ELSEVIER

Decreasing malathion application time for lice treatment reduces transdermal absorption

Rhonda M. Brand *, Anna R. Charron, Randall E. Brand

Department of Internal Medicine, Evanston Northwestern Healthcare and Feinberg School of Medicine at Northwestern University, 1001 University Place, Evanston, IL 60201, USA

Abstract

Objective: Head lice are the most common parasitic infestation in the United States requiring topical treatment with pediculicides. Ovide®, the 0.5% malathion formulation used in treatment of head lice requires placement on dry hair for 8–12 h. Malathion, however, is effective at killing lice and nits in 10 min. Our concern of over exposing children to malathion has led us to examine whether significantly more malathion will penetrate transdermally when applied for the recommended 8 h than for a shorter but apparently equally effective period.

Methods: In vitro absorption studies were performed across haired rat skin and human abdominal skin to determine whether reducing malathion application time decreased skin absorption.

Results: A 0.5 h exposure caused $0.36 \pm 0.14\%$ of the donor malathion to penetrate through human skin after 24 h and $2.1 \pm 0.6\%$ remained in the skin after washing with shampoo. After 8 h of topical applications penetration was approximately three-fold greater (1.02 ± 0.41) and $3.4 \pm 0.5\%$ remained in the skin ($p < 0.05$ versus 0.5 h). The relationship between absorption and exposure time also occurred for haired rat skin ($p < 0.05$). This differential continued for 72 h even after removal of the source.

Conclusions: Significantly less malathion penetrated from Ovide® after 0.5 h versus the suggested 8 h application, without decreasing the product's efficacy. Further clinical studies in children are warranted to confirm the efficacy of this shortened application time.

© 2005 Elsevier B.V. All rights reserved.

Keywords: Head lice; Malathion; Transdermal

1. Introduction

Head lice (pediculosis capitas) is the most common parasitic infestation in the United States (Yoon et al., 2003). Topical lice treatments usually contain the pediculicides lindane, permethrin or malathion. Lindane

* Corresponding author. Tel.: +1 847 570 4074;
fax: +1 847 733 5451.
E-mail address: rhbrand@enh.org (R.M. Brand).

and permethrin resistance is increasing in the United States, encouraging malathion use in the form of a 0.5% solution (Ovide®, Medcis–Phoenix, AZ) (Burkhart, 2004). Malathion (MW = 330, log $K_{o/w}$ = 2.3) is a widely used organophosphate pesticide, which inhibits acetylcholinesterase and alters cholinergic synaptic transmission. It is readily absorbed transdermally, so skin contact can result in an acute exposure risk (Tos-Luty et al., 2003).

Children are commonly infected with head lice requiring topical treatment with pediculicides, as these agents are more effective at treating lice than wet combing with fine tooth combs (Roberts et al., 2000). Their surface area to weight ratio is larger than adults leading to greater toxicity risk due to transdermal absorption. Furthermore, their ability to metabolize toxicants changes with age, which can cause them to be more sensitive than adults to pesticide effects (Padilla et al., 2004). There are no studies that have directly examined malathion toxicity in children other than to note that the clinical symptoms of organophosphate or carbamate poisoning in children are different from those described in adults (Lifshitz et al., 1999). Animal studies, however, have shown that adverse effects of malathion decrease with increasing age (ATSDR, 2003).

The instructions for the Ovide® 0.5% malathion formulation include placing formulation on dry hair and leaving it on for 8–12 h. Ovide®, however, is effective at killing 100% of both lice and nits in 10 min (Meinking et al., 2001). Our concerns over limiting exposure in children led us to examine whether significantly more malathion will penetrate transdermally when applied for the recommended 8 h than for a shorter but apparently equally effective period. In vitro dermal absorption studies were therefore performed to determine malathion penetration from Ovide® across both rat and human abdominal skin.

2. Methods

2.1. Chemicals

The donor solution consisted of Ovide® (Ovide®, Medcis–Phoenix, AZ) spiked with [14C] malathion (specific activity 16.9 μCi/mg, Sigma, St. Louis, MO). The receiving solution was Hanks balanced saline solution (HBSS) supplemented with 4% (w/v) bovine serum albumin (BSA) (Fisher Chemicals, Pittsburgh,

PA). The BSA supplement increases the hydrophobicity of the solution, thus improving the partitioning of lipophilic molecules like malathion into the receiver compartment, with viable skin maintenance and metabolism, for more than 24 h (Collier and Bronaugh, 1991).

2.2. Skin models

Male Wistar rats were used for all animal experiments and were treated according to the NIH guide for the care and use of laboratory animals. Each rat was euthanized with carbon dioxide gas and cervical dislocation and the full-thickness skin removed. Full thickness rat skin was selected because its high concentration of hair follicles (289 hair folicles/cm^2) (Bronaugh et al., 1982) make this is a good representation of the human scalp (293 hair folicles/cm^2) (Birch et al., 2001). Rat skin, however, tends to be more permeable than human skin, so a follow-up study was performed with human skin. Abdominal skin from healthy human volunteers was obtained after plastic surgery, dermatomed to a thickness of 300 μm using a Padgett Electrodermatome Model B dermatome (Padgett Instruments, Kansas City, MO) and frozen for later use at −80 °C to not compromise the barrier (Bronaugh et al., 1986).

2.3. Diffusion studies

Skin was placed epidermal side up in an in vitro flow-through diffusion cell system maintained at 32 °C (PermeGear, Riegelsville, PA). The exposed surface area of the skin was 0.79 cm^2 (circular chamber with 1 cm diameter). The epidermal side was exposed to 100 μl of Ovide® (0.5 mg) and 50,000 dpm ^{14}C-labeled malathion. The solution was allowed to remain unoccluded on top of the skin for 0.5, 2, 4, or 8 h of exposure at which time malathion was removed and skin was thoroughly washed with a 10% shampoo solution (Suave, Balsam & Protein, Chicago, IL). Penetration was allowed to continue for either 24 h (rat and human), 48 h (rat) or 72 h (rat) in order to examine the skin's ability to act as a reservoir for malathion (Kraeling et al., 2004). The hydrophobic malathion will readily partition into the lipid portions of the skin and will remain there for greater periods of time before partitioning into the more hydrophilic receiver solution. Longer experiments were therefore used for the rat studied because

the skin is so thick that it can act as a depot for topically applied chemicals. This reservoir effect leads to continued absorption long after removal of the chemical and is especially pronounced with lipophilic molecules like malathion (Nielsen and Nielsen, 2000). This can also be seen in other fatty tissue and will provide an additional exposure source after treatment termination. The dermal side was in contact with the HBSS receiver fluid which was continuously perfused. The fluid then passed to a fraction collector via Teflon tubing. Eluent was assayed for radioactivity by liquid scintillation counting (LSC) (Packard, Tricarb Model 1600CA).

Upon completion of the transport experiments, the skin was washed three times with a 10% soap solution, removed from the diffusion chamber and placed in tissue solubilizer (NCS®-II, Amersham, Piscataway, NJ). Once the skin had completely dissolved it was neutralized and counted using LSC.

2.4. Data analysis

Studies were repeated between 4 and 12 times. Data was analyzed by determining the total amount of pesticide penetrating through or into the skin throughout the course of the experiment. Statistical differences were determined by a repeat measure ANOVA followed by a Dunnett's Multiple Comparison post-test (GraphPad Prism, GraphPad, San Diego, CA). The criterion for significance was set at $p < 0.05$.

3. Results

The rows in Table 1 shows that penetration continues well after the removal of the source. Absorption after 72 h increased 2.4 and 2.8-fold compared to 24 h for the 0.5 and 8 h exposure, respectively ($p < 0.01$). The columns in Table 1 demonstrates that penetration increases with longer exposure times for each experimental duration. The exception is that the 2 h exposure does not result in additional malathion crossing through the skin compared to the 0.5 h treatment. The absorption at 24 h, after the 30 min treatment (1.78 ± 0.13), however, is significantly smaller ($p < 0.01$) than after an 8 h exposure (2.18 ± 0.09). At 48 h, penetration increased to 3.11 ± 0.24 and 4.52 ± 0.34 ($p < 0.01$) for the short and long exposures, respectively, while at 72 h these values increased to 4.34 ± 0.60 and 6.20 ± 0.96, respectively ($p < 0.01$). Although these values are statistically significant their toxicological relevance is not clear.

The amount of malathion remaining in the skin upon completion of the experiments was also determined. After 24 h there was a trend toward greater skin levels as exposure duration increased with levels of 8.5 ± 0.3, 12.7 ± 1.5, 11.9 ± 1.2, and $13.8 \pm 1.8\%$ after 0.5, 2, 4 and 8 h, respectively. This trend was not found at either 48 or 72 h. Mass balances resulted in >96% recovery for all experiments (data not shown).

Human abdominal skin was also examined for its sensitivity to Ovide® application duration. Transdermal absorption at 24 h after an 8 h exposure was 2.8-fold greater than the 0.5 h exposure (1.02 ± 0.41 versus 0.36 ± 0.14) ($p < 0.05$) as seen in Table 2. Upon completion of the studies, the skin was thoroughly washed, dissolved in tissue solubilizers and counted via LSC so any ^{14}C malathion remaining in the skin could be quantitated. Table 2 also demonstrates that significantly more malathion ($p < 0.05$) remains in the skin after an 8 h treatment (3.4 ± 0.5) than a 0.5 h exposure

Table 1

Effect of treatment duration on the transdermal absorption of malathion across rat skin at 24, 48 and 72 h post application

Treatment (h)	Percentage of penetration at 24 h (mean ± S.E.M.)	Percentage of penetration at 48 h (mean ± S.E.M.)	Percentage of penetration at 72 h (mean ± S.E.M.)
0.5	1.78 ± 0.13[**]	3.11 ± 0.24[**]	4.34 ± 0.60[**,††]
2.0	1.73 ± 0.08[**]	3.35 ± 0.27[**]	4.29 ± 0.43[**,†]
4.0	2.10 ± 0.13[*]	3.87 ± 0.41[*]	4.86 ± 0.98[**,††]
8.0	2.18 ± 0.09	4.52 ± 0.39[†]	6.20 ± 0.96[††]

[*] $p < 0.05$ vs. 8 h treatment.

[**] $p < 0.01$ vs. 8 h treatment.

[†] $p < 0.05$ vs. 24 h of penetration.

[††] $p < 0.01$ vs. 24 h of penetration.

Table 2
Effect of treatment duration on the transdermal absorption of malathion across human skin 24 h post application

Treatment (h)	Percentage of penetration at 24 h (mean ± S.E.M.)	Percentage remaining in skin (mean ± S.E.M.)[a]
0.5	0.36 ± 0.14[*]	2.1 ± 0.6[*]
2.0	0.46 ± 0.10[*]	2.1 ± 0.3[*]
4.0	0.56 ± 0.11[*]	2.0 ± 0.3[*]
8.0	1.02 ± 0.41	3.4 ± 0.5

[a] Skin was washed with shampoo prior to calculating residual.
[*] $p < 0.05$ vs. 8 h treatment.

(2.1 ± 0.6). This indicates that continued absorption after 24 h is likely because malathion remained in the skin upon completion of the experiment.

4. Discussion

Ovide® is 0.5% (0.5 g/100 mL or 5 mg/mL) malathion and comes in a bottle containing 59 mL. Assuming that the maximal dose of 59 mL Ovide® is applied to the scalp, the total malathion dose will be 295 mg. Since approximately 1% of the applied dose crossed human abdominal skin in the first 24 h, the transdermal penetration is about 3 mg. The haired rat model, which may better mimic human scalp had 2% absorption at 24 h, suggesting a doubling of the transdermal penetration of malathion in the scalp. Extending penetration to 72 h causes this value to climb to 6% or 18 mg. Continued absorption through 72 h even though the source has been removed, demonstrates that the skin does act as a depot for malathion and that the 24 h penetration values are an underestimate of actual in vivo absorption. Adding the receiver fluid values to the skin residuals can provide a more accurate estimate of in vivo penetration (Reifenrath et al., 1991) and would modify the human abdominal absorption values to 4.4% or 13 mg.

The stratum corneum acts as a reservoir for chemicals that come into contact with the skin prior to being washed off. This reservoir is responsible for continued absorption through the skin which may occur even after removal. A linear relationship exists between the chemical level in the stratum corneum after a 30 min application and the total amount penetrated in 4 days (Rougier et al., 1983, 1985; Dupuis et al., 1984). In vitro studies can underestimate the in vivo transdermal absorption of lipopholic compounds due to the preferential partitioning of these molecules toward the skin as opposed to the receiver fluid. Addition of 4% BSA, however, can shift the partitioning towards the receiver solution, thereby improving penetration (Collier and Bronaugh, 1991).

There is good agreement (within a factor of 2–3) between in vitro experiments and in vivo experiments for pesticides (Scott et al., 1992). The transdermal absorption of malathion from a 1% aqueous ethanol solution across human skin in vitro was 8.8% (Wester et al., 1996). Topical application of 4 μg/cm^2 malathion for 24 h resulted in an in vivo absorption of 9.4% through abdominal skin and 6.8% through the forearm (Wester and Maibach, 1985). The interrelationship between malathion application and penetration was tested on the forearms of human volunteers. Skin was exposed to 4 μg/cm^2 of the pesticide for a set period of time and then the skin was washed with soap and water and the absorption was determined at 24 h. Transdermal penetration was 1.3, 4.3 and 4.5% after 1, 15 and 30 min, respectively. Absorption increased to 6.1% after 1 h, 8.3% after 2 h and 12.1% after 4 h, but decreased to 6.8% after 24 h of continuous application (United States Task Group on Occupational Exposure to Pesticides, 1974). Furthermore, percutaneous penetration can increase to 63.8% if the site is occluded (Wester and Maibach, 1985). Washing the skin after malathion application can increase penetration 2–3-fold (Bucks et al., 1985). These findings suggest that our estimate of 1% penetration (3 mg) is quite conservative for the in vivo exposure situation on human scalp and the haired rat model penetration of 6% (18 mg) after 72 h may be more accurate.

In general, rat skin is more permeable than human skin, with most studies finding the differential to be between 1.7- and 5.8- fold, with an average of approximately three times more penetration for most chemicals (Priborsky and Muhlbachova, 1990; Barber et al., 1992; van de Sandt et al., 2000). The difference depends on the physical properties of the chemical. Rat skin was selected because the hair follicle density (289 hair folicles/cm^2) (Bronaugh et al., 1982) is similar to human scalp (293 hair folicles/cm^2) (Birch et al., 2001). Skin appendages, form an important pathway for absorption lipid-soluble substances such as malathion (Scheuplein, 1967). This may explain why the results from our rat data were closer to those seen in vivo across human studies than the human abdominal studies.

Regional variations in transdermal absorption occur in human skin, with the scrotal region being the most permeable, followed by the axilla, jaw angle and scalp (Wester and Maibach, 1985). The in vivo absorption of pesticide parathion is 1.7 times greater across scalp skin than abdominal skin (Maibach et al., 1971). This differential is 1.3, 1.6 and 1.4 for the moderately hydrophobic coumarin, griseofulvin and propranolol respectively (Ritschel et al., 1989), while the transdermal penetration of lipophilic melatonin through human scalp skin is 27 times higher than its absorption through abdominal skin (Ogiso et al., 2002). Multiplying the total estimated exposure through human skin (3 mg) by the conservative factor of 1.3 would increase it to approximately 4 mg, while using the more aggressive factor of 27 would increase the dose to 81 mg. It is not clear whether the lower penetration reported here is related to techniques used or differences in formulation. In any event, the 1% estimate is conservative and inclusion of the malathion remaining in the skin (3.4%) could account for some of this differential.

Most studies show no acute or chronic toxicity after exposure to malathion levels described here so the biological importance of these results may not be significant. There are some instances, however, of erythema in humans and inhibition of plasma cholinesterase and RBC activity in dogs (Vestweber and Kruckenberg, 1972). Furthermore, dermal exposure to 8 and 16 mg malathion daily for a month led to ultrastructural changes in the liver (Tos-Luty et al., 2003). There is also a report of a pregnant woman using a 0.5% malathion hair lotion in the 11–12th week of pregnancy and giving birth to a severely malformed child (Lindhout and Hageman, 1987). There is no direct evidence, however that malathion caused the defect.

Additionally, interactions between circulating malathion and other environmental toxins that may be present in the blood stream are unclear, especially in children. Children are at risk for inadvertent pesticide exposure after spraying at daycare or residential locations (Wilson et al., 2003). Children of pesticide applicators have higher organophosphorus exposure than reference children in the community. Younger children in these families have significantly higher concentrations compared to their older siblings (Loewenherz et al., 1997). Furthermore, those who live in areas where malathion is used for public health purposes and who spend time outdoors are also at higher risk than the general population (Marty et al., 1994). Diet is also a major source of pesticides. In one study, malathion was found in 75% and chloropyrifos in 38.3% of solid food samples (MacIntosh et al., 2001). Children who eat conventional diet have significantly greater blood pesticide levels than those who eat organic fruit and vegetables with an estimated daily dietary dose for malathion of 2.3 µg/kg/day (Curl et al., 2003).

Reducing Ovide® application from the suggested 8–12 h to 30 min can significantly reduce transdermal absorption of malathion, without decreasing the product's efficacy. While there appears to be little acute toxicity directly associated with malathion shampoos, there is no data regarding the potential long-term effects of exposure in children. The risk may be even greater when combined with malathion already present from other sources such as diet and other pesticides or toxins that may be in the body. It therefore, seems prudent to decrease the Ovide® exposure time to 30 min or less. Further clinical studies in children are warranted to confirm the efficacy of this shortened application time.

Acknowledgement

References

ATSDR., 2003. Toxicological profile for Malathion. U.S. Department of Health and Human Services, Public Health, Atlanta, GA.

Barber, E.D., Teetsel, N.M., Kolberg, K.F., Guest, D., 1992. A comparative study of the rates of in vitro percutaneous absorption of eight chemicals using rat and human skin. Fundam. Appl. Toxicol. 19, 493–497.

Birch, M.P., Messenger, J.F., Messenger, A.G., 2001. Hair density, hair diameter and the prevalence of female pattern hair loss. Br. J. Dermatol. 144, 297–304.

Bronaugh, R.L., Stewart, R.F., Congdon, E.R., 1982. Methods for in vitro percutaneous absorption studies. II. Animal models for human skin. Toxicol. Appl. Pharmacol. 62, 481–488.

Bronaugh, R.L., Stewart, R.F., Simon, M., 1986. Methods for in vitro percutaneous absorption studies. VII: Use of excised human skin. J. Pharm. Sci. 75, 1094–1097.

Bucks, D.A., Marty, J.P., Maibach, H.I., 1985. Percutaneous absorption of malathion in the guinea-pig: effect of repeated topical application. Food Chem. Toxicol. 23, 919–922.

Burkhart, C.G., 2004. Relationship of treatment-resistant head lice to the safety and efficacy of pediculicides. Mayo Clin. Proc. 79, 661–666.

Collier, S.W., Bronaugh, R.L., 1991. Receptor fluids. In: Bronaugh, R.L., Maibach, H.I. (Eds.), In Vitro Percutaneous Absorption, 32–49. CRC Press, Boca Raton.

Curl, C.L., Fenske, R.A., Elgethun, K., 2003. Organophosphorus pesticide exposure of urban and suburban preschool children with organic and conventional diets. Environ. Health Perspect. 111, 377–382.

Dupuis, D., Rougier, A., Roguet, R., Lotte, C., Kalopissis, G., 1984. In vivo relationship between horny layer reservoir effect and percutaneous absorption in human and rat. J. Invest. Dermatol. 82, 353–356.

Kraeling, M.E., Yourick, J.J., Bronaugh, R.L., 2004. In vitro human skin penetration of diethanolamine. Food Chem. Toxicol. 42, 1553–1561.

Lifshitz, M., Shahak, E., Sofer, S., 1999. Carbamate and organophosphate poisoning in young children. Pediatr. Emerg. Care 15, 102–103.

Lindhout, D., Hageman, G., 1987. Amyoplasia congenita-like condition and maternal malathion exposure. Teratology 36, 7–9.

Loewenherz, C., Fenske, R.A., Simcox, N.J., Bellamy, G., Kalman, D., 1997. Biological monitoring of organophosphorus pesticide exposure among children of agricultural workers in central Washington State. Environ. Health Perspect. 105, 1344–1353.

MacIntosh, D.L., Kabiru, C.W., Ryan, P.B., 2001. Longitudinal investigation of dietary exposure to selected pesticides. Environ. Health Perspect. 109, 145–150.

Maibach, H.I., Feldman, R.J., Milby, T.H., Serat, W.F., 1971. Regional variation in percutaneous penetration in man. Pesticides Arch Environ. Health 23, 208–211.

Marty, M.A., Dawson, S.V., Bradman, M.A., Harnly, M.E., Dibartolomeis, M.J., 1994. Assessment of exposure to malathion and malaoxon due to aerial application over urban areas of southern California. J. Expo. Anal. Environ. Epidemiol. 4, 65–81.

Meinking, T.L., Entzel, P., Villar, M.E., Vicaria, M., Lemard, G.A., Porcelain, S.L., 2000. Comparative efficacy of treatments for pediculosis capitis infestations: update. Arch Dermatol. 137, 287–292.

Nielsen, J.B., Nielsen, F., 2000. Dermal in vitro penetration of methiocarb, paclobutrazol, and pirimicarb. Occup. Environ. Med. 57, 734–737.

Ogiso, T., Shiraki, T., Okajima, K., Tanino, T., Iwaki, M., Wada, T., 2002. Transfollicular drug delivery: penetration of drugs through human scalp skin and comparison of penetration between scalp and abdominal skins in vitro. J. Drug Target 10, 369–378.

Padilla, S., Sung, H.J., Moser, V.C., 2004. Further assessment of an in vitro screen that may help identify organophosphorus pesticides that are more acutely toxic to the young. J. Toxicol. Environ. Health A 67, 1477–1489.

Priborsky, J., Muhlbachova, E., 1990. Evaluation of in-vitro percutaneous absorption across human skin and in animal models. J. Pharm. Pharmacol. 42, 468–472.

Reifenrath, W.G., Hawkins, G.S., Kurtz, M.S., 1991. Percutaneous penetration and skin retention of topically applied compounds: an in vitro-in vivo study. J. Pharm. Sci. 80, 526–532.

Ritschel, W.A., Sabouni, A., Hussain, A.S., 1989. Percutaneous absorption of coumarin, griseofulvin and propranolol across human scalp and abdominal skin. Meth. Find Exp. Clin. Pharmacol. 11, 643–646.

Roberts, R.J., Casey, D., Morgan, D.A., Petrovic, M., 2000. Comparison of wet combing with malathion for treatment of head lice in the UK: a pragmatic randomised controlled trial. Lancet 356, 540–544.

Rougier, A., Dupuis, D., Lotte, C., Roguet, R., 1985. The measurement of the stratum corneum reservoir. A predictive method for in vivo percutaneous absorption studies: influence of application time. J. Invest. Dermatol. 84, 66–68.

Rougier, A., Dupuis, D., Lotte, C., Roguet, R., Schaefer, H., 1983. In vivo correlation between stratum corneum reservoir function and percutaneous absorption. J. Invest. Dermatol. 81, 275–278.

Scheuplein, R.J., 1967. Mechanism of percutaneous absorption. II. Transient diffusion and the relative importance of various routes of skin penetration. J. Invest. Dermatol. 48, 79–88.

Scott, R.C., Batten, P.L., Clowes, H.M., Jones, B.K., Ramsey, J.D., 1992. Further validation of an in vitro method to reduce the need for in vivo studies for measuring the absorption of chemicals through rat skin. Fundam. Appl. Toxicol. 19, 484–492.

Tos-Luty, S., Obuchowska-Przebirowska, D., Latuszynska, J., Tokarska-Rodak, M., Haratym-Maj, A., 2003. Dermal and oral toxicity of malathion in rats. Ann. Agric. Environ. Med. 10, 101–106.

United States Task Group on Occupational Exposure to Pesticides., 1974. Occupational Exposure to Pesticides, Washington DC, pp. 120–126.

van de Sandt, J.J., Meuling, W.J., Elliott, G.R., Cnubben, N.H., Hakkert, B.C., 2000. Comparative in vitro-in vivo percutaneous absorption of the pesticide propoxur. Toxicol. Sci. 58, 15–22.

Vestweber, J.G., Kruckenberg, S.M., 1972. The effect of selected organophosphorus compounds on plasma and red blood cell cholinesterase in the dog. Vet. Med. Small Anim. Clin. 67, 803–806.

Wester, R.C., Maibach, H.I., 1985. In vivo percutaneous absorption and decontamination of pesticides in humans. J. Toxicol. Environ. Health 16, 25–37.

Wester, R.C., Quan, D., Maibach, H.I., 1996. In vitro percutaneous absorption of model compounds glyphosate and malathion from cotton fabric into and through human skin. Food Chem. Toxicol. 34, 731–735.

Wilson, N.K., Chuang, J.C., Lyu, C., Menton, R., Morgan, M.K., 2003. Aggregate exposures of nine preschool children to persistent organic pollutants at day care and at home. J. Expo. Anal. Environ. Epidemiol. 13, 187–202.

Yoon, K.S., Gao, J.R., Lee, S.H., Clark, J.M., Brown, L., Taplin, D., 2003. Permethrin-resistant human head lice, Pediculus capitis, and their treatment. Arch. Dermatol. 139, 994–1000.