East African Scholars Journal of Medicine and Surgery
Abbreviated Key Title: EAS J Med Surg
ISSN: 2663-1857 (Print) & ISSN: 2663-7332 (Online)
Published By East African Scholars Publisher, Kenya

OPEN ACCESS

Volume-6 | Issue-3 | Mar-2024 | DOI: 10.36349/easjms.2024.v06i03.005

Review Article

Harnessing Photo-Dynamic Treatment for Immune System Diseases: A Promising Therapeutic Approach: A Systematic Review

Imadoudini Hassimi Safia[1,2*], Yao-Yun Tang[1], Wu Ping[1], Jiang Jie[1]

[1]Department of Otorhinolaryngology Head and Neck Surgery, Xiangya Hospital, Central South University, Changsha, China, National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Changsha, Hunan, China
[2]Tongji University School of Medicine, Shanghai, China

Article History
Received: 12.02.2024
Accepted: 18.03.2024
Published: 21.03.2024

Journal homepage:
https://www.easpublisher.com

Quick Response Code

Abstract: Photodynamic treatment (PDT) has emerged as a promising therapeutic approach for immune system diseases due to its ability to selectively target abnormal cells while modulating the immune response. This review explores the mechanisms by which PDT activates the immune system to target diseased cells, including the induction of immunogenic cell death, activation of dendritic cells, release of tumor-associated antigens, modulation of immune checkpoints, and induction of cytokines and chemokines. Additionally, PDT can generate reactive oxygen species, induce apoptosis, and exhibit anti-inflammatory and vascular effects, all of which contribute to its therapeutic potential in immune system diseases [1]. Harnessing PDT for immune system diseases offers a unique opportunity to leverage the immune system's inherent ability to recognize and eliminate abnormal cells, providing a targeted and potentially less toxic treatment option. Further research and clinical studies are warranted to fully elucidate the potential of PDT in the management of immune system diseases and to optimize its clinical application.

Keywords: Photodynamic treatment (PDT), immune system diseases, toxic treatment option, Photo-Dynamic Treatment.

INTRODUCTION

The immune system is crucial in protecting the body from infections and diseases [2, 1]. Immune system malfunctions can lead to various immune system diseases, such as autoimmune disorders, immunodeficiency, and hypersensitivity reactions. Traditional treatment approaches for these diseases often involve immunosuppression drugs, which can have significant side effects and may not always provide long-term relief [3].

In recent years, photodynamic treatment has emerged as a promising therapeutic approach for immune system diseases. Photodynamic treatment, also known as photodynamic therapy (PDT), is a non-invasive treatment that uses light and a photosensitizing agent to kill targeted cells [4]. PDT has gained attention as a potential therapeutic approach for immune system diseases, such as cancer, autoimmune disorders, and infectious diseases. This is due to its ability to selectively target diseased cells and modulate the immune response.

The basic principle involves the administration of a photosensitizing agent, which accumulates in the target tissue, followed by exposure to light of a specific wavelength [5]. This activates the photosensitizer, leading to the production of reactive oxygen species (ROS) and the induction of localised cytotoxic effects [6]. In the context of immune system diseases, PDT has shown promise in modulating immune responses, suppressing inflammatory processes, and targeting abnormal immune cells. This has sparked interest in exploring the potential of photodynamic treatment as a novel approach to managing immune system diseases to achieve better efficacy and fewer side effects compared to traditional therapies.

Background

Harnessing photo-dynamic treatment for immune system diseases is a promising therapeutic approach that involves the use of light-activated compounds to target and destroy abnormal immune cells.[7]This treatment method has shown great potential in the treatment of various immune system diseases, including autoimmune disorders, inflammatory conditions, and certain types of cancers [8].

Photo-dynamic treatment works by first administering a photosensitizing agent to the patient,

***Corresponding Author:** Imadoudini Hassimi Safia
Department of Otorhinolaryngology Head and Neck Surgery, Xiangya Hospital, Central South University, Changsha, China, National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Changsha, Hunan, China

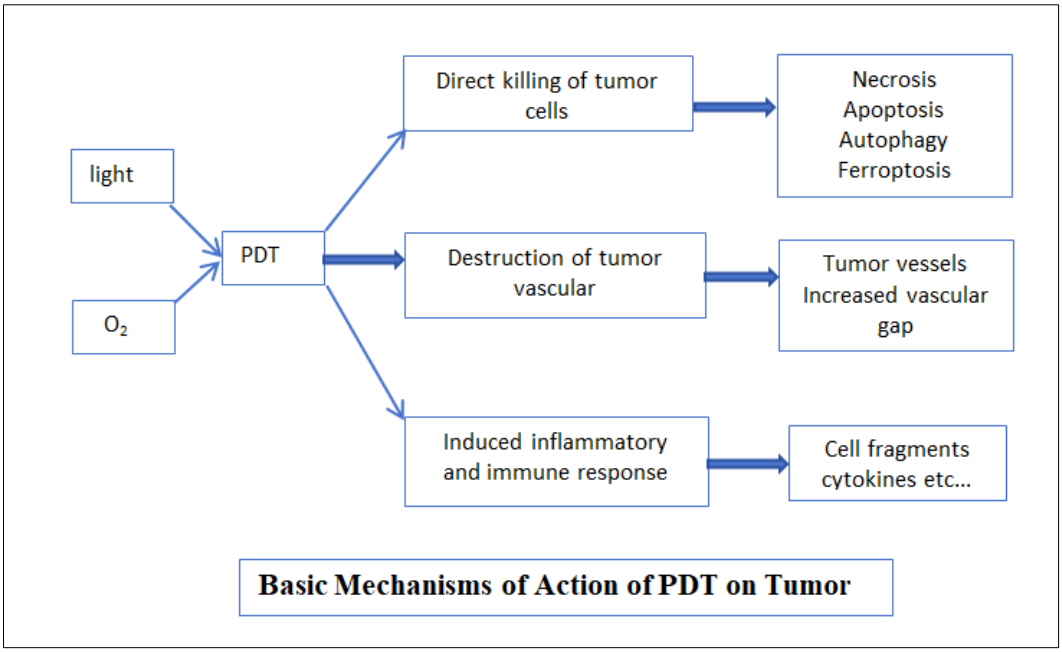
which is then activated by specific wavelengths of light [9]. When exposed to light, the photosensitizing agent produces a form of reactive oxygen species that can selectively target and destroy abnormal immune cells, while leaving healthy cells unharmed [10].

This targeted approach has several advantages over traditional therapies for immune system diseases, such as reduced side effects and improved efficacy. Additionally, photo-dynamic treatment can be easily tailored to target specific types of immune cells or tissues, making it a highly versatile and customizable treatment option.

Research into harnessing photo-dynamic treatment for immune system diseases is ongoing, with promising results being reported in preclinical and clinical studies. As our understanding of the immune system continues to grow, this innovative therapeutic approach holds great promise for improving the treatment outcomes of patients with a wide range of immune system diseases [11].

Mechanisms of Photodynamic Treatment in Immune System Diseases

PDT Activates the Immune System to Target Diseased Cells



Basic Mechanisms of Action of PDT on Tumor

Photodynamic treatment (PDT) is a type of therapy that uses a photosensitizing agent and light to target and destroy abnormal cells, including those involved in immune system diseases [1-12]. The mechanisms of PDT in immune system diseases involve several key processes.

PDT, or photodynamic therapy, activates the immune system to target diseased cells through a process called immunogenic cell death [13]. When a photosensitizing agent is activated by light, it produces reactive oxygen species (ROS) that can cause damage to the targeted cells. This damage triggers a series of cellular events that lead to the release of damage-associated molecular patterns (DAMPs) and the exposure of antigens on the surface of the dying cells [14]. These DAMPs and antigens act as signals to the immune system, alerting it to the presence of damaged or dying cells. This triggers an immune response, leading to the recruitment of immune cells such as dendritic cells, macrophages, and T cells to the site of treatment [15]. These immune cells recognize the exposed antigens and DAMPs, and begin to engulf and destroy the targeted cells [16].

Furthermore, the immune response triggered by PDT can also lead to the release of cytokines and other signaling molecules that help to further activate and coordinate the immune system's attack on the diseased cells. This process ultimately results in the elimination of the targeted cells and the development of a specific immune memory against the antigens associated with the diseased cells, providing long-term protection against recurrence [17].

Induction of Immune Response and Immunomodulatory Effects

The induction of an immune response and immunomodulatory effects are important aspects of photodynamic therapy (PDT) in targeting diseased cells.[18] PDT can activate the immune system and modulate its responses in several ways:

Immunogenic cell death (ICD) is a form of cell death that can stimulate an immune response against

dying cells. When it comes to photodynamic therapy (PDT), the induction of ICD is a crucial mechanism through which the treatment activates the immune system to target diseased cells, particularly in the context of cancer therapy.

PDT involves the administration of a photosensitizing agent followed by exposure to light of a specific wavelength, leading to the generation of reactive oxygen species (ROS) that can cause damage to the targeted cells [19]. This damage triggers a series of cellular events that ultimately result in immunogenic cell death. The release of damage-associated molecular patterns (DAMPs) and the exposure of antigens on the surface of the dying cells serve as signals to the immune system, alerting it to the presence of damaged or dying cells [20]. This process triggers an immune response, leading to the recruitment of immune cells such as dendritic cells, macrophages, and T cells to the site of treatment [21]. These immune cells recognize the exposed antigens and DAMPs, and begin to engulf and destroy the targeted cells [22]. Furthermore, the immune response triggered by PDT can also lead to the release of cytokines and other signaling molecules that help to further activate and coordinate the immune system's attack on the diseased cells. The induction of ICD by PDT is crucial for its effectiveness in cancer therapy, as it not only directly targets cancer cells but also activates the immune system to recognize and eliminate cancer cells more effectively [23]. Additionally, the immune response triggered by PDT can lead to the development of a specific immune memory against the antigens associated with the cancer cells, providing long-term protection against cancer recurrence [24]. Therefore, the induction of immunogenic cell death is a key aspect of how PDT activates the immune system to target diseased cells, particularly in the context of cancer treatment.

Activation of dendritic cells is a significant aspect of the immune response induced by photodynamic therapy (PDT). Dendritic cells (DCs) play a crucial role in initiating and regulating immune responses, particularly in the context of recognizing and presenting antigens to T cells, which are key components of the adaptive immune system [25]. In the context of PDT, the process involves the administration of a photosensitizing agent followed by exposure to light, leading to the generation of reactive oxygen species (ROS) and subsequent damage to the targeted cells. This cellular damage can lead to the release of damage-associated molecular patterns (DAMPs) and the exposure of antigens on the surface of the dying cells. Dendritic cells recognize these antigens and DAMPs, and upon activation, they undergo a maturation process [26]. Mature dendritic cells are highly efficient at capturing antigens and presenting them to T cells, thereby initiating an adaptive immune response against the antigens associated with the diseased cells targeted by PDT [27]. The activation of dendritic cells by PDT is critical in the context of cancer therapy. By presenting tumor-associated antigens to T cells, activated dendritic cells can help initiate a specific immune response against cancer cells, leading to the recruitment of cytotoxic T cells and other immune effectors that target and eliminate the cancer cells. The activation of dendritic cells by PDT can lead to the development of long-term immune memory against the antigens associated with the cancer cells [28]. This memory response can provide ongoing protection against cancer recurrence.

Recruitment of immune cells: Photodynamic therapy (PDT) plays a significant role in the recruitment of immune cells to the site of treatment, which is a crucial aspect of its mechanism of action in targeting diseased cells, particularly in the context of cancer therapy. The recruitment of immune cells is an essential part of the immune response induced by PDT and contributes to the overall effectiveness of the treatment [29].

When PDT is performed, a photosensitizing agent is administered, followed by exposure to light of a specific wavelength. This leads to the generation of reactive oxygen species (ROS) and subsequent damage to the targeted cells. The cellular damage caused by PDT triggers a series of events that result in the release of signaling molecules and the exposure of antigens and damage-associated molecular patterns (DAMPs) on the surface of the dying or damaged cells. These signals act as a beacon for the immune system, attracting various immune cells to the site of treatment. Immune cells such as macrophages, neutrophils, dendritic cells, and T cells are recruited to the area where the PDT was applied [30]. These immune cells play different roles in the immune response and can contribute to the elimination of the diseased cells. Macrophages and neutrophils, for example, are phagocytic cells that can engulf and destroy the damaged or dying cells. Dendritic cells play a crucial role in capturing antigens and presenting them to T cells, initiating an adaptive immune response. T cells, including cytotoxic T cells, are critical in directly targeting and eliminating the diseased cells [31].

The recruitment of immune cells by PDT also leads to the release of cytokines and other signaling molecules that further modulate and coordinate the immune response. These molecules can promote inflammation, activate immune cells, and contribute to the elimination of diseased cells [32].

Cytokine release is a crucial aspect of the immune response induced by photodynamic therapy (PDT). PDT, which involves the use of a photosensitizing agent and light to target and destroy diseased cells, triggers a series of events that lead to the release of various cytokines and other signaling molecules. These cytokines play a significant role in modulating and coordinating the immune response to the treated cells, particularly in the context of cancer therapy. When PDT is performed, the generation of reactive oxygen species (ROS) and subsequent damage to the

targeted cells lead to the release of damage-associated molecular patterns (DAMPs) and other signals that act as danger signals to the immune system. These signals trigger the activation of immune cells and the release of cytokines.

Cytokines are signaling molecules that can have diverse effects on the immune system. Some cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6), can promote inflammation and activate immune cells, contributing to the recruitment and activation of immune effectors at the site of treatment [33].

Additionally, certain cytokines released in response to PDT can contribute to the maturation and activation of dendritic cells, which play a crucial role in initiating adaptive immune responses. Activated dendritic cells are efficient at capturing antigens from the damaged cells and presenting them to T cells, thereby initiating an immune response against the antigens associated with the treated cells. The release of cytokines in response to PDT can contribute to the development of a specific immune memory against the antigens associated with the treated cells. This memory response can provide ongoing protection against disease recurrence.

Photodynamic therapy (PDT) has significant immunomodulatory effects, meaning it can influence and regulate the immune response. These effects are particularly important in the context of cancer therapy, as PDT can stimulate the immune system to recognize and eliminate cancer cells [34]. The immunomodulatory effects of PDT involve various mechanisms that impact the activity and function of immune cells and the overall immune response. The immunomodulatory effects of PDT are essential for its effectiveness in targeting and eliminating cancer cells. By activating and modulating the immune response, PDT can enhance the immune system's ability to recognize and eliminate diseased cells, making it a valuable approach in cancer therapy and other immunomodulatory applications.

Enhancement of Immune Cell Function and Cytotoxicity

Photodynamic therapy (PDT) has been shown to enhance immune cell function and cytotoxicity, contributing to its effectiveness in the treatment of various diseases, particularly cancer [35]. The interaction between PDT and the immune system leads to several beneficial effects on immune cells, ultimately resulting in improved immune surveillance and the elimination of diseased cells.

PDT enhances immune cell function and cytotoxicity through a combination of mechanisms, including the activation of immune cells, induction of immunogenic cell death, increased susceptibility of treated cells to immune-mediated cytotoxicity, cytokine release, and antigen presentation. These effects collectively contribute to the immune system's ability to recognize and eliminate diseased cells, making PDT a promising approach in cancer therapy and other immunomodulatory applications.

Photodynamic Treatment for Specific Immune System Diseases

Review of Studies and Clinical Trials on PDT for Autoimmune Diseases

Photodynamic therapy (PDT) has primarily been studied and utilized for the treatment of cancer and certain infectious diseases, its application in autoimmune diseases has also been explored in preclinical and clinical studies [36, 1]. However, the use of PDT for autoimmune diseases is not as extensively researched as its application in cancer therapy.

Several preclinical studies have investigated the potential of PDT in modulating immune responses and treating autoimmune conditions [37]. These studies have focused on animal models of autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus, and autoimmune skin disorders. The findings from these preclinical studies have suggested that PDT may have immunomodulatory effects that could be beneficial in managing autoimmune diseases [38]. While there is limited clinical trial data specifically focused on PDT for autoimmune diseases, some clinical studies have explored the use of PDT in dermatological conditions with autoimmune components, such as psoriasis and cutaneous lupus erythematosus [39]. These studies have demonstrated the potential of PDT in managing skin manifestations of autoimmune diseases, with some evidence of improvement in symptoms and disease activity [40].

In addition to clinical studies, mechanistic research has provided insights into the immunomodulatory effects of PDT that could be relevant to autoimmune diseases [41]. These studies have investigated the impact of PDT on immune cell function, cytokine production, and the induction of immunogenic cell death, all of which have implications for modulating autoimmune responses [42]. Despite the potential benefits of PDT in autoimmune diseases, there are challenges and considerations that need to be addressed. These include optimizing treatment parameters, understanding the specific mechanisms of action in autoimmune settings, and identifying appropriate patient populations for clinical trials [43].

Application of PDT in the Treatment of Immunodeficiency Disorders

Immunodeficiency disorders are characterized by a compromised or dysfunctional immune system, leading to an increased susceptibility to infections and other complications [44]. While PDT has been primarily studied in the context of cancer therapy and certain infectious diseases, its potential application in

immunodeficiency disorders is being explored due to its immunomodulatory effects. PDT was considered in the treatment of immunodeficiency disorders as potential ways in which.

Immunodeficiency disorders can predispose individuals to recurrent or severe infections [45]. PDT has been investigated as a potential adjunctive treatment for localized infections in immunocompromised patients. By targeting and destroying pathogens in localized areas, PDT may help reduce the burden of infections and support the immune system's response. PDT has been shown to modulate the immune response, including the activation of immune cells and the release of cytokines [46]. In the context of immunodeficiency disorders, PDT may be explored for its potential to enhance immune cell function and improve immune surveillance, thereby helping to mitigate the impact of immunodeficiency on the body's ability to fight infections [47].

Immunodeficiency disorders can be associated with secondary conditions, such as skin infections, oral mucosal infections, and certain types of cancer. PDT has been utilized for the treatment of localized infections and malignancies in these contexts, and its potential role in managing secondary conditions associated with immunodeficiency disorders could be further investigated. PDT is a minimally invasive and localized treatment, it may offer advantages in terms of safety and tolerability for individuals with immunodeficiency disorders who may be more susceptible to systemic treatments and their associated side effects.

Use of PDT in the Management of Allergic and Hypersensitivity Reactions

In the case of allergic reactions, PDT can be used to reduce the symptoms and severity of conditions such as atopic dermatitis, allergic rhinitis, and allergic asthma.[48] By targeting the inflammatory response and immune cells involved in the allergic reaction, PDT can help alleviate symptoms and improve the overall management of these conditions.

Similarly, in the case of hypersensitivity reactions, such as contact dermatitis or drug-induced hypersensitivity, PDT can be used to reduce inflammation and immune response in the affected area. This can help alleviate symptoms and promote healing of the affected skin or tissues.

Challenges and Limitations of Photodynamic Treatment in Immune System Diseases

Potential Side Effects and Complications Associated with PDT

Photodynamic therapy (PDT) is generally considered to be a safe treatment option, but like any medical procedure, it can have potential side effects and complications [49]. Some of the potential side effects and complications associated with PDT may include skin sensitivity [50]. After PDT, the treated area may be sensitive to light for a period of time. Patients are typically advised to avoid direct sunlight and bright indoor light for a few days following the procedure [51].

Skin Irritation and Redness

The treated area may experience temporary redness, swelling, and irritation. This is a common side effect and usually resolves within a few days [52].

Pain or Discomfort

Some patients may experience mild to moderate pain or discomfort during or after the PDT procedure. This can usually be managed with over-the-counter pain medications.

Skin Changes

The skin in the treated area may become temporarily discolored, crusty, or develop blisters. These changes typically resolve as the skin heals.

Scarring

In rare cases, PDT may cause scarring, particularly if the treatment is not administered properly or if the patient has a predisposition to scarring.

Risk of Infection: Any procedure that breaks the skin barrier carries a risk of infection. Care instructions to minimize this risk.

Eye Sensitivity: If the face or head is treated with PDT, there is a risk of eye sensitivity to light.

Factors Affecting the Efficacy of PDT in Immune System Diseases

The efficacy of photodynamic therapy (PDT) in immune system diseases can be influenced by several factors such as Photosensitizer choice [53]. The selection of an appropriate photosensitizer is crucial for the success of PDT. Different photosensitizers have varying abilities to target specific cells or tissues, and their efficacy can vary depending on the type of immune system disease being treated [54].

Light Dose and Wavelength

The light source used to activate the photosensitizer must be carefully chosen to match the absorption spectrum of the photosensitizer [55]. The light dose and wavelength can impact the depth of tissue penetration and the overall effectiveness of the treatment.

The effectiveness of PDT can be influenced by the specific immune response in the affected area. In some cases, PDT may modulate the immune response, which can impact the overall efficacy of the treatment [56].

The stage and severity of the immune system disease can also affect the efficacy of PDT [57]. Early-

stage diseases may respond more effectively to PDT compared to advanced or severe cases.

Patient-specific factors such as skin type, overall health, and medical history, can impact the efficacy of PDT.

The specific treatment protocol, including the number of PDT sessions, interval between treatments, and the combination with other therapies, can influence the overall efficacy of PDT in immune system diseases.

The experience and expertise of the healthcare provider performing the PDT procedure can also impact its efficacy. Proper administration and management of PDT are essential for achieving optimal results. Additionally, individualized treatment plans and close monitoring of patients are essential to optimize the outcomes of PDT in the management of immune system diseases.

Current Limitations and Areas for Improvement in PDT Techniques

Photodynamic therapy (PDT) has shown promise in treating a variety of conditions, but there are several limitations and areas for improvement in PDT techniques [57]. One of the primary limitations of PDT is its restricted ability to penetrate deep into tissues [58]. This limits its effectiveness in treating larger or deeper tumors or lesions. Improving the depth of treatment without causing damage to surrounding healthy tissues is a key area for development.

Current photosensitizers used in PDT may not exclusively target diseased or cancerous tissues, leading to potential damage to healthy cells. Developing photosensitizers with greater specificity for diseased tissues could improve the overall safety and efficacy of PDT [59].

Ensuring precise and uniform delivery of light to the treatment area is essential for optimal PDT outcomes. Innovations in light delivery technologies, such as fiber optic systems and light-emitting diodes (LEDs), could enhance treatment precision [60].

Real-time monitoring of the treatment area during PDT is limited [61]. Improved techniques for monitoring the distribution of the photosensitizer, the oxygen levels in the tissue, and the extent of cellular damage during treatment could enhance the precision and effectiveness of PDT.

While PDT can be effective on its own, combining it with other treatment modalities, such as chemotherapy, immunotherapy, or targeted therapies, may lead to synergistic effects [62]. Identifying optimal combinations and treatment sequences is an area of ongoing research [63].

There is a need for standardized treatment protocols in PDT to ensure consistent and reproducible outcomes across different clinical settings. This includes standardizing parameters such as photosensitizer dose, light dose, and treatment intervals.

Identifying which patients are most likely to benefit from PDT, as well as predicting response to treatment, remains an area for improvement. Personalized approaches based on individual patient characteristics and disease profiles could optimize treatment outcomes.

PDT can be costly, and improving cost-effectiveness through the development of more affordable photosensitizers, light sources, and treatment protocols is important for broader accessibility.

Future Directions

Promising Advancements in PDT for Immune System Diseases

Research has shown that PDT can induce immunomodulatory effects, such as the activation of immune cells and the release of cytokines, which may have beneficial effects in immune system diseases [64]. Advancements in understanding these immunomodulatory mechanisms could lead to targeted PDT approaches to modulate the immune response in conditions such as autoimmune diseases and immunodeficiencies.

Advancements in nanotechnology and drug delivery systems have facilitated the development of targeted photosensitizer delivery to specific immune cells or tissues [65]. This targeted approach could improve the precision and efficacy of PDT while minimizing off-target effects.

Combining PDT with immunotherapy or other immune-modulating agents holds promise for enhancing the treatment of immune system diseases. Synergistic effects between PDT and immunotherapies, such as checkpoint inhibitors or adoptive cell therapies, are being explored to improve treatment outcomes.

Advancements in precision medicine and patient stratification may lead to personalized PDT approaches tailored to individual immune system diseases and patient characteristics. This could optimize treatment efficacy while minimizing adverse effects.

Ongoing research into the development of novel photosensitizers with improved targeting, selectivity, and activation properties may expand the applicability of PDT in immune system diseases [66].

PDT has been shown to induce immunogenic cell death, which can stimulate an immune response against cancer cells [67]. Harnessing this mechanism could have implications for immune system diseases by

modulating the immune response and promoting the clearance of abnormal cells.

Advancements in light sources and delivery systems, including light-emitting diodes (LEDs) and fiber optic devices, could improve the precision and depth of light penetration, expanding the potential applications of PDT in immune system diseases.

Ongoing preclinical and clinical studies are exploring the use of PDT in various immune system diseases, providing valuable insights into its safety and efficacy, as well as identifying potential areas for further development.

Potential Combination Therapies with PDT to Enhance Treatment Outcomes

There are several potential combination therapies with photodynamic therapy (PDT) that could enhance treatment outcomes across various medical fields.

Combining PDT with chemotherapy has shown promise in enhancing the treatment of various cancers. PDT can sensitize cancer cells to chemotherapy, potentially reducing the required chemotherapy dosage and minimizing systemic side effects [68].

PDT has been investigated in combination with immunotherapies, such as checkpoint inhibitors, adoptive cell therapies, and cancer vaccines. The immunomodulatory effects of PDT can enhance the immune response against cancer cells, leading to improved treatment outcomes [67, 68].

Also, Combining PDT with radiotherapy, known as photo-radiotherapy, has been explored as a potential synergistic approach to enhance tumor control and minimize radiation doses. The combination of these modalities may lead to improved local tumor control and reduced side effects.

PDT can be combined with targeted molecular therapies, such as tyrosine kinase inhibitors or monoclonal antibodies, to enhance the specificity and effectiveness of treatment for certain cancers and other diseases.

In the treatment of localized infections, such as periodontal disease or skin infections, combining PDT with antibiotic therapy may provide synergistic antimicrobial effects, potentially reducing the development of antibiotic resistance.

Combining PDT with photothermal therapy, which uses light to generate heat in targeted tissues, may offer a complementary approach for tumor ablation and enhanced treatment of solid tumors.

PDT can be combined with gene therapy to deliver therapeutic genes to targeted cells, potentially enhancing the treatment of genetic disorders or certain cancers.

PDT can be combined with anti-angiogenic agents to target tumor vasculature, potentially enhancing the destruction of tumor blood vessels and inhibiting tumor growth. This emerging approach combines PDT with immunotherapy agents to stimulate the immune system and enhance the anti-tumor immune response, potentially leading to improved treatment outcomes [66-68].

In certain hormone-sensitive cancers, combining PDT with hormonal therapies may provide a synergistic approach to target hormone receptor-positive tumor cells [53-68].

These potential combination therapies with PDT highlight the diverse opportunities for enhancing treatment outcomes in various medical conditions.

CONCLUSION

In conclusion, photodynamic therapy (PDT) has shown great potential as a therapeutic option for immune system diseases. By targeting specific cells and modulating the immune response, PDT has the ability to effectively treat conditions such as autoimmune disorders, allergies, and certain cancers. With further research and development, PDT has the potential to become a valuable tool in the treatment of immune system diseases, offering patients a promising alternative to traditional therapies. Its ability to selectively target diseased cells while minimizing damage to healthy tissue makes PDT a promising option for the future of immune system disease treatment.

REFERENCES

1. Van Straten, D., Mashayekhi, V., De Bruijn, H. S., Oliveira, S., & Robinson, D. J. (2017). Oncologic photodynamic therapy: basic principles, current clinical status and future directions. *Cancers*, *9*(2), 19.
2. Jerjes, W., Upile, T., Akram, S., & Hopper, C. (2010). The surgical palliation of advanced head and neck cancer using photodynamic therapy. *Clinical Oncology*, *22*(9), 785-791.
3. Kwiatkowski, S., Knap, B., Przystupski, D., Saczko, J., Kędzierska, E., Knap-Czop, K., ... & Kulbacka, J. (2018). Photodynamic therapy–mechanisms, photosensitizers and combinations. *Biomedicine & pharmacotherapy*, *106*, 1098-1107.
4. Ackroyd, R., Kelty, C., Brown, N., & Reed, M. (2001). The history of photodetection and photodynamic therapy¶. *Photochemistry and photobiology*, *74*(5), 656-669.
5. BW, H. (1991). How does photodynamic therapy work?. *Photochem Photobiol*, *55*, 145-157.

6. Wagnieres, G. A., Star, W. M., & Wilson, B. C. (1998). In vivo fluorescence spectroscopy and imaging for oncological applications. *Photochemistry and photobiology*, *68*(5), 603.
7. Foote, C. S. (1991). Definition of type I and type II photosensitized oxidation. *Photochemistry and photobiology*, *54*(5), 659-659.
8. Dysart, J. S. (2007). Photosensitizer Photobleaching for Singlet Oxygen Dose Estimation During Photodynamic Therapy. *Library an d Archives Canada= Bibliothèque et Archives Canada, Ottawa*.
9. Castano, A. P., Demidova, T. N., & Hamblin, M. R. (2004). Mechanisms in photodynamic therapy: part one—photosensitizers, photochemistry and cellular localization. *Photodiagnosis and photodynamic therapy*, *1*(4), 279-293.
10. Igney, F. H., & Krammer, P. H. (2002). Death and anti-death: tumour resistance to apoptosis. *Nature Reviews Cancer*, *2*(4), 277-288.
11. Kessel, D., & Reiners Jr, J. J. (2007). Apoptosis and autophagy after mitochondrial or endoplasmic reticulum photodamage. *Photochemistry and photobiology*, *83*(5), 1024-1028.
12. Oleinick, N. L., Morris, R. L., & Belichenko, I. (2002). The role of apoptosis in response to photodynamic therapy: what, where, why, and how. *Photochemical & Photobiological Sciences*, *1*(1), 1-21.
13. Wu, S., & Xing, D. (2012). Mechanism of mitochondrial membrane permeabilization during apoptosis under photofrin-mediated photodynamic therapy. *Journal of X-ray Science and Technology*, *20*(3), 363-372.
14. Lavie, G., Kaplinsky, C., Toren, A., Aizman, I., Meruelo, D., Mazur, Y., & Mandel, M. (1999). A photodynamic pathway to apoptosis and necrosis induced by dimethyl tetrahydroxyhelianthrone and hypericin in leukaemic cells: possible relevance to photodynamic therapy. *British journal of cancer*, *79*(3), 423-432.
15. Castano, A. P., Mroz, P., & Hamblin, M. R. (2006). Photodynamic therapy and anti-tumour immunity. *Nature Reviews Cancer*, *6*(7), 535-545.
16. Levine, B., & Klionsky, D. J. (2004). Development by self-digestion: molecular mechanisms and biological functions of autophagy. *Developmental cell*, *6*(4), 463-477.
17. Buytaert, E., Callewaert, G., Hendrickx, N., Scorrano, L., Hartmann, D., Missiaen, L., ... & Agostinis, P. (2006). Role of endoplasmic reticulum depletion and multidomain proapoptotic BAX and BAK proteins in shaping cell death after hypericin-mediated photodynamic therapy. *Faseb Journal*, *20*(6), 756-758.
18. Inguscio, V., Panzarini, E., & Dini, L. (2012). Autophagy contributes to the death/survival balance in cancer photodynamic therapy. *Cells*, *1*(3), 464-491.
19. Kessel, D. H., Price, M., & Reiners, Jr, J. J. (2012). ATG7 deficiency suppresses apoptosis and cell death induced by lysosomal photodamage. *Autophagy*, *8*(9), 1333-1341.
20. Maeda, H., Nakamura, H., & Fang, J. (2013). The EPR effect for macromolecular drug delivery to solid tumors: Improvement of tumor uptake, lowering of systemic toxicity, and distinct tumor imaging in vivo. *Advanced drug delivery reviews*, *65*(1), 71-79.
21. Peng, Q., & Nesland, J. M. (2004). Effects of photodynamic therapy on tumor stroma. *Ultrastructural Pathology*, *28*(5-6), 333-340.
22. Dvorak, H. F. (2003). How tumors make bad blood vessels and stroma. *The American journal of pathology*, *162*(6), 1747-1757.
23. Guo, W., & Giancotti, F. G. (2004). Integrin signalling during tumour progression. *Nature reviews Molecular cell biology*, *5*(10), 816-826.
24. Celli, J. P. (2012). Stromal interactions as regulators of tumor growth and therapeutic response: A potential target for photodynamic therapy?. *Israel journal of chemistry*, *52*(8-9), 757-766.
25. Hanahan, D., & Weinberg, R. A. (2000). The hallmarks of cancer. *cell*, *100*(1), 57-70.
26. Belal Al-Husein, M. S., Abdalla, M., DeRemer, D. L., & Somanath, P. R. (2012). Antiangiogenic therapy for cancer: an update. *Pharmacotherapy*, *32*(12), 1095-1111.
27. Star, W. M., Marijnissen, H. P., van den Berg-Blok, A. E., Versteeg, J. A., Franken, K. A., & Reinhold, H. S. (1986). Destruction of rat mammary tumor and normal tissue microcirculation by hematoporphyrin derivative photoradiation observed in vivo in sandwich observation chambers. *Cancer research*, *46*(5), 2532-2540.
28. Ben-Hur, E., Heldman, E., Crane, S. W., & Rosenthal, I. (1988). Release of clotting factors from photosensitized endothelial cells: a possible trigger for blood vessel occlusion by photodynamic therapy. *FEBS letters*, *236*(1), 105-108.
29. Fingar, V. H., Wieman, T. J., & Haydon, P. S. (1997). The effects of thrombocytopenia on vessel stasis and macromolecular leakage after photodynamic therapy using photofrin. *Photochemistry and Photobiology*, *66*(4), 513-517.
30. Kurohane, K., Tominaga, A., Sato, K., North, J. R., Namba, Y., & Oku, N. (2001). Photodynamic therapy targeted to tumor-induced angiogenic vessels. *Cancer letters*, *167*(1), 49-56.
31. Chen, B., Pogue, B. W., Hoopes, P. J., & Hasan, T. (2005). Combining vascular and cellular targeting regimens enhances the efficacy of photodynamic therapy. *International Journal of Radiation Oncology* Biology* Physics*, *61*(4), 1216-1226.
32. Castano, A. P., Mroz, P., & Hamblin, M. R. (2006). Photodynamic therapy and anti-tumour immunity. *Nature Reviews Cancer*, *6*(7), 535-545.

33. Korbelik, M., Sun, J., & Cecic, I. (2005). Photodynamic therapy–induced cell surface expression and release of heat shock proteins: relevance for tumor response. *Cancer research*, *65*(3), 1018-1026.
34. Beg, A. A. (2002). Endogenous ligands of Toll-like receptors: implications for regulating inflammatory and immune responses. *Trends in immunology*, *23*(11), 509-512.
35. Vabulas, R. M., Wagner, H., & Schild, H. (2002). Heat shock proteins as ligands of toll-like receptors. *Toll-like receptor family members and their ligands*, 169-184.
36. Reginato, E., Wolf, P., & Hamblin, M. R. (2014). Immune response after photodynamic therapy increases anti-cancer and anti-bacterial effects. *World journal of immunology*, *4*(1), 1.
37. Agarwal, M. L., Clay, M. E., Harvey, E. J., Evans, H. H., Antunez, A. R., & Oleinick, N. L. (1991). Photodynamic therapy induces rapid cell death by apoptosis in L5178Y mouse lymphoma cells. *Cancer research*, *51*(21), 5993-5996.
38. Krosl, G., Korbelik, M., & Dougherty, G. J. (1995). Induction of immune cell infiltration into murine SCCVII tumour by photofrin-based photodynamic therapy. *British journal of cancer*, *71*(3), 549-555.
39. Matroule, J. Y., Volanti, C., & Piette, J. (2006). NF-κB in Photodynamic Therapy: Discrepancies of a Master Regulator. *Photochemistry and Photobiology*, *82*(5), 1241-1246.
40. Gollnick, S. O., Evans, S. S., Baumann, H., Owczarczak, B., Maier, P., Vaughan, L., ... & Henderson, B. W. (2003). Role of cytokines in photodynamic therapy-induced local and systemic inflammation. *British journal of cancer*, *88*(11), 1772-1779.
41. de Vree, W. J., Essers, M. C., de Bruijn, H. S., Star, W. M., Koster, J. F., & Sluiter, W. (1996). Evidence for an important role of neutrophils in the efficacy of photodynamic therapy in vivo. *Cancer research*, *56*(13), 2908-2911.
42. Kousis, P. C., Henderson, B. W., Maier, P. G., & Gollnick, S. O. (2007). Photodynamic therapy enhancement of antitumor immunity is regulated by neutrophils. *Cancer research*, *67*(21), 10501-10510.
43. Cantl, G., Lattuada, D., Nicolin, A., Taroni, P., Valentinl, G., & Cubeddu, R. (1994). Antitumor immunity induced by photodynamic therapy with aluminum disulfonated phthalocyanines and laser light. *Anti-Cancer Drugs*, *5*(4), 443-447.
44. Korbelik, M., Krosl, G., Krosl, J., & Dougherty, G. J. (1996). The role of host lymphoid populations in the response of mouse EMT6 tumor to photodynamic therapy. *Cancer research*, *56*(24), 5647-5652.
45. Korbelik, M., & Dougherty, G. J. (1999). Photodynamic therapy-mediated immune response against subcutaneous mouse tumors. *Cancer research*, *59*(8), 1941-1946.
46. Larsson, M., Fonteneau, J. F., & Bhardwaj, N. (2001). Dendritic cells resurrect antigens from dead cells. *Trends in immunology*, *22*(3), 141-148.
47. Kabingu, E., Vaughan, L., Owczarczak, B., Ramsey, K. D., & Gollnick, S. O. (2007). CD8+ T cell-mediated control of distant tumours following local photodynamic therapy is independent of CD4+ T cells and dependent on natural killer cells. *British journal of cancer*, *96*(12), 1839-1848.
48. Yoon, I., Li, J. Z., & Shim, Y. K. (2013). Advance in photosensitizers and light delivery for photodynamic therapy. *Clinical endoscopy*, *46*(1), 7.
49. Szaciłowski, K., Macyk, W., Drzewiecka-Matuszek, A., Brindell, M., & Stochel, G. (2005). Bioinorganic photochemistry: frontiers and mechanisms. *Chemical reviews*, *105*(6), 2647-2694.
50. Szaciłowski, K., Macyk, W., Drzewiecka-Matuszek, A., Brindell, M., & Stochel, G. (2005). Bioinorganic photochemistry: frontiers and mechanisms. *Chemical reviews*, *105*(6), 2647-2694.
51. Henderson, B. W., Busch, T. M., & Snyder, J. W. (2006). Fluence rate as a modulator of PDT mechanisms. *Lasers in Surgery and Medicine: The Official Journal of the American Society for Laser Medicine and Surgery*, *38*(5), 489-493.
52. Henderson, B. W., Gollnick, S. O., Snyder, J. W., Busch, T. M., Kousis, P. C., Cheney, R. T., & Morgan, J. (2004). Choice of oxygen-conserving treatment regimen determines the inflammatory response and outcome of photodynamic therapy of tumors. *Cancer research*, *64*(6), 2120-2126.
53. See, K. L., Forbes, I. J., & Betts, W. H. (1984). Oxygen dependency of photocytotoxicity with haematoporphyrin derivative. *Photochemistry and photobiology*, *39*(5), 631-634.
54. Casas, A., Di Venosa, G., Hasan, T., & Batlle, A. (2011). Mechanisms of resistance to photodynamic therapy. *Current medicinal chemistry*, *18*(16), 2486-2515.
55. Castano, A. P., Mroz, P., Wu, M. X., & Hamblin, M. R. (2008). Photodynamic therapy plus low-dose cyclophosphamide generates antitumor immunity in a mouse model. *Proceedings of the National Academy of Sciences*, *105*(14), 5495-5500.
56. Akilov, O. E., Kosaka, S., O'Riordan, K., Song, X., Sherwood, M., Flotte, T. J., ... & Hasan, T. (2006). The role of photosensitizer molecular charge and structure on the efficacy of photodynamic therapy against Leishmania parasites. *Chemistry & biology*, *13*(8), 839-847.
57. Dummin, H., Cernay, T., & Zimmermann, H. W. (1997). Selective photosensitization of mitochondria in HeLa cells by cationic Zn (II) phthalocyanines with lipophilic side-chains. *Journal of Photochemistry and Photobiology B: Biology*, *37*(3), 219-229.
58. Jensen, T. J., Vicente, M. G. H., Luguya, R., Norton, J., Fronczek, F. R., & Smith, K. M. (2010). Effect of overall charge and charge distribution on cellular

uptake, distribution and phototoxicity of cationic porphyrins in HEp2 cells. *Journal of Photochemistry and Photobiology B: Biology*, *100*(2), 100-111.

59. Woodburn, K. W., Vardaxis, N. J., Hill, J. S., Kaye, A. H., & Phillips, D. R. (1991). Subcellular localization of porphyrins using confocal laser scanning microscopy. *Photochemistry and photobiology*, *54*(5), 725-732.
60. Pavani, C., Uchoa, A. F., Oliveira, C. S., Iamamoto, Y., & Baptista, M. S. (2009). Effect of zinc insertion and hydrophobicity on the membrane interactions and PDT activity of porphyrin photosensitizers. *Photochemical & photobiological sciences*, *8*, 233-240.
61. Pavani, C., Uchoa, A. F., Oliveira, C. S., Iamamoto, Y., & Baptista, M. S. (2009). Effect of zinc insertion and hydrophobicity on the membrane interactions and PDT activity of porphyrin photosensitizers. *Photochemical & photobiological sciences*, *8*, 233-240.
62. Rosenthal, I., Sostaric, J. Z., & Riesz, P. (2004). Sonodynamic therapy—a review of the synergistic effects of drugs and ultrasound. *Ultrasonics sonochemistry*, *11*(6), 349-363.
63. Miller, D. L., Smith, N. B., Bailey, M. R., Czarnota, G. J., Hynynen, K., Makin, I. R. S., & Bioeffects Committee of the American Institute of Ultrasound in Medicine. (2012). Overview of therapeutic ultrasound applications and safety considerations. *Journal of ultrasound in medicine*, *31*(4), 623-634.
64. Polat, B. E., Hart, D., Langer, R., & Blankschtein, D. (2011). Ultrasound-mediated transdermal drug delivery: mechanisms, scope, and emerging trends. *Journal of controlled release*, *152*(3), 330-348.
65. Pavani, C., Uchoa, A. F., Oliveira, C. S., Iamamoto, Y., & Baptista, M. S. (2009). Effect of zinc insertion and hydrophobicity on the membrane interactions and PDT activity of porphyrin photosensitizers. *Photochemical & photobiological sciences*, *8*, 233-240.
66. Rosenthal, I., Sostaric, J. Z., & Riesz, P. (2004). Sonodynamic therapy—a review of the synergistic effects of drugs and ultrasound. *Ultrasonics sonochemistry*, *11*(6), 349-363.
67. Miller, D. L., Smith, N. B., Bailey, M. R., Czarnota, G. J., Hynynen, K., Makin, I. R. S., & Bioeffects Committee of the American Institute of Ultrasound in Medicine. (2012). Overview of therapeutic ultrasound applications and safety considerations. *Journal of ultrasound in medicine*, *31*(4), 623-634.
68. Polat, B. E., Hart, D., Langer, R., & Blankschtein, D. (2011). Ultrasound-mediated transdermal drug delivery: mechanisms, scope, and emerging trends. *Journal of controlled release*, *152*(3), 330-348.

Cite This Article: Imadoudini Hassimi Safia, Yao-Yun Tang, Wu Ping, Jiang Jie (2024). Harnessing Photo-Dynamic Treatment for Immune System Diseases: A Promising Therapeutic Approach: A Systematic Review. *East African Scholars J Med Surg*, *6*(3), 105-114.