

Dipotassium Glycyrrhizate Selectively Inhibits the Periodontal Pathobiont *Porphyromonas gingivalis**¹ A New Approach to Periodontal Disease Prevention: Balancing the Oral Microbiome*²

Lion Corporation (Representative Director, President and Executive Officer: Masayuki Takemori) has discovered the selective inhibitory effect of dipotassium glycyrrhizate (hereinafter GK2) on a specific periodontal disease-causing bacterium, a function that helps balance the oral microbiome.*³ The findings of this research were published in the September 2024 issue of the Journal of Oral Biosciences, a global journal devoted to the dissemination of fundamental knowledge concerning every aspect of oral biology, and relevant information will be presented at the 68th Autumn Meeting of the Japanese Society of Periodontology at the Niigata Convention Center in Niigata prefecture from Friday, October 17 to Saturday, October 18, 2025.

*1 *Porphyromonas gingivalis* (*P. gingivalis*), a representative bacterial species associated with periodontal disease. This bacterium not only causes inflammation in the gums but has also been reported as a keystone bacterium that disrupts the oral microbiome. (G. Hajishengallis, et al. Low-abundance biofilm species orchestrates inflammatory periodontal disease through the commensal microbiota and complement. *Cell Host Microbe*, 10(5)(2011):497–506., J. Mysak, et al. Porphyromonas gingivalis: major periodontopathic pathogen overview. *J Immunol Res*, (2014):476068.)

*2 Refers to groups of bacteria that live in the oral cavity

*3 The action of regulating the balance of the oral microbiome to a state with a low proportion of *P. gingivalis*

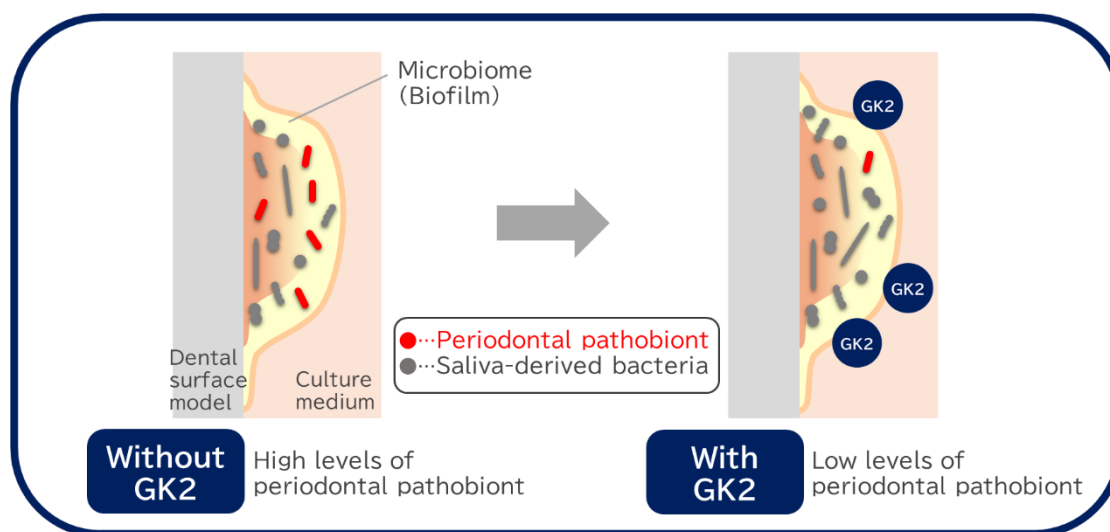


Figure 1. Summary of Research Findings (Image)

■ Research Background

Periodontal disease is a disease of the mouth caused by oral bacteria that can lead to tooth loss. As the disruption of the oral microbiome has been linked to the onset and progression of periodontal disease,*⁴ achieving a balanced oral microbiome, along with the use of conventional plaque control methods, is believed to play a key part in its prevention. For more than 10 years, Lion has conducted research focused on the importance of the oral microbiome. This research revealed that individuals with disrupted oral microbiomes harbored high levels of periodontal pathobionts in their saliva even after dental treatment.*⁵ Based on these findings, we conducted this study on the premise that effective prevention of the onset and recurrence of periodontal

disease requires first selectively inhibiting *P. gingivalis*, a periodontal pathobiont known to be a potential factor in oral microbiome disruption, and then restoring oral microbial balance.

*4 M. Kilian, et al. The oral microbiome – an update for oral healthcare professionals. *British Dental Journal*, 221(10)(2016):657–666.

*5 K. Yama, et al. Dysbiosis of oral microbiome persists after dental treatment-induced remission of periodontal disease and dental caries. *mSystems*, 26;8(5)(2023):e0068323.

■ Key Research Results

1. Established a proprietary system capable of assessing the inhibitory effect on oral microbiome imbalance

Based on an experimental model*⁶ developed by the world-renowned dental research institute ACTA (Academisch Centrum Tandheelkunde Amsterdam), we collaborated with Kanagawa Dental University to investigate a new experimental system for evaluating the inhibitory effects on periodontal pathobionts in the microbiome. Leveraging the unique expertise we have accumulated over the years through extensive research in oral microbiology, we successfully established a proprietary system capable of assessing microbiome where periodontal pathogens coexist with oral bacteria derived from human saliva.

*6 The Amsterdam Active Attachment biofilm model is an experimental model capable of forming and evaluating biofilms composed of human-derived oral bacteria. Using human saliva, it can form an oral microbiome comprising multiple oral bacteria on a dental surface model. Furthermore, it features the ability to easily modify culture medium components, allowing the presence of target bacteria to be adjusted through medium optimization.

2. Confirmed GK2's effect on balancing the oral microbiome

In our search for components with inhibitory effects against *P. gingivalis*, we discovered that GK2 suppresses its proliferation. Furthermore, using the evaluation system established in (1), we confirmed that adding GK2 significantly reduced the level of *P. gingivalis* within the microbiome, approaching a balance between the bacteria present in a microbiome without added *P. gingivalis**⁷ (Figure 2).

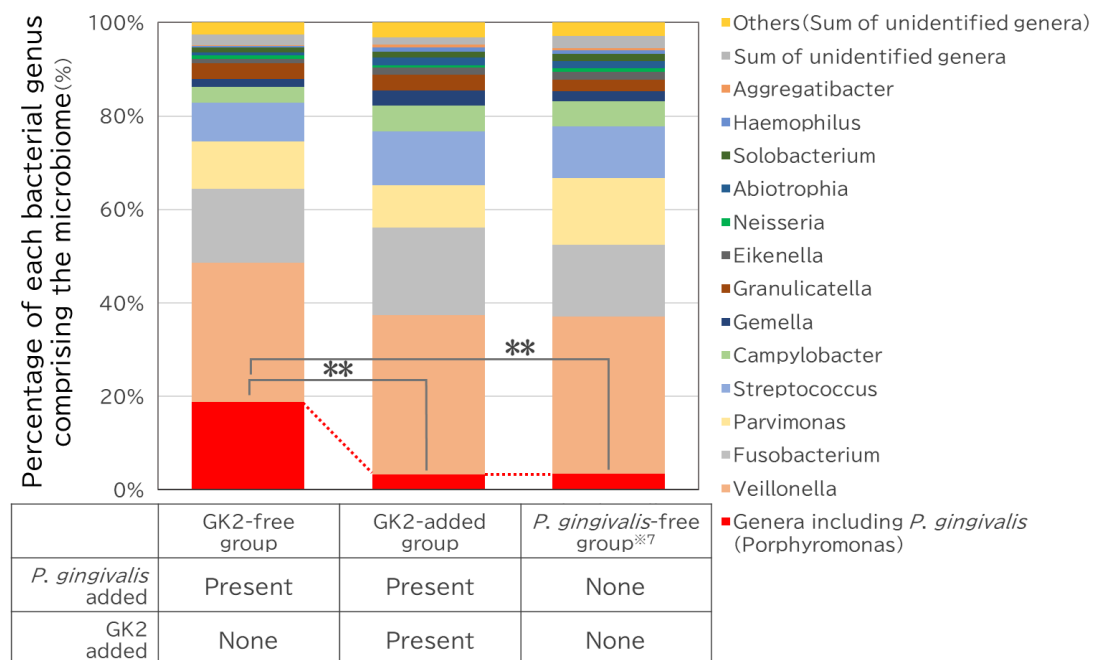


Figure 2. Percentage of each bacterial genus comprising the microbiome
Microbiome formation conditions: Cultured for one week at 37° C under anaerobic conditions

** Steel-Dwass test results for Porphyromonas genus

*7 A model representing a state where the microbiome has been undisturbed by *P. gingivalis*. The red segments in the bar graph for the group without added *P. gingivalis* indicate the levels of bacteria other than *P. gingivalis* belonging to the genus Porphyromonas.

Furthermore, a principal coordinate analysis*⁸ was performed to understand differences in the overall bacterial composition of the microbiome. This analysis showed that group supplemented with GK2 approached those without *P. gingivalis* more closely than group without GK2 supplementation (Figure 3). These results suggest that GK2 suppresses *P. gingivalis* within the microbiome and has a balancing effect on the oral microbiome.

*8 A method for plotting bacterial information constituting microbiomes in two dimensions and analyzing similarity. Microbiomes with similar compositions are positioned closer together.

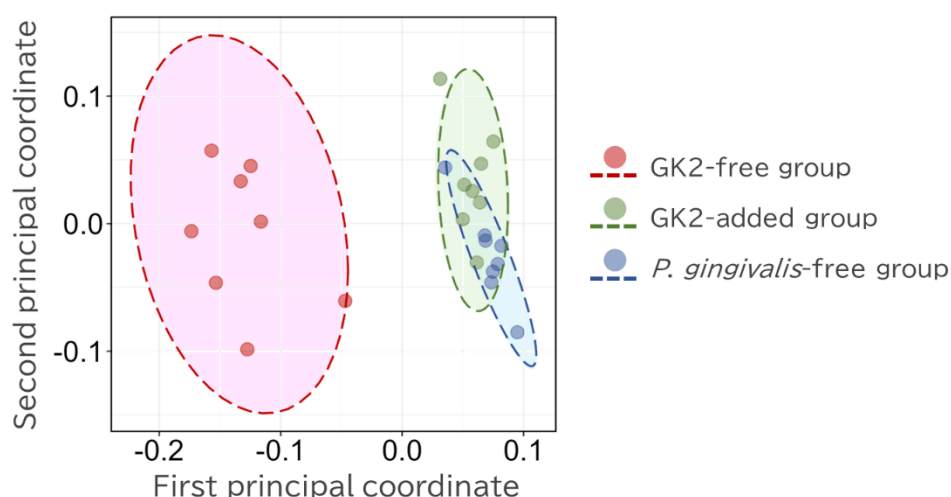


Figure 3. Evaluation of microbiome similarity

The dotted-line enclosures indicate the predicted distribution range (95% confidence interval, t-distribution) from each plot with N=8 conditions.

Based on the above results, it has been demonstrated that GK2 reduces the proportion of *P. gingivalis* present in the oral microbiome and prevents bacterial composition disruptions caused by *P. gingivalis*. Consequently, it is expected that GK2 suppresses the disruption of the oral microbiome caused by *P. gingivalis*, thereby contributing to the suppression of inflammation that leads to periodontal disease.

■Future Outlook

Lion believes that maintaining oral health requires not only temporarily eliminating the causative bacteria but also balancing the entire oral microbiome through preventive “oral flora care” to guard against recurring issues.*⁹ We will continue to focus on the importance of preventive approaches based on this new perspective, aiming to contribute to promoting healthy habits.

*9 Microbiome Control Research Aiming to Prevent Repeated Issues by Building Beneficial Relationships Between Humans and Microorganisms

<https://www.lion.co.jp/ja/rd/basic/analysis/case01.php>

【Published Paper】

Title: “Dipotassium Glycyrrhizate Prevents Oral Dysbiosis Caused by *Porphyromonas gingivalis* in an *in vitro* Saliva-Derived Polymicrobial Biofilm Model”

Authors: Kanta Ohara, Kiyoshi Tomiyama, Takuma Okuda, Kota Tsutsumi, Chikako Ishihara, Daiki Hashimoto, Yuto Fujii, Takashi Chikazawa, Kei Kurita, Yoshiharu Mukai

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【Presentation Information】

Conference: The 68th Autumn Meeting of the Japanese Society of Periodontology

Presentation Title: “Effects of Dipotassium Glycyrrhizate on Dysbiosis of Polymicrobial Biofilm Model”

Date: Friday, 17 October – Saturday, 18 October 2025

Venue: TOKI MESSE, Niigata Convention Center (Niigata, Japan)

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【Related Information】

- Oral Care From Infancy Is Crucial! Children Aged 6 to 18 Months Are Going Through a critical Development Stage in Which Their Oral Microbiome Is Rapidly Maturing Toward That of an Adult [Japanese only]

https://doc.lion.co.jp/uploads/tmg_block_page_image/file/8021/20220324.pdf

- The Foundation of the Oral Microbiome Is Established by Age 3—Longitudinal Study of Infants and Young Children Clarifies the Period of Accelerated Oral Microbiome Formation [Japanese only]

https://doc.lion.co.jp/uploads/tmg_block_page_image/file/10319/20241114_01.pdf

- Lion Discovers that Oral Microbiomes of Those with Dental Caries and Periodontal Disease Differ from Those with Healthy Oral Condition, Even After Dental Treatment: Aiming to Propose Preventive Methods that Take into Account the Oral Microbiome

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