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HANDHELD LED ARRAY DEVICE IN THE TREATMENT OF ACNE VULGARIS

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Abstract
The successful treatment of acne still remains problematic. Conventional therapies often prove inconsistent with unacceptable side effects and recurrence rates, leading to patient noncompliance. A thermal phototherapy treatment using a combination of blue light and red light has recently attracted much attention and seems to offer an effective alternative. The objective of this study was to evaluate the efficacy of blue light (415 nm) in combination with red light (633 nm) in the reduction of inflammatory lesions on the face of subjects (n=21) with mild to moderate acne vulgaris after a course of 8 20-minute (blue) or 30-minute (red) alternated light treatments, self-administered by a handheld unit over a period of 4 weeks. Lesion counts progressively reduced throughout the 4-week light therapy period and continued to reduce up to 8 weeks posttherapy, with a final average reduction of 69% seen 8 weeks after the treatment course ($P>.001$). This pattern is similar to previously reported studies.

Introduction
Acne is a chronic, inflammatory disease of the pilosebaceous units of the face, chest, and back. In the US, census data and prevalence reports indicate approximately 40 million adolescents and 25 million adults (85% of the population) have some form of acne, with 30% requiring physician intervention.[1-3]

The mainstays of current acne treatments are retinoids and antibiotics, however treatment failure rates vary. Retinoid therapy carries a poor side-effect profile and displays teratogenicity [4] and can only be prescribed by member physicians of the System to Manage Accutane-Related Teratogenicity (SMART) program and the development of bacterial resistance in antibiotic therapy is widely documented.[5] Topical preparations may also cause significant side effects including skin irritation and these effects may lead to noncompliance with treatment.[6] Such noncompliance is one of the most common aspects of regimen failure in acne therapy,[7] which highlights the need for an alternative therapy or a combination of therapies for patients who fail to respond adequately to current treatments, develop problematic side effects, or are noncompliant.

Photodynamic therapy is the use of light to activate exogenously administered or endogenously formed photosensitizers within the cell, forming singlet oxygen and other transient free radicals, inducing cellular death by apoptosis .The success of blue light for treating mild to moderate acne has been proven to varying degrees of success using photodynamic therapy.[8-12] *Propionibacterium acnes* is known to produce endogenous photosensitizers called porphyrins, the major components of which are coproporphyrin III[13,14] and protoporphyrin IX (PPIX).[15] Coproporphyrin III and protoporphyrin IX mainly absorb visible light at 400 nm to 415 nm.[13,14]

Blue light in combination with red has been proven to be an effective therapy in the treatment of acne vulgaris.[15-17] Papageorgiou et al, and subsequently Golberg and Russell and Lee et el, proposed that blue light and red light acted synergistically in improving acne by combining the antibacterial and anti-inflammatory action of blue and red light, respectively.[15-17]

The objective of this study was to evaluate the efficacy of blue light (415 nm) in combination with red (633 nm) in the reduction of inflammatory lesions on the face of subjects with mild to moderate acne vulgaris after a course of 8 light treatments delivered by a handheld unit, and self-administered by the patient over a period of 4 weeks.

Materials and Methods

Subjects
Twenty-one subjects (38% male, 62% female; age range: 14-21 years) with Burton grades 3 to 4 were recruited. Subjects had not used topical, oral or systemic treatments for 4 weeks and had not received oral retinoids for 6 months prior to the study. Subjects were recruited during December 2006. Treatments were administered between January and February 2007. All subjects gave informed consent to the treatment and had been prescreened before inclusion on the study. Subjects were allocated to a single treatment group. No control group was used in this study. An independent ethics review panel approved the study.

Light Source
The handheld unit (Omnilux clear-U™, Photo Therapeutics Inc, Carlsbad, CA) consisted of an air cooled, fixed planar array of light-emitting diodes emitting at 415 nm (40 mW/cm^2) and 633 nm (70 mW/cm^2). The active light-emitting diode area measured 60 mm by 50 mm and was used to illuminate the subject treatment area.

Treatment
Before the treatment course, subjects were instructed to read the user manual on the use of the handheld light source and were monitored during the study to assess the subjects' understanding of how to operate the equipment. Each subject was given 1 of 6 locations on the face to treat: left or right forehead, left or right cheek, nose or chin. Chest and back were excluded. Locations were randomly allocated using a modification of the Global Acne Grading System (GAGS).

Subjects were issued with a nonmedicated soap for the duration of the trial.

Each week, the subject administered 2 alternate exposures: blue light (415 nm; 40 mW/cm^2, 48 J/cm^2) for a 20-minute duration and red light (633 nm; 70 mW/cm^2, 126 J/cm^2) for a 30-minute duration. The unit was operated by each subject and held in contact with the subject's face for the duration of the treatment. A 2 to 3 day interval was instructed between blue and red light treatments. The weekly treatments were continued for the full study period of 4 weeks (total of 8 treatments).

Clinical Assessments

Burton acne grading and Fitzpatrick skin type were recorded for all subjects at baseline. Acne assessments were conducted using lesion counts to include the treated area as identified by the GAGS system. Lesions included in the count were comedones, papules, pustules and nodules. Each lesion present was assigned a value of 1 in the lesion count. Acne was assessed at baseline and weeks 2, 4, 8, and 12. The principle-investigating physician (nonblinded) conducted assessments.

Digital photographs (Canon 300D, Tokyo, Japan) of subjects were taken for lesion assessment at baseline and weeks 2, 4, 8, and 12. Head position, angle, framing, exposure, and lighting conditions were standardized for all photograph documentation.

Statistical Methods

Statistical significance of lesion count reductions, from baseline at 2-week, 4-week, 8-week, and 12-week follow-up, were analysed with a standard student's *t* test using a confidence level of *P*=.001.

Results

Subjects were well matched at baseline in terms of both age and duration of acne. Of the 21 subjects recruited, 19 subjects (8 male, 11 female, mean age 17 years, range: 14-21 years) completed follow up; 10 subjects had Burton grade 3 acne, 9 were grade 4. Two subjects withdrew from the study due to personal circumstances unrelated to the trial, and these subjects' data were subsequently excluded from analysis.

The average percentage reductions in inflamed lesions at all follow-up points are detailed in Table 1. Significant reductions in inflamed lesions were noted from week 4 onwards, with a final average reduction of 69% seen at the week 12 assessment (*P*>.001) (Figures 1 and 2). However the difference from baseline was significant as early as the second assessment at week 4. There appeared to be little or no change in comedones from baseline (Table 2).

Unlike previous work by Goldberg and Russell, there appeared to be no significant difference in average clearance rates between the 2 Burton grades. Subject self-assessments (categorized as "marked improvement," "moderate improvement," "mild improvement," or "no improvement") were interesting: the majority graded the light treatment as having moderate or marked improvement 68% in comparison to 32% of subject who only rated their improvement as mild. Of those 6 subjects who reported only mild improvement, 3 (50%) had clearances of >70% when compared to baseline. There were no reports from subjects of overall response being graded as no improvement (Table 3).

Subjects were also asked to rate the ease of use of the system after reading and understanding the user guide. Assessments

Table 1. Mean reduction in inflamed lesions.

Assessment Time	Mean Lesion Count of Inflamed Lesions (n)	Mean Reduction of Inflamed Lesions (%)
Baseline	16	
Week 2	13	20
Week 4	10	38
Week 8	6	63
Week 12	5	69

Table 2. Mean reduction in noninflamed lesions.

Assessment Time	Mean Lesion Count of Noninflamed Lesions (n)	Mean Reduction of Noninflamed Lesions (%)
Baseline	8	
Week 2	9	13
Week 4	8	0
Week 8	7	12
Week 12	7	12

Table 3. Subject assessment of overall treatment response.

	Marked Improvement	Moderate Improvement	Mild Improvement	No Improvement
Subject assessment (%)	16	52	32	0

were categorized as "extremely easy," "very easy," "slightly easy," or "difficult." Seventy-four percent rated the product very easy or extremely easy to use. Only 2 subjects (11%) rated the product as only slightly easy. No subject rated the product as difficult to use.

Two subjects reported side effects of the light treatment in the form of mild facial erythema, occurring for one subject after the first light treatment and for the other after the second light treatment. These events were self-limiting in both cases and resolved within 24 hours of the treatment.

Discussion

The pathogenesis of acne is still not fully realized. However, in the context of light therapy, one of the major causative factors of acne is the multiplication of *P acnes* in the follicular canal. The presence of actively replicating *P acnes* in the sebaceous glands has been associated with the production of proinflammatory cytokines such as interleukin (IL-1), tumour necrosis factor (TNF) and granulocyte/macrophage colony stimulating factor (GM-CSF).[18]

Although the exact mode of action is still to be elucidated it is believed that the effectiveness of phototherapy is brought about by the destruction of *P acnes* through the mechanism of photodynamic therapy combined with the stimulation of cellular activity by intracellular and intercellular pathways. Red light (633 nm) although less effective at activating coproporphyrin III than blue light, penetrates more deeply into the tissue and importantly has noted anti-inflammatory properties. It has been demonstrated *in vitro*, that red light has influenced anti-inflammatory cytokines from macrophages and increased the synthesis of fibroblast growth factor from photoactivated cells[17] and low-level laser irradiation within the visible red waveband can produce various beneficial effects such as stimulation of cell proliferation, release of growth factors, collagen deposition, and neovascularization.[19-21]

Several reports now exist on use of light emitting diodes for the successful treatment of acne using blue light alone (415 nm)[12] or a combination of blue (415 nm) and red light (633 nm),[15-17] delivered twice weekly over a 4 week period. All of these studies have used a wide area arrays of LEDs and have involved subjects attending a clinic on a twice-weekly basis. Although these studies reported good subject compliance, it was the intention of this study the efficacy of a handheld unit to deliver an acceptable clearance rate for acne vulgaris in a setting where treatment is self-administered by the patient.

Initial findings were comparable to those cited in the literature for a static full-face treatment; however these counts were restricted to a particular area of the face and should be viewed as such. The results from this study support earlier findings indicating that combination red and blue light therapy is a safe and efficacious treatment for acne vulgaris.

Lesion counts progressively reduced throughout the 4-week light therapy period. This pattern reflects the results of studies previously cited[11-13,16] and is evidence for the proposed photobiomodulation cellular effects attributable to light treatment using a nonthermal LED light source for acne treatment.

A substantial and significant 69% reduction in mean lesion count was observed at the final 12-week follow-up. Although clinically evident that the light therapy course achieved considerable reduction in papules and pustules, comedone counts were minimally affected, unlike previous studies, which have demonstrated both positive[17] and negative[12] outcomes. This may be an indication for the addition of an anticomedonal preparation used adjunctively with light therapy treatments for acne.

Conclusion

This study has successfully demonstrated the use of a handheld LED device for the treatment of inflammatory acne. A significant reduction in acne lesions from baseline was seen from week 4 to final assessment at week 12.

The light treatments were well received by subjects, 68% reporting moderate to marked improvement at final follow-

Figure 1. Appearance of chin at baseline.

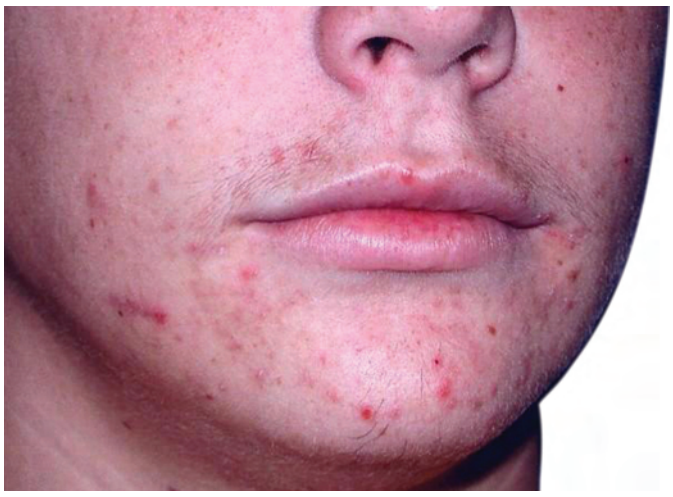
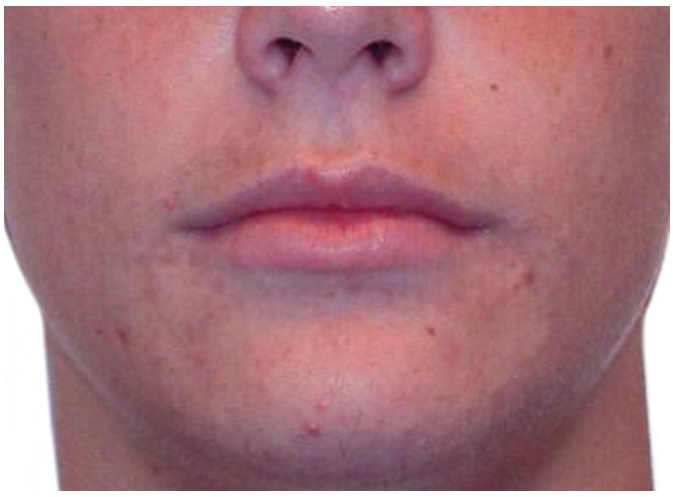


Figure 2. Appearance of chin at 8 weeks posttherapy.



up. None of the included subjects reported the handheld LED device as difficult to use or that their acne had not improved posttreatment. These results lead to further the consideration of this handheld system as a successful adjunct to mainstay acne therapy, as the hand-held functionality enables the patient to self-administer treatment, which could be effective as an additional tool in the clinician's armamentarium.

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