Malathion lotions for head lice — a less reliable treatment than commonly believed

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Recently-developed testing methods were used to compare the *in vitro* efficacy of malathion lotions for head lice. The results suggest that the insecticide alone does not always penetrate and kill louse eggs. Some marketed formulations appeared more effective than others. This is attributed to excipients that assist in the ovicidal action. For most formulations the results indicate that a 10 hour or overnight treatment is required with a second application after one week.

THE introduction of malathion in 1971 as an active ingredient in formulations for head louse treatment was a significant advance at a time when resistance to organochlorine insecticides was becoming apparent.[1] Its acceptance was greatly assisted by evidence of ovicidal activity and residual action which eliminated the need for thorough "nit combing" following treatment.[2]

Until recently the efficacy of malathion formulations has been unquestioned. Some health authorities and organisations have even advocated continual use of malathion for head louse treatment rather than rotation between different insecticides.[3,4]

Despite its previously good track record, reports of treatment failures with malathion-based lotions began to be received by the Medical Entomology Centre in December 1988, some six months after the first inquiries about carbaryl efficacy, reported previously.[5] As with carbaryl, many of these were either cases in which newly hatched lice had been found soon after treatment or else individuals who required repeated treatments every three or four weeks. In some cases there had been no possibility of re-infection by contacts.

Tests performed when malathion treatment was introduced were primarily field trials.[1,2] Laboratory tests to confirm ovicidal activity were not performed until some time later. Those subsequently performed suffered the same drawbacks in methodology as early tests of carbaryl formulations.[5] Consequently, any variation of efficacy between formulations may have been missed.

This paper describes a new series of tests to examine the efficacy of malathion lotion formulations produced for the British market against laboratory bred lice and their eggs.

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Materials and methods

Head louse lotions were obtained from local pharmacies and all samples tested had a minimum of one year before their expiry date. A standard solution for comparison was made using 99 per cent pure malathion dissolved in a mixture of 60 per cent analytical grade propan-2-ol (isopropanol) and 40 per cent distilled water to give 0.5 per cent w/v concentration.

The method of testing was as described previously.[5] Young adult lice and third instar nymphs were obtained from the Cambridge reference strain culture colony of clothing lice. Eggs up to 48 hours old were obtained from the same source. On each occasion, eggs were randomised between treatments in an attempt to eliminate variations in susceptibility between eggs laid by different lice.

In each test, the insects or eggs were immersed in the test formulations for 10 seconds, drained of excess liquid and incubated for either two hours or overnight at 30°C ± 2°C and 70 per cent relative humidity. They were than washed in a 1:15 mixture of Boots frequent wash shampoo in tap water (FWS 1:15), rinsed and incubated again until the results were read.

As in the carbaryl study, controls were only subjected to washing with FWS 1:15. In all batches, washes were subsequently performed on alternate days with the shampoo mix in order to mimic normal hair washing procedures.

In previous tests of carbaryl formulations it appeared that excipients affected efficacy. Prioderm underwent a formulation change in 1988. "Before" and "after" formulations were tested to look at possible differences of activity due to excipients. These tests followed the same procedure as above but were conducted separately.

Any surviving lice or hatching nymphs were checked for their ability to feed when placed on the back of a hand. Those that were able to walk normally but failed to take a blood meal were considered incapable of survival. Nymphs that died in the process of escaping from the egg were recorded as half-hatched and included in mortality figures.

Treatments were compared using Chi-squared analysis.

Results

Treatment of lice with any of the formulations or the 0.5 per cent malathion in isopropanol caused complete immobilisation within two hours with no subsequent recovery (Table 1). However, when tested against louse eggs, a marked difference was apparent between formulations.

With a two hour treatment time, only Suleo-M was effective against eggs (Table 2). There was no significant difference between the performance of either of the other two formulations or malathion in simple solution in preventing hatching.

In all groups the majority of eggs that failed to hatch reached an advanced stage of embryonic development and in most cases the fully developed nymphs were seen to be swallowing air, a process that precedes hatching. Subsequent failure of these nymphs to hatch indicates that malathion had been trapped in the cavities of the egg shell cap, rather than penetrating

Table 1: Efficacy of malathion-based lotions against clothing lice *in vitro* after two hours' treatment

Formulation	Number of lice	Mortality (per cent)*
Isopropanol 60 per cent	100	12 (9.3)
Malathion 0.5 per cent	100	100 (100)
Derbac-M	100	100 (100)
Prioderm	100	100 (100)
Suleo-M	100	100 (100)

* Percentage mortality adjusted using "Abbott's correction" for control mortality[6]

Table 2: Efficacy of malathion-based lotions against louse eggs *in vitro*

Formulation	Two hours† Treatment Time				"Overnight" (10 hours)‡			
	Number of eggs				Number of eggs			
	Total	Hatched	Half-hatched	Mortality per cent* (±SD)	Total	Hatched	Half-hatched	Mortality per cent* (±SD)
Isopropanol 60 per cent	1438	1236	30	[−2.2] (3.6)	974	786	27	1.7 (1.4)
Malathion 0.5 per cent	1415	570	247	52.1 (30.7)	1091	214	121	76.1 (31.3)
Derbac-M	1762	736	199	50.3 (14.4)	770	7	37	98.9 (0.9)
Prioderm	2530	955	438	55.1 (18.7)	1615	529	199	60.1 (26.0)
Suleo-M	1622	0	2	100	902	0	0	100

* Percentage mortality adjusted using "Abbott's correction" for control mortality.[6] Figure in square brackets indicates a lower mean mortality than the control group

† This series of tests consisted of 17 replicates conducted in six test groups over a period of seven months

‡ This test series consisted of 12 replicate tests conducted in six groups over a period of seven months

the embryo, and that a toxic dose was only delivered after the nymph had broken through the chorionic membranes as it started to hatch, which is confirmed by the relatively high numbers of nymphs that died in the process of hatching and are listed as half-hatched in Table 2. Whether the louse dies before or during hatching may be relevant to degradation of insecticide. It has always been thought that malathion which penetrated the egg was "safe" from environmental degradation. Insecticide not penetrating the egg could be washed out.

The relatively poor performance of Derbac-M here was expected since the manufacturer's instructions call for an overnight treatment in order to obtain complete evaporation of the water base which concentrates the insecticide into a small volume of lipid. Of the lice that managed to complete the hatching process only those emerging from eggs treated with Prioderm were able to feed.

When eggs were treated "overnight", a minimum of 10 hours, the performance of all lotions, except Prioderm, improved. However, improvement was only statistically significant for Derbac-M. Prioderm gave no overall improvement on a two hour application. Some individual Prioderm test replicates were significantly better than others. However, its overall performance was not as good as 0.5 per cent malathion solution and, as with a two hour treatment, some of the nymphs emerging were capable of feeding successfully. In contrast, Derbac-M gave complete kill most of the time but occasionally a few eggs survived. Nevertheless it performed significantly better than malathion in isopropanol alone.

As with the previous tests of carbaryl products, a comparison was made of a single application of lotion with two treatments seven days apart. The results of these tests are shown in Table 3. As with earlier tests, Suleo-M gave complete kill of eggs. Malathion and Derbac-M improved their performance significantly ($p<0.05$) by using two applications. Prioderm applied overnight failed to improve its performance using a second treatment.

When different formulations of Prioderm, marketed before and after summer 1988 were compared, a marked difference was seen between them ($p<0.001$) at both time exposures (Table 4).

Discussion

Malathion has been regarded as having a strong ovicidal action since its introduction for treatment of head lice. At that time its performance, even in crude formulations, clearly outstripped all other treatments available.[2,7] However, the ovicidal activity of organophosphorus insecticides, such as malathion, is not confirmed in all insects. Some species' eggs seem to be less easily penetrated than others.[8,9]

Over the years, there have been a number of anecdotal reports of treatment failure with malathion lotions. Generally, these have been explained by inadequate application of lotion. However, some evidence that malathion is not necessarily effective at penetrating louse eggs has come from Holland where a product containing 0.5 per cent malathion in ethanol was available until recently. Following reports of suspected resistance, the susceptibility of head louse eggs was investigated by de Boer. Around half the eggs grown and tested in the laboratory survived the treatment, even with a 24 hour application time. De Boer found inconsistent activity and that mortality was not entirely dependent on exposure time.[10] It appeared that the deposition of a residue of malathion in the egg shell, sufficient to kill the emerging nymph, depended on the individual batch of eggs as much as the formulation.

The results of the current series of tests show wide variations of activity of some formulations when used on different occasions. In contrast, the same test method used for carbaryl formulations showed a high consistency even for the least successful formulations.[5] Consequently, it can be concluded that the variations are a characteristic of the malathion molecule rather than the test method. If this is so, it is clearly necessary to formulate malathion carefully in order to deliver it to the louse and its eggs. In the case of malathion this may be more critical since it is more readily degraded in the presence of oxygen. Samples of lotions exposed to air acquire a highly disagreeable odour in time. This characteristic of the apparently less well stabilised Dutch formulation may have been caused by its ethanol solvent. Such degradation greatly reduces the product's efficacy.

As with carbaryl formulations, much of the difference of activity of malathion lotions appears to be due to excipients. This is most clearly demonstrated by the change of efficacy of Prioderm which, from its introduction in 1970, was considered the industry "standard'. Comparison of the original formulation with the one currently available shows that difference.

The original formulation, which is still available in the United States under the name Ovide (Genderm Corp), contained approximately 21 per cent oily excipient material which included terpineol, limonene and pine needle oil.[11] These compounds gave the original its distinctive "disinfectant" smell and were supposedly incorporated as perfumes, although the concentrations used were probably higher than would be necessary just to impart an odour. A similar formulation is still used for Suleo lotions.

The formulation of Prioderm introduced from the summer of 1988 appears to contain none of the terpene compounds of its predecessor and has a much more pleasant smell. Unfortunately, as can be seen from Table 4, the terpene "excipients" appear to make a considerable difference to the ovicidal efficacy of the lotion. In preliminary experiments I have found that terpenes alone can be just as insecticidal and often more ovicidal than conventionally accepted insecticides when used against human lice (unpublished data). However, this does not mean that the presence of terpenes in a formulation ensures a successful treatment, although returning to the pre-1988 formulations of Prioderm and Carylderm would help. Properly controlled field studies are now required to confirm the results of this trial *in vivo*.

Even if lotions are effective they may fail if not used correctly. During 1990, I received at least one report of product failure for each formulation currently marketed.

In many reported failures consumers have used far too little lotion to give adequate coverage or to deliver an effective dose of active components to eggs.

The principal difficulty encountered in applying alcoholic formulations is that they spread freely on the scalp and along hair shafts with the result that the hair and scalp may appear to be wetted after the application of very little lotion. This no doubt gave rise to the World Health Organisation

Table 3: Efficacy of malathion-based lotions against louse eggs *in vitro* using either a single application or two treatments one week apart†

Formulation	Treatment time: Two hours — Percentage mortality of eggs* (± SD)		"Overnight" (10 hours) — Percentage mortality of eggs* (± SD)	
	Single treatment	Two treatments	Single treatment	Two treatments
Malathion 0.5 per cent	74.7 (13.9)	96.0 (1.4)	97.4 (3.1)	100
Derbac-M	64.2 (5.8)	79.7 (6.4)	100	100
Prioderm	75.2 (11.6)	89.0 (10.7)	66.0 (30.0)	67.9 (24.0)
Suleo-M	100	100	100	100

* Percentage mortality using "Abbott's correction" for control mortality[6]

† This test series was performed concurrently with the tests shown in Table 2. Three of the test batches used to construct Table 2 also constituted the single application batches in this Table. The corresponding double application groups were treated concurrently using eggs laid at the same time. This series consisted of eight replicate tests performed in three batches over a period of seven months

Table 4: Comparison of efficacy of the old and new formulations of Prioderm lotion against louse eggs

Formulation	Two hours: Total	Hatched	Half-hatched	Mortality per cent* ±SD	Overnight (10 hours): Total	Hatched	Half-hatched	Mortality per cent* ±SD
Old Prioderm (pre-summer 1988)	379	5	7	98.4 (1.5)	373	4	3	98.7 (0.7)
New Prioderm (since 1988)	226	127	34	33.3 (15.9)	315	154	57	42.0 (4.6)

* Percentage mortality adjusted using "Abbott's correction" for control mortality[6]

This test series consisted of three replicate tests from a single batch of eggs

recommended application of just 5 to 10ml per treatment.[12] This is sufficient to give the appearance of wetting the hair but is unable to wet all the eggs.

In practice, it is necessary to apply approximately one small bottle (55ml) to most adult patients and proportionately less to smaller heads or less thick hair. For example, three-year-olds need 20-30ml per application for fine hair and 30-40ml for thick hair. The lotion should be applied in small quantities to a small area of scalp working systematically over the whole head. The procedure should be repeated after allowing a short period for the solvent to evaporate. A thorough treatment may thus be achieved without the liquid running into the eyes, ears or down the patient's neck. This, coupled with the previous recommendations for two overnight treatments one week apart,[5] should help restore confidence in the efficacy of our most widely used head louse treatments and preserve them from the risk of resistance that could develop as a result of louse eggs surviving a low dose of insecticide.

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REFERENCES

1. Maunder JW. Resistance to organochlorine insecticides in head lice, and trials using alternative compounds. *Med Offr* 1971; **125**: 27-9.
2. Maunder JW. Use of malathion in the treatment of lousy children. *Community Med* 1971; **126**: 145-7.
3. Anon. NPA survey reveals treatment bias in district head lice policies. *Pharm J* 1989; **242**: 311.
4. Anon. The treatment of head lice in 1990. Isleworth: Community Hygiene Concern, 1990.
5. Burgess I. Carbaryl lotions for head lice — new laboratory tests show variations in efficacy. *Pharm J* 1990; **245**: 159-61.
6. Abbott WS. A method of computing the effectiveness of an insecticide. *J Econ Entomol* 1925; **18**: 265-7.
7. Coates KG. Control of head infestation in schoolchildren. *Community Med* 1971; **126**: 148-9.
8. Smith EH, Salkeld EH. The use and action of ovicides. *Annu Rev Entomol* 1966; **11**: 331-68.
9. Zschintzsch J, O'Brien RD, Smith EH. The relation between uptake and toxicity of organophosphates for eggs of the large milkweed bug. *J Econ Entomol* 1965; **58**: 614-21.
10. De Boer R. Efficacy of malathion and synergised bioallethrine in the treatment of head louse, *Pediculus humanus* spp *capitis* infestations. *Acta Leidensia* 1984; **52**: 53-9.
11. Physician's desk reference. 44th ed. Oradell: Medical Economics Co, 1990: 999.
12. Smith A (ed). Chemical methods for the control of arthropod vectors and pests of public health. Geneva: World Health Organization, 1984: 60.

FUTURE EVENTS

Dermatological drugs A one day meeting on "The clinical development of dermatological agents", London, November 14. The meeting is aimed at those involved in clinical programme implementation, protocol design, and trial monitoring. Details from Ms S. McCarron, Sussex Clinical Research Consultants, Sussex House, Grange Road, Uckfield, East Sussex TN22 1QU (telephone: 0825 765025).

Respiratory drug delivery A symposium devoted to current biological and pharmaceutical issues related to optimising drug delivery by aerosols for systemic and local therapeutic purposes. The symposium, Respiratory Drug Delivery III, will be held on May 17-22, 1992 and is organised by the College of Pharmcy, Virginia Commonwealth University, Richmond, Virginia 23298, USA.

Patient information leaflets A two day conference on "Patient information and package inserts in Europe", London, November 28-29. Details from the Management Forum, 48 Woodbridge Road, Guildford, Surrey GU1 4RL (telephone: 0483 570099).

Marketing A Pharmaceutical Marketing Society meeting on "Quality in marketing", Royal Pharmaceutical Society headquarters, London, November 27. Details from Mrs V. Bennett, Pharmaceutical Marketing Society, PO Box 200, Horsham, West Sussex RH12 3FA (telephone: 0403 64898).

Demography and health care A one day symposium on "Demographic changes, health care and the NHS: Is time running out?", organised by the MSD Foundation in London, November 13. Details from the Symposium Office, MSD Foundation, 11 Carteret Street, London SW1H 9DL.

Water A one day meeting on "Water for the pharmaceutical industries", organised by the Institution of Chemical Engineers, at Cranfield Institute of Technology, Bedford, November 13. Details from Mr G. Cole, 29 Vernons Close, Henham, Bishops Stortford, Hertfordshire CM22 6AE.

Impurities A one day conference on "Impurities in pharmaceutical products", Royal Pharmaceutical Society headquarters, London, December 12. Details from Mr J. Clements, Royal Pharmaceutical Society, 1 Lambeth High Street, London SE1 7JN (telephone: 071-735 9141).

New Zealand conference The 1992 New Zealand pharmacy conference will be held in Dunedin from April 24-27, 1992. This will be the first ever combined conference of the Pharmaceutical Society of New Zealand, the Pharmacy Guild of New Zealand and the New Zealand Hospital Pharmacists Association. The theme of the conference is "Pharmacy — The contemporaneous mixture that works". Details from Conference Secretary, c/o the School of Pharmacy, PO Box 913, Dunedin, New Zealand.

Cardiac rehabilitation A one day meeting on "Cardiac rehabilitation: a multidisciplinary approach", London, November 21. Details from Mrs A. McPherson-Davis, Department of Education, Royal Brompton National Heart and Lung Hospital, Sydney Street, London SW3 6NP (telephone: 071-351 8059).

Online searching A one day seminar introducing online science and technology search techniques, equipment and databases, London, November 28, 1991. Details from The British Library, Science Reference and Information Service, Marketing and Public Relations, 25 Southampton Buildings, London WC2A 1AW (telephone: 071-323 7473).

Clinical pharmacy A meeting for hospital pharmacists within the South West Thames region with an interest in clinical pharmacy has been arranged for November 20 at the Lavis Room, Level A, West Wing, Royal Surrey County Hospital, Guildford. Details from Ms H. Tomlinson (telephone: 0293 527866).

Pharmaceutical officers The annual general meeting of the National Association of Pharmaceutical Officers will be held at the Royal Pharmaceutical Society headquarters, London, on November 11. Details from Mr R. Higson (telephone: 0753 34567).

ABOUT PEOPLE

Mr David Haythornthwaite, MRPharmS, a former principal medicines inspector, and a head of quality assurance in industry, has set up his own pharmaceutical and quality consultancy as well as a clinical trial packaging partnership. He may be contacted at 12 Lower Park Road, Queen's Park, Chester CH4 7BB (telephone: 0244 675407).

Miss Elizabeth Sutton, MRPharmS, has been appointed principal pharmacist, clinical support services, for Aylesbury Vale health authority.

Dr M. Davies, MRPharmS, a lecturer in pharmaceutics at the department of pharmaceutical sciences, University of Nottingham, has received an award from Pfizer. Six awards are made annually to support scientists in academia. Dr Davies's award was for his "surface analysis studies (including scanning tunnelling microscopy) which have contributed to the structural characterisation of pharmaceuticals and biomaterials to optimise the rational design of drug delivery systems."

Professor J. W. Gorrod, research professor in biopharmacy, King's College London, has been awarded the gold medal of Comenius university "for his research, co-operation and publications in the field of metabolism of drugs." He was also elected honorary fellow of the Bohemslovakia Pharmaceutical Society and had the title visiting professor conferred upon him by the Chinese Academy of Preventative Medicine.