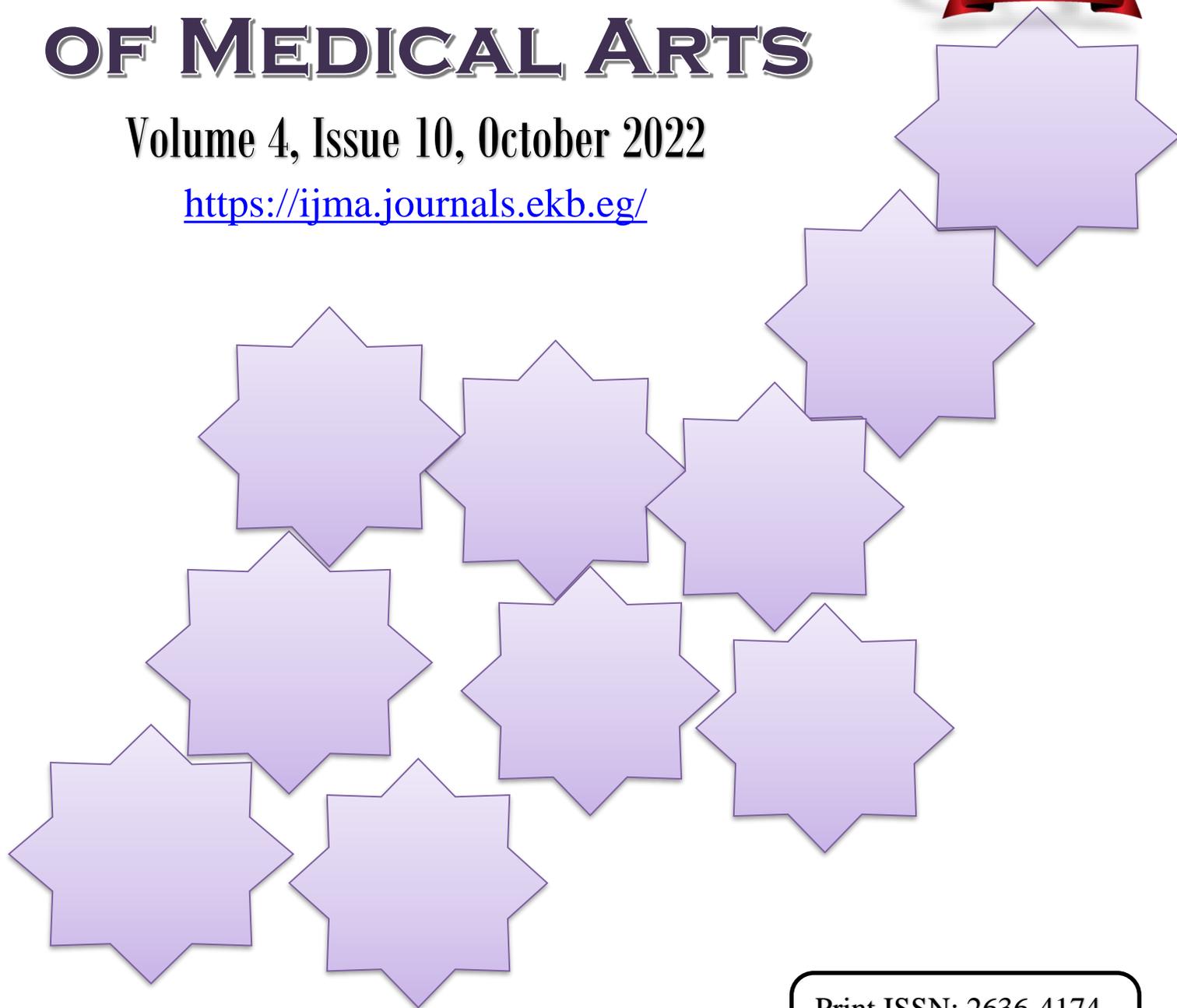


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## Original Article

# Monochromatic Excimer Light [308nm] versus Monochromatic Excimer Light [308nm] and 4% Khellin Extract in Treatment of Vitiligo

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## ABSTRACT

### Article information

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**Background:** Vitiligo is very common skin disease resulting from absence of active melanocytes and characterized by focal regions of depigmentation, which may induce great psychological problems for the patients. Many therapies such as topical, systemic and phototherapy are not always successful, and re-pigmentation is often incomplete.

**Aim of the work:** We aimed to compare between the efficacies of topical Khellin 4% and excimer light versus excimer light alone in treatment of vitiligo.

**Patients and methods:** A comparative study that was carried out on 100 patients with 200 patches of vitiligo lesions, divided into **group I**; 100 patches treated with topical khellin 4% solution before excimer light, and **group II**; 100 patches treated with excimer light alone, for 30 minutes, two sessions per week for six months.

**Results:** We found a significant difference decrease in surface area in group I when compared to the surface area in group II. The degree of improvement measured by quartile grading scale in the group I was higher than in group II. Moreover, the improvement rate in group I was faster than group II. Topical khellin 4% solution and excimer light, were safe and well tolerated, however, mild erythema and burning sensation were observed and resolved after that.

**Conclusion:** Topical khellin 4% solution and excimer light, are faster, effective, safe and well tolerated combination in treatment of vitiligo.

**Keywords:** Vitiligo; Topical khellin; Excimer light.



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## INTRODUCTION

Vitiligo is a chronic, pigmentary skin disease with a selective and progressive loss of functioning melanocytes of epidermis and hair follicle, which clinically translates to depigmented patches over the skin [1]. It estimated about 1% and range from 0.1 to more than 8.8% in different areas of the world [2]. Therefore, among factors regulating melano-genesis, the melanocortin/MC1R complex stands out as being the most important. The demonstration of receptor upregulation by UV light is particularly interesting, indicating a novel site for physicochemical interactions with the environment. Other important positive regulators of melanin pigmentation include endothelins, histamine, eicosanoids, and SCF acting via interaction with cell surface receptors [3].

The pathophysiology of vitiligo includes intrinsic and extrinsic melanocyte defects, T cell-mediated melanocyte destruction and innate immune inflammation [4].

There are different treatment modalities of vitiligo, topical calcineurin inhibitors, including topical and systemic steroids, phototherapy, surgery and JAK inhibitors as [as Tofacitinib, ruxolitinib] have been shown to block interferon-gamma signaling, contributing to re-pigmentation in individuals with vitiligo. However, these treatment options not always successful, and re-pigmentation is often incomplete [5].

A 308 nm excimer laser is the latest alternative NB-UVB treatment for vitiligo [6]. The safety and effectiveness of excimer laser phototherapy making it superior to that of NB-UVB phototherapy, because 308 nm excimer laser allow re-pigmentation within a shorter period of time than NB UVB phototherapy does, while limiting exposure to only selected areas. Also, the rapid onset of re-pigmentation may play an important role in supporting patients' motivation and compliance, and, importantly, the cumulative UV dose at the end of the treatment is significantly lower than with conventional NB UVB [7]. Phototherapy increased vitamin D levels in patients with low initial levels of 25-hydroxyvitamin D [25[OH] D], which indicates that the beneficial effect of phototherapy, on the induction of vitamin D and re-pigmentation [8].

Khellin has a chemical structure close to psoralens with similar phototherapeutic effects

but with less carcinogenic and phototoxic side effects. It has previously proven its efficacy in vitiligo, since it can stimulate a photosensitization and induce melanocyte proliferation and melanogenesis [9]. So, this work was aimed to compare between efficacy and safety of topical khellin 4% and excimer light versus excimer light alone in treatment of vitiligo.

## PATIENTS AND METHODS

The study was carried out after being approved by the local Ethics Committee of the Faculty of Medicine, Al-Azhar University, Assiut, Egypt, and informed written consent was obtained from all patients. The study was conducted by Helsinki standards as revised in 2013.

This is a comparative prospective clinical trial that was carried out on 100 patients presented with vitiligo. The patients selected from those attending the phototherapy unit at Dermatology and Andrology department of Al-Azhar University Hospital in [Assiut], between November 2020 and September 2021.

Patients with history of systemic or topical therapy for vitiligo and phototherapy during the last 2 months, patients with history of photosensitivity, photo-aggravated disorders, patients presented with segmental vitiligo, as well as, pregnant and breast-feeding women were excluded from the study.

All patients were subjected to complete history taking include: Personal history: as name, age, occupation, residence; Present history as: onset, course, and duration of vitiligo; Past history of any chronic or associated disorders; Family history of vitiligo, premature graying of hair, or other general diseases; and Drug history: as oral medications, topical medications, or phototherapy. Then, general examination and dermatological evaluation were done to detect the distribution and type of vitiligo, as well as, Wood's light examination to confirm diagnosis of vitiligo.

As regard the treatment protocol, 200 patches of vitiligo lesions [2 different patches of vitiligo at the same patient], were selected and divided into; **Group I:** 100 patches treated with topical khellin 4% solution and excimer light, patients were instructed to apply khellin 4 % solution to the depigmented skin patch as a thin film sufficient to cover the affected area, before

excimer light session, and **Group II:** 100 patches treated with excimer light alone.

Excimer light [Excilite  $\mu^{\text{TM}}$  [DEKA, Florence, Italy] was used, with a wave length 308 nm, a light spot sizes of 10, 20 and 25 mm, pulse width of 60 ns, and a light impulse energy of 6.5 mJ/cm<sup>2</sup> with a repeat frequency of 200 Hz. All patients were subjected to do 2 sessions per week for 6 months.

**Follow up:** Evaluation of clinical response included extent of recovery [pigmentation], recurrence, and possible side effects, as well as, comparing photos of the patient before and after treatment using Optimas photo analyzer program in which we analyzed photo diameter, perimeter, length and area of the lesions.

**Statistical methods:** Statistical analysis was performed using GraphPad Prism version 8.0.2 [GraphPad Software, La Jolla, CA]. Descriptive statistics for quantitative data were expressed in tables as the mean  $\pm$  SD, while qualitative data were expressed as number and percentage. We checked the normality of continuous data using Shapiro Walk test. We used unpaired Student's t-test to compare between two groups of normally distributed variables, while ANOVA test was used to compare between more than two groups of normally distributed variables. ANOVA repeated measure post hoc test [Bonferroni] was used to detect significance between periods. P-value was considered significant if  $< 0.05$ .

## RESULTS

Regarding clinic-demographic data of studied patients, the mean age was 34.89  $\pm$

14.42 years ranging between 18 and 60 years. Out of those patients, 79 [79 %] patients were female, and the others were male. The baseline characteristics of our studied population are shown in [Table 1].

The vitiligo lesions treated with khellin plus excimer light as well as, the lesions treated excimer alone showed a statistically significant reduction in surface area, at 3rd month and 6th month when compared to the baseline with p-value  $< 0.001$ , as shown in [Table 2].

There was a significant reduction in the surface area of the group I when compared to the surface area of the group II at the period between the baseline and 3 months. At the period between 3rd and 6th months, changes were no longer statistically significant, but there was a continual trend showing decreasing surface area. Moreover, there was a significant increase in improvement percentage in group I more than in group II, as shown in [Table 3].

As regard the degree of improvement we found a statistically significant increase in regimentation in the group I underwent the combination therapy versus group II after both three and six months [p=0.01] and 0.025 respectively. Moreover, about 77% of patients were satisfied in Group I, in comparison to 62 % of patient were satisfied in Group II, with P-value 0.016, as shown in [Table 4].

There was a significant difference between khellin plus excimer, versus excimer alone as regard adverse effects, as shown in [Table 5].

**Table [1]:** Demographic and clinical characteristics of vitiligo patients

Variables		Total number [100]
Age [years]	Mean $\pm$ SD	[18-60] 34.89 $\pm$ 14.42
	18-40 y	64 [64.0]
	41-60 y	36 [36.0]
Sex	Females	79 [79.0]
	Males	21 [21.0]
Smoking	No	86 [86.0]
	Yes	14 [14.0]
Duration [years]		[1-22] 8.07 $\pm$ 4.44
Course	Stable	74 [74.0]
	Unstable	26 [26.0]
Family history	Yes	35 [35.0]
	No	65 [65.0]
Pattern	Focal	74 [74.0]
	Acral	25 [25.0]
	Generalized	1 [1.0]

**Table [2]:** Comparison between the surface area of vitiligo before and after treatment

Surface area [cm <sup>2</sup> ]	Mean ± SD		95% CI	P <sub>a</sub> -value
<b>Khellin + Excimer light</b>				
At baseline	131.37 ± 133.76		[104.83-157.91]	<0.001*
After 3 months	87.82 ± 78.57		[72.23-103.41]	
After 6 months	55.48 ± 46.01		[46.35 - 64.61]	
Sig bet period	P <sub>1</sub> < 0.001*, P <sub>2</sub> <0.001*, P <sub>3</sub> <0.001*			
<b>Excimer light alone</b>				
At baseline	111.75 ± 104.18		[91.08 - 132.42]	<0.001*
After 3 months	86.24 ± 77.11		[70.94 - 101.54]	
After 6 months	62.62 ± 52.78		[52.15 - 73.10]	
Sig bet period	P <sub>1</sub> < 0.001*, P <sub>2</sub> <0.001*, P <sub>3</sub> <0.001*			

CI, confidence interval. P<sub>a</sub>-value for comparing between group at baseline and 3 and 6 months after application of excimer light. Sig bet periods were done using post hoc test [Bonferroni] for ANOVA with repeated measures. P<sub>1</sub>: P-value for comparing between pre and 3 months after treatment. P<sub>2</sub>: P-value for comparing between pre and 6 months after treatment. P<sub>3</sub>: P-value for comparing between 3 and 6 months after treatment

**Table [3]:** Comparison between group I and group II according to surface area reduction and percentage of improvement

	Group I	Group II	Mean difference	P- value
	Mean ± SD			
<b>Surface area reduction [cm<sup>2</sup>]</b>				
Baseline – 3 months	43.54 ± 61.73	25.51 ± 36.48	18.04	<b>0.013*</b>
Baseline -6 months	75.89 ± 100.28	49.12 ± 62.83	26.765	<b>0.025*</b>
3 months -6 months	32.34 ± 41.32	22.61 ± 33.11	9.73	<b>0.068</b>
<b>Percentage of improvement</b>				
Baseline – 3 months	28.94 ± 26.66	18.80 ± 10.51	10.14	<b>0.001*</b>
Baseline -6 months	48.22 ± 20.05	37.56 ± 18.09	10.66	<b>0.001*</b>
3 months -6 months	19.28 ± 23.29	18.76 ± 10.90	0.52	0.840

**Table [4]:** Comparison between group I and group II according to degree of improvement and patients' satisfaction

	Group I	Group II	p-value
<b>Quartile Grading Scale [3months]</b>			
Marked re-pigmentation >75%	4 [4.0]	1 [1.0]	0.010*
Moderate re-pigmentation 50-75%	11 [11.0]	8 [8.0]	
Mild re-pigmentation 25-49%	48 [48.0]	31 [31.0]	
Treatment failure; re-pigmentation < 25	37 [37.0]	60 [60.0]	
<b>Quartile Grading Scale [6months]</b>			
Marked re-pigmentation >75%	15 [15.0]	12 [12.0]	0.025*
Moderate re-pigmentation 50-75%	41 [41.0]	26 [26.0]	
Mild re-pigmentation 25-49%	31 [31.0]	34 [34.0]	
Treatment failure; re-pigmentation < 25	13 [13.0]	28 [28.0]	
<b>Patients' satisfaction</b>			
Very satisfied	52 [52.0]	33 [33.0]	0.016*
Satisfied	25 [25.0]	29 [29.0]	
Poorly satisfied	23 [23.0]	38 [38.0]	

**Table [5]:** Comparison between group I and group II according to degree of improvement and patients' satisfaction

	Group I	Group II	P-value
<b>No side effect</b>	68 [68.0]	92 [92.0]	<0.001*
<b>Erythema</b>	23 [23.0]	5 [5.0]	
<b>Bullae</b>	5 [5.0]	0 [0.0]	
<b>Burning sensation</b>	4 [4.0]	3 [3.0]	

## DISCUSSION

Treatment of vitiligo is challenging and unsatisfactory [5]. Therefore, in our study we used combination of topical khellin 4% with excimer light in group I and excimer light alone in group II to evaluate the percentage of improvement before and after treatment.

Our study encountered 100 patients with vitiligo, with 200 patches of vitiligo divided into 2 equal groups, **group I** 100 patches treated with topical khellin 4% and excimer light, and **group II** 100 patches treated with excimer light alone

Regarding to the descriptive data of our patients, the mean age was  $34.89 \pm 14.42$  years ranging between 18 and 60 years, incidence was [64%] in age group 18-40 years and [36%] in the age group 41-60 years. In continuation with our findings, **Nistico et al.** [10], found that, the mean age of their participants was 41.2 years.

Out of our 100 patients, 79 [79 %] patients were female. In agreement with the current finding, several studies as **Zhang et al.** [6], and **Majid** [11]. They explained female predominance by the high cosmetic concern in females than males.

In our study, 35 [35%] of patients had positive family history. Positive family history of vitiligo was variable in different studies, it was 26% in **Karelson et al.** [12], and 36% in **Gopal et al.** [13].

In our study, we found that, the vitiligo lesions treated with khellin plus excimer light as well as, the lesions treated excimer alone showed a statistically significant reduction in surface area, at 3rd month and 6th month when compared to the baseline. Moreover, there was a significant reduction in surface area of the group I when compared to the surface area of the group II at the period between the baseline and 3 months. At the period between 3<sup>rd</sup> and 6<sup>th</sup> months, changes were no longer statistically significant, but there was a continual trend showing decreasing surface area. Also, there was a significant increase in improvement percentage of regimentation in group I more than in group II.

In agreement with our findings, **Nistico et al.** [10], conducted a study on 16 vitiligo patients. They divided into two equal groups, **Group I** included 8 patients, treated with excimer light; **Group II** included 8 patients treated with excimer light associated with topical khellin

4%. At the end of the study, Group I showed marked and moderate re-pigmentation in 50 % of patients while in Group II showed marked and moderate re-pigmentation in 75 % of patients.

Similarly, **Saraceno et al.** [14], conducted a prospective study on 32 vitiligo patients. They divided into 2 groups, **group I** [16 patients treated with excimer light 308 nm once-weekly and oral vitamin E]; **group II** [16 patients treated with excimer light once-weekly combined with application of khellin 4% ointment and oral vitamin E]. Considering each study group, **group I** showed good and excellent re-pigmentation in [87.5%] patients, and **group II** showed good and excellent re-pigmentation in [87.5%].

The previous results can be explained by the fact that, the great efficacy of Khellin in treatment of vitiligo as it has a furanochromone action which induces a photosensitization and stimulates melanocyte proliferation and melanogenesis [15].

In our study, there was a significant difference between group I and group II as regard adverse effects, in group I there is mild erythema in [23%], bullae in [5%] and burning sensation in [4%]. In group II there is mild erythema in [5%] and burning sensation in [3%]. In agreement with our findings, **Nistico et al.** [10], found mild erythema 50%. Group I: 4/8 patients; Group II: 5/8 patients; burning/pain 18.7%. Group I: 1/8; Group II: 2/8.

As regard patients' satisfaction, the majority of patients satisfied more with combined therapy [khellin plus excimer light] than patients treated with excimer light alone, in group I: 52 % very satisfied, 25 % satisfied 23 % poorly satisfied, in group II: 33% very satisfied, 29 % satisfied, 38 % poorly satisfied.

In agreement with our findings, **Nistico et al.** [10], found that all patients in their study were satisfied since the therapeutic protocol was well tolerated, easy to administer, and not time-consuming. Moreover, patients showed a significant improvement of their life quality, improvement of their body image, less embarrassment during relationships, and a more optimistic attitude towards life in general and their disease.

**Limitations:** Our study has some limitations: first, we included only patients from Upper Egypt area, which may stress on the significance of geographical and ethnic

background in the clinical presentation and improvement of vitiligo. Second, small sample size and a relatively short period of study suggest significant differences in our findings with the other studies.

**Recommendations:** For safe, easy, inexpensive method we recommend the use of combination of topical khellin 4% and excimer light in treatment of vitiligo. We also recommend confirmation of our results by further studies with high-quality randomized controlled trials, long period of study and follow-up and selection of different ethnic groups.

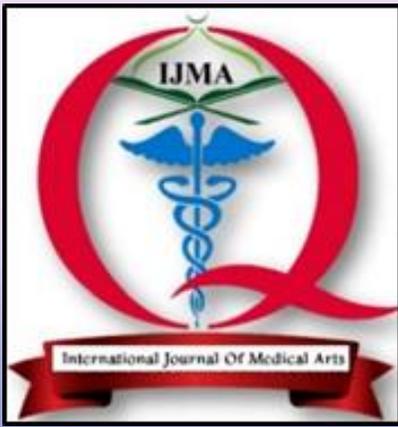
**Conclusion:** We concluded that, topical khellin 4% solution and excimer light, are effective, faster, safe, and well tolerated combination in treatment of vitiligo. Khellin is a furanochromone which induces a photosensitization and stimulates melanocyte proliferation and melanogenesis.

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**Conflicts of interest:** We declare that we have not any conflict of interest.

## REFERENCES

1. Taïeb A, Seneschal J, Mazereeuw-Hautier J. Special Considerations in Children with Vitiligo. *Dermatol Clin.* 2017 Apr;35[2]:229-233. doi: 10.1016/j.det.2016.11.011.
2. Sehgal VN, Srivastava G. Vitiligo: compendium of clinico-epidemiological features. *Indian J Dermatol Venereol Leprol.* 2007 May-Jun;73[3]:149-56. doi: 10.4103/0378-6323.32708.
3. Slominski A, Tobin DJ, Shibahara S, Wortsman J. Melanin pigmentation in mammalian skin and its hormonal regulation. *Physiol Rev.* 2004 Oct;84[4]:1155-228. doi: 10.1152/physrev.00044.2003.
4. Rashighi M, Harris JE. Vitiligo Pathogenesis and Emerging Treatments. *Dermatol Clin.* 2017 Apr; 35[2]:257-265. doi: 10.1016/j.det.2016.11.014.
5. Alhwaish AK, Dietrich N, Onder M, Fritz K. Effectiveness of a 308-nm excimer laser in treatment of vitiligo: a review. *Lasers Med Sci.* 2013 May;28[3]:1035-41. doi: 10.1007/s10103-012-1185-1.
6. Zhang XY, He YL, Dong J, Xu JZ, Wang J. Clinical efficacy of a 308 nm excimer laser in the treatment of vitiligo. *Photodermatol Photoimmunol Photomed.* 2010 Jun;26[3]:138-42. doi: 10.1111/j.1600-0781.2010.00509.x.
7. Hong SB, Park HH, Lee MH. Short-term effects of 308-nm xenon-chloride excimer laser and narrow-band ultraviolet B in the treatment of vitiligo: a comparative study. *J Korean Med Sci.* 2005 Apr;20[2]:273-8. doi: 10.3346/jkms.2005.20.2.273.
8. Ibrahim H, El Taieb M, El Gamel Z, El Saied AR. Effect of narrow-band ultraviolet B on the serum of 25-hydroxyvitamin D in vitiligo patients. *J Cosmet Dermatol.* 2018 Oct;17[5]:911-916. doi: 10.1111/jocd.12515
9. Hashim S, Jan A, Marwat KB, Khan MA. Phytochemistry and medicinal properties of Ammi visnaga [Apiaceae]. *Pak J Bot.* 2014 Jun 1;46[3]:861-7.
10. Nistico S, Cannarozzo G, Sannino M, Del Duca E, Bottoni U. 308 nm UV excimer light in monotherapy or combined to topical khellin 4% and/or tacrolimus 0.1% in the treatment of vitiligo. *Glob Dermatol.* 2015;2:93-6. doi: 10.15761/GOD.1000129
11. Majid I. Does topical tacrolimus ointment enhance the efficacy of narrowband ultraviolet B therapy in vitiligo? A left-right comparison study. *Photodermatol Photoimmunol Photomed.* 2010 Oct;26[5]:230-4. doi: 10.1111/j.1600-0781.2010.00540.x.
12. Karelson M, Kingo K, Salum T, Kõks S, Silm H. An Adults Vitiligo in Estonia: Study of 155 Patients. *Open Dermatol J.* 2009;3[1]:68-72. doi: 10.2174/1874372200903010068
13. Gopal KV, Rama Rao GR, Kumar YH, Appa Rao MV, Vasudev P; Srikant. Vitiligo: a part of a systemic autoimmune process. *Indian J Dermatol Venereol Leprol.* 2007 May-Jun;73[3]:162-5. doi: 10.4103/0378-6323.32710.
14. Saraceno R, Nisticò SP, Capriotti E, Chimenti S. Monochromatic excimer light 308 nm in monotherapy and combined with topical khellin 4% in the treatment of vitiligo: a controlled study. *Dermatol Ther.* 2009 Jul-Aug;22[4]:391-4. doi: 10.1111/j.1529-8019.2009.01252.x.
15. Carlie G, Ntusi NB, Hulley PA, Kidson SH. KUVVA [khellin plus ultraviolet A] stimulates proliferation and melanogenesis in normal human melanocytes and melanoma cells in vitro. *Br J Dermatol.* 2003 Oct;149[4]:707-17. doi: 10.1046/j.1365-2133.2003.05577.x.



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