Original Article

Effect of 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one-containing lactic acid bacterial beverages on skin moisture: a randomized, double-blind, placebo-controlled, parallel study

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Although we previously reported that 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one has antioxidant properties, its effect on the skin remains unclear. This study aimed to investigate the effects of beverages containing 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one on skin moisture. This study enrolled 220 healthy Japanese participants with dry skin who were randomly assigned to the test or placebo group (*n* = 110 each). Each group received either a beverage containing 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one or a placebo for 12 weeks. The primary outcome was stratum corneum water content. Secondary outcomes were transdermal water loss, number of blemishes and wrinkles, and blood antioxidant markers such as biological antioxidant potential and diacron-reactive oxygen metabolites. Visual analog scale was used to assess skin improvement. Stratum corneum water content and visual analog scale scores differed significantly between the test and placebo groups. Water content significantly increased in the test group compared to the placebo group at 4 and 8 weeks. Subjective skin symptoms significantly improved with the test beverage intake compared with the placebo. No other significant or adverse effects were observed. In conclusion, the of 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one-containing beverage for 12 consecutive weeks significantly increases stratum corneum water content. The study findings could aid in the development of safe functional foods enriched with this compound.

***Key Words*:** **2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one, skin, polyphenol, antioxidant, stratum corneum water content**

Skin aging is caused by both extrinsic and intrinsic factors; intrinsic factors are age-related, whereas external factors are caused by environmental conditions, such as exposure to direct sunlight, leading to the production of reactive oxygen species (ROS) in the skin and triggering an inflammatory reaction.(1) This inflammatory reaction activates various enzymes, such as elastase, collagenase, hyaluronidase, and tyrosinase. Elastase and collagenase break down important skin components that are associated with skin elasticity and flexibility, such as elastin and collagen, leading to wrinkles. Hyaluronidase breaks down hyaluronic acid which plays a significant role in maintaining skin moisture. Tyrosinase is involved in melanin synthesis, leading to blemishes.(2–4)

Research on developing beauty products has focused on reducing ROS, inflammatory reactions, and enzyme activity.(3–6) In recent years, studies have focused on natural compounds. Many beauty products are consumed orally, and safety is the highest priority. Polyphenols are natural products with high antioxidant properties. They are highly safe and have several hydroxyl groups and aromatic ring compounds identified in many foods, such as chocolate, green tea, and wine.(7) They have many anti-skin-aging characteristics, such as reducing ROS, inflammatory reactions, and activities of tyrosinase, elastase, collagenase, and hyaluronidase.(8–11) The effects of polyphenols on the skin have been demonstrated in human clinical trials. Coffee polyphenol improves skin hydration and barrier function.(12) Further, dietary cocoa polyphenol prevents the progress of skin aging processes such as facial wrinkles and elasticity.(13) Consumption of polyphenol-containing foods is expected to reduce skin aging.

2,3-Dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one (DDMP), isolated from food, is a type of polyphenol; it is expected to be a promising agent to maintain and improve skin condition.(14,15) DDMP has recently been identified as a major antioxidant produced by the Maillard reaction in beverages containing lactic acid bacteria.(16) The correlation between DDMP and skin health is still unclear, but consuming these beverages may improve skin condition.

In this study, we investigated the effect of a DDMP-containing lactic acid bacteria beverage on the skin by measuring stratum corneum water content, transdermal water loss (TEWL), number of blemishes and wrinkles, visual analog scale (VAS), and blood antioxidant markers.

Materials and Methods

Approval of the ethics committee. We conducted a randomized, double-blind, placebo-controlled study to evaluate the effects of a beverage containing DDMP on the skin between February 2024 and April 2024. This clinical trial was conducted in accordance with the Declaration of Helsinki (2000). This study was approved by the Ethics Committee of the Medical Corporation Kyosokai AMC Nishi-Umeda Clinic (Osaka, Japan; reference number 20000026) and was registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN 000052867). The procedures were explained in detail to all participants in advance, and their informed consent was freely obtained.

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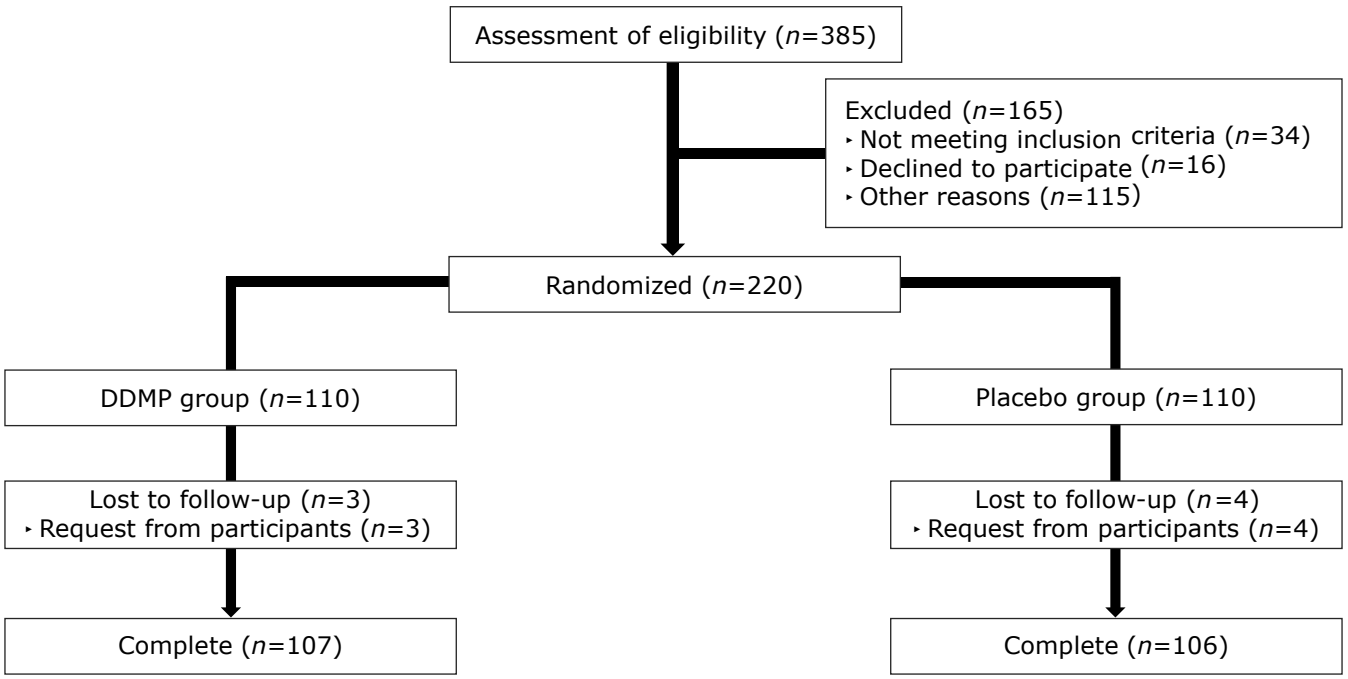

Fig. 1. Flow chart showing the trial design. DDMP, 2,3-Dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one.

Samples. The lactic acid bacteria beverage used in this study was provided by Nissin York Co., Ltd. (Tokyo, Japan). For the test group (DDMP group), 65 ml of lactic acid bacteria beverage containing 2.2 mg DDMP was prepared. For the placebo group, a 65 ml beverage was prepared that was composed of the same test beverage components but without DDMP. The placebo drink was indistinguishable from the DDMP-containing test drink in terms of flavor, taste, and color. The participants consumed placebo- or DDMP-containing beverages (65 ml per day) for 12 weeks. As a trend of improvement in oxidative stress levels was observed after consumption of 65 ml of a beverage containing DDMP for 12 weeks in a previous preliminary study (UMIN000051522, unpublished data), this guideline and inoculation period were used in this study.

Participants. The participants were healthy Japanese adults between the ages of 20 and 65 years who had dry or rough skin and provided written informed consent. The exclusion criteria were those who regularly ate fermented foods, health foods, or medicines at least three times a week; were under medication or outpatient treatment for certain serious disease; were under the supervision of a physician for exercise or diet therapy; had developed an allergy to the test food; were presently or previously suffering from drug dependence or alcohol dependence; had a mental disorder or were presently visiting the hospital for mental or sleep disorders, or had a history of mental illness in the past; had an irregular rhythm of life due to night or shift work; had extremely irregular eating, sleeping, or other personal behavior habits; were extremely picky eaters; had a serious current or previous illness such as brain disease, malignant tumor, immunological disease, diabetes, liver disease, renal disease, heart disease, thyroid disease, adrenal gland disease, or other metabolic disease; had a history of cosmetic treatment that may affect the test site; had skin diseases, traumatic injuries, or subjective symptoms such as pain that may affect the study; were using health foods, supplements, or medicines that may affect the test; had used beauty devices or equipment within a month prior to obtaining consent; had participated in another clinical trial within 3 months prior to the date of consent or planned to participate in another clinical trial during the study period; had donated more than 200 ml of blood within a month or 400 ml of blood within 3 months prior to the date of consent; were pregnant or lactating at enrolment or would be during the study period; were unable to comply with the recording of various questionnaires; were unsuitable as participants based on clinical laboratory values and measurements at screening; or were otherwise decided by the investigator to be unsuitable as participants.

Evaluation items. Stratum corneum water content was the primary outcome because of its physiological and cosmetic importance compared to other outcomes. Secondary outcomes were TEWL, number of blemishes and wrinkles, and blood antioxidant markers such as biological antioxidant potential (BAP) and diacron-reactive oxygen metabolites (d-ROMs). Further, a VAS was used to assess skin improvement. Skin and VAS measurements were conducted every 4 weeks for each participant. Blood antioxidant markers were measured twice before and after 12 weeks of test food consumption.

The water content of the stratum corneum was measured at one location on the inner forearm using a Corneometer CM 825 (Courage+Khazaka Electronic GmbH, Cologne, Germany). TEWL was measured at one location on the inner forearm using a Tewameter TM HEX (Courage+Khazaka Electronic GmbH). The number of blemishes and wrinkles was evaluated from images of the front, left, and right faces using VISIA Evolution (Canfield Scientific, Parsippany, NJ). All skin measurements were performed after the test site was washed and acclimated to a constant temperature and humidity chamber (temperature: 21 ± 1°C, humidity: 50 ± 5%) for 20 min in a resting state and were repeated for each participant every fourth week (four times).

BAP and d-ROM measurements were performed using the BAP TEST reagents (R1 and R2) and d-ROM TEST reagents (R1 and R2) (Wismerll, Tokyo, Japan) according to the manufacturer's protocols.

Skin symptoms were assessed using the VAS. The survey items were as follows: Q1, skin wrinkles; Q2, skin elasticity; Q3, skin blemishes; Q4, dry skin; Q5, skin roughness; Q6, skin moisture; Q7, skin texture; and Q8, glossy skin. For Qs 1, 3, 4, and 5,

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Table 1. Baseline skin characteristics of study groups

Characteristics	DDMP group (n = 107)	Placebo group (n = 106)	p value
	Mean ± SD	Mean ± SD	
Gender, n (%)			
Male	51 (48)	50 (47)	0.841
Female	55 (52)	57 (53)	
Age (years)	45.6 ± 11.7	45.1 ± 11.7	0.759
Height (cm)	165.5 ± 8.3	165.1 ± 8.3	0.763
Weight (kg)	59.6 ± 10.1	60.5 ± 10.1	0.488
Body mass index (kg/m^2)	21.6 ± 2.6	22.1 ± 2.7	0.209
Blood pressure (mmHg)			
Systolic blood pressure	119.4 ± 13.0	121.4 ± 11.8	0.232
Diastolic blood pressure	77.1 ± 10.5	77.6 ± 9.7	0.743
Pulse (beats/min)	72.4 ± 9.8	70.1 ± 9.2	0.087
Corneum value (arbitrary units)	21.8 ± 3.8	21.6 ± 4.6	0.733

DDMP, 2,3-Dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one.

the closer the number was to 0, the more the participant was "not concerned at all", with 100 being the maximum score for "very concerned". For Qs 2, 6, 7, and 8, a score of 0 corresponded with "very much concerned", while 100 corresponded with "not concerned at all".

The safety of the test food was evaluated using clinical laboratory values (blood pressure, pulse rate, body weight, body mass index, and biochemical, hematological, and urinalysis) as well as adverse events.

Statistical analysis. Results are expressed as means ± SD. All statistical analyses were performed using two-tailed tests with significance set at 5%. The software used for data analysis was IBM® SPSS® Statistics 29 (IBM Japan, Tokyo, Japan). Differences between the groups at each measurement were evaluated using t tests. The change in value represents the value at the time of measurement minus the base value. We further performed a linear mixed model analysis with corneal water content as the objective variable and tested beverage and time as fixed effects. Participants were used as variable effects to compare between groups, with Bonferroni correction for significant differences in intervention terms and interactions in measured values and changes.

Results

Participant analysis. Of the 385 participants, 220 met the selection criteria and were randomly divided into two groups (DDMP and placebo groups, n = 110 each). Seven participants met the rejection and exclusion criteria in the blinded review after the completion of the study; the main analysis was conducted as a population conforming to the study protocol, analyzing 213 participants (DDMP group: 107; placebo group: 106). Figure 1 shows a follow-up flowchart of the study participants. No significant differences were observed in the baseline characteristics between the two groups (Table 1).

Measurement of skin parameters. No significant differences in skin parameters, such as TEWL and the number of blemishes and wrinkles, were observed between the DDMP and placebo groups (Table 2). Corneal water content was significantly different for those taking DDMP-containing beverages compared to placebo food at 4 and 8 weeks of intake (Student's t test, p<0.001 at 4 weeks and p<0.01 at 8 weeks), but was almost the same between the two groups at 12 weeks. In addition, significant differences between the two groups were observed using a linear mixed model with fixed effects for the test beverage and time (p<0.001; Fig. 2).

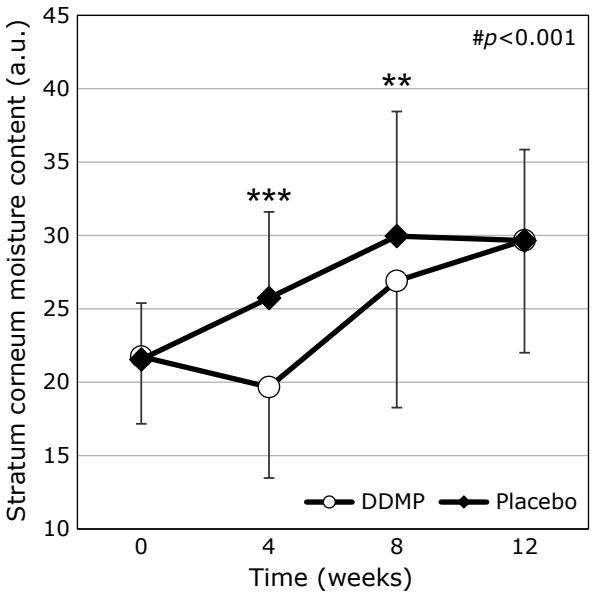

Fig. 2. Effects of 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one on the stratum corneum moisture content values. a.u., arbitrary units. Each bar shows the mean ± SD for experiments. Differences between groups at each measurement time point are evaluated by student's t test and represented as **p<0.01 and ***p<0.001. Differences between groups using a linear mixed model with fixed effects of test beverage and time as the main effects are expressed as #p<0.001. DDMP, 2,3-Dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one.

Blood antioxidant markers. No significant differences in BAP and d-ROM were observed between the DDMP and placebo groups.

Self-assessment of skin symptoms. Table 3 provides the results of the skin symptom self-assessment using the VAS; lower scores indicated greater perceived skin improvement. The DDMP group showed a significantly lower score (improved skin texture) than the placebo group in Q1 (wrinkles) at 8 weeks, Q2 (skin elasticity) at 8 and 12 weeks, Q3 (skin blemishes), Q4 (skin dryness), and Q6 (skin moistness) at 12 weeks; Q7 (skin texture) at 4, 8, and 12 weeks; and Q8 (glossy skin) at 0, 4, 8, and 12 weeks. The placebo group did not have significantly lower scores compared with the DDMP group.

Table 2. Changes in skin parameters

Item (unit)		Sample type	0 week			4 weeks			8 weeks			12 weeks		
			n	Means ± SD	*p* value	*n*	Means ± SD	*p* value	*n*	Means ± SD	*p* value	*n*	Means ± SD	*p* value
Stratum corneum moisture content (arbitrary units)	Measured value	Placebo	106	21.8 ± 3.84	0.733	105	19.7 ± 5.87	**<0.001*** **	103	26.9 ± 8.5	**0.0116***	105	29.7 ± 6.19	0.985
		DDMP	107	21.6 ± 4.59		103	25.7 ± 6.19		102	30 ± 8.64		106	29.7 ± 7.67	
	Change value	Placebo				105	–2.09 ± 4.74	**<0.001*** **	103	5.17 ± 7.53	**0.00200****	105	7.92 ± 5.97	0.877
		DDMP				103	4.28 ± 4.20		102	8.47 ± 7.57		106	8.05 ± 6.85	
Trans-epidermal moisture transpiration rate (g/m²/h)	Measured value	Placebo	106	9.09 ± 1.60	0.0990	105	9.29 ± 1.46	0.457	103	11.2 ± 3.01	0.315	105	12.2 ± 5.50	0.673
		DDMP	107	9.44 ± 1.46		103	9.44 ± 1.40		102	11.7 ± 4.54		106	11.9 ± 3.90	
	Change value	Placebo				105	0.164 ± 1.58	0.366	103	2.12 ± 3.02	0.726	105	3.07 ± 5.70	0.376
		DDMP				103	–0.0316 ± 1.54		102	2.30 ± 4.35		106	2.48 ± 3.88	
Blemishes (right face)	Measured value	Placebo	106	103 ± 41.9	0.538	105	106 ± 43.6	0.326	103	102 ± 43.3	0.396	105	107 ± 44.3	0.340
		DDMP	107	99.4 ± 39.1		103	100 ± 38.0		102	96.9 ± 40.4		106	101 ± 40.0	
	Change value	Placebo				105	2.88 ± 14.4	0.089	103	–0.223 ± 13.5	0.561	105	4.44 ± 13.3	0.241
		DDMP				103	–0.340 ± 12.7		102	–1.28 ± 12.6		106	2.25 ± 13.8	
Blemishes (left face)	Measured value	Placebo	106	99.2 ± 41.9	0.694	105	102 ± 44.2	0.386	103	98.2 ± 43.9	0.489	105	102 ± 44.5	0.583
		DDMP	107	97.0 ± 39.6		103	97.4 ± 38.8		102	94.2 ± 39.3		106	98.3 ± 41.7	
	Change value	Placebo				105	3.25 ± 14.5	**0.0434***	103	–0.505 ± 12.1	0.444	105	3.06 ± 15.1	0.577
		DDMP				103	–0.563 ± 12.5		102	–1.75 ± 11.0		106	1.94 ± 13.8	
Wrinkles (right face)	Measured value	Placebo	106	274 ± 105	**0.0490***	105	232 ± 88.8	0.201	103	222 ± 86.8	0.258	105	221 ± 92.8	0.378
		DDMP	107	246 ± 103		103	215 ± 100		102	208 ± 97.1		106	209 ± 101	
	Change value	Placebo				105	–43.0 ± 87.1	0.366	103	–49.1 ± 77.8	0.143	105	–51.3 ± 88.7	0.207
		DDMP				103	–32.2 ± 85.5		102	–33.4 ± 76.0		106	–36.1 ± 85.8	
Wrinkles (left face)	Measured value	Placebo	106	235 ± 91.3	0.0960	105	202 ± 81.7	0.383	103	195 ± 81.6	0.431	105	184 ± 89.6	0.721
		DDMP	107	212 ± 103		103	191 ± 95.4		102	184 ± 101		106	180 ± 101	
	Change value	Placebo				105	–33.6 ± 70.1	0.373	103	–36.4 ± 69.6	0.230	105	–48.2 ± 69.4	0.131
		DDMP				103	–23.8 ± 87.8		102	–24.2 ± 75.5		106	–32.5 ± 80.0	

DDMP, 2,3-Dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one. Stratum corneum water content, transepidermal water transpiration, number of blemishes, and wrinkles were measured before the test and after 4, 8, and 12 weeks of DDMP, with or without beverage consumption. Values are expressed as the mean ± SD of each group. Differences between groups at each measurement time point were evaluated using Student's *t* test and are represented as *p<0.05, **p<0.01, and ***p<0.001. The change in value represents the value measured at the time of measurement minus the value measured at week 0.

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Table 3. Changes in VAS scores of symptoms of the skin

		Sample type	0 week			4 weeks			8 weeks			12 weeks		
			n	Means ± SD	*p* value	*n*	Means ± SD	*p* value	*n*	Means ± SD	*p* value	*n*	Means ± SD	*p* value
Q1 Skin wrinkles	Measured value	Placebo	106	61.5 ± 25.5	0.501	105	54.6 ± 25.3	0.169	103	52.9 ± 24.2	**0.0371***	105	51.0 ± 24.7	0.128
		DDMP	107	59.0 ± 28.2		103	49.6 ± 26.6		102	45.8 ± 24.0		106	45.8 ± 24.5	
	Change value	Placebo				105	−6.72 ± 19.2	0.365	103	−9.32 ± 23.9	0.178	105	−10.3 ± 22.5	0.421
		DDMP				103	−9.58 ± 25.9		102	−14.0 ± 25.9		106	−13.1 ± 28.0	
Q2 Skin elasticity	Measured value	Placebo	106	62.5 ± 23.6	0.748	105	59.0 ± 18.8	0.181	103	57.6 ± 18.2	**0.0227***	105	54.9 ± 19.1	**0.00457****
		DDMP	107	61.5 ± 22.9		103	55.5 ± 19.6		102	51.2 ± 21.3		106	47.3 ± 19.5	
	Change value	Placebo				105	−3.47 ± 26.9	0.300	103	−5.08 ± 26.1	0.0700	105	−7.38 ± 28.1	0.0760
		DDMP				103	−6.90 ± 20.3		102	−11.6 ± 25.0		106	−14.0 ± 26.3	
Q3 Skin blemishes	Measured value	Placebo	106	66.2 ± 25.5	0.585	105	60.3 ± 23.8	0.284	103	57.0 ± 23.5	0.339	105	57.3 ± 23.8	0.163
		DDMP	107	68.2 ± 26.4		103	56.5 ± 26.9		102	53.8 ± 24.7		106	52.7 ± 24.5	
	Change value	Placebo				105	−5.83 ± 24.7	0.077	103	−8.85 ± 23.3	0.0890	105	−9.00 ± 23.1	**0.0492***
		DDMP				103	−11.8 ± 23.5		102	−14.4 ± 23.5		106	−15.5 ± 24.5	
Q4 Dry skin	Measured value	Placebo	106	81.3 ± 13.2	0.184	105	67.3 ± 21.1	0.326	103	61.3 ± 21.9	0.298	105	57.1 ± 22.4	**0.0302***
		DDMP	107	78.5 ± 17.3		103	64.4 ± 21.0		102	58.0 ± 22.7		106	50.2 ± 23.2	
	Change value	Placebo				105	−14.2 ± 18.6	0.933	103	−20.1 ± 22.0	0.807	105	−24.3 ± 24.4	0.243
		DDMP				103	−14.4 ± 21.9		102	−20.9 ± 24.6		106	−28.2 ± 24.8	
Q5 Roughness of skin	Measured value	Placebo	106	65.8 ± 22.3	0.815	105	54.7 ± 24.3	0.561	103	51.0 ± 25.6	0.197	105	50.0 ± 24.9	0.0660
		DDMP	107	66.5 ± 22.3		103	52.7 ± 24.7		102	46.5 ± 24.1		106	43.8 ± 23.7	
	Change value	Placebo				105	−11.2 ± 23.0	0.422	103	−15.1 ± 25.0	0.165	105	−16.0 ± 26.8	0.0650
		DDMP				103	−14.0 ± 26.9		102	−20.4 ± 28.9		106	−22.8 ± 26.9	
Q6 Moistness of skin	Measured value	Placebo	106	71.5 ± 18.9	0.150	105	60.1 ± 17.9	0.183	103	54.6 ± 21.1	0.119	105	52.5 ± 19.7	**0.00647****
		DDMP	107	67.9 ± 18.3		103	56.8 ± 18.2		102	50.1 ± 20.6		106	44.8 ± 20.7	
	Change value	Placebo				105	−11.4 ± 21.6	0.895	103	−17.4 ± 24.8	0.842	105	−18.9 ± 23.4	0.214
		DDMP				103	−11.0 ± 21.1		102	−18.1 ± 22.5		106	−22.9 ± 23.2	
Q7 Skin texture	Measured value	Placebo	106	70.7 ± 18.4	0.156	105	62.9 ± 18.2	**0.00433****	103	60.5 ± 17.5	**0.0108***	105	57.0 ± 18.9	**0.0186***
		DDMP	107	67.1 ± 18.3		103	55.8 ± 17.3		102	54.1 ± 17.9		106	50.8 ± 18.6	
	Change value	Placebo				105	−7.76 ± 20.8	0.202	103	−9.70 ± 19.8	0.146	105	−13.6 ± 24.0	0.404
		DDMP				103	−11.1 ± 17.1		102	−13.9 ± 21.0		106	−16.2 ± 22.2	
Q8 Glossy skin	Measured value	Placebo	106	73.1 ± 17.0	**0.0411***	105	64.3 ± 17.9	**0.00305****	103	59.8 ± 19.9	**0.00973***	105	57.9 ± 19.5	**0.00299****
		DDMP	107	67.7 ± 21.0		103	56.6 ± 19.2		102	52.5 ± 20.3		106	49.7 ± 20.5	
	Change value	Placebo				105	−8.74 ± 19.5	0.442	103	−13.1 ± 21.0	0.456	105	−15.0 ± 23.0	0.373
		DDMP				103	−10.9 ± 21.4		102	−15.4 ± 24.2		106	−17.9 ± 24.7	

DDMP, 2,3-Dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one. Values are expressed as the mean ± SD of each group. Differences between groups at each measurement time point were evaluated using Student's *t* test and are represented as *p<0.05, **p<0.01, and ***p<0.001. The change in values represents the measured value at the time of measurement minus the measured value at week 0. Qs 1, 3, 4, and 5: The closer the number is to 0, the more "not concerned at all", and the closer it is to 100, the more "very concerned". Qs 2, 6, 7, and 8: The closer the number is to 0, the more "very concerned"; the closer it is to 100, the more "not concerned at all".

Test food safety. No serious adverse events related to consuming the test food occurred in this study, confirming the safety of beverages containing DDMP.

Discussion

In this study, DDMP-containing lactic acid bacterial beverages significantly increased the stratum corneum water content, showing that DDMP maintains skin moisture and improves subjective skin conditions. These results were partially consistent with the VAS results. In contrast, the DDMP and placebo groups showed similar final stratum corneum water content; we speculate that this result at week 12 may reflect the effect of the intake of lactic acid bacteria, which are present in the placebo beverage, and/or seasonal changes in atmospheric humidity. A previous study showed the intake of lactic acid bacteria-fermented milk improved hydration levels in the stratum corneum in young women.[17] Additionally, both the test beverage and placebo contained *Lacticaseibacillus paracasei* NY1301. We previously reported that culture supernatant fermented by NY1301 inhibited hyaluronidase, which degrades hyaluronic acid, a component involved in skin moisturization.[18] Furthermore, a study of seasonal changes in skin water content in Japan reported an increase in stratum corneum water content in the summer compared to winter, with values ranging from 25–35 a.u.[19] The measurements in this study were performed from winter to spring (December to April), meaning the stratum corneum water content may have been affected by seasonal factors. The stratum corneum water content of the DDMP group showed little change between weeks 8 and 12, suggesting that the upper limit of water content (approximately 30 a.u.) was reached at week 12. The effect of NY1301 on skin moisture should be investigated further in future studies.

The DDMP group showed increased skin moisture content from an early stage of consumption; analysis with the linear mixed model showed a significant difference from the placebo group, suggesting that DDMP has a positive effect on stratum corneum water content. Although the detailed mechanism of the DDMP-induced increase in skin water content remains to be elucidated, we speculate that reduction of ROS production, inhibition of inflammatory reactions, and inhibition of the activity of skin component-degrading enzymes might be responsible for this effect. Cell experiments have confirmed the anti-inflammatory effects of the exosome-like nanoparticles derived from papaya, which contain DDMP,[20] and rat experiments have confirmed that DDMP has antioxidant effects.[21]

Our study has several limitations. Further research is needed to clarify the relationship between DDMP and skin health, as the main objective of this study was to determine its effect on stratum corneum water content. Screening was performed by considering the distribution of stratum corneum water content among the participants, meaning that the mean baseline values of the secondary parameters differed in distribution even if the values were similar; this may have affected other secondary outcomes, including TEWL, number of blemishes and wrinkles, and blood antioxidant markers, which showed no significant differences between the DDMP and placebo groups.

In conclusion, we have clarified for the first time that oral intake of DDMP significantly increased stratum corneum water content. DDMP is recognized as a particularly safe compound because it is naturally present in various foods and can be consumed for a long time.[16,20,22] In addition, it is produced by the Maillard reaction and can be easily produced during the manufacturing of various foods. The findings of this study could help in better understanding the relationship between skin health and DDMP, as well as developing safe functional foods enriched with DDMP.

Author Contributions

TS, SS, and MM designed the research; TS and MT conducted the research; TS and MT provided essential materials; MT and MM analyzed the data; TS wrote the manuscript; TA had primary responsibility for the final content. All authors read and approved the final manuscript.

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Conflict of Interest

TS, MT, and SS are associated with Nissin York Co., Ltd. MM is associated with M&I Science CORP. TA is also affiliated with Tokyo Shinjuku Clinic; he did not receive any research funding. This study was properly conducted by a third-party organization, M&I Science CORP. There are no other conflicts of interest to declare.

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