

ASPIRIN LEADS MULTI THERAPEUTIC INDEX

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Introduction

Salicylic acid the main metabolite of aspirin, is an integral part of human and animal metabolism. It was discovered by Arthur Eichengrün, a chemist with the German company Bayer. It is rapidly converted in the body to salicylic acid which is responsible for most of the action as analgesic, anti-inflammatory, Platelet aggregation inhibitor. [1, 2] (by inhibiting the production of thromboxane), Anticoagulant [3, 6]. It's actions are the result of acetylation of certain macromolecules including cyclooxygenase. It is one of the oldest analgesics, anti-inflammatory drugs and still widely used [4]. Aspirin is also used long-term, at low doses, to help prevent heart, strokes, and blood clot formation in people at high risk of developing blood clots. It has also been established that low doses of aspirin may be given immediately after a heart attack to reduce the risk of another heart attack or of the death of cardiac tissue & in Myocardial Infarction [5].

Therapeutic uses

1. As analgesic: For headache (including mild migraine), backache, myalgia, joint pain, pulled muscle, toothache, neuralgias & dysmenorrhea; it is effective in low dose (0.3-0.6 g 6-8 hourly). Analgesic effect is maximal at ~1000mg (single dose).
2. As antipyretic: It is effective in fever of any origin; dose is same as for analgesia but not used in fever due to heat stroke; only external cooling lowers body temperature.
3. Acute rheumatic fever: Aspirin is the first drug to be used in all cases; other drugs are added or substituted only when it fails or in severe cases. Granulomatous lesions, nodules, cardiac complications, valvular defects, chorea and duration of disease are not altered by salicylates therapy.
4. Rheumatoid arthritis: Aspirin in a low dose 3-5 g/day is effective in most cases; produces relief in pain, swelling & morning stiffness, but progress of disease the disease process is not affected. Since larger doses of aspirin are poorly tolerated for long periods it is rarely used now; other non-steroidal anti-inflammatory drugs are preferred.
5. Osteoarthritis: It affords symptomatic relief only; may be used on 'as when required'.
6. Postmyocardial infarction & poststroke patients: By inhibiting platelet aggregation aspirin lowers the incidence of reinfarction TXA₂ synthesis in platelets is inhibited at low doses. It has been argued that high doses can reverse the beneficial effects by concurrently inhibiting PGI₂ (anti-aggregatory & vasodilatory) synthesis in vessel wall. Large studies have demonstrated that aspirin 60-100 mg/day reduces the incidence of myocardial infarction; it is now routinely

prescribed to post-infarct patients. Many recommend it for primary prophylaxis as well. Aspirin reduces “Transient ischaemic attacks” & lowers incidence of stroke in such patients. But the risk of stroke in post-myocardial infarction patients is not reduced.

7. Other less well established uses of aspirin are:

- a. Pregnancy-induced hypertension & pre-eclampsia: imbalance between TXA_2 & PGI_2 is believed to be involved: aspirin 80-100 mg/day benefits many cases by selecting suppressing TXA_2 production.
- b. Patent ductus arteriosus: aspirin can bring about closure and avoid surgery.
- c. To prevent flushing attending nicotinic acid ingestion.

Mechanism of action

1. The analgesic action is mainly due to obtunding of peripheral pain receptors & prevention of prostaglandin mediated sensitization of nerve endings. A central subcortical action raising threshold to pain perception also contributes, but morphine like action component of the pain missing with no sedation. It resets the hypothalamic thermostat & rapidly reduces fever by promoting heat loss by sweating & cutaneous vasodilatation.

2. Aspirin irreversibly inhibit TXA_2 synthesis by platelets & thus interferes with platelet aggregation & bleeding time is prolonged to nearly twice the normal value

Adverse effect

1. Side effect : side effect occurs at analgesic dose 0.3-1.5 g/day are nausea, vomiting, epigastric distress, increased occult blood loss in stool, gastric mucosal damage % peptic ulceration important.

2. Hypersensitivity& idiosyncrasy: Reactions include rashes, fixed drug eruption, urticaria, asthma, anaphylactic reaction.

3. Anti-inflammatory doses (3-5 g/day): An association between salicylate therapy and Reye’s syndrome, a rare form of hepatic encephalopathy seen in children having viral (varicella, influenza) infection has been noted.

4. Salicylate Poisoning: Serious toxicity is seen at serum salicylate levels >50 mg/dl. Manifestation are vomiting, dehydration, acidotic breathing, electrolyte imbalance, hallucination, convulsion, coma & death due to respiratory failure + cardiovascular collapse. **[Treatment: i.v. fluid with Na^+ , K^+ , HCO_3^- % Glucose. Gastric lavage to remove un absorbed drug; forced alkaline diuresis, blood transfusion & Vit-K should be given if bleeding occurs].**

5. Precautions & Contraindications: aspirin is contraindicated to peptic ulcer, in children suffering from chicken pox, influenza. In case of hepatic necrosis, diabetics, juvenile rheumatic arthritis patients, in pregnancy & lactating mothers should be avoided the use of it.

Drug interaction

Aspirin interacts with warfarin, naproxen, sulfonylureas, phenytoin. It inhibits tubular secretion of uric acid & antagonise uricosuric action of probenecid. It blunts diuretic action of furosemide & thiazide. Aspirin reduces protein bound iodine levels by displacement of thyroxin but hypothyroidism dose not occurs.

Caution: Dosage as directed by Physician.

Availability details

Brand name	Composition	Tablet (in mg)	Action
aspirin	Aspirin	350	Nsaids, Platelet aggregation inhibitor, Anticoagulant
Disprin	Aspirin	350	Nsaids, Platelet aggregation inhibitor, Anticoagulant
Loprin	Aspirin	75, 162.5	Nsaids, Platelet aggregation inhibitor, Anticoagulant
Clopiwas (Combined Therapy)	Aspirin + Clopidogrel bisulphate	150 + 75	Platelet aggregation inhibitor, Anticoagulant
Arreno (Combined Therapy)	Aspirin + dipyridamol	25 + 200	Platelet aggregation inhibitor, Anticoagulant

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