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Letter

Inhibitory effect of mozuku seaweed-derived ultra-high-molecular-weight fucoidan on the growth of indigenous skin bacteria

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ABSTRACT — Fucoidan, a sulfated polysaccharide found abundantly in brown algae such as mozuku seaweeds, is classified as a water-soluble dietary fiber. Fucoidan reportedly exerts antitumor, anti-inflammatory, immunomodulatory, antioxidant, whitening, antibacterial, and antiviral activities. Owing to these properties, fucoidan has been widely used as an active ingredient for skin care purposes, including quasi-drug serums and hair growth products. However, fucoidan effects differ depending on the algal species, molecular weight, and other factors. Thus, it is crucial to thoroughly test fucoidan preparations and determine their suitability for individual applications. In this study, we probed the effects of mozuku-derived ultra-high-molecular-weight fucoidan (1700 kDa, normally ~300 kDa) preparations on indigenous skin bacteria and general bacteria. We observed that fucoidan preparations derived from Tongan mozuku *Cladosiphon novae-caledoniae* and Amami mozuku *Cladosiphon okamuranus* inhibited the growth of skin bacteria, such as *Staphylococcus aureus* and *Staphylococcus epidermidis*. However, no growth inhibition was observed for the skin bacterium *Cutibacterium acnes* or general bacteria, such as *Lactobacillus casei*, *Escherichia coli*, and *Bacillus subtilis*. Given its ability to hinder the growth of skin disease-causing bacteria, mozuku-derived ultra-high-molecular-weight fucoidan holds promise for future applications in the pharmaceutical and cosmetic industries.

Key words: Brown algae, Sulfated polysaccharide, Fucoidan, Antibacterial, *Staphylococcus aureus*, *Staphylococcus epidermidis*

INTRODUCTION

Fucoidan, a polysaccharide with sulfate groups on the fucose, is classified as a soluble dietary fiber. Fucoidan is found abundantly in brown algae, such as wakame seaweed and mozuku seaweed, as well as in marine invertebrates, such as sea urchins and sea cucumbers (Li *et al*., 2008). Fucoidan exhibits antitumor, anti-inflammatory, immunomodulatory, anticoagulant, anti-thrombogenic, lipid- and carbohydrate-loading, antioxidant, whitening, antibacterial, and antiviral activities (Jesumani *et al*., 2020; Senthilkumar and Kim, 2014; Wang *et al*., 2019a, 2019b). In addition, fucoidan exerts moisturizing, hygroscopic, and UVB-protective effects on the skin (Fernan-

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do *et al*., 2020a, 2020b; Jesumani *et al*., 2020; Lee *et al*., 2022). Notably, fucoidan inhibits the adhesion of *Staphylococcus aureus*, a causative agent of atopic dermatitis and folliculitis, and *Cutibacterium acnes*, a causative agent of acne, to human keratinocytes (Park *et al*., 2021). However, the antibacterial activity of fucoidan varies based on various factors, including the algal species. For example, fucoidan derived from *Saccharina japonica* prevents the growth of *S. aureus*, whereas fucoidan derived from *Sargassum vachellianum* does not (Jesumani *et al*., 2020; Liu *et al*., 2017). These variations in the antibacterial effects of fucoidan are likely attributed to differences in the monosaccharide and sulfate contents in fucoidan derived from different algal sources. The overgrowth of some indigenous skin bacteria, such as *S. aureus* and *C. acnes*, which are bad bacteria, can cause atopic dermatitis and folliculitis. Although *Staphylococcus epidermidis* can cause atopic dermatitis, it is generally considered to be a good bacteria because it suppresses *C. acnes* and helps maintain moisture (Park *et al*., 2021). Thus, developing skincare formulations that maintain a balanced skin flora is vital for skin health. However, the effects of fucoidans on *S. epidermidis* remain unclear.

A fucoidan-rich polysaccharide fraction extracted from *S. vachellianum* exhibited antibacterial activity against *S. aureus* and *Escherichia coli* (Jesumani *et al*., 2020). Notably, fucoidan extracted from *S. japonica* of the kelp family *Laminariaceae* did not exhibit antibacterial activity before depolymerization; however, their low-molecular-weight products effectively inhibited the growth of *S. aureus* and *E. coli* (Liu *et al*., 2017). Moreover, high-molecular-weight fucoidan inhibits angiogenesis, whereas low-molecular-weight fucoidan displays a stimulatory effect (Ustyuzhanina *et al*., 2014). These data highlight differences in fucoidan isolate action, suggesting that the antibacterial effect is caused by multiple factors, including the algal species, monosaccharide composition, sulfate content, and molecular weight (Ustyuzhanina *et al*., 2014).

Common fucoidan preparations contain naturally occurring high-molecular-weight fucoidan (molecular weight: 200–300 kDa). However, given their better intestinal absorption rate, considerably low-molecular-weight fucoidan (molecular weight < 1 kDa) has been increasingly marketed for use as a dietary supplement in recent years (Takahashi *et al*., 2018). Further, owing to its antioxidant, whitening, and antibacterial effects, fucoidan is regularly utilized as an active ingredient in skin care quasi-drugs, such as beauty salves and hair growth-promoting products. Considering that fucoidan of varying molecular weights extracted from different algal species may differ in their actions, it is crucial to ascertain the suitability of different fucoidan preparations for each application. For example, when used in skincare products, the antibacterial and growth-inhibitory effects of high-molecular-weight fucoidan must be investigated, especially on indigenous skin bacteria, as these remain largely unknown.

In this study, we investigated ultra-high-molecular-weight (>1700 kDa) fucoidan derived from mozuku. This type of fucoidan has a higher molecular weight than ordinary high-molecular-weight (200–300 kDa) fucoidans owing to its extraction and purification process. Thus, the actions of mozuku-derived fucoidan may differ from those of the previously reported low- or high-molecular-weight fucoidan. Therefore, the aim of this study was to evaluate the growth-inhibitory effects of mozuku-derived ultra-high-molecular-weight fucoidan preparation on three types of indigenous skin bacteria and three types of general bacteria.

MATERIALS AND METHODS

Materials

Tongan fucoidan preparation (TFP) or Amami fucoidan preparation (AFP) with preservatives (3% pentylene glycol and 0.5% phenoxyethanol), including preparations containing 1.2% Tongan fucoidan extract or 1.2% Amami fucoidan extract, and a preservative-free preparation containing 1.2% Tongan fucoidan extract (TFE) were used in the experiments. The preparation process for the TFP, AFP, and TFE is shown in Fig. 1. Fucoidan derived from mozuku seaweed *Cladosiphon novae-caledoniae* from the Kingdom of Tonga was mixed with 45% ethanol for 10 min, then dried using a centrifugal dehydrator to remove pigments and water, and finally treated with 0.2% hydrogen peroxide and 20 mM sodium hydroxide to yield a mild alkaline solution (pH 7.5 to 8.0). The fucoidan fraction was extracted by mixing it with 0.2% hydrogen peroxide and 20 mM sodium hydroxide and stirring at 90°C for 1 hr. The extract was neutralized with hydrochloric acid, and the TFE was concentrated via filter press filtration and ultrafiltration. A preservative was added to TFE, followed by UV sterilization and filtration through a 0.45-μm filter to remove contaminants and obtain the TFP. The AFP was prepared in the same way as the TFP using Amami mozuku seaweed *Cladosiphon okamuranus* instead of *C. novae-caledoniae*.

Analysis of the components of fucoidan preparations

The molecular weights of the components of the

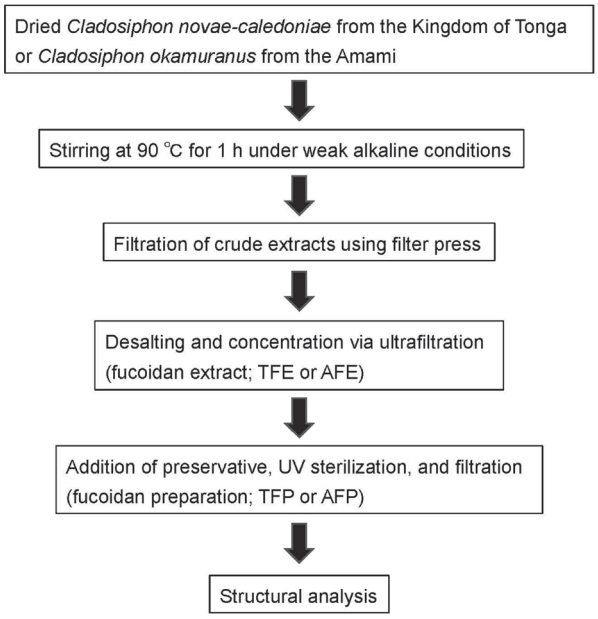

Fig. 1. Schematic workflow for the preparation of ultra-high-molecular-weight fucoidan extract of *Caladosiphon novae-caledoniae* or *Caladosiphon okamuranus*.

fucoidan preparation were determined via shim-pack gel permeation chromatography and differential refractive index detector using Shimadzu CLASS-VP software (Shimadzu, Kyoto, Japan).

In fucoidan preparation, neutral sugars were measured using the phenol-sulfuric acid method: 0.5 mL of a sample diluted 50-fold, 0.5 mL of 5% phenol, and 2.5 mL of concentrated sulfuric acid were added, stirred, and allowed to stand for 10 min. The absorbance at 490 nm was then measured. A calibration curve was prepared with fucose (12.0 mg/100 mL). Uronic acid content was determined using the carbazole sulfate method: 0.3 mL of a sample diluted 50-fold and 1.8 mL of 0.025 M sodium tetraborate/concentrated sulfuric acid solution were mixed and heated at 100°C for 10 min. After cooling, 60 mL of a carbazole solution (125 mg /100 mL ethanol) was added and heated at 100°C for 15 min. The absorbance at 525 nm was then measured. A calibration curve was prepared with glucuronic acid (9.4 mg /100 mL). Sulfate roots were assessed using the barium chloride-rodizonic acid method: 100 μL of a 1.2% concentration sample was hydrolyzed by adding 650 μL of water and 250 μL of concentrated hydrochloric acid at 100°C for 2 hr. After lyophilization, the powder was dissolved in 1000 μL of water. Next, 1.0 mL of ethanol and 0.5 mL of barium chloride buffer were added to 250 μL of the sample and stirred. Then, 0.75 mL of disodium rhodizonate reagent was added, stirred, and left in the dark for 10 min. The absorbance at 520 nm was then measured. A calibration curve was prepared with sodium sulfate (17.7 mg/100 mL).

For sugar composition, 100 μL of the sample was lyophilized, 0.5 mL of 5.0% HCl-MeOH solution was added and reacted at 90°C for 12 hr (methanolysis). After nitrogen drying, 100 μL of trimethylsilyl reagent was added and heated at 80°C for 10 min (silylation). The reaction mixture was suspended in 1.0 mL of hexane, and centrifuged, and the supernatant was subjected to gas chromatography-mass spectrometry (GC-MS) analysis, which was performed using a SHIMADZU GC-2010/QP-2010 plus gas chromatograph/mass spectrometer system (Shimadzu, Kyoto, Japan). The column was SGE-BPX5 (0.32 mm × 30 m). The column temperature was maintained at 50°C for the first minute, increased to 140°C at a rate of 20°C/min, and then increased to 250°C at a rate of 3°C/min. Sample injection was performed using the splitless injection method (1 min); the MS measurement range was *m*/*z* 50–400, sample introduction and ion source temperatures were both 250°C, and detector voltage was 1.0 KV. Compounds were identified by comparing elution times of library research and standards using the accompanying National Institute of Standards and Technology database by the U.S. Secretary of Commerce.

Preparation characteristics included osmotic pressure measured using a freezing point depression-type osmometer (Fiske Mark 3 Osmometer, Fiske Associates, Norwood, MA, USA), viscosity measured using an SV series Vibro viscometer (A&D, Tokyo, Japan), and pH value measured using a pH meter F-52 (Horiba, Kyoto, Japan).

Strains

Indigenous skin bacteria (*Staphylococcus aureus* NBRC12732, *Staphylococcus epidermidis* NBRC12993, and *Cutibacterium acnes* subsp. *acnes* NBRC107605) and general bacteria (*Lactobacillus casei* NBRC15883, *Escherichia coli* NBRC3972, and *Bacillus subtilis* NBRC3134) were used. All strains were provided by the Biological Resource Center of the National Institute of Technology and Evaluation (NBRC) in Chiba, Japan.

Bacterial culture medium

S. aureus, *S. epidermidis*, *E. coli*, and *B. subtilis* were cultured aerobically using the NBRC medium No. 802 (1% hypolypeptone, 0.2% yeast extract, 0.1% $MgSO_4 \cdot 7H_2O$). *L. casei* was cultured aerobically using

the MRS medium (Fujifilm Wako Pure Chemicals, Osaka, Japan). *C. acnes* was cultured anaerobically using the GAM medium (Nissui Pharmaceutical, Tokyo, Japan) in an AnaeroPack-Kenki system (Mitsubishi Gas Chemistry, Tokyo, Japan).

Growth test

To quantify the growth-inhibitory effect on the fucoidan preparation, the growth of the test strains was measured using a modified micro-liquid dilution method. Each test strain was cultured on the liquid medium described above. Twenty percent solutions were prepared by mixing 800 µL of the liquid medium with 200 µL of each sample (TFP, AFP, TFE, only preservatives without fucoidan, and sterile water). The solutions were then serially diluted with the liquid medium to create the following dilution series, with fucoidan contents of 0.04%, 0.08%, and 0.16%. Each test strain was inoculated into 200 µL of the dilution series to achieve an OD_{600} = 0.05 and was incubated at 37°C for 48 hr. The absorbance of the culture medium was measured over time (0, 6, 12, 24, and 48 hr) using a plate reader (200 PRO M Plex; TECAN Infinite, Männedorf, Switzerland) to measure OD_{600} and evaluate bacterial growth.

Statistical analysis

For the growth of indigenous skin and general bacteria, the mean and standard deviation were calculated for the OD_{600} measurements. Subsequently, a one-way analysis of variance (ANOVA) was performed, followed by Tukey's multiple comparison *post-hoc* test. The significance level was set at 5%. All statistical analyses were performed using Easy R software (Kanda, 2013).

RESULTS

Characteristics of ultra-high-molecular-weight fucoidan preparations

The results of the glycan analysis of the ultra-high-molecular-weight fucoidan preparation are shown in Table 1. The percentage composition of the TFP was sugar 65.4%, sulfate 11.7%, glucuronic acid 16.5%, fucose 59.7%, xylose 3.6%, mannose 0.8%, and galactose 1.3%. The percentages composition of the AFP was sugar 62.9%, sulfate 11.1%, glucuronic acid 15.8%, fucose 59.4%, xylose 2.4%, mannose 0.4%, and galactose 0.7%. Further, the osmolalities of the TFP, AFP, and only preservative without fucoidan were 390, 427, and 338 mOsm/kg H_2O; the viscosities of the 10% diluted preparations were 7.57, 7.71, and 1.11 mPa·s; the pH values were slightly acidic at 6.1, 6.1, and 6.3, respectively. In summary, the two fucoidan preparations were comparable in terms of the percentage of constituent sugars, osmolality, viscosity, and pH.

Table 1. Composition of ultra-high-molecular-weight fucoidan preparations

Seaweed composition	Tongan fucoidan preparation	Amami fucoidan preparation
Sugar (%)	65.4	62.9
Sulfate (%)	11.7	11.1
Uronic acid (%)	16.5	15.8
Fucose (%)	59.7	59.4
Xylose (%)	3.6	2.4
Mannose (%)	0.8	0.4
Galactose (%)	1.3	0.7

Evaluation of growth-inhibitory effects of ultra-high-molecular-weight fucoidan preparations

To evaluate the growth-inhibitory effect of the ultra-high-molecular-weight fucoidan preparations on indigenous skin bacteria, *S. aureus* and *S. epidermidis* were incubated for 24 hr in the presence of sterile water, preservative, TFP, or AFP. The results showed that the 0.04%, 0.08%, and 0.16% Tongan and Amami fucoidan preparations inhibited the growth of *S. aureus* and *S. epidermidis* (Fig. 2). Among the preservative solutions, only the 0.16% dilution showed growth inhibition against *S. epidermidis*. The 0.08% and 0.16% fucoidan preparations showed stronger growth inhibition of *S. aureus* and *S. epidermidis* than the preservative (Fig. 2).

Evaluation of growth-inhibitory effects of ultra-high-molecular-weight fucoidan on bacteria

To evaluate the growth-inhibitory effect of ultra-high-molecular-weight fucoidan on bacteria, all test strains were cultured in sterile water, preservative, and TFE, TFP, and AFP at 0.08% fucoidan content. In the logarithmic growth phases of each bacterium, fucoidan extract and fucoidan preparation were evaluated in terms of growth inhibition ratio with sterile water and preservatives, respectively. The results showed that TFE, TFP, and AFP more effectively inhibited the growth of *S. aureus* and *S. epidermidis* than preservative and sterile water (Fig. 3 and Table 2). However, TFE, TFP, and AFP did not inhibit the growth of *C. acnes*, *L. casei*, *E. coli*, and *B. subtilis* (Fig. 3 and Table 2).

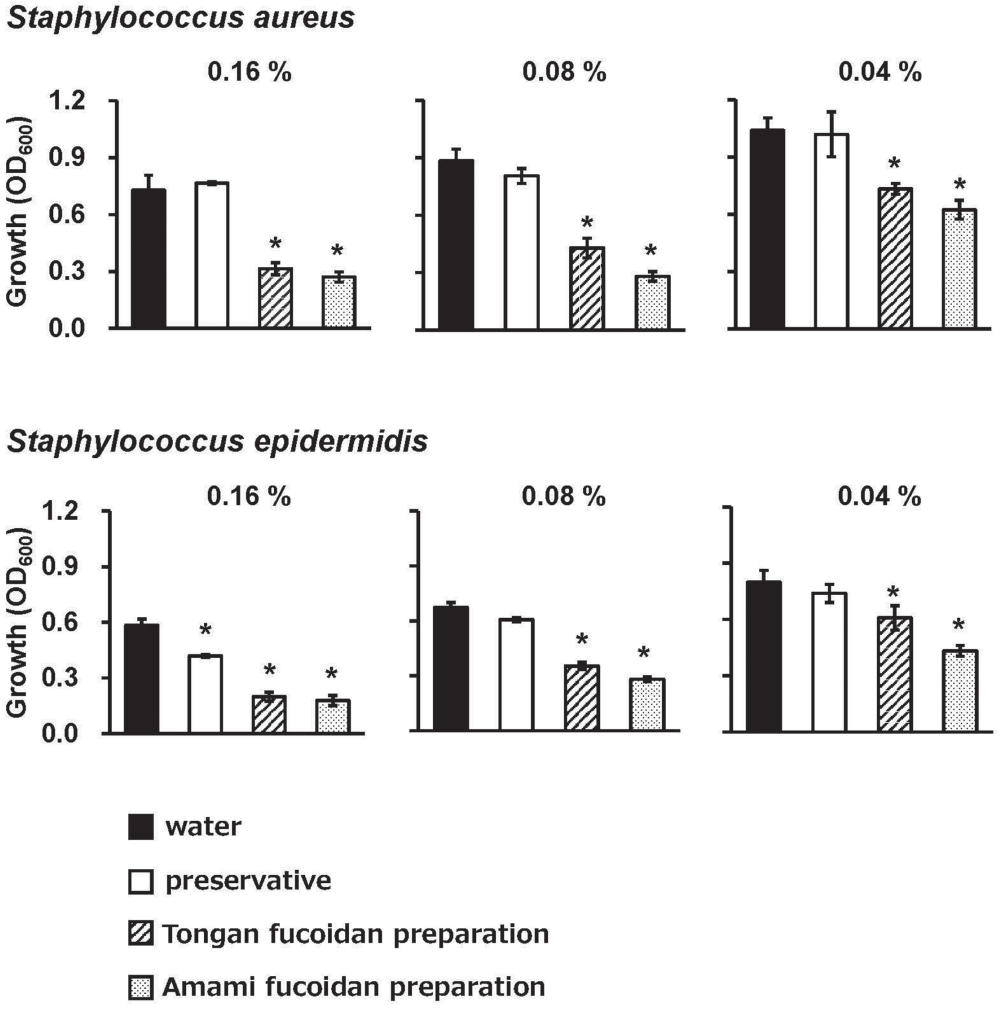

Fig. 2. Growth-inhibitory effect of ultra-high-molecular-weight fucoidan preparations on skin bacteria. *Staphylococcus aureus* and *Staphylococcus epidermidis* were cultured for 12 hr in NBRC medium No. 802 containing 0.16, 0.08, or 0.04% Tongan fucoidan preparation or Amami fucoidan preparation, and bacterial growth was measured at 600 nm absorbance. Growth inhibition by preservatives, Tongan fucoidan preparation, or Amami fucoidan preparation was evaluated using water as the standard. Data are presented as means ± standard error of the means (n = 4). * $p < 0.05$.

DISCUSSION

In the present study, using a modified micro-liquid dilution method, we examined the growth-inhibitory effects of mozuku-derived ultra-high-molecular-weight fucoidan preparation on indigenous skin and general bacteria. The results showed that fucoidan preparations derived from Tongan mozuku *C. novae-caledoniae* and Amami mozuku *C. okamuranus* inhibited the growth of *S. aureus* and *S. epidermidis*.

Effect of fucoidan on *S. aureus* and *S. epidermidis*

Our analysis indicated that the fucoidan treatments had a stronger growth-inhibitory effect on indigenous skin bacteria (*S. aureus* and *S. epidermidis*) compared to sterile water or preservatives. As the percentage of *S. aureus* correlates with the disease severity of atopic dermatitis (Kong *et al*., 2012) and relative increases in both *S. aureus* and *S. epidermidis* are reported at the onset of atopic dermatitis (Bjerre *et al*., 2017; Kong *et al*., 2012), both indigenous skin bacteria appear to be contributing factors for skin diseases (Bjerre *et al*., 2017; Kong *et al*., 2012). In our study, mozuku-derived ultra-high-molecu-

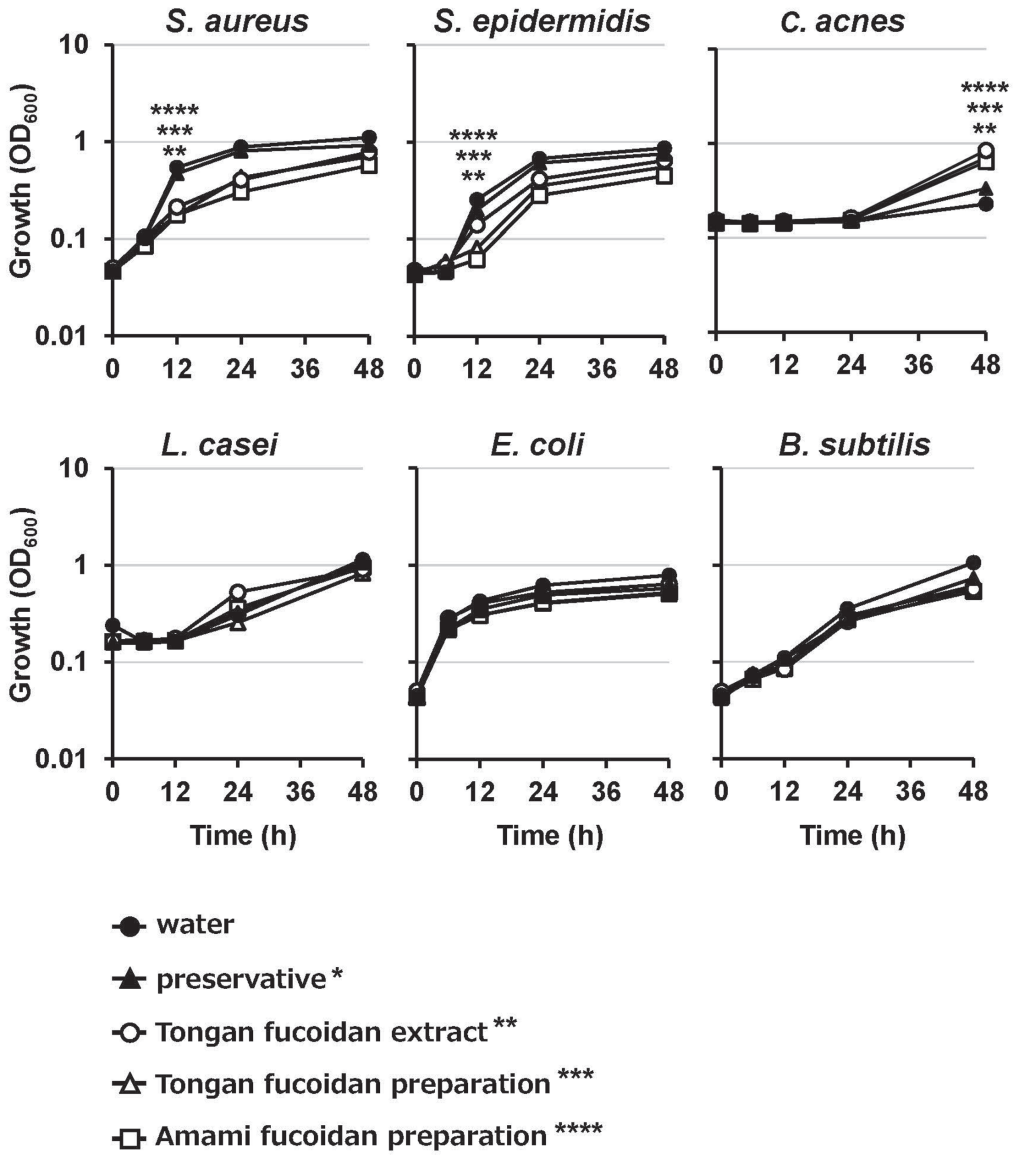

Fig. 3. Growth-inhibitory effect of ultra-high-molecular-weight fucoidan on the bacteria. Bacteria were cultured in each medium containing 0.08% Tongan fucoidan extract, Tonga fucoidan preparation, or Amami fucoidan preparation for 48 hr, and Average of bacterial growth was measured at 600 nm absorbance (n = 4). Each culture containing water as the standard was also incubated and compared to water at the log growth stage of each bacterium. Significant differences of growth-inhibitory effect are shown in preservatives, * $p < 0.05$, Tongan fucoidan extract, ** $p < 0.05$, Tongan fucoidan preparation, *** $p < 0.05$, and Amami fucoidan preparation, **** $p < 0.05$, respectively.

lar-weight fucoidan showed a growth-inhibitory effect against *S. aureus* and *S. epidermidis* during their logarithmic growth phases (6–24 hr), suggesting that the application of fucoidan preparations at intervals of 24 hr or less may help maintain their efficacy on skin diseases.

The bacterium *S. epidermidis* can hydrolyze triacylglycerol, and the glycerol it produces is involved in moisturizing effects (Puhvel *et al*., 1975). A previous study, in which *S. epidermidis* was collected from subjects and cultured, reported that its application to the face, twice a week for 4 weeks, led to increased lipid content and suppressed moisture evaporation (Nodake *et al*., 2015). Thus,

Table 2. Evaluation of the growth-inhibitory effect of ultra-high-molecular-weight fucoidan during the logarithmic growth phase of the test strains

Bacterial strain	*Staphylococcus aureus*	*Staphylococcus epidermidis*	*Cutibacterium acnes*	*Lactobacillus casei*	*Escherichia coli*	*Bacillus subtilis*
Tongan fucoidan extract	+++	++	-	-	±	+
vs water	(0.39 ± 0.02*)	(0.55 ± 0.03*)	(3.62 ± 0.89*)	(1.78 ± 0.37*)	(0.95 ± 0.03*)	(0.75 ± 0.08*)
Tongan fucoidan preparation	+++	+++	-	+	+	±
vs preservative	(0.38 ± 0.05*)	(0.40 ± 0.02*)	(2.15 ± 0.29*)	(0.79 ± 0.05*)	(0.87 ± 0.04*)	(1.13 ± 0.23)
Amami fucoidan preparation	+++	+++	-	±	+	±
vs preservative	(0.38 ± 0.03*)	(0.31 ± 0.02*)	(1.99 ± 0.45*)	(1.11 ± 0.08)	(0.87 ± 0.03*)	(1.03 ± 0.12)

Growth ratio: +++ < 0.5, ++ < 0.7, + < 0.9, 0.9 ≤ ± ≤ 1.2, - > 1.2. The growth of *S. aureus*, *S. epidermidis*, *C. acnes*, *L. casei*, *E. coli*, and *B. subtilis* during their respective logarithmic growth phases at 12, 12, 48, 24, 12, and 24 hr was measured via absorbance at 600 nm. Fucoidan extract and fucoidan preparation were evaluated in terms of growth ratio with water and preservatives as standards (1.00), respectively. Data are presented as means ± standard error of the means (n = 4). * $p < 0.05$.

S. epidermidis application improves moisture retention and maintains the skin in a slightly acidic state, suggesting that it is a suitable candidate for the treatment of skin diseases. Phenol-soluble modulins produced by *S. epidermidis* selectively inhibit *S. aureus* and *Streptococcus* (Claudel *et al*., 2019). Moreover, *S. epidermidis* reportedly exhibits antibacterial activity against *C. acnes* through glycerol fermentation (Wang *et al*., 2016). In our study, mozuku-derived ultra-high-molecular-weight fucoidan inhibited the growth of both *S. aureus* and *S. epidermidis*. In addition, the growth of *S. epidermidis* can enhance moisture retention via glycerol production, rendering the skin weakly acidic, ultimately preventing and helping treat atopic dermatitis and acne by inhibiting the growth of *S. aureus* and *C. acnes* (Park *et al*., 2021). Therefore, even if mozuku-derived fucoidan suppresses the proliferation of *S. epidermidis* and reduces water retention through glycerol production, the moisture-retaining and hygroscopic effects of fucoidan itself may compensate for the reduction.

S. epidermidis is the most frequent cause of sepsis, and *S. aureus* is a causative agent of nosocomial infections (Nguyen *et al*., 2017). Recently, a spray preparation containing mupirocin, which has shown inhibitory effects against a wide range of gram-positive bacteria, including *S. aureus* and *S. epidermidis*, has been applied clinically (Sritharadol *et al*., 2017). Therefore, based on our findings involving the suppression of *S. aureus* and *S. epidermidis*, we propose that a mozuku-derived ultra-high-molecular-weight fucoidan preparation holds the potential to be developed as a nosocomial infection prevention drug (Sritharadol *et al*., 2017).

Effect of fucoidan on *C. acnes*

The slow-growing microaerophilic and anaerobic bacterium *C. acnes* is a member of the dermal commensal flora (Lytle *et al*., 2020). In our study, the growth of *C. acnes* was slower under aerobic conditions than under anaerobic conditions (data not shown). Although the growth of *C. acnes* remained constant for up to 24 hr under anaerobic conditions, it began to increase afterward. Moreover, mozuku-derived fucoidan showed significant growth-promoting and growth-inhibitory effects against *C. acnes* and *S. epidermidis*, respectively. Considering that *C. acnes* hydrolyzes sebum triacylglycerols, secretes propionic acid to maintain an acidic pH level, and inhibits *S. aureus* growth (Claudel *et al*., 2019), mozuku-derived fucoidan may help retain skin moisture by increasing glycerol production and inhibiting *S. aureus* proliferation through ensuring a slow proliferation of *C. acnes* (Byrd *et al*., 2018). When used for atopic dermatitis with acne, mozuku-derived fucoidan products may be effective if applied after washing keratin and excess sebum from open hair pores at intervals of 24 hr or less.

Effect of fucoidan on general bacteria

Notably, in our study, mozuku-derived ultra-high-molecular-weight fucoidan showed growth inhibition against *S. aureus* and *S. epidermidis* but not against *L. casei*, *E. coli*, and *B. subtilis*, suggesting that the growth-inhibiting effect varies with bacterial species.

Effects of location and species

Fucoidan preparations from Tonga and Amami exhibited similar effects on *S. aureus*, *S. epidermidis*, *C. acnes*, *E. coli*, and *B. subtilis*. However, fucoidan preparation from these two regions displayed opposing, although

weak, effects on *L. casei*, suggesting that the effect of fucoidan on the strains used in the present study was unaffected by differences in the location of origin. The fucoidan-rich fraction derived from *S. vachellianum* did not exhibit antibacterial activity against both *S. aureus* (gram-positive bacteria) and *E. coli* (gram-negative bacteria), whereas the polyphenol-rich fraction obtained during the extraction process did (Jesumani *et al*., 2020). Further, the fucoidan extract derived from *S. japonica* did not exhibit bactericidal activity against both *S. aureus* and *E. coli*. However, its low-molecular-weight products showed bactericidal activity, with weak activity at 80 kDa or higher, and high activity by fucoidan with a molecular weight below 6 kDa. These findings are consistent with those of a previous study reporting weak bactericidal activity of fucoidan derived from *S. japonica* with a molecular weight of 80 kDa or higher (Liu *et al*., 2017), and that its bactericidal activity is more effective against *E. coli* than *S. aureus* (Liu *et al*., 2017). Although the 160 kDa high-molecular-weight fucoidan used in this study did not exhibit bactericidal activity (data not shown), it exhibited effective growth-inhibition effects against the gram-positive bacteria, *S. aureus* and *S. epidermidis*. However, it did not inhibit the growth of *E. coli*, a gram-negative bacterium. Thus, the bactericidal and growth-inhibitory effects of fucoidan on bacteria differ depending on the species, molecular weight, and composition.

Future prospects

In this study, mozuku-derived ultra-high-molecular-weight fucoidan showed growth-inhibitory activity against *S. aureus* and *S. epidermidis*, suggesting its potential for pharmaceutical and cosmetic applications. Although this study evaluated the growth-inhibitory effect of ultra-high-molecular-weight fucoidan on six bacterial strains, the safety and side effects of fucoidan on the indigenous human skin flora, including *S. aureus* and *S. epidermidis*, and on the treatment of atopic dermatitis have not yet been evaluated. Therefore, further studies are needed to clarify the effects of fucoidan on skin microflora and the pathophysiology of atopic dermatitis and other conditions.

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Conflict of interest---- The authors declare that there is no conflict of interest.

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