

ORIGINAL ARTICLE

High *in vitro* efficacy of Nyda® L, a pediculicide containing dimeticone

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Abstract

Background The therapy of pediculosis remains a common problem in clinical practice. As resistance to commonly used chemical pediculicides is constantly increasing, there is a need for new effective compounds.

Study design The efficacy of Nyda® L, a new pediculicide containing a high concentration of dimeticone, was assessed in an *in vitro* trial and compared with three reference products (Hedrin® containing 4% dimeticone, Lyclear® containing 1% permethrin, and Prioderm® containing 1% malathion) and a negative control group. Head lice were collected from heavily infested patients in a resource-poor community in Northeast Brazil, where no resistance against pediculicides has been reported thus far. In each of the five groups, 50 adult fully vital lice were tested. We used a dip test (immersing head lice in the undiluted products for 3 min, washing off products after 20 min). Using predefined criteria for mortality, the lice were monitored at different points in time, for a period of 24 h.

Results Nyda® L and Prioderm® killed all head lice already after 5 min. The efficacy of Nyda® L was better than of Lyclear®. Lice treated with Hedrin® resurrected after several hours and did not show a significantly higher mortality compared with the control group after 24 h.

Conclusion Nyda® L can be regarded as a very efficacious pediculicidal compound, killing all lice *in vitro* within 5 min.

Introduction

Head lice (*Pediculus humanus* var. *capitis*) are insects that have parasitized human beings for many thousands of years.¹ In spite of therapeutic advances, pediculosis remains a problem throughout the world, particularly in developed countries. Although the clinical effects of head lice seem to be minor,²⁻⁴ pediculosis has been considered an important cause of impetigo in developing countries and may result in stigmatization.^{3,5} Possibly, head lice play a role in the transmission of vector-borne diseases, such as bartonellosis and typhus.^{6,7}

Chemical pediculicides have been used extensively for the treatment of infestations since the early 20th century. Today, topical chemical insecticides still remain the mainstay of head lice treatment, such as pyrethrins and synthetic pyrethroids (permethrin and allethrin), organochlorines

(lindane), organophosphates (malathion), carbamates (carbaryl), and benzyl benzoate, as well as formulations based on natural products.⁸⁻¹⁰

In the last decades, as a result of extensive use, resistance to pediculicides with a neurotoxic mode of action has increased, particularly to permethrin.^{8,10-13} Permethrin is used in many countries as first-line therapy, and resistance is frequent. This pertains not only to industrialised countries, such as the USA, UK, France, Denmark, Israel, and Australia, but also to less developed countries, such as Argentina. Where resistance will develop in the future cannot be predicted.⁸

Additional reasons to investigate alternative products are failure of current chemical treatments to kill embryos in eggs, environmental and food safety, and potential toxicity of the chemical pediculicides, particularly organophosphates and organochlorines. Thus, there is a clear

need for compounds effectively killing adult lice and eggs by new modes of action.

Recently, Burgess *et al.*¹⁴ published a clinical trial comparing Hedrin®, a 4% dimeticone lotion, with Full Marks Liquid® (0.5% phenothrin). The cure rate was similar in both groups (70% and 75%, respectively).

Here, we show in an *in vitro* study that the product Nyda® L (G. Pohl-Boskamp GmbH & Co. KG, Hohenlockstedt, Germany), which has a high concentration of dimeticone, is highly effective in killing head lice.

Methods

Head lice

Adult head lice were obtained by dry combing from individuals living in the township Vicente Pinzón in the outskirts of Fortaleza, the capital city of Ceará State in Northeast Brazil. Resistance to commonly used pediculicidal agents has never been reported in the area, but formal susceptibility testing has not been done.

The individuals participated in a head lice control campaign based on combing, and we used the lice that were obtained during this campaign. Only lice were used from individuals who had not applied chemical pediculicides nor received ivermectin during the previous 4 weeks. All lice were examined for activity and morphological integrity under a dissecting microscope, and only fully active lice were tested within 60 min after collection. We used female and male adult lice and did not blood-feed the insects before or during testing.

Products

The following products were tested: Nyda® L (G. Pohl-Boskamp GmbH & Co. KG, containing a high concentration of dimeticone, as well as medium-chained triglycerides, jojoba oil, and fragrances); Hedrin® lotion (Thornton & Ross Ltd, UK, containing dimeticone 4%); Lyclair® Creme Rinse (Chefaro Ltd, UK, containing permethrin 1%); and Prioderm® Shampoo (Norpharma A/S, Denmark, containing malathion 1%).

In vitro testing

To allow a direct comparison, all products were tested according to a standard procedure. We used a dip technique in which lice attached to strands of human hair were immersed completely in the undiluted products for 3 min. The hair strands with lice were held with a forceps under the solution. We checked for the presence of air bubbles. Then, the lice were placed with hairs on Whatman filter paper in 5-cm Petri dishes. To prevent lice desiccating, the

filter paper was moistened by 200 µL tap water. Control lice were placed directly on moistened filter paper without any treatment. After lice were placed on the filter paper; obvious pools of the product were wiped from the lice with a jeweller's forceps directed under a dissecting microscope. Head lice were washed after 20 min by immersing the hair strands in tap water for 1 min and then placing them on unused filter paper in unused Petri dishes.

We tested lice in batches of 10 for each treatment and control group, repeating the tests five times to give a total of 50 lice in each group. The relative frequencies of mortality were compared using the chi-squared test.

The lice were examined after 5, 10, 20, 30, 60, 120, and 180 min as well as after 6 and 24 h. Pre-defined criteria for evaluation of the survival of lice were used, based on activity, ataxic signs, ability to stay on hair, as well as gut and leg movements.¹⁵ The vital state of each louse was classified according to the following categories: vital lice, fully active lice with normal movements; lice with major vital signs, walking, but unable to walk in a progressive fashion or no righting reflex when rolled onto the back; lice with minor vital signs, not walking, but presence of internal (gut) movements, movements of antennae, or leg movements (with or without stimulation by a forceps); lice with no vital signs at all, even after stimulation by a forceps.

For the calculation of mortality, highly stringent criteria were used: head lice were only judged as 'dead' if they were in categories 3 or 4 (i.e. no or minor vital signs observable).¹⁵

All lice were examined under a dissecting microscope by the same observer to prevent interobserver variation. Lice were maintained at 27 °C to 29 °C during the tests.

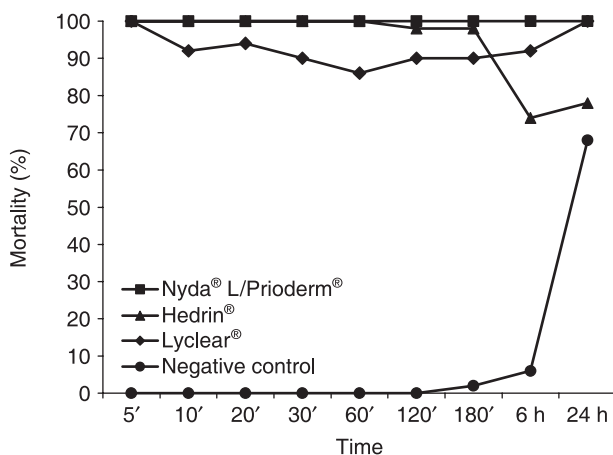
Results

All four commercial products killed lice, but efficacy differed, with Nyda® L and Prioderm® having 100% mortality at all test times (fig. 1). After 5 min, 100% of test lice had no or minor vital signs, irrespective of the product applied, compared with 0% in the negative control group. However, recovery of lice occurred over time in the Lyclair® and Hedrin® groups. The detailed vital states of the tested head lice in the five groups over time are depicted in Table 1.

Despite showing no major vital signs during the first hour, lice treated with Hedrin® recovered after several hours, with a mortality of only 74% (95% confidence interval, 59.7–85.4) after 6 h, which is significantly lower than the mortality for lice treated with Nyda® L ($P < 0.001$). After 24 h, the mortality of Hedrin®-treated lice (78%; 95% confidence interval, 64.0–88.5) was not statistically different from the control lice (68%; 95% confidence interval, 53.3–80.5; $P = 0.3$).

Table 1 Vital state of head lice in four test groups and a negative control group over time (n = 50 in each group)

	Time								
	5 min	10 min	20 min	30 min	60 min	120 min	180 min	6 h	24 h
Nyda® L									
Fully active	0	0	0	0	0	0	0	0	0
Major vital signs	0	0	0	0	0	0	0	0	0
Minor vital signs	19	15	16	7	6	5	1	2	1
No vital signs	31	35	34	43	44	45	49	48	49
Prioderm®									
Fully active	0	0	0	0	0	0	0	0	0
Major vital signs	0	0	0	0	0	0	0	0	0
Minor vital signs	1	2	5	29	35	38	40	41	0
No vital signs	49	48	45	21	15	12	10	9	50
Hedrin®									
Fully active	0	0	0	0	0	0	0	1	8
Major vital signs	0	0	0	0	0	1	1	12	3
Minor vital signs	8	2	7	3	5	11	18	18	4
No vital signs	42	48	43	47	45	38	31	19	35
Lyclear®									
Fully active	0	0	0	0	0	0	0	0	0
Major vital signs	0	4	3	5	7	5	5	4	0
Minor vital signs	12	15	20	37	33	38	32	20	0
No vital signs	38	31	27	8	10	7	13	26	50
Negative control									
Fully active	50	50	50	50	50	50	48	44	8
Major vital signs	0	0	0	0	0	0	1	3	8
Minor vital signs	0	0	0	0	0	0	1	2	11
No vital signs	0	0	0	0	0	0	0	1	23

**fig. 1** Mortality of head lice in four test groups and a negative control group over time. Results of Nyda® L and Prioderm® are identical at all times of observation.

Nyda® L performed slightly better than Lyclear®. This difference was statistically significant after 10 min ($P = 0.04$), 30 min ($P = 0.02$), 60 min ($P = 0.006$), 120 min ($P = 0.02$), 180 min ($P = 0.02$), and 6 h ($P = 0.04$).

At all points in time, Nyda® L, Lyclear®, and Prioderm® showed significantly higher mortality than the negative control lice receiving no treatment ($P < 0.001$ in all cases).

In the control group, mortality due to desiccation started after 6 h and was high after 24 h.

Discussion

Our data show that Nyda® L, based on a high concentration of dimeticone, is highly effective *in vitro* against head lice. Other components of the product are medium-chained triglycerides and jojoba oil. However, the exact concentration of dimeticone and the other ingredients is not publicly available, as the composition of Nyda® L, a medical device in the European Union, is a corporate secret of the manufacturer G. Pohl-Boskamp GmbH & Co KG.

The mortality of lice treated with this product was similar to Prioderm® (1% malathion) and higher than Lyclear® (1% permethrin). In the first hour, mortality was similar to Hedrin® (4% dimeticone). However, lice resurged after several hours in the Hedrin® group and did not show a significantly higher mortality compared with

the negative control after 24 h, although mortality in control lice was high due to desiccation.

Burgess *et al.*¹⁴ reported a cure rate of about 70% after treating head lice infestation with Hedrin®, a 4% dimeticone lotion. The lotion was left to dry naturally and not washed out; thus, the contact time was prolonged. We immersed the lice only for 3 min in the respective solutions and washed the substances away after 20 min, simulating a standard treatment with an insecticide-based pediculicide. The differences in contact time could be the reason why Hedrin® lotion was effective in a clinical trial but did not perform well after several hours *in vitro*.

As the instructions of the producers for the *in vivo* use of pediculicides vary considerably, our approach allowed the comparison of different products in a standardized manner. In addition, we could detect the products with the highest efficacy (i.e. killing most lice after a short period of contact time).

An approach of killing head lice by suffocation has been described recently by Pearlman.¹⁶ He reported excellent clinical results with a so-called 'dry-on suffocation-based pediculicide' (DSP). The DSP lotion seems to coat the lice with a film layer after drying, consequently blocking the insect's spiracles and suffocating the lice.

Pearlman's clinical study has been criticized due to the uncontrolled and open design, the outcome measures used, and a putative conflict of interest of the author.^{17,18} In addition, there are no *in vitro* data available to corroborate the clinical findings. However, the strategy to kill head lice by physical measures is a promising approach because the compounds used for this purpose are considered non-toxic if applied topically, and resistance probably cannot develop.

A possible mode of action of lowly viscous dimeticones is the penetration into the spiracles of the lice, causing asphyxia and death. The substance group of dimeticones (polydimethylsiloxane) are silicon oils also used in cosmetic products (e.g. to facilitate the use of a comb and to make the hair silky and soft).¹⁹ In addition, oral dimeticone is used as an anti-flatulent to alleviate gastrointestinal discomfort. Dimeticone is physiologically inert and non-toxic, and after oral ingestion, the oil is not absorbed but eliminated unaltered in the faeces. Topical use in humans is considered safe. In the animal model, no adverse events were observed after topical use of concentrations between 6% and 79%.²⁰

Head lice may 'resurrect' after a period without any vital signs, and pediculicidal testing has been recommended to be monitored for 24 h.^{12,21} Therefore, we obtained mortality data over 24 h. However, many lice in the control group died due to desiccation, negating the value of 24-h testing without feeding.

Commonly, less stringent criteria are used for the definition of 'mortality' of head lice: a state of reduced activity judged by the inability of the insect to walk in a progressive fashion or to show a righting reflex when rolled onto its back.^{22,23} Such outcome measures are prone to overestimate mortality. Therefore, Burkhart and Burkhart¹⁸ suggested to apply indicators of irreversible morbidity for the assessment of efficacy. In this study, we defined death as the absence of any vital signs or merely the presence of minor vital signs.

It has been suggested that *in vitro* testing done in a manner resembling the clinical application of a pediculicide may be a proxy for the results of clinical trials.²⁴ In this case, Nyda® L should be highly effective *in vivo* particularly because the usual contact time will be considerably longer than in our *in vitro* study. Albeit, clinical trials are warranted to corroborate our findings, and future studies will also have to test the efficacy of the product on head lice eggs.

In conclusion, our data show that Nyda® L is highly effective in killing head lice *in vitro*. Such products that probably kill head lice by physical means may prevent the development of resistance.

Acknowledgments

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Conflicts of interest

J. Heukelbach has been a scientific consultant to G. Pohl-Boskamp GmbH & Co KG. The company had no role in the design, execution, or interpretation of the study. R. Speare has been a consultant to an Australian producer of pediculicides in the past, but currently has no links to the pharmaceutical industry.

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