International Journal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

https://ijpsat.org/
Vol. 59 No. 1 September 2026, pp. 847-871

Photodynamic Advances In Antimicrobial Therapy And Cancer Care: Review

Maged Naser[1], Mohamed M. Nasr[2], Lamia H. Shehata[3]

[1]Mazahmiya Hospital, Ministry of Health, Kingdom of Saudi Arabia, Department of ob/gyn
[2]Consultant of General and Endoscopic Surgery (MD, FRCS)
[3]Care National Hospital, Department of Radiology

Corresponding Author: Maged Naser, maged.mahmoud42@hotmail.com

Abstract: After photodynamic therapy entered clinical practice, research and development flourished rapidly, and scientists endeavored to develop novel photosensitizers and to overcome the technology's limitations. This effort yielded numerous important advances, among them new generations of photosensitizers, increased clinical applications, nanotechnology-based systems to improve treatment efficacy, greater selectivity against diseased tissue, and combinations with other minimally invasive treatments. Researchers have also developed stimulus-responsive delivery systems, disease-targeting methodologies, and approaches that enhance the penetration depth of activating light. Collectively, these advances have greatly enhanced a technology that remains relatively new.

The main application of photodynamic therapy remains the treatment of neoplasms. Many innovations initially developed in cancer research also find their way into other realms, including microbial, fungal, and viral infections; acne; wet age-related macular degeneration; atherosclerosis; psoriasis; environmental sanitization; pest control; and dermatology. Combining photodynamic therapy with other treatments offers three main benefits: greater efficacy via additive or synergistic effects, a low likelihood of resistance, and rapid development as a targeted, high-precision treatment. Combinations with established techniques, including chemotherapy and radiotherapy, may augment their therapeutic utility. Photodynamic therapy has also proved valuable in mop-up surgery.

Published and preclinical studies, clinical trials, clinical applications, and post clinical case reports have established combination technologies. These technologies have attracted considerable research interest because they can be applied with relative ease, enhance treatment outcomes, and are rapidly advancing toward clinical relevance. They combine photodynamic therapy with chemotherapy, photothermal therapy, magnetic hyperthermia, cold plasma therapy, sonodynamic therapy, immunotherapy, or radiotherapy. Photochemical internalization is an important mechanism in several of these combinations.

Keywords: photodynamic therapy, sonodynamic therapy, photothermal hyperthermia, magnetic hyperthermia, anticancer, antimicrobial, combinations, nanomaterials chemotherapy, CAP, immunotherapy, radiotherapy

I. Introduction

Photosensitizers are compounds that absorb light energy and transfer it to oxygen in its triplet ground state, producing singlet oxygen. Other reactive oxygen species then form in biological media. Activated by light, many photosensitizers also interact directly with cell membranes and cytoplasmic components, including monosaccharides, nucleic acids, amino acids, DNA, RNA, glycans, and proteins. Photodynamic therapy (PDT) begins with a photosensitizer (PS) absorbing light, resulting in direct reactions and oxygen-dependent reactions taking place in the cell membrane and cytoplasm, respectively, leading to cell death via apoptosis or the destruction of cells by necrosis. For PDT to be selective, the PS must selectively accumulate at the disease site and within diseased cells and leave healthy cells essentially untouched or only slightly accumulated.

Early studies showed that organic photosensitizers incorporating porphyrins and phthalocyanines preferentially accumulated in tumor tissue over normal host tissue. PDT was thus introduced as an anticancer treatment [1]. As the technology was pushed into clinical practice, researchers looked to improve this preferential accumulation [2]. This led to extensive research into the selective delivery of PSs to diseased cells and sites while avoiding the delivery to healthy tissue, which remains a major focus of PDT research [3]. A main type II mechanism of PDT also relies on sufficient oxygen levels. Researchers soon realized that many disease sites had poor oxygen levels, or were hypoxic, and this was a problem in cancerous tumors as well as bacterial and fungal infections. Hypoxia limits PDT's action, and research on methods that enhance oxygen levels in the disease microenvironment has been undertaken [4].

Another limitation of PDT is the distance that light can penetrate human tissue to reach the PS and initiate the PDT reaction, which is only 2-5 mm [5]. Most skin disorders and other shallow diseases are suitable for effective treatment, but diseases deeper than 5 mm, or in dark tissues such as the liver, spleen, pancreas, and bone, cannot be treated with PDT, unless optical fibers are used to deliver the light. This remains true even with the use of near-infrared light within the therapeutic window. Optical fibers can reach some of the deep diseases and activate the PS [6,7]. The method may require costly infrastructure, and thus, is technology-intensive and less accessible to financially disadvantaged patients [8].

Sonodynamic therapy (SDT) was developed as a newer form of PDT to counter the limited light penetration of PDT [9]. In SDT, it is the ultrasound that activates the sensitizer (called the sonosensitizer) instead of light. Ultrasound can pass through the body and reach dark tissues and bones [9]. Research has therefore focused on using SDT to treat periodontal and bone diseases, as well as diseases in dark tissues such as the liver, spleen, and pancreas. X-ray-induced PDT (XPDT or PDTX) offers another method of overcoming the limited penetration of visible light used in standard PDT. In this method, nanomaterial agents are excited by X-rays, and emit visible light, which then activates the PSs [10]. Magnetic hyperthermia therapy (MGH) is already in clinical use to treat glioblastoma multiforme in the deep brain. It circumvents the tissue penetration problem because high frequency alternating magnetic field can pass through the skull and brain tissue, and it can heat glioblastoma tumors that contain magnetic nanoparticles [11]. This review addresses several combinations of PDT and MGH and the limited antimicrobial research in this area.

In most clinical PDT treatments, the PS is still administered directly to the patient and reaches the diseased tissue through systemic circulation [12]. Current research increasingly employs nanomaterials to deliver and deliver PSs to diseased tissue, and this is aimed at enhancing targeted delivery with increased selectivity for diseased cells over healthy host tissue [13]. Their small size provides a high surface-area to volume ratio, which allows them to adsorb, carry and deliver large amounts of PSs. As with porphyrin and phthalocyanine organic dye PSs, evidence suggests that the enhanced permeability and retention effect can promote nanomaterial accumulation in tumor tissue [14]. Nanoparticles have thus received extensive study as a means of enhancing PDT via more targeted PS delivery [13]. Some nanoparticles also act as PSs and promote reactive oxygen species formation [15]. These materials do not require organic dye PSs to elicit activity at the disease site, but when organic dye PSs are added, the resulting nanoconjugates show strong reactive oxygen generation and PDT activity [15].

Nanomaterials also support combination treatments that include PDT [16]. Researchers generally develop nanoconjugates that incorporate features needed for PDT and for the second treatment method [17,18]. To combine PDT with MGH, for example, magnetic nanoparticles are loaded with a PS [19]. The resulting nanoconjugate responds to a high-frequency alternating magnetic field by producing heat, raising the temperature to above the tolerance limits of diseased cells in the local tissue. For PDT combined with photothermal hyperthermia therapy (PTT), photothermal nanoparticles are loaded with a PS. Light irradiation then causes the nanoconjugate to raise the temperature beyond the tolerance limit of diseased cells in the local tissue [20]. In combined PDT and chemotherapy, nanoparticles carry both a suitable chemotherapy drug and the PS. The nanoconjugate delivers both agents to the disease site, supporting their simultaneous action [21]. This paper also examines PDT combined with cold atmospheric pressure plasma (CAP) therapy. CAP does not always require nanomaterials, but nanomaterials can carry and deliver the PS when the two treatments are combined [22].

1. Mechanism of Action of PDT

Photodynamic therapy (PDT) comprises three main components: a photosensitizer (PS), visible light, and oxygen. Individually, they are harmless, but together, they generate highly reactive oxygen species (ROS). ROS are reactive compounds formed from molecular oxygen (O2), water (H2O), and hydrogen peroxide (H2O2). They include hydroperoxyl radicals (HO2•), superoxide anions (O2•−), hydroxyl radicals (OH•), and singlet oxygen (^1O2). Singlet oxygen, also called dioxygen(singlet) or dioxidene, is a gaseous inorganic compound. It is the main active species in PDT [23,24].

1.1 The mechanism of PDT comprises two main pathways:

Type I mechanism: The excited PS transfers energy or electrons to biomolecules, resulting in the production of free radicals and other ROS that damage and destroy cancer cells [25].

Type II mechanism: The PS transfers energy directly to molecular oxygen, producing singlet oxygen, which is a strong oxidant that damages cancer cells [26].

PDT effectiveness depends on oxygen concentration, PS structure, and tissue conditions. Photodamage can cause cell death by apoptosis, which is programmed cell death, or necrosis, which is the result of severe cellular injury [27,28,29]. Several processes contribute to cell death, including the release of cytochrome c from damaged mitochondria, which activates apoptosis. Singlet oxygen does not directly "destroy cancer cells", but rather triggers pathways that result in cell death, including apoptosis. Autophagy can protect cells by recycling damaged mitochondria before they release cytochrome c.

Most organic compounds exist in the singlet ground state, but molecular oxygen has a triplet ground state and can become excited to a singlet state. As a result, excited PS molecules do not usually damage organic cellular structures directly, but they mainly interact with oxygen dissolved in the cytoplasm [30]. The type II pathway is considered the main process responsible for PDT activity, and the relative contribution of the two pathways depends on several factors, including oxygen concentration, tissue dielectric constant, tissue pH, and PS structure [31].

The type of cell death also depends on the location of the PS within the cell. Mitochondrial damage can lead to apoptosis, while damage to cell membranes, followed by the loss of membrane integrity can lead to necrosis. Injury to lysosomes or the endoplasmic reticulum can induce autophagy [31,32].

2. Innovative strategies of PDT

2.1. Photosensitizers

The PS is introduced into the body as a compound with little or no effect in the dark. Its main role is to direct pathological cells into a programmed cell death [33,34]. After a suitable time, the PS reaches a greater concentration in tumor tissue than in nearby healthy tissue. The tumor area is then exposed to light at a wavelength that matches the PS absorption maximum, usually above 500 nm. The light source must output within the dye's absorption band to be able to initiate the required photochemical reaction.

When the PS has absorbed a photon, its molecule transitions from the ground state to an excited singlet state. Two important pathways can deactivate the molecule, returning it to the ground state. In one pathway, the excited PS emits the excess energy as light, a process known as fluorescence. The measurement of fluorescence from the drug accumulated in tumor tissue can help to support a precise diagnosis by identifying the shape, size, and location of the cancerous lesion .

In the second pathway, the excited PS transitions to the triplet state. The triplet state can persist for hundreds of microseconds, allowing for the PS to interact with oxygen. Oxygen normally exists in the triplet state, and it can deactivate the excited PS while generating singlet oxygen. This deactivation pathway produces singlet oxygen, which is highly efficient in damaging cancer cells during PDT [35].

For use in cancer diagnosis or treatment, a PS should satisfy several conditions:

International Journal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

https://ijpsat.org/
Vol. 59 No. 1 September 2026, pp. 847-871

Selective accumulation in tumor tissue: The PS should be selectively accumulated in tumors while limiting the exposure of healthy tissue. No phototoxicity in healthy tissue: The PS should not produce phototoxic effects in healthy tissues exposed to light. Suitable absorption bands: The PS absorption bands should not overlap those of natural body pigments (e.g., melanin and hemoglobin) and should avoid strong water absorption near the infrared region. Efficient singlet oxygen production: The PS should produce singlet oxygen and other oxidative agents efficiently since these reactions are needed to destroy cancer cells. Limited side effects: The PS should not cause serious adverse effects that could harm the patient. Low toxicity and rapid removal: Most PSs also accumulate in host organs, including the liver. Since these organs are not generally exposed to the treatment light, they generally remain undamaged. The PS should have low toxicity and should be removed from the body easily after treatment, reducing side effects and the burden on the patient.

2.2 Anticancer Photodynamic Therapy

In cancer treatment, PDT can kill cancer cells and slow tumor growth by limiting cell proliferation. The method relies on the preferential buildup of the photosensitizer (PS) in cancer tissue. After light exposure, the PS promotes the formation of reactive oxygen species, which destroy cancer cells within the disease microenvironment. The clinical approach started with the direct administration of hematoporphyrin and hematoporphyrin derivatives that showed some preferential accumulation after systemic circulation [36]. Current research focuses on targeted PS delivery through nanomaterials, although some groups still administer free PSs without nanocarriers. One example involves coumarin incorporated into amphoteric nano capsules. These organic nanomaterials support systemic distribution through their amphiphilic nature, while the hydrophobic PS promotes accumulation at diseased sites [37].

A comparison of a new zinc (II) phthalocyanine-quinoline conjugate with Photofrin demonstrates the direct approach without a nanomaterial carrier [38]. In that study, the zinc (II) phthalocyanine-quinoline conjugate was administered to cell lines as a solution in N, N-dimethylacetamide containing 3.8% polyoxyethylene-35-castor oil. Photofrin was administered in phosphate buffered saline. Compared with free PSs, nanoparticle carriers can improve solubility, biodistribution, cellular uptake, retention, delivery to targeted cancer cells, reduce self-degradation and support combination treatments that include PDT. These benefits have been demonstrated in various studies using metal nanoparticles that are enclosed within different shells that contain the PS [39]. Silver and gold nanoparticles are among the most studied examples [40]. Metal oxide nanoparticles have also been extensively studied as carriers of organic dye PSs in targeted anticancer PDT [41]. Iron oxide nanoparticles are particularly prized for magnetic hyperthermia, magnetic tumor targeting, and magnetic resonance imaging-assisted anticancer PDT [42,43,44,45,46,47].

The main goal of nanomaterial-mediated PDT is controlled, cancer cell-specific, and stimulus-responsive PS release, which may allow metastatic cancer cells to be identified and destroyed before they develop into tumors [46,47]. Many studies have thus examined PDT methods that target metastatic cells. Photoimmunotherapy combines PDT with immunotherapy by linking the PS to a monoclonal antibody or a biologically recognizable antibody fragment. The conjugate binds selected antigens and supports precise drug delivery, and also induces an anticancer immune response [48]. In another study, a peptide that cysteine protease Cathepsin B can cleave was used to attach the PS Verteporfin to gold nanoparticles. After cancer cells had internalized the nanoconjugate, the peptide linker was cleaved and released the PS [49].

2.3 Antimicrobial Photodynamic Therapy

PDT began as a cancer treatment, but it is now used against many conditions. Antimicrobial PDT is one of its main applications, targeting bacterial, fungal, and viral infections. It is also used for environmental sanitization and pest control [50]. Researchers have studied antimicrobial PDT against viral infections, including the recent COVID-19 pandemic [51], as well as bacterial [52] and fungal infections [53]. Other studies have looked at its use in environmental sanitization [54]. Examples of antibacterial PDT include treatments for periodontal disease [55,56], superficial wounds [57], and burns [58]. The method may be valuable in developing countries, where bacterial infections cause many deaths and widespread antibiotic use is accelerating the rise of bacterial resistance [59].

Biofilm formation contributes to resistance in some bacterial and fungal infections. This process includes planktonic microbial quorum sensing [60], adhesion to a surface, colony development, maturation, and biofilm formation. Microbes can later detach from the biofilm and also attach to another site, where the cycle starts again as the biofilm expands [61,62]. During its life cycle, bacterial cells are suspended within or embedded in the biofilm. The biofilm contains an extracellular polymeric substance matrix, composed of polysaccharides, proteins, peptides, nucleic acids, and lipids. This structure makes the embedded bacterial cells difficult to reach [63,64,65]. Antibacterial PDT can overcome this resistance mechanism by breaking down the extracellular polymeric substance matrix and exposing the bacterial cells within it [66,67].

Nanoconjugates that contain PSs are the most widely reported strategy for antibacterial PDT, compared with the use of free PSs [68]. Their design allows the PS to remain loosely bound within the conjugate while retaining its ability to produce reactive oxygen species [69]. Some nanoparticles can also act as antibacterial PDT PSs without an additional carrier. Common examples include porphyrin [70] and phthalocyanine nanoparticles [71], metallic silver [72] and gold nanoparticles [73], copper sulfide nanoparticles [74], and nanographene, zinc [75], and iron oxides [76]. Many magnetic metal chalcogenide nanomaterials can convert light and magnetic energy into heat, and thus, they are used in combined therapies involving PTT, MGH, and PDT. Iron oxide nanoparticles, for example, have been applied in combinations of MGH, PTT, and PDT [63]. Studies have also found that nanographene oxide and copper sulfide nanoparticles can act as both PTT and PDT agents [70,76].

For antibacterial PDT, carefully designed nanoconjugates can release the PS in response to infection-related conditions, which include the lower pH, limited oxygen supply, and altered levels of enzymes and hydrogen peroxide found in biofilms compared with normal tissue [77,78].

3. Applications of Photodynamic Therapy

Acne develops when hair follicles become blocked with oil and dead skin cells, allowing bacteria and fungi to grow, especially on the face. Antibacterial PDT may treat these infections [70]. Wet age-related macular degeneration results from abnormal blood vessels growing at the back of the eye and damaging the macula [79]. PDT destroys these vessels, allowing for new vessels to develop normally [80]. Atherosclerosis occurs when plaque builds up along the inner arterial lining, causing the arteries to thicken or harden [81]. Psoriasis causes rapid skin-cell growth, which leads to an itchy scalp and flaky skin. [82]. Recent viral pandemics, particularly the COVID-19 pandemic, have increased interest in antiviral PDT [83]. Studies demonstrate that PDT can destroy viruses, bacteria, and fungi [84]. It has been tested for environmental sanitation, including the treatment of work surfaces, where the reactive oxygen species produced by PDT can kill microorganisms. The method has been studied as a pesticide against insect larvae [85]. PDT now extends beyond cancer and bacterial infections to acne [86,87], wet age-related macular degeneration [88,89], atherosclerosis [90,91], psoriasis [92,93], and antiviral therapy [94,95]. These antiviral applications include treatment of herpes [96,97] and COVID-19 [98]. Research has also examined PDT for environmental sanitation [99] and pest control [100]. The method is among the most widely used therapeutic techniques in dermatology [101,102].

4. Combinations of Photodynamic Therapy

PDT is a minimally invasive method for treating an expanding range of diseases [103]. Some limits affect its performance. These include poor solubility of photosensitizers (PSs), shallow tissue penetration by the activating light, and low oxygen levels in many disease sites. Other concerns include insufficient PS delivery after systemic circulation and poor selectivity at the tissue and cell levels [104]. These problems can limit PDT efficacy in vivo, even when a PS performs well in vitro. Combining PDT with other minimally invasive treatments has been studied as a way to improve its performance in these areas [105]. The aim is to increase efficacy and clinical use of the combined treatment.

The term combination has broad use in drug development. In this review, it refers to the use of several technologies, each with established therapeutic applications. The non-invasive and minimally invasive methods discussed here act through different physical and biological mechanisms. They can target different cell organelles, processes and produce several biological responses. The combined actions can produce complex effects that enhance one another, act independently, and interfere with one another. Combination therapies are therefore classified according to their effect on efficacy. If the combined treatment is more effective

than the sum of its separate effects, the result is synergistic. Equal efficacy produces an additive effect. Lower efficacy than the summed individual effects may indicate antagonism [106]. For example, an in vitro study used PDT with meso-tetrakis(3-hydroxyphenyl) chlorin as the PS and tested it with the drugs carboplatin, cisplatin, and oxaliplatin. The use of the methyl thiazole tetrazolium assay demonstrated synergy between oxaliplatin and three cancer cell lines. [107].

One cause of drug resistance is the failure of drugs to enter target cells [108]. To improve endocytosis and overcome doxorubicin resistance, researchers prepared a nanoconjugate using a doxorubicin-loaded calcium carbonate core and a shell of human serum albumin linked to the PS. The combined treatment produced a synergistic increase in antiproliferative activity in vitro [109]. By contrast, a more than two decades old proposal for combining radiotherapy with PDT indicated a generally additive effect [110]. Later studies have largely supported this finding [111]. A sub additive result was reported for PDT using methylene blue combined with erlotinib chemotherapy against human epidermoid carcinoma A431 cell lines in vitro [112].

5. Applications of Nanomaterials in Combination Therapies with Photodynamic Therapy

Before nanotechnology became widely used, studies of PDT mostly relied on the direct administration of free PSs. After remaining in systemic circulation for a period, these agents often accumulated preferentially in cancer tissue, increasing their concentration at the disease site. This selective distribution followed by photosensitization and the production of reactive oxygen species, forms the basis of PDT. It allows greater PS to reach diseased tissue and cells, than healthy cells in other parts of the body. As PDT moved towards clinical use, the level of preferential accumulation achieved by free organic dye PSs, proved too low to provide the required degree of disease targeting and selectivity. Early combination treatments used free PSs together with another therapeutic agent, either through separate administration or directly mixing the agents without nanomaterials. Many examples of this approach have been reported [113,114].

Nanotechnology not only improves PS selectivity for diseased cells over host tissue; it also supports combinations of PDT with other noninvasive treatments and can increase therapeutic efficacy [13]. This progress led to new strategies for target-cell specificity based on carefully designed nanoconjugates that contain PSs. PTT and MGH are often combined with PDT, and both already depend on nanomaterials. Nanotechnology has extended PDT beyond cancer treatment, to bacterial, fungal and viral infections. By increasing target specificity, nanomaterials can reduce the systemic dose needed to deliver large amounts of PS to diseased tissue and cells, which may help limit the development of resistance, especially among microbial pathogens [109]. Greater selectivity for diseased cells has supported combinations of PDT with chemotherapy. One possible benefit is reuse of chemotherapy drugs that became ineffective after resistance developed against them [109].

Although these systems vary widely in their design and fabrication, nanomaterials used to deliver PSs and other drugs fall into two main groups: organic and inorganic nanoparticles [115]. Organic nanoparticles include those made from carbon compounds, while inorganic nanoparticles include particles made from metals and metal chalcogenides [116]. More broadly, organic nanoparticles are produced from carbon-based compounds, whereas inorganic nanoparticles are made from noncarbon materials [117]. The boundary between these groups is not fixed. Some researchers classify carbon-based materials, including graphene, fullerenes, and carbon nanotubes, as inorganic rather than organic nanoparticles [118,119]. PSs can be added to nanoparticles through surface adsorption, absorption, covalent attachment or encapsulation. Incorporating the PS can increase preferential accumulation, as disease cells can take up and retain these particles through the enhanced permeability and retention effect. Nanoconjugates can also improve the stability and biocompatibility of systems containing PSs and other drugs, helping prevent immune responses during systemic circulation.

6. Combinations of Photodynamic Therapy with Chemotherapy

Chemotherapy refers to the use of chemical compounds to destroy rapidly growing cells in the body. It is used to treat both cancer and microbial infections [120]. Most chemotherapy drugs currently used in clinical practice originated from basic research that examined natural sources. This work was followed by chemical and biochemical studies, including synthesis and structural modification, to support structure-activity research and improve drug efficacy and selectivity [121]. Candidate compounds reach clinical use through preclinical testing and clinical trials. The growing problem of drug resistance has encouraged research into

International Journal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

https://ijpsat.org/
Vol. 59 No. 1 September 2026, pp. 847-871

PDT and other treatment options [120,122], many of which have produced encouraging clinical results [123]. Chemical changes to established drugs are one way to address chemotherapy resistance. More recently, combining chemotherapy drugs with PDT has gained attention because the approach may reduce resistance, increase treatment effects and selectivity [122]. Chemotherapy includes both antibiotic and anticancer treatments. Antibiotic chemotherapy targets infectious agents, while anticancer chemotherapy targets malignant cells. Resistance has affected both forms to varying degrees [120].

Combining antibiotic chemotherapy with PDT has generally improved activity against several microbial pathogens [124]. One example is an in vivo study of third-degree burn wounds, using the PS protoporphyrin IX with ceftriaxone sodium, a broad-spectrum antibiotic. Photoactivation produced large amounts of reactive oxygen species and caused a synergistic reduction in the growth of methicillin-resistant S. aureus, E. coli, and P. aeruginosa [125]. In another study, PDT with the PS Chlorin-e6 was combined with ciprofloxacin. The treatment improved bacterial growth inhibition and showed promise as an approach for urinary tract infections [126]. Optimization studies also examined antibacterial PDT with ciprofloxacin, amikacin, and colistin, as shown in Figure 3. For E. coli suspensions treated with ciprofloxacin, the strongest bactericidal effect occurred with 100 μg/mL Chlorin-e6 and a light energy dose of 120 J/cm2 [127].

The combined use of PDT with antibiotic chemotherapy, involving methylene blue as the PS and ciprofloxacin as the antibiotic, resulted in synergistic effects. Biofilm reduction depended on the light dose but not on the PS concentration, reaching 10^-5.4 for S. aureus and 10^-7 for E. coli [128]. More recently, combining ciprofloxacin 1 with antibacterial PDT based on positively charged porphyrin 4 and phthalocyanine PS complexes 5 produced log10 biofilm reductions of 7.05 for S. aureus and 7.20 for E. coli. The PS-to-antibiotic concentrations were 8 μM to 2 μg/mL and 8 μM to 4 μg/mL, respectively [129]. Several reviews have reported synergistic effects when PDT is combined with chemotherapy. Ahmed El-Hussein et al. (2021) for example, found that most chemotherapy drugs used with PDT produced synergistic effects against lung cancer [130]. Reviews by Pérez-Laguna et al. (2019) also described benefits from combining aPDT with antibiotic chemotherapy, including shorter treatment periods, lower antibiotic doses and toxicity, and reduced development of drug resistance [127,131].

7. Photochemical Internalization

Photochemical internalization (PCI) was first developed to deliver macromolecular drugs into the cytosol. The method also supports PS entry into diseased cells by enclosing the PSs in endocytic liposome vesicles [132,133]. After the vesicles have entered the cell cytosol, light activation causes photodynamic breakdown of their membranes. This releases both the aqueous core contents and the compounds incorporated into the membrane bilayer into the cytosol. In PCI, the PS concentration within the vesicle membrane must be high enough to cause photodynamic rupture but low enough to avoid PDT-induced cell death [134]. Many studies have examined PCI-mediated chemotherapy drug delivery [135]. For example, PCI delivery increased the effectiveness of bleomycin [136]. The light-triggered release of chemotherapy drugs via PCI may provide an effective combination of PDT and chemotherapy [137]. For PDT, liposomal PS formulations contain enough PS to rupture the endocytosed liposome and induce PS-mediated cell death. Treatment of wet macular degeneration provides one example. It uses a liposomal formulation of benzoporphyrin derivative, marketed as Visudyne®, with a PS concentration high enough to ablate macular cells [138]. Another liposomal formulation contains meso-tetrakis(3-hydroxyphenyl)chlorin and is marketed as Foscan® for the palliative treatment of head and neck cancers [139]. In a recent review, Rak et al. (2023) described liposomal phthalocyanine complexes of aluminum, silicon and iron, marketed as Photosens, Phthalocyanine-4 and Phtalox, respectively, for anticancer and antibacterial use, along with other liposomal formulations [140].

The main distinction between PCI and liposomal PS-formulation PDT may be the PS-to-lipid ratio. A low ratio should open the PCI vesicle through photodynamic action, without causing additional PS-mediated cell ablation. For PDT, the ratio must also be high enough to produce cell death. This view agrees with a recent review that defined PCI as a specialized PDT method for combining PDT with chemotherapy and immunotherapy, among other treatments [141].

International Journal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

https://ijpsat.org/
Vol. 59 No. 1 September 2026, pp. 847-871

8. Combinations of Photodynamic Therapy with Photothermal Therapy

Nanoparticles can convert absorbed light into heat through resonance involving their low-lying conduction electrons [142,143]. This photothermal conversion forms the basis of photothermal hyperthermia therapy, which has possible uses against cancer [144] and microbial infections [145]. Combining this treatment with PDT can increase therapeutic efficacy, often through synergistic effects [146,147]. When nanoconjugates carry and release therapeutic agents, photothermal conversion can provide an external trigger for releasing PDT PSs and chemotherapy drugs from the nanoconjugate [148]. Among the many nanomaterials that show plasmon resonance and photothermal conversion, gold nanoparticles are among the most studied. Gold nanorods have the highest photothermal conversion efficiency [149]. Each nanorod has two plasmonic resonance absorption bands in its electronic absorption spectrum: a strong band in the near-infrared region and a weaker band in the blue region [150]. The near-infrared band is used to activate nanorods for photothermal conversion [151]. Some metal chalcogenide nanostructures, including copper sulfide nanoparticles, provide both photothermal conversion and reactive oxygen species generation, and are therefore well suited for combined PTT and PDT [152]. Light penetration into tissue limits PTT as well as PDT, and this also restricts their combined use [153]. Some reviews describe PDT as a way to increase the sensitivity of the cancer microenvironment to PTT [126]. Others report mutual enhancement, with PTT-generated heat improving tissue perfusion and oxygenation [147].

Nanoparticles capable of photothermal conversion can be loaded with PS molecules to combine PTT and PDT in a single nanomaterial system [154]. In one study, superparamagnetic iron oxide nanoparticles were coated with 3-aminopropyl silane and loaded with indocyanine green as the PS. The resulting nanoconjugate had a superparamagnetic iron oxide core and a shell containing 3-aminopropyl silane and labile indocyanine green. Under combined PTT and PDT conditions, in vitro treatment completely eradicated Gram-negative P. aeruginosa and produced a 7-log reduction in Gram-negative E. coli [155]. The nanoconjugate was ineffective against Gram-negative K. pneumoniae and Gram-positive S. epidermis. Temperature measurements and reactive oxygen species assays confirmed that both PTT and PDT were active in the study. The self-assembly of zinc (II) phthalocyanine functionalized with a 3-(dimethylamino) phenoxy group (6) produces phthalocyanine nanoparticles. These particles are made entirely from the organic dye PS and can convert light into heat through plasmonic effects. The reaction scheme appears in Figure 5. The particles act as both PS and photothermal agents, enabling PTT and PDT together. Under brief 655 nm laser irradiation and at an ultralow nanomolar concentration, this combination completely inhibited methicillin-resistant S. aureus growth [156]. The study confirms that organic dye PS self-assembly can generally produce nanostructures with photothermal conversion ability. In a separate study, an indocyanine green PS nanostructure was coated with poly(2-(dimethylamino)ethyl methacrylate) to create a positively charged particle. It showed strong photothermal and photodynamic antibacterial effects and eradicated P. gingivalis in vitro and in vivo [157]. Although recent reports identified several challenges, this combination can lower cytotoxicity, improve the solubility of drugs and PSs, and increase therapeutic effects through synergy [154].

9. Combinations with Magnetic Hyperthermia

Magnetic hyperthermia involves exposing magnetic nanoparticles to a high-frequency alternating magnetic field, which raises the temperature of the surrounding medium [158]. Like photothermal hyperthermia, it has gained attention as a treatment method for cancer [159] and microbial infections [160]. Researchers have also examined its possible use against atherosclerosis and thrombosis [161]. Magnetic hyperthermia does not face the light-penetration limits associated with photothermal hyperthermia. Alternating magnetic fields pass through biological materials with relative ease, reaching depths greater than 500 mm [162]. Clinical translation is illustrated by work at MagForce Charité Hospital in Berlin, where magnetic hyperthermia trials were conducted in patients with glioblastoma multiforme, prostate tumors, and pancreatic tumors [163]. The method has also been combined with PDT for cancer treatment, with promising findings [164]. In both PDT-photothermal hyperthermia and PDT-magnetic hyperthermia, PDT produces reactive oxygen species, while the hyperthermia method supplies heat. The first combination uses photothermal heating, while the second uses magnetic heating. Few studies have examined magnetic hyperthermia combined with PDT against microbial infections compared with its use in cancer and other conditions [50]. The limited research may reflect the complex equipment and infrastructure required. Photothermal hyperthermia needs much less costly and specialized equipment.

International Journal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

https://ijpsat.org/
Vol. 59 No. 1 September 2026, pp. 847-871

A direct magnetic field has also been paired with PDT using chlorin e6-loaded, mesoporous silica-capped iron oxide magnetic nanoparticles. Although this approach did not generate heat through an alternating magnetic field, it moved the magnetic particles deeper into the biofilm [165]. In another study, superparamagnetic iron oxide nanoparticles were capped with curcumin as the PS. The resulting nanoconjugate showed effective magnetothermal conversion under a high-frequency alternating magnetic field alone. It also produced strong PDT activity under blue light alone, without the alternating magnetic field, and eradicated planktonic S. aureus. However, the study did not investigate magnetic hyperthermia and PDT together through simultaneous exposure to the alternating magnetic field and blue light. Even so, it completed the key preliminary work. The researchers capped the nanoparticles with curcumin and measured the PDT effect and magnetothermal conversion curves separately, creating a basis for combined magnetic hyperthermia and PDT against bacteria [166]. Several research reports describe nanomaterial-based approaches, although reviews of PDT combined with MGH remain scarce. One example involves liposomes containing magnetic iron oxide nanoparticles in their hydrophilic core and the organic dye PS meso-tetra(3-hydroxyphenyl) chlorin within the membrane bilayer [167]. Another involves a Janus Nanobullet in which chlorin e6 is released from mesoporous silica heads in response to changes in pH and redox potential. A disulfide bond connects the PS to the nano bullet heads [168].

10. Combinations of Photodynamic Therapy with Cold Atmospheric Pressure Plasma

Cold atmospheric pressure plasma develops when gas flows between electrodes at a high direct or alternating voltage. The discharge has high concentrations of reactive gas species, including reactive oxygen species, which are also formed during PDT photosensitization [157]. Electric field causes electron removal from gas molecules and the formation of cations, radicals, and free electrons. Collisions with these particles and gas molecules lead to further ionization, radical formation, and electron release as the gas flows. The process takes place at nearly ambient temperature and pressure with only a slight temperature increase. These characteristics define CAP, whose components can destroy diseased cells on contact. CAP discharge can be applied directly to wounds during in vivo and clinical treatment [158]. In vitro studies have also applied it to the surface of growth media containing bacterial test cell lines [159]. Researchers have combined CAP therapy with PDT in basic studies [22] and preclinical research [160]. Interest in this method has grown because plasma produces reactive oxygen and nitrogen species under ambient conditions. The resulting reactive gases can be applied directly to disease sites or transferred to suitable stabilizing media, frozen at ultralow temperatures, and stored for later use [161]. These properties support combinations of CAP with other noninvasive treatments, including PDT [162], chemotherapy [163], and electrochemotherapy [164]. Such combinations have been studied for antibacterial treatment during burn and wound healing [165], tissue regeneration [166], and environmental antiseptic sanitation [167].

CAP technology has shown strong potential for anticancer applications [79,163]. Over the past two decades, research on its use against bacterial infections has also increased, with highly promising findings [168,169]. The World Health Organization has identified PDT and CAP therapy as leading new technologies for removing bacterial pathogens amid the growing problem of drug resistance [170]. Recent studies have examined the combined use of PDT and CAP against several bacterial infections. For instance, an adhesion and sealer penetration study using the pushout method found that combining CAP with PDT produced a positive effect. However, the study found no link between adhesion and sealer penetration [171].

The role of equipment and device design in studies of combined CAP and PDT treatment has also been emphasized. After a plasma device proved unsuitable in a comparative study of CAP and antimicrobial PDT, researchers recommended further work with improved study designs [172]. A later study conducted under different conditions found that CAP and PDT increased pushout bond strength [173]. The first study of its kind reported that combining CAP and PDT produced a synergistic increase in vitro against skin and wound pathogens [174]. Reviews of PDT combined with CAP remain limited [175]. Still, several reports have described new approaches that unite the two treatments. One example used a self-assembled polymer nanoconjugate containing pheophorbide as the PS, together with CAP, to improve activity against human papillomavirus (HPV)-positive cervical cancer [22]. In another study, curcumin and methylene blue served as PSs in combination with CAP and increased PDT activity against E. faecalis from molar root canal infections [176]. CAP is already used clinically in plasma medicine [177], while PDT has many FDA-approved clinical applications [178]. Their combined use therefore has strong clinical potential and may reach clinical practice rapidly.

International Journal of Progressive Sciences and Technologies (IJPSAT)
ISSN: 2509-0119.

https://ijpsat.org/
Vol. 59 No. 1 September 2026, pp. 847-871

11. Combinations of Photodynamic Therapy with Sonodynamic Therapy

Besides radiation therapy, which produces ionizing radiation, magnetic hyperthermia [146] and SDT [9] have emerged as treatments that may address the limited light penetration of PDT. Magnetic hyperthermia changes part of the energy from a high-frequency alternating magnetic field into heat through magnetic nanoparticles placed in the target tissue [11,146]. SDT has a mechanism similar to PDT, but it uses low-energy ultrasound, which penetrates tissue more deeply than light [179]. The treatment activates an SDT sensitizer with ultrasound to kill diseased cells by producing reactive oxygen species [180]. This creates oxidative stress and disrupts the biochemical systems that maintain cellular redox balance.

Combining the two methods is conceptually straightforward. Light and ultrasound can be applied at the same time after the sonosensitizer has accumulated at the disease site. Many compounds identified as sonosensitizers also function as PSs [181].

Several reviews have examined combined PDT and SDT treatments for cancer and bacterial infections [182,183]. Research interest is growing in diseases that affect bone and tissues with limited light access, including osteosarcoma [179], osteomyelitis [184], periodontal disease [185], pancreatic disease [186], hepatic disease [187], and brain disease [188]. As with PDT, SDT works by generating reactive oxygen species. Sonoporation has an important role in the absorption, distribution, and retention of the sonosensitizer [189]. The growing number of patents and clinical case studies indicates that clinical translation has begun. For example, Harbin Engineering University and Harbin Medical University filed a patent in 2011 [190]. An earlier patent was filed by Science Group Pty. Ltd. [191].

Curcumin has been widely studied as a sonosensitizer for atherosclerosis [192,193] and bacterial infections [194]. One study examined curcumin as a possible sono-PS for photo-SDT and found improved antibiofilm activity and wound healing in mice infected with A. baumannii [195]. The study demonstrates how one sensitizer can be used in combined SDT and PDT. Rose Bengal [196] and Chlorin e6 [197] can both act as PSs and sonosensitizers, although their activity differs. Combined sonodynamic therapy and PDT using Rose Bengal and Chlorin e6 at molar ratios of 1:1 and 1:3 produced a synergistic increase in reactive oxygen species and improved activity against methicillin-resistant S. aureus [198]. This work shows how two sono-PSs can be used together, with each responding mainly to one form of stimulation. Both compounds, however, can respond to light and ultrasound. These findings support synergistic increases in antibacterial activity and ROS production.

12. Combinations of Photodynamic Therapy with Immunotherapy

PDT [199] and SDT [200] can activate host immunity. The resulting immune response, however, may not be strong enough to stop bacterial or tumor growth and metastasis [201]. Antitumor immunity involves checkpoint proteins on cancer cells binding to proteins on T-cell membranes. This interaction prevents T cells from attacking the cancer cells. Checkpoint blockade immunotherapy stops these proteins from binding, allowing the induced immune response to act against the tumor [202]. The treatment uses inhibitors that attach either to checkpoint proteins or to their targets on T cells, blocking the interaction [203]. Figure 6 illustrates the mechanism of checkpoint blockade immunotherapy.

Combining SDT or PDT with checkpoint blockade immunotherapy can strengthen innate antitumor immunity and improve treatment efficacy. Reviews have identified this effect as one reason for using the combined approach [94,204]. In one study, hematoporphyrin monomethyl ether was used as the sonosensitizer with the immune-modulating adjuvant R837. Both agents were enclosed in the same liposome. The treatment stopped primary xenograft growth and prevented lung metastasis in breast and colorectal cancer models [205]. Another study used a cell membrane-coated nanometal-organic framework containing a sonosensitizer together with the R837 adjuvant. This combination produced a similar synergistic increase in treatment efficacy [206].

Pang et al. (2019) reported the first antibacterial use of this technology. They developed cell membrane nanovesicles containing a sonosensitizer and antibodies that neutralize the alpha-toxin of methicillin-resistant S. aureus. The antibodies were genetically engineered onto the vesicles' outer surface [207]. This study introduced a new approach to antibacterial immunotherapy that combines SDT with other noninvasive treatments. The authors described it as a bioinspired strategy designed to disarm bacterial pathogens rather than kill them, drawing on the natural biology of bacterial immunity. PDT is a localized treatment, but its

combination with immunotherapy could support the treatment of systemic bacterial infections by inducing strong systemic immunity [208].

12. Combinations of Photodynamic Therapy with Radiotherapy

Along with chemotherapy and surgery, ionizing radiation has long been one of the main clinical treatments for cancer [100,209]. PDT has been shown to increase the effects of radiotherapy, possibly because both treatments generate radicals and cause oxidative stress [210]. Radiotherapy and SDT can penetrate human tissue more deeply, whereas the light needed to activate PDT photosensitizers (PSs) reaches only about 2-5 mm into normal tissue [5]. Combining PDT or SDT with radiation therapy therefore provides a basis for further research [211]. Browning et al. (2021) found that SDT reduced tumor perfusion and vascularization when combined with chemotherapy and radiation. It also improved Kaplan-Meier survival curves in a treatment model that used gemcitabine as the anticancer drug [212]. Reviews have examined studies [100] and clinical trials [209] on PDT combined with radiotherapy. These reviews found greater anticancer efficacy with the combined treatment, but they included little discussion of antibacterial uses. Further research is needed. The reviews raise questions about light, ultrasound, radiation, and PS dosimetry, showing that current results remain limited by several technical challenges.

13. The Future of PDT

Interest in PDT continues to grow, supported by research groups in many countries. Current work focuses on developing new PSs, studying PDT mechanisms at the molecular level, improving treatment through combined therapies, and identifying possible clinical uses [163]. Many countries have approved PDT PSs and light applicators for clinical use, but the number of approved indications remains small. Pharmaceutical companies and research institutes are expected to continue clinical trials that assess PDT as both an addition to and a replacement for standard oncological and non-oncological treatments. Optical methods and nanotechnology will remain important for characterizing target tissues, setting the PDT dose, and measuring treatment outcomes. Combined treatments, personalized planning, and dosimetry will also remain central to PDT research. In 1993, Canada became the first country to approve Photofrin® for bladder cancer. The Netherlands and France soon approved the drug for advanced esophageal and lung cancer. Germany focused on early-stage lung cancer, while Japan expanded Photofrin® use to cancers of the esophagus, stomach, and cervix, as well as cervical dysplasia. Canadian clinical trials showed that PDT with Photofrin® greatly reduced bladder cancer recurrence after surgery. Photosensitivity and urinary symptoms remained common side effects. The results supported further studies on dose optimization. In 1995, the FDA approved Photofrin® for partially obstructive esophageal cancer after successful phase III clinical trials. Compared with Nd-YAG laser ablation, PDT produced longer tumor responses and more complete responses with fewer treatment sessions. One year later, Biel's studies of early head and neck cancers reported complete responses in patients with superficial laryngeal tumors and tumors at other head and neck sites. In 1997, the largest study of PDT for superficial esophageal cancer showed a clear reduction in dysplasia among patients with Barrett's esophagus.

Another major development came in 1999, when the FDA approved verteporfin (Visudyne®) for submacular neovascularization linked to AMD. Around the same time, dermatologists began using PDT with ALA and MAL to treat actinic keratosis, with high rates of effectiveness.

Between 2001 and 2005, the European Medicines Agency (EMA) approved Foscan® for advanced squamous cell carcinoma of the head and neck. Studies of verteporfin PDT for hemangiomas reported substantial improvements in patients' conditions. Research also began on PDT for cholangiocarcinoma (CC) and on newer drugs, including Tookad® and its derivative WST-11. These agents opened a new treatment period because they activate rapidly within blood vessels.

In 2006, studies of Photofrin® PDT for lung cancer found increased VEGF and MMP expression. The findings suggested that blocking these factors could improve treatment results. In 2007, PDT was applied in dermatology and microbiology. Studies of actinic cheilitis and Bowen's disease reported high effectiveness with MAL-based PDT. In 2009, PDT was identified as a promising treatment for localized nasopharyngeal carcinoma (NPC). Studies of anal cancer also showed that Photofrin® PDT was effective and could reduce pain and treatment-related complications. Between 2010 and 2015, further studies assessed 5-ALA and mTHPC PDT for potentially malignant oral diseases and papilloma acuminata. PDT was also shown to treat warts and peri-

implantitis effectively. A 2015 study comparing MAL PDT with imiquimod for actinic lesions found both treatments effective, although patients preferred MAL PDT. In 2016, studies confirmed the safety and effectiveness of HPPH PDT for early laryngeal disease. PDT with hemoporfin also produced substantial improvement in patients with port-wine stains. In 2017, PDT showed high effectiveness for vulvar lichen sclerosus. In 2018, it was used successfully to treat rosacea. A 2019 study found that combining PDT with minimally invasive spinal stabilization procedures for vertebral compression fractures (VCF) could improve mechanical stability. Research during the past five years has shown that PDT can treat warts and lower their recurrence rate. In 2022, studies of PDT for herpetic gingivitis reported clear improvements in patients' conditions. In 2023, indocyanine green (ICG) PDT for keloids effectively reduced the cellular activity of keloid fibroblasts. Research on PDT against SARS-CoV-2 also confirmed that the treatment is safe and can reduce viral infectivity.

PDT is a promising cancer treatment, but several barriers limit its effectiveness and remain under active study. One of the main challenges is the shallow penetration of light. PDT uses the light needed to activate the photosensitizer, which can only reach limited depths in tissue.

Another major limitation of PDT is the toxicity of photosensitizers, particularly prolonged photosensitivity. This effect may continue for several weeks after treatment. To lower this risk, researchers are developing newer photosensitizers that leave the body more quickly. ALA derivatives are one example. They are broken down faster than older photosensitizers, which shortens the period when patients remain sensitive to light. Researchers are also developing photosensitizers that respond only to selected light wavelengths. This feature may reduce accidental activation by sunlight [164]. The nonspecific spread of photosensitizers through the body creates another serious concern. These drugs may damage healthy tissues near the tumor. Several methods are being studied to direct photosensitizers toward cancer cells. Monoclonal antibodies can bind to specific targets on tumor cells and carry the drug to them. This may reduce drug buildup in healthy tissues. Nanotechnology has also produced promising results. Nanoparticles can transport photosensitizers, improve their delivery to tumors, and raise drug levels at the treatment site. One example is a nanoparticle containing protoporphyrin IX (PpIX). Such carriers have shown greater treatment effects and lower toxicity in nearby healthy tissues [165]. Tumor hypoxia is another significant limitation due to its ability to reduce the efficacy of PDT. The photodynamic reaction requires oxygen to create ROS or reactive oxygen species that are responsible for destroying cancerous cells. Many tumors, especially large tumors, have poorly oxygenated regions which considerably reduce the effectiveness of treatment. Several approaches attempt to overcome the challenge by introducing oxygen-releasing substances close to the tumor during treatment either before or during the photobleaching process. Researchers are also developing photosensitizers that operate efficiently in low-oxygen environments. These new photosensitizers may prove effective in PDT treatment of poorly oxygenated tumors.

The above developments will further increase the clinical applicability of PDT and its potential. PDT is particularly valuable for superficial tumors and as a rescue therapy for treatment-resistant diseases. The new photosensitizers, methods of using nanoparticles, and improved methods of light delivery will define the future development of PDT as a cancer treatment.

II. Conclusions

PDT has evolved over time from simple observations of the effects of light on the human body to a complex treatment involving new and sophisticated techniques for disease control and management. PDT is based on the use of photosensitizers that are activated by light of a specific wavelength to generate reactive oxygen species that target and destroy abnormal cells. PDT has become widely accepted and used in the treatment of skin cancer, head and neck cancer, bladder cancer, and gastrointestinal cancer after years of extensive clinical trials.

Developing new photosensitizers with increased targeting specificity to cancerous cells and reduced photosensitivity is among the most significant achievements in the field of PDT. The new photosensitizers have reduced unwanted side effects and enhanced patient compliance due to a shorter duration of photosensitivity. Additionally, the combination of new photosensitizers and laser technologies has enabled clinicians to target cancerous cells with more precision, minimizing tissue damage during the PDT treatment. These developments have ultimately improved the overall efficacy of PDT therapy in clinical practice.

Several challenges in the application of PDT present significant barriers to its clinical use and require further research. For example, light does not penetrate far into the tissues during PDT treatment. Therefore, clinicians can only use PDT to target superficial tumors. Researchers are working on alternative methods of delivering light to the targeted cells including the use of longer wavelengths, fiber optics, and innovative agents for increasing light diffusion. Another challenge in the application of PDT is the photosensitivity of the skin to light even weeks after administration of certain photosensitizing agents. This occurrence significantly limits the PDT-treated patients from engaging in outdoor activities. Newer photosensitizing agents with reduced photosensitivity effects and shorter duration act as an elixir to this problem.

Developing alternative and more effective photosensitizers that selectively target cancerous cells while avoiding healthy cells is another significant challenge in the field of PDT. Ideally, photosensitizing agents with targeting mechanisms should be used in cancer treatment to increase the accuracy of PDT. Another opportunity exists in the combination of PDT with immunomodulatory agents, gene therapy, and other targeted treatment to maximize efficacy and ensure long-term remission of cancer.

The establishment of standard PDT protocols in preclinical and clinical cancer research presents an opportunity for maximizing the efficacy and safety of treatment. It is critical that clinicians devise treatment regimens based on drug dosage, photosensitizing agents, wavelength, and exposure time to achieve maximum efficacy of PDT for different applications including cancer treatment. Understanding the cellular and molecular mechanisms of PDT will also enhance clinical applicability of PDT in fighting cancer. The overall role of PDT in clinical oncology will be enhanced in the future by a more comprehensive understanding of its application in patient management.

Funding

The author(s) declare that no financial support was received for the research and/or publication of this article.

Conflict of Interest

All authors declare no conflicts of interest.

Author Contribution

Authors have equally participated and shared every item of the work.

References

[1]- Auler, Hans, and Georg Banzer. "Untersuchungen über die Rolle der Porphyrine bei geschwulstkranken Menschen und Tieren." *Zeitschrift für Krebsforschung* 53.2 (1942): 65-68.

[2]- Lin, Yuyan, et al. "Chemical approaches for the enhancement of porphyrin skeleton-based photodynamic therapy." *Journal of enzyme inhibition and medicinal chemistry* 35.1 (2020): 1080-1099.

[3]- Kruger, Cherie Ann, and Heidi Abrahamse. "Utilisation of targeted nanoparticle photosensitiser drug delivery systems for the enhancement of photodynamic therapy." *Molecules* 23.10 (2018): 2628.

[4]- Hong, Liang, et al. "Recent advances in strategies for addressing hypoxia in tumor photodynamic therapy." *Biomolecules* 12.1 (2022): 81.

[5]- Barolet, Daniel. "Light-emitting diodes (LEDs) in dermatology." *Seminars in Cutaneous Medicine & Surgery*. Vol. 27. No. 4. 2008.

[6]- Songca, Sandile Phinda. "Combinations of photodynamic therapy with other minimally invasive therapeutic technologies against cancer and microbial infections." *International Journal of Molecular Sciences* 24.13 (2023): 10875.

[7]- Algorri Genaro, José Francisco, et al. "Light technology for efficient and effective photodynamic therapy: A critical review." (2021).

[8]- Liu, Hui, et al. "Development and evaluation of a low-cost, portable, LED-based device for PDT treatment of early-stage oral cancer in resource-limited settings." *Lasers in surgery and medicine* 51.4 (2019): 345-351.

[9]- Gong, Zhuoran, and Zhifei Dai. "Design and challenges of sonodynamic therapy system for cancer theranostics: from equipment to sensitizers." *Advanced Science* 8.10 (2021): 2002178.

[10]- Belanova, A., et al. "A mini-review of X-ray photodynamic therapy (XPDT) nonoagent constituents' safety and relevant design considerations." *Photochemical & Photobiological Sciences* 19.9 (2020): 1134-1144.

[11]- Mahmoudi, Keon, et al. "Magnetic hyperthermia therapy for the treatment of glioblastoma: a review of the therapy's history, efficacy and application in humans." *International Journal of Hyperthermia* 34.8 (2018): 1316-1328.

[12]- Breskey, John D., et al. "Photodynamic therapy: occupational hazards and preventative recommendations for clinical administration by healthcare providers." *Photomedicine and Laser Surgery* 31.8 (2013): 398-407.

[13]- Mokwena, Mpho Gift, et al. "A review of nanoparticle photosensitizer drug delivery uptake systems for photodynamic treatment of lung cancer." *Photodiagnosis and photodynamic therapy* 22 (2018): 147-154.

[14]- Nakamura, Yuko, et al. "Nano-drug delivery: Is the enhanced permeability and retention (EPR) effect sufficient for curing cancer?." *Bioconjugate chemistry* 27.10 (2016): 2225.

[15]- Younis, Muhammad Rizwan, et al. "Inorganic nanomaterials with intrinsic singlet oxygen generation for photodynamic therapy." *Advanced Science* 8.21 (2021): 2102587.

[16]- Hao, Yang, et al. "Combinatorial therapeutic approaches with nanomaterial-based photodynamic cancer therapy." *Pharmaceutics* 14.1 (2022): 120.

[17]- Rafique, Rafia, et al. "Photo-induced reactions for disassembling of coloaded photosensitizer and drug molecules from upconversion-mesoporous silica nanoparticles: An effective synergistic cancer therapy." *Materials Science and Engineering: C* 110 (2020): 110545.

[18]- Yu, Xiaojun, et al. "Polydopamine nanoparticle as a multifunctional nanocarrier for combined radiophotodynamic therapy of cancer." *Particle & Particle Systems Characterization* 34.2 (2017): 1600296.

[19]- Huang, Peng, et al. "Photosensitizer-conjugated magnetic nanoparticles for in vivo simultaneous magnetofluorescent imaging and targeting therapy." *Biomaterials* 32.13 (2011): 3447-3458.

[20]- Vines, Jeremy B., et al. "Gold nanoparticles for photothermal cancer therapy." *Frontiers in chemistry* 7 (2019): 167.

[21]- Aghajanzadeh, Mozhgan, et al. "Synergic antitumor effect of photodynamic therapy and chemotherapy mediated by nano drug delivery systems." *Pharmaceutics* 14.2 (2022): 322.

[22]- Ha, Ji-Hui, and Young-Jin Kim. "Photodynamic and cold atmospheric plasma combination therapy using polymeric nanoparticles for the synergistic treatment of cervical cancer." *International journal of molecular sciences* 22.3 (2021): 1172.

[23]- Allison, Ron R., and Keyvan Moghissi. "Photodynamic therapy (PDT): PDT mechanisms." *Clinical endoscopy* 46.1 (2013): 24-29.

[24]- Robertson, Claudine A., D. Hawkins Evans, and Heidi Abrahamse. "Photodynamic therapy (PDT): a short review on cellular mechanisms and cancer research applications for PDT." *Journal of Photochemistry and Photobiology B: Biology* 96.1 (2009): 1-8.

[25]- Castano, Ana P., Tatiana N. Demidova, and Michael R. Hamblin. "Mechanisms in photodynamic therapy: part two—cellular signaling, cell metabolism and modes of cell death." *Photodiagnosis and photodynamic therapy* 2.1 (2005): 1-23.

[26]- Nowak-Stepniowska, Agata, Paulina Pergoł, and Alfreda Padzik-Graczyk. "Photodynamic method of cancer diagnosis and therapy--mechanisms and applications." *Postepy biochemii* 59.1 (2013): 53-63.

[27]- Luksiene, Zivile. "Photodynamic therapy: mechanism of action and ways to improve the efficiency of treatment." (2003).

[28]- Juzeniene, Asta, and Johan Moan. "The history of PDT in Norway: Part one: Identification of basic mechanisms of general PDT." *Photodiagnosis and photodynamic therapy* 4.1 (2007): 3-11.

[29]- Fonseca, S. M., et al. "Triplet-state and singlet oxygen formation in fluorene-based alternating copolymers." *The Journal of Physical Chemistry B* 110.16 (2006): 8278-8283.

[30]- Kessel, David, and Nancy L. Oleinick. "Photodynamic therapy and cell death pathways." *Photodynamic Therapy: Methods and Protocols*. Totowa, NJ: Humana Press, 2010. 35-46.

[31]- Buytaert, Esther, Michael Dewaele, and Patrizia Agostinis. "Molecular effectors of multiple cell death pathways initiated by photodynamic therapy." *Biochimica et Biophysica Acta (BBA)-Reviews on Cancer* 1776.1 (2007): 86-107.

[32]- Mehraban, Nahid, and Harold S. Freeman. "Developments in PDT sensitizers for increased selectivity and singlet oxygen production." *Materials* 8.7 (2015): 4421-4456.

[33]- Li, Xingshu, Songyi Lee, and Juyoung Yoon. "Supramolecular photosensitizers rejuvenate photodynamic therapy." *Chemical Society Reviews* 47.4 (2018): 1174-1188.

[34]- Dyrała, Anna, et al. "Zastosowanie hiperycyny w terapii fotodynamicznej–przegląd badań preklinicznych." *Acta Bio-Optica et Informatica Medica. Inżynieria Biomedyczna* 21.4 (2015).

[35]- Brown, Guy C., and Chris E. Cooper. "Nanomolar concentrations of nitric oxide reversibly inhibit synaptosomal respiration by competing with oxygen at cytochrome oxidase." *FEBS letters* 356.2-3 (1994): 295-298.

[36]- Dougherty, Thomas J., et al. "Photoradiation therapy for the treatment of malignant tumors." *Cancer research* 38.8 (1978): 2628-2635.

[37]- Bonelli, Joaquín, et al. "Improving photodynamic therapy anticancer activity of a mitochondria-targeted coumarin photosensitizer using a polyurethane–polyurea hybrid nanocarrier." *Biomacromolecules* 23.7 (2022): 2900.

[38]- Chen, Juanjuan, et al. "Improved photodynamic anticancer activity and mechanisms of a promising zinc (II) phthalocyanine-quinoline conjugate photosensitizer in vitro and in vivo." *Biomedical Optics Express* 11.7 (2020): 3900-3912.

[39]- Shang, Liang, et al. "Metal nanoparticles for photodynamic therapy: A potential treatment for breast cancer." *Molecules* 26.21 (2021): 6532.

[40]- Shariatzadeh, Siavash, et al. "Metallic nanoparticles for the modulation of tumor microenvironment; a new horizon." *Frontiers in bioengineering and biotechnology* 10 (2022): 847433.

[41]- Kritika, and Indrajit Roy. "Therapeutic applications of magnetic nanoparticles: recent advances." *Materials Advances* 3.20 (2022): 7425-7444.

[42]- Gu, Hongwei, et al. "Synthesis and cellular uptake of porphyrin decorated iron oxide nanoparticles—a potential candidate for bimodal anticancer therapy." *Chemical Communications* 41.34 (2005): 4270-4272.

[43]- Dougherty, Thomas J. "Optical methods for tumor treatment and detection: mechanisms and techniques in photodynamic therapy IX." *Optical Methods for Tumor Treatment and Detection: Mechanisms and Techniques in Photodynamic Therapy IX* 3909 (2000).

[44]- Zhao, Shengzhe, et al. "Multifunctional magnetic iron oxide nanoparticles: an advanced platform for cancer theranostics." *Theranostics* 10.14 (2020): 6278.

[45]- Ansari, Mohammad, et al. "Synthesis and characterization of Cu0. 3Zn0. 5Mg0. 2Fe2O4 nanoparticles as a magnetic drug delivery system." *Journal of Magnetism and Magnetic Materials* 439 (2017): 67-75.

[46]- Farjadian, Fatemeh, et al. "Physically stimulus-responsive nanoparticles for therapy and diagnosis." *Frontiers in Chemistry* 10 (2022): 952675.

[47]- Rahim, Muhammad Abdur, et al. "Recent advancements in stimuli responsive drug delivery platforms for active and passive cancer targeting." *Cancers* 13.4 (2021): 670.

[48]- Songca, Sandile Phinda. "Combinations of photodynamic therapy with other minimally invasive therapeutic technologies against cancer and microbial infections." *International Journal of Molecular Sciences* 24.13 (2023): 10875.

[49]- Demiral, Ayşegül, et al. "Stimuli-responsive theranostic system: A promising approach for augmented multimodal imaging and efficient drug release." *European Journal of Pharmaceutics and Biopharmaceutics* 177 (2022): 9-23.

[50]- Songca, Sandile Phinda, and Yaw Adjei. "Applications of antimicrobial photodynamic therapy against bacterial biofilms." *International journal of molecular sciences* 23.6 (2022): 3209.

[51]- Svyatchenko, Victor A., et al. "Antiviral photodynamic therapy: Inactivation and inhibition of SARS-CoV-2 in vitro using methylene blue and Radachlorin." *Photodiagnosis and Photodynamic Therapy* 33 (2021): 102112.

[52]- Ghorbani, Jaber, et al. "Photosensitizers in antibacterial photodynamic therapy: An overview." *Laser therapy* 27.4 (2018): 293-302.

[53]- Liang, Y. I., et al. "Photodynamic therapy as an antifungal treatment." *Experimental and therapeutic medicine* 12.1 (2016): 23-27.

[54]- Brovko, Lubov Y., et al. "Photodynamic treatment: a novel method for sanitation of food handling and food processing surfaces." *Journal of food protection* 72.5 (2009): 1020-1024.

[55]- Theodoro, Letícia Helena, et al. "Comparison of repeated applications of aPDT with amoxicillin and metronidazole in the treatment of chronic periodontitis: A short-term study." *Journal of Photochemistry and Photobiology B: Biology* 174 (2017): 364-369.

[56]- Hokari, Takahiro, et al. "Effects of antimicrobial photodynamic therapy and local administration of minocycline on clinical, microbiological, and inflammatory markers of periodontal pockets: A pilot study." *International journal of dentistry* 2018.1 (2018): 1748584.

[57]- Sun, Yan, et al. "Antimicrobial photodynamic therapy in skin wound healing: A systematic review of animal studies." *International wound journal* 17.2 (2020): 285-299.

[58]- Zhao, Zhanjuan, et al. "Antimicrobial photodynamic therapy combined with antibiotic in the treatment of rats with third-degree burns." *Frontiers in microbiology* 12 (2021): 622410.

[59]- Liu, Yao, et al. "Antibacterial photodynamic therapy: overview of a promising approach to fight antibiotic-resistant bacterial infections." *Journal of clinical and translational research* 1.3 (2015): 140.

[60]- Dickschat, Jeroen S. "Quorum sensing and bacterial biofilms." *Natural product reports* 27.3 (2010): 343-369.

[61]- Kaplan, J. áB. "Biofilm dispersal: mechanisms, clinical implications, and potential therapeutic uses." *Journal of dental research* 89.3 (2010): 205-218.

[62]- Hu, Yuqing, et al. "A targeted nanozyme based on multiple porphyrins for enhanced photodynamic antibacterial application." *Chemical Engineering Journal* 431 (2022): 133704.

[63]- Muhammad, Musa Hassan, et al. "Beyond risk: bacterial biofilms and their regulating approaches." *Frontiers in microbiology* 11 (2020): 928.

[64]- Karygianni, Lamprini, et al. "Biofilm matrixome: extracellular components in structured microbial communities." *Trends in microbiology* 28.8 (2020): 668-681.

[65]- Amankwah, Stephen, Kedir Abdella, and Tesfaye Kassa. "Bacterial biofilm destruction: A focused review on the recent use of phage-based strategies with other antibiofilm agents." *Nanotechnology, science and applications* (2021): 161-177.

[66]- Kikuchi, Takeshi, et al. "Adjunctive application of antimicrobial photodynamic therapy in nonsurgical periodontal treatment: a review of literature." *International journal of molecular sciences* 16.10 (2015): 24111-24126.

[67]- Sharab, Lina, et al. "Influence of photodynamic therapy on bacterial attachment to titanium surface." *Journal of Oral Implantology* 47.5 (2021): 427-435.

[68]- Qi, Manlin, et al. "Novel nanomaterial-based antibacterial photodynamic therapies to combat oral bacterial biofilms and infectious diseases." *International journal of nanomedicine* (2019): 6937-6956.

[69]- Garapati, Chandrasekhar, et al. "Photodynamic therapy: A special emphasis on nanocarrier-mediated delivery of photosensitizers in antimicrobial therapy." *Arabian Journal of Chemistry* 16.4 (2023): 104583.

[70]- Romero, María Paulina, et al. "Graphene oxide mediated broad-spectrum antibacterial based on bimodal action of photodynamic and photothermal effects." *Frontiers in Microbiology* 10 (2020): 2995.

[71]- Wang, Dong, et al. "Synthesis of self-assembled porphyrin nanoparticle photosensitizers." *ACS nano* 12.4 (2018): 3796-3803.

[72]- Li, Yang, et al. "Surface-coating-dependent dissolution, aggregation, and reactive oxygen species (ROS) generation of silver nanoparticles under different irradiation conditions." *Environmental science & technology* 47.18 (2013): 10293-10301.

[73]- Kim, Hyung Shik, and Dong Yun Lee. "Near-infrared-responsive cancer photothermal and photodynamic therapy using gold nanoparticles." *Polymers* 10.9 (2018): 961.

[74]- Wang, Shunhao, et al. "Plasmonic copper sulfide nanocrystals exhibiting near-infrared photothermal and photodynamic therapeutic effects." *ACS nano* 9.2 (2015): 1788-1800.

[75]- Pourhajibagher, Maryam, and Abbas Bahador. "Enhanced reduction of polymicrobial biofilms on the orthodontic brackets and enamel surface remineralization using zeolite-zinc oxide nanoparticles-based antimicrobial photodynamic therapy." *BMC microbiology* 21.1 (2021): 273.

[76]- Zhang, Tiantian, et al. "Glucose oxidase and polydopamine functionalized iron oxide nanoparticles: combination of the photothermal effect and reactive oxygen species generation for dual-modality selective cancer therapy." *Journal of Materials Chemistry B* 7.13 (2019): 2190-2200.

[77]- Munir, Muhammad Usman, et al. "Recent advances in nanotechnology-aided materials in combating microbial resistance and functioning as antibiotics substitutes." *International Journal of Nanomedicine* (2020): 7329-7358.

[78]- Lv, Xinyi, et al. "Recent advances in pH-responsive nanomaterials for anti-infective therapy." *Journal of Materials Chemistry B* 8.47 (2020): 10700-10711.

[79]- Stahl, Andreas. "The diagnosis and treatment of age-related macular degeneration." *Deutsches Ärzteblatt International* 117.29-30 (2020): 513.

[80]- Browning, Andrew C., Winfried M. Amoaku, and Harminda S. Dua. "Treatment of age-related macular degeneration." *Journal of the Royal Society of Medicine* 97.4 (2004): 166-169.

[81]- Rafieian-Kopaei, Mahmoud, et al. "Atherosclerosis: process, indicators, risk factors and new hopes." *International journal of preventive medicine* 5.8 (2014): 927.

[82]- Makuch, Sebastian, et al. "An update on photodynamic therapy of psoriasis—current strategies and nanotechnology as a future perspective." *International journal of molecular sciences* 23.17 (2022): 9845.

[83]- Fekrazad, Reza, et al. "Photobiomodulation and antiviral photodynamic therapy in COVID-19 management." *Coronavirus Disease-COVID-19*. Cham: Springer International Publishing, 2021. 517-547.

[84]- Demidova, T. N., and M. R. Hamblin. "Photodynamic therapy targeted to pathogens." *International journal of immunopathology and pharmacology* 17.3 (2004): 245-254.

[85]- Shiao, Shin-Hong, et al. "Novel phthalocyanines activated by dim light for mosquito larva-and cell-inactivation with inference for their potential as broad-spectrum photodynamic insecticides." *Plos one* 14.5 (2019): e0217355.

[86]- Boen, Monica, et al. "The role of photodynamic therapy in acne: an evidence-based review." *American Journal of Clinical Dermatology* 18.3 (2017): 311-321.

[87]- Wojewoda, Karolina, et al. "Optimizing treatment of acne with photodynamic therapy (PDT) to achieve long-term remission and reduce side effects. A prospective randomized controlled trial." *Journal of Photochemistry and Photobiology B: Biology* 223 (2021): 112299.

[88]- Songca, Sandile Phinda. "Combinations of photodynamic therapy with other minimally invasive therapeutic technologies against cancer and microbial infections." *International Journal of Molecular Sciences* 24.13 (2023): 10875.

[89]- Yip, Pui Pui, et al. "Triple therapy for neovascular age-related macular degeneration using single-session photodynamic therapy combined with intravitreal bevacizumab and triamcinolone." *British Journal of Ophthalmology* 93.6 (2009): 754-758.

[90]- Houthoofd, Sabrina, et al. "Photodynamic therapy for atherosclerosis. The potential of indocyanine green." *Photodiagnosis and Photodynamic Therapy* 29 (2020): 101568.

[91]- Jain, Manish, et al. "Photodynamic therapy for the treatment of atherosclerotic plaque: Lost in translation?." *Cardiovascular therapeutics* 35.2 (2017): e12238.

[92]- Choi, Young M., Lily Adelzadeh, and Jashin J. Wu. "Photodynamic therapy for psoriasis." *Journal of dermatological treatment* 26.3 (2015): 202-207.

[93]- Tandon, Yasmeen K., Marjorie F. Yang, and Elma D. Baron. "Role of photodynamic therapy in psoriasis: a brief review." *Photodermatology, photoimmunology & photomedicine* 24.5 (2008): 222-230.

[94]- Praena, Beatriz, et al. "Potent virucidal activity in vitro of photodynamic therapy with hypericum extract as photosensitizer and white light against human coronavirus HCoV-229E." *Pharmaceutics* 14.11 (2022): 2364.

[95]- Mfouo-Tynga, Ivan S., and Augustin G. Mouinga-Ondeme. "Photodynamic therapy: A prospective therapeutic approach for viral infections and induced neoplasia." *Pharmaceuticals* 15.10 (2022): 1273.

[96]- Mfouo-Tynga, Ivan S., and Augustin G. Mouinga-Ondeme. "Photodynamic therapy: A prospective therapeutic approach for viral infections and induced neoplasia." *Pharmaceuticals* 15.10 (2022): 1273.

[97]- Marotti, Juliana, et al. "Photodynamic therapy can be effective as a treatment for herpes simplex labialis." *Photomedicine and laser surgery* 27.2 (2009): 357-363.

[98]- Conrado, Pollyanna CV, et al. "A systematic review of photodynamic therapy as an antiviral treatment: Potential guidance for dealing with SARS-CoV-2." *Photodiagnosis and photodynamic therapy* 34 (2021): 102221.

[99]- Bartolomeu, Maria, et al. "Antimicrobial photodynamic approach in the inactivation of viruses in wastewater: Influence of alternative adjuvants." *Antibiotics* 10.7 (2021): 767.

[100]- Songca, Sandile Phinda. "Combinations of photodynamic therapy with other minimally invasive therapeutic technologies against cancer and microbial infections." *International Journal of Molecular Sciences* 24.13 (2023): 10875.

[101]- Wan, Marilyn T., and Jennifer Y. Lin. "Current evidence and applications of photodynamic therapy in dermatology." *Clinical, cosmetic and investigational dermatology* (2014): 145-163.

[102]- Kalka, Katrin, Hans Merk, and Hasan Mukhtar. "Photodynamic therapy in dermatology." *Journal of the American Academy of Dermatology* 42.3 (2000): 389-413.

[103]- Benov, Ludmil. "Photodynamic therapy: current status and future directions." *Medical principles and practice* 24.Suppl. 1 (2015): 14-28.

[104]- Gunaydin, Gurcan, M. Emre Gedik, and Seylan Ayan. "Photodynamic therapy—current limitations and novel approaches." *Frontiers in Chemistry* 9 (2021): 691697.

[105]- Hua, Jianfeng, et al. "Current strategies for tumor photodynamic therapy combined with immunotherapy." *Frontiers in Oncology* 11 (2021): 738323.

[106]- Yuan, Shoujun, and Haoyu Chen. "Mathematical rules for synergistic, additive, and antagonistic effects of multi-drug combinations and their application in research and development of combinatorial drugs and special medical food combinations." *Food Science and Human Wellness* 8.2 (2019): 136-141.

[107]- Lange, Carsten, and Patrick J. Bednarski. "Evaluation for synergistic effects by combinations of photodynamic therapy (PDT) with temoporfin (mTHPC) and Pt (II) complexes carboplatin, cisplatin or oxaliplatin in a set of five human cancer cell lines." *International Journal of Molecular Sciences* 19.10 (2018): 3183.

[108]- Reygaert, Wanda C. "An overview of the antimicrobial resistance mechanisms of bacteria." *AIMS microbiology* 4.3 (2018): 482.

[109]- Yang, Yuguang, Wei Cui, and Jie Zhao. "Synergistic treatment of doxorubicin-resistant breast cancer by the combination of chemotherapy and photodynamic therapy." *Colloids and Surfaces A: Physicochemical and Engineering Aspects* 648 (2022): 129167.

[110]- Luksiene, Zivile, Audrone Kalvelyte, and Rosanna Supino. "On the combination of photodynamic therapy with ionizing radiation." *Journal of Photochemistry and Photobiology B: Biology* 52.1-3 (1999): 35-42.

[111]- Xu, Jing, Jianqing Gao, and Qichun Wei. "Combination of photodynamic therapy with radiotherapy for cancer treatment." *Journal of Nanomaterials* 2016.1 (2016): 8507924.

[112]- Gontijo, Savio ML, et al. "Sub-additive effects of photodynamic therapy combined with erlotinib for the treatment of epidermoid carcinoma: An in vitro study." *Photodiagnosis and Photodynamic Therapy* 18 (2017): 252-256.

[113]- Hosseinzadeh, Reza, Khatereh Khorsandi, and Maryam Jahanshiri. "Combination photodynamic therapy of human breast cancer using salicylic acid and methylene blue." *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 184 (2017): 198-203.

[114]- Khorsandi, Khatereh, Reza Hosseinzadeh, and Elham Chamani. "Molecular interaction and cellular studies on combination photodynamic therapy with rutoside for melanoma A375 cancer cells: an in vitro study." *Cancer cell international* 20.1 (2020): 525.

[115]- Estelrich, Joan, and Maria Antònia Busquets. "Iron oxide nanoparticles in photothermal therapy." *Molecules* 23.7 (2018): 1567.

[116]- Spirescu, Vera Alexandra, et al. "Inorganic nanoparticles and composite films for antimicrobial therapies." *International journal of molecular sciences* 22.9 (2021): 4595.

[117]- Bukhari, Bakhtawar, et al. "A comparison between organic and inorganic nanoparticles: Prime nanoparticles for tumor curation." *Nano* 16.13 (2021): 2130011.

[118]- Bodunde, Ojo P., et al. "A futuristic insight into a “nano-doctor”: A clinical review on medical diagnosis and devices using nanotechnology." *Materials Today: Proceedings* 44 (2021): 1144-1153.

[119]- Greene, Michelle K., Michael C. Johnston, and Christopher J. Scott. "Nanomedicine in pancreatic cancer: current status and future opportunities for overcoming therapy resistance." *Cancers* 13.24 (2021): 6175.

[120]- Chifiriuc, Mariana Carmen, et al. "Common themes in antimicrobial and anticancer drug resistance." *Frontiers in Microbiology* 13 (2022): 960693.

[121]- Huang, Min, Jin-Jian Lu, and Jian Ding. "Natural Products in Cancer Therapy: Past, Present and Future: M. Huang et al." *Natural products and bioprospecting* 11.1 (2021): 5-13.

[122]- Spring, Bryan Q., et al. "The role of photodynamic therapy in overcoming cancer drug resistance." *Photochemical & Photobiological Sciences* 14.8 (2015): 1476-1491.

[123]- Alsaab, Hashem O., et al. "Progress in clinical trials of photodynamic therapy for solid tumors and the role of nanomedicine." *Cancers* 12.10 (2020): 2793.

[124]- Feng, Yanfang, et al. "Photodynamic and antibiotic therapy in combination against bacterial infections: efficacy, determinants, mechanisms, and future perspectives." *Advanced Drug Delivery Reviews* 177 (2021): 113941.

[125]- Sun, Yan, et al. "Antimicrobial photodynamic therapy in skin wound healing: A systematic review of animal studies." *International wound journal* 17.2 (2020): 285-299.

[126]- Tichaczek-Goska, Dorota, et al. "Photodynamic enhancement of the activity of antibiotics used in urinary tract infections." *Lasers in medical science* 34.8 (2019): 1547-1553.

[127]- Perez-Laguna, Vanesa, et al. "Photodynamic therapy combined with antibiotics or antifungals against microorganisms that cause skin and soft tissue infections: a planktonic and biofilm approach to overcome resistances." *Pharmaceuticals* 14.7 (2021): 603.

[128]- Ronqui, Maria Rita, et al. "Synergistic antimicrobial effect of photodynamic therapy and ciprofloxacin." *Journal of Photochemistry and Photobiology B: Biology* 158 (2016): 122-129.

[129]- Openda, Yolande Ikala, and Tebello Nyokong. "Combination of photodynamic antimicrobial chemotherapy and ciprofloxacin to combat S. aureus and E. coli resistant biofilms." *Photodiagnosis and photodynamic therapy* 42 (2023): 103142.

[130]- El-Hussein, Ahmed, et al. "A review of chemotherapy and photodynamic therapy for lung cancer treatment." *Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents)* 21.2 (2021): 149-161.

[131]- Pérez-Laguna, Vanesa, et al. "A combination of photodynamic therapy and antimicrobial compounds to treat skin and mucosal infections: a systematic review." *Photochemical & photobiological sciences* 18.5 (2019): 1020-1029.

[132]- Berg, Kristian, et al. "Photochemical internalization: a novel technology for delivery of macromolecules into cytosol." *Cancer research* 59.6 (1999): 1180-1183.

[133]- Berg, Kristian, et al. "Photochemical internalization (PCI): a technology for drug delivery." *Photodynamic Therapy: Methods and Protocols*. Totowa, NJ: Humana Press, 2010. 133-145.

[134]- de Pinillos Bayona, Alejandra Martinez, et al. "Efficacy of photochemical internalisation using disulfonated chlorin and porphyrin photosensitisers: An in vitro study in 2D and 3D prostate cancer models." *Cancer letters* 393 (2017): 68-75.

[135]- Jerjes, Waseem, et al. "Photochemical internalization for intracellular drug delivery. From basic mechanisms to clinical research." *Journal of clinical medicine* 9.2 (2020): 528.

[136]- Mathews, Marlon S., et al. "Photochemical internalization of bleomycin for glioma treatment." *Journal of biomedical optics* 17.5 (2012): 058001-058001.

[137]- Martinez de Pinillos Bayona, Alejandra, et al. "Enhancing the efficacy of cytotoxic agents for cancer therapy using photochemical internalisation." *International Journal of Cancer* 138.5 (2016): 1049-1057.

[138]- Chang, Hsin-I., and Ming-Kung Yeh. "Clinical development of liposome-based drugs: formulation, characterization, and therapeutic efficacy." *International journal of nanomedicine* (2012): 49-60.

[139]- Copper, Marcel P., et al. "Meta-tetra (hydroxyphenyl) chlorin photodynamic therapy in early-stage squamous cell carcinoma of the head and neck." *Archives of Otolaryngology–Head & Neck Surgery* 129.7 (2003): 709-711.

[140]- Rak, Jakub, et al. "Advances in liposome-encapsulated phthalocyanines for photodynamic therapy." *Life* 13.2 (2023): 305.

[141]- Šošić, Lara, et al. "Photochemical internalization: light paves way for new cancer chemotherapies and vaccines." *Cancers* 12.1 (2020): 165.

[142]- Jauffred, Liselotte, et al. "Plasmonic heating of nanostructures." *Chemical reviews* 119.13 (2019): 8087-8130.

[143]- Jain, Prashant K. "Taking the heat off of plasmonic chemistry." *The Journal of Physical Chemistry C* 123.40 (2019): 24347-24351.

[144]- Zhao, Liping, et al. "Recent advances in selective photothermal therapy of tumor." *Journal of nanobiotechnology* 19.1 (2021): 335.

[145]- Chen, Yuan, et al. "Nanomaterials-based photothermal therapy and its potentials in antibacterial treatment." *Journal of Controlled Release* 328 (2020): 251-262.

[146]- Bucharskaya, Alla B., et al. "Photothermal and photodynamic therapy of tumors with plasmonic nanoparticles: challenges and prospects." *Materials* 15.4 (2022): 1606.

[147]- Kong, Cunqing, and Xingcai Chen. "Combined photodynamic and photothermal therapy and immunotherapy for cancer treatment: a review." *International journal of nanomedicine* (2022): 6427-6446.

[148]- Gao, Junbin, et al. "Hyperthermia-triggered on-demand biomimetic nanocarriers for synergetic photothermal and chemotherapy." *Advanced Science* 7.11 (2020): 1903642.

[149]- Gu, Xi, et al. "Heat generation in irradiated gold nanoparticle solutions for hyperthermia applications." *Processes* 9.2 (2021): 368.

[150]- Morales-Dalmau, Jordi, et al. "Optimum morphology of gold nanorods for light-induced hyperthermia." *Nanoscale* 10.5 (2018): 2632-2638.

[151]- Taylor, Mitchell Lee, et al. "Gold nanorod-assisted photothermal therapy and improvement strategies." *Bioengineering* 9.5 (2022): 200.

[152]- Bharathiraja, Subramaniyan, et al. "Chlorin e6 conjugated copper sulfide nanoparticles for photodynamic combined photothermal therapy." *Photodiagnosis and photodynamic therapy* 19 (2017): 128-134.

[153]- Zeng, Wenfeng, et al. "An optimal portfolio of photothermal combined immunotherapy." *Cell Reports Physical Science* 3.6 (2022).

[154]- Kadkhoda, Jamileh, et al. "Recent advances and trends in nanoparticles based photothermal and photodynamic therapy." *Photodiagnosis and photodynamic therapy* 37 (2022): 102697.

[155]- Bilici, Kubra, et al. "Broad spectrum antibacterial photodynamic and photothermal therapy achieved with indocyanine green loaded SPIONs under near infrared irradiation." *Biomaterials science* 8.16 (2020): 4616-4625.

[156]- Wang, Rui, et al. "Phthalocyanine-assembled “one-for-two” nanoparticles for combined photodynamic–photothermal therapy of multidrug-resistant bacteria." *ACS applied materials & interfaces* 14.6 (2022): 7609-7616.

[157]- Shi, Enyu, et al. "Self-assembled nanoparticles containing photosensitizer and polycationic brush for synergistic photothermal and photodynamic therapy against periodontitis." *Journal of nanobiotechnology* 19.1 (2021): 413.

[158]- Liu, Xiaoli, et al. "Comprehensive understanding of magnetic hyperthermia for improving antitumor therapeutic efficacy." *Theranostics* 10.8 (2020): 3793.

[159]- Vilas-Boas, Vânia, Félix Carvalho, and Begoña Espiña. "Magnetic hyperthermia for cancer treatment: Main parameters affecting the outcome of in vitro and in vivo studies." *Molecules* 25.12 (2020): 2874.

[160]- Alumutairi, Layla, et al. "Mild magnetic nanoparticle hyperthermia enhances the susceptibility of Staphylococcus aureus biofilm to antibiotics." *International journal of hyperthermia* 37.1 (2020): 66-75.

[161]- Liu, Junchao, et al. "Fe_3S_4 nanoparticles for arterial inflammation therapy: Integration of magnetic hyperthermia and photothermal treatment." *Applied Materials Today* (2019).

[162]- Włodarczyk, Agnieszka, et al. "Magnetite nanoparticles in magnetic hyperthermia and cancer therapies: Challenges and perspectives." *Nanomaterials* 12.11 (2022): 1807.

[163]- Włodarczyk, Agnieszka, et al. "Magnetite nanoparticles in magnetic hyperthermia and cancer therapies: Challenges and perspectives." *Nanomaterials* 12.11 (2022): 1807.

[164]- Bienia, Aleksandra, et al. "Photodynamic therapy and hyperthermia in combination treatment—Neglected forces in the fight against cancer." *Pharmaceutics* 13.8 (2021): 1147.

[165]- Balhaddad, Abdulrahman A., et al. "Magnetic-responsive photosensitizer nanoplatform for optimized inactivation of dental caries-related biofilms: technology development and proof of principle." *Acs nano* 15.12 (2021): 19888-19904.

[166]- de Santana, Willian Max OS, et al. "Conjugation of superparamagnetic iron oxide nanoparticles and curcumin photosensitizer to assist in photodynamic therapy." *Colloids and Surfaces B: Biointerfaces* 196 (2020): 111297.

[167]- Di Corato, Riccardo, et al. "Combining magnetic hyperthermia and photodynamic therapy for tumor ablation with photoresponsive magnetic liposomes." *ACS nano* 9.3 (2015): 2904-2916.

[168]- Wang, Zheng, et al. "Immunotherapy: Janus Nanobullets Combine Photodynamic Therapy and Magnetic Hyperthermia to Potentiate Synergetic Anti-Metastatic Immunotherapy (Adv. Sci. 22/2019)." *Advanced Science* 6.22 (2019): 1970136.

[169]- Kaushik, Neha, et al. "The inactivation and destruction of viruses by reactive oxygen species generated through physical and cold atmospheric plasma techniques: Current status and perspectives." *Journal of Advanced Research* 43 (2023): 59-71.

[170]- Braný, Dušan, et al. "Cold atmospheric plasma: A powerful tool for modern medicine." *International journal of molecular sciences* 21.8 (2020): 2932.

[171]- Saadati, Fariba, et al. "Comparison of Direct and Indirect cold atmospheric-pressure plasma methods in the B16F10 melanoma cancer cells treatment." *Scientific reports* 8.1 (2018): 7689.

[172]- Limanowski, Ruby, et al. "Preclinical cold atmospheric plasma cancer treatment." *Cancers* 14.14 (2022): 3461.

[173]- Yan, Dayun, et al. "Stabilizing the cold plasma-stimulated medium by regulating medium's composition." *Scientific reports* 6.1 (2016): 26016.

[174]- Wang, Mian, et al. "Killing malignant melanoma cells with protoporphyrin IX-loaded polymersome-mediated photodynamic therapy and cold atmospheric plasma." *International journal of nanomedicine* (2017): 4117-4127.

[175]- Brullé, Laura, et al. "Effects of a non thermal plasma treatment alone or in combination with gemcitabine in a MIA PaCa2-luc orthotopic pancreatic carcinoma model." *PloS one* 7.12 (2012): e52653.

[176]- Daeschlein, Georg, et al. "Comparison between cold plasma, electrochemotherapy and combined therapy in a melanoma mouse model." *Experimental dermatology* 22.9 (2013): 582-586.

[177]- Betancourt-Ángeles, Mario, et al. "Treatment in the healing of burns with a cold plasma source." *International Journal of Burns and Trauma* 7.7 (2017): 142.

[178]- Boeckmann, Lars, et al. "Cold atmospheric pressure plasma in wound healing and cancer treatment." *Applied Sciences* 10.19 (2020): 6898.

[179]- Klebes, Martin, et al. "Combined antibacterial effects of tissue-tolerable plasma and a modern conventional liquid antiseptic on chronic wound treatment." *Journal of biophotonics* 8.5 (2015): 382-391.

[180]- Jungbauer, Gert, et al. "The antimicrobial effect of cold atmospheric plasma against dental pathogens—A systematic review of in-vitro studies." *Antibiotics* 10.2 (2021): 211.

[181]- Theinkom, Felix, et al. "Antibacterial efficacy of cold atmospheric plasma against Enterococcus faecalis planktonic cultures and biofilms in vitro." *PLoS One* 14.11 (2019): e0223925.

[182]- Songca, Sandile Phinda. "Combinations of photodynamic therapy with other minimally invasive therapeutic technologies against cancer and microbial infections." *International Journal of Molecular Sciences* 24.13 (2023): 10875.

[183]- Menezes, Marilia, et al. "Effect of photodynamic therapy and non-thermal plasma on root canal filling: analysis of adhesion and sealer penetration." *Journal of Applied Oral Science* 25.4 (2017): 396-403.

[184]- Hafner, S., et al. "Comparison of the bactericidal effect of cold atmospheric pressure plasma (CAPP), antimicrobial photodynamic therapy (aPDT), and polihexanide (PHX) in a novel wet surface model to mimic oral cavity application." *Journal of Cranio-Maxillofacial Surgery* 46.12 (2018): 2197-2202.

[185]- Abdulwahed, Abdulaziz. "Canal pretreatment using cold atmospheric argon plasma, chitosan and Chlorine p6 activated by photodynamic therapy with EDTA as a final irrigant on the pushout bond strength of fiber post." *Photodiagnosis and Photodynamic Therapy* 42 (2023): 103517.

[186]- Aly, Fatma. *Synergistic antimicrobial effects of cold atmospheric pressure plasma and photodynamic therapy against common skin and wound pathogens in-vitro*. Diss. 2021.

[187]- Paschoal, Marco Aurelio, Thereza Cristina Botelho Dantas, and Simone Duarte. "Photodynamic and tissue tolerable plasma therapies as alternatives to antimicrobials to control pathogenic biofilms." *Current Oral Health Reports* 2.1 (2015): 57-62.

[188]- Haghighi, Leyli, et al. "Antibacterial efficacy of cold atmospheric plasma, photodynamic therapy with two photosensitizers, and diode laser on primary mandibular second molar root canals infected with Enterococcus faecalis: an in vitro study." *International Journal of Dentistry* 2023.1 (2023): 5514829.

[189]- Laroussi, Mounir. "Cold plasma in medicine and healthcare: The new frontier in low temperature plasma applications." *Frontiers in Physics* 8 (2020): 74.

[190]- Niculescu, Adelina-Gabriela, and Alexandru Mihai Grumezescu. "Photodynamic therapy—an up-to-date review." *Applied Sciences* 11.8 (2021): 3626.

[191]- Wan, Guo-Yun, et al. "Recent advances of sonodynamic therapy in cancer treatment." *Cancer biology & medicine* 13.3 (2016): 325-338.

[192]- Cheng, Danling, et al. "Nanosonosensitizers with ultrasound-induced reactive oxygen species generation for cancer sonodynamic immunotherapy." *Frontiers in Bioengineering and Biotechnology* 9 (2021): 761218.

[193]- Harris, Frederick, Sarah R. Dennison, and David A. Phoenix. "Sounding the death knell for microbes?." *Trends in molecular medicine* 20.7 (2014): 363-367.

[194]- Yang, Yanye, et al. "Photo-and sono-dynamic therapy: a review of mechanisms and considerations for pharmacological agents used in therapy incorporating light and sound." *Current pharmaceutical design* 25.4 (2019): 401-412.

[195]- Zheng, Yilin, et al. "Recent progress in sono-photodynamic cancer therapy: From developed new sensitizers to nanotechnology-based efficacy-enhancing strategies." *Acta Pharmaceutica Sinica B* 11.8 (2021): 2197-2219.

[196]- Youf, Raphaëlle, et al. "Antimicrobial photodynamic therapy: Latest developments with a focus on combinatory strategies." *Pharmaceutics* 13.12 (2021): 1995.

[197]- Pang, Xin, et al. "Beyond antibiotics: photo/sonodynamic approaches for bacterial theranostics." *Nano-micro letters* 12.1 (2020): 144.

[198]- Karimnia, Vida, Frank J. Slack, and Jonathan P. Celli. "Photodynamic therapy for pancreatic ductal adenocarcinoma." *Cancers* 13.17 (2021): 4354.

[199]- Yang, Huajing, et al. "Synergistic anticancer strategy of sonodynamic therapy combined with PI-103 against hepatocellular carcinoma." *Drug Design, Development and Therapy* (2021): 531-542.

[200]- Borah, Ballav M., et al. "Sonodynamic therapy in combination with photodynamic therapy shows enhanced long-term cure of brain tumor." *Scientific reports* 10.1 (2020): 21791.

[201]- Liu, Yichen, et al. "Focused ultrasound-augmented targeting delivery of nanosonosensitizers from homogenous exosomes for enhanced sonodynamic cancer therapy." *Theranostics* 9.18 (2019): 5261.

[202]- Songca, Sandile Phinda. "Combinations of photodynamic therapy with other minimally invasive therapeutic technologies against cancer and microbial infections." *International Journal of Molecular Sciences* 24.13 (2023): 10875.

[203]- Wang, Xiaohuai, et al. "Method of use of porphyrins in preparing a medicament for sonodynamic therapy and a method of sonodynamic therapy using porphyrins." U.S. Patent No. 8,318,794. 27 Nov. 2012.

[204]- Wang, Fengping, et al. "The Sonodynamic Effect of Curcumin on THP-1 Cell-Derived Macrophages." *BioMed Research International* 2013.1 (2013): 737264.

[205]- Jiang, Lei, et al. "Sonodynamic therapy in atherosclerosis by curcumin nanosuspensions: preparation design, efficacy evaluation, and mechanisms analysis." *European Journal of Pharmaceutics and Biopharmaceutics* 146 (2020): 101-110.

[206]- Pourhajibagher, Maryam, Mahshid Hodjat, and Abbas Bahador. "Sonodynamic excitation of nanomicelle curcumin for eradication of Streptococcus mutans under sonodynamic antimicrobial chemotherapy: Enhanced anti-caries activity of nanomicelle curcumin." *Photodiagnosis and Photodynamic Therapy* 30 (2020): 101780.

[207]- Pang, Xin, et al. "Beyond antibiotics: photo/sonodynamic approaches for bacterial theranostics." *Nano-micro letters* 12.1 (2020): 144.

[208]- Pang, Xin, et al. "Beyond antibiotics: photo/sonodynamic approaches for bacterial theranostics." *Nano-micro letters* 12.1 (2020): 144.

[209]- Xu, Chuanshan, et al. "Sonodynamic action of chlorin e6 on Staphylococcus aureus and Escherichia coli." *Ultrasonics* 64 (2016): 54-57.

[210]- Ziental, Daniel, et al. "The dual synergy of photodynamic and sonodynamic therapy in the eradication of methicillin-resistant Staphylococcus aureus." *Applied Sciences* 13.6 (2023): 3810.

[211]- Huang, Ying-Ying, et al. "Photodynamic therapy induces an immune response against a bacterial pathogen." *Expert review of clinical immunology* 8.5 (2012): 479-494.

[212]- Zhang, Qianyu, et al. "Sonodynamic therapy-assisted immunotherapy: A novel modality for cancer treatment." *Cancer science* 109.5 (2018): 1330-1345.

[213]- Whiteside, Theresa L. "Immune responses to malignancies." *Journal of Allergy and Clinical Immunology* 125.2 (2010): S272-S283.

[214]- Ribas, Antoni, and Jedd D. Wolchok. "Cancer immunotherapy using checkpoint blockade." *Science* 359.6382 (2018): 1350-1355.

[215]- Shiravand, Yavar, et al. "Immune checkpoint inhibitors in cancer therapy." *Current Oncology* 29.5 (2022): 3044-3060.

[216]- Hwang, Hee Sook, et al. "Combination of photodynamic therapy (PDT) and anti-tumor immunity in cancer therapy." *Journal of pharmaceutical investigation* 48.2 (2018): 143-151.

[217]- Yue, Wenwen, et al. "Checkpoint blockade and nanosonosensitizer-augmented noninvasive sonodynamic therapy combination reduces tumor growth and metastases in mice." *Nature communications* 10.1 (2019): 2025.

[218]- Luo, Jiali, et al. "Enhancement of antitumor immunotherapy using mitochondria-targeted cancer cell membrane-biomimetic MOF-mediated sonodynamic therapy and checkpoint blockade immunotherapy." *Journal of nanobiotechnology* 20.1 (2022): 228.

[219]- Pang, Xin, et al. "Sono-immunotherapeutic Nanocapturer to combat multidrug-resistant bacterial infections." *Advanced Materials* 31.35 (2019): 1902530.

[220]- Wang, Dong, et al. "Near-Infrared-Triggered Multi-Enhanced Photodynamic/Immuno Therapy with Yolk-Shell Hybrid Plasmonic Nanostructures for Multidrug-Resistant Bacterial Infection." *Immuno Therapy with Yolk-Shell Hybrid Plasmonic Nanostructures for Multidrug-Resistant Bacterial Infection*.

[221]- Debela, Dejene Tolossa, et al. "New approaches and procedures for cancer treatment: Current perspectives." *SAGE open medicine* 9 (2021): 20503121211034366.

[222]- Heckenkamp, Joerg, et al. "Different effects of photodynamic therapy and γ-irradiation on vascular smooth muscle cells and matrix: implications for inhibiting restenosis." *Arteriosclerosis, thrombosis, and vascular biology* 19.9 (1999): 2154-2161.

[223]- Wang, Geoffrey D., et al. "X-ray induced photodynamic therapy: a combination of radiotherapy and photodynamic therapy." *Theranostics* 6.13 (2016): 2295.

[224]- Browning, Richard J., et al. "Combining sonodynamic therapy with chemoradiation for the treatment of pancreatic cancer." *Journal of Controlled Release* 337 (2021): 371-377.

[225]- Allison, Ron R., et al. "The future of photodynamic therapy in oncology." *Future Oncology* 2.1 (2006): 53-71.

[226]- Lucky, Sasidharan Swarnalatha, Khee Chee Soo, and Yong Zhang. "Nanoparticles in photodynamic therapy." *Chemical reviews* 115.4 (2015): 1990-2042.

[227]- Kim, Ki Su, et al. "Bioimaging of botulinum toxin and hyaluronate hydrogels using zwitterionic near-infrared fluorophores." *Biomaterials Research* 21.1 (2017): 15.