Author's response to reviews

Title: A new paradigm in respiratory hygiene: modulators of airway secretions to improve cough interaction.

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Author's response to reviews: see over
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The BioMed Central Editorial Team
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RE: RR paper - MS: 2712263386004629

We are submitting the attached amended manuscript, “A new paradigm in respiratory hygiene: modulators of airway secretions to improve cough interaction.”, for publication in Respiratory Research. We have addressed the reviewers’ comments, and hope you find the amended article acceptable.

Sincerely,

Malcolm King, PhD, FCCP
Professor, Department of Medicine
Reviewer #1  Terry Dwyer

General Comments

Compulsory Revisions:

1. An abstract has been added.

2. Further to the comments of Reviewer #1 related to the identification of the two agents used in this study, we have clearly identified them in the different sections of the article.

3. Regarding the Reviewer’s comments on the statistical test to use, we have included the results obtained when Newman-Keuls test analysis was carried out.

4. Regarding the Reviewer’s comments on Tables that were included, we have eliminated all of them, incorporating the data in the text as appropriate. The levels of significance have been incorporated in the figures as asterisks, as suggested.

5. Regarding the number of observations, they have been incorporated in the different sections of the article.

6. Regarding the Reviewer’s comments on the spinnability data, we have incorporated these values directly in Figure 2.

7. Regarding the Reviewer’s comments that the level of significance must be shown in Figure 2, we have complied with that.

8. Regarding the question posed by the Reviewer on "whether the gum mixture ever made it out of the machine", we report in the Results section "It was also observed that as the added volume of XL “B” (borate) increased, the size of the droplets formed after the airflow interaction increased; hence few, big cohesive droplets were formed, which did not reach the target but did fall in the paper placed immediately below the exit."

9. Regarding the question posed by the Reviewer on “What did ‘C’ do?”, we found that applying mucomodulator “C” (CaCl2) on the frog palate seems to moderately slow the way that native frog mucus is transported by ciliary action in the epithelial model when using the lower concentration, but did not significantly change MTV when medium and high concentrations were used. This is shown in Figure 6, which is a new Figure.
Minor Essential Revisions

1. We have complied with the comments, adding the affiliation of the authors, and disclosing the sources of financial support.

Discretionary Revisions

Regarding the Reviewer’s comments that "Sodium borate crosslinking seems to do the opposite as the agent tested here; if so why?" In model studies using vegetable polysaccharides, sodium tetraborate preferentially raises elasticity relative to viscosity, and current knowledge prior to the development of mucomodulators indicated that tetraborate solutions would favour mucociliary clearability at the expense of cough clearability and aerosolizability (King & Rubin 1994).

Now it appears that cough clearability and aerosolizability are both linked to cohesivity, but in opposite senses, at least within the range of the current study. Thus it appears that sodium tetraborate solutions, by altering mucous gel cohesivity, can decrease aerosolizability (fine aerosol formation during coughing) while increasing cough clearability (bulk clearance of mucus).
Reviewer #2  Bruce Rubin

General Comments

Compulsory Revisions:

1. Regarding the Reviewer’s comments on the major shortcoming of the manuscript, the use of "secret" drugs, we have clearly identified them in the different sections of the article. This was also required by Reviewer #1. We have now finalized a patent application related to some potential uses of these products.

2. Further to the comments of Reviewer #2 related to introducing new and redefining existing terminology, we find this very topic very interesting. Stedman’s Medical Dictionary (Williams and Walker) describes modulation as following from the Latin modulari to measure off properly. The Concise Dictionary of English Etymology (Oxford University Press) describes modulate as follows: regulate, adjust, attune. With this approach, by using our mucomodulators, we intend to adjust or regulate the mucin macromolecules that give respiratory mucus its physical characteristics in order to minimize the aerosolization that facilitates transmission of airborne diseases. It should be noted that it is not “normal” to cough and aerosolize particles that can be breathed in by others, although it is common. Thus a potential therapy that could reduce this tendency to aerosolize particles when coughing should be considered a form of modulation in the sense of restoring a balance or state of homeostasis. These comments have been incorporated in the Discussion.

3. Regarding the comments of the Reviewer on quantifying the results and describing the number of experiments, we have indicated these data in the different sections in the article.

4. Regarding the comments of the Reviewer on “Why to use mucus simulants and not frog or human mucus?”, what we report in this article is the very first brick of what we would like to build. We consider this the first step of a process and will continue with the steps suggested by the Reviewer.

Minor Essential Revisions

1. We have thoroughly reviewed this manuscript with a view to editing, and hopefully have an acceptable final product.