ISSN: 2577 - 8005
Research Article
Medical & Clinical Research

Photodynamic Therapy (PDT): Mechanisms, Applications, Benefits, and Limitations

Bahman Zohuri*

Adjunct Professor, Golden Gate University, Ageno School of Business, San Francisco, California, USA

*Corresponding Author
Dr. Bahman Zohuri, Adjunct Professor, Golden Gate University, Ageno School of Business, San Francisco, California, USA

Submitted: 16 Nov 2024; **Accepted**: 21 Nov 2024; **Published**: 02 Dec 2024

Citation: Zohuri, B. (2024). Photodynamic Therapy (PDT): Mechanisms, Applications, Benefits, and Limitations. *Med Clin Res, 9*(12), 01-05.

Abstract
Photodynamic Therapy (PDT) is an innovative medical treatment that harnesses the power of light to selectively target and destroy diseased cells, particularly in cancer and dermatology. This article reviews the mechanisms behind PDT, highlights its pros and cons, and discusses the potential positive and negative side effects that patients may experience. With growing applications and a unique mode of action, PDT continues to expand its role in therapeutic treatments, although certain limitations require further research.

Keywords: Photodynamic Therapy (PDT), Sun-damaged skin, Brown spots treatment, Photosensitizer drugs, Reactive oxygen species (ROS), Light-activated therapy, Skin cancer treatment, Non-invasive dermatology, Skin rejuvenation, Scalp sun exposure

1. Introduction
From the discovery of fire to the creation of the electric bulb, light has been essential to human progress (Figure 1). But in the modern day, light serves as both a source of lighting and a powerful instrument for precision-driven applications in business, defense, and health. Laser technology, a development that has allowed us to harness the power of light with previously unheard-of control and intensity, is at the center of this revolution [1].

The light in form of red or blue laser is also basics for Photodynamic Therapy (PDT) that drives this application of laser for purpose skin cancer treatment in a two steps procedure that combines a photosensitizing agent, as a usage form of Levulan, which is a 5-aminolvulinic acid or ALA and blue light at ~ nm to activate it as illustrate in Figure 2 [2-3].

(Source: www.wikipedia.org)
Figure 1: Flame and Light Power

(Source: www.wikipedia.org)
Figure 2: 7LED Light Therapy for Acne Illustration

Note That: Acne is a condition resulting from clogged or plugged hair follicles present under the skin. It presents small to large, red bumps on the skin which may be painful and pus-filled in some cases. Blue light PDT is currently FDA-approved for pre-cancerous lesions called actinic keratoses and early cancerous lesions called squamous cell carcinomas in situ. It is very effect for treating actinic keratoses, with clearance rate of greater than 70%

Photodynamic Therapy (PDT) is an innovative and minimally invasive medical treatment that harnesses the power of light to selectively target and destroy diseased cells. Originally developed to treat cancer, PDT has since broadened its scope to include applications in dermatology, ophthalmology, and infectious disease management, making it a versatile therapeutic approach. The therapy combines three essential components: a photosensitizing drug, a specific wavelength of light, and oxygen molecules within the targeted cells. When these elements interact, they produce Reactive Oxygen Species (ROS) that effectively kill or damage abnormal cells, leaving surrounding healthy tissues largely unaffected.

The unique mechanism of PDT offers several advantages over traditional treatments like surgery, radiation, and chemotherapy. It targets diseased cells with precision, minimizing harm to surrounding healthy tissues and reducing side effects. This characteristic has made PDT especially effective in treating skin conditions such as actinic keratosis, superficial basal cell carcinoma, and sun-damaged skin, which often appear on the face and scalp in older individuals. Beyond oncology, PDT is also gaining traction for its anti-inflammatory and antimicrobial properties, potentially expanding its applications in areas such as wound healing and chronic infections. Refer to Figure-3 as an illustration of this method.

(Source: www.wikipedia.org)
Figure 3: LED Light Therapy Masks

The PDT process begins with the administration of a photosensitizing drug, which is either applied topically or delivered systemically, depending on the condition being treated. After allowing time for the drug to accumulate selectively within diseased cells, the targeted area is exposed to a light source, typically a laser or Light Emission Diode (LED), calibrated to a specific wavelength that activates the photosensitizer. This light activation triggers a chemical reaction that generates ROS within the cells, leading to cellular damage and death. Importantly, PDT's effectiveness relies on localized light exposure, which ensures that only the areas treated with light will be affected, further enhancing the therapy's precision and safety profile [4-6].

However, despite its benefits, PDT is not without limitations. The therapy is most effective for superficial or surface-level lesions, as the penetration depth of light is limited, making it less suitable for deeper tumors or thick tissue masses. Additionally, patients must follow strict post-treatment guidelines to avoid exposure to sunlight, as photosensitivity is a common side effect that can lead to severe skin reactions if not managed properly.

As research into PDT continues to evolve, scientists and clinicians are exploring new ways to enhance the efficacy of this therapy, including the development of next-generation photosensitizers and light delivery systems. With its targeted, non-invasive approach, PDT holds promise not only as a treatment for cancer and skin conditions but also as a potentially valuable tool in the fields of infection control, autoimmune disease management, and even cosmetic dermatology. This review will examine the benefits, limitations, and potential side effects of PDT, providing a comprehensive understanding of its applications and role in modern medicine.

Overall, the standard PDT process involves three main steps:

- **Photosensitizer Administration:** A photosensitizing drug is introduced into the body, either topically or through intravenous injection.
- **Accumulation and Localization:** The drug accumulates in diseased cells over time due to its biochemical affinity, remaining inactive until exposed to a specific light wavelength.
- **Light Activation:** Upon light activation, the photosensitizer interacts with oxygen to produce ROS, which leads to cell death. This targeted approach makes PDT highly effective for conditions where precision is key.

In summary, Photodynamic Therapy (PDT) is a minimally invasive treatment approach that combines a photosensitizing drug, a specific wavelength of light, and molecular oxygen to produce reactive oxygen species (ROS) that selectively destroy abnormal or diseased cells. Initially developed as a tool in cancer treatment, PDT has expanded into dermatology, ophthalmology, and infectious disease therapy. Its potential lies in its ability to target cells selectively, leading to fewer side effects and reduced damage to surrounding healthy tissue.

2. Mechanism of Action

The mechanism of action in Photodynamic Therapy (PDT) involves the activation of a photosensitizer by a specific wavelength of light, producing reactive oxygen species (ROS) that selectively destroy targeted diseased cells.

Each of the above actions is described below:

2.1 Photosensitizers

Photosensitizers are unique compounds that absorb light and transfer energy to oxygen molecules, creating ROS capable of damaging cellular components. Various photosensitizers are used based on their molecular structure, which determines their ideal absorption wavelength and suitability for different treatment depths. Examples include porphyrins, chlorins, and phthalocyanines.

2.2 Light Sources

The light source used in PDT plays a critical role in treatment success. Lasers and LED lights, each emitting specific wavelengths, are carefully chosen to match the absorption spectrum of the photosensitizer. While shorter wavelengths target superficial layers, longer wavelengths penetrate deeper, allowing flexibility in treating different types of tissue.

Together, the photosensitizer and light source create a highly localized reaction. This reduces collateral damage to healthy tissues, making PDT especially useful in treating skin cancers and other superficial malignancies.

3. Advantages of PDT

PDT presents several benefits that make it an attractive alternative to traditional therapies such as surgery, radiation, and chemotherapy.

3.1 Selectivity

One of PDT's primary advantages is its selectivity. Unlike other treatments that may impact surrounding tissues, PDT targets only the diseased cells that have absorbed the photosensitizer. This precision results in fewer adverse effects on healthy cells, offering a less invasive option for sensitive areas.

3.2 Minimally Invasive

As a non-surgical method, PDT is minimally invasive, requiring only localized light exposure. Patients undergoing PDT typically experience shorter recovery times and reduced scarring compared to surgical options, as well as fewer systemic side effects associated with chemotherapy.

3.3 Repeatable Treatment

Since PDT does not induce cumulative toxicity, it can be used multiple times, which is especially valuable in conditions like skin cancer, where new lesions may form over time. PDT's repeatability makes it a versatile tool in managing chronic conditions with recurrent cell proliferation.

3.4 Cost-Effectiveness

Compared to invasive surgical procedures, PDT generally requires fewer resources, shorter hospital stays, and lower recovery costs. For healthcare systems, PDT represents an economically viable alternative that can provide high treatment quality at a lower overall cost.

In summary, PDT offers targeted, minimally invasive treatment with reduced side effects, faster recovery, and repeatability, making it ideal for superficial lesions and sensitive areas.

4. Disadvantages of PDT

Despite its benefits, PDT has several limitations that restrict its broader application.

4.1 Limited Penetration

PDT is most effective for superficial lesions due to the restricted penetration depth of light. This makes it ideal for treating skin-related conditions and surface-level tumors but less effective for deeply embedded malignancies.

4.2 Photosensitivity

Patients who undergo PDT experience heightened sensitivity to sunlight and bright indoor lighting for several days to weeks after treatment. This photosensitivity requires patients to avoid sunlight rigorously, which can be restrictive and inconvenient.

4.3 Variable Efficacy

PDT efficacy depends on numerous factors, including the type and stage of the disease, photosensitizer used, and light exposure method. This variability means that PDT may not always provide consistent results, particularly in complex cases such as advanced-stage cancers.

4.4 Limited Research in Some Applications

Although extensively studied in oncology and dermatology, PDT's potential for non-cancerous conditions remains underexplored. Further research is needed to standardize PDT protocols and evaluate its effectiveness in conditions like infections and autoimmune disorders.

In summary, PDT is limited by light penetration depth, requires strict post-treatment light avoidance, and can cause temporary skin sensitivity and discomfort.

4.5 Positive Side Effects of PDT

PDT's positive side effects include minimal scarring, potential immune system activation, and anti-inflammatory benefits, enhancing overall therapeutic outcomes.

The high-level of this aspect are listed below as:

4.5.1 Minimal Scarring: Compared to surgical methods, PDT has a lower likelihood of scarring, particularly valuable for cosmetic-sensitive areas like the face and neck. For skin conditions, PDT offers a treatment option that heals naturally without significant visible traces.

4.5.2 Immunologic Boost: In some cases, PDT appears to stimulate the immune system, enhancing its ability to attack malignant cells. This immune boost has the potential to aid in preventing recurrence and could be leveraged further in treatments where immune response is critical.

4.5.3 Reduced Inflammation: PDT has shown anti-inflammatory effects, particularly beneficial in dermatological applications. Patients with inflammatory skin conditions may find added relief through PDT's combined therapeutic effects.

PDT's positive side effects include improved cosmetic outcomes, immune response stimulation, and reduced inflammation in treated areas.

4.6 Negative Side of PDT

PDT's negative side effects include temporary skin reactions, pain, phototoxicity, and functional discomfort in sensitive treatment areas.

4.6.1 Skin Reactions: Skin reactions are common post-treatment and may include redness, swelling, and itching. These effects are usually temporary but can cause discomfort and require management with topical treatments or cold compresses.

4.6.2 Pain During and After Treatment: Some patients experience pain during and immediately after PDT, particularly in sensitive treatment areas. This pain may be managed with local anesthesia or mild analgesics; however, it remains a deterrent for some patients.

4.6.3 Phototoxicity: Phototoxicity, or sensitivity to light-induced damage, is a major drawback of PDT. Patients who inadvertently expose treated areas to sunlight may suffer from burns, blisters, or severe inflammation, underscoring the importance of patient education on post-treatment care.

4.6.4 Temporary Loss of Function: For certain PDT applications, especially in head and neck cancers, patients may experience temporary difficulties with functions such as swallowing or breathing. These side effects typically subside but may be distressing in the short term.

PDT's negative side effects are primarily temporary skin sensitivity, pain, and phototoxic reactions requiring careful post-treatment care.

5. Steps of the PDT Procedure

Photodynamic Therapy (PDT) involves three key steps:

1. **Administration of the Photosensitizer:** A photosensitizing

drug is applied topically or injected intravenously, accumulating selectively in diseased cells over hours or days.

2. **Targeted Light Activation:** The treatment area is exposed to a specific wavelength of light, activating the photosensitizer.
3. **Cellular Destruction:** The activated photosensitizer generates Reactive Oxygen Species (ROS), damaging or killing the targeted cells while sparing surrounding healthy tissues.

This precise, stepwise approach ensures effective treatment with minimal collateral damage.

On the day of treatment, you present to the office and Levulan will be applied to the treatment area by one of the operator phototherapy nurses. Then the patient will wait for 1-2 hours to allow the Levulan to absorb before being exposed to the blue light treatment for 16 minutes and 40 seconds or 1000 seconds to be precise. Sunscreen is then applied to patient face, and he/she be sent home.

Note: Levulan (generic name: aminolaevulinic acid hydrochloride) is a photosensitizing agent used in Photodynamic Therapy (PDT). It is most commonly applied topically for the treatment of skin conditions, such as actinic keratosis, a precancerous condition caused by sun damage. Additionally, the Levulan photosensitizing agent will remain active for 48 hours, so you must avoid direct sun exposure for 2 days following treatment. This is an important consideration in scheduling patient treatment.

Few additional notes are added as follows:

✓ **Number of Treatments Needed**

To achieve maximum improvement of pre-cancerous (actinic keratoses) sun damage, skin tone and texture generally a series of 2-3 treatments 6-8 weeks apart is most effective, followed by yearly maintenance.

Some patients with only actinic keratoses respond to a single treatment. Additional treatments can be done at periodic intervals in the future pending patient response and to maintain the rejuvenated appearance of the patient skin.

6. Conclusion

Photodynamic Therapy (PDT) represents a promising treatment approach that combines selectivity, minimal invasiveness, and economic viability. While it shows substantial benefits in treating skin cancers and other superficial lesions, its efficacy for deeper tissue applications remains limited. Prospective applications in infectious and autoimmune conditions continue to expand PDT's therapeutic scope, though more research is needed to standardize protocols and expand its applications.

PDT's drawbacks, including photosensitivity and the need for strict light exposure control post-treatment, highlight areas where innovation and patient education are crucial. In summary, PDT serves as a valuable tool in modern medicine, balancing high efficacy in targeted applications with manageable side effects. With ongoing research and advancements in photosensitizers and light delivery methods, PDT's future remains bright, promising wider application and improved patient outcomes across multiple medical fields.

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