

Supplementary Material

Mean changes from baseline score in clinical symptoms

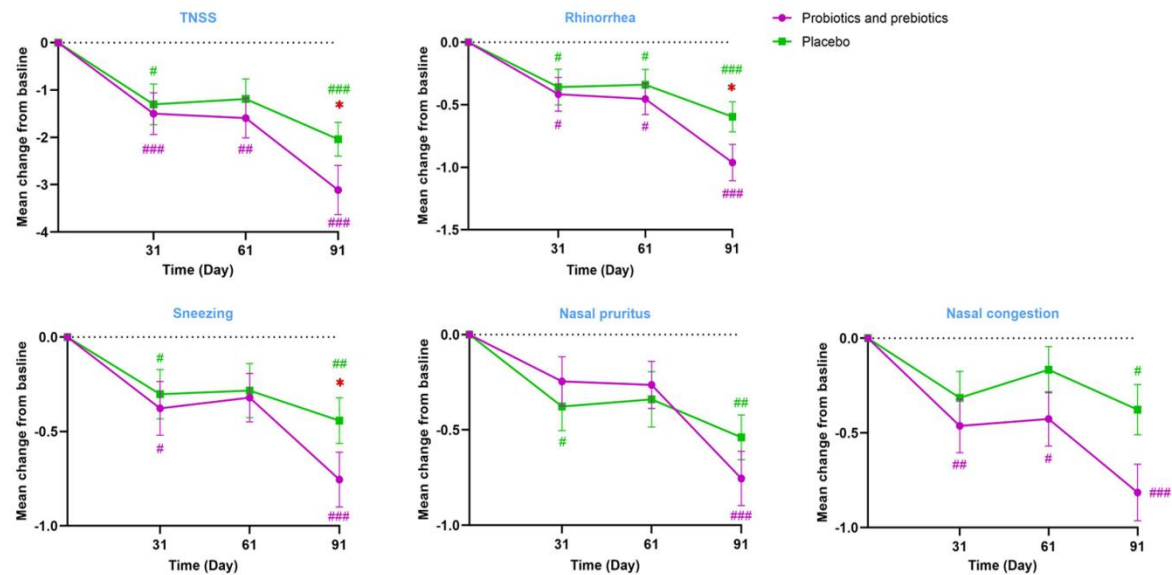


Fig. S1 Mean change from baseline score in clinical symptoms on days 31, 61, and 91. **A**, Mean change of TNSS. **B**, Mean change of rhinorrhea. **C**, Mean change of sneezing. **D**, Mean change of nasal pruritus. **E**, Mean change of nasal congestion. Data are expressed as mean \pm SE. Covariance analysis was used to compare differences from baseline scores between the two groups. # $P < 0.05$, ## $P < 0.01$, ### $P < 0.001$ for the difference from baseline within groups. * $P < 0.05$ for the difference between groups. TNSS, total nasal symptom score.

Table S1 Differences of VAS, RQLQ and FeNO between groups and within-group

| Items | | Baseline | D31 | D61 | D91 |
|------------|---------------------------|-------------|----------------|---------------|---------------|
| VAS | Probiotics and prebiotics | 20.2±7.5 | 15.8±7.9** | 15.3±9.1** | 10.8±9.7*** |
| | Placebo | 20.0±8.6 | 15.1±8.4** | 16.4±9.7* | 13.1±7.2*** |
| | Mean difference | | 0.6 | -1.1 | -2.3 |
| | (95% confidence interval) | | (-2.5, 3.7) | (-4.7, 2.4) | (-5.5, 0.8) |
| | <i>P</i> -Value | | 0.69 | 0.53 | 0.14 |
| RQLQ | Probiotics and prebiotics | 81.6±30.4 | 65.5±28.1** | 73.7±37.4 | 50.8±40.3*** |
| | Placebo | 79.0±28.6 | 66.0±37.9 | 69.1±42.3 | 52.4±31.2*** |
| | Mean difference | | -1.9 | 3.0 | -2.7 |
| | (95% confidence interval) | | (-13.3, 9.6) | (-10.9, 17.0) | (-15.7, 10.2) |
| | <i>P</i> -Value | | 0.75 | 0.67 | 0.68 |
| FeNO (ppb) | Probiotics and prebiotics | 492.2±239.7 | 461.0±252.3 | 454.6±183.2 | 393.1±152.7* |
| | Placebo | 520.7±236.6 | 496.3±229.1 | 456.6±181.8 | 389.3±174.0** |
| | Mean difference | | -24.1 | 19.0 | 10.7 |
| | (95% confidence interval) | | (-112.2, 63.9) | (-46.5, 84.4) | (-49.7, 71.2) |
| | <i>P</i> -Value | | 0.59 | 0.57 | 0.73 |

Data are expressed as mean ± SD. Wilcoxon rank sum test or t-test was used to compare differences in scores of VAS and RQLQ, and FeNO level from baseline within groups; covariance analysis was used to compare differences on days 31, 61, and 91 from baseline between the two groups. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ for the difference from baseline within groups. VAS, visual analog scale; RQLQ, rhinitis quality of life questionnaire; FeNO, fractional exhaled nitric oxide.

Table S2 Rate and intensity of Loratadine use between groups during the trial period

| Items | | 0-30 days | 31-60 days | 61-90 days | 0-90 days |
|--|---------------------------|-----------|------------|------------|-----------|
| Rate of Loratadine use [†] (%) | Probiotics and Prebiotics | 35.2 | 37.0 | 44.4 | 64.8 |
| | Placebo | 50.0 | 46.2 | 34.6 | 63.5 |
| | <i>P</i> -Value | 0.12 | 0.34 | 0.30 | 0.88 |
| Intensity of Loratadine use [‡] | Probiotics and prebiotics | 0.1±0.2 | 0.3±0.6 | 0.2±0.5 | 0.2±0.4 |
| | Placebo | 0.3±0.4 | 0.4±0.6 | 0.2±0.4 | 0.3±0.4 |
| | <i>P</i> -Value | 0.08 | 0.31 | 0.44 | 0.66 |

Data are % or mean ± SD. [†], Chi-square Test; [‡], Wilcoxon rank-sum test.

Table S3 Differences in microbiota abundance between groups at phylum level

| Species name | Time point | Baseline | D31 | D61 | D91 |
|------------------------------|---------------------------|----------|--------------|--------------|--------------|
| <i>Firmicutes</i> (%) | Probiotics and prebiotics | 78.7 | 56.7 | 62.3 | 64.5 |
| | Placebo | 72.9 | 73.1 | 76.1 | 73.9 |
| | <i>P</i> -Value | 0.06 | 0.001 | 0.001 | 0.007 |
| <i>Actinobacteria</i> (%) | Probiotics and prebiotics | 12.7 | 34.8 | 31.1 | 27.3 |
| | Placebo | 16.5 | 14.1 | 12.1 | 13.5 |
| | <i>P</i> -Value | 0.18 | 0.001 | 0.001 | 0.001 |

Data are expressed as mean abundance. Metastats analysis was used to compare differences between groups at different time points.

Table S4 Differences of intestinal beneficial bacteria between groups and within-group

| Bacteria | | Baseline | D31 | D61 | D91 |
|----------------------------------|---------------------------|----------|--------------|------------------|------------------|
| <i>Bifidobacterium</i> | Probiotics and prebiotics | 9.8±5.6 | 13.2±4.2*** | 14.0±2.9*** | 12.1±4.8*** |
| | Placebo | 10.9±4.7 | 10.5±5.3 | 10.9±4.1 | 10.0±5.2 |
| | Mean difference | | 3.5 | 4.1 | 3.1 |
| | (95% confidence interval) | | (1.1, 5.9) | (2.0, 6.1) | (0.9, 5.2) |
| | <i>P</i> -Value | | 0.004 | <0.001 | 0.005 |
| <i>Bifidobacterium animalis</i> | Probiotics and prebiotics | 0.3±2.0 | 2.0±4.5 | 1.3±3.4 | 1.1±2.9 |
| | Placebo | 0.8±3.0 | 0.6±2.3 | 0.2±1.3 | 0.3±1.8 |
| | Mean difference | | 1.8 | 1.7 | 1.3 |
| | (95% confidence interval) | | (0.4, 3.3) | (0.6, 2.7) | (0.2, 2.4) |
| | <i>P</i> -Value | | 0.02 | 0.002 | 0.02 |
| <i>Lactobacillus acidophilus</i> | Probiotics and prebiotics | 0.7±2.6 | 6.3±7.5*** | 7.2±7.6*** | 5.7±7.3** |
| | Placebo | 1.5±3.6 | 2.1±5.1 | 1.1±3.1 | 1.7±4.0 |
| | Mean difference | | 4.7 | 6.1 | 4.2 |
| | (95% confidence interval) | | (1.9, 7.5) | (3.6, 8.7) | (1.8, 6.5) |
| | <i>P</i> -Value | | 0.001 | <0.001 | <0.001 |
| <i>Lactobacillus</i> | Probiotics and prebiotics | 1.6±4.4 | 5.0±7.2* | 10.0±7.4*** | 11.2±6.4*** |
| | Placebo | 2.0±4.8 | 3.7±5.5 | 6.3±5.9 | 7.5±5.6 |
| | Mean difference | | 1.4 | 4.1 | 4.1 |

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|-------------------------------|---------------------------|----------|-------------|--------------|--------------|
| | (95% confidence interval) | | (-1.2, 4.0) | (1.3, 7.0) | (1.6, 6.5) |
| | <i>P</i> -Value | | 0.29 | 0.005 | 0.001 |
| <i>Bifidobacterium longum</i> | Probiotics and prebiotics | 9.2±6.5 | 12.7±5.6** | 14.0±4.4*** | 12.7±5.7*** |
| | Placebo | 10.5±6.2 | 10.3±5.8 | 11.1±5.1 | 11.6±5.2 |
| | Mean difference | | 3.2 | 4.0 | 2.0 |
| | (95% confidence interval) | | (0.3, 6.0) | (1.3, 6.7) | (-0.5, 4.6) |
| | <i>P</i> -Value | | 0.03 | 0.005 | 0.12 |

Data are expressed as mean ± SD. Wilcoxon rank sum test or t-test was used to compare differences in beneficial intestinal bacteria between groups at baseline and within groups; covariance analysis was used to compare differences from baseline in beneficial intestinal bacteria between groups. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ for the difference from baseline within groups.

Table S5 Differences of SCFA between groups and within-group

| SCFA | | Baseline | D31 | D61 | D91 |
|--------------------------------------|---------------------------|-----------------|--------------------|--------------------|--------------------|
| Total acids ($\mu\text{mol/g}$) | Probiotics and prebiotics | 80.6 \pm 30.4 | 63.6 \pm 42.4** | 61.4 \pm 33.4*** | 57.2 \pm 28.7*** |
| | Placebo | 83.4 \pm 30.2 | 89.4 \pm 49.6 | 83.9 \pm 35.5 | 87.3 \pm 49.1 |
| | Mean difference | | -20.3 | -21.4 | -27.5 |
| | (95% confidence interval) | | (-38.8, -2.0) | (-34.9, -7.9) | (-42.7, -12.3) |
| | <i>P</i> -Value | | 0.03 | 0.002 | 0.001 |
| Acetate (%) | Probiotics and prebiotics | 62.9 \pm 9.1 | 79.7 \pm 16.9*** | 77.6 \pm 15.1*** | 74.9 \pm 14.5*** |
| | Placebo | 63.1 \pm 8.4 | 63.4 \pm 9.8 | 64.8 \pm 7.9 | 63.7 \pm 9.1 |
| | Mean difference | | 19.8 | 12.5 | 12.4 |
| | (95% confidence interval) | | (13.1, 26.5) | (6.6, 18.4) | (7.1, 17.6) |
| | <i>P</i> -Value | | <0.001 | <0.001 | <0.001 |
| Propionate (%) | Probiotics and prebiotics | 16.6 \pm 6.1 | 9.9 \pm 9.6*** | 10.5 \pm 9.2*** | 12.1 \pm 9.1* |
| | Placebo | 17.5 \pm 7.0 | 17.9 \pm 8.1 | 18.3 \pm 8.4 | 18.0 \pm 8.5 |
| | Mean difference | | -6.6 | -7.3 | -5.3 |
| | (95% confidence interval) | | (-9.9, -3.2) | (-10.7, -4.0) | (-8.6, -1.9) |
| | <i>P</i> -Value | | <0.001 | <0.001 | 0.002 |
| Butyrate (%) | Probiotics and prebiotics | 15.8 \pm 7.3 | 8.5 \pm 10.3*** | 10.2 \pm 10.5*** | 10.6 \pm 9.7** |

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|-----------------|---|----------|--------------|--------------|---------------|
| | Placebo | 15.4±6.8 | 14.9±7.6 | 13.9±6.4 | 14.8±6.7 |
| | Mean difference | | -5.6 | -3.8 | -3.9 |
| | (95% confidence interval) | | (-9.2, -2.1) | (-7.1, -0.5) | (-7.1, -0.6) |
| | <i>P</i> -Value | | 0.002 | 0.03 | 0.02 |
| Isobutyrate (%) | Probiotics and prebiotics | 1.3±1.2 | 0.6±0.6*** | 0.5±0.5*** | 0.6±0.9*** |
| | Placebo | 1.1±1.1 | 1.0±1.0 | 0.8±0.7 | 0.9±1.0 |
| | Mean difference | | -0.5 | -0.3 | -0.3 |
| | (95% confidence interval) | | (-0.8, -0.2) | (-0.6, -0.1) | (-0.6, 0.1) |
| | <i>P</i> -Value | | 0.001 | 0.006 | 0.12 |
| Valerate (%) | Probiotics and prebiotics | 1.5±1.5 | 0.6±0.9*** | 0.7±1.0*** | 0.7±1.4*** |
| | Placebo | 1.3±1.4 | 1.2±1.3 | 1.0±1.2 | 1.1±1.2 |
| | Mean difference | | -0.6 | -0.4 | -0.4 |
| | (95% confidence interval) | | (-1.0, -0.2) | (-0.8, 0.1) | (-0.8, 0.007) |
| | <i>P</i> -Value | | 0.003 | 0.09 | 0.05 |
| Isovalerate (%) | Probiotics and prebiotics | 2.0±1.9 | 0.8±0.8*** | 0.6±0.8*** | 1.0±1.6*** |
| | Placebo | 1.6±1.6 | 1.5±1.4 | 1.2±1.1 | 1.5±1.8 |
| | Mean difference (95% confidence interval) | | -0.6 | -0.5 | -0.4 |
| | | | (-1.1, -0.1) | (-1.0, 0.04) | (-1.1, 0.2) |
| | <i>P</i> -Value | | 0.02 | 0.07 | 0.20 |

Data are expressed as mean \pm SD. Wilcoxon rank sum test or t-test was used to compare differences between groups at baseline and within groups; covariance analysis was used to compare differences in SCFAs from baseline between groups. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ for the difference from baseline within groups. SCFA, short-chain fatty acid.

16S rRNA gene sequencing data are available in the Figshare public repository (<https://doi.org/10.6084/m9.figshare.25283461>).