The history of the pyrethroid insecticides

The synthetic pyrethroid insecticides were developed at Rothamsted Research, which receives strategic funding from BBSRC, in the 1960s and 1970s. Today they account for around one sixth of global insecticide sales, and global annual sales of pyrethroids exceed US$1bn. They are also used to impregnate bed nets, which help to reduce the spread of malaria as part of the World Health Organisation’s Global Malaria Programme.

The science of pyrethroids

Natural pyrethroids are derived from Chrysanthemums, the same genus as common daisies, and are an important component of plant defences against insect pests. For thousands of years they have been extracted and used to combat insect pests. However, the natural pyrethroids are not particularly effective when used on fields of crops as they are quite unstable, breaking down quickly when exposed to sunlight.

To overcome their limitations, scientists developed synthetic compounds, called pyrethroid insecticides, based on the chemistry of the natural pyrethrons. Both work by targeting sodium channels in the cell membranes of insect nervous systems. By locking these channels open, the pyrethroids block normal nerve impulses, paralysing the insect and ultimately killing it. Compared to natural pyrethrins, the synthetic pyrethroids are more stable in direct sunlight. They are also significantly more effective against a wider range of insects, so farmers need to apply less insecticide to their crops. This also means pyrethroids are less likely to build up to dangerous levels in the environment.

However, pyrethroids can harm some beneficial insects such as bees or the parasitic wasps that prey on pests, and they are also toxic to fish and other aquatic organisms. Because humans possess enzymes that quickly break down pyrethroid insecticides, the pyrethroids are only toxic to people in large quantities or over long periods of time.

Early landmarks in the discovery of the synthetic pyrethroids

- Pyrethrin insecticides from pyrethrum daisies (Chrysanthemum cinerariaefolium) have been used in various forms for thousands of years. They were originally discovered in China and imported into Europe as ‘Persian powder’.
- Hermann Staudinger and Lavoslav Ružička published a definitive study on the structure of natural pyrethrins in 1924.
- Pest control research at Rothamsted began before the Second World War when other pest control options often relied on arsenic or cyanide. Work on plant breeding near Rothamsted in the 1920s supported the establishment of the pyrethrum industry in Kenya.

1949

The first synthetic pyrethroid, okellen and broadlanth, are developed in America by Milton S. Schlechter and colleagues. They are around twenty times more effective at killing insects than DDT without the serious environmental or health impacts.

1950s

- Bioassay in honour of the Rothamsted Experimental Station in Harpenden, UK, where the discovery was made, is much more effective against houseflies than natural pyrethroids. However, it is still unstable in sunlight and unsuitable for use outdoors.
- Michael Elliott develops permethrin, the first field-stable pyrethroid. It is much more suitable for use in agricultural settings as it does not break down so quickly in sunlight. The development of permethrin leads to a second round of licensing deals with the agro-chemical industry.
- In the UK, Michael Elliott creates resmethrin, a ‘first generation’ synthetic pyrethroid, by altering the molecular structure of naturally-occurring pyrethrons. At the time such structure-activity studies were not common practice.
- Resmethrin is a single isomer of isothian, which exists as a mixture of four different isomers, i.e. compounds with identical molecular formulas but with different shapes. At the time, other compounds with several isomers were produced as a mixture, but the agro-chemical companies, working alongside Rothamsted scientists, were able to manufacture just the resmethrin isomer.
- Professor Chris Curtis at the London School of Hygiene and Tropical Medicine begins to investigate the potential of insecticide-treated bed nets to control malaria. He campaigns for aid agencies to distribute the nets for free to communities in affected regions to help reduce mosquito numbers and W reliance.
- The results are two new pyrethroids, cypermethrin and deltamethrin, the latter in use in such nets due to their low toxicity to humans and other mammals. Their physical properties also mean manufacturers can easily incorporate pyrethroids into the fibres used to make bed nets.

1960s

- Early 1960s
  - The first generation synthetic pyrethroids are supported and commercially exploited by the National Research Development Corporation (NRDC), a group established by HM Treasury to commercially exploit the outputs of UK research, and its successor, the British Technology Group. An initial licensing deal is agreed by NRDC with six companies (Mitchell Cotts, the Wellcome Foundation, Roussel-Uclaf, Sumitomo, FMC and Penick) interested in manufacturing and selling pyrethroids.
- Late 1960s
  - Michael Elliott retires from Rothamsted.
  - Around one quarter of the profits made by UK firm Mitchell Cotts this year are attributed to the sale of pyrethroid insecticides. Mitchell Cotts were one of the original licencees for pyrethroids.
  - Japanese chemical company Sumitomo independently discovers fenvalerate. Elliott becomes aware of the development of the work through his colleague Professor Iwao Yamamoto in Japan and through the patents filed by the company. He realises he can build on their success in his own work.

1970s

- 1970s
  - The World Health Organisation (WHO) recommends using pyrethroids developed at Rothamsted, including deltamethrin and permethrin, for ITNs*. Pyrethroids are the only class of insecticides recommended for use in such nets due to their low toxicity to humans and other mammals. Their physical properties also mean manufacturers can easily incorporate pyrethroids into the fibres used to make bed nets.
  - The results are two new pyrethroids, cypermethrin and deltamethrin, the latter in particular is an extremely potent insecticide.

1980s

- 1980s
  - Professor Chris Curtis at the London School of Hygiene and Tropical Medicine begins to investigate the potential of insecticide-treatment bed nets to control malaria. He campaigns for aid agencies to distribute the nets for free to communities in affected regions to help reduce mosquito numbers and W reliance.
  - Michael Elliott retires from Rothamsted.
  - Mitchell Cotts retires from Rothamsted.
  - A Cochrane Collaboration review of earlier trials confirms that ITNs reduce deaths amongst children under the age of five by around two-thirds. The ITNs used in the study were treated with permethrin.

1990s

- Early 1990s
  - Sales of synthetic pyrethroids reach US$1.2bn per year.
  - An ARC funded study shows that using insecticide-treated mosquito nets (ITNs) in a rural region of the Gambia can reduce the number of deaths of children under the age of five by around two-thirds. The ITNs used in the study were treated with permethrin.

2000s

- 2000
  - Pyrethroids account for 17% of global insecticide sales. Total global sales of insecticides are around $8bn.

2010s

- 2010
  - The WHO recommends the use of 12 long-lasting insecticidal mosquito nets to tackle malaria. The nets all rely on pyrethroids developed at Rothamsted.

2011

- 2011
  - The WHO recommends the use of 12 long-lasting insecticidal mosquito nets to tackle malaria. The nets all rely on pyrethroids developed at Rothamsted.

- 2019
  - A Cochrane Collaboration review of earlier trials confirms that ITNs reduce deaths amongst children under the age of five by around one fifth. They also significantly reduce the incidence of illness caused by malaria.
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Notes and References
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