Chapter from the book *Insecticides - Development of Safer and More Effective Technologies*

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1. Introduction

Ectoparasites reduce significantly animal production and welfare. They cause nuisance, anaemia, irritation and transfer of pathogens of important diseases, often leading to animal death. Examples of diseases with high mortality transmitted by arthropods include viral diseases, such as the Bluetongue disease, or parasitic diseases, such as piroplasmosis and filariosis. Biting midges of the *Obsoletus* species complex of the ceratopogonid genus *Culicoides* were assumed to be the major vectors of bluetongue virus in northern and central Europe during the 2006 outbreak of bluetongue disease. Most recently, field specimens of the same group of species have also been shown to be infected with the newly emerged Schmallenberg virus in Europe, as other bloodsucking arthropods. Furthermore, ectoparasites may attack humans and threaten public health, such as diseases transmitted by mosquitoes or ticks.

The control of ectoparasites found on animals, i.e. midges, fleas, ticks, lice, flies, is largely based on the use of chemicals (insecticides). The main groups, which have been used as the basis of the common ectoparasiticides, include the synthetic pyrethroids, organochlorines, organophosphates, carbamates, formamidines and others. The macrocyclic lactones (avermectins and milbemycines) have also been shown to have a high activity against a range of ectoparasites. Furthermore, there are also compounds which affect the growth and development of insects, such as the chitin inhibitors, chitin synthesis inhibitors and juvenile hormone analogues. Insect growth regulators (i.e. lufenuron) are used mostly against fleas and certain flies.

2. Deltamethrin

Pyrethroids, synthetic analogues of pyrethrins, were developed to improve stability of the natural pyrethrins since they degraded rapidly by light. The pyrethrin insecticides were
originally derived from extracts of the flower heads of *Chrysanthemum cinerariaefolium*. There are six compounds that comprise the natural pyrethrins, namely, pyrethrins I and II, cinerins I and II, and jasmolins I and II.

Pyrethroid insecticides are attractive compounds because of their high potency and ability to reduce disease transmission, selective toxicity, relative stability in the environment and ease of degradation in vertebrates. Compared with organophosphates and carbamate insecticides, pyrethroids are less likely to cause acute and chronic health effects to vertebrates. The common synthetic pyrethrins in use include deltamethrin, permethrin, cypermethrin, flumethrin and others. The main value of these compounds is their repellent effect and since they persist well on the coat or skin, but not in tissue, they are of particular value against parasites that feed on the skin surface such as ticks, lice, some mites and nuisance flies. They can act as contact insecticides due to their property to be lipophilic. Some have the ability to repel and to affect flight and balance without causing complete paralysis (knockdown effect). They pose a strong affinity for sebum. They are widely used in veterinary medicine for agricultural and domestic purposes.

Pyrethroids are primarily targeted on the nervous system. They act as neurotoxins upon sensory and motor nerves of the neuroendocrine and CNS of arthropods. Several mechanisms of action have been proposed, including alterations in sodium channel dynamics in nerve tissues, which polarise membranes and result in abnormal discharge in targeted neurons.

Synthetic pyrethrroids are relatively safe. However, if toxicity occurs, it is expressed in the peripheral nervous system of animals as hypersensitivity and muscle tremors. They are extremely toxic to fish and aquatic invertebrates (except for molluscs and amphibians). However, it would appear that, in practice, the risks of deltamethrin are limited. Light, the pH of the water, organic or colloidal molecules in suspension, and the presence of sediment and bacteria, all contribute to a rapid breakdown of the molecule into rapidly decomposed non-toxic products. Deltamethrin does not present any toxicity problems for birds, including game birds. Regarding public health, some adverse effects on humans may occur, with neurotoxicity and developmental toxicity being potential side effects following acute high-dose exposures to pyrethroids.

Among synthetic pyrethroids, Deltamethrin (Butox, MSD) is of particular importance. Contrary to other pyrethroids, it is a single cis-isomer (Figure 1), which is considered to be more effective than isomer combinations. Deltamethrin repels ectoparasites by the “hot foot effect”, which is typical for pyrethroids. An insect after it had a “touchdown” on such an animal, redraws its feet suddenly from treated hair. Even after a very short contact, for only a few seconds, to treated hair, a “knock-down effect” occurs since insects and ticks die soon after the open nerve ends at their feet got into contact with the insecticide. This efficacy leads to a constant reduction of biting or attacks and same time dead female population stops breeding. On the other hand, studies carried out in 3 generations of rats, using daily doses of 0.15, 1 and 3.75 mg/kg in the feed, did not reveal any differences between treated and control animals with respect to fertility, duration of gestation, fecundity and viability of the litters. Finally, Deltamethrin did not show any mutagenic effects in any of the tests (both in vivo and in vitro) employed.
3. Efficacy

Several published papers exist in scientific journals demonstrating the strong properties of Deltamethrin (Butox, MSD) to repel or kill arthropods infesting livestock, such as biting midges, nuisance flies, ticks, lice, certain mites etc. Results from these field trials proved the high efficacy of this compound to protect ruminants from midges, i.e. Culicoides spp., for periods over 4-5 weeks, even if the animals became wet several times. It has been found to be effective against ticks, including all developmental stages, mosquitoes and many others.

Herein follow, in more details, the results of some studies evaluating the potential use of Deltamethrin (Butox, MSD) on farm animals.

3.1. Culicoides midges

One set of such experiments include the investigation of the control of Bluetongue disease of ruminants using this drug, carried out by Schmahl and colleagues in 2008. Bluetongue disease is a viral disease, which harms considerably farm ruminants with high mortality rates in cattle and especially in sheep, while wild ruminants become infected, serve as virus reservoirs, but show only rarely severe symptoms of disease. From several transmission experiments and epidemiological studies in South Africa and in Southern Europe, it was known that the main vector belonged to the midges (Family Ceratopogonidae, genus Culicoides). Therefore, protection methods were needed to avoid transmission of the virus from one animal to the other. Thus, the aim of this study was to compare the efficacy of Deltamethrin when Culicoides specimens come into contact with hair of cattle and sheep that had been treated for 7, 14, 21, 28, or 35 days before. This study was needed, since it had to be clarified, whether the product in this formulation of Deltamethrin can reach the hair of feet in sufficient amounts when they are applied onto the hair along the back line. The product must arrive in sufficient amounts at the feet and along the belly since there are the predominant biting sites of the very tiny (only 0.8–3 mm long) specimens of C. obsoletus, C. pulicaris and C. dewulfi, the proven vectors of Bluetongue in Europe. Towards this end, one group of three young cattle of about 400 Kg bodyweight and one group of three young sheep of 60 Kg each were treated by application (pour on) of 30 ml and 10 ml, respectively, of the product Butox® 7.5 onto the skin along the backside of the animals. Butox® 7.5 contains 7.5 g deltamethrin per liter of the ready-

Figure 1. The structure of deltamethrin
to-use solution and is a registered trademark of MSD pharmaceutical company. Seven, 14, 21, 28, and 35 days after treatment, hair was clipped off from the feet of the cattle and sheep (just above the claws), collected in separate, suitable plastic bags, and transported to the institute, where it was mixed with freshly caught midges, which had been caught in the previous night with the aid of an ultraviolet light lamp. Each vial contained at least ten *Culicoides* specimens, besides other insects. The trapped insects were incubated with treated hair or with hair of an untreated animal (control). The exposure periods of the insects to hair lasted for 15, 30, 60, or 120 seconds—a period which was thought to be realistic compared to the field conditions. The insects were thereafter separated from the hair and placed on filter paper inside closed plastic petri dishes, where they were observed at regular intervals (5–10 min) using a stereo microscope to record reactions and the time of death after the first contact with treated hair.

The midges (*Culicoides* species) were apparently highly sensitive to Deltamethrin (Butox® 7.5) since they died even after rather short contacts to hair treated even 35 days ago, which is a very satisfying effect. There were no significant differences between the species of treated animals (sheep or cattle), although the distance from the place of application (back) until the feet is longer in cattle than in sheep. Thus, the formulation can reach in sufficient amounts the region of the predominant biting sites of the *Culicoides* species (feet, belly).

The results obtained from these experiments clearly show that Deltamethrin, when applied as a pour-on solution onto the back of the animals, has a significant killing effect on the *Culicoides* species, which are known vectors of the Bluetongue virus in Europe. Furthermore, even if the protection might not be 100%, any killed female *Culicoides* prevents its possible progeny and hinders the transmission of agents of diseases.

During the above described studies, the animals were provided with adequate shelter against the rain. The efficacy of deltamethrin on wet animals was, therefore, not tested. It is common that ruminants stay under the rain or exposed to water when they stay at pasture for grazing. Therefore, the same group of researchers in 2009, carried out the next step of the above study, i.e. the new task was to determine if thoroughly wetting the test subjects, twice a week, would affect the efficacy of Deltamethrin. Cattle and sheep were treated with Butox 7.5 along the neck or dorsal midline, as described earlier. Test animals were wet thoroughly with tap water twice weekly. Control animals remained dry. Hair was clipped off the legs, near the claws, at day 7, 14, 21, and 28 after treatment of test and control animals. Recently caught *C. obsoletus* midges were then exposed to the hair for 15, 30, 60, and 120 seconds. The midges were then transferred to filter paper in plastic petri dishes and observed. The time needed for the midges to die after the exposure was recorded.

In both cattle and sheep, the product remained active for at least up to 4 weeks (28 days - end of the experiment), even in the animals wet with water twice weekly over the 4-week period. In sheep, the time between exposure and death of the midges was definitely lengthened in animals that were wet. In cattle, the results were different in that in some cases, time between exposure and death of the midges was shorter in wet animals than in dry animals, while in other cases the results were similar. Compared with the sheep, the time between exposure and death is generally quicker, probably, due to differences in hair structure. All midges exposed to hair from treated sheep or cattle, wet or dry, died even after only 15 seconds of exposure to
the hair. In cases where the period between exposure and death of the midges was very long, it is likely that the midges were unable to bite as they showed signs of paralysis immediately after contact with treated hair. The fact that Butox 7.5 pour on remains effective in animals regularly exposed to rain is an important finding towards the protection of ruminants from the attack of midges and the risk of disease transmission.

3.2. Ticks

Another study of Mehlhorn and others took place recently in 2011 in order to investigate the efficacy of Deltamethrin (Butox® 7.5 pour on) against specimens of two important species (*Ixodes ricinus* and *Rhipicephalus sanguineus*). Ticks can transmit a broad spectrum of agents of diseases in cattle or sheep and the use of an effective long lasting acaricide is needed to protect livestock. Four sheep and four young cattle were treated along the vertebral column with 10ml Butox® (deltamethrin) per sheep or 30ml Butox® per cattle. Day 7, 14, 21, and 28 after the treatment, hair was shaved off from the head, ears, the back, belly, and the feet being collected in separate, suitable plastic bags, and transported to the institute, where these hair were brought into close contact with either adult and/or nymph stages of *I. ricinus* and *R. sanguineus*. As results, strong, acaricidal effects were seen, which varied according to the parasite species, the origin of the hair (e.g., head, leg, etc.) and according to the period after the treatment.

In sheep, the acaricidal effect was noted for the whole period of 28 days along the whole body with respect to adults and nymphs of *I. ricinus*, while the acaricidal effects of Deltamethrin were reduced for *R. sanguineus* stages beginning at day 21 after treatment. In cattle, the full acaricidal effect was seen for 21 days in *I. ricinus* stages and for 14 days in *R. sanguineus*, while the acaricidal efficacy became reduced after these periods of full action—beginning at the hair taken from the legs. Only *R. sanguineus* adults did not show any reaction on day 28 after treatment. Besides these acaricidal effects, repellent effects were also noted. Full repellency for both species was seen during the first 14 days in sheep and cattle against *Ixodes* and *Rhipicephalus*, while the repellency was later reduced, especially in contact with hair from the legs. As conclusion, Deltamethrin, besides its very good effects against biting insects, brings acaricidal as well as repellent effects against ticks, thus protecting the sheep and cattle from transmission of agents of diseases.

3.3. Nuisance flies

Other researchers carried out experiments testing the efficacy of Deltamethrin against nuisance flies of ruminants. More precisely, Franc and Cadierques in 1994, applied the pour on formulation of 0.75 % Deltamethrin to cattle on 6 farms in southwest France (3 treated, 3 control). Ten ml per 100 Kg body weight were applied to the backs of 77 cattle (with a max. of 30 ml) and adequate control of hornfles (*Haematobia irritans* and *Hippobosca equina* (with a 95% or better) was achieved during 10 weeks. The protection against non biting flies *Musca autumnalis* was better than 75 % during 6 weeks and better than 50 % during the next 14 weeks in 2 farms. In the other farm the number of *Musca autumnalis* fell by 75.5% only during the first week.
3.4. Mange

Finally, in the international literature, in 2001, exists a publication of Khalaf-Allah and El-Bablly, who evaluated the effect of Deltamethrin for control of sarcoptic mange in naturally infested cattle. The infested calves (28 calves with 8-16 months of age) were randomly allocated into two groups each consisting of 14 animals. The first group was sprayed with Deltamethrin at the concentration recommended by the manufacturer using a motor sprayer, while the second group was left untreated and served as control. Besides this, 14 healthy calves at the same farm were used to compare between them and the infested calves for the haematological and biochemical parameters. Before application of the acaricide, mange lesions were carefully scraped so as to remove the scales and crusts under which sarcoptic mites are hidden. Skin scrapings were taken from the affected lesions and mites were identified at day (0) and at weekly intervals post-treatment.

The results revealed that Deltamethrin provided a high level of sarcoptic mange control which lasted up to 42 days post-treatment. The mean haematological values of RBCs, Hb, PCV were significantly lower in mange infested calves than that of control, whereas the mean WBCs was significantly higher in infested animals. As well, the mean biochemical parameters estimated in mange infested animals were significantly lower than that of controls. The mean values of the haematological and biochemical parameters in infested animals were restored and nearly returned to its normal levels one month post-treatment.

3.5. Fleas

Herein follow our results from a pilot study which was carried out in order to evaluate under field practise the effect of Deltamethrin (Butox®, MSD) against fleas infesting small ruminants in Greece.

Fleas pose a significant problem in dairy sheep and goat farms of the country, since they attack not only animals but farmers as well (Figure 2). There are several papers in the international literature, regarding flea infestation of livestock in many countries around the Mediterranean basin and elsewhere (Ethiopia, Greece, Israel, Libya, Morocco etc). In all the cases of severe infestation, fleas cause, additionally to nuisance, high mortality, morbidity and disease transfer.

Control is difficult, because fleas spend much time off the host. Furthermore, insecticide residues in milk, when treatment is applied during milk production, are a restraining factor. The great advantage of deltamethrin (Butox®, MSD) is the very short withdrawal period in milk (12 hours) making treatment against ectoparasites practically possible at any time of animal production. Very limited information, to our knowledge, exists in the scientific literature, regarding flea control using insecticides on livestock.

Twenty (15 goat and 5 sheep) farms were identified and Deltamethrin (Butox®, MSD) was applied to all animals at the recommended dose rate. Herds/flocks consisted of 100-200 head of local dairy breeds. Information was collected regarding the management system of the farms, particularly on manure handling (Figure 3).
Figure 2. Reaction on human leg after flea feeding

Figure 3. A typical farm environment favouring flea reproduction
Animals within each farm were randomly inspected and fleas, if present, were counted every week for a minimum period of one month (Figure 4). Controls, untreated animals, were not used (accepted by the WAAVP guidelines) for both ethical reasons and because the aim of the study was to eliminate fleas from the farm premises. Practically no fleas were found during the post-treatment period. In more details, the mean (±sd) number of fleas before and after the Deltamethrin treatment were 104.5 (±12.6) and 3.6 (±2.3 fleas), respectively. The overall success of flea control was >96.6%. The main flea species identified was *Ctenocephalides felis*, which is known to be very common and widespread. These results offer a sustainable approach to flea control in Greece due to the long protection period and if combined with hygienic treatment of the farm premises, may contribute significantly to flea control.

**Figure 4.** The presence of fleas was inspected using a comb

4. Concluding remarks

In conclusion, Deltamethrin (Butox®, MSD) can be successfully used for farm animal protection in control programmes against many arthropods with important vector-borne or nuisance capacity, including midges, ticks, flies and fleas. Effective control of ectoparasites is of major significance, not only for increased animal production and welfare, but for the public health protection as well.
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References


