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Review

Photodynamic therapy for onychomycosis: A systematic review

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ABSTRACT

Other than a cosmetic concern, Onychomycosis is also a prevalent nail disease, which is extremely difficult to treat, and sometimes is refractory to conventional therapy. Moreover, many patients are not eligible to take oral antifungals owing to polypharmacy and comorbidities. Systemic side effects seen with oral antifungals have lead to patient nonadherence and adverse events. Therefore, newer therapies are being investigated for onychomycosis that would be free of systemic complications posed by oral therapy. Photodynamic therapy (PDT) is one of those being currently studied, which involves the use of photosensitizer and a light source to excite the photosensitizer to generate reactive oxygen species. The present review will put some light on PDT as an upcoming treatment modality for onychomycosis. We performed a systematic review of the literature to find the articles relevant to the use of PDT for onychomycosis. From the primary search of 43 articles, 17 papers are included in this review.

Contents

1. Introduction

Onychomycosis is one of the most prevalent nail disorders, which occurs due to overgrowth of fungus in the nail bed, leading to hyperkeratinization [1]. Keratinization of the nail bed is pathologic and can lead to discolored or dystrophic nail plates [2]. While the incidence of onychomycosis is increasing across all ages, it still remains a disorder of adults with the prevalence in those younger than 18 years being <0.5% [3,4]. The mean growth rate of fingernails and toenails per month is 3 mm and 1 mm respectively, implying approximately 4–6 months to completely regenerate a fingernail or 8–12 months to replace a toenail. Nail growth is linked to a number of factors such as age, presence of systemic and localized diseases, and medications [5,6].

The available treatment options for onychomycosis are facing significant barriers in successfully eradicating the disease. This is because topical medications cannot penetrate via nail plate to reach nail bed and systemic antifungal agents possess certain adverse effects on long-term use and also has some contraindications. Moreover, some individuals have sustained infections persisting

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Table 1
Properties of some photosensitizers used in PDT-related clinical trials.

Photosensitizer compounds	Types	Chemical name	Generic Name	Trade name	FDA approved	Approved for
1st generation	Systemic		Porfimer sodium	Photofrin	Yes	Canada (1993)–bladder cancer; USA (1995)–esophageal cancer; USA (1998)–lung cancer; USA (2003)–Barrett's esophagus; Japan–cervical cancer; Europe, Canada, Japan, USA, UK–endobroncheal cancer
2nd generation	Topical	1,5-aminolevulinic acid	5-Aminolevulinic acid (ALA)	Levulan	Yes	USA (1999)–actinic keratosis
		Methyl ester	Methyl aminolevulinate (MAL)	Metvixia	Yes	USA (2004)–actinic keratosis
	Systemic	n-hexyl ester of ALA	Hexaminolevulinate (HAL)	Cysview	Yes	USA (2010)–bladder cancer diagnosis
			Meta-tetra (hydroxyphenyl)chlorin (m-THPC)	Foscan	No	Europe-neck and head cancer
			Tin ethyl etiopurpurin	Purlytin	No	Clinical trials–breast adenocarcinoma, basal cell carcinoma, Kaposi's sarcoma, age-related macular degeneration
			N-aspartyl chlorin e6 (NPe6)	Laserphyrin, Litx	No	Japan (2003)–lung cancer
			2-(1-Hexyloxyethyl)-2-devinyl pyropheophorbide (HPPH)	Photochlor	No	Clinical trials–esophogeal cancer, basal cell carcinoma, lung cancer, Barrett's esophagus
			Palladium bacteriopheophorbide (WST09)	Tookad	No	Clinical trials–prostate cancer
			WST11	Stakel	No	Clinical trials–prostate cancer
			Motexafin lutetium (Lu-Tex)	Lutrin, Optrin, Antrin	No	Clinical trials–prostate cancer, age-related macular degeneration, breast cancer, cervical cancer, arterial disease
			Aluminum phthalocyanine tetrasulfonate (AlPcS4)	Photosens	No	Russia (2001)–stomach, skin, lips, oral cavity, tongue, breast cancer
			Silicon phthalocyanine (Pc4)	–	No	Clinical trials–actinic keratosis, Bowen's disease, skin cancer, mycosis fungoides
			benzoporphyrin derivative monoacid ring A	Visudyne	No	1999, US FDA approved the use of BPD-MA as Visudyne® for age-related macular degeneration in ophthalmology
3rd generation	Systemic		Lutetium texaphyrin	Lutex	No	Cervical Intraepithelial Neoplasia, ocular fundus angiography

for months or years and, hence, they may not be motivated to initiate or complete therapy due to a perception that their condition is untreatable. Thus, these factors are seen to contribute to the suboptimal delivery of conventional therapy for onychomycosis. This gives the reason why advances in management techniques, and innovations in treatment for onychomycosis are needed.

In recent years, PDT has been extensively studied in hopes of finding efficacious and suitable treatment modality for onychomycosis. PDT is a non-invasive therapy that utilizes light to activate a photosensitizing agent applied topically or systemically, which generates reactive oxygen species (ROS) that initiate the destruction of cells by necrosis or apoptosis. Photosensitizers (PSs) act by absorbing energy from ultraviolet or visible light and transferring it to adjacent molecules. Since fungi can absorb PSs, PDT can be an alternative way of treating onychomycosis [7,8]. PDT can be used in onychomycotic patients with other comorbid condition as well because it is not known to interact with other drugs [9,10]. Another advantage of PDT is that the target cells preferentially absorb the PS, and illumination is designed to be applied only on the region to be treated [11–13]. The PDT requires the presence of three factors that interact simultaneously: a PS, a source of light emitting an appropriate wavelength, and the availability of oxygen [14].

A wide array of photosensitizers for PDT exists. In clinical practice, photosensitizers arise from three families–porphyrins, chlorophylls, and dyes [15]. Table 1 mentions some FDA approved and non-approved PSs that are commonly used in PDT in a wide variety of field in medicine. FDA-approved PSs include porfimer sodium (Photofrin), 5-aminolevulinic acid or ALA (Levulan, Ameluz, Alacare), and methyl aminolevulinate or MAL (Metvix). Photofrin is used intravenously for internal cancers while Levulan, Ameluz, Alacare and Metvix are applied topically for skin conditions [16]. Table 2 has a list of some non-porphyrin PS with their application. None have received FDA approval for their application areas. In dermatologic PDT, a 20% 5-ALA solution or MAL cream are the most common photosensitizers utilized. ALA and MAL are chemically distinct protoporphyrin IX (PpIX) precursors that are enzymatically

Table 2
Non-porphyrin sensitizers and their application.

Compound	Application
Hypericin	Squamous cell carcinoma, basal cell carcinoma
Methylene blue	Malignant melanoma, basal cell carcinoma, kaposi's sarcoma, chronic periodontitis
Merocyanine 540	Leukemia, lymphoma
Curcumin	Oral disinfectant
Toluidine blue	Chronic periodontitis
Rose bengal	Breast carcinoma, malignant melanoma
TH9402	Graft-versus-host disease

converted to PpIX, an active photosensitizer. MAL/PDT provides similar efficacy to ALA/PDT with the benefits of shorter incubation times according to the approved FDA labeling, greater selectivity, reduced pain during and immediately following therapy, and fewer systemic side effects [17]. Smijs et al. [18] studied a photodynamic and nail penetration enhancing effects of novel multifunctional photosensitizers (MFPSs) designed for the treatment of onychomycosis. This study regarded the primary characterization and evaluation of newly designed porphyrin photosensitizers for possible PDT of dermatophytic onychomycosis. Various MFPSs were synthesized to fulfill two essential effects within nail: a penetration enhancing and a PDT effect and a novel approach were provided to onychomycosis treatment that could save time and be cost-effective.

PDT light sources include lasers (mainly pulsed dye lasers and diode lasers), intense pulsed light, light-emitting diodes (LEDs), gas discharge lamps and incandescent filament lamps [16]. One or several types of light may activate photosensitizer drugs. The optimal light depends on the ideal wavelength for the particular drug being used and target tissue. A basic law of photobiology is that the longer the wavelength of light, the deeper the penetration through biological tissues. As human skin is more readily accessible to light than internal organs, dermatologic applications of PDT may be able to use a wider variety of wavelengths.

2. Method

We performed a systematic review of the literature on October 29, 2015 and updated the search on May 29, 2016. The search term "Onychomycosis" and "photodynamic therapy" was entered into the National Library of Medicine's PubMed Database. All the articles relevant to the use of PDT for onychomycosis were identified and reviewed. From the primary search of 43 articles, 17 papers are included in this review. Review articles and studies that used PDT in treating conditions other than onychomycosis were excluded. Language and study type restrictions were not imposed.

2.1. *Photodynamic effect of rose bengal on* Trichophyton rubrum

Rose Bengal (RB) is a photosensitizer that has been found to be toxic to various microbes, including *Streptococcus mutans* and *Candida albicans*, when used with PDT [19,20]. It is an amphoteric dye that absorbs visible light between the wavelengths of 500 nm to 550 nm encompassing the green light spectrum [21].

Leah Cronin et al. [22] conducted a study to assess if the photosensitization of RB using a 532 nm solid state pumped laser is fungicidal to *T. rubrum* and provided the evidence that RB photosensitization using a green laser can be a potential novel treatment for *T. rubrum* infections. They found that 140 mM Rose Bengal solution was able to induce a fungicidal effect on *T. rubrum* when photosensitized with the fluence of 228 J/cm2.

2.2. *Photogem-photodynamic therapy*

Photogem, a photosensitizer is a hematoporphyrin derivative made by Photogem LLC Co. (Moscow, Russia). It is usually described as chemically similar to Photofrin. Both Photogem and Photofrin are mixtures of monomers, dimers, and oligomers of hematoporphyrin derivatives and first-generation photosensitizers [23,24].

Silva et al. [25] presented a case report of onychomycosis that was completely cured by photogem-photodynamic therapy. The case was about a 59-year-old male patient with two onychomycotic nails who was treated with photogem-PDT once a week for a period of six weeks. An hour after the photosensitization, the nails were illuminated using a light source based on light emitting diodes (LEDs) in the red wavelength of 630 nm, at a total dose of 54 J/cm2.

da Silva et al. [26], in another study used two different photosensitizers: a hematoporphyrin derivative (photogem) and a mix of curcumins and curcumoids. The study presented two devices based on light-emitting diode arrays as light sources for the treatment of onychomycosis by photodynamic therapy. These prototype devices were successfully used on two patients to treat onychomycosis. First patient was a 55-year-old female with toenail onychomycosis for more than 5 years who was cured with PDT sessions with photogem and 630-nm LED device. The second patient was a 46-year-old female patient with toenail onychomycosis for more than 10 years who was cured with PDT sessions with curcumin and curcuminoids, which was activated by 470 nm LED device.

2.3. *ALA-photodynamic therapy*

ALA itself is not photodynamically active but when taken up by target cells, it can act as a prodrug, inducing the accumulation of endogenous PS whose light activation can lead to a range of antimicrobial effects [27–31]. Based on these observations, ALA-based PDT has been increasingly researched for medical application in addition to a number of nonmedical uses [32,33]. The major absorption peak for ALA is seen in the blue light range, between 410 to 420 nm.

Other light sources that can be used to activate ALA include potassium titanyl phosphate (KTP) lasers, pulsed dye lasers (PDL), and intense pulsed light (IPL).

Kamp et al. [34] showed for the first time that onychomycosis inducing dermatophyte *Trichophyton rubrum* was able to metabolize ALA to protoporphyrin IX (PpIX) in liquid culture medium. Their study with ALA treatment and irradiation of *T. rubrum* clearly demonstrated the growth-inhibiting effect of ALA PDT, either leading to reduced numbers of colonies or reduced diameters of single fungal colonies and summarized the results that ALA PDT might be a promising approach in the reduction of *T. rubrum* colonization in onychomycosis.

Donnelly et al. [35] conducted a study where bioadhesive patch-based delivery of ALA to the nail for photodynamic therapy of onychomycosis was studied and found that incubation of *Candida albicans* and *Trichophyton interdigitale* with ALA concentrations of 10.0 mM for 30 min and 6 h respectively caused reductions in viability of 87% and 42% respectively following irradiation with red light. Incubation with 0.1 mM ALA for 30 min and 6 h respectively caused reductions in viability of 32% for *Candida albicans* and 6% for *Trichophyton interdigitale* following irradiation. Hence, they concluded that, with suitable modifications, ALA-PDT might prove to be a viable alternative in the treatment of onychomycosis.

Piraccini et al. [36] presented a case reported of a 78-year-old woman with onychomycosis in both the big toenails caused by *Trichophyton rubrum* who had failed to respond to treatment with topical antifungals and had conditions that contraindicated the administration of systemic antifungals. After treatment with ALA-PDT, both the toenails were considered clinically cured with

mycologic and clinical cure persisting until the last follow-up at 24 months.

2.4. MAL-photodynamic therapy

MAL is a methylated ester of photosensitizer prodrug ALA. In topical PDT, both MAL and ALA are converted to endogenous photosensitizer PpIX. MAL is best utilized with a red light source at 630 nm.

Aspiroz et al. [37] presented a case report of a 75-year-old woman with onychomycosis caused by Acremonium sclerotigenum in the 5th finger who was treated with 3 sessions of MAL-PDT at an interval of 15 days. The patient achieved mycological and clinical cure and remained asymptomatic after 12 months of follow up.

2.5. Methylene blue light emission diode/PDT

Methylene blue (MB) is a well-known histological stain, which has been used for many years and has played an important role in microbiology and pharmacology [38]. Dermal exposures to MB have no reported side effects aside from photosensitivity [39]. Studies have demonstrated clinical efficacy and safety of MB light emission diode/PDT (MBLED/PDT) with response rates of approximately 85–100% [40,41].

Figueiredo Souza et al. [42] conducted a clinical study to evaluate the efficacy of the MBLED/PDT compared with fluconazole in patients with toenail onychomycosis. The use of PDT consisted of sessions of MBLED with an interval of 15 days between each session for 6 months where 2% MB aqueous solution was applied to the lesion followed by illumination with noncoherent red light (630 nm, 18 J/cm^2) from a LED device. The study found that patients treated with MBLED/PDT showed a significant response with a clinical cure rate of 90% compared to those treated with fluconazole who responded poorly. The MBLED/PDT was found to be safe, effective, and was well tolerated.

2.6. Hypericin- photodynamic therapy

Hypericin is a natural photoactive pigment found in Hypericum perforatum plants, commonly known as St. John's wort [43]. Since many years in the past, hypericin has been extensively investigated for its use in wide variety of fields in medicine [44–47]. More recently, studies have revealed a photodynamic fungicidal effect of hypericin against Candida spp., especially *Candida albicans* [48]. It is one of the photosensitizers being investigated as a promising PDT agent.

Paz-Cristobal et al. [49], in their in vitro study demonstrated the fungicidal effect of hypericin-PDT on dermatophytes. *Trichophyton rubrum* and *Trichophyton mentagrophytes* strains were incubated with different concentrations of hypericin for different times and exposed to light emitting diode lamp emitting at 602 ± 10 nm with a fluence of energy at 37 J cm^2. Using the optimal incubation time, 60 min, a 3-log fungicidal effect was achieved with hypericin concentration ranges of 10–20 μM for *T. rubrum* and 20–50 μM for *T. mentagrophytes*.

2.7. Result

Our search yielded a total of 43 sources of which 17 articles met the inclusion criteria. 5 were in vitro and 12 were in vivo studies. 16 studies were published in English and 1 in Spanish. These articles were published between the year 2005 and 2015. A total of 214 patients were included in this review of which 21 were men, 18 were women and the gender of the remainder was not reported. The reported age of patients range from 18–85 years. Age of 95 patients was not reported. The photosensitizers used included: 5 studies using ALA, 3 studies using MAL, 4 studies using methylene blue dye, 2 studies with a haematoporphyrin derivative Photogem, 1 study with rose bengal dye, 1 study with porphyrin, and 1 study with hypericin. The number of treatment sessions varied from 1 to 22 sessions and interval time between each session varied from 1 to 8 weeks. The wavelength of light used to excite the photosensitizer range from 470–750 nm. Typical fluence delivered during a treatment session was from 18–228 J/cm^2 (See Table 3).

3. Discussion

Onychomycosis is an exceptionally common problem, with studies estimating its prevalence around 14% in the general population [50]. A number of organisms responsible for this fungal nail infection include dermatophytes, nondermatophyte molds, and yeast. Multiple factors are known to predispose this condition such as, hyperhidrosis, wearing occlusive shoes, participation in sports, use of commercial swimming pools, contact with sources of fungal infection, nail trauma, immunodeficiency, diabetes mellitus, and old age. Many treatment modalities for the treatment of onychomycosis have been studied, including topical lacquers and ointments, oral antifungals, surgical and chemical nail avulsion, and more recently lasers and PDT [51,52].

Therapeutic modality with minimal systemic side effects, a reasonable duration of therapy, and an ability to deliver treatment to a confined area has made PDT the topic of interest. This might be the reason for several studies being conducted in recent years to see its effect for onychomycosis. Most of the studies published so far are case reports except for 5 clinical trials of which only 1 is randomized controlled trial. These studies show that PDT may have a successful therapeutic benefit for onychomycosis without systemic side effects. The reported side effects include mild pain, burning, erythema, edema and blistering which were well tolerated, did not demand additional treatment, and resolved within few days. Even a study with no side effects at all was reported [53]. But in this study several patients discontinued treatment due to dislike of the blue coloration of the nail and peripheral tissues caused by solutions of methylene blue and toluidine blue. This indicates that not only side effects, but also other factors need consideration while choosing PSs. In contrast to above-mentioned successful studies, one study [54] reported unsatisfactory outcome on distal lateral subungual onychomycosis (DLSO) with ALA-PDT. There may be several possible explanations for the unsatisfactory outcome like, PS, light source as well as therapeutic cycles. This demands larger prospective studies for the assessment of the efficacy of PDT using a variety of PSs, light sources and different treatment regimen.

Studies have shown that PDT can successfully treat onychomycosis in patients where conventional therapy failed or patient could not continue therapy due to adverse effects [55,56]. PDT is seen to be effective in treating onychomycosis caused by different fungal species such as *T. rubrum*, *T. mentagrophytis*, *T. interdigitale*, *Epidermophyton Floccosum*, *Candida albicans*, Acremonium sclerotigenum, *Fusarium Oxysporum* and *Aspergillus terreus*. In addition, a study [57] has reported successful use of PDT in different severity of onychomycosis from mild to severe. However, clinical response was significantly better in mild-to-moderate onychomycosis (100%) compared to severe onychomycosis (63.6%). Other than DLSO, which is the most common type of onychomycosis, PDT has shown good response in endonyx onychomycosis as well, which is considered an unusual variant of onychomycosis [58].

The main problem in using PDT for onychomycosis is inadequate penetration of photosensitizing drug via nail plate. To overcome this hurdle, most of the studies used urea as a pre treatment to soften the nail or microabrasion of the nail and/or complete

Table 3
Studies demonstrating the effect of PDT in the treatment of onychomycosis.

Study type/Reference	Causative agent	Photosensitizer	Light source	Wave length	Fluence of energy	Treatment session and duration	Outcome
Case report/research letter [25]	–	Porphyrin (photogem)	LEDs in red wavelength	630 nm	54 J/cm^2	6 Sessions at 1 week interval	Complete healing was reported after an irradiation over six weeks and in addition, the microorganism culture indicated negative for fungi.
In vivo [26]	–	Mix of curcumins and curcuminoids/hematoporphyrin-derivative (Photogem)	LED arrays	470 nm blue light/630 nm red light	120 J/cm^2	–	Use of a portable and secure light source device in patients with onychomycosis has additional advantages of low cost, possibility of topical treatment rather than systemic and the simplicity of operation.
In vitro [35]	*Candida albicans* and *Trichophyton interdigitale*	5-ALA	–	–	–	–	Incubation of Candida albicans and Trichophyton interdigitale with ALA concentrations of 10.0 mM for 30 min and 6 h, respectively, caused reductions in viability of 87% and 42%, respectively, following irradiation with red light
Case report [36]	*Trichophyton rubrum*	5-ALA	Lamp equipped with LED	630 nm	37 J/cm^2	3 sessions at 15 days interval	Treatment was well tolerated with no side effects. Mycologic and clinical cure persisted until the last follow-up at month 24.
In vitro [34]	*Trichophyton rubrum*	5-ALA	N_2 laser	420 nm	128 J/cm^2	–	Growth-inhibiting effect of ALA PDT was clearly demonstrated, either leading to reduced numbers of colonies or reduced diameters of single fungal colonies.
Report of cases [55]	–	5-ALA	Excimer-dye laser	630 nm	100 J/cm 2	6 to 7 Sessions at 1 week interval	The lesion substantially improved, and no dermatophyte was detected by KOH or by culture
Single-centre Open Trial [54]	*T. rubrum*	5-ALA	Non-coherent light source	570–670 nm	40 J/cm^2	3 Sessions at 2 week interval	A cure rate of 43.3% 12 months after treatment was seen, which reduced to 36.6% 18 months after treatment. Only 11 of the cured patients at the first follow-up visit had persistent clearance.
In vitro [49]	*Trichophyton rubrum* and *Trichophyton mentagrophytes*	Hypericin	LED lamp	602 ± 10 nm	37 J/cm^2	–	Hypericin-PDT has a fungicidal effect in vitro on dermatophytes. Hypericin seems to be a promising photosensitizer to treat localized dermatophytic infections such as tinea pedis and onychomycosis.
In vitro [22]	*Trichophyton rubrum*	Rose bengal	Green laser (diode-pumped solid state laser)	532 nm	68, 133 and 228 J/cm2	–	Growth of T. rubrum was significantly inhibited when compared to the control. In particular, the treatments with fluences at 228 and 133 J/cm2 were highly effective, reducing the area of fungal growth to 15% that of the control.

Table 3 (*Continued*)

Study type/Reference	Causative agent	Photosensitizer	Light source	Wave length	Fluence of energy	Treatment session and duration	Outcome
In vitro [18]	*Trichophyton mentagrophytes*	Porphyrin (PORTH, PORTHE, Sylsens B)	Laser light (± argon/mannitol/NaN3).	532 nm	0.15 to 36 J/cm^2	–	PDT (0.6 J/cm^2, 2 μM) showed 4.6 log kill for PORTH, 4.4 for Sylsens B and 3.2 for PORTHE (4.1 for 10 μM). Argon increased PORTHE, but decreased PORTH PDT efficacy; NaN3 increased PDT effect of both MFPSs whereas mannitol increased PDT effect of PORTHE only.
Case report [42]	Acremonium sclerotigenum	MAL	Lamp (Atkilite)	630 nm	37 J/cm^2	3 sessions at 15 days interval	The patient achieved mycological and clinical cure and remained asymptomatic after 12 months of follow up.
Report of cases [56]	*Fusarium Oxysporum* or *Aspergillus terreus*	MAL	LED	635-nm	–	3 Sessions at 2 week interval	The patients were clinically and microbiologically cured. After 6 months of follow-up, recurrences were not detected.
Case study [59]	*Trichophyton rubrum* or *Epidermophyton floccosum*	MAL	LED	–	–	2 sessions at 60 days interval	After one year of follow-up, all of the patients presented negative mycological test results, with mycological cure in every case
Randomized controlled trial [41]	–	Methylene blue	Noncoherent red light from LED device	630 nm	18 J/cm^2	12 Sessions at 15 days interval	Patients treated with PDT showed a significant response compared with those treated with fluconazole. PDT was effective and well tolerated.
Small-scale trial [53]	*Trichophyton rubrum*, *T. mentagrophytis* or *Candida albicans*	Methylene blue and toluidine blue	In-house light source	600 to 750 nm	18 J/cm2	1 to 22 Sessions at 1 month interval	45% patients completing the treatment exhibited complete clearance of fungal nail infection, with 40% partial clearances. 15%showed no change.
Open-label controlled clinical trial [57]	*Trichophyton rubrum*	Methylene blue	LED	630 nm	36 J/cm2	12 Sessions at 2 week interval	The clinical response was significantly better in patients with mild-to-moderate (100%) onychomycosis compared with patients with severe onychomycosis (63.6%).
Preliminary open clinical trial [58]	*Trichophyton rubrum*	Methylene blue	LED	630 nm	36 J/cm2	12 Sessions at 2 week interval	Complete clinical response was evident, with mycological cure in all cases. No patient showed dense opacification of the nail plate. No adverse effects were observed.

(–): Information not provided, PDT: Photodynamic therapy, LEDs: light-emitting diodes, MAL: methyl aminolevulinate, ALA: aminolevulinic acid, MFPSs: multifunctional photosensitizers, PORTH: 5,10,15-tris (4-*N*-methylpyridinium)-20-(4-phenylthio)-[21H,23H]-porphine trichloride, PORTHE: 5,10,15-tris(4-*N*-methylpyridinium)-20-(4-(butyramido-methylcysteinyl)-hydroxyphenyl)-[21H,23H]-porphine trichloride.

removal of nail plate was employed. In contrast, one study [59] used fractional CO2 laser 10.600 nm to assist photosensitizer penetration via nail plate. The studies have reported a clinical and microbiological cure rate of 90% to 100% but this percentage were seen to decrease on follow-up. It seems that the efficacy of PDT depends on the pretreatment of the nail. However, more work needs to be done on the effect of various treatment variables, on the efficiency and adverse effects of PDT, in order to develop an optimum treatment protocol.

Although research is still limited, some big and small studies utilizing PDT for the treatment of onychomycosis have achieved exciting results. This new style of treatment approach can be advantageous because they are conducted within a clinic and only require patient compliance. However, more large-scale randomized control clinical trials are needed to assess the efficacy of PDT treatments.

Conflicts of interest

The authors have no conflict of interest to declare.

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None.

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