



# 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**