**Pharm-08B7** List the agents used to therapeutically reduce platelet function. Outline their mechanism of action, adverse effects, mode of elimination and duration of action.

**Antiplatelet agents**

- **COX inhibitors**
  - aspirin
  - non-steroidal anti-inflammatory drugs
- **ADP receptor inhibitors**
  - clopidogrel
  - prasugrel
  - ticagrelor
- **GPIIb/IIIa inhibitors**
  - abciximab
  - tirofiban
- **Phosphodiesterase inhibitors**
  - dipyridamole
- **Other agents**
  - Dextrans
  - Heparin

<table>
<thead>
<tr>
<th>Example</th>
<th>irreversible COX inhibitor</th>
<th>reversible COX inhibitor</th>
<th>ADP receptor inhibitor</th>
<th>GPIIb/IIIa inhibitor</th>
<th>PDE inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>aspirin</td>
<td>e.g. diclofenac</td>
<td>clopidogrel</td>
<td>abciximab</td>
<td>dipyrdiamole</td>
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<tr>
<td>acetylate COX → irreversible inhibition → ↓TxA → ↓plt aggregation, ↓adhesiveness</td>
<td>reversibly inhibits COX → ↓TxA → ↓plt aggregation</td>
<td>prodrug → activated by liver → irreversible block ADP receptor → ↓plt aggregation</td>
<td>tightly complexes GPIIb/IIIa receptor → block fibrinogen, fibronectin and vWF binding → ↓plt aggregation (final common pathway)</td>
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<td>rapid hydrolysis by intestinal and hepatic esterases → salicylate → further hepatic metabolism → salicylic acid + glucuronide → renal excretion</td>
<td>hepatic hydroxylation + conjugation → inactive metabolites → excretion in urine (60%) and bile (40%)</td>
<td>hepatic metabolism → activation of prodrug → excreted in urine and faeces</td>
<td>rapid metabolism by plasma proteases</td>
<td>hepatic metabolism → biliary excretion</td>
<td></td>
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<tr>
<td>7 ~ 10 days (until formation of new platelets)</td>
<td>4 ~ 8 hours</td>
<td>7 ~ 10 days (until formation of new platelets)</td>
<td>duration 48 hrs</td>
<td>24 hours</td>
<td></td>
</tr>
<tr>
<td>bleeding peptic ulcer ↓renal blood flow, Reye’s syndrome salicylate tox</td>
<td>bleeding peptic ulcer ↓renal blood flow closes ductus arteriosus</td>
<td>bleeding neutropaenia</td>
<td>bleeding ↓plt hypersensitivity anaphylaxis</td>
<td>vasodilatation hypotension coronary steal bronchospasm</td>
<td></td>
</tr>
</tbody>
</table>

**Examiner’s comments** – 82% of candidates passed this question.
Relevant agents for this question include **aspirin**, pro-drugs at **ADP receptor**, **antagonists at the IIb/IIIa receptor** and **phosphodiesterase inhibitors**.

This question had the option of being answered in the form of a 'table' format using dot points outlining the components asked for about platelet function reduction. Marks were enhanced by including explanation of how the drug action interferes e.g. blocking the IIb/IIIa receptor interrupts the binding of fibrinogen hence the failure of adhesion and aggregation of platelets.

The 'thrombus/platelet' diagram in Katzung page 544 illustrates in summary form the information and it was included in some candidate answers.

There is always a risk of elaborating on adverse effects probably more than the mark allocated at the expense of time spent on other agents. Medications who unwanted side effects include platelet inhibition are not used therapeutically for that ideal purpose thus not gaining marks. Comments on **dextran** and **thrombin inhibitors** gained credit.