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# Investigation of the effect of low power laser used in photodynamic therapy for treatment of psoriasis

Wirksamkeit von Low-Power-Lasern in der photodynamischen Therapie der Schuppenflechte

## Abstract

**Objective:** The objective of this study was to investigate the effect of power on low-level lasers used in photodynamic therapy (PDT) to treat chronic plaque psoriasis in a group of Sudanese patients.

**Materials and methods:** Twenty-four patients with chronic plaque psoriasis were randomly selected to enter this study from a total of 100 patients who attended the Khartoum Dermatology Teaching Hospital between 2010 and 2011. The lasers used for PDT were three continuous wave diode lasers in the red portion of the electromagnetic spectrum (671–675 nm) with output powers of 16, 50 and 100 mW to activate the chemical photosensitizer (Levulan® Kerastick® topical solution), i.e., the 24 patients were divided into three treatment groups (eight patients for each laser power group). Each patient received three sessions at 2-week intervals. The exposure time was 15 min for each laser session.

**Results:** This study showed that 62% of the patients treated with 100 mW achieved complete clearance compared with 25% for those treated with 50 mW and 0% for those treated with 16 mW.

**Conclusions:** The results showed that increasing the power of low-level laser in PDT increased the clearance of plaque psoriasis. PDT can be used as an alternative method for treatment of psoriasis.

**Keywords:** photodynamic therapy; low-level laser therapy; psoriasis; laser in dermatology.

## Zusammenfassung

**Zielsetzung:** Ziel dieser Studie war es, die Wirksamkeit von Low-Power-Lasern in der photodynamischen Therapie

(PDT) der Schuppenflechte in einer Gruppe sudanesischer Patienten zu untersuchen.

**Material und Methoden:** Von 100 Patienten, die sich zwischen 2010 und 2011 am Khartoum Dermatology Teaching Hospital vorstellten, wurden 24 Patienten mit chronischer Schuppenflechte randomisiert und in die Studie aufgenommen. Für die PDT wurden drei kontinuierlich abstrahlende (cw) Laserdioden im roten Wellenlängenbereich (671–675 nm) mit einer Ausgangsleistung von 16, 50 bzw. 100 mW verwendet, um den Photosensibilisator (Levulan® Kerastick® für die topische Lösung) zu aktivieren, d.h. die 24 Patienten wurden in 3 Behandlungsgruppen unterteilt mit jeweils 8 Patienten je Laserleistung. Jeder Patient wurde dreimal im Abstand von 2 Wochen behandelt. Die Bestrahlungszeit betrug jeweils 15 min.

**Ergebnisse:** Bei 62% der mit 100 mW Laserleistung behandelten Patienten konnte eine komplette Remission der Schuppenflechte erzielt werden. Dies konnte nur für 25% der Patienten in der Leistungsgruppe “50 mW” und für keinen der mit 16 mW behandelten Patienten erreicht werden.

**Schlussfolgerung:** Die Ergebnisse zeigen, dass eine Steigerung der Laserleistung und damit der Leistungsflussdichte zu einer Verbesserung der Clearance-Rate bei photodynamischer Behandlung der Schuppenflechte führte. Die PDT stellt somit eine alternative Behandlungsmethode für dieses Krankheitsbild dar.

**Schlüsselwörter:** Photodynamische Therapie; Low-Level-Laser-Therapie; Schuppenflechte; Dermatologische Laser.

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## 1 Introduction

Photodynamic therapy (PDT) is a treatment modality based on a photochemical reaction involving oxygen. It is a relatively new technique for local treatment, which is mostly applied to malignant tumors. PDT requires three simultaneously present components for cytotoxicity: a photosensitizer, light and oxygen. A photosensitive compound or pro-drug is administered systemically or topically to the patient, and the photoactive agent utilized is usually selectively accumulated in the tissue. The chemical reaction occurs at that point when the irradiation starts [1, 2]. The use of PDT to treat psoriasis was reported first in 1937 with systemically administered hematoporphyrin and ultraviolet radiation [3].

Porphyrin precursors or derivatives, with peak absorption in the 400–650 nm range, are used as photosensitizers. Most recently, 5-aminolevulinic acid (5-ALA), a porphyrin precursor converted intracellularly to protoporphyrin IX, has been used clinically. It has the advantage of having a short half-life, reducing the risk of prolonged systemic photosensitivity [3, 4].

5-ALA has been shown to selectively accumulate in psoriatic plaques and to induce apoptosis of lesional T helper lymphocytes. Topical ALA is applied 4–5 h prior to photoactivation with lasers or light sources in the 400–700 nm range. Short topical contact, i.e., 30 min to 2 h, of ALA-PDT has proved to be a safe and effective treatment for a variety of dermatological disorders including psoriasis [5–8]. A series of treatments is usually necessary with variable clinical response. To date, a long-term follow-up has not been reported [3, 4].

Treatment may be associated with pain, and it may be prudent to use topical anesthesia prior to treatment [3].

Potential side effects of PDT vary with the photosensitizer and light source used. Cutaneous photosensitivity is common and patients should avoid exposure to any intense light for 24 h after application of the photosensitizer to avoid a ‘sunburn’ reaction. Occasional blistering may occur and hyperpigmentation can occur at treated sites. Scarring can occur on very rare occasions, particularly on the lower extremities [3, 4].

The aim of this study was to provide a new method of treatment for chronic plaque psoriasis using PDT. This is the first study in this field in Sudan where the incidence of psoriasis is about 1–3% in the general population. There has been no satisfactory method of treatment until now and the remission rate of the available treatments is not long. Photo-chemotherapy presents a future risk of malignancy. No previous study has been carried out on black skin using the laser for treating psoriasis in the Sudan.

## 2 Materials and methods

### 2.1 Patients

#### 2.1.1 Study area

The study was conducted at the Institute of Laser, Sudan University of Science and Technology (SUST), Khartoum Plastic Surgery Department and Khartoum Dermatology Teaching Hospital (KDTH).

#### 2.1.2 Study population

This study was conducted on Sudanese patients with chronic plaque psoriasis attending KDTH.

#### 2.1.3 Sample size

Twenty-four patients were randomly selected to enter into this study from 100 patients with chronic plaque psoriasis who attended KDTH between 2010 and 2011.

The inclusion criteria were:

- Stable, chronic plaque psoriasis.
- Ability to understand and sign the informed consent form.

The exclusion criteria were:

- Female subjects of reproductive age who are pregnant, attempting to conceive, or nursing an infant.
- Subjects who have received either psoralen and UVA treatment (PUVA) between 320 and 400 nm, UVB treatment between 290 and 320 nm or systemic antipsoriatic therapy within 4 weeks before this study treatment.
- Subjects who have received any approved biologic drug therapy for psoriasis within 3 months before the study.
- Subjects with a history of porphyria, systemic lupus erythematosus or xeroderma pigmentosum.
- Subjects with clinical conditions that, in the opinion of the investigator, may pose a health risk to the subject by being involved in the study or detrimentally affect the regular follow-up of the subject.

#### 2.1.4 Patients’ records

A record for each patient in this study was documented and contained the following details:

1. Name, age, sex, skin type, history, examination notes and results of investigations.
2. Duration of the lesions.
3. Sites of the lesions.
4. Baseline and follow-up photographs.
5. Baseline and follow-up histopathology for some patients.
6. Date and laser parameters of each session.
7. Notes about the progress of the treatment, and notes about the adverse sequels and complications.
8. Consent form for laser treatment.

## 2.2 Materials

### 2.2.1 Photosensitizer

Topical 20% aminolevulinic acid hydrochloride solution (ALA HCl) (Levulan® Kerastick® topical solution; DUSA Pharmaceuticals, Inc., Wilmington, MA, USA) was used in this study.

### 2.2.2 Lasers used to activate 5-ALA

Different continuous wave (cw) low power diode lasers were used in this study to activate 5-ALA. The first cw diode laser (Omega XP Laser; Omega Laser Systems Limited, Essex, UK) had a 675 nm wavelength and 16 mW output power. The second cw diode laser (RLTMRL-671-50; Roithner Lasertechnik GmbH, Vienna, Austria) had a 671 nm wavelength and 50 mW output power, while the third cw diode laser (RLTMRL-671-100; Roithner Lasertechnik GmbH, Vienna, Austria) had a 671 nm wavelength and 100 mW output power. The exposure time was 15 min in each laser session.

### 2.2.3 Other materials

Bleaching agents (hydroquinone 2% cream) were prescribed for patients with lesions on sun-exposed areas to avoid post-inflammatory hyperpigmentation. Sunscreens (aloe vera cream with sun protection factor 30) were prescribed for patients with lesions on exposed areas.

## 2.3 Method

### 2.3.1 Photodynamic therapy

Levulan® Kerastick® topical solution containing 20% ALA HCl was applied to the target psoriatic plaque for

a 2 h incubation time (short contact application) before irradiation.

Immediately before laser application, the area with ALA was rinsed with water and patted dry. Dark blocking protective goggles were worn both by the patient and the operator. The patients were divided into three treatment groups:

- Eight patients received 675 nm, 16 mW (power density, 31.8 mW/cm<sup>2</sup>) for 15 min.
- Eight patients received 671 nm, 50 mW (power density, 995 mW/cm<sup>2</sup>) for 15 min.
- Eight patients received 671 nm, 100 mW (power density, 1990 mW/cm<sup>2</sup>) for 15 min.

After light treatment, patients were warned not to expose themselves to sunlight or intense light for at least 48 h and that non-compliance could result in a severe phototoxic reaction.

Each patient received three sessions at 2-week intervals. The patients were seen on the next day, and 48 h from the first session to check for early post-operative complications and then followed-up every 2 weeks for about 1 year. The patients' response to PDT was evaluated clinically and histopathologically.

### 2.3.2 Clinical evaluation

The clinical evaluation was performed by means of the psoriasis area and severity index (PASI), which is a measure of overall psoriasis severity and coverage. It is a commonly used measure in clinical trials for psoriasis treatments. Typically, the PASI is calculated before, during, and after a treatment period in order to determine how well the psoriasis responds to the treatment under test (a lower PASI generally means less psoriasis).

For the PASI, the body is divided into four areas. Each of these areas is scored by itself, and the four scores are combined into the final PASI. The four areas are: the legs, which have 40% of a person's skin, the body (trunk area, abdomen, chest, back, etc.) with 30%, the arms with 20%, and the head with 10%. For each skin section the amount of skin involved is measured, as a percentage of the skin in that part of the body, and then it is assigned a score from 0 to 6. The severity is measured by four different parameters: itching, erythema (redness), scaling and thickness (psoriatic skin is thicker than normal skin). Again, each of these is measured separately for each skin section. These are measured on a scale of 0 to 4, from none to maximum, according to the Table 1.

Severity	Score	Site of the lesion	Total number of lesions	Percentage (%)
None	0			
Some	1	Face	3	8.6
Moderate	2	Neck	1	2.9
Severe	3	Chest and breast	2	5.7
Maximum	4	Dorsa of the hands	5	14.3
		Forearms/arms	15	42.8
		Legs and feet	9	25.7
		Total	35	100.0

**Table 1** PASI scores.

### 2.3.3 Histopathological evaluation

The biopsies were taken under local anesthesia with 5% xylocaine without adrenaline in a minor operation room in the dermatology hospital using 5 mm diameter disposable punches. The specimens were placed in 10% formalin in bottles. The bottles were labeled with the patient's name, with details of the date, specimen site and professional diagnosis. Then the probes were sent to the histopathological laboratory. The specimens were fixed in 10% formalin then stained with hematoxylin and eosin (H&E), then processed for light microscope examination. The results obtained were registered on the study sheet. The data collected were analyzed using the program for statistical package for social studies (SPSS).

## 3 Results

### 3.1 Age and sex

The ages of the patients enrolled in this study ranged from 18 to 60 years as listed in Table 2. Fourteen patients (58.3%) were males and 10 patients (41.7%) were females.

### 3.2 Sites and size of the plaques

The lesions of the patients selected in this study were located in different sites as listed in Table 3. The sizes of the plaques ranged from 4 cm<sup>2</sup> to 24 cm<sup>2</sup>.

Age group (years)	Number of patients	Percentage (%)
18–40	13	54.2
41–60	11	46.8
Total	24	100.0

**Table 2** Age distribution.

**Table 3** Sites of the plaques.

Table 4 summarizes the age and sex of the patients, the sites, size, and number of the lesions and the laser parameters used for each patient in this study.

### 3.3 Response of chronic plaque psoriasis to PDT using 675 nm diode laser, 16 mW output power and 15 min exposure time

Four patients showed 50% reduction in PASI after three sessions using PDT with 675 nm and 16 mW cw diode laser irradiation for 15 min, while the other four patients showed 25% reduction in PASI after three sessions, as listed in Table 5.

Figure 1 shows a comparison between plaques in a 60-year-old male with chronic plaque psoriasis on the left forearm before and after treatment with the cw laser of 675 nm and 16 mW, where 50% reduction was observed. Figure 2 shows the histological findings of this patient.

### 3.4 Response of chronic plaque psoriasis to PDT using 671 nm diode laser, 50 mW output power and 15 min exposure time

Two patients showed complete clearance after three sessions using PDT with the 671 nm cw diode laser with 50 mW power and irradiation for 15 min, two patients showed a reduction of 75% while the other four patients showed 50% reduction in PASI after three sessions, see Table 6.

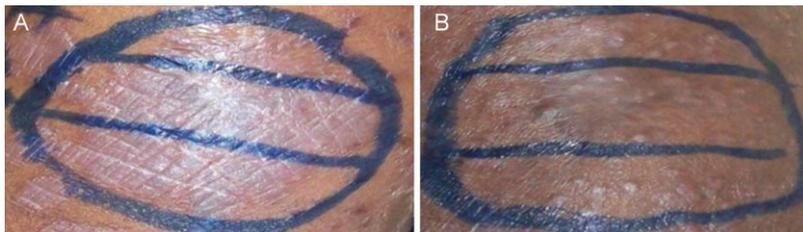
Figure 3 shows a comparison between plaques in a 29-year-old male with chronic plaque psoriasis on the left arm before and after treatment, using the cw laser of 671 nm and 50 mW. Figure 4 shows the histological findings of this patient.

Patient no.	Age (year)	Sex	Site of lesions	Total number of lesions	Size of lesions (cm <sup>2</sup> )
Group 1 (675 nm, 16 mW, 15 min)					
1	34	M	Face and neck	2	4/6
2	20	M	Forearms	2	16
3	18	F	Hands	1	12
4	60	M	Left forearm	1	10
5	41	M	Right leg, face	2	20/6
6	23	F	Left leg, left forearm	2	6/10
7	30	F	Right forearm	1	12
8	53	M	Right leg	1	24
Group 2 (671 nm, 50 mW, 15 min)					
9	46	M	Left forearm	1	8
10	37	F	Right hand	1	10
11	29	M	Left arm	2	6/4
12	44	M	Left forearm, left hand	2	14/8
13	20	F	Right leg, left hand	2	9/8
14	27	F	Left and right forearms	2	20/6
15	57	M	Right leg	1	24
16	51	M	Right forearm	1	16
Group 3 (671 nm, 100 mW, 15 min)					
17	25	M	Right and left forearms	2	4/14
18	35	F	Right leg	1	20
19	43	M	Right chest	1	4
20	42	M	Left forearms	1	14
21	31	F	Left forearm, face	2	8/6
22	40	F	Left breast	1	12
23	41	F	Right hand	1	18
24	50	M	Right leg, right forearm	2	14/4

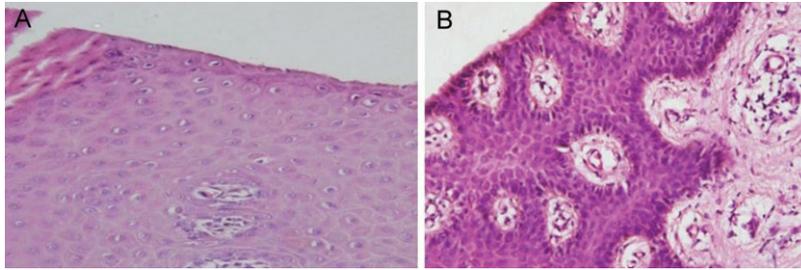
**Table 4** Age and sex of patients; site, size, and number of lesions and laser parameters used for each patient. M, male; F, female.

Response to laser therapy	Patients no. 3 and 8	Patients no. 1 and 4	Patients no. 5 and 7	Patients no. 2 and 6
Complete clearance				
75% reduction				
50% reduction		+		+
25% reduction	+		+	
No response				

**Table 5** Response of chronic plaque psoriasis to photodynamic therapy using 675 nm cw diode laser, 16 mW output power, for 15 min exposure time.



**Figure 1** Chronic plaque psoriasis on the left forearm of a 60-year-old man. (A) Before treatment and (B) 2 months after three PDT sessions using 675 nm cw diode laser, 16 mW output power. Fifty per cent clearance was achieved.



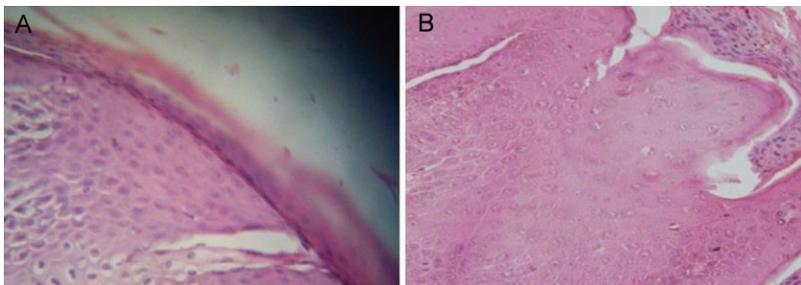
**Figure 2** Histological findings of the same patient as in Figure 1. (A) Before treatment: hyperkeratosis, parakeratosis, and absence of granular cell layer (H&E staining, magnification: ×40). (B) After treatment: small changes in stratum corneum, granular cell layer, and squamous cell layer (H&E staining; magnification: ×40).

Response to laser therapy	Patients no. 9 and 12	Patients no. 13 and 16	Patients no. 11 and 14	Patients no. 10 and 15
Complete clearance			+	
75% reduction				+
50% reduction	+	+		
25% reduction				
No response				

**Table 6** Response of chronic plaque psoriasis to photodynamic therapy using 671 nm cw diode laser, 50 mW output power, for 15 min exposure time.



**Figure 3** Chronic plaque psoriasis on the left arm of a 29-year-old male. (A) Before treatment and (B) 3 months after three PDT sessions using a 671 nm cw diode laser, 50 mW output power. Complete clearance was achieved.



**Figure 4** Histological findings of the same patient as in Figure 3. (A) Before treatment: hyperkeratosis, acanthosis, absence of granular cell layer, Munro's microabscess (H&E staining, magnification: ×40). (B) After treatment: less hyperkeratosis and parakeratosis, less acanthosis and restoration of granular cell layer (H&E staining; magnification: ×40).

Response to laser therapy	Patients no. 17 and 21	Patients no. 18 and 19	Patients no. 20, 23 and 24	Patients no. 22
Complete clearance		+	+	
75% reduction				+
50% reduction	+			
25% reduction				
No response				

**Table 7** Response of chronic plaque psoriasis to photodynamic therapy using 671 nm cw diode laser, 100 mW power, and 15 min exposure time.

### 3.5 Response of chronic plaque psoriasis to PDT using 671 nm diode laser, 100 mW power, and 15 min exposure time

Five patients showed complete clearance after three sessions using PDT with 671 nm cw diode laser of 100 mW power and irradiation for 15 min; one patient showed 75% reduction in PASI, while the other two patients showed 50% reduction after three sessions as listed in Table 7.

Figure 5 shows the complete clearance of a 43-year-old man treated by PDT on the dorsum of the left leg with the cw laser of 671 nm wavelength and 100 mW power for 15 min. Figure 6 shows the histological findings of this patient.

Figure 7 shows a comparison between plaques in a 40-year-old woman with chronic plaque psoriasis on the left breast, before and after treatment.

Figure 8 shows a comparison between plaques in a 43-year-old man with chronic plaque psoriasis on the right side of the chest, before and after treatment with PDT. Complete clearance can be seen here.

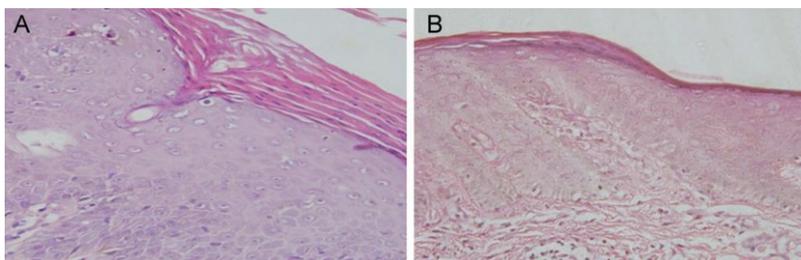
### 3.6 Adverse events

At each appointment, before starting the laser therapy, the adverse events following the laser session were evaluated and recorded in the patient sheet. No adverse sequels or complications were observed in patients treated with the laser; however one patient developed a phototoxic reaction 24 h after exposure to excessive sunlight.

Slight pain in the areas treated by PDT using laser with 671 nm, 100 mW output power, was recorded in



**Figure 5** Chronic plaque psoriasis on the dorsum of the left leg of a 43-year-old male. (A) Before treatment and (B) 1 month after three PDT sessions. Complete clearance was achieved.



**Figure 6** Histological findings of the same patient as in Figure 5. (A) Before treatment: hyperkeratosis, parakeratosis, acanthosis, absence of granular cell layer, dilated papillary dermal vascular (H&E staining, magnification:  $\times 40$ ). (B) After treatment: less hyperkeratosis, less parakeratosis and restoration of granular cell layer (H&E staining; magnification:  $\times 40$ ).



**Figure 7** Chronic plaque psoriasis on the left breast of a 40-year-old woman. (A) Before treatment and (B) 1 month after three PDT sessions using 671 nm cw diode laser, 100 mW output power, 15 min irradiation time. A 75% reduction in PASI was obtained.



**Figure 8** Chronic plaque psoriasis on the right side of the chest of a 43-year-old man. (A) Before treatment and (B) 1 month after three PDT sessions using 671 nm cw diode laser, 100 mW output power, 15 min irradiation time. Complete clearance was achieved.

three patients. It lasted for 1–2 days after PDT, but it didn't prevent the patients from continuing their therapy.

Discomfort was also observed in some of the patients treated with 50 mW and 16 mW output power diode lasers.

## 4 Discussion

Treatment of chronic plaque psoriasis by PDT achieved different results. The results with the cw diode laser using 16 mW output power for 15 min, were not bad, but after using cw diode laser with 50 mW output power for 15 min, we found that the response was better. Furthermore, using the cw diode laser with 100 mW for 15 min, the results were much better than using 50 mW for 15 min. The obtained results indicated the importance of choosing both the optimal exposure time and the laser power in order to achieve good results.

These results are consistent with those obtained by Radakovic-Fijan et al. [9] and by Fransson and Ros [10]. Peng et al. [11] concluded that optimizing parameters of ALA-based PDT gives promising results in different dermatological conditions. This is consistent with the results obtained in this study i.e., when the output power is increased, PASI is reduced significantly.

In a study carried out by Smits et al. [5], eight patients with stable, symmetrical psoriasis plaques were irradiated with 600–750 nm, 40 mW/cm<sup>2</sup>, once a week for 4 weeks

and the treatment led to a significant improvement. The sum score of PASI were also significantly lower in the ALA-treated plaques. They concluded that optimizing the current treatment protocol may further increase clinical efficacy.

In a another study conducted by Robinson et al. [6] using broad-band visible radiation, 15 mW/cm<sup>2</sup>, four out of 19 treated sites were cleared, 10 responded but did not clear and five showed no improvement.

With regard to short-contact ALA in epithelial skin tumors and psoriatic lesions, another study by Fritsch et al. [12] showed that a maximum concentration of ALA in the tumors and psoriatic skin was reached between 2 and 6 h.

## 5 Conclusions

From the results of this study one can conclude that:

1. PDT can be used as an alternative method for treatment of plaque psoriasis.
2. Increasing the power of low-level laser in PDT increased the clearance of plaque psoriasis.
3. The cost and availability of ALA remains a problem for using PDT to treat different skin diseases, including chronic plaque psoriasis.

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