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RESEARCH ARTICLE

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Anti-acne properties of hydrophobic fraction of red ginseng (*Panax ginseng* C.A. Meyer) and its active components

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Acne is a chronic inflammatory disease of the skin that occurs when bacteria abnormally grow in hair follicles. The most common treatment is antibiotics, but they are limited due to antibiotic resistance. The purpose of this study was to identify the active ingredients of the antimicrobial effects of red ginseng (*Panax ginseng* C.A. Meyer), compare it to existing antibacterial substances, and determine its potential efficacy as a natural drug product. The hydrophobic fraction in red ginseng ethanol extract (RGEF) showed the same or better antimicrobial activity against *Propionibacterium acnes* than benzoyl peroxide or azelaic acid. In addition, the antimicrobial component derived from red ginseng selectively showed a high antimicrobial effect on *P. acnes*. Nuclear magnetic resonance spectroscopic analysis showed that the active antimicrobial substance in this fraction was panaxynol and panaxydol. Twenty subjects who had acne symptoms were treated with cream containing 3 mg/g of RGEF for 4 weeks. It was found that oxidized sebum contents and redness of the skin were reduced, and symptoms of the early to middle stage of acne were effectively improved. This study showed that red ginseng extract containing panaxynol and panaxydol can effectively control the symptoms of acne.

KEYWORDS

anti-acne, antibacterial ingredient, *Panax ginseng* C.A. Meyer, panaxydol, panaxynol, red ginseng

1 | INTRODUCTION

Acne is a chronic inflammatory disease of the skin involving the sebaceous glands and hair follicles and is characterized by comedones, papules, pustules, cysts, and nodules that appear on the face, chest, back, and shoulders (Williams, Dellavalle, & Garner, 2012). It is known that acne is caused by a combination of various factors such as hereditary, fatigue, or stress, and it is generally known that acne develops by excessive sebum production, *Propionibacterium acnes* proliferation, and inflammation reaction (Contassot & French, 2014). Particularly, skin damage caused by excessive and repetitive inflammatory reactions leaves scars even after complete recovery, which lowers a patient's self-esteem psychologically, often leading to an unfulfilling social life (Darji, Varade, West, Armbrecht, & Guo, 2017).

Various methods have been used for the treatment of acne: inhibition of excessive sebum production using hormone agents; inhibition of proliferation of *P. acnes* using lasers, antibacterial agents, or antibiotics; prevention of pore blockages through chemical peels, etc. (Fox, Csongradi, Aucamp, du Plessis, & Gerber, 2016). Among these methods, topical agents are most widely used to inhibit the proliferation of *P. acnes*. It is recommended to use antibacterial materials such as benzoyl peroxide rather than antibiotics such as erythromycin or clindamycin due to tolerance issues (Gollnick & Krautheim, 2003). In particular, in order to maximize the effects of such antibacterial substances, a combination therapy of various components was performed (Gollnick, 2003). To that end, it is required to develop a variety of antibacterial materials that are both safe and effective (Fu & Vender, 2011).

As a natural medicine, ginseng (*Panax ginseng* C.A. Meyer) is known as a medicinal plant that has minimal side effects on the human body and various biologically active effects. In general, it is typically known that ginseng improves immunity (Sohn et al., 2008), enhances blood flow (Lee et al., 2008) and memory (Zhang et al., 2008), prevents skin

damage from ultraviolet rays (Lee et al., 2009), and increases antioxidant effects (Kang, Yokozawa, Yamabe, Kim, & Park, 2007). These physiologically beneficial effects of ginseng are known to be caused by saponin, a main ingredient of ginseng. However, in recent years, many pharmacological effects of nonsaponin components have been reported, too. Polyacetylene, one of the typical nonsaponin components, has been found in about 20 kinds of ginseng and red ginseng (Yeo, Yong, & Popovich, 2017). Polyacetylene reportedly has positive effects such as anti-inflammation (Lee et al., 2006), anticancer (Mayer, Steinreiber, Orru, & Faber, 2002), improved blood circulation (Teng et al., 1989), prevention of brain damage (Nie et al., 2008), and antibacterial effects (Bae, Han, Baek, & Kim, 2001). Usually, ginseng refers to white ginseng and is produced by air-drying fresh ginseng. Red ginseng is produced by repeatedly steaming and air-drying fresh ginseng (Im, Kim, & Min, 2016).

This study aims to identify the active antimicrobial ingredients from red ginseng (*P. ginseng* C.A. Meyer) to treat *P. acnes*. Its efficacy is compared with other over-the-counter (OTC) ingredients, benzoyl peroxide, and azelaic acid. We also performed a human clinical trial with topical formulation containing antibacterial ingredients and analyzed the in vivo efficacy.

2 | MATERIALS AND METHOD

2.1 | Sample preparation and isolation

The 6-year-old fresh ginseng roots (*P. ginseng* C.A. Meyer) were prepared by steaming and drying to make red ginseng in the red ginseng manufacturing plant of Korea Ginseng Corporation (Buyeo, Chungnam, Korea). Red ginseng samples (dry weight, 5 kg) were macerated and extracted repeatedly with distilled water (20 L × 2) at 70°C for 8 hr to prepare samples of red ginseng extracts with water (RGW). Red ginseng ethanol extracts (RGE) were prepared as an extraction with 70% ethanol at 70°C for 8 hr. The crude extract was separately fractioned with a Diaion® HP-20 column. The hydrophilic fraction was eliminated sequentially by eluting with ethanol gradient beginning with 100% water and increasing with 30% and 50% ethanol aqueous solution. A hydrophobic fraction of red ginseng extracts with water (RGWF) and hydrophobic fraction of RGE (RGEF) were obtained by eluting with ethanol.

The RGEF was subjected to medium-pressure LC (CombiFlash Rf 200, Teledyne Isco, Lincoln, NE, USA) with a reversed silica column (YMC-Dispopack AT. ODS-25 g: 40 g) using sequential mixtures of MeOH and H_2O (50% aq. MeOH to 100% MeOH for 50 min). Guided by the results of bioactivity, MPLC-2 was purified by reversed silica semipreparative HPLC (YMC-Pack ODS-A, 250 × 10 mm, 40% aq. AcCN to 90% aq. AcCN for 55 min.) to yield 17.2mg of compound 1 (Rt = 44.3 min) and MPLC-3 was purified by reversed silica semipreparative HPLC (YMC-Pack ODS-A, 250 × 10 mm, 70% aq. AcCN to 100% aq. AcCN for 60 min.) to yield 60.0 mg of compound 2 (Rt = 57.5 min). Benzoyl peroxide, azelaic acid, and tea tree oil were purchased from Sigma-Aldrich (Saint Louis, MO, USA).

Compound **1** (Panaxydol): clear oil; ^{1}H-NMR ($CDCl_3$) δ 5.94 (1H, ddd, *J* = 17.0, 10.1, 5.6 Hz, H-2), 5.47 (1H, br d, *J* = 17.0 Hz, H-1a), 5.25 (1H, br d, *J* = 10.1 Hz, H-1b), 4.92 (1H, d, *J* = 5.2 Hz, H-3), 3.15 (1H, ddd, *J* = 7.0, 5.4, 4.3 Hz, H-9), 2.97 (1H, dd, *J* = 6.0, 4.3 Hz, H-10), 2.70 (1H, dd, *J* = 17.7, 5.5 Hz, H-8b), 2.38 (1H, dd, *J* = 17.7, 6.8 Hz, H-8a), 1.41 ~ 1.57 (4H, m, H-11~12), 1.20 ~ 1.39 (8H, m, H-13~16), 0.88 (3H, t, *J* = 7.0 Hz, H-17); ^{13}C-NMR ($CDCl_3$) δ 136.0 (C-2), 117.2 (C-1), 76.7 (C-7), 74.9 (C-4), 70.9 (C-5), 66.3 (C-6), 63.5 (C-3), 57.1 (C-10), 54.4 (C-9), 31.8 (C-15), 29.4 (C-13), 29.2 (C-14), 27.5 (C-11), 26.5 (C-12), 22.6 (C-16), 19.4 (C-8), 14.1 (C-17); HRFABMS *m/z* 283.1670 $[M + Na]^+$ (calculated for $C_{17}H_{24}O_2Na$, *m/z* 283.16741).

Compound **2** (Panaxynol): clear oil; ^{1}H-NMR ($CDCl_3$) δ 5.94 (1H, ddd, *J* = 17.0, 10.2, 5.4 Hz, H-2), 5.51 (1H, m, H-10), 5.49 (1H, br d, *J* = 17.0 Hz, H-1a), 5.36 (1H, m, H-9), 5.23 (1H, br d, *J* = 10.1 Hz, H-1b), 4.90 (1H, d, *J* = 5.3 Hz, H-3), 3.03 (2H, d, 7.0 Hz, H-8), 2.02 (2H, q, *J* = 7.3 Hz, H-11), 1.20 ~ 1.36 (10H, m, H-12~16), 0.88 (3H, t, *J* = 7.0 Hz, H-17); ^{13}C-NMR ($CDCl_3$) δ 136.2 (C-2), 133.1 (C-10), 121.9 (C-9), 117.0 (C-1), 80.2 (C-7), 74.3 (C-4), 71.2 (C-5), 64.0 (C-6), 63.5 (C-3), 31.8 (C-15), 29.2 (C-12), 29.2 (C-13), 29.2 (C-14), 27.2 (C-11), 22.7 (C-16), 17.7 (C-8), 14.1 (C-17); HRCIMS *m/z* 245.1904 $[M + H]^+$ (calculated for $C_{17}H_{25}O$, *m/z* 245.19055).

2.2 | HPLC analysis of RGEF

HPLC analysis of RGEF was performed on a Waters 2695 system (Waters, Milford, MA, USA) equipped with a Waters 996 photodiode array detector, auto-sampler, and degasser. The RGEF was separated on a phenomenex kinetex C18 column (150 × 4.6 mm, 5 μm) with isocratic elution system. The mobile phase consisted of 20:80 of Solvents A (water) and B (ACN:MeOH = 2:1). The injection volume was 10 μl, and the flow rate was 0.4 ml/min. The chromatogram of RGEF was monitored at 203 nm.

2.2.1 | Microorganisms and culture method

The standard strains of *P. acnes* (ATCC 6919, American Type Culture Collection, Manassas, VA, USA), *Streptococcus mutans* (KCTC 3065, Korean Collection for Type Cultures, Jeonbuk, South Korea), and *Fusobacterium nucleatum* (KCTC 2640) were cultured in reinforced clostridial agar medium (Difco Laboratories Inc., Franklin Lakes, NJ, USA). *Escherichia coli* (KCTC 2448), *Pseudomonas aeruginosa* (KCTC 1637), *Bacillus subtilis* (KCTC 1666), and *Staphylococcus aureus* (KCTC 1916) were cultured in tryptic soy agar medium (Difco Laboratories Inc.). *Candida albicans* (KCTC 27386) and *Aspergillus niger* (KCTC 6911) were cultured in potato dextrose agar medium (Difco Laboratories Inc.). The strains of *P. acnes*, *S. mutans*, and *F. nucleatum* were cultured at 37°C in anaerobic atmosphere containing 10% (v/v) CO_2, 10% (v/v) H_2, and 80% (v/v) N_2. Other strains were cultured at aerobic atmosphere containing 10% (v/v) CO_2, 10% (v/v) H_2, and 80% (v/v) N_2. Each cell suspension was diluted with sterile phosphate-buffered saline to provide initial cell counts of 10^{6-8} CFU/ml, and inoculation was performed by spreading the microorganism on an agar plate.

2.2.2 | Anti-acne activity measurement

The antimicrobial activity was analyzed by the disc-diffusion method. Each sample, fraction, and control group were dissolved in ethanol with concentrations of 50.0, 25.0, and 12.5 mg/ml. Ethanol was used

as a negative control. All samples were loaded on 13-mm paper discs and were applied on an inoculated agar plate. After 5 days of incubation in anaerobic conditions, the antimicrobial activity was determined by measuring the zones of inhibition (ZOI) around the discs.

2.2.3 | Determinations of antimicrobial spectrum

The RGEF was dissolved in ethanol with a concentration of 12.5 mg/ml, and triclosan was dissolved in ethanol with a concentration of 3.0 mg/ml. All samples were loaded on 13-mm paper discs and applied to an inoculated agar plate. Aerobic bacteria were cultured for 1 day in aerobic condition, and the antimicrobial activity was determined by measuring the ZOI around the discs. Anaerobic bacteria were cultured for 5 days in anaerobic condition, and then, the ZOI was measured. The fungi were cultured for 5 days in aerobic condition, and the ZOI was measured. The antimicrobial spectrum of the RGEF and triclosan was compared through the ZOI of the two substances.

2.2.4 | Skin safety test

The RGEF was diluted with a saline buffer to concentrations of 12.5, 6.25, and 3.12 mg/ml. The 35 μl of RGEF dilute and saline buffer were loaded into a Van der Bend Chamber® (Brielle, The Netherlands). The patch-test chambers were applied to the upper backs of 31 female volunteers. Following occlusion for 24 hr, the patch-test chambers were removed, and readings were performed on Days 0, 1, and 2. The intensity of the reaction was scored and recorded according to the rules of the Draize Dermal Irritation Scoring System (Table 1). The mean scores were calculated by Equation (1). The response grade was then judged using the decision table for skin patch-test result (Table 2).

$$\text{Mean Irritation Index (M.I.I.)} = \frac{\Sigma \text{quotation of the 3 readings (all volunteers)}}{\text{No. of volunteers} \times 3 \text{ (readings)}}. \quad (1)$$

2.2.5 | Clinical trials

The facial cream containing 3 mg/g of RGEF was applied twice a day to 20 men and women age 19 to 40 years for 4 weeks (Approval number: PNK-17810-S1R). The subjects had mild to moderate acne symptoms, and they were selected as healthy persons without severe or chronic physical illnesses including skin diseases. At Weeks 0, 2, and 4 after the start of the study, the oil contents, oxidized sebum contents, and redness of skin were measured using the Sebumeter SM 815 (Courage-Khazaka Electronic GmbH, Germany), Facial Stage DM-3 (Moritex, Japan), and Visia-CR (Canfield Imaging Systems, USA). The number of white/blackheads, papules, and nodules on the face of the subjects were evaluated by two experts as evaluators. When there were differences in the evaluation of the experts, we selected the larger number.

TABLE 1 Notation for patch test results from Draize Dermal Irritation Scoring System

Erythema and eschar formation	Value	Edema formation
No erythema	0	No edema
Very slight erythema	1	Very slight edema
Well-defined erythema	2	Slight edema (edges of area well-defined by definite raising)
Moderate to severe	3	Moderate edema (raised approximately 1 mm)
Severe erythema (beet redness) to slight, eschar formation (injuries in depth)	4	Severe edema (raised more than 1 mm and extending beyond the area of exposure)

TABLE 2 Decision table for skin patch-test result (EPA Dermal Classification System)

Grade	Mean score
Negligible	$0.00 \leq$ M.I.I. < 0.50
Slight reaction	$0.50 \leq$ M.I.I. < 2.00
Moderate reaction	$2.00 \leq$ M.I.I. < 5.00
Strong reaction	$5.00 \leq$ M.I.I. ≤ 8.00

3 | RESULTS AND DISCUSSION

3.1 | Anti-acne activities of samples and OTC drug ingredients

Our results showed that RGEF was the most effective in inhibiting *P. acnes* activity among the samples (Figure 1). Compared with the active ingredients in OTC drugs, the RGEF showed better antimicrobial activities than azelaic acid and benzoyl peroxide at 12.5 mg/ml and higher concentrations. Antimicrobials derived from natural products such as tea tree oil have a low effect compared with the OTC drug ingredients, whereas RGEF has an equivalent or superior antibacterial effect. Additionally, the minimum inhibitory concentrations of benzoyl peroxide, azelaic acid, RGE, and RGEF against *P. acnes* were measured. Minimum inhibitory concentrations of benzoyl peroxide, RGEF, and RGE were 156.3, 625, 10,000 μg/ml, respectively. Azelaic acid showed a slight growth inhibition effect at the maximum concentration (10,000 μg/ml). No growth inhibitory effect was observed in RGW or RGWF.

3.2 | Identification of antimicrobial active components and chemical composition of RGEF

In order to find the antimicrobial active components, RGEF was fractionated by reversed silica semipreparative MPLC. Total four fractions were obtained, and their antibacterial effects were compared. The best antimicrobial effect was confirmed by the MPLC-2 and MPLC-3 fractions (data not shown). Panaxydol (compound **1**) and panaxynol (compound **2**) were isolated from the MPLC-2 and MPLC-3 fractions, respectively, using prep-HPLC (Figure 2b). The structure of the compounds was identified based on combined spectroscopic analyses and comparison to the published spectral data (Yang, Seo, Choi, Park, & Lee, 2008). The antimicrobial activity of the isolated compounds (**1**–**2**) was measured (Figure 2c). As shown

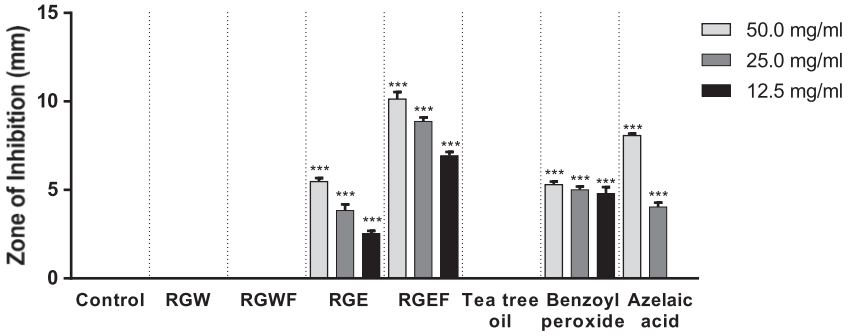

FIGURE 1 Diameter of inhibition zone of RGW, RGWF, RGE, RGEF, tea tree oil, benzoyl peroxide, and azelaic acid against *Propionibacterium acnes*. Results were represented as means ± *SD* (n = 3). *** Significantly different from control group (p < 0.001). Control: Ethanol; RGW: red ginseng extracts with water; RGWF: hydrophobic fraction of RGW; RGE: red ginseng 70% ethanol extracts; RGEF: hydrophobic fraction of RGE

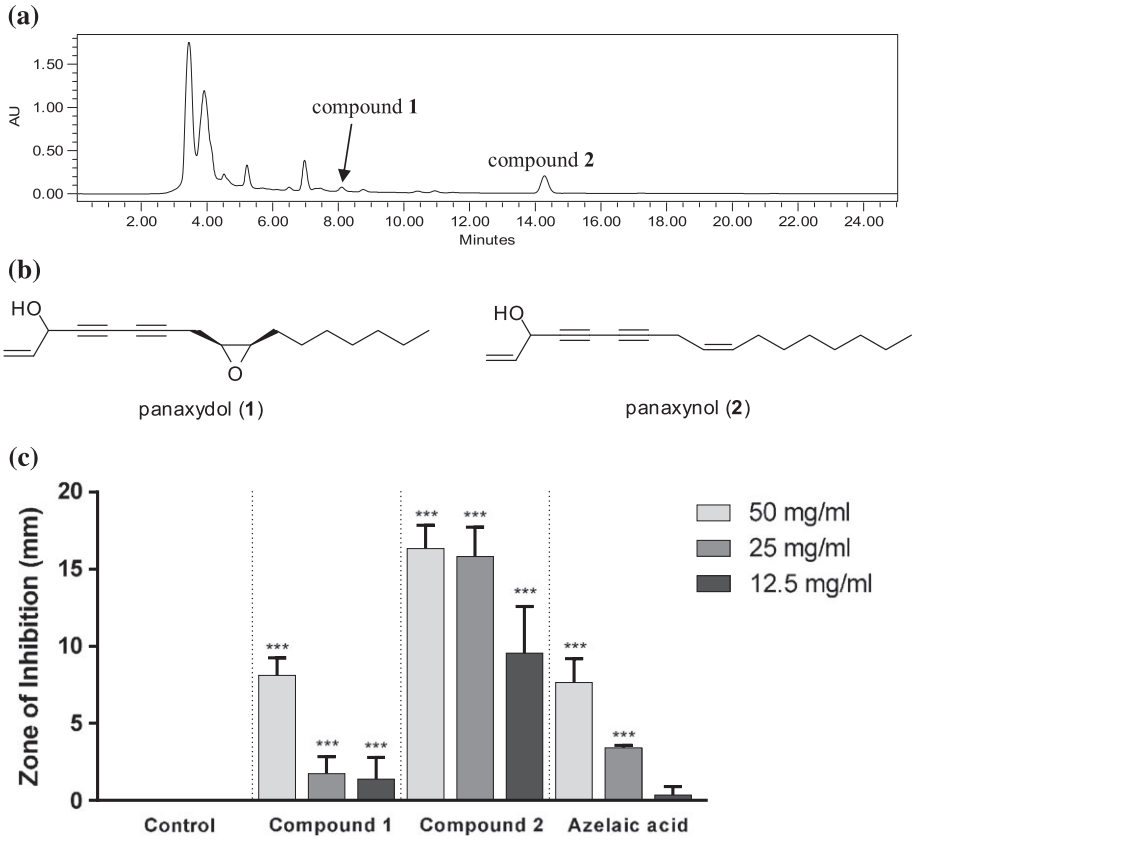

FIGURE 2 (a) UV chromatogram of RGEF (203 nm), (b) structure of compounds **1** and **2**, and (c) diameter of inhibition zone of compounds **1** and **2** against *Propionibacterium acnes*. Results were represented as means ± *SD* (n = 3). *** Significantly different from control group (p < 0.001)

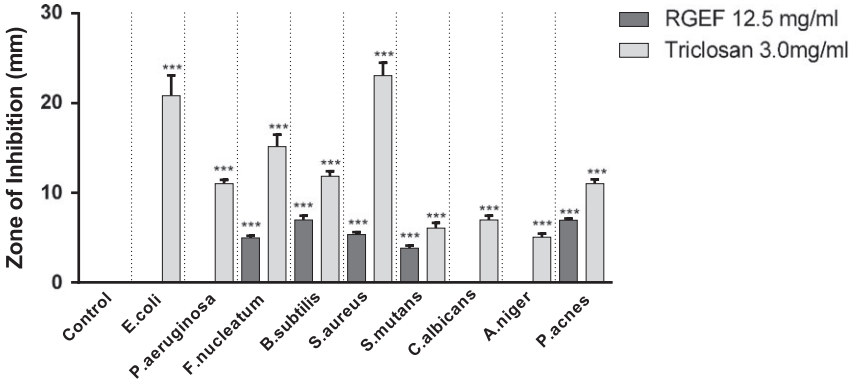

FIGURE 3 Diameter of inhibition zone of the RGEF and triclosan against various strains. Results were represented as means ± *SD* (n = 3). *** Significantly different from control group (p < 0.001). RGEF: hydrophobic fraction of RGE

in Figure 2c, the antimicrobial activity of panaxynol (**2**) was excellent. Previous studies have shown that panaxydol (**1**) or panaxynol (**2**) possess antiproliferation effects on various cancer cell lines including colon cancer, renal cell carcinoma, malignant melanoma, ovarian carcinoma, and hepatocellular carcinoma (Guo et al., 2009; Siddiq & Dembitsky, 2008).

TABLE 3 The results of the skin patch test (n = 31)

		Concentration (mg/ml)																							
		12.50						6.25						3.12						Distilled water					
		Day 0		Day 1		Day 2		Day 0		Day 1		Day 2		Day 0		Day 1		Day 2		Day 0		Day 1		Day 2	
No.	Age	R[a]	E[b]	R	E	R	E	R	E	R	E	R	E	R	E	R	E	R	E	R	E	R	E	R	E
1	46																								
2	23																								
3	21			1		1				1										1		1			
4	52																							1	
5	51																								
6	48	1						2		1		1		1		1				2					
7	47																								
8	52																			1		2			
9	20	1		1				1						1		1									
10	38			2		1				2		1				1									
11	36																			1					
12	54																								
13	45																							1	
14	48													1						1				1	
15	51																			1		1		1	
16	46																								
17	23																								
18	39																								
19	49																	1							
20	44																								
21	40																	1							
22	49																								
23	49																			1					
24	38																					1	1	1	2
25	41																								
26	21																			1		1		1	
27	30																								
28	49																			1					
29	54											1						1							
30	51	1						1												1					
31	29																								
Sum		3	0	4	0	2	0	4	0	4	0	3	0	3	0	3	0	3	0	11	0	6	1	6	2
Value	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1	3	0	2	0	2	0	2	0	2	0	3	0	3	0	3	0	3	0	9	0	4	1	6	0
	2	0	0	1	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	1	0	1	0	0	1
	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.I.I.[c]		0.10						0.12						0.10						0.30					
Grade		Negligible						Negligible						Negligible						Negligible					

[a]R, red spots.

[b]E, edema.

[c]M.I.I. notation in Table 1.

Also, based on the previous studies of the antimicrobial effect (Sung & Lee, 2008; Xue, Yao, Yang, Feng, & Ren, 2017) of red ginseng, saponins were identified as an effective ingredient having a pharmacological effect. However, this study demonstrated that red-ginseng-derived polyacetylenes, in particular, panaxynol and panaxydol, have antimicrobial activities against *P. acnes*.

The chromatographic condition established according to the previously reported literature (Woo et al., 2011) was applied for the simultaneous determination of active constituents in RGEF. RGEF was standardized on the basis of panaxydol (**1**) and panaxynol (**2**). The chromatographic separation of these two compounds in the hydrophobic fraction was successfully achieved (Figure 2a). The

TABLE 4 Changes in oil, oxidized sebum contents, and skin redness after skin application

Period of application	Oil contents of skin (ug/cm^2)	Oxidized sebum contents of skin (ea)	Skin redness
0 day	79.350 ± 28.969	386.45 ± 563.316	11.516 ± 2.909
14 days	54.700 ± 29.439*	347.10 ± 535.230**	10.818 ± 2.584
28 days	35.800 ± 22.860*	284.40 ± 492.249**	10.773 ± 2.529*

*$p < 0.05$.

**$p < 0.025$ by Friedman test, post hoc Wilcoxon signed rank test Bonferroni correction.

contents of panaxydol (**1**) and panaxynol (**2**) in RGEF were 2.77 ± 0.11 and 8.36 ± 0.00 mg/g, respectively.

3.3 | Antimicrobial spectrum of RGEF

The antimicrobial range of the RGEF was determined by measuring the antimicrobial activity against the major microorganisms. A triclosan treatment used as a control showed antimicrobial activities at 3 mg/ml on all types of microorganisms, whereas the RGEF at 12.5 mg/ml showed selective antimicrobial activities on some of the microorganisms (Figure 3). The RGEF showed antimicrobial activities on gram-positive strains (*Bacillus subtilis*, *S. aureus*, *and S. mutans*) and gram-negative and anaerobic *F. nucleatum*. In particular, the antimicrobial activities on gram-positive and anaerobic strains, namely, *P. acnes* and *S. mutans*, were 63.6% (*P. acnes*) and 66.7% (*S. mutans*), respectively, and more effective than on other strains (23.9–41.7%). This characteristic serves as an advantage to reduce the risks of side effects caused by antimicrobial agents for the symptoms of acne. Antimicrobial agents such as erythromycin and clindamycin have strong antimicrobial effects, but they should be used under prescription to avoid resistance caused by mutant strains. Triclosan was also reported to facilitate the proliferation of *S. aureus*, and its use should be limited (Syed, Ghosh, Love, & Boles, 2014). Therefore, the combination therapy using red-ginseng-derived antimicrobial substances and existing antimicrobial substances is highly required to minimize these side effects.

3.4 | Skin safety of RGEF

To evaluate the skin allergies and/or adverse reactions by the RGEF, a skin patch test was conducted on 31 female subjects. Distilled water was used as a negative control. As described in Table 3, no adverse reactions were observed when the RGEF was applied to the skin at concentrations between 12.50 and 3.12 mg/ml, with no significant differences with distilled water as the negative control.

3.5 | Clinical trials

The cream containing 3 mg of RGEF was applied to subjects twice daily for 4 weeks. As a result, the oil contents were significantly decreased after 2 and 4 weeks (<0.05) after application. The oxidized sebum contents of skin also decreased after 2 and 4 weeks (<0.025), and skin redness statistically decreased only 4 weeks (<0.05) after application (Table 4).

Clinical evaluation of 4 weeks showed that white/blackheads and papules decreased significantly after 2 and 4 weeks (<0.025) compared with before use. On the other hand, no statistically significant improvement was found in the nodules (Figure 4).

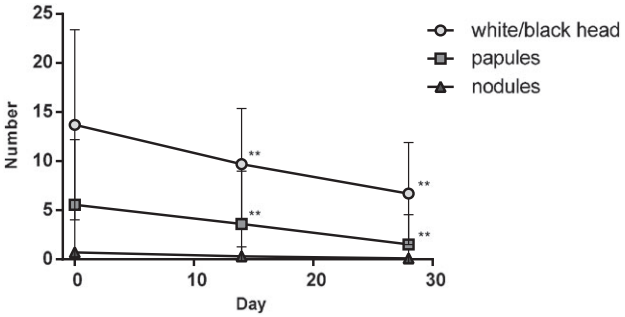

FIGURE 4 Clinical evaluation result of acne symptom through visual judgment. **$p < 0.025$ by Friedman test, post hoc Wilcoxon signed rank test Bonferroni correction

The symptoms of acne are worsen when excessive sebum blocks pores create an anaerobic environment favorable for the over proliferation of *P. acnes*, which, in turn, causes inflammation. To improve these symptoms effectively, controlling sebum excretion and/or removing it to avoid favorable environments for *P. acnes* should be accompanied by controlling inflammatory reactions to prevent inflammation-caused skin tissue necrosis (Yu et al., 2017). This study provides a clinical demonstration that the red-ginseng-derived antimicrobial substances not only have antimicrobial activities against *P. acnes* but also reduce the oil and sebum present in the skin. This effect is thought to be associated with the fact that saponins present in red ginseng have both hydrophobic and hydrophilic properties; hence, they play surfactant roles just as soap does. Similar results were reported by a study that demonstrated saponins obtained from *Camellia oleifera* effectively removed sebum (Chen, Yang, Chang, Ciou, & Huang, 2010). In addition, red ginseng has been reported by various studies to have anti-inflammatory effects in vitro (Baek et al., 2016) and in vivo (Lee & Cho, 2017), and in this study, too, improvement of early stage inflammatory symptoms such as papules was clinically demonstrated. Thus, red ginseng extracts that contain red-ginseng-derived antimicrobial substances are expected to control the symptoms of acne effectively by not only killing *P. acnes* but also removing sebum and exerting anti-inflammatory effects.

4 | CONCLUSION

The hydrophobic fraction of red ginseng (*P. ginseng* C.A. Meyer; RGEF) showed strong antimicrobial effect against *P. acnes*, and panaxynol (**2**) is confirmed as key antimicrobial constituent of RGEF. RGEF showed antimicrobial activity on various strains as well. Furthermore, the cream containing RGEF not only exhibited antimicrobial activity on *P. acnes* but also removed sebum in the skin in clinical trial. Therefore, red ginseng extracts is predicted to be good antimicrobial agent for the treatment of inflammation diseases including acne.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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