

New shampoo additive to eliminate head lice from scalp hair

A novel use of the cooling agent, menthol propyleneglycol carbonate

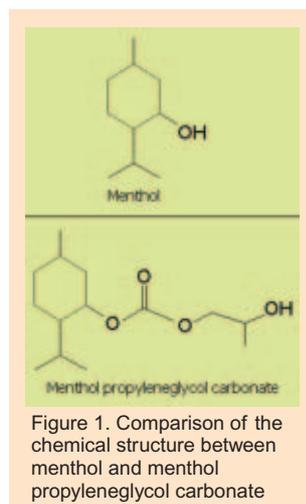
ABSTRACT

The head louse, *Pediculus capitis*, is an ectoparasite in man since pre-historic times. Although head lice cause no serious medical problems, head lice infestation in modern times, particularly in children, remains a public health issue because of the itching and social stigma attached to their presence in the scalp. Resistance to the pesticides normally used to kill head lice is prevalent. While repellents, such as DEET, and other natural products are of little efficacy, recent work on menthol propyleneglycol carbonate (MR-08), a menthol derivative on the FDA GRAS list, demonstrated efficacy against head lice. MR-08 was added to a conventional shampoo and applied to hair of children. After washing and towel drying of the scalp, a normal comb was used to remove lice. The MR-08 shampoo treatment reduced the head lice population by as much as 90 percent and daily treatment regimen resulted in complete elimination of the lice from the scalp. The lice collected from MR-08 treated group were alive demonstrating no toxicity associated with the treatment. Laboratory analysis showed that lice were rendered unable to hold on to the hair shaft and preferentially avoid hair treated with MR-08. The volunteers did not report any discomfort with the MR-08 shampoo and experienced relief of the itch caused by previous head lice infestation. This anti-itch effect is likely due to the known anti-inflammatory action of MR-08. The results demonstrated the potential use of MR-08 in shampoos as a possible method of hair management against insecticide-resistant head lice in children and as a pro-active means of preventing infestation during daily grooming.

INTRODUCTION

The head louse (*Pediculus capitis*) has been part of the human experience for at least 1.2 million years and had evolved efficient means of hanging on to human hair (1). This dependence on human hair for the louse is so extreme that, once detached from the hair, the head louse survives only for a few hours unless it finds a new host. The louse clings to the hair near the scalp and survives by sucking blood multiple times each day. Despite this parasitic relationship, humans and the louse have coexisted well until modern times when pyrethrins and pyrethroids changed this balance towards man's favour. However, the last decade saw a major change, with the head louse taking the upper hand yet once again. Resistance to the pesticides normally used to kill head lice are increasing so that management problems now exist, particularly in school children. An alarming trend of chemical resistance has been documented in various parts of the world, ranging from 50 percent to as high as 98 percent. Some lice

populations, called super-lice, even showed resistance to as many as five different chemicals (2). As last resort, even more toxic pesticides such as lindane and malathion, have been included in the armamentarium to treat resistant head lice infestations. However, levels of resistance were reported to reach as high as 87 percent for permethrin and 64 percent for malathion (3). It is just a matter of time when the louse develops resistance to these chemicals as well and the human-lice ecologic relationship returns to its pre-historic balance.



THE MARKET

Head lice treatment products had been on the fringe of the personal care industry market until more recent times when the magnitude of the problem began to get more attention. In the United States alone, head lice infests up to 12 million people each year. Although accurate estimates are difficult to make especially in developing countries, this problem may likely affect as much as 500 million people on a global scale, particularly since head lice affects both children and adults alike in tropical countries. From the hair care perspective, this is an emerging market opportunity that has not been adequately addressed with the portfolio of products that can be brought to bear against the problem. This is primarily because the current 'official' treatment methods invariably include highly regulated pesticidal products. However, with emerging chemical resistance also came the proliferation of alternative, non-pesticidal approaches, many of which rely on anecdotal evidence rather than being based on sound science. This market is wide open for novel products that are safe, convenient and effective.

A PUBLIC HEALTH ISSUE

Head lice infestation is a public health issue because of the itching and social stigma attached to their presence in the scalp. The frequent blood meal eventually causes pruritus reaction on the scalp skin from the lice saliva. In Western countries, pyoderma of the scalp has been



suggested as a direct result of lice infestation (4). The continued use of increasingly toxic pesticides to treat pyrethroid-resistant lice also poses serious medical risks especially when the end users are primarily children. In a study of 280 children, scientists at INSERM in France concluded that insecticidal shampoos doubled the risk of developing leukemia (5). The medical issues are far from clear at this time. While lice had been known to transmit trench fever and typhus in World War I, there has been no active research on possibilities of disease transmission from head lice.

NATURAL PRODUCTS AND REPELLENTS

Except for a few exceptions, most herbal over-the-counter remedies are of limited value in head lice management. Many of these products include extracts of citronella, peppermint, eucalyptus and many others. Even the commonly used repellent, DEET (*N, N-diethyl-m-toluamide*) as a method of deterrence was ineffective. For these reasons, the concept of using repellents as part of the management of head lice infestation had not been considered a viable one in the past. However, recent studies on new analogues of menthol, the cooling agent extracted from peppermint, provided new insights in resurrecting the repellent/deterrent approach to hair lice management.

MENTHOL PROPYLENEGLYCOL CARBONATE IN HAIR LICE MANAGEMENT

Menthol is used for over 100 years as a treatment for a wide variety of medical ailments, including as repellent against various insects. But, it has gained a much wider use in the last decades as a cooling agent for food and cosmetics. As the industry develops even better cooling agents, new synthetic molecules have been synthesized that increased the cooling effect while reducing the associated heavy menthol smell. Although menthol has weak insect control properties, it became apparent that the new synthetic molecules that possess higher cooling efficiency also have higher efficiency as a repellent than the parent compound. As the recent research on menthol derivatives shows, these compounds also have heightened efficacy not only as an insect repellent (6), but also as anti-inflammatory agents as well (7). However, not all synthetic cooling agents show efficacy in other applications outside of the cooling effect. Structure activity studies indicate that only certain conformations of menthol derivatives are suitable for non-cooling applications. A novel compound derived from menthol has now been identified to have superior repellent action against a wide range of insect pests. This compound, menthol propylene glycol carbonate, is referred to as MR-08 in Poseidon's inventory of menthol analogues. A comparison of the chemical structure of menthol and MR-08 is shown in Figure 1. While the repellent activity may likely be insufficient as a stand technology, the combination of cooling, analgesia, anti-inflammatory and repellency may provide a multi-target approach within a single molecule that can act in concert to address the problem of head lice management. For the industry to begin looking at possibilities in a more aggressive manner, it is important to discover new ways to find solutions using materials already available in the cosmetic and

food industries to avoid the necessity of using more toxic chemicals. The concept of using MR-08 as a possible new approach for personal care was explored in this study.

LABORATORY STUDIES

Menthol propylene glycol carbonate (MR-08) was added directly to Johnson's Baby Shampoo (Johnson & Johnson) that was purchased over the counter. MR-08 mixed very well with this hair shampoo and no further processing was necessary. The MR-08 shampoo solution was prepared each day prior to use. The control test groups comprised those treated with Johnson's Baby Shampoo alone. Black human hair in a bundle (10 cm in length) was treated by dipping half of the hair in the test shampoo for five seconds. This was immediately followed by removal of excess liquid by wiping with paper towel and air drying for 1 hour at room temperature prior to use. The hair was held stationary on a plastic petri dish by taping both ends on the surface. After collection from human volunteers, 10 lice were immediately placed in between the MR-08 treated and control hairs in a two-choice test. The number of lice that migrated to each hair group was counted. All the studies were repeated five times for each group with a total of 50 lice per test in the dark at ambient room temperature. The results in Table 1 show that lice preferentially avoided attaching to hair previously exposed to MR-08. In a second study, the lice were not provided

any choices and immediately placed on the surface of the 10 percent MR-08 treated and control hair. After 30 minutes, the hair was lifted off the surface of the dish and the total numbers of lice that had fallen off the hair was counted. The data in Table 2 showed that lice were unable to cling on to MR-08 treated hair and found to fall off the hair with minor hair movement. More lice actively came off in MR-08 treated hair than in control hair.

Treatment	Number of attached lice Mean ± SEM	P*
MR-08	1.0 ± 0.6	P < 0.006
Control	6.7 ± 0.9	

* Student's t-test

Table 1. The preference of head lice in MR-08 treated and control hair

Treatment	Number of detached lice Mean ± SEM	P*
MR-08	13.6 ± 1.4	P < 0.008
Control	2.6 ± 1.1	

* Student's t-test

Table 2. The efficiency of attachment of head lice when placed directly on hair treated with or without MR.08. Each test is comprised of five repeat tests

CLINICAL STUDY

Twenty-five female children (ages 4 to 12) with confirmed head lice infestation were recruited as volunteers from July to September 2006. Randomly assigned groups of five children each were placed in both the control group that received only the shampoo and the test groups that received MR-08 shampoo at various concentrations. The scalp of each child was shampooed for a total of 3 minutes, rinsed with tap water for 2 minutes and towel dried. Immediately after towel drying, the hair is combed with a regular comb. Fine-toothed combs were specifically not used for this study. The number of head lice that falls out of the hair

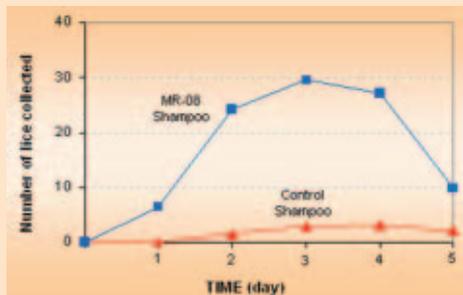


Figure 2. The number of head lice collected each day from normal shampooing with and without 3 percent MR-08 in children with confirmed head lice infestation. Mean of five volunteers per data point

after normal combing were counted for each child. The head lice were collected, examined visually and also under a dissecting microscope.

The treatments were continued daily in the morning, once each day, for a period of five days. All studies were conducted in the presence of an attending paediatrician and under informed consent from the parents. Each child was interviewed for any comments associated with the treatment process and special attention was placed on any side effects. The data in figure 2 show the number of lice collected each day from normal combing while figure 3 shows the total number of lice collected over the 5-day treatment regimen. The results indicated that shampooing with MR-08 optimized the collection of lice from the hair with the use of a common hair comb. There was no incidence of irritation associated with the shampoo treatment in either control or experimental groups. When examined under the microscope immediately after collection, the lice appeared normal and no unusual behaviour was observed. Survival of the lice was the same in both groups suggesting that toxic effects were not associated with the treatment regimen. More important, the children experienced relief from the itching of the scalp after the MR-08 shampoo and this relief persisted throughout the night.

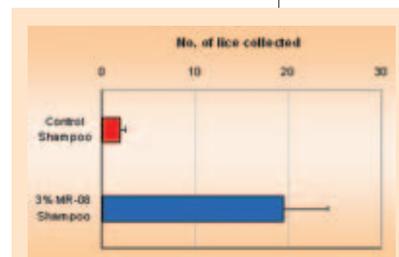
DISCUSSION

The increasing risks to human health, heightened public awareness on the toxicity of pesticides, pest resurgence and resistance to insecticides have prompted us to search for environmentally-friendly, safe and non-toxic alternatives. Natural compounds and analogues that showed promising results were evaluated for improved efficacy under laboratory and field conditions. The selection of these compounds took into account their potential for further development, their impact on the environment and their safety for human use. As a "generally recognized as safe" (GRAS) compound, menthol would have been an ideal eco-friendly material for a repellent. However, its use for this purpose is impractical because of its marginal repellent potency. The synthesis of the menthol analogue, menthol propyleneglycol carbonate, opened new opportunities for menthol-like compounds. MR-08 received GRAS status as a food ingredient and is referenced as number 3806 in the U.S. FEMA GRAS list and as number 444 on the JECFA (Joint FAO/WHO Expert Committee on Food Additives) list. New applications were discovered soon after. MR-08 showed practical applications in preventing attachment of fouling organisms (barnacles and oysters) in marine coatings (8), as an anti-inflammatory agent (9), as an anti-angiogenic chemical (7) and as an insect repellent (6). The prospect of employing this molecule for hair care is a new opportunity presented by this multifunctional compound. The concept of combining cooling, analgesia, anti-inflammatory and repellency as a multi-target approach within a single molecule

showed good promise. The studies described in this report demonstrated that MR-08 can be incorporated into a hair shampoo to provide a more efficient removal of lice from the hair. The scalp irritation due to pruritus is reduced and the worrisome use of pesticidal treatment can be completely avoided. The presence of MR-08 does not kill the lice, but renders them unable to cling to human hair through a mechanism yet to be identified. Once removed from the host, head lice die in a matter of hours so that daily use will produce an effective non-toxic approach to lice removal from the hair. Equally important is the fact that this removal can be accomplished with the use of a common comb rather than the typical fine-toothed comb normally employed. The use of a fine-toothed comb is cumbersome and creates discomfort and scalp irritation in children. In summary, MR-08 containing shampoo presents a simple, effective, non-toxic alternative to the use of pesticidal compounds in the removal of head lice from human hair. This finding opens new market opportunities in preventing lice infestations and by making MR-08 shampoo as an integral part of the daily grooming activity.

REFERENCES

1. Reed, D.L., Smith, V.S., Hammond, S.L., Rogers, A.R., Clayton, D.H. (2004) Genetic analysis of lice supports direct contact between modern and archaic humans. *PLoS Biol.*, 2(11):2340.
2. Nowak, R. (2004). Hair wars. *New Scientist*, 25 Dec 2004/ 1 Jan 2005, p 64-67.
3. Downs, A.M.R., Stafford, K.A., Coles, H.I. (1999). Evidence for double resistance to permethrin and malathion in head lice. *Br. J. Dermatol.*, 141:508-511.
4. Burgess, I.E. (1995). Human lice and their management. *Adv. Parasitol.*, 36:271-342.
5. Menegaux, F., Baruchel, A., Bertrand, Y., Lescoeur, B., Leverger, G., Nelken, B., Sommelet, D., Hémon, D., Clavel, J. (2006) Household exposure to pesticides and risk of childhood acute leukaemia. *Occupational and Environ. Med.*, 63:131-134.
6. Matias JR (2005). Menthol propyleneglycol carbonate and analogs thereof as insect pest repellents. World Intellectual Property Organization. PCT Intl. Publication No. WO 2005/025313 A1. 24 March 2005.
7. Matias (2006). Methods of using menthol propyleneglycol carbonate and analogs thereof for producing anti-inflammatory and anti-angiogenic effects. World Intellectual Property Organization. PCT Intl Publication No. WO 2006/034495 A2. 30 March 2006.
8. Matias JR, Mary A (2002). On the antifouling properties of menthol and related compounds. Results from Poseidon's Natural Products Screening Program. 11th International Congress on Marine Corrosion and Fouling. University of San Diego, July 21-25.
9. Matias JR (2005). Anti-angiogenic and anti-inflammatory action of menthol propyleneglycol carbonate in experimental models. Proceedings: Soc. Cosmetic Chem. Annual. Scientific Meeting, June 2-3, 2005. pp 80-81.



collected by normal combing after the 5-day treatment regimen with and without 3percent MR-08 shampoo. Mean ± SEM of five volunteers per test. (P<0.01)

JONATHAN R. MATIAS*,
ARACELI A. LORELLA,
COLEEN P. SUCGANG,
LOURDES Q. ADRIAS

*Corresponding author
Poseidon Sciences Group
122 East 42nd Street, Suite 1700
New York, NY 10168 USA