Light Emitting Diodes (LEDs) in Dermatology

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Light-emitting diode photobiomodulation is the newest category of nonthermal light therapies to find its way to the dermatologic armamentarium. In this article, we briefly review the literature on the development of this technology, its evolution within aesthetic and medical dermatology, and provide practical and technical considerations for use in various conditions. This article also focuses on the specific cell-signaling pathways involved and how the mechanisms at play can be put to use to treat a variety of cutaneous problems as a stand-alone application and/or complementary treatment modality or as one of the best photodynamic therapy light source.

Semin Cutan Med Surg 27:227-238 © 2008 Elsevier Inc. All rights reserved.

LED photobiomodulation is the newest category of nonthermal light therapies to find its way to the dermatologic armamentarium and will be the focus of this review. Initial work in this area was mainly developed by National Aeronautics and Space Administration (NASA). NASA research came about as a result of the effects noted when light of a specific wavelength was shown to accelerate plant growth. Because of the deficient level of wound healing experienced by astronauts in zero-gravity space conditions and Navy Seals in submarines under high atmospheric pressure, NASA investigated the use of LED therapy in wound healing and obtained positive results. This research has continued and innovative and powerful LEDs are now used for a variety of conditions ranging from cosmetic indications to skin cancer treatment (as a photodynamic therapy light source).

LED Technology

LEDs are complex semiconductors that convert electrical current into incoherent narrow spectrum light. LEDs have been around since the 1960s but have mostly been relegated to showing the time on an alarm clock or the battery level of a video camera. They have not until recently been used as sources of illumination because, for a long time, they could not produce white light—only red, green, and yellow. Nichia Chemical of Japan changed that in 1993 when it started producing blue LEDs which, combined with red and green, produce white light, opening up a whole new field for the technology. The industry has been quick to exploit it. LEDs are based on semiconductor technology, just like computer processors, and are increasing in brightness, energy efficiency, and longevity at a pace reminiscent of the evolution of computer processors. Emitted light are now available at wavelengths ranging from ultraviolet (UV) to visible near infrared (NIR) bandwidth (247 to 1300 nm).
LED arrays are built using diverse methods each hinges on the manner in which the chips themselves are packaged by the LED semiconductor manufacturer. Examples of packaged, lensed LEDs are t-pack LED and surface mount LEDs (Figs 3-5). These packages can be affixed to a heat-sinking substrate by using either a "through hole" mounting or surface mounting. Through hole mounted devices are often referred to as t-pack LEDs. Importantly, it is also possible to procure wafers of bare, unpackaged chips, also called "dice." By using automated pick-and-place equipment, some manufacturers take such individual chips and affix them to printed circuit boards, creating so-called "chip-on-board" LED arrays. LED array is thus assembled on a printed circuit board. The pins or pads or actual surfaces of the LED chips are attached to conductive tracks on the PCB (printed circuit board). Assemblies built from t-pack LEDs are often unsatisfactory in that they do not always provide sufficiently uni-

form lighting, are not well heat-sinked, and they are bulky due to the size (several millimeters) of each t-pack device. Nonetheless, for certain applications, t-packs prove to be the most appropriate, cost-effective solution. However, when t-packs cannot provide the required performance, however, chip-on-board emerges as the answer.

A significant difference between lasers and LEDs is the way the light energy is delivered [optical power output (OPD)]. The peak power output of LEDs is measured in milliwatts, whereas that of lasers is measured in watts. LEDs provide a much gentler delivery of the same wavelengths of light compared to lasers and at a substantially lower energy output. LEDs do not deliver enough power to damage tissues and do not have the same risk of accidental eye damage that lasers do. Visible/NIR-LED light therapy has been deemed a non-significant risk by the Food and Drug Administration and has been approved for use in humans. Other advantages over lasers include the possibility to combine wavelengths with an array of various sizes. LED disperses over a greater surface area than lasers and can be used where large areas are targeted, resulting in a faster treatment time.

**Mechanism of Action**

In the same way that plants use chlorophyll to convert sunlight into plant tissue, LEDs can trigger natural intracellular photo-biochemical reactions. To have any effect on a living biological system, LED-emitted photons must be absorbed by a molecular

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**Figure 1** Niels Ryberg Finsen (1860-1904). Courtesy of the Clandening History of Medicine Library, University of Kansas Medical Center.

**Figure 2** Finsen's phototherapy. Due to expense of carbon arc lighting, single lamp directed light through four water-cooled focusing lenses, allowing several patients to be treated simultaneously. Each patient had nurse attendant to focus light to single small region for up to 1 hour. (Reprinted from Bie V. Finsen's phototherapy. BMJ 1899;2:825)

**Figure 3** LED technology. The red arrows indicate the flow of heat. Courtesy of Stocker Yale, Inc.

**Figure 4** A t-pack LED.
spontaneous, between the mitochondria and genes in the nucleus for which we are just beginning to explore the mechanism at play. If we can better modulate this signaling, we might be able to influence the life or death of cells in many pathologies as it is more and more demonstrated in its anti-aging effects on collagen metabolism.

A recent discovery has revealed that NO eliminates the LLLT-induced increase in the number of cells attached to the glass matrix, supposedly by way of binding NO to cytochrome c oxidase. Cells use NO to regulate respiratory chain processes, resulting in a change in cell metabolism. In turn, in LED-exposed cells like fibroblasts increased ATP production, modulation of reactive oxygen species (such as singlet oxygen species), reduction and prevention of apoptosis, stimulation of angiogenesis, increase of blood flow, and induction of transcription factors are observed. These signal transduction pathways lead to increased cell proliferation and migration (particularly by fibroblasts), modulation in levels of cytokines (eg. interleukins, tumor necrosis factor-α), growth factors and inflammatory mediators, and increases in anti-apoptotic proteins.

The photodissociation theory incriminating NO as one of the main players suggests that during an inflammatory process, for example, cytochrome c oxidase is clogged up by NO. LED therapy would photodissociate NO or dump it to the extracellular matrix for oxygen to bind back again to cytochrome c oxidase and resume respiratory chain activity. Understanding the mechanisms of cutaneous LED-induced specific cell-signaling pathway modulation will assist in the future design of novel devices with tailored parameters even for the treatment of degenerative pathologies of the skin.

**Optimal LED Parameters**

In LED, the question is no longer whether it has biological effects but rather what the optimal light parameters are for different uses. Biological effects depend on the parameters of the irradiation such as wavelength, dose (fluence), intensity (power density or irradiance), irradiation time (treatment time), continuous wave or pulsed mode, and for the latter, pulsing patterns. In addition, clinically, such factors as the frequency, intervals between treatments and total number of treatments are to be considered. The prerequisites for effective LED clinical response are discussed hereafter.

**Well-Absorbed Deeply Penetrating Wavelength**

Light is measured in wavelengths and is expressed in units of nanometers (nm). Different wavelengths have different chromophores and can have various effects on tissue (Fig. 6). Wavelengths are often referred to using their associated color and include blue (400-470 nm), green (470-550 nm), yellow (550-600 nm), and NIR (700-2000 nm). In general, the longer the wavelength, the deeper the penetration into tissues. Depending on the type of tissue, the penetration depth is less than 1 mm at 400 nm, 0.5 to 2 mm at 514 nm, 1 to 6 mm at 630 nm, and maximal at 700 to 900 nm.
The various cell and tissue types in the body have their own unique light absorption characteristics, each absorbing light at specific wavelengths. For best effects, the wavelength used should allow for optimal penetration of light into the targeted cells or tissue. Red light can be used successfully for deeper localized target (eg, sebaceous glands), and blue light may be useful for the treatment of skin conditions located within the epidermis in photodynamic therapy (PDT) (eg, actinic keratoses). To reach as many fibroblasts as possible, which is often the aim of LED therapy, a deeply penetrating wavelength is desirable. At 660 nm, for instance, light can achieve such a goal reaching a depth of 2.3 mm in the dermis, therefore covering fibroblasts up to the reticular dermis. The wavelength used should also be within the absorption spectrum of the chromophore or photosensitizer molecule and will often determine for which applications LEDs will be used. Because cytochrome c oxidase is the most likely chromophore in LLLT, 2 absorption peaks are considered in the red (~660 nm) and NIR (~850 nm) spectra.

Two major wavelength boundaries exist for LED applications: at wavelengths <600 nm, blood hemoglobin (Hb)
is a major obstacle to photon absorption because blood vessels are not compressed during treatment. Furthermore, at wavelengths \( >1000 \text{ nm} \), water is also absorbing many photons, reducing their availability for specific chromophores located, for instance, in dermal fibroblasts. Between these 2 boundaries, there is a valley of LED possible applications (see Fig. 7).

**Fluence and Irradiance**

The Arndt-Schulz law states that there is only a narrow window of opportunity where you can actually activate a cellular response using precise sets of parameters, i.e., the fluence or dose (see Fig. 8). The challenge remains to find the appropriate combinations of LED treatment time and irradiance to achieve optimal target tissue effects. Fluence or dose is indicated in joules per cm\(^2\) (J/cm\(^2\)). The law of reciprocity states that the dose is equal to the intensity \( \times \) time. Therefore, the same exposure should result from reducing duration and increasing light intensity, and vice versa. Reciprocity is assumed and routinely used in LED and LLLT experiments. However, the scientific evidence supporting reciprocity in LED therapy is unclear.\(^{11}\)

Dose reciprocity effects were examined in a wound healing model and showed that varying irradiance and exposure time to achieve a constant specified energy density affects LED therapy outcomes.\(^{12}\) In practice, if light intensity (irradiance) is lower than the physiological threshold value for a given target, it does not produce photostimulatory effects even when irradiation time is extended. Moreover, photoinhibitory effects may occur at higher fluences.

In Fig. 9, different light delivery patterns are shown. Interestingly, they are all of the same fluence but over time, the energy of photons does not reach the biological targets in the same way. This may alter the LED biological response significantly. The importance of pulsing will be discussed in the next section.

Certainly a minimal exposure time per treatment is necessary—in the order of several minutes rather than only a few seconds—to allow activation of the cell machinery; otherwise, tissue response is evanescent and no clinical outcome is expected. The ideal treatment time has to be tailored according to the skin condition or degree of inflammation present at the time of treatment.

**Pulsing and Continuous Modes**

Both pulsed wave and continuous wave (CW) modes are available in LED devices, which add to the medical applicability. The influence of CW versus pulsing mode, as well as precise pulsing parameters (eg, duration, interval, pulse per train, pulse train interval), on cellular response has not been fully studied. To date, comparative studies have shown conflicting results.\(^{13}\) In our own experience, sequentially pulsed optical energy (proprietary pulsing mode with repeated sequences of short pulse trains followed by longer intervals) has been shown to stimulate more collagen production than CW mode.\(^{11}\)

Under certain conditions, ultra-short pulses can travel deeper into tissues than CW radiation.\(^{15,6}\) This is because the first part of a powerful pulse may contain enough photons to take all chromophores moecules in the upper tissue layer to excited states, thus literally opening a road for itself into tissue. Moreover, too long a pulse may produce cellular exhaustion whereas too short a pulse may deliver insufficient energy for a biologic effect to occur. Targeted molecules and cells may-on a smaller scale than selective photothermolysis-have their own thermal relaxation times.\(^{14}\)

The NO photodissociation theory could also be part of the answer, especially the need for pulsing characteristics during LED therapy. Interestingly, fireflies use such pulsing phenomenon. There, oxygen reacts with the luciferyl intermediate to produce a flash of light. The glory is that the flash switches itself off. Light dissociates NO from cytochrome oxidase, allowing oxygen to bind again. Then, the mitochondria consume oxygen once more, allowing the luciferyl intermediate to build up until another wave of NO arrives.\(^{17}\)

**Precise Positioning of Treatment Head**

Very precise positioning or working distance is mandatory to ensure optimal beam delivery intensity covering the treatment area so as to achieve maximum physiological effects. Accurate positioning ensures that the proper amount of photons is delivered to the treated skin to avoid hot or cold spots in the treatment field. This is especially important in photobiology as a required amount of energy must be delivered to the target to trigger the expected cell response. If insufficient photons reach the target, no cell response will result. Some LED devices even provide optical positioning systems to allow reproducible treatment distance within precise limits (±3 mm).

**Timing of Treatments’ Outcomes**

There are some indications that cellular responses after light irradiation are time dependent. A recent study suggests that responses such as ATP viability can be observed directly (1 hour) after the irradiation, whereas other responses such as cell proliferation require at least 24 hours before the true
effect can be observed.\textsuperscript{19} It is thus important to establish time-dependent responses to adequately assess photomodulatory effects. Fibroblasts in culture show physiological cyclical patterns of procollagen type I up-regulation and metalloproteinase-1 (MMP-1) down-regulation that can be emphasized by LED treatments every 48 hours.\textsuperscript{10}

**State of Cells and Tissues**

The magnitude of the biostimulation effect depends on the physiological condition of the cells and tissues at the moment of irradiation.\textsuperscript{10} Compromised cells and tissues respond more readily than healthy cells or tissues to energy transfers that occur between LED-emitted photons and the receptive chromophores. For instance, light would only stimulate cell proliferation if the cells are growing poorly at the time of the irradiation. Cell conditions are to be considered because light exposures would restore and stimulate procollagen production, energizing the cell to its own maximal biological potential. This may explain the variability in results in different studies.

**Effects of LED**

LED therapy is known for its healing and antiinflammatory properties and is mostly used in clinical practice as a supplement to other treatments such as nonablative thermal technologies. Different LED applications can now be subdivided according to the wavelength or combination of wavelengths used (see Fig. 10). LED therapy can be used as a standalone procedure for many indications, as described herein. A summary of recommended LED parameters for various clinical applications are presented in Table 1.

When reviewing the literature, one needs to keep in mind that results from different studies may be difficult to compare because the potential effects of variation of treatment parameters (eg, wavelength, fluence, power density, pulse/continuous mode and treatment timing) may vary from one study to the next. Moreover, there is the possibility that the photobiomodulatory effects are dissimilar across different cell lines, species and patient types. We will now discuss current LED applications.

**Wound Healing**

Early work involving LED mainly focused on the wound healing properties on skin lesions. Visible/NIR-LED light treatments at various wavelengths have been shown to increase significantly cell growth in a diversity of cell lines, including murine fibroblasts, rat osteoblasts, rat skeletal muscle cells, and normal human epithelial cells.\textsuperscript{21} Decrease in wound size and acceleration of wound closure also has been demonstrated in various in vivo models, including toads, mice, rats, guinea pigs, and swine.\textsuperscript{22,23} Accelerated healing and greater amounts of epithelialization for wound closure of skin grafts have been demonstrated in human studies.\textsuperscript{24,25} The literature also shows that LED therapy is known to positively support and speed up healing of chronic leg ulcers: diabetic, venous, arterial, pressure.\textsuperscript{26}

According to our experience, LED treatments are also very useful after CO\textsubscript{2} ablative resurfacing in reducing the signs of the acute healing phase resulting in less swelling, oozing, crusting, pain, and prolonged erythema thereby accelerating wound healing (see Fig. 11). It is important to keep in mind that to optimize healing of necrotic wounded skin, it may be useful to work closer to the near infrared spectrum as an increase in metalloproteinases (ie, MMP-1, debridement-like effect) production accelerates wound remodeling.

**Inflammation**

Free radicals are known to cause subclinical inflammation. Inflammation can happen in a number of ways. It can be the result of the oxidation of enzymes produced by the body’s defense mechanism in response to exposure to trauma such as sunlight (photodamage) or chemicals. LED therapy brings a new treatment alternative for such lesions possibly by countering inflammatory mediators.

A series of recent studies have demonstrated the antiinflammatory potential of LED. A study conducted in arachidonic acid-treated human gingival fibroblast suggests that 635 nm irradiation inhibits PGE\textsubscript{2} synthase like COX inhibitor and thus may be a useful antiinflammatory tool.\textsuperscript{27} LED photobiomodulation treatment has also been shown to accelerate the resolution of erythema and reduce posttreatment discomfort in pulsed dye laser (IPL)-treated patients with photodamage and to prevent radiation-induced dermatitis in breast cancer patients.\textsuperscript{28,29} Patients with diffuse type rosacea (unstable) (see Fig. 12), keratosis pilaris rubra, as well as postintervention erythema (eg, IPL, CO\textsubscript{2}) (Fig. 11) can benefit from a quicker recovery with complementary LED therapy. (See also section on wound healing).

Because LED is known to reduce MMPs, it might be useful in conditions in which MMPs are implicated. One such case is lupus erythematosus (LE). LE is a heterogeneous autoimmune disease associated with aberrant immune responses including production of autoantibodies and immune complexes and specific MMPs have been implicated in its etiol-
Table 1 LED Parameters for Various Clinical Applications Used in our Practice

<table>
<thead>
<tr>
<th>Applications</th>
<th>Wavelength (nm)</th>
<th>No. of Treatments</th>
<th>Irradiance (mW/cm²)</th>
<th>Fluence (J/cm²)</th>
<th>Treatment Time (min:sec)</th>
<th>Interval Treatment Time (hours)</th>
<th>Mode (Pulsed/CW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound healing</td>
<td>660 &amp; 850</td>
<td>3-12</td>
<td>50 (minimal)</td>
<td>4</td>
<td>2:40</td>
<td>24-72</td>
<td>Sequential pulsing**</td>
</tr>
<tr>
<td>Inflammation/erythema/edema (diffuse type rosacea, post-procedure erythema) (eg, IPL, CO₂)</td>
<td>630-660</td>
<td>3-12</td>
<td>50 (minimal)</td>
<td>4</td>
<td>2:40</td>
<td>48-72</td>
<td>Sequential pulsing</td>
</tr>
<tr>
<td>PDT</td>
<td>405-630</td>
<td>3+</td>
<td>50-100</td>
<td>&gt;50</td>
<td>13-45</td>
<td>3 weeks</td>
<td>CW or pulsed</td>
</tr>
<tr>
<td>Photorejuvenation</td>
<td>630-660</td>
<td>12</td>
<td>50-100</td>
<td>4</td>
<td>2:40-16</td>
<td>48-72</td>
<td>Sequential pulsing</td>
</tr>
<tr>
<td>Sunburn prevention††</td>
<td>660-970</td>
<td>ad 7</td>
<td>50</td>
<td>4</td>
<td>2:40-15</td>
<td>24-48</td>
<td>Sequential pulsing or CW</td>
</tr>
<tr>
<td>PIH prevention††</td>
<td>870-970</td>
<td>ad 8</td>
<td>50-80</td>
<td>45-96</td>
<td>15-20</td>
<td>24-48</td>
<td>Sequential pulsing or CW</td>
</tr>
<tr>
<td>Scar prevention*</td>
<td>805-970</td>
<td>Multiple</td>
<td>50-80</td>
<td>45-72</td>
<td>15</td>
<td>24</td>
<td>CW</td>
</tr>
<tr>
<td>Photopreparation</td>
<td>870-970</td>
<td>3 (before every PDT Treatment§)</td>
<td>&gt;80</td>
<td>72-100</td>
<td>15</td>
<td>Pre-PDT (q 3 weeks)</td>
<td>CW</td>
</tr>
<tr>
<td>Photoregulation</td>
<td>660-850</td>
<td>Long-term</td>
<td>8-50</td>
<td>4-7.5</td>
<td>5-16</td>
<td>24-48</td>
<td>Sequential pulsing</td>
</tr>
<tr>
<td>UV-free phototherapy</td>
<td>405-850</td>
<td>Depends on inflammatory disease</td>
<td>30-50</td>
<td>27-135</td>
<td>15-45</td>
<td>48</td>
<td>Sequential pulsing or CW</td>
</tr>
</tbody>
</table>

*Sunburn, PIH, and scar-prevention methods = Photoprophylaxis.
**Sequential pulsing mode with proprietary pulsed characteristics (50% duty cycle).
†LED treatments should be preferably performed in the week before UV insult or skin trauma to better prevent sunburn or PIH, respectively.
ogy. MMP inhibition through LED treatments may reduce lupus-induced damage in inflamed tissues.

Photorejuvenation

In aged photo-damaged human skin, collagen synthesis is reduced with a concomitant elevation of matrix MMP expression.36 Hence, a possible strategy for treating and preventing the clinical manifestations of skin aging is the restoration of the collagen deficiency by the induction of new collagen synthesis and reduction of MMP.

Using a variety of LED light sources in the visible to NIR regions of the spectrum, in vitro studies have revealed that LED can trigger skin collagen synthesis with concurrent reduction in MMP. A significant increase in collagen production after LED treatment has been shown in various experiments, including fibroblasts cultures, third-degree burn animal models, and human blister fluids, and skin biopsies.11,31-34 In clinical studies, the increase in collagen production with concurrent MMP-1 reduction has been seen in association with improved appearance of photodamaged skin. Table 2 shows currently available LED sources for skin rejuvenation.

Photoprophylaxis or Photoprevention

Photoprophylaxis is a novel approach that we were the first to introduce—to the best of our knowledge—in the use of LEDs for the prevention of cutaneous manifestations after a trauma. If LED therapy is administered several times prior to a UV insult, a mechanical trauma such as a CO2 laser treatment or a surgery, one may prevent undesirable consequences such as sunburn, postinflammatory hyperpigmentation (PIH), or hypertrophic scarring, respectively. These LED-preventative modalities will be discussed hereafter.

Sunburn Prevention

Beyond the repair of previous UV insults to the skin, visible to NIR light might offer protection against upcoming photodamage. It has been suggested that protective mechanisms against skin UV-induced damage may be activated by IR exposure in a number of in vitro studies using primary-culture human fibroblasts.35,36 Therefore, LED treatment could stimulate skin resistance to UV damage.

Results from our own laboratory testing suggest that LED 660 nm treatment before UV exposure provides significant protection against UV-B induced erythema.37 The induction of cellular resistance to UV insults may possibly be explained by the induction of a state a natural resistance to the skin (possibly via the p53 cell signaling pathways) without the drawbacks and limitations of traditional sunscreens.38 These results represent an encouraging step toward expanding the potential applications of LED therapy and could be useful in the treatment of patients with anomalous reactions to sunlight such as polymorphous light eruption or lupus.

Postinflammatory Hyperpigmentation Prevention

PIH is a frequently encountered problem and represents the sequelae of various cutaneous disorders as well as therapeutic interventions especially on Asian and dark complexion patients. A preventative and complementary approach to thermal laser induced PIH using LED therapy is possible. According to unpublished work performed in our laboratory, the use of LED 660 nm therapy can prevent or treat PIH. On the basis of photographic analysis and melanin content measurements, most patients can achieve substantial reduction or absence of PIH lesions in the LED-treated areas (versus con-

<table>
<thead>
<tr>
<th>Wavelength (nm)</th>
<th>System Name</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>590</td>
<td>GentleWaves</td>
<td>Light Bioscience</td>
</tr>
<tr>
<td>630</td>
<td>Omnilux Revive</td>
<td>Phototherapeutics</td>
</tr>
<tr>
<td>660</td>
<td>LumiPhase-R</td>
<td>OpusMed</td>
</tr>
</tbody>
</table>
 Scar Prevention

Hypertrophic scars and keloids can form after surgery, trauma, or acne and are characterized by fibroblastic proliferation and excess collagen deposition. An imbalance between rates of collagen biosynthesis and degradation super-

imposed on the individual's genetic predisposition have been implicated in the pathogenesis of these scar types. It has recently been proposed that interleukin (IL)-6 signaling pathways play a central role in this process and thus, that IL-6 pathway inhibition could be a promising therapeutic target for scar prevention. As LED therapy has been shown to decrease IL-6 mRNA levels, it may potentially be preventing aberrant healing. A recent study conducted by our research group revealed significant improvements on the treated versus the control side in appearance and outline of scars (Fig. 14).

Photopreparation

Photopreparation is another new concept that we have been working on that characterizes a way to enhance the delivery, through a substantially unform penetration, of a given compound in the skin resulting in more active conversion of such topical agents (ie, ALA to PpIX) in targeted tissues. Radiant IR photopreparation increases skin temperature, which may lead to an increase in pore size (diameter) for enhanced penetration of a given topical in the pilosebaceous unit.

The efficacy of aminolevulinic acid photodynamic therapy (ALA-PDT), for instance, is dependent on ALA absorption and remains one of the main challenges of PDT. We have recently showed that increasing the skin temperature for 15 minutes with radiant IR (CW LEDs emitting @ λ 970 nm, irradiance 50 mW/cm², total fluence 45 J/cm²) before ALA-PDT in the treatment of a cystic acne patient significantly
conditions bear similarities with some of those associated with blue LEDs and IR phototherapy with LEDs, including singlet oxygen production and modulation of interleukins. This provides a unique opportunity to explore the use of LED in skin conditions where UV therapy is used without the downside of inherent side effects. This approach has been termed UV-free therapy.

For instance, the mode of action of UVA phototherapy for atopic dermatitis was found to involve the induction of apoptosis in skin-infiltrating T-helper cells through a mechanism that requires the generation of singlet oxygen. A recent study demonstrated that visible light (400-500 nm) can be successfully used for the treatment of patients with atopic eczema. In our hands, even resistant KPR (keratosis pilaris rubra) may respond to LED therapy in the visible-NIR spectrum (Fig. 16). These promising results introduce a wide range of new potential application for LED.

Photodynamic Therapy (PDT)

PDT can best be defined as the use of light to activate a photosensitive medication that is applied to the skin prior to treatment. The PDT light source has a direct influence on treatment efficacy. Nowadays, the importance of treatment parameters of this light source is unfortunately greatly underestimated. High-end LED devices meet this challenge and can be used as the light source of choice for PDT (Table 3). Thus, PDT can serve as a treatment that complements other skin rejuvenation therapies or topical agents used to enhance collagen production. The use of a dual wavelength (red and blue) LED light source enhances PDT results for acne and other sebaceous disorders. Red wavelength (630 nm) can reach the sebaceous glands and blue (405 nm) light photobleaches any residual protoporphyrin IX (PpIX) in the epidermis, thereby reducing posttreatment photosensitivity (Fig. 17). The way light photons are delivered seems to hold the answer for more effective PDT. Hence, dose rate is becoming one of the important criteria as opposed to total dose (fluence). Also, it is now suggested to avoid peak power effects on the photosensitizer—so-called thermal effects—that are usually encountered with light sources (thermal technologies) such as IPLs and lasers (ie, PDL). PDT frequent indications, both cosmetic and medical, are described in Table 4. LED technology clearly brings several advantages to

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**Table 3: Fluorescent and High end LED Systems for PDT**

<table>
<thead>
<tr>
<th>Device Parameters</th>
<th>Blu-U</th>
<th>LumiPhase-R/B</th>
<th>Omniflux Revive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wavelength (nm)</td>
<td>Fluorescent tubes</td>
<td>LED</td>
<td>LED</td>
</tr>
<tr>
<td></td>
<td>417</td>
<td>405/630 (R/B)</td>
<td>633</td>
</tr>
<tr>
<td>Power density (mW/cm²)</td>
<td>10</td>
<td>150/60 (R/B)</td>
<td>105</td>
</tr>
<tr>
<td>Working distance gauge</td>
<td>No</td>
<td>Optical Positioning</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>System on both R &amp; R/B Models</td>
<td></td>
</tr>
<tr>
<td>Treatment time (sec)</td>
<td>1000</td>
<td>160-1000</td>
<td>1200-1800</td>
</tr>
<tr>
<td>PDT light source</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
envelope PDT clinical efficacy: progressive photoactivation of photosensitizers, large uniform beam profile, reduced procedural pain, and multiple wavelengths available.

**Other Potential Applications**

Rapidly emerging areas in light-based therapy include the treatment of cellulite and hair loss. Both conditions are very prevalent for which acceptable treatment options are lacking. Genetic, hormonal, and vascular factors have been implicated etiologies. Cellulite manifests as herniations of the subcutaneous fat into the dermis. It has been suggested that light therapy can improve the appearance of cellulite through the contracture and increase in deep dermal collagen, resulting in skin tightening and hypothetically providing a stronger dermo-subcuticular junction barrier to herniation. A recent study demonstrated that cellulite responded positively to an anticellulite gel combined with red/NIR LED light exposure. Light-based treatment (laser and LED) has also been shown to promote hair regrowth and increased hair tensile strength. These effects are thought to be due to the dilation of blood vessels and increase in blood supply to hair follicles.

**Safety**

LED is safe, nonthermal, nontoxic and noninvasive, and to date, no side effects have been reported in published literature. Caution must be emphasized especially for epileptic and photoophbic patients especially if LEDs are pulsed.

**Conclusion**

We are now part of an exciting era in which complex subcellular reactions can actually be influenced favorably with the help of sophisticated configured LED ballistic photons to obtain excellent outcomes in a variety of skin conditions. Safer than sunlight, this new low level light therapy allows for the treatment of patients without pain, downtime or side effects. On the basis of sound photobiology principles, scientific and clinical studies conducted so far have shown promising results. The future seems limitless for LED therapy with innovative methods such as photophyllaxis, photo-reparation, and home use photoregulation although many challenges lie ahead. Future research should focus on investigating specific cell-signaling pathways involved to better understand the mechanisms at play, search for cellular activation threshold of targeted chromophores, as well as study its effectiveness in treating a variety of cutaneous problems as a stand alone application and/or complementary treatment modality or as one of the best PDT light source.

**References**
