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ORIGINAL ARTICLE

A randomized, comparative study on the efficacy and safety of mangosteen 1% extract gel versus benzoyl peroxide 5% gel in the treatment of mild to moderate acne vulgaris

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ABSTRACT

INTRODUCTION Acne vulgaris is a common dermatologic disorder caused by follicular epidermal hyperproliferation, excess sebum production, inflammation, and *Cutibacterium acnes (C. acnes)*. The mangosteen fruit rind contains large amount of xanthones, which has high antimicrobial activity against *C. acnes*.

OBJECTIVES To compare the efficacy and safety of mangosteen 1% extract gel versus benzoyl peroxide (BPO) 5% gel in the treatment of mild to moderate acne vulgaris.

METHODS A total of 60 participants with mild to moderate acne or a rating of 2 or 3 in the Investigator's Global Assessment (IGA) for acne were randomized to receive either mangosteen 1% extract gel or BPO 5% gel applied on the face twice daily over an 8-week period. Primary outcomes measured in the study were clinical remission graded as "clear" or "almost clear" (rating of 0 or 1) based on the IGA and any adverse reaction.

RESULTS At week 8, 73% (23/30) in the BPO group and 53% (16/30) in the mangosteen group achieved clinical remission, although the difference between the two groups were not statistically significant (P = 0.108). In the BPO group, 4% (1/27) had a weak reaction during the 2nd follow up, while in the mangosteen group all participants did not have any reactions; however, this was not statistically significant (P = 0.627).

CONCLUSION Mangosteen 1% extract gel is a safe and effective alternative treatment for mild to moderate acne vulgaris.

KEYWORDS acne vulgaris, mangosteen extract, benzoyl peroxide

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INTRODUCTION

Acne vulgaris is a common dermatologic disorder caused by follicular epidermal hyperproliferation, excess sebum production, inflammation, and the activity of *Cutibacterium acnes (C. acnes)*.[1,2] The *C. acnes* is a gram-positive, anaerobic and microaerobic bacterium found within the sebaceous follicle.[2]

Acne can cause emotional distress, reduced self-esteem and impaired psychosocial development due to perceived disfigurement.[3] The peak incidence is in the middle-to-late teenage period, affecting more than 85% of adolescents between ages 12 and 24.[3] It was reported in 8% of adults aged 25 to 34 years and 3% of adults aged 35 to 44 years.[3] The Philippine Dermatological Society-Health Information System (PDS-HIS) ranked acne as the most commonly diagnosed skin disease in 2016.[4]

The treatment includes benzoyl peroxide (BPO), tretinoin, and doxycycline.[5] However, these can produce a number of side effects and has a high cost of treatment.[6] BPO is a broad-spectrum bactericidal agent known to have powerful oxidizing activity with very mild comedolytic properties.[3] The main adverse effect is irritant contact dermatitis (ICD); and it can also bleach fabric, hair, clothes, and other colored materials.[7]

Mangosteen *(Garcinia mangostana)* is called "the queen of fruits" due to its pleasant taste and aroma.[5,8] It is one of the most economical tropical fruits found among the Southeast Asian countries.[8,9] Most common mangosteen-producing

areas in the Philippines are found in Mindanao, which includes Davao City.[10]

The mangosteen fruit rind is described as firm, spongy, and thick that is composed of a yellow, resinous juice.[11] Experimental studies demonstrated that the mangosteen extract has antifungal, antibacterial, antiviral, anti-inflammatory, and antioxidant properties.[5,11] The fruit rind contains large amounts of xanthones, such as α-mangostin, that have high antimicrobial activity against *C. acnes*.[5,8,9,12,13]

The concentration of mangosteen fruit rind crude extract used in the development of an anti-acne gel was 1%, based on the study by Jansook et al.[14] The mangosteen acne gel was evaluated for its consumer acceptance and had a mean overall preference of 71.7%.[15] However, it was not mentioned in the study on how the gel decreased the acne lesions, and there was no comparison done with a standard anti-acne drug.[15] A recent study done in Thailand reported that 0.5% topical mangosteen extract gel was comparable to 1% clindamycin gel in the treatment of mild to moderate acne vulgaris, in terms of improvement in comedones, inflammatory lesion count, clinical evaluation, porphyrin, and post-acne erythema after 12 weeks of treatment.[16]

The safety of using of mangosteen extract on human subjects has been well discussed in several studies. A clinical study done in the Philippines showed that mangosteen 40% extract ointment used in the treatment of plaque-type psoriasis had no adverse reactions.[17] Another study used 400 mg mangosteen rind extract taken orally thrice a day and was compared with a placebo. The mangosteen group showed a cure rate of 73%, but it was not statistically significant. There were no known adverse reactions in the treatment group.[13]

Mangosteen rind extract was used as a periodontal gel that was applied topically at the subgingival area. After 3 months of treatment, the subgingival microbial composition improved with no adverse reactions.[18]

OBJECTIVES

Our study aimed to compare the efficacy and safety of mangosteen 1% extract gel versus BPO 5% gel in producing clinical remission in patients with mild to moderate acne vulgaris. Specifically, the following outcomes were determined in both groups: Investigator's Global Assessment (IGA) for acne score, the total number of lesions, number of weeks to achieve clinical remission, quality of life of the participants using dermatology life quality index (DLQI), and the incidence of adverse reactions.

METHODS

TRIAL DESIGN AND PARTICIPANTS

This was a prospective, randomized, double-blind trial conducted at the dermatology out-patient department of a tertiary hospital from January to April 2016. The research protocol was approved by the Hospital Research and Ethics Committee (P16052601). Informed consent from all participants was obtained prior to treatment. Minor participants had to sign an assent form together with the parent consent form.

This study included male and female participants, aged 12 years old and above, diagnosed with mild to moderate acne vulgaris, characterized clinically by non-inflammatory lesions (open and closed comedones) and inflammatory lesions (papules to pustules) with a rating of 2 or 3 based on the IGA for acne. Participants should have no anti-acne procedures (acne surgery, intralesional glucocorticoids, phototherapy, or lasers) done for the past 2 weeks. Excluded from this study were participants who are allergic to the active ingredients and who exhibited other facial dermatological conditions that could hinder or obstruct clinical assessments. Those who needed to use another non-acne topical medication that could interfere with study treatment were also excluded. Participants with any serious and/or uncontrolled cutaneous problems, systemic disease, or comorbidities such as hypertension, diabetes, acquired immunodeficiency syndrome (AIDS), pulmonary, renal, or heart disease, cancer, or mental illness were likewise excluded.

MATERIALS

The study intervention is the application of either mangosteen 1% extract gel or BPO 5% gel. The mature mangosteen rind was grinded into a powder by Hale and Hearty Herbaceuticals and it was extracted by an industrial pharmacist using 95% ethanol for 3 days, done 3 times at room temperature. The filtrates were pooled and concentrated by a rotary evaporator at 40°C. The extract was sent to Jaskin Cosmeceutical Products, at Biñan Laguna, for compounding of the mangosteen 1% extract gel. The formulation of the gel was composed of carbopol 0.2%, triethanolamine 0.15%, glycerine 1%, preservatives (phenoxyethanol and ethylhexylglycerin) 0.2%, alcohol 20%, water 74.45%, and mangosteen crude extract 1%.

In a previous study, they formulated the mangosteen crude extract as a gel with 0.5% concentration that had a high efficacy in inhibiting the growth of acne.[15] We increased the concentration of the extract to 1% gel based on the mangosteen anti-acne formulation done by Jansook et al.[14]

Another study showed that the mangosteen crude extract (95% ethanol) had a minimum bactericidal concentration (MBC) against *P.acnes* of 15.63 ug/ml, which was equivalent to 0.0001563%. Hence the 1% concentration of the gel was used in this study.[5] The control intervention was BPO 5% gel obtained from a dermatological pharmaceutical company.

RANDOMIZATION, TREATMENT ALLOCATION, AND BLINDING

Investigator B, who was not involved in the assessment of outcome, measures randomized the participants using a computer-based randomization list. This was a double-blind study, both the participants and investigator A did not know the treatment

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allocation.

INTERVENTIONS

Both interventions were placed in identical 10-gram plastic containers that were pre-coded by investigator B. The mangosteen gel had a yellow color with a mild mangosteen smell, while the BPO gel was colorless and had no smell.

The participants were also provided with a transparent and odorless soap, obtained from a dermatological pharmaceutical company. After cleansing, the participants were instructed to wait 10 minutes to allow the skin to dry completely before applying the intervention. The intervention was applied twice daily for 8 weeks avoiding the areas around the eyes and lips. They were advised to apply the intervention using the 1 fingertip unit (FTU) per application.

OUTCOME MEASURES

The participants were evaluated by investigator A at baseline, 2-, 4-, 6- and 8-week follow-up. The primary outcome of the study was the clinical remission defined as “clear” or "almost clear" (IGA score 0 or 1). Treatment failure was defined as IGA score same as baseline (IGA 2 or 3) or an increase in the baseline. Secondary outcomes include the mean percentage reduction of the total lesion count per treatment group at week 8 and the number of participants in either group who had adverse reactions.

The IGA acne score, lesion count, and adverse reactions such as erythema, stinging/burning, pruritus, and eczema was evaluated by Investigator A. The adverse reaction grading was based from the International Contact Dermatitis Research Group and was categorized as negative (0), weak (1+), strong (2+), and extremely strong reaction (3+).[19] Participants with a score of 3 + were advised to discontinue the treatment. Participants with a score of 1 + or 2 + were advised to continue with every other day application of the intervention. If there was an improvement in the reaction, they will be advised to return to daily application. On the final follow-up (8th week), participants were asked to answer the Dermatology Life Quality Index (DLQI) and those considered as treatment failure, were given the standard treatment.

SAMPLE SIZE COMPUTATION

The sample size computation was based on the following assumptions: population 1 is BPO 5% with a proportion of 1.00 based from the study of Busa et al. and population 2 is mangosteen 1% extract gel with a proportion of 0.67 based on the study of Delima et al.[20,21] The confidence level was set at 0.95, with the power of 0.8 and a ratio of 1:1 using a two-tailed test. A total number of at least 60 participants, 30 in each group, was the sample size for this study.

STATISTICAL METHODS

The data gathered were encoded into Microsoft Excel. Descriptive analysis was used for the demographic data. The significant difference was analyzed using either the t-test for two samples or Mann-Whitney U test. The significant association between categorical variables and the treatment groups was analyzed using Chi-Square test or Fisher’s exact test. Survival analysis was used to compare time (in weeks) to clinical remission in both groups.

The primary analysis was carried out using the intention-to-treat (ITT) principle. A separate analysis excluding patients lost to follow-up (LTFU) was done in the per-protocol (PP) analysis. Sensitivity analysis with three scenarios was also performed to test the robustness of the primary analysis.

RESULTS

STUDY POPULATION

A total of 60 participants were recruited and randomized to treatment (mangosteen gel, n=30) and control (BPO gel, n=30) groups. Of these, 9 participants were LTFU as shown in Figure 1. The demographic and clinical profile of the participants showed no significant difference between the two treatment groups at baseline (Table 1).

All drop-outs were not included in the PP analysis, as presented in Table 2. In the BPO group, 81% had “almost clear” score at week 8 (P = 0.035). In the mangosteen group, 4% had “clear” score and 63% had “almost clear” score at week 8 (P = 0.017).

CLINICAL REMISSION (PP ANALYSIS AT WEEK 8)

Using the PP analysis, all LTFU were not included. At week 8, the BPO group had 81% clinical remission compared to mangosteen group with 67%.

CLINICAL REMISSION (ITT ANALYSIS AT WEEK 8)

Using the ITT analysis, all LTFU were included. At week 8, the BPO group had 73% clinical remission compared to mangosteen group with clinical remission of 53%.

SENSITIVITY ANALYSIS

Sensitivity analysis was done to test for the robustness of the primary analysis. Three case scenarios were used:

In the 1st scenario, we assumed that all LTFU from both groups achieved clinical remission with an IGA score of 0-1 (clear/almost clear). At week 8, the BPO group had a clinical remission rate of 83% compared to 73% in the mangosteen group (P = 0.347).

In the 2nd scenario, it was assumed that all LTFU from the BPO group have achieved clinical remission with an IGA score of 0-1 (clear/almost clear) and all LTFU of from mangosteen group were considered as treatment failure having an IGA score of 2-3 (mild/moderate). At week 8, the BPO group had a clinical remission rate of 83% compared to 53% in the mangosteen group (P =0.012).

In the 3rd scenario, it was assumed that all LTFU from BPO group had treatment failure having an IGA score of 2-3 (mild/moderate) and all LTFU from mangosteen group have achieved

Table 1. Baseline demographic and clinical data of the participants.

Characteristics	BPO 5% gel (n=30)	Mangosteen 1% extract gel (n=30)	Total (n=60)	p-value
Gender				0.518*
Male	12 , 57%	9 , 43%	21 , 35%	
Female	18 , 46%	21 , 54%	39 , 65%	
Age, Mean ± SD	21.73 ± 5.42	21.37 ± 4.69	21.55 ± 5.055	0.780¥
10 - 20 years old	11 , 46%	13 , 54%	24 , 40%	0.844*
21 to 30 years old	17 , 50%	17 , 50%	34 , 57%	
31 to 40 years old	2 , 100%	0 , 0%	2 , 3%	
Occupation				0.617*
Student	15 , 48%	16 , 52%	31 , 52%	
Employed	13 , 52%	12 , 48%	25 , 42%	
Unemployed	2 , 50%	2 , 50%	4 , 7%	
Clinical severity based on IGA (baseline)				0.508*
Mild	16 , 55%	13 , 45%	29 , 48%	
Moderate	14 , 45%	17 , 55%	31 , 52%	
Number of lesions, mean ± SD	63.57 ± 23.24	67.3 ± 28.05	65.44 ± 25.65	0.576¥
Inflammatory	14.27 ± 7.44	15.77 ± 8.9	15.02 ± 8.17	0.481¥
Non-Inflammatory	49.3 ± 19.86	51.53 ± 21.49	50.42 ± 20.68	0.677¥
Duration, mean ± SD	4.42 ± 3.42	5.1 ± 4.61	4.76 ± 4.02	0.519¥
Family history (acne)				0.317*
Yes	20 , 50%	20 , 50%	40 , 67%	
No	10 , 50%	10 , 50%	20 , 33%	
Acne procedures				0.319*
No	22 , 51%	21 , 49%	43 , 72%	
Yes	8 , 47%	9 , 53%	17 , 28 %	
Acne surgery	8 , 47%	9 , 53%	17 , 28 %	
Intralesional glucocorticoid injection	1 , 33%	2 , 67%	3 , 5%	
Phototherapy	0 , 0%	0 , 0%	0 , 0%	
Lasers	0 , 0%	0 , 0%	0 , 0%	
Others (chemical peel)	2 , 40%	3 , 60%	5 , 8%	
Previous treatment				
Total oral	4 , 50%	4 , 50%	8 , 13%	0.321*
Total topical	26 , 49%	27 , 51%	53 , 88%	0.254*
Medicated cleansers	10 , 38%	16 , 62%	26 , 43%	
Topical retinoids	11 , 48%	12 , 52%	23 , 38%	
Topical antimicrobials	13 , 41%	19 , 59%	32 , 53%	
Astringents	21 , 54%	18 , 46%	39 , 65%	
Other topical	1 , 25%	3 , 75%	4 , 7%	
Oral antibiotics	3 , 60%	2 , 40%	5 , 8%	
Oral contraceptives	2 , 67%	1 , 33%	3 , 5%	
Oral glucocorticoids	0 , 0%	1 , 100%	1 , 2%	
Current Treatment				
Total oral	0 , 0%	0 , 0%	0 , 0%	0.687*
Total topical	3 , 38%	5 , 63%	8 , 13%	0.642*
Topical retinoids	2 , 50%	2 , 50%	4 , 7%	
Topical antimicrobials	2 , 50%	2 , 50%	4 , 7%	
Astringents	1 , 33%	2 , 67%	3 , 5%	

* - Chi-square test; ¥ - t-test; IGA - Investigator's Global Assessment.

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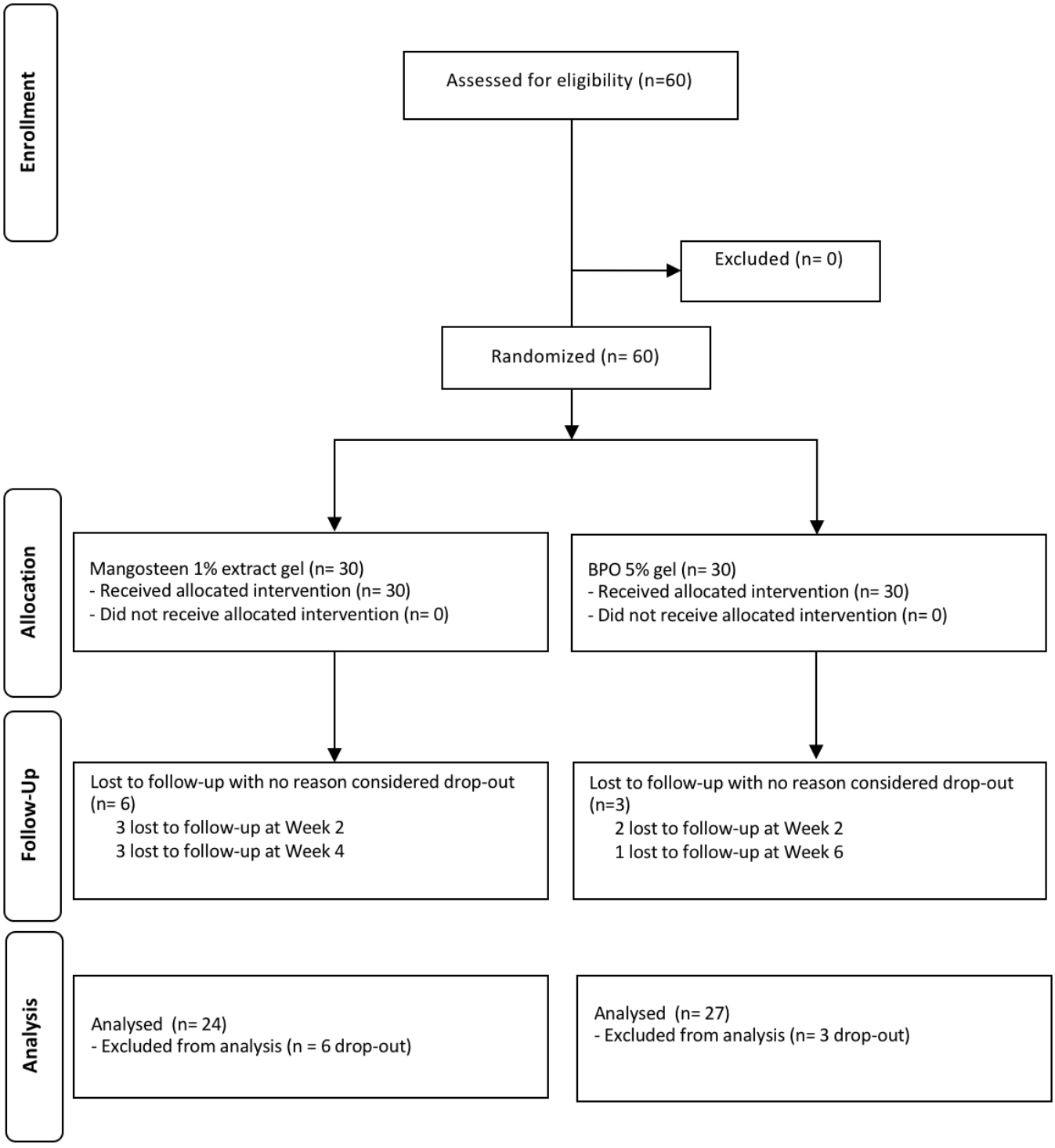

Figure 1. Flow chart of participants.

Table 2. Comparison of IGA score before and after the treatment in each study arm (per-protocol analysis).

Treatment	Baseline	Week 8	p-value
BPO 5% gel (n=27)			0.035*
Clear	0 , 0%	0 , 0%	
Almost Clear	0 , 0%	22 , 81%	
Mild	16 , 53%	5 , 19%	
Moderate	14 , 47%	0 , 0%	
Mangosteen 1% extract gel (n=24)			0.017*
Clear	0 , 0%	1 , 4%	
Almost Clear	0 , 0%	15 , 63%	
Mild	13 , 43%	8 , 33%	
Moderate	17 , 57%	0 , 0%	
Note: Chi-square test			

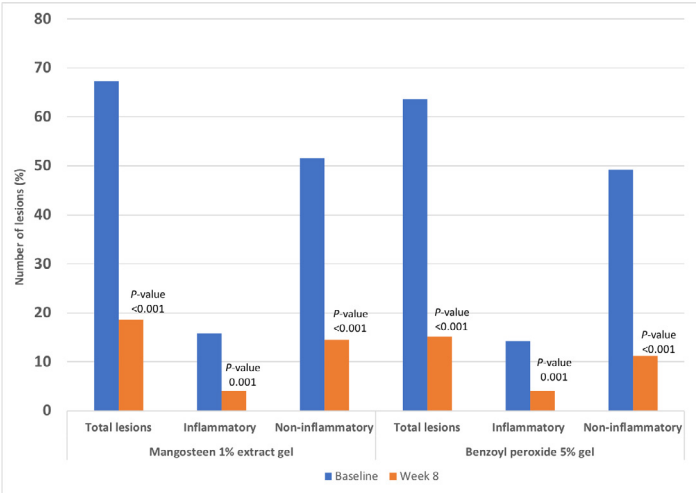

Figure 2. Comparison of the number of lesions after 8 weeks of treatment between both groups.

clinical remission with an IGA score of 0-1 (clear/almost clear). At week 8, the BPO group had a clinical remission rate of 73% compared to 73% of mangosteen group (P =0.991).

COMPARISON OF THE NUMBER OF LESIONS AFTER TREATMENT BETWEEN BOTH GROUPS

In the BPO group, the percent decrease in the total number of lesions at week 8 was (76.06%), inflammatory lesions (71.69%), and non-inflammatory lesions (77.3%) as presented in Figure 2. In the mangosteen group, a decrease was noted in the total number of lesions (72.32%), inflammatory (73.81%), and non-inflammatory lesions (71.86%). The decrease in the number of lesions in both groups had a P-value < 0.05.

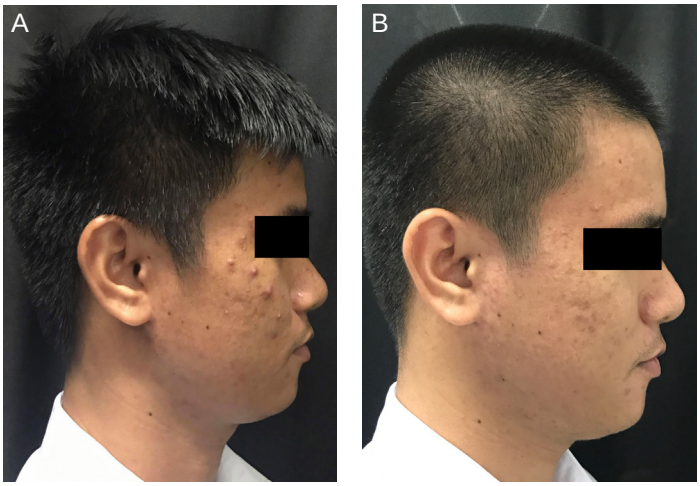

Figure 3. A. Representative clinical photo of a patient treated with BPO 5% gel at baseline. **B.** At 8 weeks follow-up.

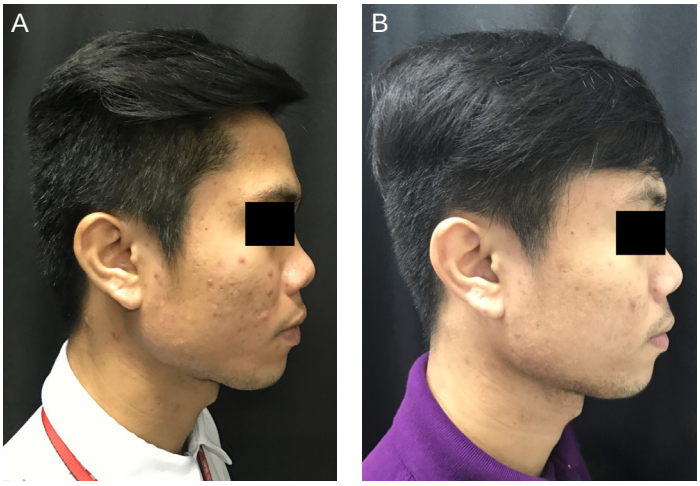

Figure 4. A. Representative clinical photo of a patient treated with mangosteen 1% gel at baseline. **B.** After 8 weeks.

Survival analysis was done using the Kaplan-Meier curve and the log rank test, to determine the number of weeks to achieve clinical remission. At weeks 4 and 6, BPO group showed a lower cumulative survival than mangosteen group. It took 6 weeks for the BPO group compared to 6.3 weeks for the mangosteen group to achieve clinical remission (P > 0.05).

ADVERSE REACTION RATE

In the BPO group, 4% (1/27) presented with a weak reaction on the 2nd follow-up. The medication was tapered to every other day application. On the succeeding follow-up, the patient did not have any reaction so the treatment was continued to twice a day application. In the mangosteen group, all participants did not

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have any adverse reactions.

QUALITY OF LIFE

The quality of life of the participants on both groups were compared at baseline and at week 8 follow-up. The improvement was graded as none, 1 scale, 2 scale, and 3 scale. Majority of the participants in the BPO group reported no improvement and 1 scale improvement (44%, 44% respectively). In the mangosteen group, most (42%) had 1 scale improvement. Below are the representative photos of the participants treated with BPO 5% gel and mangosteen 1% extract gel (Figures 3 and 4).

DISCUSSION

Using the ITT analysis, all LTFU in either group were considered as treatment failure. The clinical remission rate after 8 weeks in BPO group was slightly higher (73%) compared to mangosteen group (53%) however, the difference was not statistically significant (P=0.108).

PP analysis was also done, which did not include LTFUs in both groups. The BPO group had a higher clinical remission rate (81%) compared to (67%). The difference between the two groups was not statistically significant (P =0.634).

In both ITT analysis and PP analysis of the clinical remission rate, statistical results showed no significant difference between the two treatment groups (P = 0.108, 0.634 respectively). These would indicate that the treatment group (mangosteen) is comparable with the control group (BPO) in achieving clearance.

Mangosteen extract is effective in reducing acne lesions because it can target the two main pathogenesis of acne: inflammation and *P.acnes*. Its major component α-mangostin has a potent anti-inflammatory activity and also a high antimicrobial activity towards *C. acnes*.[22,23] A study was done to determine the antimicrobial activity of 19 medicinal plant extracts from Thailand against *C. acnes*. Among these, mangosteen extract had the greatest antimicrobial effect. On broth dilution method, the minimum inhibitory concentration (MIC) and (MBC) values against *C. acnes* were both 0.039 mg/ml.[23] Bioautography assay showed that mangosteen extract produced strong inhibition zones (≥ 15 mm) against C. acnes.[23] The mature mangosteen rind contained more α-mangostin and had better bactericidal activity against *C. acnes* at 15.63 µg/ml as compared to 31.25 µg/ml of the young rind.[8]

Mangosteen extract is also known to have anti-oxidant activity that can inhibit reactive oxygen species (ROS) and prostaglandin E2 (PGE2).[9,24] These molecules can attract more inflammatory cells, thereby leading to the development of more inflammatory acne lesions.[25]

Sensitivity analysis was done using a worst case-best case scenario. In the 1st case, we assumed that all the LTFU on both groups achieved clearance rate after 8 weeks, the difference between two groups was not statistically significant (P =0.347). The 2nd case was the worst case scenario, we assumed that after 8 weeks, all LTFU of BPO group achieved clearance while all LTFU of EVCO group had treatment failure. This was assigned as the worst-case scenario because the best possible outcome was assigned to all the LTFU of BPO group and the worst outcome were assigned to all LTFU on the mangosteen group. In this worst-case scenario, the difference between 2 groups was statistically significant (P = 0.012). The 3rd case was the best-case scenario, we assumed that after 8 weeks, all LTFU of the BPO group were treatment failure and all LTFU from the mangosteen group achieved clearance rate after 8 weeks. The difference between two groups was not statistically significant (P =0.991). Therefore, we can assume that the possible dropouts in mangosteen group can significantly alter our conclusion.

In terms of observed adverse reactions, BPO group had more reactions compared to mangosteen group, although the difference was not statistically significant. According to published literature, BPO can cause irritant contact dermatitis manifesting as erythema, pruritus, stinging/burning, and eczema.[1-3,7] In addition, the adverse effects of BPO were also recorded in the several local studies.[20,21] In our study, tapering of the medication was done in the BPO group because there was 1 participant who had a weak reaction (1+). The medication was tapered to every other day. On week 4, there was improvement in the reaction and was advised to return to daily application of the medication. In the mangosteen group, several studies established a good safety profile of the drug.[16-18] Mangosteen could be an alternative natural treatment for patients with acne vulgaris who experienced irritation towards BPO.

In terms of achieving clinical remission, the standard drug for acne- BPO group achieved clinical response at 6 weeks. Based on the number of weeks, BPO group had a slightly faster effect in terms of clinical remission when compared to mangosteen group. Thus, clinically this would translate that mangosteen group needs to be applied longer compared to BPO, but it is still effective in achieving clinical response.

In our study, we also assessed the lesion reduction from baseline until 8 weeks. The inflammatory lesion reduction on BPO group was 71.69% compared to 73.81% of mangosteen group. This finding was consistent with the mentioned properties of mangosteen. The non-inflammatory lesions (open and closed comedones) reduction on BPO group was 77.3%, while in the mangosteen group it was 71.86%. The results for BPO was already expected since it is known to have mild comedolytic properties.[1,2,7] For the mangosteen group, the findings of our study could suggest that it has comedolytic effects. The reduction in non-inflammatory lesions could be explained by its antibacterial activity against *C. acnes*, since *C. acnes* is also involved in the process of comedogenesis.[16] A previous study used a combination of herbal extracts that included mangosteen and it was found to be effective in the treatment of acne, possibly due to the synergistic effect of each component.[25]

During the initial recruitment and completion of the study (8 weeks), the participants were asked to fill up a DLQI question-

naire. In the BPO group, 7% had 2 scale improvement compared to 33% of mangosteen group. Both groups showed almost similar percentage in the 1 scale improvement. However, the difference in the quality of life of both groups was not statistically significant. These would indicate that the participants from both treatment group had comparable quality of life.

One limitation of this study was the short duration of follow-up because some topical acne treatment may need a longer duration to achieve complete remission as seen in other studies.[26,27] The study participants were all Southeast Asians and different skin types among races have different skin characteristics that might lead to a different effect of the drug. This study was also limited by the use of monotherapy and cannot predict the possible interactions with other anti-acne medications which is important in clinical practice since the current treatment approach to acne vulgaris is combination therapy.

We recommend further studies with a longer duration to further evaluate its efficacy and safety and to accurately assess the length of time needed to achieve clinical remission. We also recommend to compare the anti-acne effect of the test drug using different bases to determine the most appropriate formulation and to conduct a study on different skin types. The test drug can also be combined with other anti-acne medications such as BPO, to evaluate its possible synergistic effect that might lead to faster clinical remission.

CONCLUSION

Mangosteen 1% extract gel had comparable clearance rate with BPO 5% gel in the treatment of mild to moderate acne vulgaris. The raw materials of the test drug are indigenous to our locality and readily accessible even in remote areas. Hence, mangosteen extract 1% gel is an efficacious and safe alternative treatment for acne vulgaris.

REFERENCES

1. Zaenglein A, Thiboutot D. Acne vulgaris. In: Bolognia J, Jorizzo J, Schaffer J, eds. Dermatology. 3rd ed. Edinburgh: Elsevier; 2012:545-559.
2. Zaenglein A, Graber E, Thiboutot D. Acne Vulgaris and Acneiform Eruptions. In: Goldsmith L, Katz S, eds. Fitzpatrick's dermatology in general medicine. 8th ed. New York: McGraw-Hill; 2012:897-917.
3. Leyden J. A review of the use of combination therapies for the treatment of acne vulgaris. J Am Acad Dermatol. 2003 Sep 30;49(3). DOI: 10.1067/s0190-9622(03)01154-x.
4. Philippine Dermatological Society Health Information Systems. Philippine Dermatological Society; 2011. pdshis@outlook.com. Accessed October 3, 2016.
5. Pothitirat W, Chomnawang MT, Gritsanapan W. Anti-acne-inducing bacterial activity of mangosteen fruit rind extracts. Med Princ Pract. 2010;19(4):281-286. DOI: 10.1159/000312714.
6. Azimi H, Fallah-Tafti M, Khakshur AA, Abdollahi M. A review of phytotherapy of acne vulgaris: perspective of new pharmacological treatments. Fitoterapia. 2012;83(8):1306-1317. DOI: 10.1016/j.fitote.2012.03.026.
7. Motaparthi K, Hsu S. Topical Antibacterial Agents. In: Wolverton S, ed. Comprehensive Dermatologic Drug Therapy. 3rd ed. Edinburg: Elsevier; 2012:454.
8. Khumsupan P, Gritsanapan W. Anti-acne activity of Garcinia mangostana L.: A review. Plant Science Today. 2014 Aug 14;1(3):147-150. DOI: 10.14719/pst.2014.1.3.39.
9. Pedraza-Chaverri J, Cárdenas-Rodríguez N, Orozco-Ibarra M, Pérez-Rojas JM. Medicinal properties of mangosteen (Garcinia mangostana). Food Chem Toxicol. 2008;46(10):3227-3239. DOI: 10.1016/j.fct.2008.07.024.
10. Osman M, Milan A. Mangosteen Garcinia mangostana L. In: Williams JT, Smith RW, Haq N, Dunsiger Z, eds. Chichester, England, UK: Southampton Centre for Underutilised Crops; 2006.
11. Dweck A. A review of Mangosteen (Garcinia mangostana) Linn. 2003:8. Accessed 2016 Sept 27.
12. Priya V, Jainu M, Mohan S, Saraswathi P, Gopan S. Antimicrobial activity of pericarp extract of Garcinia mangostana Linn. Int J Pharm Sci Res. 2010;1:278-281.
13. Sutono T. Efficacy of Garcinia mangostana L. (mangosteen rind extract) to reduce acne severity. Med J Indones. 2013 Aug 1;22(3):167-172. DOI: 10.13181/mji.v22i3.586.
14. Jansook P, Sompukdee A, Rattranakosekit M, Kokiatinun A, Pothitirat W. Development and evaluation of anti-acne microemulsion gel containing extracts of mangosteen fruit rind. Thai J Pharm Sci. 2010;36:158-161.
15. Sukatta U, Rugthaworn P, Pitpiangchan P, Dilokkunanant U. Development of mangosteen anti-acne gel. Kasetsart J (Nat Sci). 2008;42(5):163-168.
16. Lueangarun S, Sriviriyakul K, Tempark T, Managit C, Sithisarn P. Clinical efficacy of 0.5% topical mangosteen extract in nanoparticle loaded gel in treatment of mild-to-moderate acne vulgaris: A 12-week, split-face, double-blinded, randomized, controlled trial. J Cosmet Dermatol. 2019. DOI: 10.1111/jocd.12856.
17. Gallega G, Bunagan M, Visitacion L. A pilot study on the efficacy of mangosteen 40% extract ointment compared to clobetasol propionate 0.05% ointment in the treatment of plaque type psoriasis vulgaris. In: Philippines; 2009.
18. Rassameemasmaung S, Sirikulsathean A, Amornchat C, Maungmingsook P, Rojanapanthu P, Gritsanaphan W. Topical application of Garcinia mangostana L. pericarp gel as an adjunct to periodontal treatment. Complement Ther Med. 2008;16(5):262-267. DOI: 10.1016/j.ctim.2007.12.004.
19. Fonacier L, Bernstein DI, Pacheco K, et al. Contact dermatitis: a practice parameter-update 2015. J Allergy Clin Immunol Pract. 2015;3(3

Suppl):S1-39. DOI: 10.1016/j.jaip.2015.02.009.
20. Delima C, Belisario M, Bunagan M. A randomized investigator-blinded clinical trial evaluating the efficacy and safety of Ocimum basilicum (Sweet Basil) 2% cream vs benzoyl peroxide 5% cream in the treatment of mild to moderate acne vulgaris. In: Philippines; 2010.
21. Busa M, Ng J, Lacuesta-Gutierrez M. A prospective, randomized, double-blind, comparative study on the efficacy and safety of 2% enzymatic virgin coconut oil monoglyceride cream versus 5% benzoyl peroxide cream in the treatment of mild to moderate acne vulgaris. J Phil Dermatol Soc. 2018;27(2):18-30.
22. Chomnawang MT, Surassmo S, Nukoolkarn VS, Gritsanapan W. Effect of Garcinia mangostana on inflammation caused by Propionibacterium acnes. Fitoterapia. 2007;78(6):401-408. DOI: 10.1016/j.fitote.2007.02.019.
23. Chomnawang MT, Surassmo S, Nukoolkarn VS, Gritsanapan W. Antimicrobial effects of Thai medicinal plants against acne-inducing bacteria. J Ethnopharmacol. 2005;101(1-3):330-333. DOI: 10.1016/j.jep.2005.04.038.
24. Nakatani K, Atsumi M, Arakawa T, et al. Inhibitions of histamine release and prostaglandin E2 synthesis by mangosteen, a Thai medicinal plant. Biol Pharm Bull. 2002;25(9):1137-1141. DOI: 10.1248/bpb.25.1137.
25. Yang JH, Hwang EJ, Moon J, et al. Clinical efficacy of herbal extracts in treatment of mild to moderate acne vulgaris: an 8-week, double-blinded, randomized, controlled trial. J Dermatolog Treat. 2021;32(3):297-301. DOI: 10.1080/09546634.2019.1657792.
26. Schmidt N, Gans EH. Clindamycin 1.2% Tretinoin 0.025% Gel versus Clindamycin Gel Treatment in Acne Patients: A Focus on Fitzpatrick Skin Types. J Clin Aesthet Dermatol. 2011;4(6):31-40. PMCID: PMC3140902.
27. Gold LS, Tan J, Cruz-Santana A, Papp K, Poulin Y, Schlessinger J, Gidner J, Liu Y, Graeber M; Adapalene-BPO Study Group. A North American study of adapalene-benzoyl peroxide combination gel in the treatment of acne. Cutis. 2009 Aug;84(2):110-6. PMID: 19746769.