

Exploratory Single-Arm Trial on the Effects of keora™ Oral Moisture Mist/Gel on Halitosis and Periodontitis

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Abstract

Objectives

Dry mouth reduces the self-cleansing and antimicrobial properties of saliva, which can worsen periodontitis and halitosis caused by volatile sulfur compounds (VSCs) in a self-reinforcing cycle. This exploratory, single-arm trial evaluated the short-term and sustained effects of the oral moisturizer keora™ Oral Moisture Mist/Gel on halitosis, periodontal inflammation, and oral environmental parameters in patients with periodontitis, dry mouth, or halitosis.

Materials and Methods

Twenty subjects took part. Concentrations of three VSCs (hydrogen sulfide, methyl mercaptan, and dimethyl sulfide) were measured 10 minutes after mist application, and again on Day 8 after five days of home brushing with the gel. Periodontal Inflamed Surface Area (PISA), resting and stimulated salivary flow rates, Tongue Coating Index (TCI), oral bacterial count, salivary viscosity, masticatory efficiency, occlusal force, and oral moisture level were also assessed.

Results

VSC concentrations fell sharply 10 minutes after mist application (hydrogen sulfide: 87.0% reduction; methyl mercaptan: 80.2% reduction; dimethyl sulfide: 57.3% reduction) and remained low with continued use. From Day 1 to Day 8, all three VSCs, PISA, oral bacterial counts, and TCI scores decreased significantly, while salivary flow rates and oral moisture increased significantly.

Conclusions

keora™ Oral Moisture Mist and Gel rapidly reduced halitosis and, over one week, also improved periodontal inflammation, lowered oral bacterial load, and enhanced oral physiological function. Larger controlled trials are warranted.

Clinical Relevance

Combining an immediate-acting mist with a moisturizing gel for daily brushing may offer clinicians a practical, dual-action strategy for managing patients whose halitosis and periodontal inflammation are compounded by xerostomia.

Trial registration

Introduction

The number of patients reporting xerostomia (dry mouth) has risen in recent years, driven by an aging society and increased everyday stress [1]. Xerostomia is more than a discomfort: it substantially weakens saliva's natural functions, including self-cleansing, antimicrobial activity, buffering, and tissue repair [2]. This allows the oral microbiota to shift and colonize more readily, which increases periodontitis activity and worsens halitosis — a condition driven mainly by volatile sulfur compounds (VSCs) [3]. Because of this vicious cycle, modern periodontal care increasingly requires an approach that goes beyond mechanical plaque control to also improve the moisture balance of the oral environment.

We focused on the keora™ series of oral moisturizers (Nissin Dental Products Inc., Kyoto, Japan), which combine strong moisturizing power with tissue-protective and antimicrobial properties. Rather than offering only a temporary feeling of moisture, these products are formulated to improve the oral environment at a more fundamental level.

The series contains high-molecular-weight polysaccharides such as hyaluronic acid and collagen, which support both water retention and tissue repair, together with anti-inflammatory ingredients that help limit colonization by oral pathogens and calm inflammation in the local microenvironment. The two formulations play distinct clinical roles. keora™ Oral Moisture Mist has high fluidity and spreads instantly over the fine irregularities of the oral mucosa and tongue surface, giving a chemical deodorizing/adsorbing effect while also forming a thin coating film that physically limits gas release. keora™ Oral Moisture Gel, by contrast, is viscoelastic and adhesive, and serves as a carrier during brushing: it keeps active ingredients in contact with the gingival sulcus and deep lingual papillae for longer, reduces frictional irritation from brushing, and supports anti-inflammatory and metabolic processes in the tissue.

This study therefore had two aims: first, to evaluate the acute halitosis-reducing effect of keora™ Oral Moisture Mist 10 minutes after a single application; and second, to explore — through a single-arm trial — how five subsequent days of home brushing with keora™ Oral Moisture Gel affected periodontal status, oral physiological function, and the oral microbial environment.

This study is distinguished by evaluating the moisturizer's efficacy from several angles rather than relying on a single subjective measure such as a reported sensation of moisture. Objective indicators were drawn from three domains: clinical status, environment (microbiology and chemistry), and oral function. For clinical status, instead of relying solely on pocket-probing depth, we calculated the Periodontal Inflamed Surface Area (PISA) — which reflects the total area of micro-ulceration and vascularized tissue within periodontal pockets — to sensitively quantify how much inflammation resolved with gel use and brushing [4]. We also tracked the Tongue Coating Index (TCI) to capture macroscopic changes in oral deposits [5]. For the microbiological and chemical domain, we monitored total bacterial counts with an oral bacteria counter and separately quantified the three VSCs (hydrogen

sulfide:H₂S, methyl mercaptan:CH₃SH, and dimethyl sulfide:DMS) by gas chromatography, allowing us to examine how periodontal improvement related to breath chemistry and total bacterial load [6]. For oral physiological function, we measured mucosal moisture with an oral moisture meter along with resting and stimulated salivary flow, to see whether the moisturizing gel and the mechanical stimulation of brushing secondarily activated the host's own salivary gland function and supported a broader functional recovery.

Most earlier studies of oral moisturizers (gels, sprays, mouthwashes) have focused on short-term, symptomatic effects seen soon after use, such as temporary odor masking or a physical sensation of moisture [7, 8]. Comparatively little clinical research has shown that one week of continuous gel use restores intrinsic physiological functions – mucosal hydration and salivary secretion – in a way that is directly linked to a meaningful reduction in periodontitis activity (PISA) and a lower total oral bacterial count, as one integrated process [9]. This study aims to show that continuously managing the oral moisture environment does more than relieve short-term discomfort: it can help drive a broader cycle of oral health improvement.

Materials and Methods

Study design and ethical considerations

This study was an exploratory, prospective, single-center, single-arm clinical trial conducted at Hiroshima University Hospital. The protocol was approved by the Certified Clinical Research Review Committee of Hiroshima University (Approval No. CRB2025-0002) and complied with Japan's Clinical Research Act and the Declaration of Helsinki. Written informed consent was obtained from all subjects before participation. The trial was registered in the Japan Registry of Clinical Trials (jRCT) under registration number jRCTs061250080.

Subjects and eligibility criteria

Subjects were recruited from outpatients aged 18 years or older attending the Department of Periodontics at Hiroshima University Hospital. Eligible participants had been diagnosed with periodontitis requiring periodontal treatment or supportive periodontal therapy (SPT), had at least 15 remaining teeth, and reported or requested evaluation for oral dryness or halitosis. Participants also needed to be available for clinic visits on the study start date and again 7 days later, at the same time of day, and to provide written informed consent. The sample consisted of 20 participants (12 men and 8 women), with a mean age of 76.9 ± 7.1 years.

Exclusion criteria were: a history of severe hypersensitivity or allergy to components of keora™ Oral Moisture Mist/Gel; active periodontal treatment or professional mechanical cleaning within 1 month before consent; systemic antimicrobial use within 1 month before consent, or oral, intravenous, or ophthalmic antibiotic use within 14 days before the intervention; intravenous or oral immunosuppressant

or steroid use within 14 days before the intervention; an anticipated ongoing need for antibiotics or anti-inflammatory drugs during the study; a Plaque Control Record (PCR) of 20% or less before the intervention; difficulty holding or moving a toothbrush in the mouth; an expected change in living environment during the study; pregnancy, lactation, or possible pregnancy; or any condition judged by the investigator to make the subject unsuitable.

Because this study compares each patient's own measurements before and after the intervention rather than comparing between patients, confounders such as systemic disease and lifestyle did not require extensive control. Based on prior literature, the target sample size was set at 20 subjects [10].

Intervention protocol

The clinical timeline comprised a run-in and baseline day (Day 1), a home-care period (Days 3–7), and a final evaluation (Day 8) (Fig. 1).

Day 1 (baseline evaluation and mist intervention): subjects underwent baseline oral, periodontal, halitosis, and oral function examinations. A single dose of 0.6 g keora™ Oral Moisture Mist (Nissin Dental Products Inc., Kyoto, Japan) was then applied, and halitosis was re-measured exactly 10 minutes later to assess the immediate gas-reduction effect. A 1-day washout period followed (Day 2), during which subjects used their usual oral hygiene routine without the study products.

Days 3–7 (home-care period): subjects applied 0.6 g of keora™ Oral Moisture Gel (Nissin Dental Products Inc., Kyoto, Japan) after their normal morning and evening toothbrushing, followed by 5 minutes brushing with the gel, for a total of 5 days.

Day 8 (final evaluation): clinical, microbial, and functional assessments were repeated using the same methods as on Day 1.

Clinical and periodontal assessment

Halitosis measurement

VSC concentrations were measured with a gas chromatography system (Oral Chroma; Japan Dental Supply, Tokyo, Japan), as previously described [6]. Measurements were taken between 9:00 and 11:00 am. Subjects kept their mouths closed for 1 minute before sampling; a disposable 1 mL syringe was then used to collect 1 mL of oral air, which was injected into the device. VSCs were analyzed automatically and reported in ppb. The oral malodor thresholds used in this study were those reported previously: hydrogen sulfide > 112 ppb, methyl mercaptan > 26 ppb, and dimethyl sulfide > 8 ppb [11].

Periodontal Inflamed Surface Area (PISA)

Periodontal status was assessed by a calibrated examiner. PISA (mm²) was calculated from periodontal pocket depth (PPD) and bleeding on probing (BOP) at six sites per tooth, using a validated algorithm to quantify total inflammatory burden [4].

Resting saliva collection

Subjects avoided eating, drinking, smoking, and toothbrushing for 30–60 minutes before testing, then relaxed and allowed saliva to pool naturally, spitting it into a container over 5 minutes.

Stimulated saliva collection

After the same 30–60 minute preparation period, subjects chewed a tasteless, odorless gum (paraffin gum) for 5 minutes and spat the resulting saliva into a container; the volume (mL) collected over 5 minutes was measured.

Tongue coating evaluation

Tongue coating was scored with the Tongue Coating Index (TCI). The tongue surface was divided into nine regions, each scored on a 0–2 scale (maximum 18, minimum 0), and the total was expressed as a percentage [12].

Oral bacterial count

A Panasonic bacterial counter (NP-BCM01-A; Panasonic Corporation, Osaka, Japan) measured bacterial concentration (CFU/mL) on a seven-point scale using dielectrophoresis and impedance spectroscopy. A dedicated swab was used to sample the tongue surface, mixed with the supplied liquid in a disposable cup, and measured in the device.

Oral moisture level

Oral moisture was measured with an oral moisture meter (Mucus®, approval No. 22200BZX00640000; LiFE Co., Ltd., Koshigaya, Saitama, Japan) at the midline of the tongue dorsum, 10 mm posterior to the tip, by pressing the sensor against the mucosa. Three measurements were averaged [13].

Salivary viscosity

Salivary viscosity (stringiness) was measured with a NEVA meter (IMI-0501; Ishikawa Iron Works Co., Ltd., Kobe, Japan). A 50-μL saliva sample was placed on the measuring platform, and the device's probe touched and automatically drew up the sample, recording the string length (mm) until it broke.

Masticatory efficiency

A gummy candy test (UHA Mikakuto Co., Ltd., Osaka, Japan) assessed chewing ability from the amount of glucose released. Subjects chewed the candy for 20 seconds, then spat it out with water into a

container; glucose concentration in the water was measured with a glucose sensor (GC Glucosensor GS-II; GC Corporation, Tokyo, Japan). The test was performed twice and averaged.

Occlusal force

Subjects bit down on a pressure-sensitive film (Dental Prescale II; GC Corporation, Tokyo, Japan) for approximately 3 seconds. The film was scanned and analyzed with dedicated software (Bite Force Analyzer; GC Corporation, Tokyo, Japan) to quantify and visualize the magnitude and balance of occlusal force across the dentition.

Statistical analysis

Continuous variables are expressed as mean $\pm$ SD. Paired comparisons between Day 1 and Day 8 (or Day 1 and 10 minutes post-mist) were made with the Wilcoxon signed-rank test. Relationships between the magnitude of change in paired parameters were assessed with Spearman's rank correlation coefficient (ρ). Principal component analysis (PCA) was used to summarize the interrelationships among parameters that changed significantly. A p value < 0.05 was considered statistically significant. Analyses were performed with EZR and JMP.

Results

Changes in intraoral measurements and clinical parameters

To capture both the short-term and medium-term effects of the intervention, we measured the immediate change in VSC concentrations from baseline (Day 1) to 10 minutes post-mist, and the longitudinal change in oral functional and biological indices from Day 1 to Day 8.

Ten minutes after mist application, all three VSCs — hydrogen sulfide (H_2S), methyl mercaptan (CH_3SH), and dimethyl sulfide (DMS) — fell markedly and consistently across subjects (Fig. 2, H_2S : 87.0% reduction, $p = 0.0002$; CH_3SH : 80.2% reduction, $p = 0.0001$; DMS: 57.3% reduction, $p = 0.001$).

From Day 1 to Day 8 (Table 1, Fig. 2), all three VSCs decreased significantly (H_2S : 194.20 ± 196.08 ppb to 33.80 ± 63.42 ppb, $p = 0.002$, threshold 112 ppb; CH_3SH : 38.35 ± 42.63 ppb to 5.65 ± 4.63 ppb, $p = 0.002$, threshold 26 ppb; DMS: 20.00 ± 17.01 ppb to 3.65 ± 1.95 ppb, $p = 0.0003$, threshold 8 ppb), consistent with previously reported clinical malodor thresholds [11]. PISA decreased substantially, from 255.62 ± 135.59 mm² to 64.33 ± 56.47 mm² ($p < 0.0001$), indicating a marked anti-inflammatory effect [4]. Oral bacterial count also decreased significantly, from 5.45 ± 0.60 to 4.40 ± 0.75 ($p = 0.0016$).

Table 1
Clinical, microbiological, and functional parameters at Day 1 and Day 8 (n = 20, mean $\pm$ SD)

Evaluation item	Day 1 (mean $\pm$ SD)	Day 8 (mean $\pm$ SD)	p value	Interpretation
Hydrogen sulfide (H ₂ S)	194.20 $\pm$ 196.08 ppb	33.80 $\pm$ 63.42 ppb	0.002	Significant decrease
Methyl mercaptan (CH ₃ SH)	38.35 $\pm$ 42.63 ppb	5.65 $\pm$ 4.63 ppb	0.002	Significant decrease
Dimethyl sulfide (DMS)	20.00 $\pm$ 17.01 ppb	3.65 $\pm$ 1.95 ppb	0.0003	Significant decrease
Periodontal Inflamed Surface Area (PISA)	255.62 $\pm$ 135.59 mm ²	64.33 $\pm$ 56.47 mm ²	< 0.0001	Significant decrease
Resting salivary flow rate	0.35 $\pm$ 0.28 mL/min	0.50 $\pm$ 0.33 mL/min	0.002	Significant increase
Stimulated salivary flow rate	1.10 $\pm$ 0.55 mL/min	1.25 $\pm$ 0.62 mL/min	0.0368	Significant increase
Tongue Coating Index (TCI)	54.16 $\pm$ 15.59%	38.89 $\pm$ 15.92%	< 0.0001	Significant decrease
Oral bacterial count (level)	5.45 $\pm$ 0.60	4.40 $\pm$ 0.75	0.0016	Significant decrease
Oral moisture level (moisture meter)	28.18 $\pm$ 2.43	29.55 $\pm$ 1.79	0.0212	Significant increase
Salivary viscosity	2.46 $\pm$ 0.72 mm	2.24 $\pm$ 0.47 mm	0.1242	No significant difference
Masticatory efficiency	168.85 $\pm$ 53.81 mg/dL	178.78 $\pm$ 39.41 mg/dL	0.3335	No significant difference
Occlusal force	766.74 $\pm$ 478.86 N	803.23 $\pm$ 369.88 N	0.6079	No significant difference

Resting salivary flow rate increased from 0.35 $\pm$ 0.28 to 0.50 $\pm$ 0.33 mL/min (p = 0.002), and stimulated salivary flow rate increased from 1.10 $\pm$ 0.55 to 1.25 $\pm$ 0.62 mL/min (p = 0.0368). TCI, scored with a validated nine-region method [12], decreased from 54.16 $\pm$ 15.59% to 38.89 $\pm$ 15.92% (p < 0.0001), and oral moisture (Mucus meter) increased from 28.18 $\pm$ 2.43 to 29.55 $\pm$ 1.79 (p = 0.0212).

Salivary viscosity (2.46 $\pm$ 0.72 mm to 2.24 $\pm$ 0.47 mm; p = 0.1242), masticatory efficiency (168.85 $\pm$ 53.81 mg/dL to 178.78 $\pm$ 39.41 mg/dL; p = 0.3335), and occlusal force (766.74 $\pm$ 478.86 N to 803.23 $\pm$ 369.88 N; p = 0.6079) all trended toward improvement but did not reach statistical significance, reflecting the varied clinical background of individual cases.

Correlations among changes in measured parameters

Spearman's rank correlation analysis was used to examine relationships between the magnitude of change (Day 8 minus Day 1) for each parameter (Fig. 3). The strongest positive correlation was between the change in oral bacterial count and the change in masticatory efficiency ($\rho = 0.61$), consistent with the established role of mastication in stimulating salivary flow and mechanical oral clearance [14]. Bacterial count change also correlated positively with PISA change ($\rho = 0.36$), suggesting that suppression of periodontal inflammation and improved chewing function are linked to changes in the oral microbiota.

Among halitosis-related gases, H₂S and DMS showed a mild positive correlation ($\rho = 0.32$), while H₂S and CH₃SH showed almost no correlation ($\rho = 0.08$), and DMS and CH₃SH showed a weak negative correlation ($\rho = -0.16$) – suggesting that, even within the same malodor category, these gases are produced and regulated through partly independent pathways.

Among salivary and dryness-related parameters, resting saliva change correlated positively with TCI change ($\rho = 0.43$) and stimulated saliva change ($\rho = 0.41$). Local moisture change showed only weak negative correlations with stimulated saliva change ($\rho = -0.20$) and bacterial count change ($\rho = -0.17$), following a distinct pattern from overall salivary secretion and bacterial dynamics. Occlusal force change correlated positively with CH₃SH change ($\rho = 0.39$), viscosity change ($\rho = 0.37$), and masticatory efficiency change ($\rho = 0.37$).

Comprehensive evaluation by multivariate analysis

Principal component analysis (PCA) was performed on the magnitude of change for all parameters to summarize their interactions and the distribution of subjects (Fig. 4). The first two components (PC1 and PC2) explained 26.5% and 19.2% of the variance, respectively (cumulative 45.7%).

On the biplot, the vectors for H₂S_diff and CH₃SH_diff ran almost parallel toward the negative PC1 direction, showing that these two gases behaved very similarly along the dataset's dominant axis of variation. DMS_diff and SalRest_diff (resting salivary flow) extended in the opposite, positive PC1 direction, indicating an opposing trend to the main halitosis-gas vectors. Moisture_diff extended strongly in the negative PC2 direction, forming a functional axis distinct from SalStim_diff and TCI_diff, which sat in the upper-right quadrant.

Projecting the subjects (IDs 1–20) onto this space showed clear groupings: subjects such as ID3, ID4, and ID6 (negative PC1) were mainly driven by changes in malodor gases, while subjects such as ID1 and ID20 (positive PC2) were mainly driven by changes in stimulated salivary flow. ID14, plotted in isolation at the far positive end of PC1, stood out with elevated DMS and resting salivary flow relative to the overall trend. Together, these results show that this integrated approach reveals not only isolated pairwise correlations but also meaningful, patient-level patterns of clinical change.

Discussion

This single-arm exploratory trial of keora™ Oral Moisture Mist/Gel, in patients with dry mouth, halitosis, and periodontitis, aimed to characterize the product's clinical effects and underlying mechanisms. The

most notable finding was a distinct two-stage halitosis-suppressing pattern: a rapid drop in VSC concentrations immediately after use (acute effect), followed by cumulative improvement in the underlying pathology (biological effect) after five days of continued use (Day 8).

Just 10 minutes after application, hydrogen sulfide and methyl mercaptan – the main contributors to halitosis – dropped sharply, in many cases below the detection threshold (Fig. 2). This immediate effect likely reflects both the physical rinsing action and chemical deodorizing/adsorbing properties of the mist, together with the mechanical suppression of gas release from the coating film it forms over the mucosa and tongue. VSC levels also remained low over the medium term (Day 8). Because effective halitosis care requires both immediate relief and a lasting, cause-directed effect, these results suggest the product meets both requirements. The combination of sustained low VSC levels at Day 8 with a substantial reduction in PISA – a precise marker of periodontal inflammation – suggests that the product's benefit goes beyond temporary masking and reflects a genuine anti-inflammatory, therapeutic effect.

Methyl mercaptan, a particularly malodorous VSC, is generally produced when periodontal pathogens such as *Porphyromonas gingivalis* metabolize sulfur-containing amino acids via methionine γ -lyase (encoded by the *mgl* gene) [6]. The parallel reduction in oral bacterial load and PISA observed here suggests that continued combined use of the mist and gel acted on both the bacterial source of halitosis and the underlying microenvironmental inflammation. This link was supported by the Spearman correlation analysis (Fig. 3), where the strongest correlation observed ($\rho = 0.61$) was between the change in oral bacterial count and the change in masticatory efficiency. Because the overall trend was a significant decrease in bacterial count alongside an improving trend in masticatory efficiency (Table 1), this positive correlation does not mean “more bacteria, better function”; rather, it indicates that cases with the largest functional gains also showed the most active turnover in the oral microbial community. Improved masticatory efficiency generally smooths food-bolus formation, stimulates salivary secretion through tongue and buccal-mucosa movement, and activates the mouth's mechanical self-cleansing mechanisms [14]. The significant positive correlation between bacterial count change and PISA change ($\rho = 0.36$) further supports cross-talk between oral function, host immunity, and the microbial environment, consistent with a sequence in which better oral moisture and chewing function contribute to resolving tissue inflammation, which in turn feeds back into microbiota composition.

Applying the product also increased both resting and stimulated salivary flow, contributing to improved oral moisture. Reduced salivary flow is known to impair oral self-cleansing and promote plaque and tongue-coating accumulation [2]. In this study, increased salivary flow was accompanied by a marked reduction in TCI – a validated index that correlates with the anaerobic bacterial burden on the tongue dorsum [12] – suggesting that the product's moisturizing action – including the gel's physical properties – protected the mucosa while restoring self-cleansing, allowing more efficient removal of tongue coating.

Interestingly, at baseline, correlation analysis showed a positive association between oral moisture level and CH₃SH concentration ($r = 0.40$), consistent with the fact that oral bacteria draw on sulfur-containing substrates in the moist periodontal environment to generate CH₃SH via the same enzymatic pathway [6]. With continued product use, however, moisture was replenished and maintained even as bacterial counts and gas concentrations both fell significantly. This suggests that the product's moisturizing, antibacterial, and anti-inflammatory properties — together with a properly structured oral care routine — outweighed any theoretical risk that added moisture might otherwise pose for bacterial growth, shifting the oral environment toward a healthier state.

Correlation analysis also revealed a related pattern among functional measures: modest positive associations linking changes in masticatory efficiency and occlusal force ($r = 0.37$), with weaker positive links from oral moisture to each of these measures ($r = 0.19$ – 0.20). Although the one-week study period was too short to produce large, statistically significant shifts in these functional parameters individually, the pattern is consistent with the idea that a well-maintained moist oral environment can support smoother bolus formation and chewing movement, potentially contributing over time to broader improvements in oral function [14]. In addition, among subjects with high baseline salivary viscosity (stickiness) — a high-risk group for xerostomia-related symptoms — product use was followed by a significant reduction in viscosity alongside a trend toward improved occlusal force ($r = 0.37$), suggesting a meaningful clinical benefit for patients with more severe dry-mouth symptoms.

The multivariate PCA (Fig. 4) showed clearly that the product's mechanism of action is multifaceted rather than dependent on a single pathway. H₂S, CH₃SH, and bacterial count all loaded strongly in the negative direction of PC1 (26.5% of variance), indicating that the product's primary contribution is to reshape the dynamics of halitosis-causing gases through control of the bacterial population. Notably, although the pairwise correlation between H₂S and CH₃SH was very low ($p = 0.08$), their vectors in PCA space overlapped almost completely and moved in parallel. This apparent contradiction is, in fact, consistent from both a biological and a statistical standpoint: Spearman correlation captures fragmented, case-by-case local dynamics — distinguishing, for example, physiological from periodontitis-driven halitosis — whereas PCA extracts the single dominant common trend across the whole dataset (PC1), here representing comprehensive, potent suppression of the major malodor gases. In other words, regardless of variation in individual clinical background, the product's benefit acted uniformly and synergistically on the microenvironments where H₂S and CH₃SH are produced.

By contrast, DMS_{diff} and SalRest_{diff} sat at the opposite pole (positive PC1), graphically reflecting the fact that dimethyl sulfide is governed by regulatory mechanisms distinct from — and sometimes inversely related to — those of the other VSCs, since a portion of DMS in the breath can originate from blood-borne, extra-oral sources rather than purely local oral metabolism [15]. Along PC2 (19.2% of variance), Moisture_{diff} extended strongly in the negative direction, forming a functional axis distinct from the improvements in stimulated salivary flow and tongue coating seen in the upper-right quadrant. The distribution of subjects across this space was informative: ID3, ID4, and ID6 (negative PC1) were cases driven mainly by changes in malodor gas levels, while ID1 and ID20 (positive PC2) were driven

mainly by changes in stimulated salivary flow — a pattern consistent with the product optimizing the oral environment through multiple pathways, tailored to whether periodontitis or xerostomia predominated in each patient's baseline condition.

This study has several limitations, including its small sample size and single-arm design, which cannot fully exclude a placebo effect or the influence of reinforced routine brushing. Even so, the data — from a rapid drop in halitosis-causing gases within 10 minutes to a substantial reduction in PISA after one week — were highly consistent, and this consistency was reinforced by correlation and multivariate analyses. In conclusion, keora™ Oral Moisture Mist/Gel showed strong immediate halitosis-suppressing effects together with meaningful clinical benefits from continued use, including moisturizing action, reduced oral bacterial counts, and resolution of periodontal inflammation (reduced PISA). Future randomized controlled trials with a control group are warranted to confirm long-term outcomes and effects on oral function.

Declarations

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Author Contributions

Author Contributions: Study conception was performed by Kazuhisa Ouhara and Mikihiro Kajiya, and study design by Noriyoshi Mizuno. Material preparation was performed by Yuri Taniguchi. Data collection was performed by Ryouzuke Fujimori, Naoya Kuwahara, Shoya Ueda, Daigo Omokawa, Tomoyuki Iwata, Yukiko Nagatani, Tomoaki Shintani, and Takumi Memida. Data analysis was performed by Shinji Matsuda. The first draft of the manuscript was written by Kazuhisa Ouhara, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Compliance with Ethical Standards

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Conflict of Interest

The study products, keora® Oral Moisture Gel and Mist, were provided free of charge by Nissin Dental Products Inc., Ltd. The authors declare no other conflicts of interest.

Ethics Approval

This study was performed in line with the principles of the 1964 Declaration of Helsinki and its later amendments. Approval was granted by the Certified Clinical Research Review Committee of Hiroshima University (Approval No. CRB2025-0002).

Consent to Participate

Written informed consent was obtained from all individual participants included in the study.

Consent for Publication

Not applicable.

Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1. Nederfors T (2000) Xerostomia and hyposalivation. *Adv Dent Res* 14:48–56
2. Humphrey SP, Williamson RT (2001) A review of saliva: normal composition, flow, and function. *J Prosthet Dent* 85:162–169
3. Scully C, Greenman J (2008) Halitosis (breath odor). *Periodontol* 2000 48:66–75
4. Nesse W, Abbas F, van der Ploeg I, Spijkervet FKL, Dijkstra PU, Vissink A (2008) Periodontal inflamed surface area: quantifying inflammatory burden. *J Clin Periodontol* 35:668–673
5. Miyazaki H, Sakao S, Katoh Y, Takehara T (1995) Correlation between volatile sulphur compounds and certain oral health measurements in the general population. *J Periodontol* 66:679–684
6. Ouhara K, Iwasaki Y, Kajiya M, Savitri IJ, Kitagawa M, Tokunaga N, Shintani T, Ogawa I, Hino T, Fujita T, Shiba H, Kurihara H (2015) The differential expression of mgl mRNA by *Porphyromonas gingivalis* affects the production of methyl mercaptan. *Oral Dis* 21:626–633.
<https://doi.org/10.1111/odi.12326>
7. Saad S, Greenman J, Shaw H (2011) Comparative effects of various commercially available mouthrinse formulations on oral malodour. *Oral Dis* 17:180–186
8. Seemann R, Filippi A, Michaelis S, Lauterbach S, John HD, Huismann J (2016) Duration of effect of the mouthwash CB12 for the treatment of intra-oral halitosis: a double-blind, randomised, controlled trial. *J Breath Res* 10:036002
9. Liu SS, Fu E, Tu HP, Fu MW, Lin CT, Shen EC (2017) Comparison of oral malodors before and after nonsurgical periodontal therapy in chronic periodontitis patients. *J Dent Sci* 12:156–160.
<https://doi.org/10.1016/j.jds.2016.12.004>
10. Nakano M, Shimizu E, Wakabayashi H, Yamauchi K (2016) A randomized, double-blind, crossover, placebo-controlled clinical trial to assess effects of the single ingestion of a tablet containing

lactoferrin, lactoperoxidase, and glucose oxidase on oral malodor. BMC Oral Health 16:37.

<https://doi.org/10.1186/s12903-016-0199-7>

11. Tonzetich J (1977) Production and origin of oral malodor: a review of mechanisms and methods of analysis. J Periodontol 48:13–20
12. Shimizu T, Ueda T, Sakurai K (2007) New method for evaluation of tongue-coating status. J Oral Rehabil 34:442–447. <https://doi.org/10.1111/j.1365-2842.2007.01733.x>
13. Yamada H, Nakagawa Y, Nomura Y, Suzuki M, Nomoto K (2005) Preliminary results of moisture checker for Mucus in diagnosing dry mouth. Oral Dis 11:405–407
14. Pedersen AM, Bardow A, Jensen SB, Nauntofte B (2002) Saliva and gastrointestinal functions of taste, mastication, swallowing and digestion. Oral Dis 8:117–129. <https://doi.org/10.1034/j.1601-0825.2002.02851.x>
15. Tagerman A, Winkel EG (2007) Intra- and extra-oral halitosis: finding of a new form of extra-oral blood-borne halitosis caused by dimethyl sulphide. J Clin Periodontol 34:748–755. <https://doi.org/10.1111/j.1600-051X.2007.01116.x>

Figures

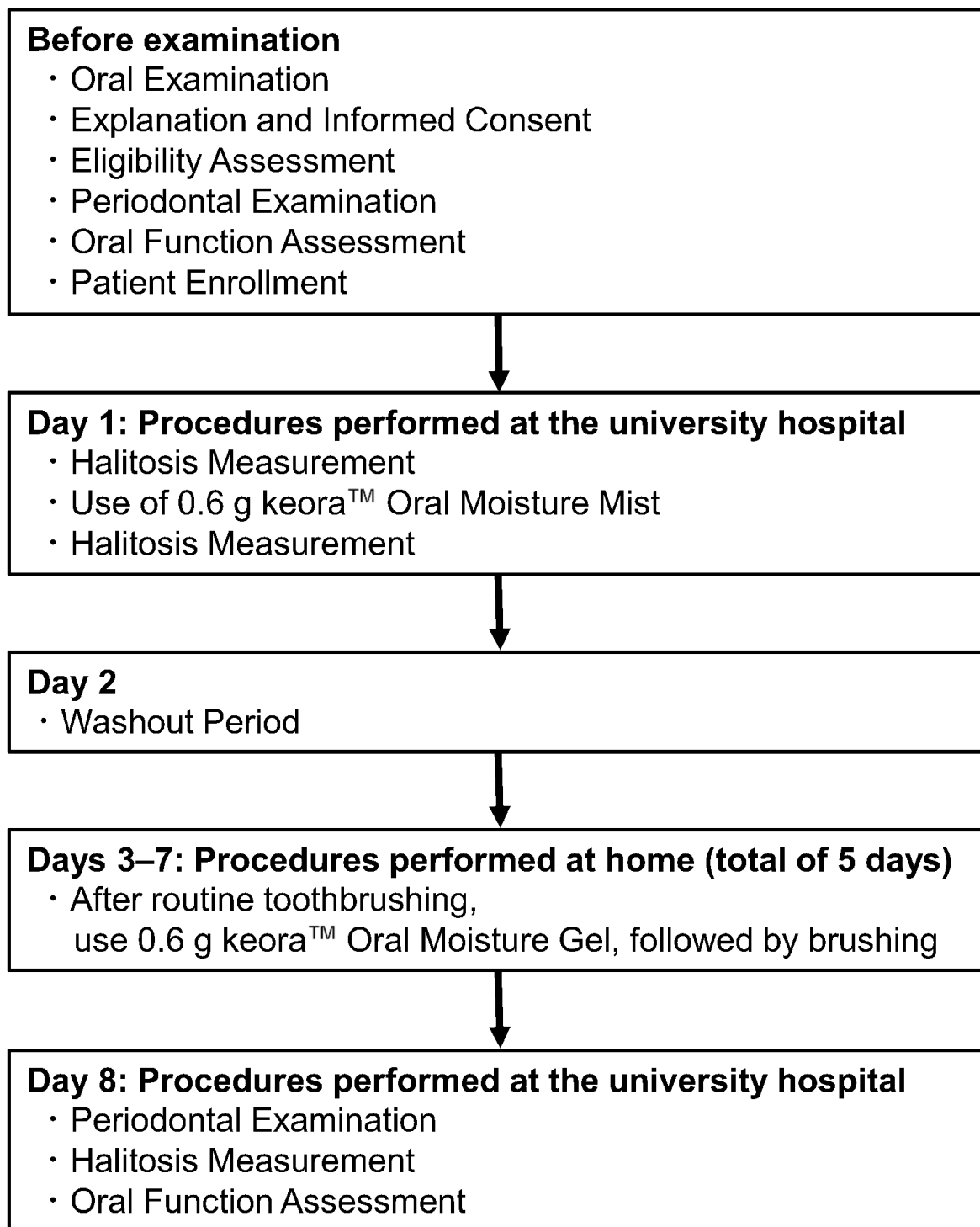


Figure 1

Study design and protocol. Schematic timeline and evaluation items of the exploratory single-arm trial, comprising a run-in/baseline day, a 5-day home-care period with keora™ Oral Moisture Mist and Gel, and clinical evaluations (oral, periodontal, halitosis, and oral function assessment) performed at the university hospital on Day 1 and Day 8

Fig. 2

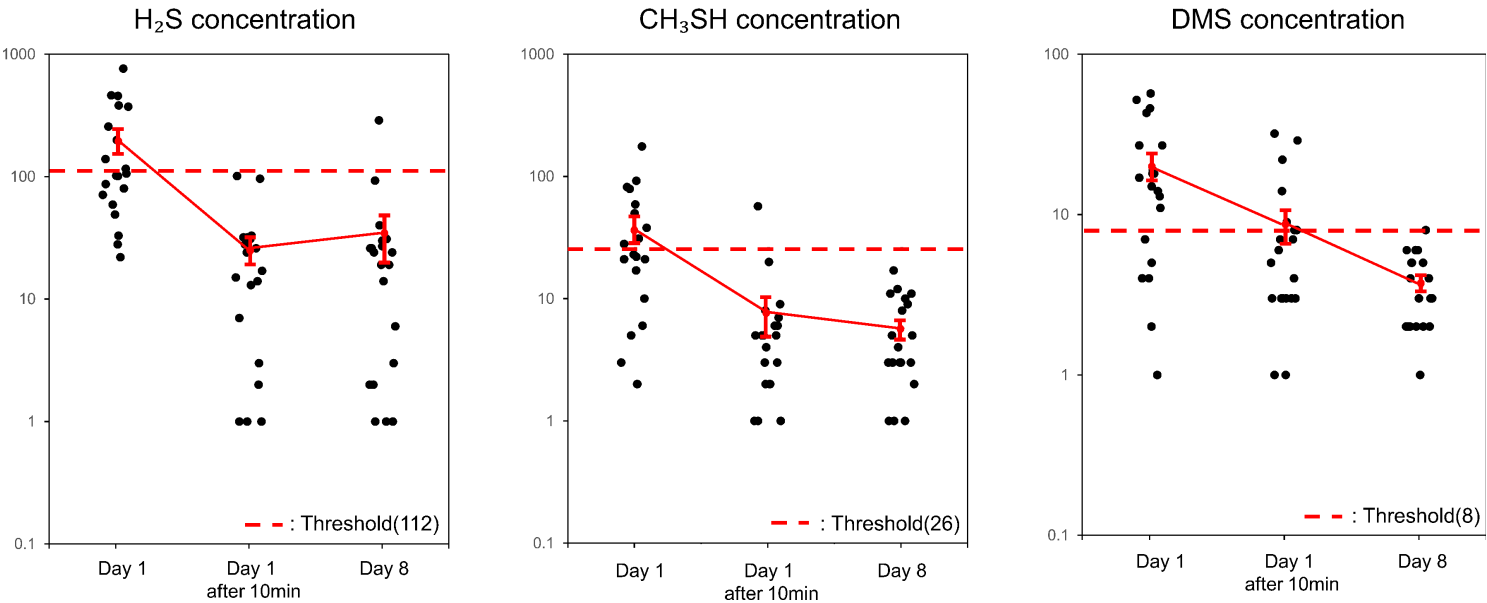


Figure 2

Changes in volatile sulfur compound (VSC) concentrations. Log-scale plots of (left) hydrogen sulfide (H₂S), (middle) methyl mercaptan (CH₃SH), and (right) dimethyl sulfide (DMS) concentrations at baseline (Day 1), 10 minutes after keora™ Oral Moisture Mist application, and after continued use to Day 8. Red dashed lines indicate the clinical oral-malodor thresholds (H₂S: 112 ppb; CH₃SH: 26 ppb; DMS: 8 ppb). Error bars show mean ± SD. All three gases decreased significantly from Day 1 to Day 8 (p < 0.01 for H₂S and CH₃SH; p < 0.001 for DMS)

Fig. 3

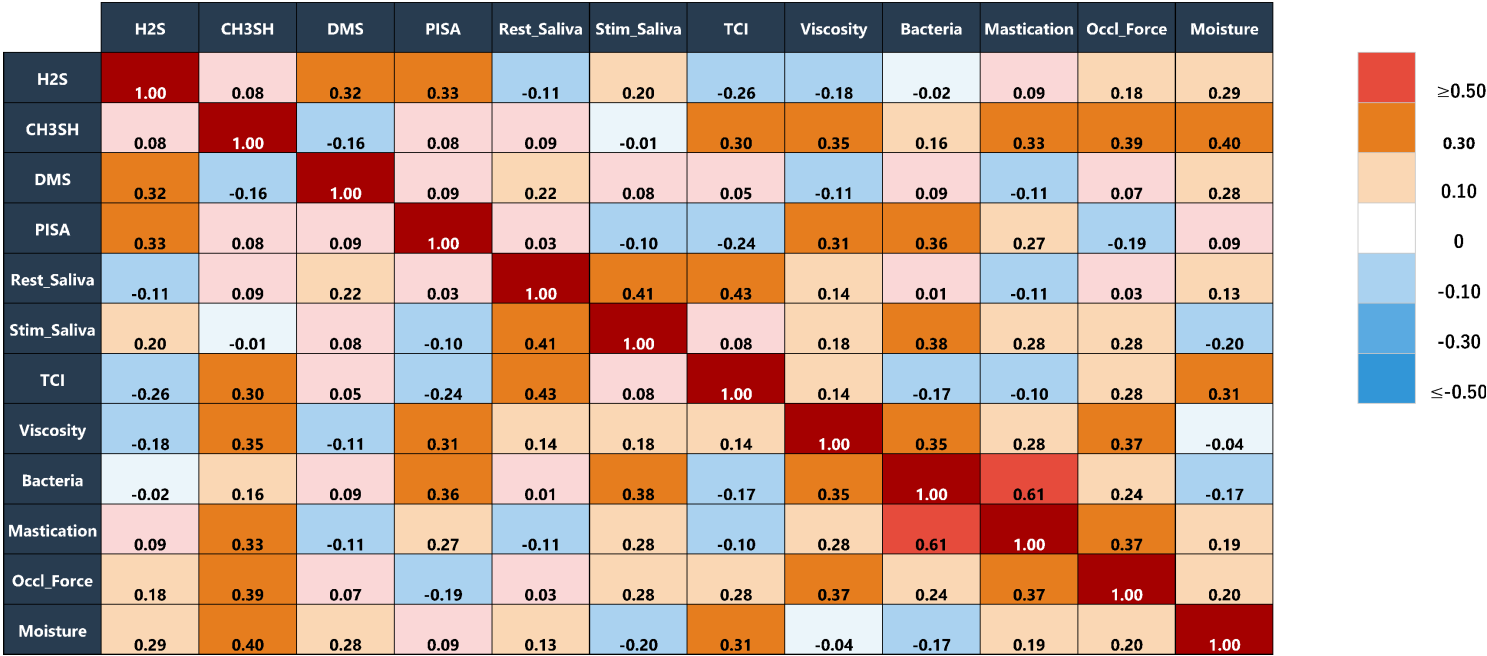


Figure 3

Spearman's rank correlation heatmap of changes in clinical parameters from Day 1 to Day 8. The matrix shows pairwise Spearman correlation coefficients (r) calculated from the delta values (Day 8 minus Day 1) of each parameter ($n = 20$). The color scale indicates correlation strength and direction: red, strong positive ($r > 0.50$); orange, moderate positive ($r > 0.30$); light orange, weak positive ($r > 0.10$); white, no correlation ($r \approx 0$); blue shades, negative correlations ($r < -0.10$ to < -0.50)

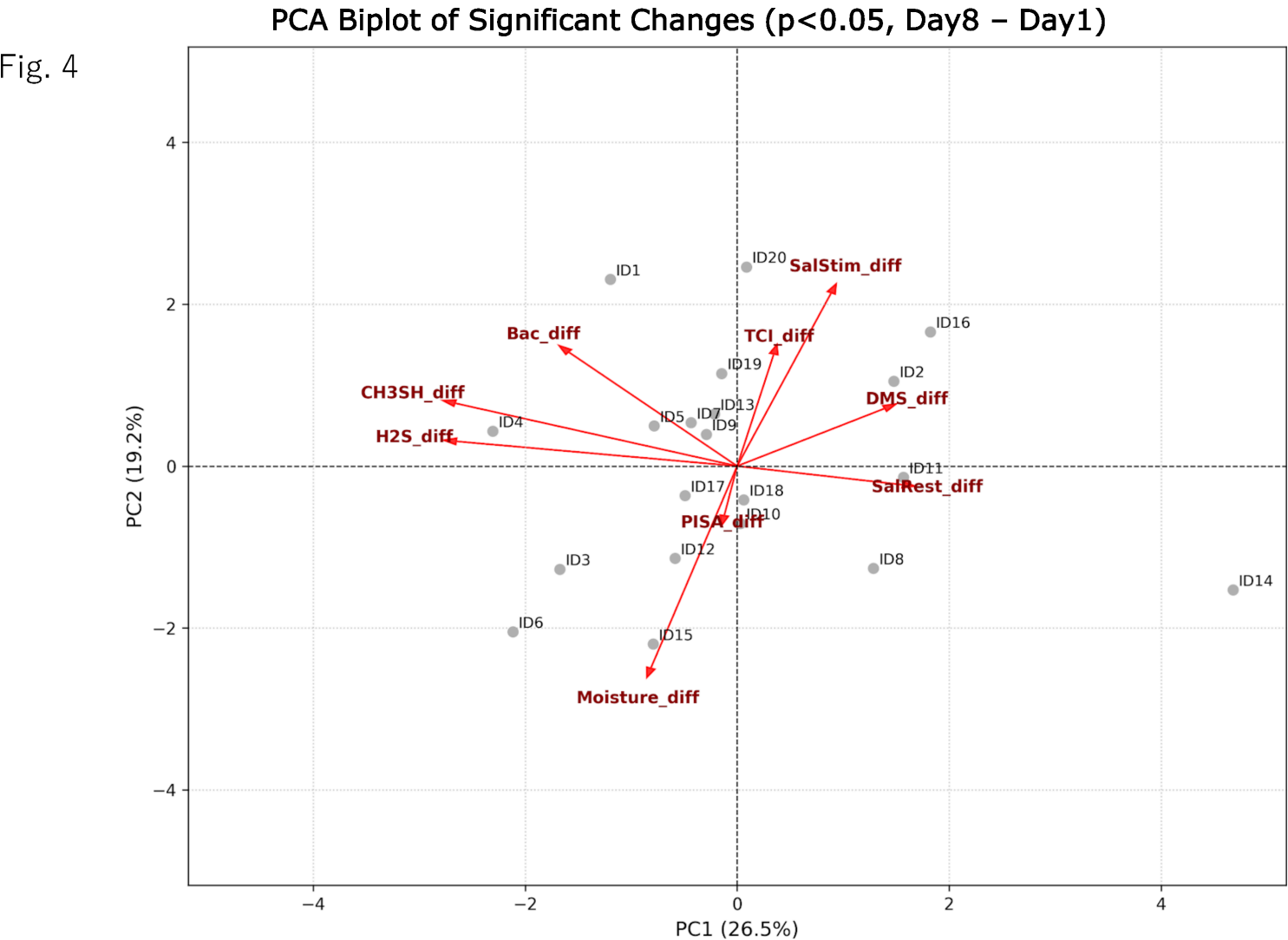


Figure 4

Principal component analysis (PCA) biplot of significant clinical changes. Biplot visualizing the relationships among parameters that changed significantly ($p < 0.05$) from Day 1 to Day 8. The horizontal axis (PC1, 26.5% variance) and vertical axis (PC2, 19.2% variance) capture the main trends in the data. Red arrows indicate the direction and strength of each variable's contribution. Individual subjects (ID1–ID20) are plotted as gray dots, showing a primary shift toward VSC and bacterial reduction (leftward) and varied individual patterns balancing periodontal healing (PISA) and moisture improvement (downward)