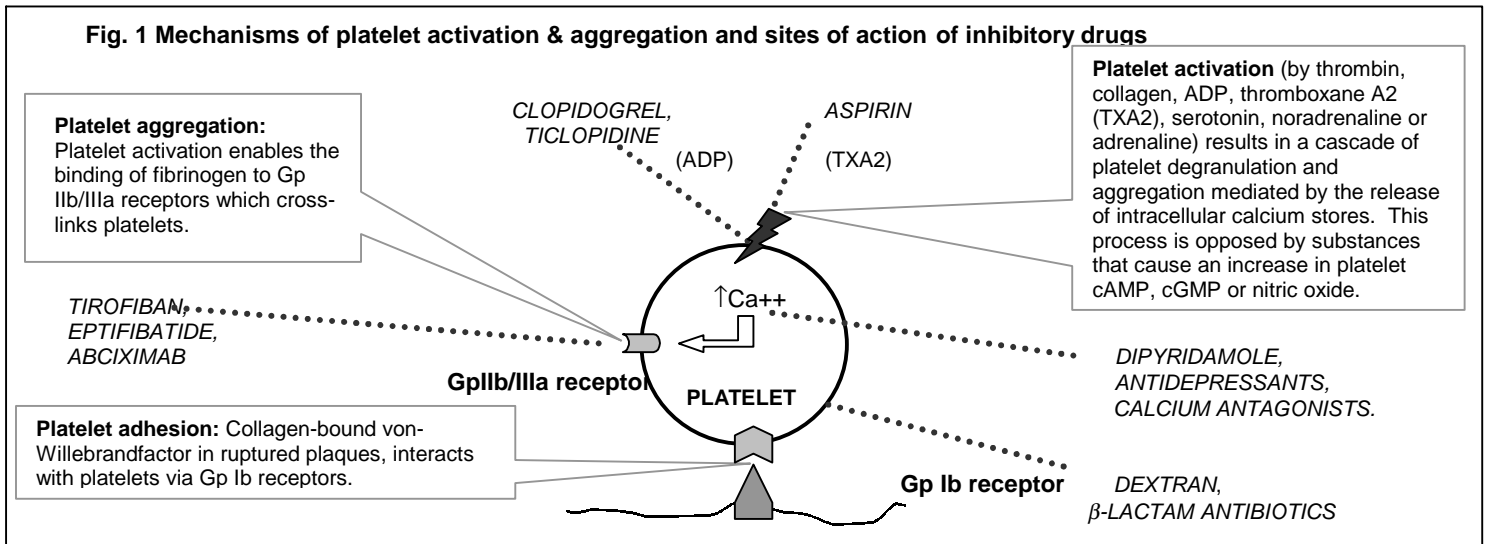


## Drugs Affecting Platelet Function

Although some drugs are used specifically for their antiplatelet effects, other commonly used drugs may affect platelet function causing prolongation of the bleeding time. The mechanisms behind the antiplatelet effects of drugs are described below. Drugs that cause thrombocytopenia are not discussed.



### Drugs inhibit platelet aggregation by three major mechanisms:

#### 1) Interaction with platelet surface receptors

- The peptides **tirofiban** and **eptifibatide** and the monoclonal antibody **abciximab** reversibly inhibit platelet glycoprotein (Gp) IIb/IIIa receptors. They are indicated for the management of acute coronary syndromes. The antiplatelet effects of tirofiban and eptifibatide dissipate within 4-8hrs of stopping treatment. In contrast, abciximab alters platelet function for >48hrs, but its antiplatelet effects can be reversed by a platelet infusion.
- Beta-lactam antibiotics** (penicillins and some cephalosporins) bind to platelet membranes impairing platelet aggregation. Bleeding has occurred in chronically ill and malnourished patients receiving these agents. Increased perioperative bleeding has also been reported, but without apparent clinical significance<sup>1</sup>.
- Dextran** molecules adsorb onto platelet surfaces impairing aggregation and adhesion. Dextran should be used cautiously in patients with thrombocytopenia or active haemorrhage.
- Clopidogrel** and **ticlopidine** block ADP receptors, inhibiting platelet aggregation for 4-7 days.

#### 2) Reducing calcium availability

- Dipyridamole** inhibits phosphodiesterase-mediated breakdown of cAMP thus decreasing intracellular calcium availability and platelet aggregation. **Theophylline** and **caffeine** affect platelet function *in vitro* via their effects on phosphodiesterase and adenosine receptors<sup>2</sup>, however there is no clinical evidence that significant antiplatelet effects or bleeding problems occur.
- Some **herbal medicines** such as ginkgo biloba, ginseng, St John's wort and garlic are thought to impair platelet aggregation through reducing available intracellular calcium. They can increase the risk of bleeding with anticoagulants.

- Antidepressants** with high affinity for the serotonin transporter, namely the **SSRIs** and **tertiary tricyclics** (eg clomipramine & amitriptyline), deplete platelet serotonin thus decreasing one of the signals for intracellular calcium release. In case-control studies they were associated with up to a 10% increase in the rate of gastrointestinal tract (GIT) bleeding, with the risk being highest for octogenarians and those with previous upper GIT bleeding<sup>3</sup>. SSRIs should be discontinued in this group in the setting of an acute GIT bleed, but for most patients these precautions are probably unnecessary.
- Calcium antagonists, β-blockers** and **nitrates** have antiplatelet effects *in vitro*, but information on their *in vivo* effect is limited. **Verapamil** and **diltiazem** have the most consistent evidence supporting an antiplatelet effect. They inhibit platelet aggregation in whole blood. In a case-control study they were associated with an increased incidence of GIT bleeding in elderly hypertensive patients<sup>4</sup>. Caution is required when prescribing these calcium antagonists to elderly patients with other risk factors for GIT bleeding.

#### 3) Inhibition of prostaglandin metabolism, thereby reducing platelet thromboxane A2 levels

**Aspirin** irreversibly inhibits cyclo-oxygenase-1 (COX-1), inhibiting platelet aggregation for 7-10 days.

- Conventional **NSAIDs** reversibly inhibit COX-1. The drug half-life determines the duration of the antiplatelet effect.
- Selective **COX-2 inhibitors** have no appreciable effects on COX-1 at therapeutic doses and thus no antiplatelet action.

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