



SDI Review Form 1.6

Journal Name:	Advances in Research
Manuscript Number:	2014_AIR_9580
Title of the Manuscript:	A Phytotherapeutic Formulation for Allergic Rhinitis in Autistic Children
Type of the Article	

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<u>Compulsory</u> REVISION comments	<p>Needs rewriting by a native English speaker – almost every sentence needs grammatical corrections.</p> <p>Line 160: explain how patients were assigned to groups A and B (randomly?); Were the physicians and parents blinded as to which group the children were in? Was the person conducting the microscope measurements blinded?</p> <p>Line 255: explain the results of group B</p>	<p>As suggested by the reviewer, the text has been revised for the English language.</p> <p>Line 160: This study was a randomised placebo-controlled, double-blind procedure. Randomised controlled trials (RCT) are experimental studies that allow the evaluation of the effectiveness of a specific treatment in a given population. The assignment of the subjects to the different treatment arms of the protocol was made by a random method. The randomisation increased the likelihood that other variables, not considered in the study design, were distributed uniformly in the experimental group and in the controls. In this way, the possible differences observed between the two groups could be attributed to the treatment. This was a double-blind procedure such that both the parents of the subjects and the experimenters were unaware of any information that could have affected the results of the experiment.</p> <p>Line 255: As requested by the reviewer the following sentence has been integrated: After ten days of topical administration of the lemon spray, rhinocytograms of the patients in group A showed an almost complete disappearance of</p>



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		<p>eosinophils and mast cells, with the persistence of some neutrophilic and eosinophilic granules, while the patients in group B did not show any significant changes after the saline treatment.</p>
	<p>Line 255-257: the sentence starting “It is therefore” is very unclear</p>	<p>Line 255-257: the sentence has been replaced for clarity: Moreover, during treatment, it is important to perform constant hygienic nasal washes with saline solution to remove all the conditions favourable for an allergic reaction. Sometimes, the severity and subjective symptoms made it necessary to increase the dose of the lemon-based spray and there were no observable side effects.</p>
	<p>Liine 258-259 – what fraction of patients used a higher dose? Did the placebo group also use a higher dose?</p>	<p>Line 258-259: Two patients in group A used a higher dose (two puffs - 0.14 ml 5 times a day instead of 3). Similarly, two patients in group B were given an equal amount of saline. Neither group showed any side effects, such as redness or irritation of the nose (data not shown).</p>
	<p>Add a discussion about how quickly there was a change in symptoms (1 week, 2 weeks, etc) if known.</p>	<p>In all the subjects in group A, an improvement was observed in the first ten days of the treatment.</p>
	<p>Line 259: be more specific about side-effects</p>	<p>Line 259: The side effects such as irritation and redness of the nasal cavities were not observed during the entire treatment period.</p>



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	<p>Lines 290-293 – very unclear</p> <p>Line 296-297 - give a reference</p> <p>Line 332-387 should be move to results</p> <p>The abstract should state that this is a placebo-controlled study.</p> <p>All the figures should have scale bars showing the dimension of the figure.</p> <p>Add a section discussing limitations of the study.</p>	<p>Lines 290-293: According to the suggestion of the reviewer, the sentence “The essential oils present exert a cooling effect contributing sanitizing action” has been changed and a new reference has been added: Furthermore, the essential oils present exert beneficial effects that contribute to the sanitising action [33]. 33 Bakkali F, Averbeck S, Averbeck D, Idaomar M. Biological effects of essential oils – A review. Food and Chemical Toxicology 2008, 46(2): 446-475.</p> <p>Line 296-297: As recommended by the reviewer, the authors have inserted a reference that has been previously reported [22]. 22 Gattuso G, Barreca D, Gargiulli C, Leuzzi U, Caristi C. Flavonoid Composition of <i>Citrus</i> Juices. Molecules 2007, 12: 1641-1673.</p> <p>Line 332-387: According to the suggestion of the reviewer, Line 332-387 has been moved to the results section.</p> <p>In the abstract, the statement that this was a placebo-controlled study has been included.</p> <p>All the figures have been modified</p> <p>Citrus fruits and Citrus juices stand out among the most common phenolic rich dietary sources [22]. Epidemiological studies have shown an inverse association between risk and the intake</p>
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	<p>Add general comments that this therapy may be helpful for non-autistic individuals with allergic rhinitis</p>	<p>level of some particular flavonoids, but further clinical trials are needed to assess a more precise correlation between the level of flavonoid intake and the human health benefits.</p> <p>The nasal spray based on extract of lemon pulp tested in this work has been used for the treatment of allergic rhinitis in autistic subjects, in order to avoid possible harmful side effects related to traditional therapy long term, but certainly could also be applied to non- autistic. Moreover, the advantage of this sprays is that it could be administered in very small children, being devoid of alcohol.</p>
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<p>Minor REVISION comments</p>	<p>Line 49-62 – the discussion of flavonoids should have its own paragraph</p> <p>Lines 101-114 – the health claims for lemon need references</p> <p>Line 119-120 should be moved to the end of the intro, with a transition sentence.</p> <p>Line 143-144 – the scale of 0-3 is unclear and needs more explanation of each number (0, 1, 2, 3)</p> <p>Line 157 “cell phones” – typo?</p> <p>Line 202: “ast cells” – should be “mast cells”</p> <p>Table 1 – for number of cells observed, please clarify the volume or area examined</p> <p>Table 3 – the before and after colors are too similar</p>	<p>Line 49-62: the authors have added a new paragraph to the discussion of flavonoids</p> <p>Lines 101-114: the authors have added a new reference to the health claims for lemon [22] 22 Gattuso G, Barreca D, Gargiulli C, Leuzzi U, Caristi C. Flavonoid Composition of <i>Citrus</i> Juices. <i>Molecules</i> 2007, 12: 1641-1673.</p> <p>Line 119-120: the sentence has been moved in the introduction and modified</p> <p>Line 143-144: the scale has been clarified.</p> <p>Line 157: “cell phones – typo” has been replaced with cell phenotype</p> <p>Line 202: “ast cells” has been replaced with mast cells.</p> <p>Table 1: the table has been clarified.</p> <p>Table 3: the colors have been changed.</p>
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<u>Optional/General</u> comments	<p>This is a very interesting study with very striking results, but it needs a total rewrite to correct the grammar, and clarification of study procedures and results.</p> <p>Did the study receive approval from a human subjects board? Did the parents sign informed consents about the study including possibility of receiving a placebo?</p>	<p>As suggested by reviewer the text was revised for the english language and study procedures and results were clarified, in addition the references were implemented and the order was changed.</p> <p>The study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures were according to those approved by Federico II University Ethics Committee. Moreover, after describing the design of the study, all children parents signed the informed consent form about the study including possibility of receiving a placebo.</p>
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