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Photodynamic therapy based on magnetic field stimulation: new directions in diverse medicine applications

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ABSTRACT

Despite the growing interest in photodynamic therapy (PDT) and the granting of regulatory approvals for many photosensitivity drugs and light applicators worldwide, there are many endeavors involving the search for a new physical mechanism that underpins PDT to influence various biological processes that are necessary for and contribute to In healing processes and in reducing pain, inflammation and other forms of damage. Electromagnetic and magnetic fields appear to be unique in their safety during clinical use. This review will focus on new clinical research advancements and will explore the value of incorporating external magnetic and electromagnetic fields for PDT technologies for the treatment of malignant and non-malignant disorders.

Keywords: *Photodynamic therapy; Electromagnetic and magnetic fields; Clinical application; Future studies; Combined therapeutic effect.*

INTRODUCTION

Today, photodynamic therapy (PDT) is a well-known and predominant treatment for both clinical and non-clinical diseases [1]. This treatment requires a precise light source and non-toxic photosensitizers that respond to light at the target site in order to induce selective tissue damage in the presence of singlet oxygen ($^1O_2$) without harming adjacent tissues [2], [3]. Based on the beneficial interaction between oxygen and photosensitive substances or compounds [4], [5], PDT has grown in popularity among many different forms of therapy. The main benefits that make this method more promising than traditional treatment methods such as chemotherapy, radiotherapy, and surgery are better clinical outcomes, assistance in minimal functional disturbances, patient suffering, continuity of advanced treatment results, and reduced systemic toxicity [6], [7].

However, many defects have been found, which are mainly caused by either conventional organic photosensitizers, the light sources used, or the pathology to be treated. These drawbacks include issues of limited solubility, optical absorption and ability to target the tumor, the doses of light used, and the biology of the target tissue, all of which have a somewhat negative impact on treatment outcomes [5], [8], [9]. Many clinical users have turned to more potent treatment alternatives in this area, such as magnetic fields of various kinds [10], [11]. Several studies indicate that external electromagnetic and magnetic fields can have significant effects on a wide range of biological processes, most of which are essential and critical for diagnosis and treatment [12]. In addition, many basic logical-physical processes are directly related to those intrinsic electromagnetic and magnetic fields ranging from molecular modification in the cell membrane and ionic bonding to the macroscopic mechanical properties of tissues in vivo and in vitro [13]–[15]. Accordingly, various cutting-edge researches has demonstrated that MFs have the ability to interact with other therapeutic agents, such as lasers, photosensitizers, or other chemicals, to produce physiologically relevant co-effects at the organelle and cellular level of the organism [16]–[18]. In sum, the aim of this review is to encourage readers to look forward to further reading and related research that provides strong scientific evidence regarding the feasibility of using magnetic or electromagnetic fields as a safe multi-product treatment regimen or as a supplement to others, such as PDT or low-level laser therapy (LILT), to become A sustainable approach to the clinical environment.

ESSENTIAL QUESTION

The task that this paper focused on was: “Should magnetic fields be applied as adjuncts to photodynamic therapy to give more accurate and realistic results for clinical medicine?”

RESEARCH PROTOCOL

According to the Department of Phototherapy Transactions, the details of the trial show the most important results of this treatment either alone or in combination with magnetic fields.

FUNDAMENTALS OF PHOTODYNAMIC THERAPY

PDT is a unique form of light therapy that relies on the interaction of three key components: molecular oxygen, a light source, and a photosensitizer (PS) (Figure 1) [19], [20]. The three major light source types utilized in PDT are lasers, light-emitting diodes, and lamps. The choice is made based on the target's location, the photosensitizer's absorption spectrum, and the required light dose [9]. When the PS is exposed to the right amount of light in the target area, it is able to absorb and transfer electrons, while the electron is received by oxygen molecules already in the same location [21], [22]. Thus, cytotoxic reactive oxygen species (ROS) are produced, triggering cell membrane rupture and cell death by necrosis or apoptosis in the target microorganisms and tissues [23], [24].

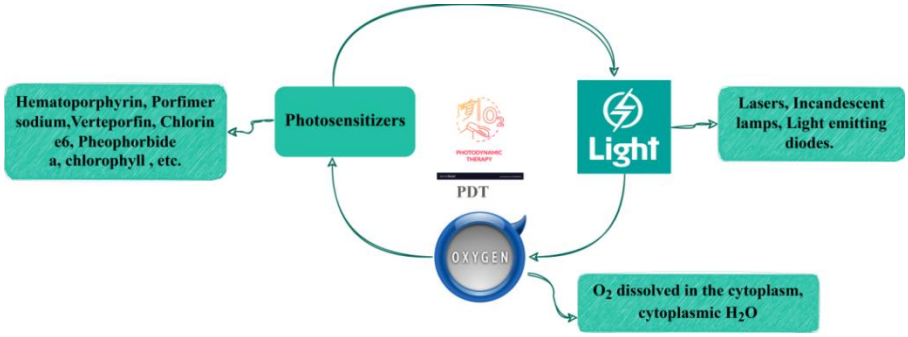

FIGURE 1: The basic components of PDT, it was designed on the basis of the mentioned literature studies [9], [19]–[24].

As is known, there are two basic classes of ROS (**Figure 2**), and each has a mechanism with a unique PDT. Hydroxyl radical $HO^{\bullet}$, superoxide anion $O^{2\bullet-}$, hydroperoxyl radical $HOO^{\bullet}$ or so-called oxygen radicals, are generated by free electron transfer, while energy transfer leads to the production of single oxygen ($^1O_2$) [25]. According to the mechanism of the first type of photoreaction, PS molecules move from their basic state to the single excited state and then the triple excited state [26]–[28]. Then, through electron transfer, a sequence of modifications occurs in which the activated PS molecules interact with the substrate to produce the resultant free radicals [22], [27]. Second, the triple-excited PS can immediately transfer its energy to molecular oxygen, resulting in mono-excited active oxygen, which can readily react with amino acids, proteins and lipids, to cause necrosis or apoptosis [27], [29]. Similarly, both reactions can happen at the same time and are mostly determined by the type and grade of PS utilized as well as the oxygen content in the substrate [30].

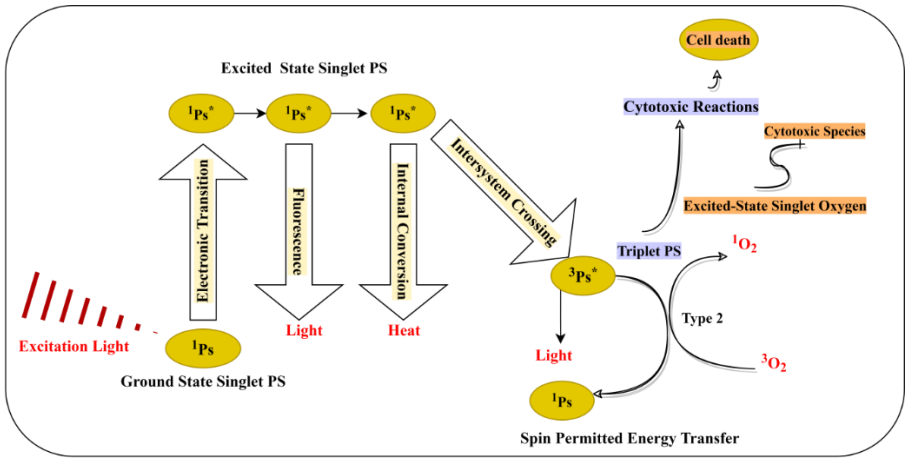

FIGURE 2: Illustration of the photodynamic processing (PDT) mechanism generated on the basis of literature references [22], [26], [27], [29].

Light delivery

When initiating any photodynamic therapy treatment, it must be ensured that sufficient light reaches the target tissues successfully in vivo. This gives an explanation of the understanding of the relative effects of the transmission of the light beam through the different layers of tissues and the relative effects that follow such as scattering and absorption [31]. Predicting the spatial distribution of light within the target tissue is crucial for PDT. Depending on the type of tissue and the wavelength of light employed, light enters the fabric and is either dispersed or absorbed to varying degrees. Measurements of tissue structures' spatiotemporal distribution, size distribution, and absorption and diffusion characteristics are all part of the field of tissue optics. Since biological tissues are heterogeneous and turbidity is caused by microscopic heterogeneity (macromolecules, cell organelles, structured cell structure, interstitial layers), this is a rather implicated situation [32]. Light beam propagation and direction loss are caused by multiple scattering in a turbid medium. Endogenous production is mostly responsible for absorption. The precise location of PS sub-cells within the cell determines the sort of photo damage that happens in bright and PS-loaded cells. Therefore, when choosing the best PS for each application, knowing PS localization is a key factor to take into account [33].

Photosensitizers (PSs)

PSs are an essential component of PDT, along with light and oxygen. The intrinsic features of these compounds influence their efficacy and efficacy as safe therapeutic agents as PSs can absorb light at a particular wavelength and cause

photophysical or photochemical responses [34], [35]. These particles are used for local administration to collect in the tissues to be treated to give an excellent opportunity for local treatment under the influence of absorbing wavelengths ranging between 200-900 nm to produce individual oxygen, allowing the passage of light through the layers of tissues through the chromosphere [36]. Ps need sufficient energy to generate enough reactive oxygen species during excitation to function properly and cleanse normal tissues with minimal risk of damage [37]. For this reason, many previous results have shown that excessive PSs during treatment is avoided, to give less risk and accurate results, because it can simply cause significant damage to the blood vessels and tissue layers. PSs were first used in the 1970s on a commercial scale by testing a "hematoporphyrin derivative" (HpD) by Dr. Thomas Dougherty and colleagues. These sensitizers are represented as a water-soluble mixture of protoporphyrin, hematoporphyrin, deuteroporphyrin, and are the derivatives of monomers, oligomers, dimers and esters [34], [35].

Over the years, despite its wide applications, a series of flaws have been discovered. Chief among these drawbacks is the low chemical purity, which is particularly evident in the first generation of those sensors, which show weak photoactivation and can only be activated at wavelengths shorter than 640 nm, which limits tissue penetration [28], [38]. In addition, the extended half-life of PSs causes the skin to become hypersensitive to light for many weeks, forcing treated patients to stay in dark locations for up to six weeks or more [29], [39]. To get beyond these restrictions, theories have been created to investigate how steady-state and optical emission can be affected by the physical characteristics that support these PS. For example, magnetic fields have been used to support the optical motion path of those compounds by affecting the pairs of ionic radicals associated with type I optical motion, and magnetic fields can be used for the purpose of enhancing or suppressing to achieve a dynamic equilibrium between the type I and type II dynamic pathways [40], [41].

PHOTODYNAMIC THERAPY APPLICATIONS

PDT has made substantial improvements in the treatment of both cancerous and non-cancerous disorders [Table1]. This treatment has received a lot of criticism, yet it has been widely used in a variety of medical specialties, including oncology, dermatology, urology, dentistry, and ophthalmology, where its outcomes have been acceptable and effective in treating a variety of disorders [42], [43].

TABLE 1: List a group of clinically relevant treatment conditions in PDT.

Photosensitizer Ps	Wavelength(nm)	Application	Structure	Reference
Photofrin (HPD)	625 630 635	Cancer (lung, brain, bladder, Breast, bile, colorectal)	Porphyrins	[44], [45]
Toluidine Blue O	630	Antimicrobial, in vitro, in vivo, clinical	Phenothiazinium salt	[46]
Foshan (mTHPC)	652	Cancer (Head and neck, skin, bile, lung, breast)	Chlorine	[47]
Rose Bengal	540	Cancer, antimicrobial, tissue bonding, in vitro, in vivo, clinical	fluorescent	[48]
Methylene Blue	660	Cancer, antimicrobial, in vitro, in vivo, clinical	Phenothiazinium salt	[49]
Cationic	380	Antimicrobial, in vitro	cationic derivative	[50]
Aminolevulinic acid (5-ALA)	635	Skin, bladder, brain, Mitochondria, cytosolic membrane	Porphyrins	[51]

Hypocretin	470 nm	Cancer, antimicrobial, in vitro, in vivo, clinical.	Perylenequinone	[52]
Motexafin lutetium (LuTex)	732	texaphyrin	Breast cancer, Arteriosclerosis, prostate, in vivo, clinical.	[53]
Chlorine E6 (Ce6)+Up conversion nanoparticles	980, 405	Chlorine	THP-1 macrophages, in vivo, clinical.	[54]

RELATED PRINCIPLES AND THEORIES IN PHOTODYNAMIC THERAPY

Low-Level Laser (Light) Therapy and Its Mechanism of Action

Photo-bio-modulation (PBM), often known as low-level laser therapy, is the modification of biological activity through the use of photons in non-thermal or cold radiation. LILT helps to heal tissue, lessen pain and inflammation, encourage tissue and nerve regeneration, and stop harm in circumstances where it is likely to happen [55], [56]. In photo-bio stimulation, excitation of intracellular chromospheres such as endogenous porphyrins, mitochondrial and membrane cytochromes, and flavoproteins is attributed to the interaction of light with the cell. Chromospheres transfer their excited electrons to nearby oxygen, thus, activating and supporting many cellular processes, including the release of gene expression factors, transcription, muscle contraction, and cell growth [57].

However, intra-tissue penetration must be taken into account when using light therapeutically in a variety of applications. In the current study, we do this without taking into account the higher epidermal layer by applying a photon migration model in the tissue's dermis layer. To determine penetration depth as a function of visible wavelengths, the mean absorption coefficients of the dermis layer are calculated and replaced with theoretical expressions of penetration depth [55], [58]. It can be considered that the best wavelengths for clinical treatments are those that fall within the appropriate wavelength range and that penetrate deeper into tissues. Therefore, it is possible to use various numerical techniques and methodologies, including Monte Carlo simulations, finite difference methods, diffusion approximations for radioactive transmission equations, etc., to examine how light moves through tissue boundaries [55], [59].

Wavelength

The absorption spectrum of important tissue chromospheres with the wavelengths of the lasers is widely used in PDT. Hemoglobin has several different absorption peaks whereas absorption by melanin gradually diminishes with longer wavelengths of incident light [9]. Consideration must also be given to the depth of the target structure, as scattering in the dermis is strongly influenced by wavelength, making a longer wavelength, which may be relatively poorly absorbed often preferable, to a short wavelength with the opposite characteristics [60].

LIGHT-TISSUE INTERACTIONS

When light reaches the skin's surface, a portion of it is absorbed by the skin's biological characteristics, while the rest is reflected and dispersed at various temperatures over the electromagnetic radiation spectrum. As a result, the remaining portion begins to penetrate the skin's barrier, and different physical and chemical processes begin to show variations to the target tissues under the effect of wavelength and pulse duration, without causing damage to the surrounding tissues [61], [62].

Besides, the mechanism of light transmission through tissues can be divided into several main ways, the most important of which are:

Light transitions

Determining the basics of treatment in PDT depends on determining the light source, radiation dose, wavelength, and intensity. Also,

the spectral properties of the light source must display the largest band for PS absorbing wavelength, generating toxic effects during sufficient reactive oxygen species (ROS) production [22], [63]. The greatest penetration depth, on the other hand, is governed by the wavelength (630-800 nm) and ranges from (3-8 mm), and this phenomenon is known as the "healing window". The fluency (W/cm^2) and fluency (J/cm^2) of light radiation doses are also provided. When high optical rates are employed, however, PSs begin to degrade during the induced biological responses, resulting in situations including skin sensitivity, tumor development, and therapy delay [64].

Photochemical

The PS excitement undergoes two types of interactions. The first kind delivers an electron or a proton to the cell by interacting directly with the target (cell membrane or molecule), producing a superoxide anion or a radical cation, respectively [Figure2]. When these anions come into contact with light, they produce reactive oxygen species. Second, the triple-excited PS can immediately transmit its energy to molecular oxygen, resulting in mono-excited oxygen. Similarly, both reactions can happen at the same time and are mostly determined by the type and grade of PS utilized as well as the oxygen content in the substrate [30]. The superoxide interacts with itself to generate hydrogen peroxide and oxygen during the development of biological systems, but it does not harm the organism. It is easily permeable across cell membranes, can be catalyzed by the enzyme superoxide dismutase (SOD), and is as vital to health as oxygen in replenishing enzyme function [65].

Photophysical

The wavelength is a photophysical property that aids in the activation and efficiency of the PS exciter's triple state. The wavelength of the tissue's greatest penetration is between 650 and 850 nm, which is adequate for single oxygen production [66]. By modifying the wave by flashing the target location, this producing efficacy, as well as the long-term triple case, aids in detecting the tumor and manufacturing poisonous products or repairing damaged tissues, and this should display more work and shine for PS [67].

BENEFITS AND DRAWBACKS OF PHOTODYNAMIC THERAPY

Given the widespread use of photodynamic therapy, it is clear that it offers a number of benefits compared to traditional therapeutic alternatives. This property enables minimal systemic toxicity, poor invasiveness, tumor invasion, and unsolvable functional problems by allowing control of the spatiotemporal selectivity of the radiation used [68], [69]. Based on the current analysis of the relevant literature, PDT appears to be a good and promising technology for all types of cancers and superficial infections, as well as bacterial and fungal infections, and may in the future be repeatedly applied at the same site [70]. Another key advantage that has made this treatment acceptable is the ability to generate ROS that damage a wide variety of cells from both clinical and non-clinical applications [71].

Despite the clinical efficacy of photodynamic therapy, there are some persistent problems associated with conventional PDT that are frequently encountered. These problems include the poor water solubility imposed by many classical PS, poor dose regulation that prevents sufficient energy delivery to activate the PS, and limited optical penetration depth [28], [72], [73]. These restrictions damage adjacent healthy tissues and somehow interfere with the organization of treatment. Therefore, the development of new therapeutic approaches that advance the fundamentals of photodynamic therapy is essential in the advancement of clinical practice.

However, the limitations of photodynamic therapy can be overcome by a more effective alternative, which allows its use in conjunction with basic photodynamic therapy, and has a significant impact on biological properties and

cellular systems in vivo and in vitro [75] ,[74]. In this way, the advantages of magnetic fields can be exploited in the regulation of PDT, overcoming many of the limitations imposed. For example, these areas may improve immune function, cellular control, ionic bonding, and tissue support when combined with basic PDT, such as LILT or PS [75] ,[74]. This is expected to help reduce pain and speed up the healing process within the tissue boundaries.

MAGNETIC FIELD

Therapeutic Magnetic Fields

After the magnetic field (MF) became one of the sources of confusion regarding its use to treat many medical problems. Many international organizations have generated numerous reports resulting from inspired clinical indications confirming the effective use of MFs in humans. Unfortunately, many studies lack a clear description of MFs in order to determine the proper dose to give to target tissues. As a result, some of the findings reached may be misleading or confusing [11]. Despite this, interest in the use of MF has grown for several years, however many researchers regard it as a supplemental or transitory treatment for a variety of disorders, particularly inflammatory ones. This misunderstanding arose as a result of the treatment's parameters, such as the quantity of energy or capacity delivered in the treatment, being misinterpreted as benign, damaging, or curative [76].

As a result, the main question remains: what is the appropriate application of the MF, and where should it be applied? In my opinion, these parameters should be used in conjunction with other therapeutic regimens, such as PDT, to allow many researchers to gain more experience and competence in applying these physical approaches in order to prescribe such physiologically relevant therapies to the body.

Tissue magnetic interference

Various parameters about the interaction of low, high and medium magnetic fields with living organisms have recently been reported, which aroused the interest of many disciplines both in physics, chemistry, medicine and nanotechnology to reveal the levels and variables expected within molecules and cells as a result of this technique [77], [78]. The magnetic effect causes biological and physiological changes that dramatically alter the functioning of cells and organisms by stimulating ions and supporting cells [Figure 3], affecting to some extent the energy houses (mitochondrial) and the endoplasmic reticulum in addition to increasing the number of lysosomes [79]. In other words, the magnetic effect can cause morphological and biological changes in cells, allowing them to be reprogrammed, migration of proteins and cell membrane receptors, activation of ion channels via mechanical membrane pressure, and arrest of harmful cell growth by magnetic stress and cell fission [76]. According to some research, human tissues contain a tiny amount of chemicals and mineral compounds like manganite (up to a few hundred micrograms), which has biomedical effects and has high electrical conductivity for any cellular material [80]. However, there are several crystals per gram, each of which interacts powerfully with external magnetic fields and has an impact on the cellular level, particularly the immunological and neurological systems, as well as their relevance to human health.

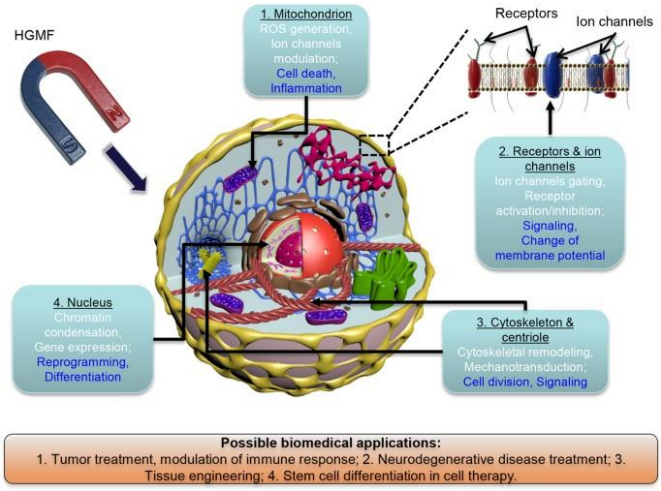

FIGURE 3: Outline of the applications of magnetic potential affecting cells [79].

Is PDT affected by magnetic interference?

As it has been shown, when PDT made significant progress to improve treatment efficacy, the depth of optical penetration through the layers of the skin became more exciting to the target tissue. This progress highlighted the response of these nanomaterial's or PS to physical forces such as the external magnetic field (MF) [41]. Another reason, this method has been used to address the limitations of conventional treatment, such as the lack of photosensitizer accumulation in the tumor or its spread to adjacent tissues, and the dependence on external light alone, which makes the photosensitizers lower in tissues[81].

The Hyperfine and Zeeman reactions influence the absorption, dissolution, and emission characteristics between S, T0, T + 1, and T-1, as well as the photoluminescence properties. The amount of nuclear spin and the non-paired electrons of radical ion pairs are affected by these factors. This division reduces the electron state, which may impact the pace of the system crossing over and the generation of reactive roots. Lower the rate of lunar oxygen production, or put another way, reduce the rate of lunar oxygen production [82]. Laboratory studies, on the other hand, show that when cells are excited by light, MF impacts cell survival, decreasing toxicity by reducing conjugation and promoting the mitotic state. This stimulation enhances porphyrin emission and life, allowing it to absorb light and create radical ions, potentially increasing the photo catalytic absorption state of PS, as well as the rate of light penetration and reactive oxygen production [40].

Low-level laser therapy versus magnetic field

Low-intensity laser magnetic interference is a therapy strategy that has a combined impact on the body and is based on the degree of biological reactions and the synergy between therapeutic physical variables. This use can be regarded as a thermo therapeutic interaction with an anti-sedating effect, edema, inflammation, pain alleviation, and other disorders. As a result, combining MF with LLLT may improve the efficacy of medical synergists that are dependent on biological activity, as well as enhance sensitivity to supra molecular effects and biological compositions to light beam penetration [83], [84].

The MF reduces the dispersion and lateral diffusion of the electron beam by boosting dose only in inaccessible areas and achieving stability in those areas, resulting in a more compact and focused beam. Similarly, the laser beam stimulates therapeutic effects and organizes internal functions to achieve biological stability and produce an effective therapeutic effect, whereas magnetic interference affects functional changes in biological tissues, which are linked to sodium and potassium ion movement in the blood [85], [86]. Thus, when laser light is

momentarily concentrated on a point with a diameter of 1 micrometer, high-pressure waves are generated per nanosecond of the light energy employed, resulting in transient holes in the cell membrane.

What needs to be done?

Any photodynamic therapy should begin with an assessment of the clinical problem, identification of the source of that problem (i.e. the target organs/tissues), and selection of appropriate means of application, such as wavelength and power output, and finally, the type of PS that are appropriate for treatment. Most importantly, the strength of the low-level laser light beam that must be delivered to the desired target tissue must be determined. The ability and efficacy of photosensitizers to alter biological processes and physiological condition are investigated. They're likely to be unequally soluble in water, resulting in malfunctions or inconsistent treatment results. In fact, according to recent research and studies, employing magnetic fields in conjunction with photodynamic therapy with a parallel strength of magnetic flux may result in more successful treatment results than using photodynamic therapy alone. It must be remembered that the basic physical principle of static or variable magnets is biologically and clinically relevant at the target site. The biological response to the applied MF indicates the existence of biological "windows" that allow the penetration of magnetic flux density through tissue chromosomes to the target site and change the dynamics of the optical beam to behave clearly with PS and nanostructures. The 'windows,' in general, reflect combinations of amplitude, frequency, and duration of exposure during which the optimal reaction to magnetism is observed, and once outside this range, the effect is smaller and conventional, as with any phototherapy.

GENERAL APPLICATIONS AND RELATED FEATURES

Potential Targets for Biological a-MF Effects and Related Mechanisms

The use of the weak, medium, and strong magnetic fields shows that they have different effects on biological processes in vivo [Table.2] [79], [87]. Utilizing low frequencies, particularly those between 50 Hz and 60 Hz, is one of the most up-to-date and effective approaches to studying the antibacterial effects of MF [87]. The magnetic effect causes biological and physiological changes that dramatically alter the functioning of cells and organisms by stimulating ions and supporting cells, affecting to some extent the energy houses (mitochondrial) and the endoplasmic reticulum, in addition to increasing the number of lysosomes, and then affect the immune system of the body [79], [88]. The effects of external magnetic fields on the body's organs and cells are known. Living tissues' ion channels are mechanically altered by the low-frequency magnetic field, and as a result, these fields extend the range of ion gates like Ca^{2+}, Na^{+}, and other ions [76]. Since a number of other organs/tissue interfaces are considered the first line of defence against disease-causing viruses and bacteria, it necessitates their preservation as they are the main frontiers of the body [88]. Therefore, these borders must be carefully guarded, repaired, and protected because any damage to them may weaken the human immune system and cause death.

The antimicrobial combined effect of low-level laser therapy and magnetic fields

The fibroblast layer of the skin, which contains necessary proteins like elastin and collagen, is one of the five major layers that make up the skin [89]. The primary purposes of these components are to protect the skin; if this layer is compromised; the skin loses its texture, allowing infection to spread to the dermis layer's base, damaging the keratinocytes and blood vessel endothelium, which then enables the blood vessels to deliver platelets and monocytes to the injured area [90], [91].

According to a number of researches, important biological responses and features can be observed in vitro within the so-called biological 'windows' when dealing with target tissues, these

windows represent the best interaction that can be seen from basic physical and physiological properties. For example, low-dose LLLT has demonstrated positive effects on cellular immunity, enzymatic chain reactions, cell proliferation process, quantity and quality of immune cells, tissue perfusion, and improvement of surgical incision scar tissue by strengthening the cell cycle and directing it to generate Producing and replacement cells, etc. regardless of whether the wound is deep or superficial [92], [93]. In contrast, another biologically relevant characteristic is the static magnetic field strength at the target site [94]. The best biological response is predicted by several factors including exposure time, dose, frequency, and amplitude, and once outside this range, the response is much smaller. In the case of dipole magnets, there will be important biological responses, especially if there is close affinity between the magnet surface and the target area (usually 1–1.5 cm) [95], [96]. In this context, when these two physical features are combined, cooperation occurs between the complex biological systems, and inflammatory phenomena begin to decrease as a result of the formation of cutaneous scars by granulation tissue due to stimulation of fibrosis by adult macrophage [91], which changes its dynamics to fibroblasts to replace fibroblasts from their own.

Light sources in antimicrobial photodynamic therapy

Multiple light sources at low intensity are necessary for the treatment of bacterial infectious diseases in photodynamic therapy [97], [98]. As the light beam passes through the skin, the light intensity decreases due to attenuation [99]. Accordingly, it is necessary to apply red (600±10 nm) and green (530±10 nm) light to nearby lesions and cause a variety of effects in order to achieve PDT under one set of irradiation conditions [100]. This property can be used in combination with other therapeutic methods such as the presence of magnetic fields to cause selective damage or tissue regeneration without surgery [Table 2] [101], [102]. Different lasers are thought to cause a variety of cellular reactions, including an increase in mast cells and glycolysis, an improvement in procollagen production in dermal fibroblast cultures, and an increase in fibroblast and mesenchyme cell proliferation.

TABLE 2: Examples of randomized studies that used photodynamic treatment in the presence or / absence of magnetic fields.

Sample	Treated	Laser parameters	Photosensitizes (PSs)	Magnetic field (MF)	Compared	Effect	Author
Mice	Cancer treatment	Red diode650nm, 704nm (5mW/cm^2 ,27 J/cm^2)	Chlorine e6 (Ce6)	gradual	Improved treatment efficiency, improved tissue penetration, non-toxicity, and good cellular absorption.	High therapeutic efficacy with significantly delayed tumour growth.	[103]
Mice	Tumours	Diode laser600–700 nm, (425–1050) nm.	ZnPor-C60, L-CuPor-C60	0-350 MT and 115mT.	Achieve treatment efficiency, amplify the curative effect.	Tumour targeting accuracy, fast inhibition	[81]
Human	Brain attack	Infrared (840 nm/12 watts), for 5 days, 45 minutes / day.	Not	power (1 MT 50 Hz).	A significant difference before and after the intervention (P < 0.001).	A decrease in temperature for the experimental group increases with the effect of treatment.	[75]
Human	Acute	-pulsed diode laser (904 nm, (1, 10, 100, 1000) Hz.	Not	Fixed (not specified), Exposure	Pain relief, mobility restored, limb	It was noted that the success rate in both	[17]

	and chronic pain	-pulsed diode laser (635 nm), with (2) Hz. -IR LED's (780-950) nm with (1, 10, 100, 1000) Hz.		times are (1 or 5) minutes.	swelling reduced.	groups is 70%.	
Mice	Toxic cells	UV and Red diode laser (673nm, 380nm, 430nm), (10 J /cm^2), output power 96mW.	(4hydroxyphenyl) Porphyrin.	(0-350mT).	Increase the mean effect of wavelength by (+ 4 nm), while increasing luminosity intensity when increasing the B-field.	Produce root pairs with elevated degeneration of three triple states (T_0, T_{+1}, T_{-1}).	[82]
Human	Stem cell damage	808nm, 200mW power output, 0.2W / cm^2 power density.	Not	3 MT (50Hz).	Stem cells multiply and change their geometric shape.	Changes in cell morphology, and an increase in its area.	[104]
Athletes	Apoplexy	Diode laser (840nm)	Not	1 MT	Improved muscle performance and fast post-workout recovery.	Power generation	[105]
Human	Diabetic foot ulcers	He-Ne (632 nm to 904 nm), density (10 J/cm^2).	Curcuma longa (CL)	0.5 Gauss	Not	Wound regeneration, pain relief	[106]

CONCLUSIONS AND FUTURE PERSPECTIVES

The total advantages of clinically relevant combination events of photodynamic treatment and magnetic fields are highly striking. However, due to the fact that each of these therapeutic techniques has a unique mechanism of action in terms of administering the treatment and regulating biological processes in vivo, it is necessary to have in-depth knowledge of both the parameters in terms of light management and its biological interactions as well as the efficiency of the PSs to match the parameters of the MFs that is being used. These parameters include things like field type, magnetic gradient, gradient intensity, penetration depth, and so on. These characteristics offer a substantial contribution to the process of overcoming hurdles and producing an effect of accurate application dosage. Light's selective absorption and biological response by malignant and non-malignant cells can vary depending on factors like energy density, and penetration depth, including scattering, absorption, and selection of PSs like the natural and synthetic chlorophyll sensitizers discussed in this article. a greater understanding of the fundamental concept of magnetism and the physiological basis for employing an MF to realign and encourage tissue repair and other illnesses increases the likelihood of positive outcomes.

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COMPETING INTERESTS

The authors declare that there are no conflicts of interest.

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