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Action Spectrum for Phototherapy of Psoriasis

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Using a monochromator the action spectrum for ultraviolet phototherapy of psoriasis was determined for radiation between 254 and 313 nm and compared to the action spectrum for erythema of uninvolved adjacent skin. Daily exposures of different doses of 254, 280, 290, 296, 300, 304 and 313 nm radiation were observed. Wavelengths of 254, 280, and 290 nm were erythemogenic but not therapeutic even at 10 to 50 times the minimal erythema dose. At the other wavelengths studied, the 2 action spectra were similar. In general, fixed daily doses cleared at lower cumulative dose than did incrementally increased daily doses. The small number of suberythemogenic exposure doses required suggests that monochromatic radiation may have advantages over broadband sources.

Phototherapy and heliotherapy with and without tar products have been standard moderately effective therapies for psoriasis for many decades. Although several observations define its general shape, the action spectrum for the therapeutic effects of ultraviolet radiation (UVR) has not been precisely defined. When considering the spectral sensitivity of skin, commonly used broadband exposure devices can be considered essentially UVB (290-320 nm) sources. Phototherapy, using these sources, improves psoriasis with exposure to erythemogenic doses [1–4]. High-pressure mercury lamps, mercury xenon sources, fluorescent "sunlamps" and sunlight are all moderately effective if repeated erythemogenic exposure doses are used. Fischer [5] showed that a narrow waveband at 313 nm was effective in clearing small exposure sites within plaques of psoriasis. Parrish [6] has shown that large doses of broadband UVA (60-300 J/cm^2, 320-400 nm) similarly cleared small areas of psoriasis.

All phototherapy of psoriasis is limited by the acute injurious effects of ultraviolet radiation on normal uninvolved skin. In order to design maximally safe and effective treatment systems and protocols, it is important to know the action spectrum of phototherapy of psoriasis and compare it with the action spectrum for phototoxicity of normal skin manifest by delayed erythema. Such a comparison is the subject of this report.

MATERIALS AND METHODS

Four male Caucasian volunteers with 50% or greater body involvement of psoriasis were studied. An Optical Radiation Corporation V-4500 housing with a 5000 W Xe-Hg d.c. compact arc lamp optically matched to a Jobin Yvon HL300 holographic grating monochromator was used to obtain radiation at 280 nm, 290 nm, 296 nm, 300 nm, 304 nm, and 313 nm (6 nm half-bandwidths). Low-pressure mercury discharge lamps filtered with a cyanine periodate/Bäckstrom liquid solution [7] were used to obtain 253.7 nm radiation. Irradiance measurements were made with either an Eppley (Model 16170E4) or Oriel (Model 7102) thermopile and a Keithley (Model 150B) microvoltmeter. At least 3 irradiance measurements were taken in different areas of each field site to insure uniform irradiance within ± 10%. Irradiance measurements were done prior to each experiment and again at its conclusion. Stray light was less than 10^{-5} for both sources.

For each wavelength used, the minimal erythema dose (MED) was determined on normal (uninvolved) skin adjacent to treatment sites by using geometric increments of 20%. Delayed erythema was read at 24 hr after exposure, except for the 254 nm MED, which was read at 8 hr after exposure. Experimental irradiation sites within plaques of psoriasis vulgaris ranged in area from 5 cm^2 to 12.5 cm^2. At each wavelength at least 9 different sites were exposed daily (6 times/week) for 4 weeks. Exposure doses on 7 of these sites were 0.2, 0.4 , 0.6, 0.8, 1.0, 1.5, and 2.0 or 2.5 times the previously determined MED. Two additional sites for each wavelength were irradiated initially with 1 MED then with daily increases in exposure dose of 10% and 20% respectively. At 254, 280 and 290 nm, additional sites were exposed daily to greater doses up to 53 × MED. All experimental sites were lubricated with mineral oil twice daily, immediately before bed and 15 min before irradiation. No other topical lubricants or systemic or topical medications were used during the course of the study. One additional patient (#5) was treated for 28 days with 10, 28 and 43 × MED at 254 nm.

Treated sites were observed daily. The following grading was used:

O:No change.
SPR:Slight regression—minimal but definite reduction in plaque induration.
PR:Plaque regression—marked improvement, considerable reduction in plaque induration.
PC:Plaque clear—complete disappearance of induration in 90% of the treated site. Reappearance of normal skin texture.

Subjects #2 and #4 were skin type III, subject #1 was skin type II, and subject #3 was skin type I. Erythema and pigmentation within the treated sites were recorded on a 0–4+ scale [8].

RESULTS

At 254, 280 and 290 nm no exposure sites showed any improvement at any exposure dose. At these wavelengths the lowest effective daily dose for complete clearing (LEDD) must be greater than the highest exposure dose tested in this experiment because no improvement was seen even though 10 to 53 times MED were used (see Table I). Subject #5 showed no response to exposures of 10, 28 and 43 × MED at 254 nm.

At 296 nm, results ranged from no effect to complete clearing depending upon daily exposure dose. In 2 subjects, repeated suberythemogenic exposure doses led to clearing. That is, in both patients #1 and #3 the LEDD was lower than the MED. In one subject (#4) repeated exposure to 1.5 times MED was required for complete clearing and the other subject showed improvement but not clearing at the highest dose used (2.5 × MED in subject #2).

At both 300 and 304 nm, complete clearing occurred with daily exposures to doses equal to or less than MED in all but subject #2. In subject #2, the 1 × MED site at 300 nm was improved but repeated exposures to 2.5 × MED was required for complete clearing.

In every subject, suberythemogenic exposure doses of 313 nm led to complete clearing. As little as 0.2 × MED was effective in subject #1. 0.4 × MED showed improvement in every subject but led to complete clearing only in subject #1. But because the MED for 313 nm radiation is more than 10 times greater than that for shorter wavelengths, LEDD was at least 10 times greater at 313 nm than LEDD at 300 or 304 nm. Furthermore, sites treated with 2.0 or 2.5 × MED at 313 nm or with incre-

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TABLE I. *Comparison of Minimal Erythema Dose of Normal Skin and Lowest Effective Daily Dose to Clearing of Psoriasis*[a]

λnm	Pt. 1			Pt. 2			Pt. 3			Pt. 4		
	mJ/cm² MED	mJ/cm² LEDD	LEDD/ MED	mJ/cm² MED	mJ/cm² LEDD	LEDD/ MED	mJ/cm² MED	mJ/cm² LEDD	LEDD/ MED	mJ/cm² MED	mJ/cm² LEDD	LEDD/ MED
254	19.0	>1007	>53	18	>900	50	ND	ND	ND	ND	ND	ND
280	49.0	>1029	>21	49	>1225	>25	45	>1125	>25	59	>590	>10
290	33	>924	>28	48	>1200	>25	17	>425	>25	31	>310	>10
296	26	21	0.8	22	>55	>2.5	17	10	0.6	26	39	1.5
300	41	16	0.4	34	85	2.5	27	21	0.8	32	19	0.6
304	76	30	0.4	119	72	0.6	28	28	1	62	62	1
313	1971	400	0.2	1643	986	0.6	478	287	0.6	1100	660	0.6

[a] Minimal erythema dose (MED) and lowest effective daily dose to clearing (LEDD) in 4 subjects. Doses preceded by > give the highest dose tested in this experiment. Because clearing was not achieved at this dose the actual LEDD will be greater than this dose. Suberythemogenic exposure doses lead to clearing if LEDD/MED <1.

TABLE II. *Comparison of number of treatments to clear with lowest effective daily dose to clearing (LEDD) and with incrementally increasing doses*[a]

Subject Number	$(1.1)^N$ MED			4	$(1.2)^N$ MED				LEDD			
	1	2	3		1	2	3	4	1	2	3	4
λnm												
296	10	×	15	×	10	×	14	ND	5	×	19	15
300	5	11	20	16	5	11	21	ND	5	12	23	21
304	7	6	17	12	7	6	17	ND	4	9	23	12
313	7	8	18	5	7	ND	ND	ND	6	13	23	12

[a] Number of treatments required to achieve complete clearing at each waveband for each of 3 daily exposure doses. MED = minimal erythema dose. $(1.1)^N$ MED refers to daily increase in dose by 10%, $(1.2)^N$ MED refers to daily incremental increase of 20%, N = treatment number. Numbers at top of each column refer to subject number. X means that complete clearing was never achieved. ND means not done.

TABLE III. *Lowest number of treatments to clear*[a]

λnm	Subject 1		Subject 2		Subject 3		Subject 4	
	Treatments	MED Multiple	Treatments	MED Multiple	Treatments	MED Multiple	Treatments	MED Multiple
296	5	0.8*	>14	>2.5	14	$(1.2)^N$	11	2.0
300	5	0.4*	11	$(1.1)^N$	20	$(1.1)^N$	11	2.0
304	4	0.4*	6	1.0	17	$(1.1)^N$	6	1.2
313	5	1.0	7	1.0	18	$(1.1)^N$	5	$(1.1)^N$

[a] The lowest number of treatments to clear and the exposure dose in multiples of minimal erythema dose (MED) leading to this clearing are listed. $(1.1)^N$ and $(1.2)^N$ refer to 10% and 20% daily increases in dose where N = treatment number. The MED multiples with asterisks are equal to those lowest effective daily doses which cleared psoriasis (LEDD).

TABLE IV. *Cumulative dose to clearing at lowest effective daily dose to clearing of psoriasis (LEDD) and incrementally increasing doses*[a]

Subject #	$(1.1)^N$ mJ/cm²				$(1.2)^N$ mJ/cm²				LEDD mJ/cm²			
	1	2	3	4	1	2	3	4	1	2	3	4
λnm												
296	740	>614	578	>1,857	1,032	1,298	1,176N	105[b]	>7	19[b]	58[b]	
300	430	634[b]	1,703	1,151	459	1,098	4,152 D	80[b]	70	0[b]	5[b]	
304	1,258	920	1,226	1,327	1,480	1,183	3,495N	120[b]	1,0[b]	48[b]	39[b]	
313	32,640	18,784	23,950	6,700[b]	34,521	ND	ND D	2,400[b]	32[b]	3[b]	9	
							N		64	64	74	
							D		8	4	4	
							N		12,	6,6	7,9	
							D		81	01	20	
									8			

[a] Cumulative dose to clearing in mJ/cm² at sites treated with 10% increments [$(1.1)^N$ MED], 20% increments [$(1.2)^N$ MED], and daily dose which proved to be lowest effective daily dose to clear psoriasis (LEDD). N = treatment number.

[b] The lowest cumulative dose at each wavelength leading to clearing. In all but 2 cases the lowest cumulative dose to clearing occurred at fixed LEDD and not with incrementally increasing doses.

mentally increasing doses showed tenderness, increase in induration and scaling, and occasionally petechiae.

At some sites complete clearing was achieved in as few as 4 to 7 treatments (see Table II). Except for subject #1, in general, but not always, sites exposed to incrementally increased doses cleared quicker (fewer number of treatments) than sites exposed repeatedly to fixed doses that later proved to be LEDD, but the differences were small. However, exposure doses greater than LEDD often led to complete clearing in even fewer treatments (see Table III).

At each wavelength causing clearing, sites exposed to fixed daily doses cleared with smaller cumulative dose than sites treated with incremental increasing doses (Table IV). The only exceptions were seen in subject #2 at 300 nm and in subject #4 at 313 nm. At 300 nm in subject #2, the site treated daily with 10% increase in dose had lower cumulative dose to clearing than was accomplished with a fixed dose at LEDD. At 313 nm in subject #4 10% incremental increases led to lower cumulative dose to clear than with the fixed dose that proved to be LEDD.

With 2 exceptions (subject #2 at 300 nm and subject #4 at

TABLE V. *Lowest cumulative dose to clearing*[a]

λnm	Dose mJ/cm²	MED multiple	Dose mJ/cm²	MED multiple	Dose mJ/cm²	MED multiple	Dose mJ/cm²	MED multiple
296	105	0.8	>770	>2.5	190	0.6	572	2.0[b]
300	80	0.4	634	$(1.1)^N$	483	0.8	399	0.6
304	120	0.4	648	0.6	644	1.0	446	1.2[b]
313	2,400	0.2	11,501	1.0[b]	6,601	0.6	6,700	$(1.1)^N$

[a] Lowest cumulative dose to clearing at each waveband. MED = Minimal erythema dose of adjacent uninvolved skin prior to any phototherapy. $(1.1)^N$ = Daily doses increased by 10%, N = treatment number.

[b] In 3 sites a fixed daily dose greater than lowest effective daily dose to clearing (LEDD) led to a lower cumulative dose because at the higher dose fewer treatments were required.

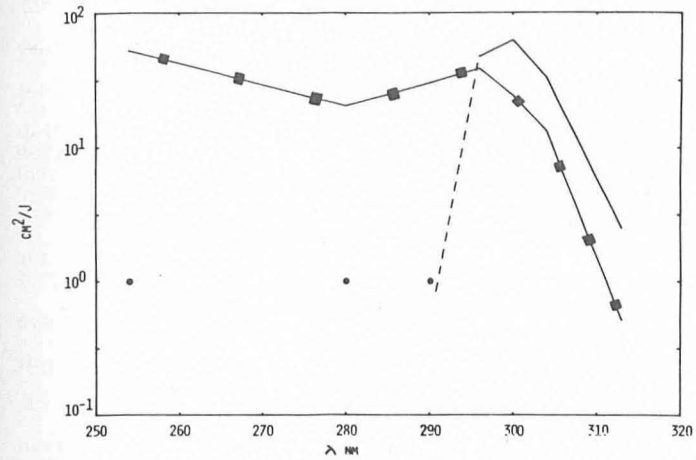

FIG 1. The erythema action spectrum (subject 1) (the reciprocal of the minimal erythema dose vs. λ nm) is indicated by the line with *squares*. The phototherapy action spectrum (reciprocal of lowest effective daily dose to clearing vs. λ nm) is shown by the *solid line*. The *circles* represent the highest doses tried on a daily basis at wavelengths which showed no improvement of psoriasis. The *dotted line* shows the rapid decline in therapeutic effectiveness of wavelengths less than or equal to 290 nm.

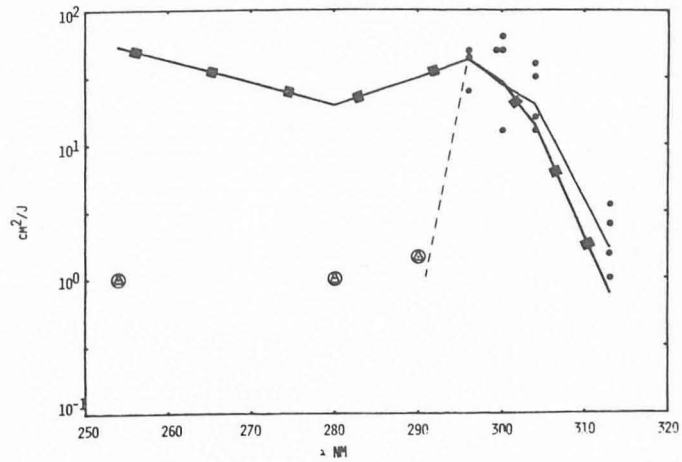

FIG 2. The erythema action spectra mean (subjects 1 to 4) is indicated by the line with *squares*. The phototherapy action spectrum mean is shown by the *solid line*. The *solid circles* represent each subject's reciprocal lowest effective daily dose to clearing. The *circles* with *triangles* represent means of the highest doses tried on a daily basis at wavelengths which showed no improvement of psoriasis. The *dotted line* shows the steep decline in therapeutic effectiveness at wavelengths less than or equal to 290 nm.

313 nm), the lowest cumulative dose to clearing was achieved with a fixed daily dose instead of incremental increasing doses (Table V). In 3 sites (footnote b in Table V) a fixed daily dose greater than LEDD led to a lower cumulative dose because fewer treatments were required at the larger exposure dose. The action spectra for delayed erythema in all of the subjects was within normal values [8]. Fig 1 gives a typical delayed erythema action spectrum (subject #1) and compares this to the action spectrum for the complete clearing of psoriasis under the conditions of this study. Fig 2 compares the combined action spectra for delayed erythema and phototherapy in all subjects.

Subsequent to this study these patients were treated with conventional treatments and proved to be difficult to manage. Two patients cleared very slowly (20 and 22 treatments) on protocols known to be effective [9]. One additional patient could not be improved at all with 14 treatments with UVB (FS40 bulbs) therapy. The final patient required both Methotrexate and PUVA to clear. This suggests that the fewer number of treatments required to clear psoriasis in small areas with monochromatic radiation was probably not due to patient selection.

DISCUSSION

The action spectra for phototherapy of psoriasis and for delayed erythema of normal skin are quite different for wavelengths less than or equal to 290 nm. Radiation of wavelengths less than 296 are very phototoxic to normal skin as manifest by a low threshold for induction of delayed erythema. This radiation is, however, not effective in phototherapy. Repeated daily exposure to as many as 50 times MED caused no gross changes in treated sites of psoriasis.

The marked decrease in effectiveness of wavelengths shorter than 296 nm may be explained by optical and structural differences between psoriatic and normal skin. In psoriasis the proliferative compartment at the bottom of the epidermis is thicker and on the average is deeper within the tissue. There is also an increased thickness of stratum corneum and an increased scale with multiple air-tissue interfaces in psoriasis. Epidermal proteins absorb wavelengths shorter than approximately 295 nm, and optical scattering also increases at shorter wavelengths. In general, transmission decreases exponentially with increasing thickness of an optical barrier. Transmission of radiation shorter than 290 nm to the proliferating epidermal cells in psoriasis may therefore be markedly reduced compared with that for normal skin. Considering thickness alone, a 4-fold increase in stratum corneum thickness over that of normal skin (8 to 10 μm) could decrease transmission of radiation at 280 nm by a factor of 10^4 or more. Other explanations for the ineffectiveness of shorter wavelengths are possible. Phototherapy and ultraviolet induced inflammation may involve entirely different chromophores. Competitive waveband interaction may occur with broadband sources with shorter wavelengths having a net proliferogenic stimulus.

In the region of 296-313 nm the action spectrum for phototherapy appears to be similar to that for delayed erythema. At 296, 300 and 304 nm the exposure dose required to induce delayed erythema is similar to the daily dose required to clear psoriasis from small sites within psoriatic plaques.

Previous studies suggest that the action spectra for delayed erythema of normal skin and for therapy of psoriasis may also be closely aligned in the UVA region. UVA is markedly less erythemogenic than is UVB, requiring as much as 1000 times greater doses [6]. Young and van der Leun [10] found that 14 daily exposures to 7-14 J/cm² of UVA had no effect on psoriasis. No erythema was reported to occur on normal skin. Fischer [5]

found 30 J/cm^2 of primarily 365 nm radiation to be ineffective in most test sites. Normal skin was not irradiated but this dose may be minimally erythemogenic to some, but not all, light Caucasians. Parrish [6], using larger exposure doses of 50 to 300 J/cm^2, found broadband UVA (320-400 nm) to be effective in clearing psoriasis from small exposure sites. Comparative studies showed these doses of UVA to be as effective as doses of UVB 1000 times less. The UVA MED with the same exposure sources was 20 to 100 J/cm^2.

The results of this study suggest that eliminating radiation of wavelengths less than 296 nm, which are erythemogenic but apparently not phototherapeutic, may improve the efficacy of phototherapy. This may in part explain the effectiveness of so-called selective ultraviolet phototherapy [11–13] which has peak emission at 300 to 325 nm and heliotherapy at the Dead Sea where increased solar ultraviolet pathlengths may decrease photon flux of shorter wavelength ultraviolet radiation [14]. This work also suggests that monochromatic radiation may be more therapeutic than exposures to broadband sources. The number of treatments and cumulative dose to clearing was considerably less than required with conventional UVB sources [9, 15]. This difference may be related to the small experimental sites employed, but this appears unlikely. At the end of this study, 2 patients were treated with total body UVB using fluorescent FS40 Westinghouse bulbs, which have a broad emission spectrum including wavelengths as short as 275 nm, and it was found that within 7 days psoriasis selectively returned to sites previously exposed and cleared using the monochromatic source at 300, 304, 313 nm. This suggests that broadband sources may not be unnecessarily erythemogenic but may contain nontherapeutic, proliferogenic components.

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