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Ex vivo effectiveness of French over-the-counter products against head lice (*Pediculus humanus capitis* De Geer, 1778)

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Abstract Head lice infestation is still a public health problem worldwide, with an intracountry and intercountry prevalence variation of 0.7 to 59 %. There is a large variety of over-the-counter anti-louse products, but their efficacy is not always well assessed. Our objective was to test the pediculicidal and ovicidal efficacy of 21 over-the-counter head louse products, available in France during the period of 2008 to 2012. We tested children living in Tours City in central France and visiting preschools, primary schools, kindergarten, camps, and child care facilities, as well as children in their family houses, and were examined for the presence of lice. The products were collected from randomly selected pharmacies by covert investigators and then tested in the laboratory on an ex vivo sample of head lice and their eggs, collected from the hair of infested children. Living lice and unharmed eggs were collected from the scalps of 3–12 years old. The laboratory conditions for ex vivo testing mimicked the manufacturers' instructions for exposure time and application method. In 21 runs, 3919 living lice and 4321 undamaged living eggs were collected from the scalp of over 400 children. The 21 products were classified in three groups: 6 products in a group of potentially 100 % pediculicidal activity and potentially 100 % ovicidal activity, 8 products in a group of potentially 100 % pediculicidal activity but insufficient ovicidal activity (including 2 products with claims of single application treatment), and 7 products in a group of insufficient pediculicidal activity and ovicidal activity. The pharmaceutical market for head lice products in France is swamped with poorly tested and ineffective products. Rigorous efficacy testing preregistration and periodic screening and testing of effectiveness in the post-registration period should be endorsed by the health authorities.

Keywords Pediculosis · *Pediculus humanus capitis* · Pediculicides · France · Effectiveness · Ex vivo assays

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Introduction

Head lice (*Pediculus humanus capitis*) are obligate blood-sucking parasites of humans since ancient times (Filer 1996; Mumcuoglu et al. 1989) and still continue to be a worldwide public health problem. Their prevalence vary within a given country and between countries (Portenart et al. 1984; Combescot-Lang et al. 1986; Combescot 1990; Mumcuoglu et al. 1995; Gratz 1997; Refaat 2000; Counahan et al. 2004;

Falagas et al. 2008; Rukke et al. 2011). Mostly children between 3 and 13 years are infested (Combescot-Lang et al. 1986 Mumcuoglu 1991) across all socioeconomic levels (Mumcuoglu 1991; Willems et al. 2005). From 1950s to 1970s, research interest in pediculicides was low, as lice infestations were controlled with dichlorodiphenyltrichloroethane (DDT). However, as early as 1958, the international research community was aware of the problem of resistance.

In 1970, an international expert committee recommended that the World Health Organization (WHO) "should encourage the development of a tentative method to physical resistance" (Rao 1958). Subsequently, the WHO has approved methodologies for measuring susceptibility or resistance of body lice with standardized protocols and dose (WHO 1970, 1975, 1981). In several assays throughout, the world resistance to neurotoxic pediculicides was documented (WHO 1976). Since the middle of 1960s, the prevalence of pediculosis increased worldwide, mainly as a result of developing resistance (Maunder 1971; Combescot 1990; Coz et al. 1993; Downs et al. 1999; Hemingway et al. 1999; Aydemir et al. 1993; Chosidow et al. 1994; Mumcuoglu et al. 1990, 1995; Picollo et al. 1998; Burgess 2004; Meinking et al. 2002; Vassena et al. 2003; Burkhart 2004; Bouvresse et al. 2012). Accordingly, the environmentally hazardous pesticide DDT was gradually banned for agriculture and pharmaceutical use, as was lindane in most countries.

New topical treatments of head lice were developed, and their efficacies were reviewed first by Vander Stichele et al. (1995) and later in a Cochrane review (Dodd 2000, which was updated in 2001, 2006, and withdrawn in 2007). Concomitantly, new reports of resistance to the new pediculicides were published (Mumcuoglu et al. 1995, 2007; Yoon et al. 2004). Although many publications on head lice resistance formally refer to the standardized protocols recommended by the WHO (1981), these protocols were seldom applied rigorously. WHO did establish formal outcome criteria for pediculicidal and ovicidal activity in terms of 100 % of dead lice and 100 % of dead larvae in eggs (B.O.M.S. 1988). Concerning the establishment of the exposure time, the method recommended for body lice is not satisfactory for head lice, due to the high control mortality of the latter (Zeichner 1999). In the standardized protocols, the WHO (1981) recommends that the susceptibility to insecticides be determined by using a single concentration and changing the exposure time. This should come as no surprise as the WHO's protocols were developed in the era of DDT for longitudinal follow-up of development of resistance in neurotoxic products (Wright et al. 1957), and accordingly, they are no longer up-to-date. These recommendations were issued for the measurement of resistance but are not suitable to measure efficacy of anti-louse formulations sold over-the-counter. However, no gold standard method for proving efficacy in a registration procedure has been established (Burkhart et al. 2001, 2006). To evaluate efficacy of formulations sold over-the-counter, several recommendations and designs for ex vivo, in vivo, and clinical studies of anti-louse products had been proposed (Combescot et al. 1996; Burkhart et al. 2001). Regulatory authorities of different countries of the world have their own criteria to test products prior to registration. However, the methods to test such products were not always well specified or were difficult to fulfill pragmatically. For instance in France, the official requirement was to test the product in an ex vivo study with a sample of five patients per site, with three sites per region, and four different metropolitan areas (AFSSAPS 1999).

As in many countries, in France, head louse infestation is no longer considered as a disease, and accordingly, pediculicides are no longer seen as a medicine and therefore subjected to a less rigorous administrative registration procedure (Cour de Cassation, chambre criminelle 1924). The status of pediculicides changed from medicinal product to medical device or "natural product" in many countries, as manufacturers preferred less stringent registration procedures. Hence, regulatory authorities shifted their focus of attention from rigorous preregistration efficacy testing to limited preregistration toxicity testing and post-marketing surveillance of safety.

A number of occasional studies in a limited number of countries have shown that some of the formulations sold over the counter did not show satisfactory effectiveness against head lice (Mumcuoglu et al. 1991; Vander Stichele et al. 1995; Burkhart 2004; Burkhart et al. 2006; Asenov et al. 2010). Mumcuoglu et al. (1991) conducted an in vitro evaluation on body lice of the efficacy of 14 pediculicides, at that time available over-the-counter in Israel. The assay was performed in respect of the manufacturer recommendations on a laboratory colony of body lice (*P. humanus humanus*) and their eggs. In other similar studies, the contact time in the assay differed from the contact time recommended by the manufacturer (Meinking et al. 1986; Meinking et al. 2001; Heukelbach et al. 2008a, 2009; Abdel-Ghaffar 2010; Gallardo et al. 2012).

The aim of the present study was to conduct an evaluation of the effectiveness of 21 topical anti-louse products, available over-the-counter in France. Head lice were collected from the heads of infested children, and ex vivo tests were performed in respect of the manufacturer's recommendations.

Material and methods

Schools examined

During the years 2008 to 2012 and using the media (TV, radio, newspapers, and internet), children living in Tours (France) and visiting preschools, primary schools, kindergarten, child care facilities, as well as private houses, in which an outbreak

of head lice was suspected, were visited and children were examined for the presence of lice. A permission was obtained from the appropriate authorities, while parents or the responsible fosters of the children were requested to sign an informed consent, before the child's head was examined and existing lice and eggs removed. As the present investigation was not an interventional study as stated by the European Directive and the French regulations, acceptance of the protocol by an ethical commission was not required at the time of this research work.

Children examined

Before the examination, children and their teachers and/or parents were informed about the biology, epidemiology, and control of head lice. While examining children outside their homes, maximum care was taken to ensure that nobody except the examiner knows the results of the examination, i.e., whether living lice and/or eggs has been found on the scalp. The hair of each child was first checked visually, and those children who were likely to be infested with lice or eggs were examined more thoroughly. The child was asked to lean the head forward over a table covered with a white paper sheet, previously folded in the middle. If necessary, a regular comb or brush was used to straighten the hair and to open the tangled hair. The scalp was examined with the help of a louse comb by starting from the middle of the anterior part of the scalp. Lice and eggs, which fall on the white sheet were collected with the help of an insect forceps and transferred to a 5.5-cm diameter Petri dish.

Selection of living lice and eggs

In the laboratory, collected lice and eggs were examined under the stereo microscope (Nikon, Type 115), and 50 living lice originated from the head of several children were pooled to Petri dishes (5.5-cm diameter) with a Whatman filter paper (No. 1) using an insect tweezers. While lice were tested the same day, intact eggs were transferred to an incubator at 28 °C and 50 % relative humidity until they were tested the following day.

Products tested

Lice products were purchased from random pharmacies and malls by covert investigators and were divided in three categories: those having neurotoxic activity, those having a physical action (coating agents), and remedies which were combining both actions (Box 1).

Bioassay

The assays were performed with maximum compliance to the manufacturer's instructions for use in the labeling, faithfully mimicking the application time and other aspects of administration.

After examination and sorting under the stereo microscope, healthy living lice were selected and divided in three batches of at least 50 lice each, i.e., 150 lice minimum by product to test.

Each batch of lice was deposited in the lid of a Petri dish and then exposted to the product.

Depending on the formulation of the product, different strategies of application of the product were used.

In the case of lotion, 300 μl of the product was poured into the lid of the Petri dish, assuring full immersion.

In the case of , cream gel, balm, or, foam 500 mg of the product was prelevated with a microspatule in inox 18/10. The lice were enrobed, and the product lice mix was gently stirred with a flat ended inox pincet, for 1 min.

In the case of shampoo, recommended to be applied on dry hair, 300 μl of product is poured over the lid. In the case of shampoo recommended to be applied on wet hair, first 100 μl of distilled water is poured over the lice and then 300 μl of product. In both instances, the product lice mix is gently stirred with a flat ended inox pincet, for 1 min.

The next step in the exposure process was to transfer the content of the lid (product and lice) to the bottom of the Petri disk, covered with a round Whatman paper. In the case of crème, gel, balm, and mousse, the Whatman paper was covered with a fine layer of the product. With lotion or shampoo, a dry Whatman paper was used, as the liquid product quickly diffuses into the paper.

The contact between product and lice in the bottom of the open Petri dish was continued for exactly the time recommended by the manufacturer and at room temperature (19–23 °C).

After the set contact time, the lice were washed with a regular children shampoo (Bébé Extra-Doux®, Repère®, Scamark®), diluted 1 in 3 *v*/*v* distilled water. The absence of toxicity of these shampoos for lice and eggs has previously been tested. The Whatman filter paper with the lice attached was placed on a strainer, and the shampoo was versed over the lice and eggs. Then, the lice were rinsed with distilled water in different crystallizers (100 ml). The washing step was done by successive shaking/rinsing with distilled water, until the last rinsing water become clear. Then, treated lice were dried on a filter paper to absorb excess water, transferred in a new Petri dish, covered with a new and dry filter paper disk (diameter 5.5 cm). Petri dishes with lice were transferred to an incubator at 34.2±0.05 °C and 51±1 % relative humidity. As control, healthy living lice were selected and divided into three batches of at least 50 lice each, i.e., 150 lice minimum by product to

Box 1 Identification and characteristics as indicated in the labeling of 21 tested products in France (ex vivo tests)

Type of action categories product names	Trade names in other countries	Galenic form	Principal component(s)	Percent	Other component(s)	Application time	Repeat instructions after first treatment according to manufacturer	Inflammability/ flash point[a]	Company	Bar code or ACL code/batch number/expiration date	Trial date
Agents with neurological action											
Pyrethrins											
Marie-Rose®	?	Lotion without pressure	Pyrethrin	0.3	Acetic acid 4 %, perfume excipient	2–3 h	Several consecutive days and after 7 days	?	LJP Technopole Forbach Sud (France)	3 160 920 964 909/ ML070301/ 03 2010	Jul 2009
Pyrethroids											
Pyreflor® *lotion*	None	Pressurized lotion with gas	Permethrin 25/75	0.3	1 % Piperonyl butoxyde, ricin oil, ß-glycyrrhetinic acid	5 min	After 1 day	?	Medganix (Belgium)	328 370 2[a]/2005 F 28/06 2008	Feb 2008
Para® *special Poux*	Para® Poux	Pressurized lotion with gas	Alethrin (pallethrin)	1.8	7.2 % Piperonyl butoxyde, 91 % isododecane propellant: HFA 134 a	30 min	One application followed by fine tooth combing. Adapt application time and mode for children under 2	<55 °C	Pharmygiene-Scat (France)	349 384 2[a]/ BH020/10 2008	Feb 2008
Pyrethroids+organophosphates											
Para® *plus*	Para® special lice	Pressurized lotion with gas	Malathion, permethrin	0.5 1.0	4 % Piperonyl butoxyde, 94.5 % Isododecane, propellant: HFA 134 a	40 min	One application followed by fine tooth combing. Adapt application time and mode for children under 2. Second application recommended at days 10 to 12	<55 °C	Omega Pharma (France)	349 383 6[a]/QH 336/06 2010	Feb 2008
Organophosphates+essential oils											
Prioderm®	Radikal®; Derbac-M®; Kurllada®; Suleo®; Zipotok®; Ovide®; Rafa®	Lotion without pressure	Malathion	0.5	Terpineol, Siberian pine scent, isopropyl alcohol	8 h	If necessary after 7 days	<55 °C	Meda Manufacturing (France)	325 542 7[a]/ 102251/02 2012	Feb 2011
Agents with physical action											
Vegetable oils+mineral oils											
Parasidose® *lotion traitante*	?	Lotion spray without gas	Ricinus, paraffine, cocamide DEA, cocos	?	Capric acid, citric acid, perfume	45 min	After 3 to 5 days	?	Gilbert (France)	448 292 9[a]/2311-967/ 01PLT0606/ 06 2011	Jul 2010
Silicones											
Itax®	?	Pressurized lotion with gas	Oily silicone based complex	?	Agents to untangle and style hair	1 h	After 7 and 14 days	20 °C[b]	Pierre Fabre/ Ducray (France)	3 282 779 158 336/	Jul 2008

Box 1 (continued)

Type of action categories product names	Trade names in other countries	Galenic form	Principal component(s)	Percent	Other component(s)	Application time	Repeat instructions after first treatment according to manufacturer	Inflammability/ flash point[a]	Company	Bar code or ACL code/batch number/expiration date	Trial date
										449178.5/F 105/11 2009	
Altopou®	Piojito®	Lotion without spray	Cyclometicone 5, dimeticone	?5	Isodecyl neopentanoate, perfume	8 h	After 7 and 14 days	83 °C[b]	Arkopharma (France)	3 578 830 149 307/ 4626819[a]/ SSM006/08 2010	Nov 2008
Pouxit®	Etopril®; Silicom®; XTLuis®; Piky®; Headring®; Neositrin®; Hedrin®	Lotion without spray	Cyclometicone 5, dimeticone	?4		8 h or overnight	After 7 days	78 °C[b]	Thornon & Ross Ltd (Ireland)	3401044856269/ 4485626/ VE93/ 08 2010	Jul 2010
Pouxit® *XF extra fort*	?	Lotion without spray	Dimeticone-1.6, dodecatrien-3-ol 3,7,11-trimetyl-PEG/PPG dimeticone co-polymersilica silylate	?		15 min	One application	?	Thornon & Ross Ltd, (UK)	3 401596 695491/ AE83/09 2013	Mar 2011
Silicones+mineral oils											
Paranix® *mousse*	?	Lotion spray without gas	Dimeticone, paraffine oil	?		15 min	After 7 days	?	Chefaro Ltd (Ireland) not internationally available	3 595 894 848 205/4848201/ 08060701/06 2010	Oct 2008
Paranix® *NEW Formule Action Double*	Paranit®	Lotion without spray	Dimeticone, mineral oil	?		15 min	After 7 days	?	Chefaro Ltd (Ireland)	2 596 476/ 10100610/1/ 10 2012	Jun 2011
Other non-identified agents											
Duo LP Pro®	Liberalice® Paranix® sensitive	Lotion without spray	Triglycerides, lipid esters (Oxyphthirine®)	?		8 h	One application	No	Duhot S A (Belgium)	3 700 006 250 030/4625777/ 07040/07 2009	Jul 2009
Parasidose® *Nouvelle formule biococidine®*	?	Lotion without spray	Biococidine®	?	Conservators, perfume, exipients	45 min	After 3–5 days in case of wrong application (sic) or reinfestation	?	Laboratoires Gilbert (France)	3 518646 041 259/3 401095 075220/ GOB0295/08 2012	Mar 2011
Vegetable oils +/or Vegetable derivative oils											
Yapapou®	Piojito®	shampoo	Cocos nucifera, cocamide DEA, citric acid, cocamidopropyl	?	Sodium laureth sulfate, betaine, sodium chloride, akyposal, chlorhexidine digluconate	10–15 min	Repeat every 2–3 days in case of epidemic as a preventive measure	?	Axiane (France)	ACL 450 635 7[a]/ 60690/02 2009	Feb 2008

Box 1 (continued)

Type of action categories product names	Trade names in other countries	Galenic form	Principal component(s)	Percent	Other component(s)	Application time	Repeat instructions after first treatment according to manufacturer	Inflammability/ flash point[a]	Company	Bar code or ACL code/batch number/expiration date	Trial date
Poux Apaisyl®	None	shampoo	Coconut oil derivatives	?	Triethanolamin, disodium EDTA	15 min	After 7 and 14 days	No	Merck Médication Familiale (France)	3 401 345 516 367/455163-6/20701134/03 2010	Oct 2009
Marie-Rose® *une seule application*	None	Lotion without spray	Cocamidopropyl betaine cocamide DEA	?	D-panthenol, EDTA, polysorbate 20, polyquaternium 6, chlorhexidine digluconate, phenoxyethanol, citric acid, perfume	6 h or all night	One application	?	LJP Technopole Forbach Sud (France)	3 160 920 964 909/Ref 096490-EMB 57227E - RX14/08 2013	Sep 2011
Agents combining neurological /physical action											
Essential oils+vegetable oils											
Paranix®	Paranit® lotion, Lyclear® lotion, Chick Chuck®	Pressurized lotion with gas	Coconut, anise, Ylang Ylang (essential oil)	?		15 min	After 9–10 days	20 °C[b]	Teva Pharmaceutical Ind. Ltd (Ireland)	3 595 894 360 080/4360089/WB 6E24-5/05 2009	Jul 2008
Puressentiel®	?	Lotion spray without gas	Essentials oils of lavender, clove, tea tree, geranium, vegetables oils of cocos, Calophyllum, jojoba, sunflower, almond, ricin	?		10 min	After 3 days	?	Puressentiel (France)	3 401098 489505/9848950/CNK 2783-124/F103001/03 2014	Dec 2011
Essential oils+silicones											
Ecoprioderm®	Linicin®	Liniment	Dimeticone, Prunus armeniaca, Prunus dulcis	?	Tocopheryl acetate	15 min	After 8 days	<55 °C	Meda AB (Sweden)	3 401 097 41867 4/608 803 08/2013 07 08	Mar 2011
Essential oils+vegetable oils+silicones											
Nyda®	None	Lotion spray without gas	Dimeticone 92 %, medium chain triglycerides, jojoba wax	92	Aromatic substances	8 h	After 8–10 days if necessary	34 °C[b]	G Pohl - Boskamp GmbH &Co (Germany)	4 029 125 050 512/4678779/123286/05 2009	Nov 2008

[a] From a legislative point chemical materials are only considered flammable if they have a flash point under 55 °C

[b] COOPER (2008) -Pouxit® and anti-lice products: what you should know about the risk of flammability. Website Pouxit®: www.pouxit.fr, last accessed 2008

test. Each batch of lice is then deposited in the lid of a Petri dish and then submitted to the same procedures as the experimental group, except that distilled water replaced the testing product. During an assessment of several products on the same day, only one control group was used.

The next day, the same procedure of exposure was repeated on the eggs, collected on the previous day, and kept in an incubator at 28 °C and 50 % relative humidity. Only viable eggs (checked under stereo microscope) are selected for the bioassay.

Outcome assessment on living mobile lice (pediculicidal activity)

After the exposure to the product or control, at the contact time recommended by the manufacturer, the viability of lice was examined under a stereo microscope by the same observer in each case to prevent inter observer variation, at room temperature (19 to 23 °C) at 5 min, 1 h, 3 h, and 24 h after the last rinsing of the regular washing step.

Preliminary studies showed that physical conditions observed at 3 h after the washing step were fully reliable to assess anti-lice effectiveness. At this observation time, it was possible to detect the possibility of lice recovering after the exposure to pediculicides. After 3 h, external factors (starvation or dehydration) could interfere with the pediculicidal effectiveness and give false positive results. Therefore, to assess pediculicidal efficacy, 3 h after treatment was considered as the observation reference period. However, lice were observed for 24 h, as sometimes a few lice remained alive in the control and treated group, which gave further indications regarding the efficacy of some anti-louse products.

The physical conditions of lice observed after treatment were classified as follows: normal, lice behaving and moving normally; knockdown (KD), showing signs of ataxia in legs, antenna, and intestinal tract; and dead, no signs of biological life.

The Knock-Down group was subdivided into

- KD^{+} Lice showing some abnormal movements, but able of turning over quickly when placed on their backs.
- KD^{++} Lice showing some abnormal movements and having difficulties turning over.
- KD^{+++} Lice showing some movements after being touched or stimulated by forceps.
- KD^{++++} Lice showing no apparent external or internal movements, except for slight contractions of the digestive tube after stimulation with tweezers.

After 3 h of observation, lice were dichotomously classified as alive or dead: Alive were the moving lice and the lice in the KD^{+} and KD^{++} group, while lice from the groups KD^{+++} and K^{++++} were considered as dead.

In the case that the percentage of lice considered dead was lower at 24 h, because some lice considered dead at 3 h apparently recuperated, then this percentage of 24-h results was considered as the primary outcome.

Outcome assessment on viable eggs (ovicidal activity)

After the exposure procedure, Petri dishes with eggs were transferred to an incubator at 34.2±0.05 °C and 51±1 % relative humidity and observed under a stereo microscope by the same observer daily for 12 days, and the number of hatching lice was counted. Eggs were classified as hatched, dead (non-hatched), and still born (dead during the hatching process). The primary outcome was the percentage of mortality at day 12, while the outcome evaluation was not blinded.

Statistical analysis

The minimum sample size of 150 lice per experimental group was chosen to ensure sufficient power to assess with great precision the true prevalence of lice or eggs that were killed by the tested products and to ascertain with a 95 % confidence interval that whether effectiveness in the treated group is different from 100 % or not. The hypothesis to reject was that effectiveness was 100 %. Due to observed proportions of dead lice or eggs close to 100 %, we performed exact 95 % confidence interval calculations.

Results

In 21 runs, 3919 living lice and 4321 undamaged living eggs were collected from the scalp of over 400 children, 3–12 years old. The pediculicidal and ovicidal activity of the 21 tested products and the control groups (in which the majority of the lice were still alive and behaved normally) is shown in Table 1.

The 21 products were classified in three groups, according to the results of ex vivo testing: a first group of six products of potentially 100 % pediculicidal activity (which kill 100 % of the mobile stage of lice) and potentially 100 % ovicidal activity (which kill 100 % of the viable eggs), a second group of eight products in a group of potentially 100 % pediculicidal activity and insufficient ovicidal activity, and a third group of seven products of insufficient pediculicidal activity and insufficient ovicidal activity (see Table 2).

In the first group of six products, there was one agent with neurological action, *Prioderm*® malathion+essential oils), two agents with physical action, *Pouxit*® XF *Extra Fort* (silicones) and *Duo LP Pro*® (oxyphthirine), and three agents with combined neurological and physical action *Paranix*® (essential oils+vegetable oils), *Ecoprioderm*® (essential

Table 1 Mortality of lice (pediculicidal activity) and eggs (ovicidal activity) after one ex vivo exposure

Products	Lice						Eggs			
	Experimental group			Control group			Experimental group		Control group	
	N	5 min *n* (% dead [95 %CI])	3 h *n* (% dead [95 %CI])	*N*	5 min *n* (% dead [95 %CI])	3 h *n* (% dead [95 %CI])	*N*	After 12 days *n* (% dead [95 %CI])	*N*	After 12 days *n* (% dead [95 %CI])
Agents with neurological action										
Pyrethrins										
Marie-Rose®[b]	153	153 (100 [98–100])	153 (100 [98–100])	168	0 (0 [0–2])	9 (5 [3–10])	286	226 (79 [74–84])	84	17 (20 [12–30])
Pyrethroids										
Pyreflor® *lotion*[a]	150	0 (0 [0–2])	87 (58 [50–66])	112	0 (0 [0–3])	11 (10 [5–17])	158	57 (36 [29–44])	138	32 (23 [16–31])
Para® *special Poux*[b]	215	0 (0 [0–1])	215 (100 [99–100])	159	0 (0 [0–2])	15 (9 [5–15])	164	144 (88 [82–92])	192	42 (22 [16–28])
Pyrethroids+Organophosphates										
Para® *plus*[a]	200	0 (0 [0–1])	170 (85 [79–90])	159	0 (0 [0–2])	15 (9 [5–15])	246	215 (87 [83–91])	192	42 (22 [16–28])
Organophosphates+Essential oils										
Prioderm®[c]	183	183 (100 [98–100])	183 (100 [98–100])	176	0 (0 [0–2])	27 (15 [10–22])	261	258 (99 [97–100])	208	20 (10 [6–15])
Agents with physical action										
Vegetable oils+Mineral oils										
Parasidose® *lotion traitante*[a]	153	0 (0 [0 – 2])	75 (49 [41–57])	112	0 (0 [0–3])	3 (3 [1–8])	187	117 (63 [55–70])	441	92 (21 [17–25])
Silicones										
Itax®[b], Altopou®[b], and Pouxit®[b]	163	163 (100 [98–100])	163 (100 [98–100])	229	8 (4 [2–7])	37 (16 [12–22])	202	67 (33 [27–40])	441	92 (21 [17–25])
Pouxit® *XF extra fort*[c]	60	160 (100 [98–100])	160 (100 [98–100])	162	0 (0 [0–2])	18 (11 [7–17])	172	171 (99 [97–100])	187	59 (32 [25–39])
Silicones+Minerals oils										
Paranix® *mousse*[a]	158	141 (89 [83–94])	157 (99 [97–100])	162	0 (0 [0–2])	18 (11 [7–17])	171	167 (98 [94–99]	172	67 (39 [32–47])
Paranix® *New formule action double*[b]	181	181 (100 [98–100])	181 (100 [98–100])	134	0 (0 [0–2])	0 (0 [0–2])	188	137 (73 [66–79])	297	65 (22 [17–27])
Other non-identified agents										
Duo LP Pro®[c]	159	159 (100 [98–100])	159 (100 [98–100])	203	2 (1 [0–4])	54 (27 [21–33])	232	232 (100 [99–100])	262	105 (40 [34–46])
Parasidose® *Nouvelle formule biococidine*®[a]	153	0 (0 [0–2])	75 (49 [41–57])	112	0 (0 [0–3])	3 (3 [1–8])	150	93 (62 [54–70])	194	50 (26 [20–33])
Vegetable oils +/or vegetable derivative oils										
Yapapou®[a]	154	0 (0 [0–2])	132 (86 [79–91])	159	0 (0 [0–2])	15 (9 [5–15])	236	121 (51 [45–58])	192	42 (22 [16–28])
Poux Apaisyl®[a]	155	84 (54 [46–62])	122 (79 [71–85])	229	8 (4 [2–7])	37 (16 [12–22])	195	81 (42 [35–49])	441	92 (21 [17–25])
Marie-Rose® *une seule application*[b]	201	201 (100 [99–100])	201 (100 [99–100])	161	0 (0 [0–2])	19 (12 [7–18])	174	134 (77 [70–83])	60	16 (27 [16–40])
Agents combining neurological/physical action										
Essential oils+vegetable oils										
Paranix®[c]	152	152 (100 [98–100])	152 (100 [98–100])	229	8 (4 [2–7])	37 (16 [12–22])	171	171 (100 [98–100])	441	92 (21 [17–25])
Puressentiel®[a]	179	0 (0 [0–2])	61 (34 [27–42])	44	0 (0 [0–2])	2 (2 [1–16])	214	94 (44 [37–51])	212	21 (10 [6–15])
Essential oils+silicones										

Table 1 (continued)

Products	Lice						Eggs				
	Experimental group			Control group			Experimental group		Control group		
	N	5 min *n* (% dead [95 %CI])	3 h *n* (% dead [95 %CI])	*N*	5 min *n* (% dead [95 %CI])	3 h *n* (% dead [95 %CI])	*N*	After 12 days *n* (% dead [95 %CI])	*N*	After 12 days *n* (% dead [95 %CI])
Ecoprioderm®[c]	150	150 (100 [98–100])	150 (100 [98–100])	144	0 (0 [0–2])	0 (0 [0–2])	321	321 (100 [99–100])	280	110 (39 [34–45])
Essential oils+vegetable oils+silicones										
Nyda®[c]	153	153 (100 [98–100])	153 (100 [98–100])	139	0 (0 [0–2])	29 (21 [14–29])	155	155 (100 [98–100])	180	25 (14 [9–20])

[a] Products that kill lice and nits incompletely

[b] Products that kill 100 % of lice and nits incompletely

[c] Products that kill 100 % of lice and 100 % of nits

oils+silicones), and *Nyda*® (essential oils+vegetable oils+silicones).

In the second group of eight products, there were two agents with neurological action, *Marie Rose*® (pyrethrins) and *Para*® *special poux* (*pyrethroid*), and six products with physical action, Itax®, Altopou®, and Pouxit® (silicones), *Paranix*® *Mousse* and *Paranix*® *NEW Formule Action Double* (silicones+mineral oils), and *Marie Rose*® *1 seule application* (vegetable oils +/or vegetable derivate oils).

In the third group of seven products, there were two agents with neurological action, *Pyreflor*® *lotion* (pyrethroids) and *Para*® *Plus* (pyrethroids+organophosphates), four agents with physical action, *Parasidose*® *lotion traitante* (vegetable oils+mineral oils), *Parasidose*® *Nouvelle formule biococidine*® (other non-identified agents), *Yapapou*® (vegetable oils +/or vegetable derivate oils), and *Poux Apaisyl*® (vegetable oils), and one agent with combined neurological and physical action, *Puressentiel*® (essential oils+vegetable oils).

Discussion

This examination of 21 pediculicidal products on the French market during the period of 2008–2012 is a pragmatic ex vivo assay, testing the products according to the manufacturer's instructions. It is the first attempt for a comprehensive appraisal of the efficacy of the therapeutic arsenal of a European nation (France) with ex vivo tests conducted within the country on samples collected from the country and according to the manufacturer's instructions.

The 21 pediculicidal products were classified into three groups. A first group of six products of potentially 100 % pediculicidal activity and potentially 100 % ovicidal activity can be regarded as effective. It is suitable for individual treatment and for a public health approach directed at communities.

A second group of eight products of potentially 100 % pediculicidal activity and insufficient ovicidal activity is less suitable to a public health approach, because of the possibility of recontamination with lice, hatched after the first treatments. These products might still be effective for individual treatment. It takes 7 to 10 days for all eggs to hatch (Barker et al. 2012; Nuttall 1917). Such products need an additional application after 10 days, in order to kill all the lice, which hatched from the surviving eggs. There is an ongoing debate as to when the second/last treatment should be done after the initial treatment at day 0 (Barker et al. 2012). A second treatment on day 10 would eliminate all lice, which hatched in the meantime from the eggs (Mumcuoglu 2006). Treating after 1 week has the advantage for helping people not to forget the second treatment, on the same day of the week as the first treatment. Some authors argue that in case D7 is chosen for the second

Table 2 Ex vivo effectiveness classification of 21 French over-the-counter products against head lice

Products	Group 1 100 % peliculicidal activity and 100 % ovicidal activity	Group 2 100 % peliculicidal activity and insufficient ovicidal activity	Group 3 Insufficient peliculicidal activity and insufficient ovicidal activity
Agents with neurological action			
Pyrethrins		Marie-Rose®	
Pyrethroids		Para® *special Poux*[a]	Pyreflor® *lotion*
		Pyrethroids+organophosphates	
Para® *plus*[a]			
Organophosphates+essential oils	Prioderm®		
Agents with physical action			
Vegetable oils+mineral oils			Parasidose® *lotion traitante*
Silicones	Pouxit® *XF extra fort*[a]	Itax® Altopou®	
		Pouxit®	
Silicones+mineral oils		Paranix® *mousse* Paranix® *NEW Formule Action Double*	
Other non-identified agents	Duo LP Pro®[a]		Parasidose® *Nouvelle formule biococidine®*
Vegetable oils +/or vegetable derivate oils		Marie-Rose® *une seule application*[a]	Yapapou® Poux Apaisyl®
Agents combining neurological/physical action			
Essential oils+vegetable oils	Paranix®		Puressentiel®
Essential oils+silicones	Ecoprioderm®		
Essential oils+vegetable oils+silicones	Nyda®		

[a] Product claiming that only one application is needed

treatment, a third treatment is needed on day 14 (Barker et al. 2012).

A third group of seven products of insufficient pediculicidal activity and insufficient ovicidal activity would be not effective.

For products with insufficient ovidicidal activity but claims in their labeling that one application is sufficient, labeling should be changed or the license withdrawn.

Similar surveys of the therapeutic arsenal of some nations were conducted to assess the efficacy of all pediculicides available on their market. In Israel (Mumcuoglu et al. 1991), the efficacy of 14 products had been tested according to the manufacturer's instructions but with in vitro tests with raring body lice (*Pediculus humanus humanus*). Other similar ex vivo efficacy tests of pediculicides available on their market are as follows: one in Egypt (Abdel-Ghaffar et al. 2010) on 13 anti-head-lice products, not according to the manufacturer's instructions and without testing ovicidal efficacy, another in the USA (Meinking et al. 1986), testing the pediculicidal activity of six pediculicides but not according to the manufacturer's instructions.

Strengths and limitations

The strength of this pragmatic survey methodology is its ability to identify signals of ineffectiveness for products already on the market, which were either inefficacious from the start but slipped through sloppy registration procedures or either have become ineffective because of developing resistance. These signals should be the starting point of further investigation or an invitation to the marketing company to withdraw the product if no convincing clinical information can be produced. The ex vivo method proposed here should be further discussed, refined, and validated against clinical studies with application on heads of infested children. Passing this pragmatic test cannot be considered as proof for clinical efficacy. It is also possible that under this experimental conditions, e.g., optimal submersion of lice and eggs into relatively large quantities of the pediculicide, and respecting fully the exposure times, perform better than in real live application.

With this sample size, survival of four or more lice or hatching of four or more eggs was considered as treatment failure, and accordingly, the hypothesis that the product is fully effective was rejected. If there were no treatment failures or there were less than four treatment failures, the hypothesis that the product is effective could not be rejected. However, this should not be considered as proof of effectiveness, i.e., that the product will be clinically efficacious. Moreover, clinical efficacy can only be fully ascertained in a randomized controlled clinical trial.

Discussion per product

In the group of agents with neurological action, in France, the only available potentially effective product is Prioderm®

(0.5 % malathion Lotion+essential oils). The clinical efficacy of malathion was tested in several clinical trials (Mathias et al. 1984; Meinking et al. 2004, 2007), and it is considered an effective active ingredient in previous systematic reviews (Vander Stichele et al. 1995; Dodd 2000). There are clinical indications that resistance to malathion is rising (Burgess 2007; Bouvresse 2012).

In France, surprisingly, permethrine 1 % crème rinse (considered effective in previous systematic reviews (Vander Stichele et al. 1995; Dodd 2000) is no longer commercially available, possibly due to perceived resistance problems.

In the group with physical action, two potentially effective products were available. Regarding *Duo LP Pro®*, a controlled clinical study (Militao de Sousa et al. 2009) and an ex vivo experiment with *Liberalice®* (*Duo LP Pro®*) (Heukenbach et al. 2009) were conducted. However, in the latter study, the authors observed that Liberalice® was less effective, but they did not expose the lice for 8 h as it is asked in the manufacturer's instructions. For *Pouxit ®XF Extra Fort* (dimeticone), only an uncontrolled clinical study but no RCTs is available (Burgess et al. 2011).

Among the products with physical action and insufficient ovidicidal activity, *Pouxit®* (also known under the name *of Etopril®*, *Silicom®*, *XTLuis®*, *Piky®*, *Headring®*, *Neositrin®*, *Hedrin®*) was tested in clinical trials (Burgess et al. 2005, 2007; Kurt et al. 2009).

Among the products combining neurological and physical action, we classified three potentially effective products. *Paranix®* (essential oils+vegetable oils) was tested in an open clinical study (Mumcuoglu et al. 2002). *Nyda®* (essential oils+vegetable ois+silicones) was tested in a randomized, controlled, observer-blinded clinical trial (Heukelbach et al. 2008a, b). For *EcoPrioderm®* (essential oils+silicones), to the best of our knowledge, no data from RCTs are available.

For the other products in this survey of 21 products, to the best of our knowledge, no data from RCTs are available.

Products such as *Paranix® mousse* and *Pyreflor® lotion* were in the meantime removed from the French market.

Recommendations for regulatory authorities

In general, companies should make verifiable labeling claims. It is of paramount importance that the instructions for use should indicate how long each treatment should last and exactly when consecutive treatments should be conducted (Mumcuoglu et al. 2007). It is imperative to avoid instructions which could be interpreted differently by the users, i.e., "leave the product for 6 h or overnight," "use the product for several consecutive days and 7 days after," leaving the product on the hair for 8 h in the case of "strong" infestation, using the product for "several" "consecutive days" or in case the eggs "persist." For that matter, even the instruction for an "overnight" treatment is vague and should be replaced with the exact hours of treatment. Sometimes unclear or unsubstantiated recommendations are made as to the timing of the second treatment and even third treatments and more: e.g., to use the products 3 to 5 days in the case of "wrong application" or "reinfestation" or unacceptable recommendations for preventive use, such as "repeat every 2–3 days in the case of epidemic as a preventive measure."

Three products claimed to be effective with one application, while our test revealed that they were not fully ovicidal (*Marie Rose® une seule application* and *Para ® Special Poux* and even not fully pediculicidal *Para® Plus*).

Apparently, the regulatory authorities accepted that companies launched products with similar names containing different active substances (e.g., *Ecoprioderm®* and *Prioderm®*; *Marie Rose®* and *Marie Rose® une seule application*; *Parasidose® lotion traitante* and *Parasidose® Nouvelle formule biococidine®*; *Paranix® and Paranix® mousse*, *and Paranix® NEW Formule Action Double*) or with unsubstantiated claims included in the brand name (*Marie Rose®* and *Marie Rose®* "*une seule application*," meaning one application suffices). Information on the composition of the product was sometimes insufficiently disclosed by using fantasy names for non-identified active substances (e.g., Oxyphthirine® in *Duo LP Pro®* and Biococidine® in *Parasidose® Nouvelle formule biococidine®*). Manufacturers may want to protect proprietary mixtures of active and adjuvant ingredients, but this information should be available for checking allergies.

Regulatory authorities should enforce correct information on inflammability of head lice products.

Fourteen products carry on their package unmeaningful messages such as "without insecticides" or "without chemical product."

The status for products against head lice has shifted from registered medication to medical device (Loi 7869 dite Delaneau, 1978) or cosmetic products. This has caused a degradation of the control over these products in regulatory agencies. However, more regulatory rigor is needed. It seems that all ethical pharmaceutical companies, who market fully registered medicines, have retreated from this segment of the market. Also, different departments of the regulator authorities handle these products, no longer with a full medication market authorization, but with an administrative authorization. These departments do not control the labeling as rigorously as for medicines. They do no longer require proof of efficacy in clinical trials and include only a minimal form of pharmacovigilance, which does not include monitoring of developing resistance. Theoretically, these administrative authorizations should be reaffirmed every 5 years, but no practical control activities are currently foreseen. Labeling of head lice products should be checked for inappropriate instructions, instigating patients to overconsumption, and for incomplete information on composition and inflammability. Head lice products

applying for marketing authorization should be ex vivo and clinically tested for efficacy. Marketing authorization should primarily be given to products with 100 % peliculicidal and 100 % ovicidal activity. Health agencies should also demand checks of effectiveness on a regular basis (e.g., every 5 years) in the post-marketing phase and act upon signals of ineffectiveness or growing resistance, while ineffective products should not be allowed to remain on the market.

The net result of low quality regulatory activity is that consumers are exposed to a bewildering choice of products, of which many are ineffective, either because they were never efficacious in the first place or because resistance has developed. Many families, confronted with lice infestation, frantically buy and repeatedly apply ineffective products, until financial resources are exhausted and resignation in despair reigns (Ozkan et al. 2012). This maintains the prevalence of active head lice infestation at epidemic levels in our schools and kindergarten (Vander Stichele et al. 2002).

Recommendations for practice

Pediculicides that kill 100 % lice and 100 % eggs after one treatment tested in ex vivo assays and in clinical tests are highly desirable, from a public health point of view, while wet combing can be considered as a valuable non-pharmacological treatment (Hill et al. 2005).

For physicians and pharmacists who need to advice parents in the choice of products to treat head lice, informed rational drug choice has not become easier. A protocol for a Cochrane Collaboration systematic review on the subject has been published (Vander Wouden et al. 2011), and results are now awaited. Relying on products alone to contain head louse infestations at a reasonable level will not be sufficient. Public health programs at local community level involving parents, schools, and community services with accurate screening methods (Combescot 1990; Demaeseneer et al. 2000; Mumcuoglu et al. 2007; Jahnke 2009) and synchronized treatment campaigns with effective treatments will be needed (Meinking et al. 1986; Combescot 1990; Ibarra et al. 2007; Feldmeier 2012).

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Conflict of interest Combescot-Lang C. and Toubate B performed as university experts tests for the evaluation of numerous products, including products in this study. However, for this study, all tests were performed independently, with products bought by the researchers in pharmacies.

Mumcuoglu K.Y. has participated in the development of Paranix®.

Vander Stichele RH and Veirron E have no potential conflicts of interest to declare.

References

[WHO] World Health Organization (1970) Insecticide resistance and vector control. Seventeenth Report of WHO Expert Committee on insecticides .Technical report series no 443 - Geneva

[WHO] World Health Organization (1975) Instruction for determining the susceptibility or resistance of body lice and head lice to insecticides. WHO/VBC/75.585 - Geneva

[WHO] World Health Organization (1976) Resistance of vectors and reservoirs of disease to pesticides. 22nd Report of the WHO Expert Committee on Insecticides. Technical Report Series no 585 - Geneva

[WHO] World Health Organization (1981) Instruction for determining the susceptibility or resistance of body lice and head lice to insecticides. WHO/VBC/81.808 - Geneva

Abdel-Ghaffar F, Semmler M, Al-Rasheid K, Klimpel S, Mehlhorn H (2010) Comparative in-vitro test on the efficacy and safety of 13 anti-head-lice products. Parasitol Res 106:423–429

Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS) - Procédure nationale: note explicative concernant les produits pédiculicides pour application locale soumis à autorisation selon l'art. L658-11 du code de la Santé publique. Commission d'Autorisation de Mise en Marché (AMM) du 07 juillet 1999

Asenov A, Oliviera FA, Speare R, Liesenfeld O, Hengge U, Heukelbach J (2010) Efficacy of chemicals and botanical over-the-counter pediculicides available in Brazil, and off-label treatments, against lice ex vivo. Int J Dermatol 49:324–330

Aydemir EH, Unal G, KutlarM ON (1993) Pediculosis in Istanbul. Int J Dermatol 32:30–32

Barker SC, Burgess IF, Meinking TL, Mumcuoglu KY (2012) International guidelines for clinical trtials with pediculicides. Int J Dermatol 51:853–858

Bouvresse S, Berdjane Z, Durand R, Bouscaillou J, Izri A, Chosidow O (2012) Permethrin and malathion resistance in head lice: results of ex vivo and molecular assays. J Am Acad Dermatol 67:1143–1150

Bulletin Organisation Mondiale de la Santé (BOMS) (1988 oct. 29th) Recommandations concernant les études biocliniques des préparations anti poux. AVIS du 8 septembre 1988.

Burgess IF (2004) Human lice and their control. Annu Rev Entomol 49: 457–81

Burgess IF, Burgess NA (2011) Dimeticone 4% liquid gel found to kill all lice and eggs with a single 15 minute application. BMC Res Notes 4: 15

Burgess IF, Brown CM, Lee PN (2005) Treatment of head louse infestation with 4% dimeticone lotion: randomised controlled equivalence trial. BMJ 330(7505):1423

Burgess IF, Lee PN, Matlock G (2007) Randomised, controlled, assessor blind trial Comparing 4% dimeticone lotion with 0.5% malathion liquid for head louse infestation. PLoS One 2(11):e1127

Burkhart CG (2004) Relationship of treatment-resistant head lice to the safety and efficacy of pediculicides. Clin Proc 79:661–666

Burkhart CG, Burkhart CN (2001) Recommendation to standardize pediculicidal and ovicidal testing for head lice (Anoplura: Pediculicidae). J Med Entomol 38:127–129

Burkhart CG, Burkhart CN (2006) Safety and efficacy of pediculicides for head lice. Expert Opin Drug Saf 5:169–179

Chosidow O, Chastang C, Btue C, Bouvet E, Mohand I, Monteny N, Bastuji-Garin S, Rousset J-J, Revuz J (1994) Controlled study of malathion and d-phenothrin lotions for *Pediculus humanus var capitis*-infested schoolchildren. Lancet 344:1724–1727

Combescot C (1990) Current epidemiology of *Pediculosis capitis*. Bull Acad Natl Med 174:231–236

Combescot C, Combescot-Lang C, de Nadon J, Remy-Kristensen A, Richard-Lenoble D (1996) Interest and limits of tests to evaluate pediculicides efficacy. Bull Acad Natl Med 180:1315–1324

Combescot-Lang C, Fournon M, Pioux R, Delemos-Ribeiro A, Combescot C (1986) Enquête épidémiologique sur la pédiculose dans la région de Fortaleza (Brésil-Nordeste). Bull Soc Parasitol 4: 113–117

Counahan M, Andrews R, Bütner P, Bymes G, Speare R (2004) Head lice prevalence in primary school in Victoria, Australia. J Paediatr Child Health 40:616–619

Cour de cassation, chambre criminelle (10 mai 1924) Pourvoi en Cassation contre un arrêt de la cour d'appel de Rouen du 18 fev 1924; Delaneau law no 78 699, 6 july 1978; Code de la Santé publique Art. L.5136-1 Ord no 2000-548, 15 juin 2000; Art. L5136-1 Abrogé par Ordonnance no 2007-613 du 26 avril 2007- art. 28 JORF (27 Avril 2007).

Coz J, Combescot-Lang C, Verdier V (1993) Resistance of head lice *Pediculus capitis* L. 1758 to pyrethroïds: d-phenothrin and permethrin in France. Bull Soc Fr Parasitol 11:245–452

de Maeseneer J, Blokland I, Willems S, Vander Stichele R, Meersschaut F (2000) Wet combing versus traditional scalp inspection to detect head lice in schoolchildren: observational study. BMJ 321:1187–1188

Dodd CS (2000) Interventions for treating headlice. Cochrane Database Syst Rev 2001 (3): CD001165 update in Cochrane Database Syst Rev 2006; (4):CD001165, Withdrawn in 2007

Downs AMR, Stafford KA, Harvey I, Coles GC (1999) Evidence for double resistance to permethrin and malathion in head lice. Br J Dermatol 141:508–511

Falagas ME, Matthaiou DK, Rafailidis PI, Panos G, Pappas G (2008) Worldwide prevalence of head lice. Emerg Infect Dis 14:1493–1494

Feldmeier H (2012) Pediculosis capitis: new insights into epidemiology, diagnosis and treatment. Eur J Clin Microbiol Infect Dis 3:2105–2110

Filer J (1996) Egyptian bookshelf diseases. University of Texas Press, Austin, TX

Gallardo A, Mongabure-Cueto G, Vassena C, Piccollo MI, Toloza AC (2012) Comparative efficacy of new commercial pediculicides against adult and eggs of *Pediculus humanus capitis* (head lice). Parasitol Res 110:1601–1606

Gratz NG (1997) Human lice, their prevalence, control and resistance to insecticides. Geneva WHO/CTD/WHOPES 957(8):3–28

Hemingway J, Miller J, Mumcuoglu KY (1999) Pyrethroid resistance mechanisms in the head louse *Pediculus capitis* from Israel: implications for control. Med Vet Entomol 13:89–96

Heukelbach J, Canyon DV, Oliveira FA, Muller R, Speare R (2008a) In vitro efficacy of over-the-counter botanical pediculicides against the head louse *Pediculuss humanus* var *capitis* based on a stringent standard for mortality assessment. Med Vet Entomol 22:264–272

Heukelbach J, Pilger D, Oliveira FA et al (2008b) A highly efficacious pediculicide based on dimeticone: randomized observer blinded comparative trial. BMC Infect Dis 8:115

Heukenbach J, Asenov A, Liesenfeld O, Mirmohammadsadegh A, Oliveira FA (2009) A new two-phase dimeticone pediculicide shows high efficacy in a comparative bioassay. BMC Dermatol 9:12

Hill N, Moor G, Cameron M, Butlin A, Williamson M, Bass C (2005) Single blind randomized, comparative study of the Bug Buster kit and over the counter pediculicide treatments against head lice in the United Kingdom. BMJ 331:384–387

Ibarra J, Fry F, Clarice W, Olsen A, Vander Stichele RH, Lapeere H, Maryan J, Franks A, Smith JL (2007) Overcoming health inequalities by using the Bug Busting 'whole-school approach' to eradicate head lice. J Clin Nurs 16:1955–1965

Jahnke C, Bauer E, Hengge UR, Feldmeier H (2009) Accuracy of diagnosis of pediculosis capitis: visual inspection vs. wet combing. Arch Dermatol 145:309–313

Kurt O, Balcioglu IC, Burgess IF et al (2009) Treatment of head lice with dimeticone 4% lotion: comparison of two formulations in a randomised controlled trial in rural Turkey. BMC Public Health 9: 441

Loi 78 699 dite Delaneau (du 6 juillet 1978), portant sur l'autorisation de mise sur le marché des insecticides et acaricides et modifiant certaines dispositions du code de la santé publique (Art. L. 658-11)

Mathias RG, Huggins DR, Leroux SJ, Proctor EM (1984) Comparative trial of treatment with Prioderm lotion and Kwellada shampoo in children with head lice. Can Med Assoc J 130:407–409

Maunder JW (1971) Resistance to organochlorine insecticides in head lice, and trials using alternative compounds. Med Officer 125:27–29

Meinking TL, Taplin D, Kalter DC, Eberle MW (1986) Comparative efficacy of treatments for Ovide lotion (0.5% malathion) compared to Nix creme rinse (1% permethrin) for the treatment pediculosis capitis Infestation. Arch Dermatol 122:267–271

Meinking TL, Entzel P, Villar ME, Vicaria M, Lemard G, Porcelain C (2001) Comparative efficacy of treatments for pediculosis infestations. Arch Dermatol 137:287–292

Meinking TL, Serrano L, Hard B, Entzel P, Lemard G, Rivera E, Villar ME (2002) Comparative in vitro pediculicidal efficacy of treatments in a resistant head lice population in the United States. Arch Dermatol 138:220–224

Meinking TL, Vicaria M, Eyerdam DH et al (2004) Efficacy of a reduced application time of head lice. Pediatr Dermatol 21:670–674

Meinking TL, Vicaria M, Eyerdam DH et al (2007) A randomized, investigator-blinded, time-ranging study of the comparative efficacy of 0.5% malathion gel versus Ovide Lotion (0.5% malathion) or Nix Crème Rinse (1% permethrin) used as labeled, for the treatment of head lice. Pediatr Dermatol 24:405–411

Militao de Sousa F, Vasconcelos AW, de Nadon J, Duhot PY (2009) Treatment of human head lice infestations in a single application with a new galenic lotion. Int J Cosmet Sci 17:1–7

Mumcuoglu KY (2006) Effective treatment of head louse with pediculicides. J Drugs Dermatol 5:451–452

Mumcuoglu KY, Miller J (1991) The efficacy of pediculicides in Israel. Isr Med Sci 27:562–565

Mumcuoglu KY, Zias J (1989) How the ancients de-loused themselves. Biblic Archaeol Rev 15:66–69

Mumcuoglu KY, Miller J, Galun R (1990) Susceptibility of human head and body louse, *Pediculus humanus* (Anoplura: Pediculidae) to insecticides. Insect Sci Applic 11:223–226

Mumcuoglu KY, Hemingway J, Miller J, Ioffe-Uspensky I, Klaus S, Ben-Ishai F, Galum R (1995) Permethrin resistance in the head louse *Pediculus capitis* from Israel. Med Vet Entomol 9:427–432

Mumcuoglu KY, Miller J, Zamir C, Zentner G, Helbin V, Ingber A (2002) The in vivo pediculicidal efficacy of a natural remedy. Isr Med Assoc J 4:790–793

Mumcuoglu KY, Barker SC, Burgess IE, Combescot-Lang C, Dalgleish RC, Larsen KS, Miller J, Roberts RJ, Taylan-Oskan A (2007) International guideline for effective control of head louse infestations. J Drugs Dermatol 6:409–414

Nuttall GHF (1917) The biology of *Pediculus humanus*. Parasitology 10: 80–185

Ozkan O, Sikar-Aktürk A, Mert K, Bilen N, Mumcuoglu KY (2012) Difficulties experienced by families following unsuccessful treatment of pediculosis capitis: the mothers' perspective. Turk Parazitol Derg 36:82–86

Picollo MI, Casadio AA, Massimo J, Zerba EN (1998) Laboratory studies of susceptibility and resistance to insecticides in *Pediculus capitis* (Anoplura; Pediculidae). J Med Entomol 35:814–817

Portenart M, Combescot-Lang C (1984) La pédiculose a *Pediculus humanus capitis* en Touraine. Ouest Med 37:321–325

Rao R (1958) Seminars on susceptibility of insect to insecticide. Resistance test for lice. Panama City, Republic of Panama, 23-28 June. PASB/WHO report

Refaat GAE, Tosson AM, Mamdouh MIN, Samy AAK (2000) Evaluation of four pediculicides against the head lice *Pediculus humanus capitis*. J Egypt Soc Parasitol 30:51–58

Rukke BA, Birkemoe T, Soleng A, Linstedt HH, Ottesen P (2011) Head lice prevalence among households in Norway: importance of spatial variables and individual and household characteristics. Parasitology 138:1296–1304

Vander Stichele RH, Dezeure EM, Bogaert MG (1995) Systematic review of clinical efficacy of topical treatments for head lice. BMJ 311:604–608

Vander Stichele RH, Gyssels L, Bracke C, Meersschaut F, Blokland I, Wittouck E, Willems S, De Maeseneer J (2002) Wet combing for head lice: feasibility in mass screening, treatment preference and outcome. J R Soc Med 95:348–352

Vander Wouden JC, Klootwijk T, Le Cleach L, Do G, Vander Stichele R, Neven K, Eekhof JAH. Intervention for treating head lice. 2011 Protocol Cochrane Systematic Review. http://onlinelibrary.wiley.com/cochranelibrary/ : last accessed on Febr 20, 2014.

Vassena CV, Mougabure Cueto G, González Audino P et al (2003) Prevalence and levels of permethrin resistance in *Pediculus humanus capitis* De Geer (Anoplura: Pediculidae) from Buenos Aires, Argentina. J Med Entomol 40:447–450

Willems S, Lapeere H, Haedens N, Pasteels I, Naeyaert J-M, De Maeseneer J (2005) The importance of socio-economic status and individual characteristics on the prevalence of head lice in schoolchildren. Eur J Dermatol 15:387–392

Wright JW (1957) Brown AWA (1957) Global survey of the susceptibility of body louse to insecticides, based on the standard kit developed and distributed by [WHO] in 1953. Bull Wld Hlth Org 16:9–31

Yoon KS, Gao JR, Lee SH, Coles GC, Meinking TL, Taplin D, Edman JD, Takano L, Clark JM (2004) Resistance and cross-resistance to insecticide in human head lice from Florida and California. Pestic Biochem Physiol 80:192–201

Zeichner BC (1999) Baseline susceptibility of a laboratory strain of *Pediculus humanus humanus* (Anoplura Pediculidae) using a modified world health organization testing protocol. J Med Entomol 36: 903–905