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Low-level Light Therapy for Treatment of Acne and Rejuvenation of Photoaged Skin

Narrow bands of non-thermal visible or non-visible infrared light generated by light-emitting diodes (LEDs) have the potential to improve certain cosmetic-related facial issues. This article reviews low-level light therapy using LEDs in the treatment of acne and for rejuvenation of photoaged skin, with a focus on the Neutrogena® Light Therapy Mask.

About the Reviewers

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David J. Goldberg is a Board-Certified Dermatologist and is recognized nationally and internationally for his work with skin lasers, cosmetic dermatology and facial rejuvenation techniques.

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He has published over 165 peer-reviewed manuscripts and and has contributed to many academic textbooks and is on the editorial boards of the Lasers in Surgery and Medicine and Dermatologic Surgery and is the current Senior Chief-Editor of the Journal of Cosmetic and Laser Therapy.

Dr. Goldberg is active in professional societies and has sat on the board of directors of the American Academy of Dermatology, the American Society for Lasers in Medicine and Surgery, the American Society for Dermatologic Surgery and the International Society for Dermatologic Surgery. He has also served as a co-vice-president of the Skin Cancer Foundation.

The Skin Laser & Surgery Specialists of New York & New Jersey, directed by Dr. Goldberg, have been the site of FDA research on laser hair removal and skin rejuvenation and he has been instrumental in bringing this technology to the public

As a physician, he has garnered a host of accolades, including being the recipient of the ASLMS's first Leon Goldman Memorial Award, which recognizes contributions in clinical laser research, laser patient care and medical laser education.

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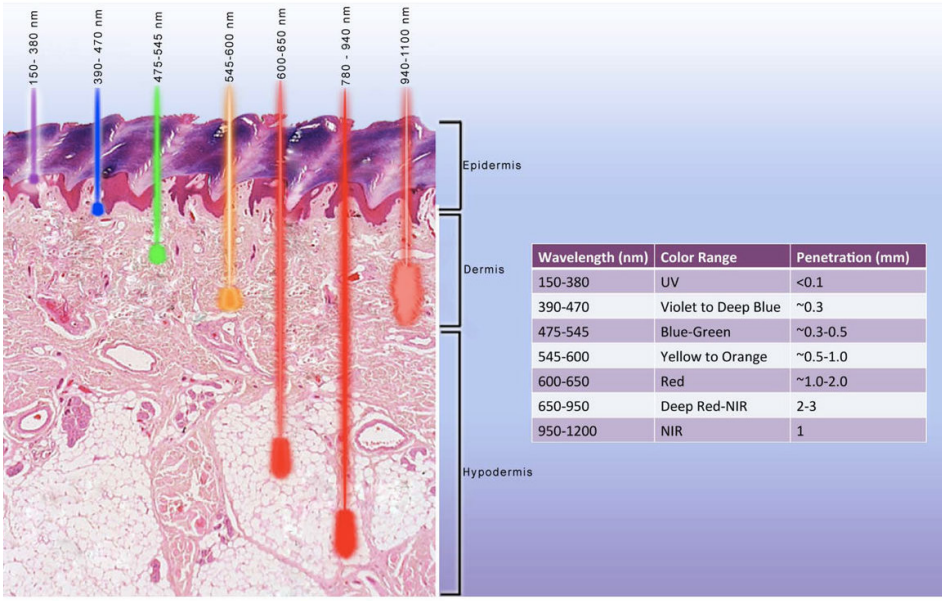
Dr See has served on the State and Federal boards of the Australasian College of Dermatologists as well as having been a guest examiner for the Fellowship examinations. Her practice covers a broad spectrum of cases which often times require innovative methods of treatment. Her key interests are skin care, sun damage, skin cancer and acne.

She is co-chair of All About Acne, an online acne resource as well as a regular national and international speaker on acne. She is a key opinion leader regarding acne and chairs several advisory boards looking at new acne treatments as well as education resources for the public and doctors. She appears regularly in the media talking about acne and skin care.

LED-based low-level light therapy

Low-level light therapy (LLLT) refers to the use of photons at a non-thermal intensity (irradiance) to alter biological activity, i.e. photo-bioactivation or photo-biomodulation of a cell's biological processes without damaging or destroying the treated cell.[1,2] Photons are discrete particles of pure light energy that must be absorbed by a target cell for a reaction to occur.[2] LLLT employs light in the visible to near-infrared (IR) spectrum, i.e. wavelengths of 390–1100nm (**Figure 1**).[1,3] In general, shorter wavelengths of 390–600nm are used to treat superficial layers of the skin and longer wavelengths of 600–1100nm, which penetrate deeper, are used to treat the deeper skin layers.



Wavelength (nm)	Color Range	Penetration (mm)
150-380	UV	<0.1
390-470	Violet to Deep Blue	~0.3
475-545	Blue-Green	~0.3-0.5
545-600	Yellow to Orange	~0.5-1.0
600-650	Red	~1.0-2.0
650-950	Deep Red-NIR	2-3
950-1200	NIR	1

Figure 1. Skin penetration depths of various wavelengths of light (visible to near-infrared light). The epidermis, the outermost layer of skin, provides a waterproof barrier and creates skin tone.[1,3] It is primarily composed of keratinocytes and dentritic cells but also contains melanocytes, Merkel cells, and Langerhans cells. Beneath the epidermis is the dermis, which contains collagen, capillary networks, hair follicles, and sweat glands. The deepest layer of skin is the hypodermis or subcutaneous tissue. It is composed of fat, collagen, and larger blood vessels.[4]

Typically, LLLT uses either coherent light sources (lasers) or non-coherent light sources in the form of filtered lamps and light-emitting diodes (LED).[1] LEDs are semiconductors that convert electrical current into non-coherent and divergent narrow band light.[2,3] Non-coherent means that the amplitude and phase of the emitted light waves fluctuate randomly. Due to being a non-coherent divergent light source, LEDs emit the same wavelengths of light as lasers but with less intensity and at a substantially lower energy output.[2,3] Hence, LEDs do not deliver sufficient energy to damage tissues and have a lower risk of accidental eye damage. LEDs are also suitable for use in LLLT systems because:[2]

- They require a small amount of electricity to produce a great deal of light.
- Being solid state they require neither filaments nor flash-lamps for activation.
- Their narrow bandwidth allows precise target specificity.
- They can be mounted in large-area planar arrays, which allows hands-free irradiance of a large area (versus the point-by-point application of a laser system).
- They are significantly less expensive than other light sources.

There is increasing evidence that light of varying wavelengths delivered at low level has a beneficial effect on a variety of dermatological conditions, including acne and photoaged skin.[2,3,5-7] Moreover, LLLT has been shown to be safe and well tolerated.[2,3,7] However, some users may experience mild reddening of the skin and/or tingling sensations.[8]

Light Therapy Mask

The Neutrogena Light Therapy Mask is a wearable, non-thermal, non-ablative, LED-based device for home-use LLLT.[8,9] The design incorporates a parabolic shape and an internal reflector to maximize photon recycling and delivery to the skin. The Light Therapy Mask connects to a controller that houses a battery pack sufficient to power a total of 30 daily LLLT sessions of 10 minutes duration each. The Light Therapy Mask is available in two variations:

Acne Light Therapy Mask

This mask uses a combination of LED red light (630nm) and blue light (445nm) delivered at an irradiance of <85 mW m^{-2} for treatment of mild to moderate facial acne.[8] The Acne Light Therapy Mask has been approved by the FDA for this indication.[10]

Fine Fairness Light Therapy Mask

This mask uses a combination of LED red light (630nm; minimum mean peak power 400μW) and near-infrared (850nm; minimum mean peak power 150μW) light for rejuvenation of photoaged skin.[9] The Fine Fairness Light Therapy Mask features an LED array (as distinguished from the typical 'row and column' array) arranged to maximize irradiance over the most common skin aging zones, i.e. the periocular and perioral regions.

** The Neutrogena Fine Fairness Light Therapy Mask is not available in Australia or New Zealand.

Precautions

The Light Therapy Mask should not be used if a person has light-sensitive skin or if they are currently using medication that may cause their skin to be light sensitive. The Light Therapy Mask should also not be used if a person is pregnant, may be pregnant, or is breast feeding because at the present time any potential risks are unknown. Use of the Light Therapy Mask should be discontinued if discomfort or skin reddening or discoloration lasting >24hrs is experienced.

Treatment of acne

Acne vulgaris is a common skin condition that presents with non-inflammatory (closed and open comedones) and inflammatory lesions (papules, pustules, and nodules or cysts).[11,12] Acne can lead to scarring and psychological distress. In some people, the use of oral or topical treatments is of limited utility due to inconvenience, lack of efficacy, or poor tolerability.

Phototherapy has been proposed as a convenient alternative treatment modality for people whose acne is non-responsive to standard acne therapies or who are unable or unwilling to tolerate standard therapies.[13,14] Phototherapy with visible light, mainly blue light, red light, or combination of both, started being used in the treatment of acne during the early 2000s.[15]

Mode of action

Blue light has been shown to have beneficial effects on acne vulgaris.[16-18] The bacterium *Propionibacterium acnes*, which plays an important role in the aetiology of acne, is known to produce large quantities of intracellular porphyrins.[19-21] The most abundant is coproporphyrin III, which has peak absorption at 415nm, i.e. in the wavelength range of blue light.[7] The absorption of blue light by protoporphyrins leads to the formation of reactive free radicals and subsequent destruction of the cell membrane of *P. acnes*.[19,22]

Additionally, numerous *in vitro* studies have shown the anti-inflammatory effects of blue light via modulation of inflammatory mediators implicated in acne.[23] The anti-inflammatory effects of blue light have also been demonstrated in an acne animal model.[24] Devices that employ blue light-emitting diodes (LEDs) have been shown to have reduce lesion counts in the treatment of acne vulgaris in randomised controlled trials (RCTs).[25,26]

Red light can also improve acne vulgaris. Compared with blue light, it penetrates more deeply into the skin (**Figure 1**).[1,3] Red light has been shown to reduce levels of inflammatory biomarkers (including neutrophils, interleukin, and matrix metalloproteinase) in an acne animal model and to moderate cytokine production by macrophages *in vitro*.[27,28] Confirming its anti-inflammatory effects, including lesion count reduction, red light has been demonstrated to be beneficial in the treatment of patients with acne vulgaris in prospective controlled trials and RCTs.[29-31]

Moreover, in a recent *in vitro* study, 415nm blue light suppressed cell human sebocyte proliferation and 630nm red light strongly downregulated sebocyte lipid production.[32] These results indicate that both 415nm blue light and 630nm red light have beneficial effects on acne by suppressing sebum production.

Combining blue light, which is effective against *P. acnes* and has anti-inflammatory and anti-sebum effects, with red light, which also has anti-inflammatory and anti-sebum effects, provides complementary and synergistic mechanisms in the treatment of acne vulgaris.

Clinical studies

Multiple published RCTs have demonstrated that combination blue-red LED LLLT is effective and well tolerated in the treatment of acne.[33-38] Notably, blue-red LED phototherapy was associated with reductions in the number of inflammatory acne lesions and treatment was well tolerated with no serious adverse events observed. Additionally, a reduction in melanin levels after red-light LLLT (alone and sequentially with blue light) was demonstrated in one study with brightening of skin tone being spontaneously reported by almost 60% of the acne patients.[38]

Acne Light Therapy Mask

One of the published RCTs evaluated the clinical performance of the (445nm blue/630nm red) Acne Light Therapy Mask in patients with mild to moderate acne.[37]

This 12-week, randomised, evaluator-blinded study assessed the efficacy and tolerability of the Acne Light Therapy Mask used alone (MASK) and with topical 1% salicylic acid plus retinol (MASK-SA) versus 2.5% benzoyl peroxide (BPO) in 105 individuals (aged 12–35 years) with mild-to-moderate facial acne vulgaris who were all using the same brand of skin cleanser.[37]

The MASK group showed a 24.4% improvement in inflammatory acne lesions at week 12 ($p<0.01$ vs baseline) versus 22.7% ($p<0.01$) and 17.2% ($p<0.05$) improvements in the MASK-SA and BPO groups, respectively (**Figure 2**).[37] The MASK-treated subjects also showed a 19.5% improvement in non-inflammatory lesions at week 12 ($p<0.001$ vs baseline) versus 4.8% and 6.3% improvements in MASK-SA-treated and BPO-treated subjects, respectively. In terms of the Investigator Global

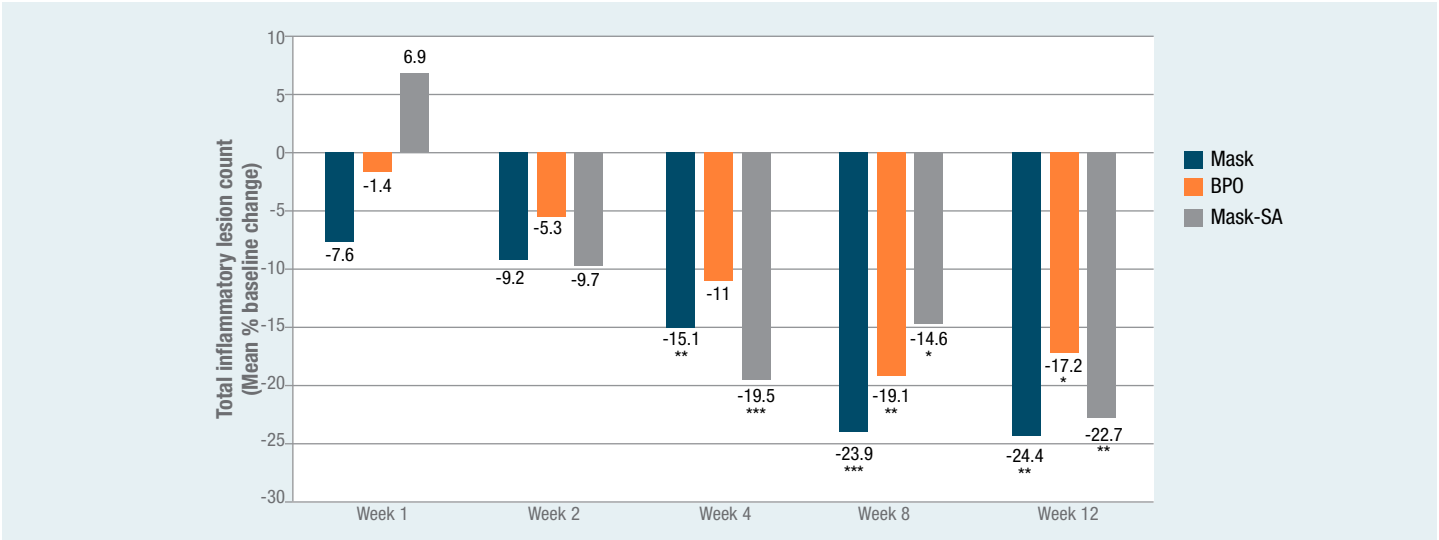


Figure 2. Change in number of inflammatory lesions (primary endpoint) over 12 weeks of treatment in people with acne.[37] Abbreviations: Mask = Acne Light Therapy Mask plus skin cleanser; BPO = skin cleanser and 2.5% benzoyl peroxide lotion; Mask-SA = Acne Light Therapy Mask plus skin cleanser and 1% salicylic acid + retinol. Statistically significant differences versus baseline: *p=0.05; **p=0.01; ***p=0.001.

Acne Assessment, subjects in MASK group achieved a 19% improvement (p<0.001 vs baseline) compared with improvements of 13.9% and 4.7% in the MASK-SA (p<0.01) and BPO groups, respectively.

The three treatments were well-tolerated overall, with a trend toward less early irritation noted in the MASK group.[37]

Similar improvements were also apparent in another 12-week, randomised, evaluator-blinded study, which evaluated the use of the Acne Light Therapy Mask and topical benzoyl peroxide in individuals (aged 12-40 years) with mild to moderate acne.[39] In this study, treatment with the Acne Light Therapy Mask was well tolerated and significantly reduced total acne lesion counts versus baseline (p<0.05). Subjects also reported significant improvements (p<0.05) in their acne and overall skin appearance.

Skin rejuvenation

The first signs of skin aging, such as wrinkling, dyspigmentation, and spider veins (telangiectasia), appear in a person's late 20s to early 30s.[1] Skin aging involves the complex interaction of intrinsic biological aging with the influence of external environmental factors, especially solar ultraviolet light.[1,2] This interaction results in the degradation of the extracellular matrix with loss of collagen, fragmentation of collagen fibres, and increased levels of matrix metalloproteases. With other effects of skin aging being a disorganized stratum corneum and poor cellularity, epidermal thinning also occurs.[2]

While the dermis is considered to be the supporting layer of the skin, it is the epidermis that is visible. Non-ablative skin rejuvenation modalities, including LLLT, aim to improve photoaged skin without damaging the epidermis.[1]

Mode of action

LED energy must pass through the epidermis on its way to the dermis. Visible red light 633nm and near-infrared light 830nm are known to beneficially affect epidermal basal layer cells.[2] These wavelengths of light will photo-bioactivate the epidermal basal layer cells, including keratinocytes, melanocytes, Merkel cells, and Langerhans cells without thermal or traumatic damage.

Many theories exist regarding the specific mechanisms of skin rejuvenation using red light.[23] One of the more likely explanations is that the absorption of red and near-infrared light by mitochondrial chromophores, especially cytochrome C oxidase (which is a terminal enzyme in the mitochondrial electron transport chain), results in elevated levels of adenosine triphosphate (ATP) and reactive oxygen species (ROS), which can enhance the cellular functions of dermal cells through specific signalling pathways.[1,23]

For example, by acting on different signalling-transduction pathways, red light helped to moderate UVA-induced aging of human skin fibroblasts in an *in vitro* study.[40] Increased collagen production (via an increase in numbers of fibroblasts and levels of platelet-derived growth factor) with a concomitant reduction in collagen degradation (via reduced levels of matrix metalloproteases and interleukin-6) has been proposed as a mechanism by which photo-bioactivation aids skin rejuvenation (**Figure 3**).[1] Indeed, a marked increase in the amount of collagen and elastic fibres was demonstrated by histology in subjects with facial wrinkles who received red (with or without near-infrared) LLLT in a recent RCT.[41]

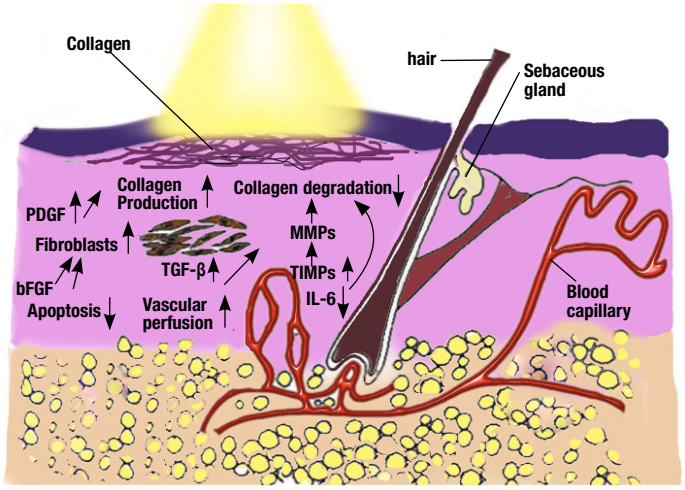


Figure 3. Proposed mechanism whereby LLLT aids skin rejuvenation via concurrently increasing collagen production and decreasing collagen degradation.[1] Abbreviations: bFGF = basic fibroblast growth factors; IL-6 = interleukin-6; MMP = matrix metalloproteases; PDGF = platelet-derived growth factor; TGF-β1 = transforming growth factor; TIMP = tissue inhibitors of metalloproteases.

Clinical studies

In randomised and non-randomised clinical studies, red (with or without near-infrared) LED-based LLLT has variously demonstrated statistically significant improvements in subjective parameters of skin rejuvenation (e.g. skin complexion, appearance, and feeling), with subjective/instrumental assessments (e.g. skin wrinkle severity, skin elasticity, and skin tone) generally showing moderate to slight improvements.[41-45]

For example, in one of these studies, red (633nm) light alone was associated with a statistically significant reduction (vs baseline) in melanin levels in patients with facial wrinkles and statistically significant baseline increases in skin elasticity were observed with red (633nm) light alone, near-infrared (830nm) light alone, and both in combination.[41]

Fine Fairness Light Therapy Mask

Two unpublished RCT studies have evaluated the skin rejuvenation effects and tolerability of the (630nm red/850nm near-IR) Fine Fairness Light Therapy Mask.[46,47]

One of these studies was a 12-week, double-blind, split-faced assessment in 30 women (aged 50–65 years) with moderate to severe facial photoaging.[46] It demonstrated significant (p<0.001 vs baseline) improvements in physician-assessed parameters of skin rejuvenation (radiance, skin roughness, pigmentation, and wrinkles) with the Fine Fairness Light Therapy Mask as well as high rates of patient satisfaction and adherence to treatment. No statistically significant differences (vs baseline) were observed for any physician-assessed tolerability parameter (dryness, erythema, oedema, burning, stinging, itching, and tightness).

The other RCT was an 8-week randomised, double-blind evaluation in women (aged 40–65 years) with moderate to severe facial photoaging and wrinkling. Subjects (n=50) were randomly assigned to treatment with the Fine Fairness Light Therapy Mask (n=30) or a control (sham) mask (n=20).[47]

In the clinical assessment of efficacy, 94% (16/17) of the physician-assessed measures of skin rejuvenation in the Fine Fairness Light Therapy Mask group showed statistically significantly higher scores at 8 weeks than at baseline (including all measures of wrinkling) compared with 23.5% (4/17) of attributes in the control mask group.[47] Compared with the control mask group, the Fine Fairness Light Therapy Mask showed statistically significantly greater improvement for 59% (10/17) of physician-assessed efficacy measures of rejuvenation (including eye-area Crow's Feet and under-eye area wrinkles) in terms of the percentage of subjects who improved from baseline. The control mask did not perform statistically significantly better than the Fine Fairness Light Therapy Mask for any of the rejuvenation parameters.

The Fine Fairness Light Therapy Mask group also outperformed the control mask group for all attributes for subject self-assessment of rejuvenation parameters.[47] In the clinical grading assessment, the Fine Fairness Light Therapy Mask group outperformed the control mask group for the four rejuvenation attributes, which included skin radiance, assessed at both week 4 and week 8 in terms of average improvement score and the proportion of patients who improved (**Table 1**). The physician assessment of tolerability did not reveal issues in either treatment group.

	Fine Fairness Light Therapy Mask		Control Light Therapy Mask	
	Week 4	Week 8	Week 4	Week 8
Patients with improvement in overall:				
• Clarity/brightness/radiance	83%*	86%*	21%	21%
• Appearance of youthfulness	72%*	83%*	21%	21%
• Skin texture	79%*	83%*	21%	21%
• Contrast between dark spots and surrounding skin	72%*	83%*	21%	21%

Table 1. Proportions of patients who demonstrated overall improvement in physician clinical grading of attributes of facial skin rejuvenation in the Fine Fairness Light Therapy Mask and control mask treatment groups.[47] Significant difference vs control mask group: *p<0.001. Attributes were scored on a 5-point scale: 1=much worse; 2=worse; 3=no improvement; 4=better; 5=much better

** The Neutrogena Fine Fairness Light Therapy Mask is not available in Australia or New Zealand.

EXPERTS' CONCLUDING COMMENTS

Dr David Goldberg

Low-level light therapy (LLLT) has been recognized as a potential treatment modality in medicine for many years. In the past, such devices were only available in physician offices. Recently, effective LLLT devices have become available to the public as home devices. Such home devices, like their larger in-office physician devices, have shown efficacy in the treatment of acne, pigment irregularities, and anti-aging of the skin.

What makes such devices useful in the home setting is not only their efficacy but also the incredibly low risk of side effects – in part because such devices photomodulate cells rather than inducing a laser-like photothermal effect. Because of this, LLLT treatments also are painless.

Whether LLLT will be used at home as a sole device or as an adjunct to other agents in the treatment of acne has yet to be fully evaluated. It is likely though that LLLT may, in some individuals with acne, obviate the need for oral and/or topical antibiotics. Because LLLT devices are effective and have such a favourable side effect profile, it is also likely that patients using such devices will show greater adherence in their treatment protocols.

Dr Jo-Ann See

Acne can be a frustrating condition to treat as many younger patients, and their parents, are concerned with the side effects of both topical and oral treatments. Acne patients want to see a quick result, i.e. effective therapy, while not enduring any side effects and many patients do not like the skin irritation of topical treatments nor the possible long-term side effects of oral acne therapy.

Many acne treatments, acne information, or even recommendations are not provided by physicians. So, it is important to understand any new treatment, which includes the light therapy acne mask, and the science behind it.

The benefits of red and blue light therapy, or the combination of the two, have been noted to be effective in acne management but have not been widely adopted due to their cost, inaccessibility (as multiple in-clinic visits are required), and the chronicity of treatment. Synergistic benefits of decreasing *P. acnes* and immunomodulatory anti-inflammatory effects are thought to be effective in decreasing overall inflammatory and non-inflammatory lesions.

The light therapy delivery system as a home device may be easy, relatively cost effective, and safe to use. However, only with more studies, more widespread use, and a longer time frame to gather experience will the true benefits be known. In the short term, however, it will appeal to those patients who want a "safe" novel treatment.

TAKE-HOME MESSAGES

- Multiple clinical trials have demonstrated the efficacy and safety of red-blue LED LLLT in the treatment of acne vulgaris.
- Combination red-blue LED LLLT is destructive to P. acnes and has anti-inflammatory and anti-sebum effects.
- Combination red-near-infrared LED LLLT improved subjective and objective measures of skin rejuvenation in clinical studies, which may be at least partially due to increased levels of collagen in the skin.
- In clinical trials, local adverse events have been rare with LED LLLT and systemic adverse events absent.
- The Neutrogena® Light Therapy Mask is a chemical-free, non-thermal, home-use, LED-based LLLT device.
- The Neutrogena® Light Therapy Mask has been shown to be beneficial and well tolerated in the treatment of mild to moderate acne.

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