MedCrave
Step into the World of Research

Journal of Dermatology & Cosmetology

Research Article

Open Access

CrossMark

Safety and efficacy of two botanical based topical anti-acne products in treatment of mild to moderate acne subjects

Abstract

Background: Acne is a chronic inflammatory skin condition that causes spots and pimples on the face due to excessive skin sebum.

Objectives: To evaluate efficacy and safety of Rosa T Mild Cleanser and Rosa T Serum in volunteers with mild to moderate facial acne lesions with oily skin/excessive skin sebum.

Methods: 37 subjects were randomized in a double-blind, two arm, parallel study conducted in healthy males and females aged≥18 to≤35 years. Each subject applied Placebo Cleanser /Rosa T Mild Cleanser along with Rosa T Serum on face BID for 42 days.

Effect of Placebo Cleanser and Rosa T serum (Test Product 1) and RosaT Mild Cleanser and Rosa T Serum (Test Product 2)was evaluated for sebum level, skin hydration, cutaneous inflammatory and non-inflammatory acne lesions, skin pigment, acne severity and acne scars assessment.

Results: Combined usage of Rosa T serum along with the cleanser proved to be effective where significant reduction in sebum level on cheek and forehead ($p<0.001$), cutaneous inflammatory ($p<0.05$) and non-inflammatory ($p<0.01$) acne lesions skin pigment ($p<0.001$), till Day 42, with sufficient skin hydration level (MS>40) and no apparent adverse event was observed.

Conclusions: Significant improvement in acne, overall skin condition with lowered sebum level, decrease in skin pigment, sufficient skin hydration, improved acne condition and reduction in acne scars. The botanical based Rosa T Mild Cleanser and Rosa T Serum (Test Product 2) can be employed as a safer and effective substitute to current change of synthetic topical anti acne product in patients with acne severity grade II and III.

Keywords: acne vulgaris, adult acne, scar, post-inflammatory hyperpigmentation

Volume 4 Issue 5 - 2020

Trusha Gajjar,[1] Nayan Patel,[1] Maheshvari Patel,[1] Soon-Keong Chew[2]

[1]Karmic Lifesciences LLP (Cliantha Research), India

[2]Maxwell Pharma Sdn Bhd, Malaysia

Correspondence: Soon-Keong, Chew, Maxwell Pharma Sdn Bhd, 73-3 Block G, Zenith Corporate Park, Jalan SS7/26, Selangor, Malaysia, Email sk.chew@maxwellpharma.com

Received: August 28, 2020 | **Published:** September 16, 2020

Abbreviations: AE, adverse event; CADI, cardiff acne disability index; IUD, intrauterine device; MS, mean score; OCP, oral contraceptive pill

Introduction

Acne vulgaris is a common skin disease that affects 85% to 100% of people at some time during their life time. It is characterized by non-inflammatory follicular papules or comedones and by inflammatory papules, pustules and nodules in its more severe forms. Acne vulgaris affects the areas of skin with the highest population of sebaceous follicles; these areas include the face, upper part of the chest, and the back. The pathogenesis of acne vulgaris is multifactorial. Four key factors are responsible for the development of an acne lesion. These factors are follicular epidermal hyperproliferation with subsequent plugging of the follicle, excess sebum, the presence and activity of *Propionibacterium* acnes, and inflammation.[1,2]

The literature reveals no discernible differences in the sebum composition of acne patients as compared to age-matched controls. There is an inverse relationship between sebum secretion and linoleic acid concentration in the sebum of acne patients. The higher the sebum secretion, the lower the linoleic acid concentration and vice versa. This leads to a localized deficiency of linoleic essential fatty acid of follicular epithelium. This deficiency then contributes to diminished epithelial barrier function and follicular hyperkeratosis, which aggravates acne.[3,4]

Topical treatment is enough for comedonal acne. In case of more severe acne, topical treatment can be combined with systemic treatment.[5]Agents containing sulphur or resorcinol were used in especially the first part of the 20th century. Salicylic acid, which is a keratolytic agent, was popular for some time. Nowadays, the most popular topical agents in use are retinoids, benzoyl peroxide, sulfacetamide, azelaic acid, erythromycin, doxycycline, tetracycline, or Minocycline and topical antibiotics.[6,7]

The objectives of the present research is to observe the effect of two botanical products on inflammatory and non-inflammatory acne lesions; evaluate sebum secretion rate on forehead and cheeks by Sebumeter; acne severity by using evaluator's acne severity scale; assess skin hydration using Corneometer; quality of life by Cardiff Acne Disability Index (CADI); subject self-assessment on effect of acne on skin and acne scar assessment by Goodman and Baron's Qualitative scarring grading system. Excessive sebum is the precursor of acne. Yet there are very few botanical anti-acne products that reduces sebum, Hence the study was conducted on volunteers with mild to moderate facial acne lesions with oily /excessive sebum skin

to know the effectiveness and safety of two Botanical based topical Anti-Acne products i.e. Placebo Cleanser with Rosa T Serum and Rosa T Mild Cleanser with Rosa T Serum.

Material and methods

Study design and participants

The study was a double-blind, randomized, two-arm study to evaluate the efficacy and safety of skin care formulation (i.e. Rosa T serum plus Rosa T Mild Cleanser) in terms of reduction in inflammatory and non-inflammatory facial acne lesions in healthy male and female subjects. This study comprised of screening phase (Day -28 to Day 00), Enrolment Phase (Visit 1, Day 01) baseline before test products application, Treatment Phase (Visit 2, Day 07; Visit 3, Day 14 and Visit 4, Day 21), and End of study (Visit 5, Day 42) after test product application. A randomization allocation of 1:1 was utilized to assign subjects to any of the two groups as per the "Master Randomization List" for 42 days. Subjects were randomly allocated to one of the treatment groups, as per the "Master Randomization list". Neither the subjects nor the Investigator were aware of study products being allocated. The potential subjects were screened as per inclusion and exclusion criteria only after procurement of a signed written informed consent from the subject. A total of 60 subjects were screened and signed the informed consent document for the study. Out of these 60 subjects, 37 subjects who met the study criteria were enrolled and randomized in the study. Total 35 subjects (24 Females, 11 Males) completed all the phases of the study.

Inclusion criteria

Healthy subjects aged ≥ 18 to ≤ 35 years, having mild to moderate acne and Fitzpatrick skin type III and IV, with oily skin i.e. > 150µg/cm^2 sebum level was determined from forehead and cheek area (using Sebumeter® SM-815). Other enrolment criteria include subject's permission to take facial photographs and agreement in writing to allow sponsor to use photograph; female subjects with child bearing potential must report on the first day of menstruation on enrolment day, as during this period the hormonal changes cause increase in sebum secretion; subject has not participated in a similar clinical investigation in the past 4 weeks; subjects willing to visit the site regularly for follow up visits; subject must agree to use an active form of birth control other than oral contraceptives (i.e. condom and/or spermicidal foam, IUD, implant or diaphragm) during study duration; subjects who are willing to refrain from the use of new personal care products and treatments (cleansers/cosmetics etc.) during the study period.

Exclusion criteria

Subjects were excluded from the study for the reasons as follows: Manual workers, construction workers and those who work in the sun or cooks and those who work close to fire; pregnant and lactating female subjects; subjects having a known history or present condition of allergic response or sensitivity to any cosmetic products, and with any skin allergies or infections; skin disease (e.g. psoriasis, atopic dermatitis or any other condition as per Investigator's discretion); using medications e.g. steroids or antihistamines, skin disorders or applying any topical medication (including cosmetic) to face; taking any medications as determined by the Investigator that could potentially influence the study outcome; not willing to abstain from spa treatments throughout the study period; currently or previously has undergone facial treatments or procedures by dermatologist within the last 1 month or any additional condition(s) that would warrant exclusion from the study or prevent the subject from completing the study.

Study product

All enrolled subjects received Placebo Cleanser or Rosa T Mild Cleanser along with Rosa T Serum as per randomization code. Subjects were advised to use the Placebo Cleanser or Rosa T Mild Cleanser first, then apply the serum. For cleansing subjects were advised to take a small amount (3-4ml) of the cleanser into their palm and work up a lather by rubbing both the palms together. Apply the cleanser on the whole face and massage in circular motion excluding lips and area around the eyes. Rinse the cleanser thoroughly with plain water. Pat dry the face using a towel. Then, one or two drops of serum was taken on the index finger and rubbed between thumb and index finger before applying to the acne and also the rest of the face which tends to get oily.

Placebo Cleanser or Rosa T Mild Cleanser and Rosa T Serum both were applied twice daily, once in the morning and once at night before retiring to bed for a consecutive 42 days.

Safety assessments

Subjects were enquired about AEs at each clinic visit and were informed to contact the investigator at any time to report the possible AEs. However, no AEs occurred in the study. Also, no clinically significant changes were observed in vital signs assessment. Both Rosa T Mild Cleanser and placebo cleanser along with Rosa T serum were found to be safe and well tolerated during the study.

Instrumental measurements

Analysis of the sebum secretion rate was done using Sebumeter® SM-815. The principle of Sebumeter® is based on photometric method, the grease spot photometer. For the determination of the sebum, the measuring head of the cartridge which exposes to a 64 mm^2 measuring section of tape is inserted into aperture of the device, where photocell measures the transparency. The light transmission represents the sebum content on the surface of the measuring area. A microprocessor calculates the result which shows on the display in units from 0-350.

Measurement of skin hydration level was done using Corneometer® CM-825. The Corneometer® works on the principle of capacitance. This measurement is based on the completely different di-electrical constant of water (81) and other substances (mostly<7). The measuring capacitor shows changes of capacitance according to moisture content of sample.

Statistical analysis

The statistical analysis was done using SAS® statistical software (Version: 9.4; SAS Institute Inc., USA). Continuous variables were described by descriptive statistics (Mean, SD, Median, Min, Max). For categorical variables, the frequency and percentage of each category was provided. All statistical tests of hypothesis employed a level of significance of 0.05.

Ethics

The clinical investigation, including the informed consent document (ICD), was reviewed by Riddhi Medical Nursing Home Institutional Ethics Committee in accordance with ICMR ethical guidelines, ICH-GCP, Schedule Y and Declaration of Helsinki.

This study was conducted according to all the relevant SOP(s), the study protocol and protocol amendment(s), the ICMR ethical guidelines, The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) (Step 5) 'Guidance on Good Clinical Practice' (E6 R2) and Declaration of Helsinki.

Results

Subject disposition and demography

In this study, a total of 60 subjects were screened, out of them 37 subjects were enrolled and randomized in the study. One subject failed to follow-up and another withdrew on his own accord. Total 35 subjects (24 Females, 11 Males) completed all the phases of the study. All the subjects included in the study were of Asian Race. (Table 1).

Table 1 Summary of demographics characteristics

Summary of Demographics Characteristics		
		Treatment Group
Age (years)	N	37
	Mean ± SD	26.7 ± 5.25
	Median	27
	Min, Max.	18, 36

N= number of subjects.

Efficacy assessments

Primary efficacy parameters

Reduction in cutaneous inflammatory acne lesions

Efficacy of both anti-acne products were measured in terms of reduction in cutaneous inflammatory and non-inflammatory acne lesions on face from baseline by clinical evaluation using counting method (Day 1, Day 7, Day 14, Day 21 and Day 42) shown in Table 2 and Figure 1.

Rosa T Mild Cleanser and Rosa T Serum (Test Product 2) shows reduction in cutaneous inflammatory acne legions after 7 and 14 days from baseline. However, significant reduction was observed after 21 and 42 days. Placebo Cleanser and Rosa T Serum (Test Product 1) shows reduction in cutaneous inflammatory acne legions after 7 days from baseline. However, significant reduction was observed after 14, 21 and 42 days.

Reduction in cutaneous non- inflammatory acne lesions

Rosa T Mild Cleanser and Rosa T Serum (Test Product 2) shows reduction in cutaneous non-inflammatory acne legions after 7, 21 and 42 days from baseline. However, significant reduction was observed after 14 days from baseline. Placebo Cleanser and Rosa T Serum (Test Product 1) shows significant reduction in cutaneous non-inflammatory acne legions after 7 days from baseline. However, significant reduction was observed after 14, 21 and 42 days after baseline as shown in Figure 2.

Table 2 Reduction in cutaneous inflammatory & non-inflammatory acne lesion using counting method and sebum secretion rate on cheek and forehead

Reduction in	**Test product 1: Placebo mild cleanser and Rosa T serum**						**Test product 2: Rosa T mild cleanser and rosa T serum**				
Days:		**Baseline**	**7**	**14**	**21**	**42**	**Baseline**	**7**	**14**	**21**	**42**
cutaneous inflammatory acne lesions	Mean value	3.8	3.1	2.5	2	1.1	4.1	3.3	2.7	2.4	2
	p-value	-	0.1105	0.1034	0.0076*	0.0021*	-	0.0947	0.0212*	0.0235*	0.0106*
	% Reduction	-	18%	1%	28%	58%	-	8%	35%	28%	49%
cutaneous non-inflammatory acne lesions	Mean value	19.9	19.1	19.7	16.2	12.9	22.9	18.4	17.6	16.9	13.6
	p-value	-	0.2907	0.0148*	0.0542	0.0834	-	0.0236*	0.0070**	0.0444*	0.0015**
	% Reduction	-	8%	15%	16%	24%	-	14%	24%	21%	38%
sebum secretion rate on cheek	Mean value	197.55	154.84	142.86	124.87	102.98	202.38	160.31	140.02	133.45	96.31
	p-value	-	0.0000**	0.0000**	0.0000**	0.0000**	-	0.0004**	0.0000**	0.0000**	0.0000**
	% Reduction	-	20%	26%	37%	48%	-	20%	29%	33%	52%
sebum secretion rate on forehead	Mean value	207.59	154.16	147.57	126.25	104.37	204.5	167.59	143.09	132.6	92.3
	p-value	-	0.0000**	0.0000**	0.0000**	0.0000**	-	0.0008**	0.0000**	0.0000**	0.0000**
	% Reduction	-	25%	27%	38%	49%	-	17%	29%	35%	54%

Citation: Gajjar T, Patel N, Chew et al. Safety and efficacy of two botanical based topical anti-acne products in treatment of mild to moderate acne subjects. *J Dermat Cosmetol.* 2020;4(5):99–107. DOI: 10.15406/jdc.2020.04.00161

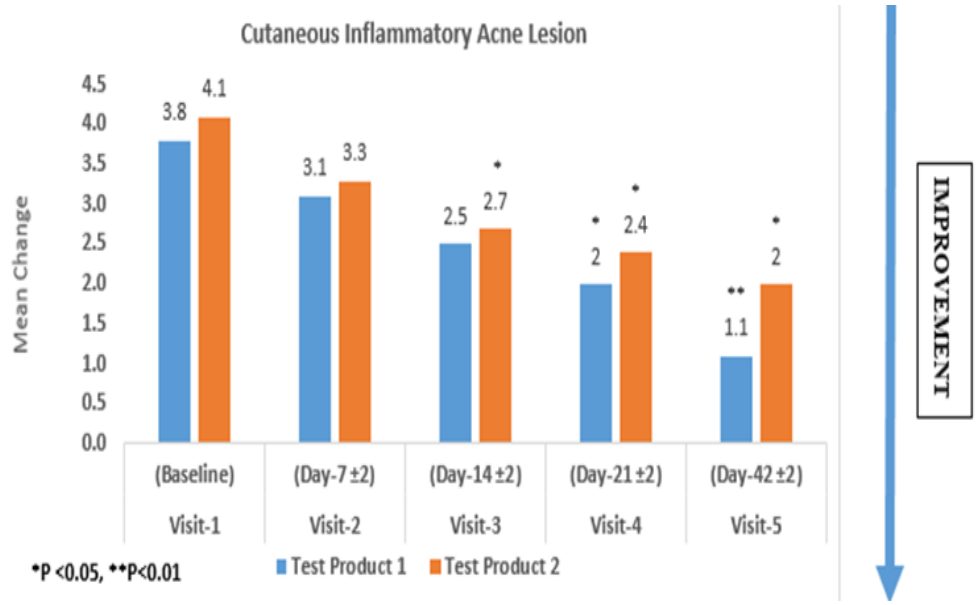


Figure 1 Analysis of the cutaneous inflammatory acne lesion [By counting method].

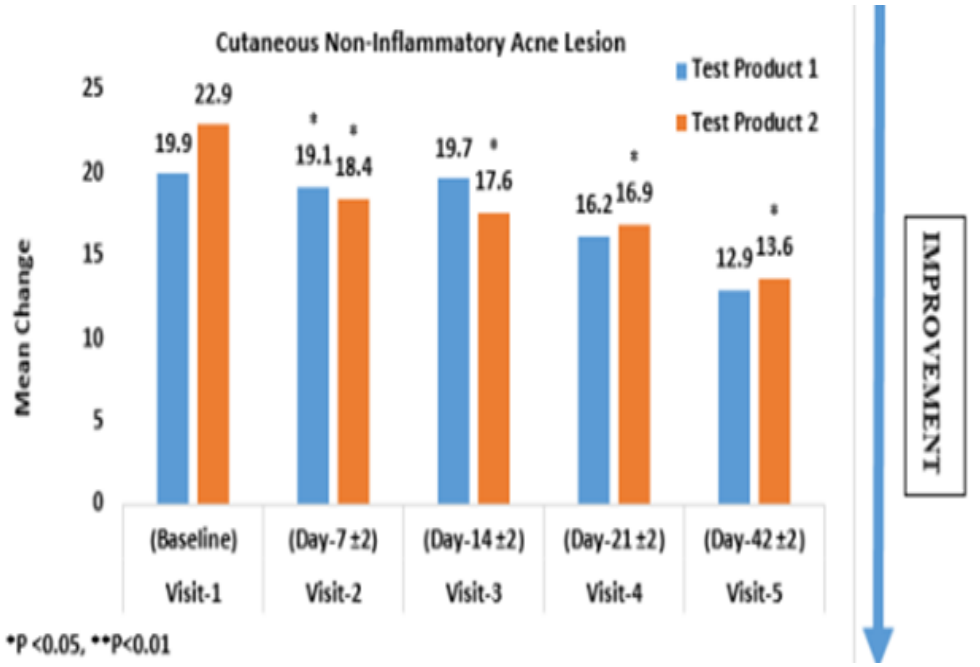


Figure 2 Analysis of the cutaneous non-inflammatory acne lesion [By counting method].

Skin Pigment assessment by photographic evaluation

Both Rosa T cleanser and Rosa T serum (Test Product 2) and Placebo cleanser along with Rosa T serum (Test Product 1) shows significant reduction in skin pigment after 7, 14, 21 and 42 days from baseline as shown in Figure 3.

Secondary efficacy parameters

Sebum secretion rate (cheek)

Efficacy of Anti-acne products were measured in terms of reduction in sebum secretion rate on forehead and cheek from baseline by using Sebumeter® (Day 1, Day 7, Day 14, Day 21 and Day 42) as shown in Figure 4.

Both anti-acne products i.e. Placebo Cleanser and Rosa T serum (Test Product 1) and RosaT Mild Cleanser and Rosa T Serum (Test Product 2) shows significant reduction in sebum secretion (cheek) after 7, 14, 21 and 42 days from baseline as shown in Figure 4.

Both the anti-acne products i.e. Placebo Cleanser and Rosa T serum (Test Product 1) and RosaT Mild Cleanser and Rosa T Serum (Test Product 2) shows significant reduction in sebum secretion (forehead) after 7, 14, 21 and 42 days from baseline as shown in Figure 5.

Citation: Gajjar T, Patel N, Chew et al. Safety and efficacy of two botanical based topical anti-acne products in treatment of mild to moderate acne subjects. *J Dermat Cosmetol.* 2020;4(5):99–107. DOI: 10.15406/jdc.2020.04.00161

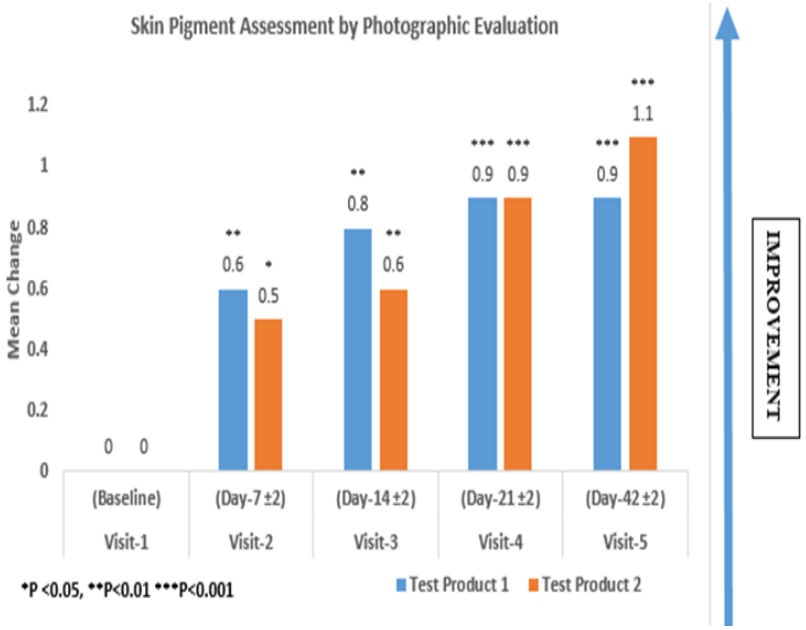
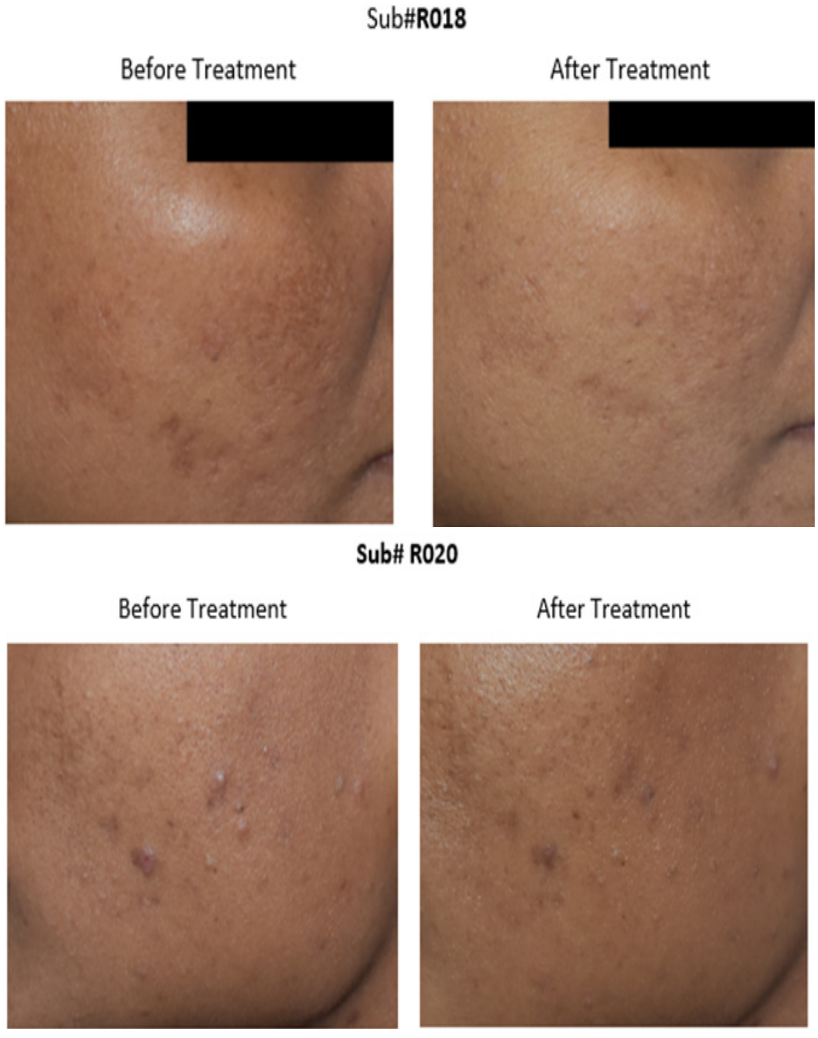


Figure 3 Analysis of the skin pigment assessment by photographic evaluation.



Citation: Gajjar T, Patel N, Chew et al. Safety and efficacy of two botanical based topical anti-acne products in treatment of mild to moderate acne subjects. *J Dermat Cosmetol.* 2020;4(5):99–107. DOI: 10.15406/jdc.2020.04.00161

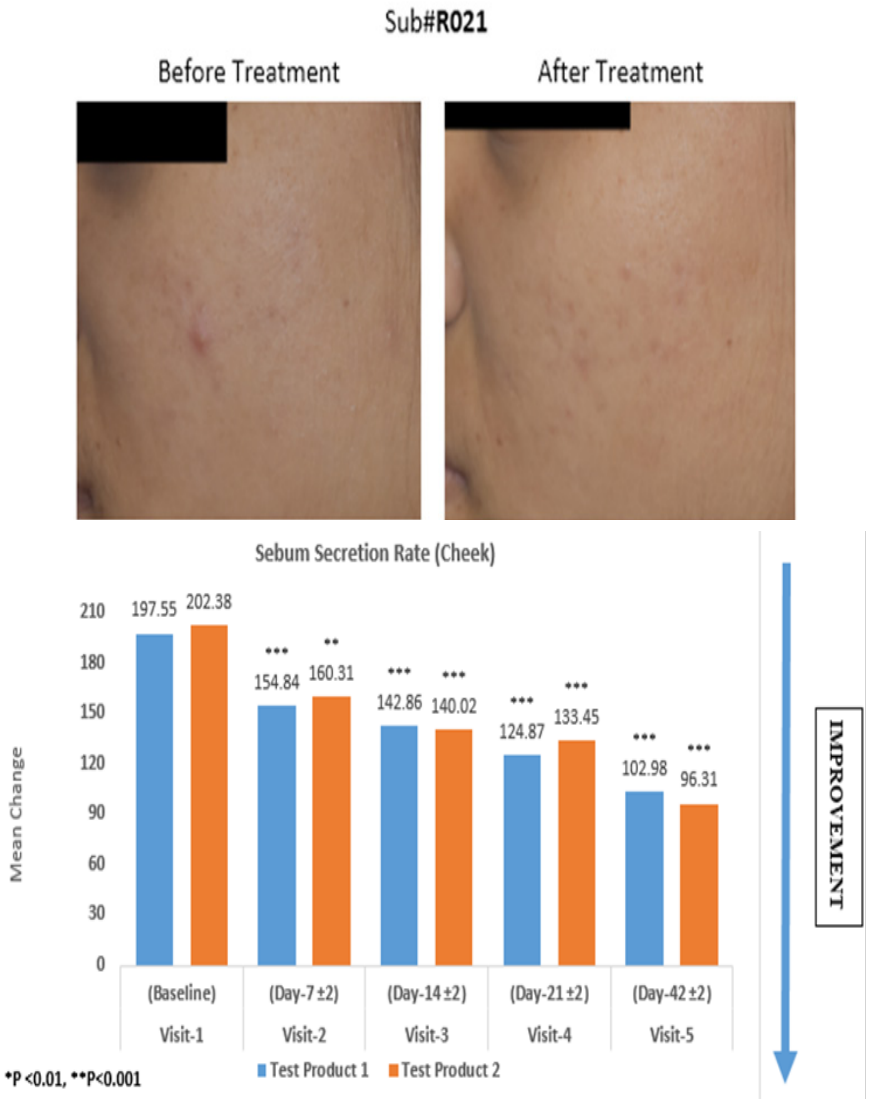


Figure 4 Analysis of the sebum secretion rate by sebumeter® (Cheek).

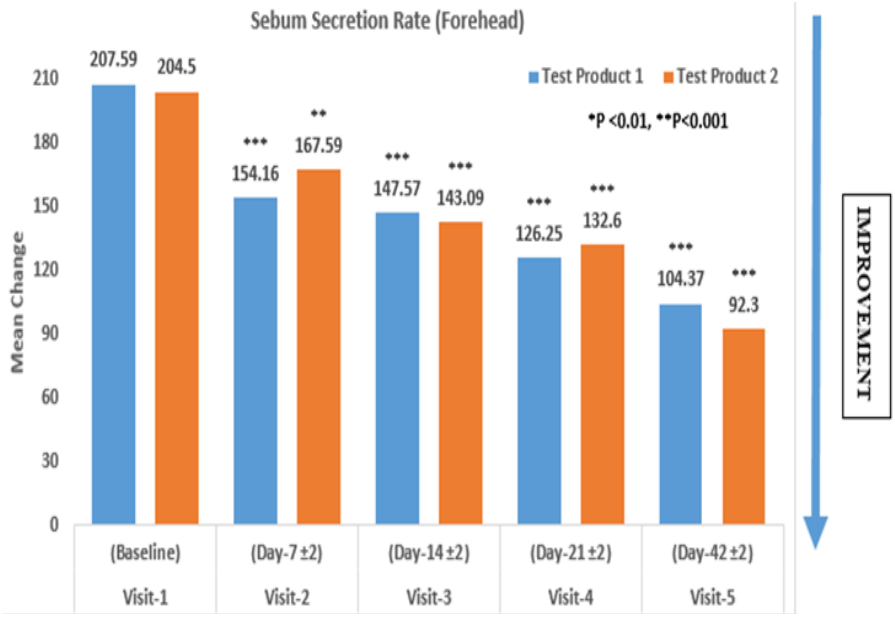


Figure 5 Analysis of the sebum secretion rate by sebumeter® (forehead).

Citation: Gajjar T, Patel N, Chew et al. Safety and efficacy of two botanical based topical anti-acne products in treatment of mild to moderate acne subjects. *J Dermat Cosmetol.* 2020;4(5):99–107. DOI: 10.15406/jdc.2020.04.00161

Effect of both the anti-acne products i.e. Placebo Cleanser and Rosa T serum (Test Product 1) and RosaT Mild Cleanser and Rosa T Serum (Test Product 2)were assessed in terms of change in acne severity from baseline by using evaluator's acne severity scale (Day 1, Day 7, Day 14, Day 21 and Day 42). Global acne severity scale is usually analysed after three months. However, even though this clinical trial lasted 42 days, there were clear evidence of improvements on Day 42.

Change in acne severity

Rosa T Mild Cleanser and Rosa T Serum (Test Product 2) shows no change in severity of acne after 7, 14 and 21 days from baseline. However, significant reduction was observed after 42 days from baseline which means acne severity changed from mild acne to almost clear skin. Placebo Cleanser and Rosa T Serum (Test Product 1)shows no change in severity of acne after 7, 21 days from baseline. However, significant reduction was observed after 14 and 42 days after baseline which means acne severity changed from mild acne to almost clear skin as shown in Figure 6.

Effect of both Anti-acne products i.e. Placebo Cleanser and Rosa T serum (Test Product 1) and RosaT Mild Cleanser and Rosa T Serum (Test Product 2)were assessed in terms of improvement in skin hydration effect from baseline by using Corneometer® on either cheek (Day 1, Day 7, Day 14, Day 21 and Day 42).

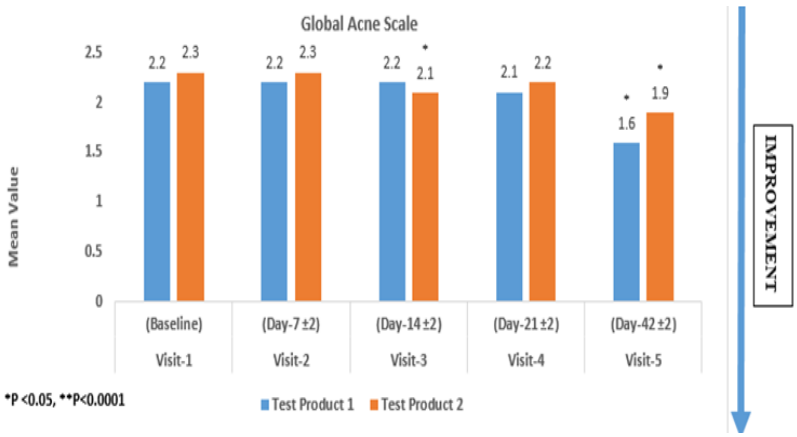


Figure 6 Analysis of the global acne severity scale.

Skin hydration

Rosa T Mild Cleanser and Rosa T Serum (Test Product 2) shows no change in skin hydration after 7, 14, 21 and 42 days from baseline which means skin hydration level maintained compared from baseline to 42 days and skin can be considered as sufficiently moisturized >40.

Placebo Cleanser and Rosa T Serum (Test Product 1) shows no change in skin hydration after 7, 14, 21 and 42 days from baseline which means skin hydration level maintained compared from baseline to 42 days as shown in Figure 7 and skin can be considered as sufficiently moisturized >40.

Effect of both anti-acne products i.e. Placebo Cleanser and Rosa T serum (Test Product 1) and Rosa T Mild Cleanser and Rosa T Serum (Test Product 2) on quality of life of subject assessed according to Cardiff Acne Disability Index (CADI) 8 (Day 1, Day 7, Day 14, Day 21 and Day 42).

Acne scar assessment

Rosa T Mild Cleanser and Rosa T Serum (Test Product 2) shows significant reduction in acne scars after 42 days from baseline as shown in Figure 8.

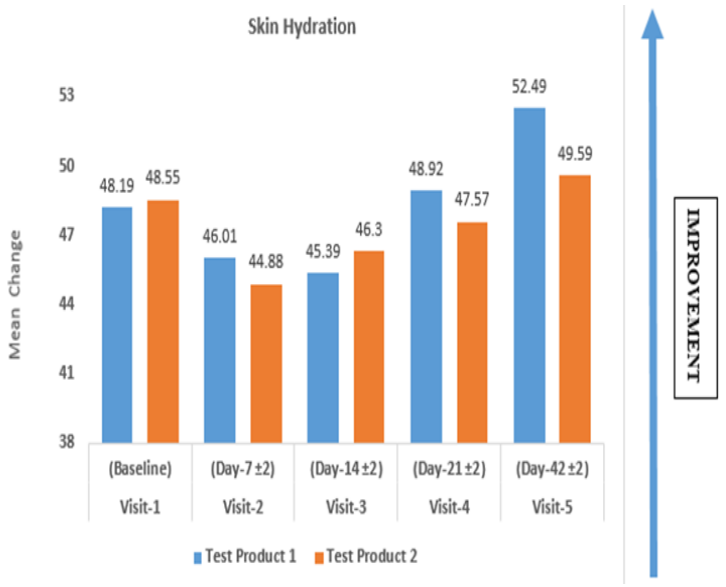


Figure 7 Analysis of the skin hydration by corneometer.

Citation: Gajjar T, Patel N, Chew et al. Safety and efficacy of two botanical based topical anti-acne products in treatment of mild to moderate acne subjects. *J Dermat Cosmetol.* 2020;4(5):99–107. DOI: 10.15406/jdc.2020.04.00161

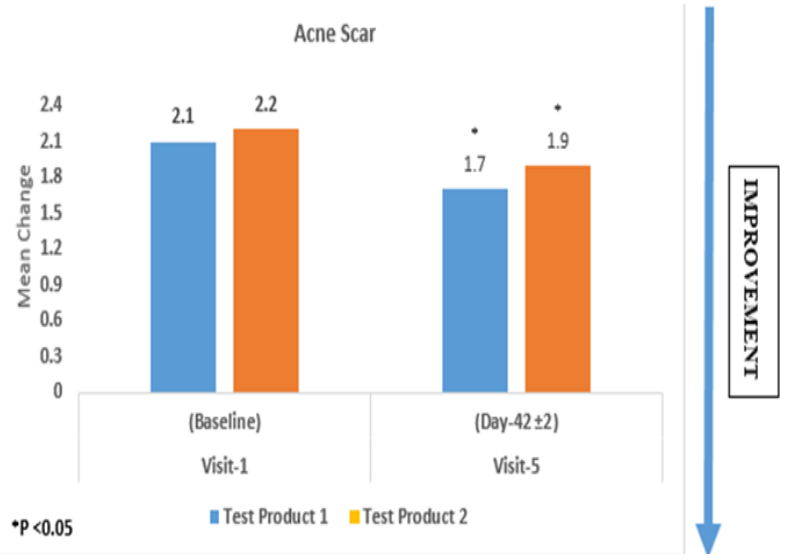


Figure 8 Analysis of the acne scar assessment.

Results

Here, the figures show significant improvement in acne and overall skin condition. The cutaneous inflammatory and non-inflammatory acne lesions are shown to have reduced evidently to baseline. Skin hydration remains unchanged compared to the baseline. Significant reduction in sebum level has been observed. Skin pigment decreased with respect to baseline and the acne scars reduced as well compared to the baseline. Based on the quality of life assessment of subjects observed remarkable improvement in acne after use and nearly all of the subjects noticed skin to be less prone to oiliness. Additionally, considerable improvement in acne scars was noted. Furthermore, the product usage was well received. Overall the subjects were satisfied with the effects shown by the Test Products.

Discussion

Many over the counter acne treatments are available to treat mild to moderate acne effectively. However, chemical treatments containing ingredients such as benzolyl peroxide, salicylic acid, azelaic acid etc. can irritate skin causing dryness, flakiness, itching, redness etc. Usage of chemically synthesized acne treatment can at certain duration lead to lose of skin hydration causing dryness, itchiness and redness due to lose of natural skin balance.

Acne is associated with a greater psychological burden than a variety of other disparate chronic disorders. Various studies have demonstrated that patients with acne vulgaris suffer psychological aberrations like depression, anxiety, psychosomatic symptoms (pain and discomfort), embarrassment and social phobia. Effective treatment of acne vulgaris is accompanied by improvements in self-esteem, social assertiveness and self-confidence.[10]

Thus, the study was conducted to determine the effectiveness and safety of using two botanical based products i.e. Placebo Cleanser and Rosa T serum (Test Product 1) and Rosa T Mild Cleanser and Rosa T Serum (Test Product 2) in treatment of mild to moderate acne subjects.

Linoleic acid is an essential building block for ceramides which is one of the skin's key moisturizing elements. And the deficiency of linoleic acid can affect the skin barrier function and result in acne breakouts.[7,8] Test product 1 (Rosa T Serum) have ingredients like Rose Hip Seed Oil, grape seed oil, Natural Vitamin E, Tea Tree Oil etc. Test product 2 (Rosa T mild cleanser) contains Hamamelis Virginia. Rosa T Serum has a high concentration of linoleic acid from two ingredients i.e. rosehip seed oil and grape seed oil, which can help in controlling sebum secretion and skin's natural oil balance. Rosa T Serum also consists of Tea Tree Oil which acts as a natural anti-inflammatory and anti-microbial agent and helps to reduce the inflammation associated with acne and prevents acne lesions.

During study conduct it was observed that Rosa T mild cleanser helps in reducing skin sebum level and improve skin hydration level after application from Day 1 to Day 07, Day 14 and Day 21. Sebum is the main cause of acne in the age group 18 to 35 years. So, we can say that Rosa T Serum is one of those few botanical anti acne products that not only reduce acne but also reduces sebum. Moreover, it has the added benefits of being hydrating, reduces redness and inflammation and reduces scars as well. Also no adverse event observed during conduct of the study.[9–17]

Conclusion

Rosa T Mild Cleanser with Rosa T Serum (Test Product 2) was found safe and effective in significant reduction of acne evaluated instrumentally, clinically and subjective self-evaluation. Rosa T serum was effective in reducing sebum level, improving skin hydration level as well as from subject's own feedback. There was also improvement in acne condition and acne scars. Rosa T is one of those few botanical anti acne products that not only reduces acne but also reduces excessive sebum, which is the main cause of acne.

Overall, the botanical based Rosa T Mild Cleanser and Rosa T Serum (Test Product 2) can be employed as an efficient substitute to present synthetic topical anti acne product in patients with mild to moderate acne [i.e. acne severity grade II and III] and safe with no AEs.

Acknowledgments

None.

Conflicts of interest

The authors has no conflict of interest to declare.

Funding

None.

References

1. Lizelle Fox , Candice Csongradi , Marique Aucamp, et al. Treatment Modalities for Acne. *Molecules*. 2016;13;21(8):1063.
2. Feldman S, Careccia RE, Barham KL, et al. Diagnosis and treatment of acne. *Am Fam Physician*. 2004. 2004;69(9):2123–2130.
3. Strauss JS, Thiboutot DM: Diseases of the sebaceous glands. In: Freeberg I, Eisen A, editors. Fitzpatrick's Dermatology in General Medicine. 5th edn.usa, NY: McGraw–Hill. 199:769.
4. Downing DT, Stewart ME, Wertz PW, et al. Essential fatty acids and acne. *J Am Acad Dermatol*. 1986; 14(2):221–225.
5. Nil Froushzadeh MA, Siadat AH, Baradaran EH. Clindamycin lotion alone versus combination lotion of clindamycin phosphate plus Tretinoin versus combination lotion of clindamycin phosphate plus salicylic acid in the topical treatment of mild to moderate acne vulgaris: A randomized control trial. *Indian J Dermatol Venerol Leprol*. 2009;75(3):279–282.
6. Irby CE, Yentzer BA, Feldman SR. A Review of Adapalene in the Treatment of Acne Vulgaris. *Journal of Adolescent Health*. 2008;43(5):421–424.
7. Iraji F, Sadeghinia A, Shahmoradi Z, et al. Efficacy of topical azelaic acid gel in the treatment of mild–moderated acne vulgaris. *Indian J Dermatol Venerol Leprol*. 2007;73(2):94–96.
8. Gabriella Fabbrocini et al. Acne Scars: Pathogenesis, Classification and Treatment. *Dermatology Research and Practice*. 2010. p. 13.
9. Gollnick HP, Zouboulis CC, Akamatsu H, et al. Pathogenesis and pathogenesis related treatment of acne. *J Dermatol*. 1991;18(9):489–499.
10. Tan JK. Psychosocial impact of acne vulgaris: Evaluating the evidence. *Skin Therapy Lett*. 2004;9(7):1–3,9.
11. SM– The Sebumeter® SM 815 Manual – Courage + Khazaka.
12. CM– The Corneometer® CM 825 Manual – Courage + Khazaka.
13. G. Ravichandran, M Derm, V Shivaram Bharadwaj, and S.A. Kolhapure.
14. Kligman AM. An overview of acne. *J Invest Derm*. 1974;62(3):268–287.
15. Webster GF. Inflammation in acne vulgaris. J Am Acad Derm. 1995;33:247–253.
16. Manoj A, Suva, Ankita M. Patel, Neeraj Sharma, et al. A Brief Review on Acne Vulgaris: Pathogenesis, Diagnosis and Treatment. *Research & Reviews: A Journal of Pharmacology*. 2014;4(3).
17. Youn SW. The Role of Facial Sebum Secretion in Acne Pathogenesis: Facts and Controversies. *Clin. Dermatol.* 2010;28(1):8–11.