




Pyrethrins and pyrethroids

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- ▶ Pyrethrins are active extracts of the chrysanthemum plant(*Chrysanthemum cinerariaefolium*), and include pyrethrum and piperonyl butoxide.
 - ▶ Pyrethroids are synthetic analogues and number over 1000 varieties which are used as insecticides to incapacitate or “knock out” insects

Pyrethroids are of 2 types

- ▶ **Type I** pyrethroids do not contain a cyano group, e.g. permethrin.
- ▶ **Type II** pyrethroids contain a cyano group, e.g. deltamethrin, cypermethrin, fenpropathrin, fenvalerate, etc.
- ▶ They are sold as liquids, sprays, dusts, powders, mats, and coils.

USE

- ▶ They are also used to prevent pest infestation in granaries, and in agriculture as pesticides.
- ▶ These compounds are used as household insect repellants and insecticides.
- ▶ Pyrethrum extract is effective for treating pediculosis of the head, body and pubic area.

Usual Fatal Dose

- ▶ Pyrethrum has an LD50 of over 1 gm/kg.
- ▶ The minimal lethal dose of pyrethrum is not clearly established, though it is probably in the range of 10 to 100 grams.
- ▶ Most cases of toxicity are actually the result of allergic reactions.

MOA

- ▶ Pyrethroids modify the gating characteristics of voltage-sensitive **sodium channels to delay their closure.**
- ▶ A protracted sodium influx (referred to as a sodium 'tail current') ensues which, if it is sufficiently large and/or long, **lowers the action potential threshold** and causes **repetitive firing**; this may be the mechanism causing **paraesthesiae**.


MOA




- ▶ Type II pyrethroids also decrease chloride currents through voltage-dependent chloride channels and this action probably contributes the most to the features of poisoning with type II pyrethroids.
- ▶ At relatively **high concentrations**, pyrethroids can also **act on GABA-gated chloride channels**, which may be responsible for the **seizures** seen with severe type II poisoning

Allergens

- ▶ Two types of allergens present in crude pyrethrum oleoresin have been identified: glycoproteins or glycopeptides, sesquiterpene lactones, principally pyrethrosin
- ▶ Refined pyrethrins and synthetic pyrethroids are said to have little or no allergenic effect

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- ▶ pyrethrum is broken down mainly by oxidation of the
 - ▶ isobutenyl side chain of the acid moiety and of the unsaturated
 - ▶ side chain of the alcohol moiety with ester hydrolysis playing
 - ▶ a role. Some organophosphates may enhance pyrethrin toxicity
 - ▶ due to competition for carboxyesterases responsible for rapid
 - ▶ detoxification of pyrethrins via ester hydrolysis. Very young
 - ▶ children are perhaps more susceptible to poisoning by pyrethroids
 - ▶ because they may not hydrolyse the pyrethrum esters
 - ▶ efficiently.

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- ▶ ester pyrethroids are rapidly detoxified in humans by hydrolysis, oxidation, and
 - ▶ conjugation. After oral, inhalative or dermal intake, both acid and alcohol
 - ▶ moieties of the pyrethroids are metabolized into carboxylic acids. The water-
 - ▶ soluble metabolites and their conjugates are excreted with the urine by the same
 - ▶ renal mechanisms the body uses to remove end products from intermediary
 - ▶ metabolism. In addition, no accumulation of pyrethroids in tissues have been
 - ▶ reported in the literature so far

Toxicokinetics

- ▶ Absorbed **dermally, orally** and through **inhalation**.
- ▶ Pyrethroids rapidly distribute to **tissues with a high lipid content, including fat and central and peripheral nervous tissues** due to its **lipophilic nature**
- ▶ Pyrethroid **metabolites** are **less lipid soluble** than the parent compound

Toxicokinetics

- ▶ Biotransformation takes place through **hydrolysis** of the central ester bond, **oxidative** attacks at several sites, and **conjugation** reactions to produce a complex array of primary and secondary **water-soluble** metabolites that undergo **urinary and biliary excretion**.
- ▶ Excreted through **urine, bile, fecal, milk**.

Clinical features

- ▶ *Skin contact:* dermatitis, blistering. Mild erythematous dermatitis with vesicles, papules in moist areas, and intense pruritus; a bulbous dermatitis may also occur. Skin contamination with pyrethrins can cause localised paraesthesia.
- ▶ 2. *Eye contact:* Eye exposures may result in mild to severe corneal damage, Corneal denudation and decreased visual acuity during normal use of pediculicide shampoos containing pyrethrin. Chemical conjunctivitis.

Clinical features

- ▶ Inhalation: rhinorrhoea, sore throat, wheezing, dyspnoea. Asthma or reactive airways disease syndrome, hypersensitivity pneumonitis with chest pain, cough, dyspnoea and bronchospasm. Eosinophilia, Dizziness and headache.
- ▶ Ingestion (large doses): paraesthesias, nausea, vomiting, vertigo, fasciculations, hyperthermia, altered mental status, seizures, pulmonary oedema, coma.
- ▶ Nausea, vomiting and abdominal pain develop within 10 to 60 minutes.
- ▶ Hypotension and tachycardia, associated with anaphylaxis, may occur.

Diagnosis

- ▶ ECG may demonstrate ST-T changes, sinus tachycardia, and ventricular premature beats.
- ▶ A colour test with 2-2 (2-aminoethylamine) ethanol produces red to violet colour in the presence of pyrethroidal substances. It is however not suitable for analysis of pyrethrins in body fluids, except, possibly at very high concentrations.

Treatment

- ▶ Skin contact—decontaminate with soap and water.
- ▶ Eye contact—irrigate with normal saline or water for 10 to 15 minutes.

Treatment

- ▶ Mild to moderate allergic reactions may be treated with antihistamines
 - ▶ Diphenhydramine 50 mg orally, intravenously, or intramuscularly initially, then 25 to 50 mg orally every 4 to 6 hours for 24 to 72 hours) with or without inhaled beta agonists,
 - ▶ Corticosteroids (e.g. methyl prednisolone 1 to 2 mg/kg intravenously every 6 to 8 hours) or
 - ▶ Adrenaline (1:10,000 solution, 3 to 5 ml diluted in 10 ml 0.9% saline slow intravenous push over 5 to 10 minutes).
- ▶ Treatment of severe anaphylaxis also includes oxygen supplementation, aggressive airway management, adrenaline, ECG monitoring and IV fluids.

Treatment

- ▶ Stomach wash can be done after making sure that there are no petroleum distillate additives.
- ▶ Activated charcoal is beneficial
- ▶ Oils and fats (including milk) promote the intestinal absorption of pyrethroids and should be avoided.
- ▶ Bronchospasm-Administer beta2 adrenergic agonists, Consider use of inhaled ipratropium and systemic corticosteroids (prednisone 60 mg/day (adult), or 1 to 2

Treatment

- ▶ Monitor for hypoxia and respiratory failure, and administer oxygen as necessary.
- ▶ If hypotensive give 500 to 2000 ml crystalloid initially (20 ml/kg in children) and titrate to desired effect (stabilisation of vital signs, mentation, urine output); adults may require up to 6 to 10 litres/24 hours.
- ▶ Dopamine should be used in refractory cases unresponsive to repeated doses of adrenaline, and after vigorous intravenous crystalloid rehydration

Treatment

- ▶ Atropine and oximes are contraindicated
- ▶ Cutaneous paraesthesias are said to respond to topical applications of vitamin E.



Thank you