

The efficacy of d-phenothrin and permethrin formulations against head lice: a comparison

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The efficacy of d-phenothrin and permethrin formulations for treating head lice were compared using laboratory-bred lice and their eggs. Both products were wholly effective at killing lice but the phenothrin lotion was significantly better ($P < 0.001$) at killing nymphs before they could begin to emerge from the egg shell. In contrast, the permethrin creme rinse appeared to rely on residual action for its efficacy in order to kill surviving nymphs after they had hatched.

SYNTHETIC pyrethroid insecticide-based formulations for the treatment of head lice were obvious successors to natural pyrethrin-based products for reasons of stability, safety and lack of allergenic activity.¹ However, their introduction to the British market was somewhat late, when compared with North America and parts of Europe, possibly because a range of effective products with other active ingredients was already established.

Two formulations containing different pyrethroid active ingredients are currently available in Britain. They are d-phenothrin 0.2 per cent lotion (Full Marks) and permethrin 1 per cent creme rinse (Lyclear). The active ingredients in these products are very similar chemically and both formulations have performed well in field trials.^{2,5} However, since they differ so much in their presentation there is some confusion among professionals and consumers regarding efficacy and appropriate use.

This study was undertaken with a view to clarifying the situation since no previous direct comparative tests have been performed.

Materials and methods

Samples of formulations used were obtained from local pharmacies. In each case the product had a minimum of one year remaining before its expiry date.

Young adult lice and third instar nymphs were obtained from the Cambridge reference strain culture colony of clothing lice.

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Eggs up to 48 hours old were obtained from the same source. In each test eggs were allocated randomly to treatments in order to eliminate variation in susceptibility of eggs laid by different lice.

The two formulations under test differ in presentation and in their intended modes of use.

In each case the test used attempted to mimic actual use by consumers as follows.

Full Marks lotion is an evaporating lotion in a water and alcohol base and was tested as described previously⁶ by dipping lice or eggs on nylon gauze into the formulation for 10 seconds, draining of excess fluid and incubating at $30 \pm 2^\circ\text{C}$ and 70 per cent relative humidity for the appropriate period. This was followed by washing in a 1:15 mixture of Boots frequent wash shampoo in tap water (FWS 1:15) followed by rinsing and further incubation until the results were read.

Lyclear, in contrast, is a creme rinse formulation to which 20 per cent alcohol and insecticide have been added. It is applied to clean, damp hair. In this case lice or eggs on gauze were first washed with FWS 1:15, rinsed and distributed onto dampened medical wipe tissues. The creme rinse was then poured onto the gauze squares and spread with the tip of a finger, so that all parts were impregnated, after which they were incubated for 10 minutes followed by rinsing in warm tap water. The insects or eggs were subsequently incubated until the results were read.

For comparison, a simple solution of d-phenothrin in 70 per cent isopropanol was also tested against eggs in the same way as Full Marks lotion together with a temporary emulsion of permethrin 1 per cent. The latter was made by dissolving permethrin in pure isopropanol to produce a 5 per cent solution which was then mixed with water in a 1:5 ratio and vigorously shaken immediately before use.

Control lice and eggs were only subjected to washing with FWS 1:15.

Hatching nymphs were checked for their ability to feed when placed on the back of a hand. Any that were able to walk but were unable to feed were considered incapable of survival and recorded as "hatched but non viable". Nymphs that died in the process of emerging from their eggs were recorded as "half-hatched" and included in mortality figures.

The performance of products was assessed statistically using the binomial distribution analysis described by Armitage and Berry.⁷

Results

Lice treated with either of the formulations were immobilised immediately. Toxic effects on those exposed to Lyclear were not immediately apparent because they had already been wetted which causes them to cease activity. Once dried few showed any movement for some time, presumably because the insecticide had already taken effect. The reaction of lice treated with Full Marks was in marked contrast since as soon as the alcohol base had evaporated the lice began to show signs of activity. However, whereas in controls treated with isopropanol alone the movement was normal walking activity, the Full Marks treated lice showed immediate signs of insecticide intoxication with jerky and spasmodic movements. After 16 hours when mortality was assessed all lice treated with Lyclear or Full Marks were effectively killed (Table 1). However, 9 per cent of Lyclear and 36 per cent of Full Marks treated lice still showed some twitching of limbs although it was clear none would be capable of surviving.

Table 1: Efficacy of pyrethroid formulations against clothing lice in vitro after 10 minutes treatment

Formulation	Number of lice	Mortality %
Isopropanol 60 per cent	100	5 (2.1)
Full Marks	100	100 (100)
Lyclear	100	100 (100)

*Percentage mortality adjusted using "Abbott's correction" for control mortality. Abbott's correction uses the formula:

$$\text{Corrected mortality} = \frac{\text{Test mortality} - \text{Control mortality}}{100 - \text{Control mortality}} \times 100$$

Treatments of louse eggs showed a difference of direct efficacy between the formulations. Since the recommended application times of Full Marks (two hours) and Lyclear (10 minutes) differ so much an additional set of tests was performed in which Full Marks was applied for 10 minutes so that a direct comparison could be made (Table 2). At both application times Full Marks performed significantly better (binomial distribution analysis $P < 0.001$) than Lyclear in prevention of hatching. Nymphs that emerged from eggs in all tests rapidly showed signs of intoxication. It was not clear whether the insecticide was picked up from the egg shells, as the insect emerged, or from the gauze substrate. In all cases this resulted in a lethal dose and even those that were able to take a blood meal failed to recover.

In order to assess the difference in residual effect of the two formulations identical

Table 2: Efficacy of pyrethroid formulations against louse eggs *in vitro*

Formulation	Exposure period	Number of eggs			
		Total	Hatched but non-viable	Half-hatched	Mortality (%) \pm SD
Full Marks	2 hours	2473	20	8	99.1 \pm 2.4
Full Marks	10 minutes	4596	61	44	98.5 \pm 3.5
Lyclear	10 minutes	4103	557	329	84.2 \pm 11.0
d-Phenothrin 0.2%	10 minutes	850	0	0	100
Permethrin 1% emulsion	10 minutes	621	1	33	99.8 \pm 0.5
Control		3825	3290	82	14.0 \pm 5.7

*Percentage mortality adjusted using "Abbott's correction" for control of mortality. This series of tests consisted of 34 replicates conducted in four groups over a period of three months.

human hair samples were treated with either Full Marks or Lyclear for 10 minutes and washed in accordance with the instructions. Both samples were tested against lice after three hours and were equally effective at killing them. The hair was then exposed to natural light from a north-west facing window over a period of 24 hours following which the phenothrin-treated hair killed seven of 20 lice whereas the permethrin-treated hair killed all lice placed in it. Following four further days of exposure the Full Marks treated hair showed no residual activity in contrast to that treated with Lyclear in which persistence was detectable for several weeks.

A further test to examine the residual effect of d-phenothrin was performed in which identical hair locks were treated with Full Marks for either 10 minutes or two hours followed by a wash. Small samples were removed from each piece of hair at intervals over the next two weeks. During this period the hair was carried around by an experimenter to simulate natural exposure to light and washed on alternate days with FWS 1:15. The samples removed from each hair lock were placed in individual Petri dishes and stored in the dark at 30°C until tested for residual activity by placing lice on the hair and checking for ability to feed 24 hours later. The results are shown in Table 3. A number of lice that failed to feed were able to walk, often with erratic movements. These were designated as moribund.

Discussion

Both phenothrin and permethrin were discovered during programmes to develop more effective and safer insecticides during the 1970s. As chemicals they are very similar, differing only in that permethrin is a modified form of phenothrin in which chlorine atoms have been substituted for methyl groups in the light sensitive chrysanthemoid acid portion of the molecule, thus increasing the photostability.⁸ This stability is of significance since it means that permethrin will persist on hair for some time after treatment despite regular washing^{2,3} and even when exposed to sunlight as has been shown in this study. Taplin *et al.*² attributed the success of Nix (the USA brand name for Lyclear) in their *in vivo* study to residual permethrin on hair since 30 per cent of eggs removed from patients immediately following treatment, and then incubated *in vitro*, hatched out viable nymphs. It appears from

our study also that Lyclear depends on residual activity for success since at least one nymph hatched successfully in 29 of 34 test replicates.

Residual effect was one of the great advantages of malathion lotion when it was first introduced.⁹ Under conditions of high prevalence of louse infection, when a freshly cured patient runs a severe risk of immediate reinfection, the advantages of a residual insecticide effect are obvious. This was certainly the case at the time of Maunder's study in Britain⁹ and that of Taplin *et al.*² and others in America recently. It is also certain to apply in many parts of the developing world today. However, the situation in most parts of Britain is now different. Whether a residual action confers any advantage on the patient is a matter of conjecture since most health authorities currently encourage people to contact trace the source of their infection, and in this way avoid reinfection, rather than rely on a residual effect which may have a variable duration and efficacy as has been found with malathion. It has been suggested that the slow wearing away of the residuum of insecticide will ultimately result in levels that are too low to kill insects coming into contact with them and could result in some becoming resistant.¹⁰

Phenothrin is photolabile and in sunlight appears to break down quite rapidly. We have shown that hair treated with Full Marks lotion and then exposed to daylight loses its toxicity for lice within a few days. A similar breakdown was described by Miyamoto¹¹ after applying the insecticide to inert base materials. Consequently it will be essential for consumers using this product to perform adequate contact tracing if they wish to avoid the risk of reinfection. Whether the lack of residual effect will have any bearing on the possible development of resistance to phenothrin will need to be tested in field trials.

It is clear that both products are effective. Also, they have active ingredients that are not only considered highly safe in acute toxicity but also have low dermal absorption,¹¹⁻¹³ together with a low level of reported side effects.^{1,4} It is likely that the presentation of Lyclear may make it more attractive to consumers. However, the mode of application may render it less effective in some cases as a result of dilution by water remaining on the hair after partial drying,¹⁴ especially if a whole bottle of formulation is not used for each person treated. Comparison of efficacy under conditions

Table 3: Residual insecticide of activity of hair samples treated with Full Marks lotion

Time hair exposed in hours	Treated 10 minutes			Treated 2 hours		
	Feeding	Moribund	Killed	Feeding	Moribund	Killed
0*	3	5	2	0	3	7
0+	8	1	1	0	8	2
48	8	2	0	2	7	1
72	9	0	1	2	8	0
144	9	1#	0	7	3	0
264	10	0	0	7	3	0

* This test was performed within three hours of lotion application.

+ This test was performed after two weeks storage in the dark.

This louse tried to feed several times but was unable to withdraw blood.

of actual use will, therefore, need to be undertaken in field trials.

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