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Photodynamic Therapy: A Successful Alternative for Dermatological Medicine

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ABSTRACT

This paper shows the basics of Photodynamic Therapy (PDT), aiming to expand the knowledge of the benefits that PDT can bring to dermatological treatments.

THE THEORETICAL BASIS OF PDT

Photodynamic Therapy (PDT) is a medical modality widely applied to treat skin diseases [1-5]. The advantage of the method involves the high selectivity to treatment local, non-invasive characteristics, low toxicity, besides the possibility of combination with other therapeutic modalities [6,7].

The treatment is based on the drug administration (photosensitizer compound PS) and the use of adequate wavelength light at the treatment site. During its excited state, the PS can spin change (singlet 1PS* to triplet 3PS* state) by intersystem conversion (ISC); [8-10]. Then, the 3PS* interacts with neighboring molecules, leading to the ROS (reactive oxygen species) formation, especially singlet oxygen ($^1O_2$). Singlet oxygen is highly cytotoxic and causes oxidative damage to cells [5,11,12]; (Figure 1).

PDT AS A POTENTIAL THERAPY FOR DISEASE TREATMENT

Recently, the clinical efficacy of PDT with Hemoporphine in the treatment of infantile facial spots (related to congenital malformation in the dermal layer) was proven. Doses of 5mg/kg Hemoporphine followed by irradiation with green LED at 532nm were administered to 100 children (between 1 and 3 years of age). Efficacy with depigmentation of the skin was achieved in 98% of cases. Adverse reactions were tolerable, and PDT was considered promising in treating port-wine stains [13].

The use of PDT (Photofrin as PS) associated with chemotherapy showed advantages in treating 90 patients (42 and 88 years old) with advanced-stage esophageal cancer. Doses of 2mg/kg Photofrin, irradiation (630nm for 8-12min) guided by fiber optics coupled to an endoscope showed therapeutic benefit [6]. A recent case report of a 52-year-old patient reported the clinical efficacy of PDT in the treatment of refractory chromoblastomycosis (long-lasting lesion caused by a fungal infection of the subcutaneous tissue) aggravated by leukopenia (low white blood cell count). Six sessions of PDT (25 min each, one week apart) mediated by the use of commercial cream containing ALA (5-Aminolevulinic Acid Hydrochloride) allowed complete cure without the occurrence of recurrence [14].

The therapeutic effects and mechanisms of action of 5-aminolevulinic acid (ALA) were studied on wounds developed in rats. The application of PDT proved advantageous as it stimulated wound healing by regulating granulation tissue formation, inflammatory process, and differentiation of M1/M2 macrophages [15]. In addition, ALA has shown potential in treating skin infections caused by Mycobacterium abscessus, which are difficult

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to treat clinically [16]. Seven patients' skin ulcers with sinus tract formation (difficult-to-treat lesions in dermatology) were treated with combination PDT therapy (using ALA) and antibiotics for three months. Local administrations every 10 days, with a total of 1-5 sessions, led to complete healing in six patients. One patient's sinus tract was healed, and this patient's ulcer area was reduced. Patients reported minimal discomfort with PDT and were satisfied with the treatment outcome [17].

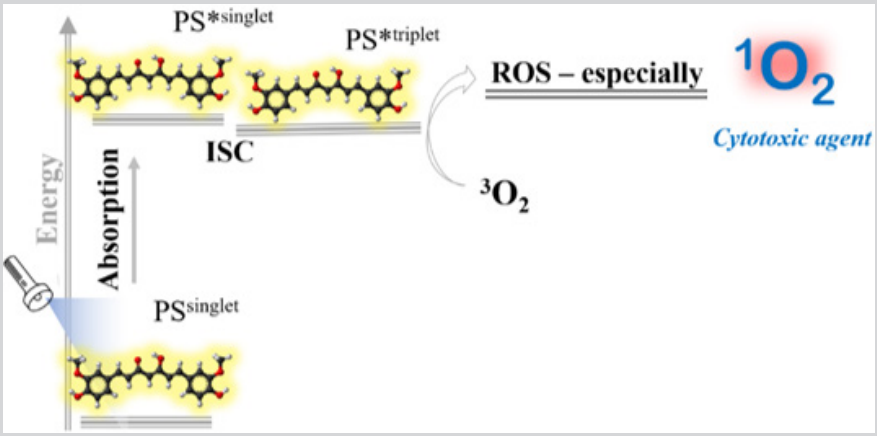

Figure 1: Jablonski diagram.

PDT IN THE WORLD: HOSPITAL USE

PDT is recognized by doctors who are members of the American Cancer Society. Besides, hospitals in Europe have employed PDT in patients for the treatment of cancer, including the Quirónsalud Madrid University Hospital (Private Hospital, Spain), Hospital Quirónsalud Barcelona (Private Hospital, Spain), Klinikum Stuttgart (Public Hospital, Germany), Centre Chirugical AMBROISE-PARÉ (Private Hospital, France), Grupo Hospitalario Quirónsalud (Hospital Group, Spain), Neolife Oncology Center (Oncology Center, Turkey), Hygeia Hospital (Hygeia Hospital, Greece), among others.

In Brazil, the Plastic Surgery Hospital HPLAS (Campo Grande-Mato Grosso do Sul) offers PDT treatment for disseminated actinic keratoses on the face, scalp, forearms, and back of the hands, superficial basal cell carcinomas, Bowen's disease and in immunosuppressed patients, when surgical excision is contraindicated. The treatment description, available on the hospital's website, includes the administration of the specific dye (PS) on the lesion. After administration, that area remains protected from light for 3h. After this period, the region receives red light, activating the dye and promoting the elimination of sick cells and those susceptible to cancer around the lesion. The application of red light in each lesion is maintained for about 8 min. The number of sessions is dependent on the clinical picture. For example, cases of actinic keratoses usually require two sessions, with an interval of one month [18]. The same procedure is offered by the Dermatology Clinic Gabriel Gontijo, located in Belo Horizonte, Minas Gerais. In addition to what has already been exposed, the doctor addresses the occurrence of a reddish and slightly swollen appearance on the skin after photodynamic treatment. However, the patient may return to normal activities after the sessions [19].

Besides the emerging hospital acceptance of PDT, researchers worldwide have invested in dermatological platforms applied to photo stimulated therapy. For example, Combuca et al. [20] published several comprehensive studies on the use of PDT in lactating animals. Their results showed that safranin, like PS, was more effective in preventing mastitis than iodine (commercial product). Thus, safranin behavior produced inactivation effects, favoring animal health and milk quality. Thermo responsive dermatological platforms were proposed by Combuca et al. [20]; Campanholi et al. [21]. The pharmaceutical bases in both works were composed of Poloxamer F127 (20%w/w) and Carbopol (0.2%w/w), with different photosensitizers. The systems were able to inactivate strains of microorganisms of hospital importance, such as Staphylococcus aureus [21,22].

CONCLUSION

PDT treatments prove the promising character of this technique. Indeed, disseminating this therapy worldwide will benefit patients seeking a cure for diseases or simply aesthetic benefits.

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