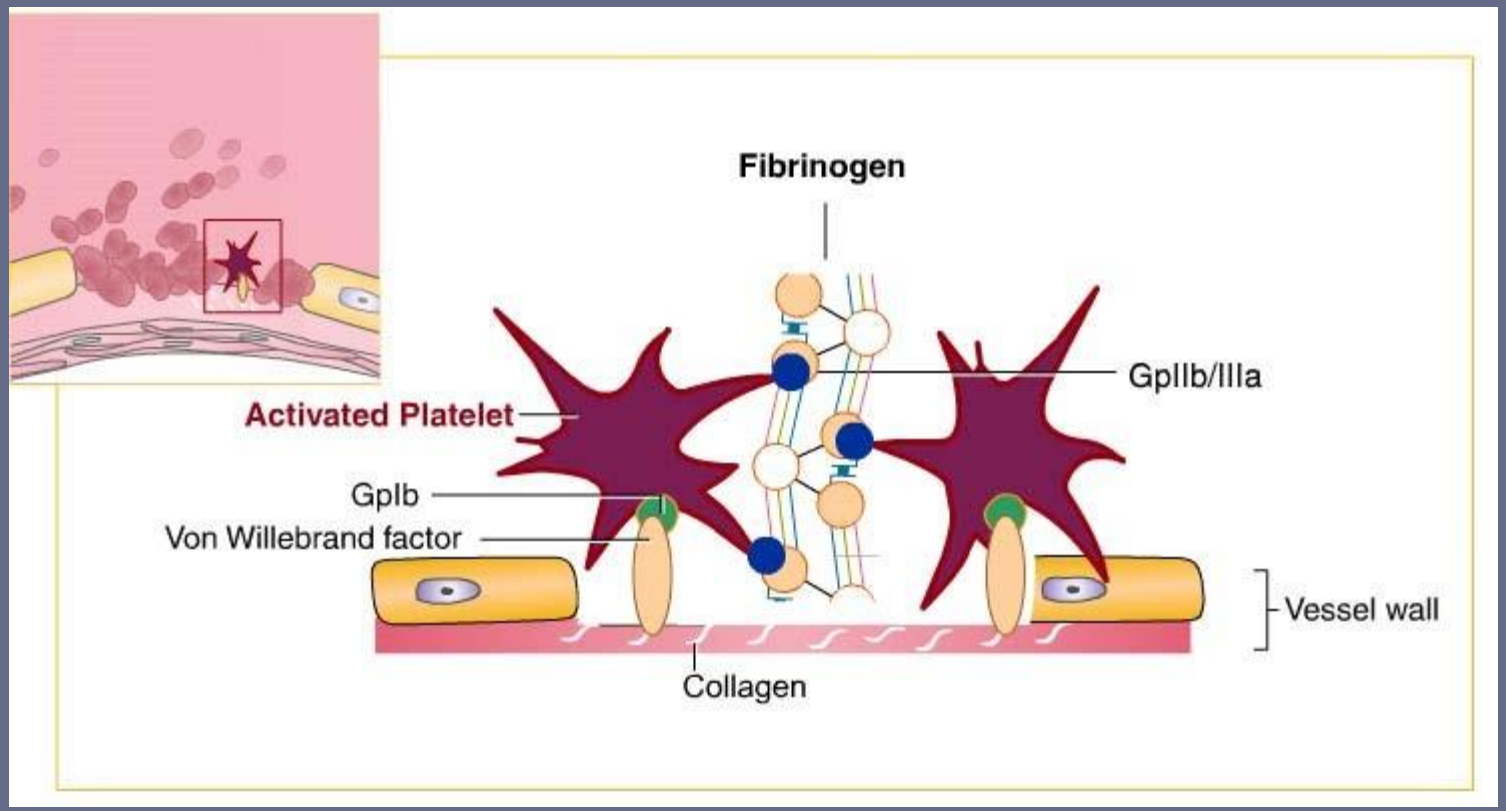
Dipyridamole – major drawbacks

- Is not a very effective antithrombotic drug
- Dipyridamole also has a vasodilatory effect and should be used with caution in patients with severe coronary artery disease; chest pain may be aggravated in patients with underlying coronary artery disease who are receiving dipyridamole

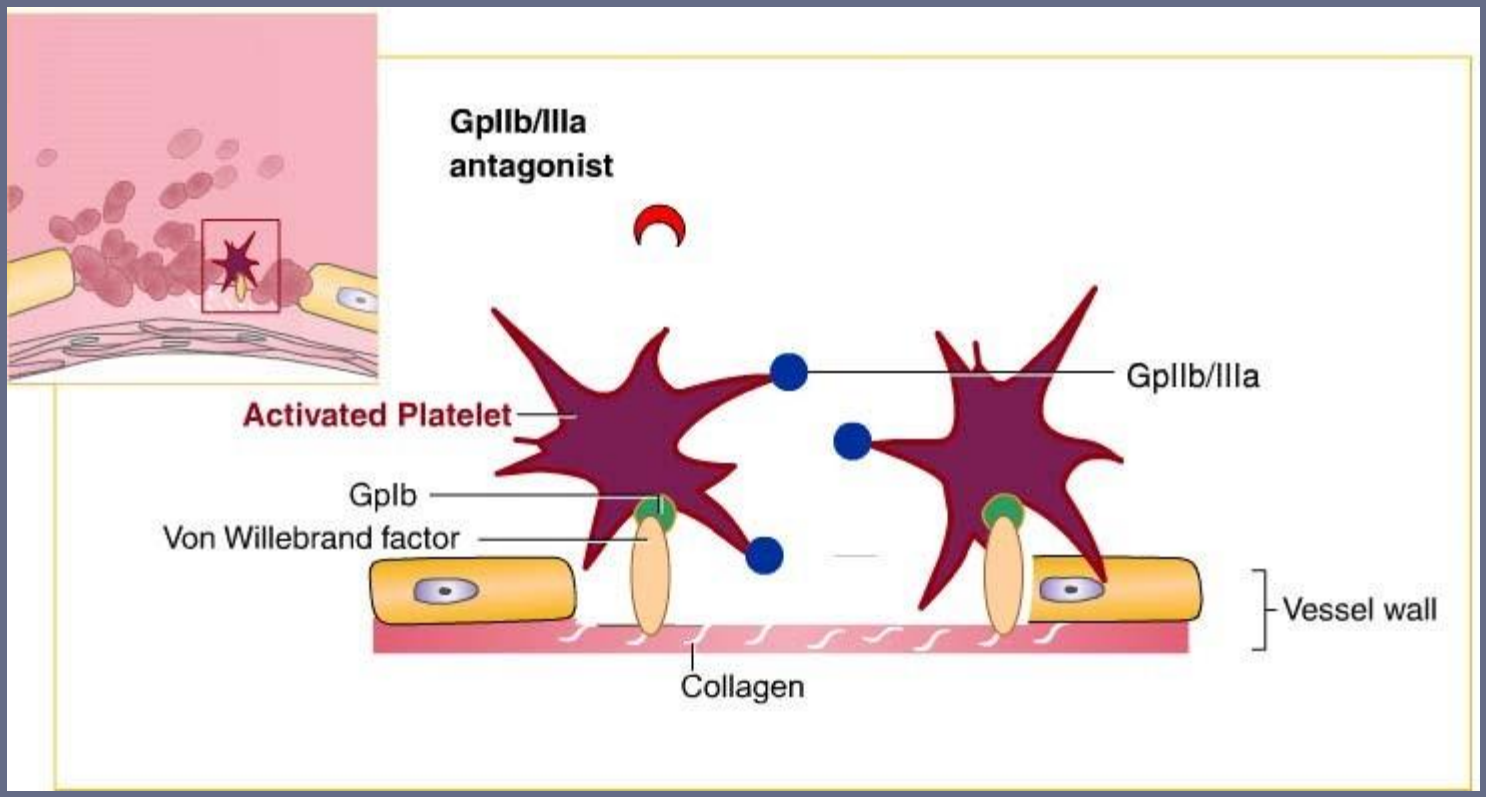
GPIIb/IIIa-receptor antagonists – mechanism of action



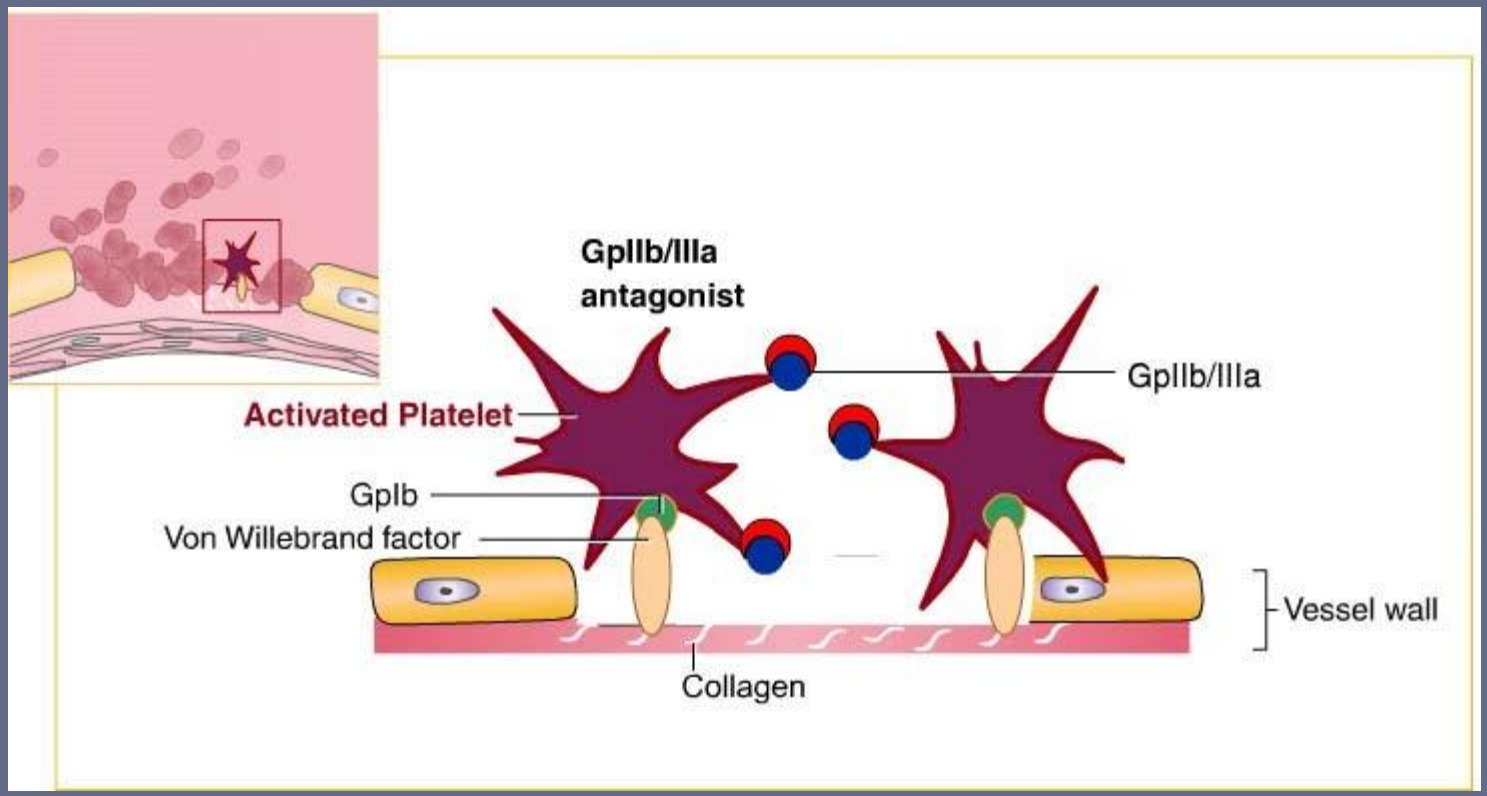
GPIIb/IIIa-receptor antagonists – mechanism of action



GPIIb/IIIa-receptor antagonists – mechanism of action



GPIIb/IIIa-receptor antagonists – mechanism of action



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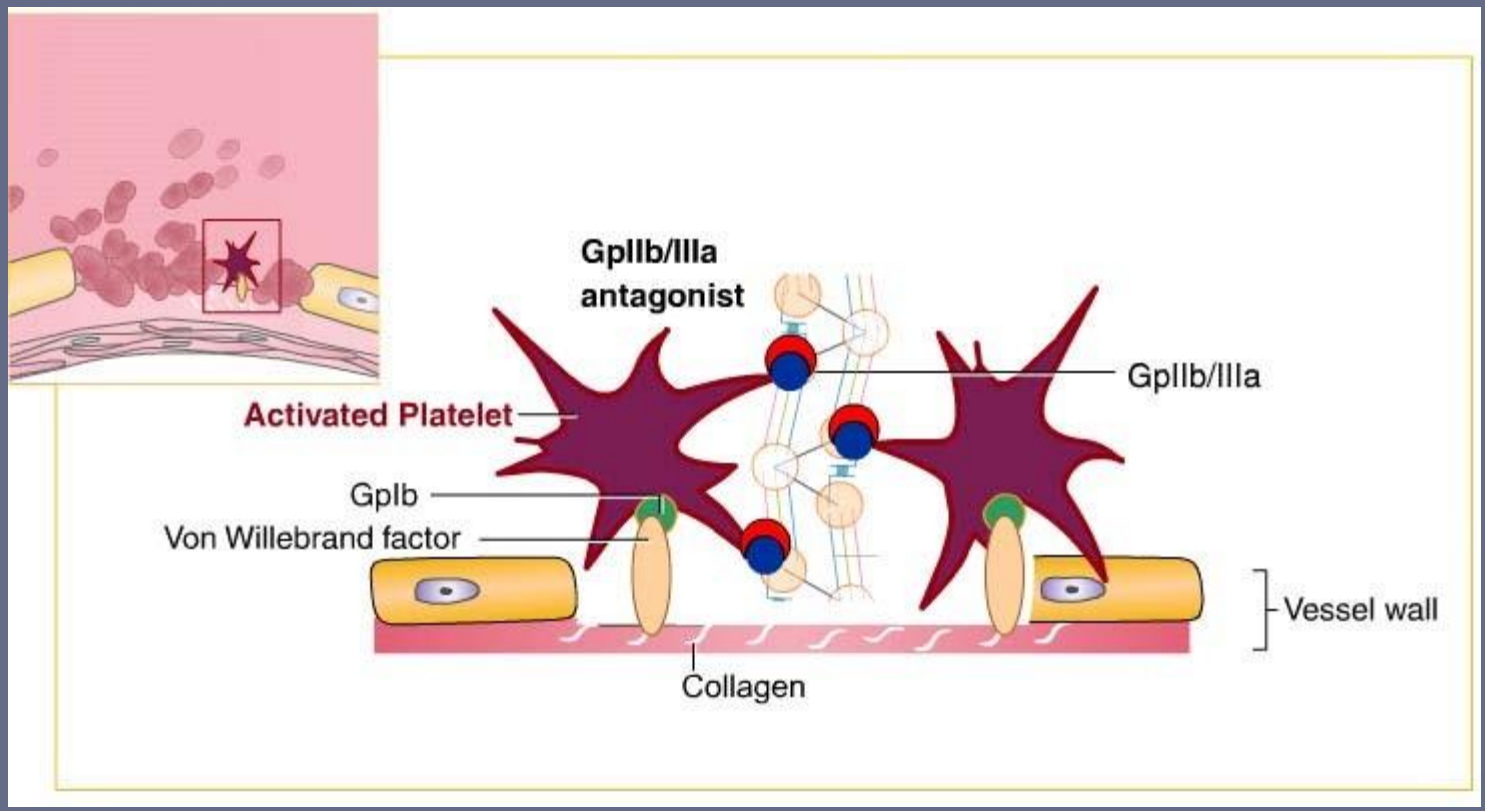

GPIIb/IIIa-receptor antagonists – pharmacokinetics

- Available only for intravenous administration
- Intravenous administration of a bolus dose followed by continuous infusion produces constant free plasma concentration throughout the infusion. At the temination of the infusion period, free plasma concentrations fall rapidly for approximately six hours then decline at a slower rate. Platelet function generally recovers over the course of 48 hours, although the GP IIb/IIIa antagonist remains in the circulation for 15 days or more in a platelet-bound state

GPIIb/IIIa-receptor antagonists – major use

- Prevention of ischaemic cardiac complications in patients with acute coronary syndrome (ACS) without ST-elevation and during percutaneous coronary interventions (PCI), in combination with aspirin and heparin

GPIIb/IIIa-receptor antagonists – major drawbacks

- Can only be administered by intravenous injection or infusion and are complicated to manufacture
- Oral drugs have been investigated but were not effective and have therefore not reached the market