Author's response to reviews

Title: Effects of Lactobacillus salivarius-containing tablets on caries risk factors: open-label clinical trial

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Author's response to reviews: see over
Replies to the reviewers’ comments.

Dr. Kamio

#1. Thank you for your comment. The misspelled words have been corrected.

#2. In previous studies, we examined salivary flow, salivary pH, and salivary buffering capacity after 2 weeks of orally administering *L. salivarius* WB21-containing tablets (Suzuki N et al. J Breath Res, 2012, 6:017106; Suzuki N et al. Oral Surg Oral Med Oral Pathol Oral Radiol, 2014, 117:462-470). Salivary flow significantly increased, but salivary pH remained unchanged. Although the results are not shown in those articles, the buffering capacity did not change. We describe our previous studies in the revised manuscript.

Dr. Oho

Thank you for your helpful comments. We have considered your comments thoroughly and have revised the manuscript. The principal aim of the study was to confirm that oral consumption of lactobacilli-containing tablets does not increase the risk of caries. As you suggested, we initially conducted a statistical analysis of all four groups. Subsequently, we compared pairs of groups. The text has been revised based on the results of the new statistical analysis. In addition, baseline data for the study population were added to Table 1. Furthermore, Figures 1A-E are now presented as Table 3.

1. The *L. salivarius* WB21-containing tablet suppressed mutans streptococci levels compared with the xylitol-containing tablet, although there were no significant differences among the four groups. Coaggregation, growth inhibition of mutans streptococci, and reduced plaque acidogenicity have been reported as potential mechanisms by which lactic acid bacteria prevent dental caries. The effects of a single tablet containing *L. salivarius* WB21 and TI 2711 are unclear. We are currently examining them in *in vitro* assays.

2. Dentocult LB tests were performed shortly after taking the tablets in the present study. In our previous study, the level of lactobacilli in saliva increased after 2 or 4 weeks of continuous oral administration of *L. salivarius* WB21-containing products (Iwamoto T et al. Oral Surg Oral Med Oral Pathol Oral Radiol, 2010, 110:201-208;

3. The taste, flavor, and texture of the products are different. These factors may have contributed to the increased salivary flow in the \textit{L. salivarius} TI 2711 group. However, there was no significant difference among the four groups.

4. The reasons for the increase in salivary buffering capacity are unclear. We describe this in the Discussion section.

5. Figure 2 (Figure 1 in the revised manuscript) now shows raw data in order to make the changes in the mutans streptococci level more obvious.

6. Mutans streptococci were detected using Dentocult SM test. Class 0 represents 0 to 5 colonies, as detected by Dentocult SM. It does not necessarily mean that there were no colonies. If one colony was detected in a subject in Class 0, he/she was regarded as positive for mutans streptococci. Therefore, the detection frequency of mutans streptococci was greater than the sum of Classes 1 to 3. Baseline data for the study population were shown in the revised Table 1.

7. To address the reviewer’s comments, we initially used the Kruskal-Wallis test to test for differences between the four groups. There were significant differences in the level of lactobacilli and salivary buffering capacity. We then compared individual pairs of groups. We are very sorry for incorrectly describing the Wilcoxon rank-sum test as the Wilcoxon signed-rank test.