

Acetylsalicylic acid (aspirin)

CAS number: 50-78-2

MF (acetylsalicylic acid): $C_9H_8O_4$

MW (acetylsalicylic acid): 180.2

MF (salicylic acid, salicylate; active part of chemical): $C_7H_6O_3$

MW (salicylic acid): 138.1

Soluble in water.

Major uses

Acetylsalicylic acid (ASA) is analgesic, anti-pyretic and anti-inflammatory drug. Low doses are used to inhibit platelet aggregation in ischemic heart disease and cerebrovascular disease [1].

Human toxicity

Therapeutic dose of ASA in an adult is between 0.5 and 1.5 g/day. Accidental ingestions of <150 mg/kg can usually be treated at home with fluids and telephone follow-up. Accidental ingestion of 150 to 300 mg/kg (moderately severe overdose): if less than 1 hour after ingestion, induction of emesis and follow-up for 24 hours is suggested. Accidental ingestion of 300 – 500 mg/kg is considered as a severe overdose and requires hospitalization. Doses higher than 500 mg/kg are potentially lethal [2]. The minimum lethal dose (MLD) was estimated to be 15 g/70 kg person [3].

Patients with mild to moderate intoxication may develop fever, tachypnea, tinnitus, respiratory alkalosis, metabolic acidosis, lethargy, mild dehydration, nausea and vomiting.

At severe intoxication, encephalopathy, coma, hypotension, pulmonary edema, seizures, metabolic acidosis, coagulopathy (clot formation), cerebral edema and dysrhythmias, as well as kidney failure may be observed [1].

Therapeutic blood concentration for adults is between 20 and 100 mg/l, whereas toxic concentration is between 150 and 300 mg/l. The minimum lethal blood concentration is 500 mg/l [4]. The mean lethal concentration, based on the data from several handbooks, was calculated to be 950 mg/l [5].

Kinetic data

Absorption of salicylic acid (salicylate, active part of chemical) after oral ingestion of therapeutic dose of ASA is >80% [6].

Salicylate exhibits dose-dependent kinetics. Overdose may change pharmacokinetic parameters [6].

The plasma half-life of ASA is 15-20 min, at the therapeutic dosage [6]. The plasma half-life for salicylate is 2-3 h in low doses and up to 12 h at the higher doses. At overdose, the half-life may be up to 15-30 h [7].

Peak plasma concentration: at the therapeutic doses, e.g. after 500 mg ingestion of ASA peak is achieved in 14 min; peak plasma concentration of salicylate is achieved in 0.5-1 h after ingestion [6, 8]. Time to peak for salicylate, after acute oral overdose, may be between 12 and 24 h [5].

Volume of distribution (ASA): 0.2 l/kg [6].

Plasma protein binding: 50-90% (ASA). Plasma salicylate is < 80% protein bound, especially to albumin [5].

The elimination half-life of plasma salicylate is dose-dependent and increases with higher doses. The reported half-lives in adults ranged between 2.4 and 19 h, at the doses of 0.25 g and 10-20 g of sodium salicylate, respectively [1].

Salicylate may pass blood-brain barrier, but this process is very slow and restricted. However, it is easily passing placenta.

Metabolism and excretion

ASA is rapidly converted by esterases presented in plasma and liver to salicylic acid. The latter is partly metabolized in the liver, mainly to salicyluric and gentisic acids.

Excretion: nearly all of a single dose is excreted as salicylic acid (5%) and as salicylic acid conjugates (95%) [8].

Toxicologic mechanism

The acute toxicity mostly is due to a high level of salicylic acid, which uncouples mitochondrial oxidative phosphorylation and also inhibits Krebs's cycle dehydrogenases [5].

Toxic effect on the CNS may be due to accumulation of CO₂ in the brain and to decreased brain glucose concentration [7].

Target organs: kidney, liver, CNS, lungs [5].

References

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