**Aspirin:**
Aspirin is an NSAID (non-steroidal anti-inflammatory drug) with a diverse range of clinical applications.

It has antiplatelet aggregatory, analgesic, anti-inflammatory and anti-pyretic effects.

Aspirin is a rapidly absorbed drug. Peak plasma level can be achieved in as short as 1-2 hours. The excretion is rapid as well through urine. The half-life of aspirin is 3-5 hours at a normal dose of 600mg/day. At a higher dose, the half-life can reach up to 6-12 hours. This is because of the saturation of aspirin metabolism. Aspirin is a highly protein-bound drug. Also, the binding is saturable and can interact with other drugs at binding sites. E.g. tolbutamide is displaced by aspirin. Aspirin causes acidification of urine so can be excreted by alkalinizing the urine.

**Pharmacological actions:**
Aspirin can be used as;

- Anti-inflammatory
- Analgesic.
- Anti-pyretic.
- Antiplatelet aggregation effect.
- Uricosuric effect. (Excretion of uric acid from the body by inhibiting its reabsorption in the nephron.)

**Mechanism of action:**
The **anti-inflammatory effect** is due to irreversible inhibition of cox-I and cox-II enzyme. Additional mechanisms include decreased chemotaxis, down-regulation of cytokine interleukin I, decrease in free radical generation and interference with calcium-mediated intracellular events.

The **analgesic effect** can be both due to central and peripheral actions by the inhibition of cox-enzyme, decreasing prostaglandins level thus minimizing pain.

The **antipyretic effect** is due to inhibition of cox enzyme thus decreasing body temperature. This effect is minimal on normal body temperature and maximum in case of elevated body temperature.

The **antiplatelet aggregation effect** is due to acetylation of a lysine residue of cox enzyme in platelets causing an irreversible blockade of cox-enzyme and hence stops platelet aggregation. The central blockade of IL-I mechanism depresses thromboxane formation and hence indirectly promote prostacyclin formation from endoperoxide which leads to platelet deaggraration and vasodilation.

The **uricosuric effect** can be effective in gout. However, it is of no clinical significance because a high dose of aspirin is required for this purpose that is 4gm/day which of course is a toxic amount. To further add up, in lower doses aspirin can cause precipitation of gout thus worsening the condition. The gout
Precipitation can be due to its effect on the active secretory mechanism of uric acid from the lumen of nephron into the blood.

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Aspirin actions and their mechanism

**Side effects of aspirin:**
Following are some of the documented side effects of aspirin use;

- At usual doses: at usual doses, aspirin can cause gastric upset, duodenal ulcers, skin rashes, and infrequently can cause asthma as well. Sometimes renal toxicities can also be caused.
- Chronic use: using aspirin for a long period of time can cause upper git bleeding due to its highly corrosive action.
- At higher doses: using aspirin in higher doses can cause vomiting, tinnitus, vertigo and decrease in hearing. Moreover, metabolic disorders, alteration in acid-base balance, electrolytic disturbances are also some of the side effects.
- Because of **uncoupled oxidative phosphorylation** aspirin can cause increased oxygen consumption and increased $\text{CO}_2$ formation thus triggering respiratory Centre which leads to hyperpnoea (increased depth and rate of respiration). The same mechanism is the cause of metabolic acidosis because of carbonic acid and other acids formation.
- After initial stimulation, aspirin causes a respiratory centre depression and hence $\text{CO}_2$ remains within the body. Aspirin also interferes with carbohydrate metabolism leading to increased production of lactic acid, acetoacetic acid, and pyruvic acid.
- In even higher doses aspirin toxicities result in “hyperpyrexia” as a result of high metabolic rate, dehydration, vomiting, fluid loss and eventually can cause cardiac collapse because of decreased blood pressure, in case if the fluid loss is severe.

**Treating aspirin toxicities:**
In aspirin toxicities, gastric lavage should be done. For this purpose, vomiting is induced by administering Apomorphine or ipecac syrup (emetics).
If aspirin has reached general circulation, hemodialysis is done. Alkalinization of urine is done by giving bicarbonates.

There is no antidote for aspirin.

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