

ASPIRIN

Tablets

Composition

Each enteric coated tablet contains 100 mg Aspirin (acetylsalicylic acid).

Action

Acetylsalicylic acid inhibits the activity of the enzyme cyclo-oxygenase and thus prostaglandins and thromboxane formation are decreased. By blocking thromboxane synthesis, acetylsalicylic acid inhibits rapidly the platelet aggregation; this action is irreversible. Acetylsalicylic acid may also inhibit formation of prostacyclin, a platelet aggregation inhibitor; this action is reversible.

Pharmacokinetics

Absorption

After oral administration the acetylsalicylic acid is rapidly absorbed partly from the stomach but mostly from the upper small intestine. The peak value is reached in about 20 to 40 minutes; the presence of food delays absorption of salicylates.

The acetylsalicylic acid is rapidly hydrolyzed into salicylic acid in the plasma. The maximal blood concentration is reached within 2 to 4 hours depending whether the subject is in fasting state or not.

Distribution

After absorption, salicylate is distributed throughout most body tissues and most transcellular fluids (synovial fluid, peritoneal fluid, cerebrospinal fluid).

The volume of distribution varies according to the dosage and averages 0.1 - 0.2 l/kg. At concentrations encountered clinically from 50 to 90% of the salicylate are bound to plasma proteins, especially albumin.

The bioavailability is about 80 to 100%.

Metabolism and elimination

A considerable fraction of an oral dose of acetylsalicylic acid is hydrolyzed presystemically, the rest is hydrolyzed rapidly ($t_{1/2} \sim 15$ minutes) after absorption. The biotransformation of salicylate takes place in many tissues, but particularly in the hepatic cells. The three chief metabolic products are salicylic acid (the glycine conjugate) the ether or phenolic glucuronide and the ester or acyl glucuronide, gentisic acid and gentisuric acid (glycine conjugate).

Salicylates are excreted in the urine as free salicylic acid (about 3 - 10%) salicylic acid (70 - 75%) and glucuronides (10 - 20%). Salicylate excretion depends on urinary pH, and is maximum for a pH equal or superior to 7.

The plasma half-life for acetylsalicylic acid is about 15 minutes, for salicylic acid is 2 to 3 hours in low doses, and increases with high doses. This dose dependent elimination is the result of the limited ability of the liver to form salicylic acid and the phenolic glucuronide.

Indications

Indications related to inhibition of platelet aggregation: To reduce the risk of myocardial infarction in patients with unstable angina or in patients who have had a previous myocardial infarction. To reduce the risk of recurrent transient ischemic attacks or stroke in men who have had transient ischemia of the brain due to fibrin platelet emboli. To reduce the risk of graft occlusion following aortocoronary by-pass surgery.

Contraindications

Patients with peptic or duodenal ulcers, hemophilia, thrombocytopenia or other bleeding tendencies, or intolerance (hypersensitivity) to aspirin or other salicylates, severe renal impairment and patients receiving oral anti-coagulant therapy.

Aspirin should not be taken during pregnancy and lactation, except under the advice and supervision of a medical doctor.

Warnings

The optimal dose for inhibition of platelet aggregation in humans is not known. Do not use Aspirin for indications related to the inhibition of platelet aggregation unless directed by a doctor. Aspirin has been implicated in Reye's syndrome, a rare but serious illness in children and teenagers with chicken pox and influenza. A doctor should be consulted before use in such patients.

Adverse Reactions

Dizziness, irritation of the gastric mucosa and resultant dyspepsia, erosion, ulceration, haematemesis, and melaena may occur. Some persons, especially asthmatics, exhibit notable sensitivity to Aspirin which may provoke various hypersensitivity reactions which may include skin eruptions, urticaria, angioedema, paroxysmal bronchospasm and dyspnoea.

Precautions

Concomitant therapy with other gastric irritants, such as non-steroidal anti-inflammatory agents may increase the risk of gastric irritation. Aspirin may increase the risk of gastrointestinal bleeding when taken simultaneously with corticosteroids or alcohol. Aspirin should be used with caution in patients who are hypersensitive to other anti-inflammatory agents or allergens.

Aspirin should be withdrawn one week before surgery because of the possibility of increasing the bleeding times. It should be administered with caution to patients with impaired renal function, in the presence of severe liver disease, in patients with a history of gastrointestinal disorders such as peptic ulcers, ulcerative colitis and Crohn's disease, dyspepsia, anemia and when the patient is dehydrated.

Prolonged use of high doses may lead to anemia, blood dyscrasia, gastro-intestinal hemorrhage and peptic ulceration.

Drug Interactions

Aspirin may enhance the activity of coumarin anti-coagulants, methotrexate, oral anti-diabetic preparations, valproic acid and sulphonamides.

Aspirin diminishes the effects of anti-gout preparations such as probenecid and sulphinpyrazone. Barbiturates and other sedatives may mask the respiratory symptoms of aspirin over dosage and have been reported to enhance its toxicity.

Diagnostic Interference

Salicylates may produce falsely increased results for blood creatinine, urate (low dose aspirin) and urea. Falsely decreased results may be obtained for blood thyroxin and urate (>4 g/day aspirin) and for urinary 5-HIAA (with nitrosonaphthol method). Urinary VMA (HMMA) levels may be falsely increased or decreased depending on the method of analysis.

Urinary glucose oxidase: Aspirin may cause a false negative test in the presence of glycosuria

Dosage and Administration

Adults: 100 to 300 mg to be taken every day, preferably at the same time each day.

The tablets should be swallowed whole. Do not chew, break or crush the tablets as this will destroy the protective effect of the enteric coating.

Over Dosage

Manifestation

These include dizziness, tinnitus, sweating, nausea, vomiting, and altered glucose metabolism, mental confusion, and hyperventilation, respiratory alkalosis, metabolic acidosis, and ketosis, fluid and electrolyte losses. Depression of the central nervous system may lead to coma, cardiovascular

collapse and respiratory failure.

In children serious signs of over dosage may develop rapidly. In cases of over dosage, consult a doctor immediately.

Treatment

Gastric lavage, forced alkaline diuresis, restoration of fluid, electrolyte and acid balance, dialysis and supportive therapy may be required.

Presentation

Aspirin 100

Box of 30 tablets