Reviewer's report

Title: A new dimeticone pediculicide (NYDA(R) sensitive) shows high efficacy in a comparative bioassay

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Reviewer: Ian Burgess

Reviewer's report:

This is an extremely interesting paper from a number of points of view. It continues elements of work from both the current authors and a number of other sources and demonstrates to a large degree the relative paucity of adequate efficacy data available for this category of therapeutic agent. I believe there are a number of areas of the manuscript that need to be re-examined by the authors and revisions made in order to make this a useful publication that fulfils its intended purpose.

Major Compulsory Revisions

Abstract:

I have one general comment about the abstract. Anyone reading this who is not familiar with the category, or even those who are familiar with it, could only come to the conclusion that there may be some commercial influence in favour of the product NYDA because you have used the name 11 times in the Abstract alone (24 times in the remaining text), in most cases specific mention of the brand is wholly unnecessary and could be replaced by a generic description of the product(s) as dimeticone lotion(s) as no other dimeticone containing product was used in the study. I can see only two points in the Abstract, once in the Background and once in the Conclusions where use of the brand name is justifiable. Also it would be better to use the terminology “NYDA® sensitiv(e)” rather than “NYDA® sensitive (also marketed as NYDA® sensitiv)”

Discussion:

General comment: This discussion has no coherent theme and has not been adequately planned. It needs complete rewriting to separate issues of a) comparative activity of the products, b) possibility of insecticide resistance, c) possible issues related to toxicity of some insecticide products and the advantages of using non-pesticide based preparations, d) novel characteristics and possible advantages for the new formulation.

Page 8, lines 4-5. It may be that adequately designed bioassays may be indicative of the possible outcome of clinical investigations but there is no real evidence so far that they could act as a proxy for clinical studies and will certainly never replace them. The reference cited in this sentence is not a good example as the test methodology used in that investigation was so wholly unlike the normal use of the products under investigation that no realistic conclusions could
be drawn from it. This section should be rephrased to avoid misunderstanding.

Page 8, paragraph 2. This should be deleted as it adds nothing to the discussion and the justification for eliminating the fragrance, i.e. to reduce the risk of adverse reactions, should be included in the reference to the formulation in the Methods section.

Page 8, paragraph 3. This is out of place here in the Discussion. I do not think it adds anything to the discussion of the investigation and so should be deleted.

Page 9, paragraphs 2 and 3. I am not sure that you understand what resistance is. The following statement is my basis for making this statement: “...survival of head lice after exposure to neurotoxic compounds does not necessarily mean that lice are resistant. Lice may have acquired a tolerance that can eventually render these chemicals ineffective.” What else is an acquired tolerance that can detoxify chemical substances other than resistance? Please do not make the mistake of believing that resistance is mediated only through mutations directed specifically against insecticide action as this is generally the least frequently encountered form of resistance mechanism.

Page 10, paragraph 3. You refer to the importance of washing off the treatment compounds in bioassays but see my point above as it is possible you may not have achieved this in your study.

Minor Essential Revisions

Abstract:

Background. There is something of a non sequitur between the first and second sentences of this section that needs to be addressed. Although the first sentence follows the introductory section of the Background section of the main text it is not necessary here and should be deleted. Although there is a need for some kind of standardised evaluation system for pediculicides development of such a methodology is not the subject of this paper so the sentence is irrelevant.

Methods. It would be useful to have more information here about the method used to expose the lice. You have not even said that the study was in vitro. Also it is important that you state that the exposure was using a standard protocol rather than following user instructions.

Results. The second sentence is easily misunderstood or misinterpreted. If you mean to say that no major vital signs were seen after five minutes please state it plainly.

Main text:

Background. In the final sentence the words “in fact” are redundant.

Methods. You state that “NYDA® sensitive contains a mixture of two dimeticones of different viscosity, in a total concentration of 92%. It differs from NYDA® by the absence of fragrances.” There are two points here.
First it would be helpful for the understanding of the reader both here and at various other points in the text where this issue is mentioned, particularly the Discussion, if you state what the fragrances are.

Second as I recall the original preparation contains 92% dimeticones as does apparently the new preparation. Therefore, some other component must have changed its proportion in the new formulation after removal of some quantity (hitherto unspecified) of fragrance. Therefore I suggest a percentage breakdown of the components would clarify this issue for all readers.

Head lice used. You state that head lice were obtained from children living in an endemic community. By this do you mean that the children were endemic to Fortaleza or that head lice were endemic within the community?

Discussion:

Page 8, line 1 and line 3. The word “excellent” is subjective and should be deleted. You should also bear in mind that the final assessment in that study was only 2 days after the second application of product whereas the FDA is currently expecting final efficacy evaluations to be made 14 days after the second application of treatment.

Conclusions: Again you refer extensively to the brand NYDA, where this name need only be used once. You have presented no conclusions regarding the other products tested.

Table 1: I think this table is unnecessarily crowded with information. It should be reformatted into landscape format and redrafted so that the components of the products are divided into active components and excipients. The names of the manufacturers only should be included in the table. If you wish to include manufacturer addresses place these in a footnote. The various alternative names for products are unnecessary.

Discretionary Revisions

Methods:

Pediculicidal bioassay. In this section you give the methodology used for the test, citing a previous study methodology as the basis. It would be helpful to understand why you have adopted this methodology as the immersion time and the period of exposure do not conform to any other published methodology (e.g. ASTM testing procedures) but possibly more importantly as far as I have been able to determine the methodology used in these tests is not representative of the normal mode of use of any of the products under evaluation. Therefore, please provide a reasoned explanation/justification for the 3 minute immersion, 20 minute exposure regimen.

Please also give more information about the washing process. Were the lice simply immersed in the water for 1 minute or was there any agitation of the water. If there was simply immersion it is unlikely that the water would actually
remove even the water soluble components of the products because, as everyone knows, even rinsing shampoo from the hair during normal hair washing requires considerable agitation to remove the surface active agents.

Results.

Figure 1 as a bar chart is not clear. I believe it would be much easier to make the comparison between the products using a conventional point and lice graphical representation.

I understand the particular criteria you are employing for measurement of mortality. These are quite clear. However, I think you should provide some additional information on the observations of the lice treated with different products at different time points. For example you record that there was a low mortality using the Goldgeist product until about 6 hours after treatment. However, this product is based on natural pyrethrin, which has a strong “knockdown” effect that persists for several hours during which time insect demonstrate a condition known as “jitters” – a series of intense tonic-clonic spasms – before death arrives due to exhaustion. Consequently, it is almost impossible for a pyrethrum product to elicit immediate mortality/immobilisation. However, I do not see it impossible that lice treated with this product might be walking around apparently unaffected. However, your data/description does not inform the reader as to which if either of these scenarios was observed. Further information is therefore required on what was actually happening to the lice that were not immobilised in order to give the study real meaning.

Discussion:

Page 8, paragraph 4 to the end of the paper. Please correct “silicon” to silicone”.

Page 8, paragraph 4. This paragraph should simply begin “Several recent studies…”

Page 9, lines 6-7. Is there evidence for the suggestion that for 4% dimeticone lotion “a higher concentration of dimeticone would be necessary to achieve irreversible death of insects”? Please either clarify or delete this possibly contentious statement.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I am involved in similar areas of research where there may be some difference of
opinion relating to the importance of certain characteristics of evaluations. I am a consultant to several companies involved in development of pediculicidal compounds and have received fees from some of the companies mentioned in the study, including the company sponsoring the research.