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ULTRAVIOLET THERAPEUTIC APPLICATIONS

Many of the therapeutic applications are still the subject of considerable controversy. Some of the beneficial results have a sound physical basis. Some may be partly psychological. Even where there is agreement as to results, the modus operandi is still in question. The whole subject is one in which much work remains to be done. In only a few areas of the biological field is the application of ultraviolet on a reasonably satisfactory quantitative basis. These are the production of erythema, prevention and cure of rickets, and the killing of bacteria and molds. With respect to these effects there exists a considerable amount of quantitative data relating the effects to the amount of energy and wavelength, and workers in the field are in rather substantial agreement.

A few hours after exposure to ultraviolet results in a reddening of the skin called erythema, or more commonly, sunburn. It ordinarily appears in 1 to 6 hours after exposure and gradually disappears in 1 to 3 days. Erythema is different from hyperemia, a reddening due to temporary excess of blood in the network of small vessels in the skin. The latter is produced by visible and infrared radiation in sufficient intensity, and disappears soon after irradiation.

The intensity of erythema depends upon the exposure. A just perceptible erythema, called minimum perceptible erythema, or MPE is used as a convenient measure of ultraviolet dosage. (An MPE disappears in 24 hours.) Greater exposure results in various degrees of inflammation or even blistering or hemorrhage. The histology and etiology have been studied in considerable detail, but the phenomena are complex and not thoroughly understood. It is known however, that histamine or histamine-like substances are formed in the skin. Erythema is followed by pigmentation or tanning of the skin which becomes noticeable two or three days after irradiation.

The relation between wavelength and erythema effects was first established by Hausser and Vahle. Others have also confirmed their work, and there is now general agreement on this relation. The erythema curve is shown in Fig.1. This curve shows the relative effectiveness of equal amounts of energy at different wavelengths in producing erythema. It can be seen, the most effective wavelength is about 297nm. Wavelengths around 250nm. are also very effective, the region between being less effective. Almost no erythema is produced by wavelengths longer than 320nm. These values differ for different individuals, and depends upon previous exposure. The curve in Fig.1 is for an average untanned skin. All observers are in good agreement on the region between 280 and 320nm.

By means of this curve it is possible to express the effectiveness of a given amount of energy at any wavelength in terms of the amount of energy of 297nm. which would have the same erythema effect. If the energy distribution of any source of ultraviolet is known, its erythema effect may be calculated by multiplying the values of energy in each wavelength region by the corresponding ordinate of the erythema curve and taking the sum of all of these values. This will be the equivalent to the amount of energy at 297nm. which would have the same effect as the source under consideration.

Minimum perceptible erythema is produced by 250,000 ergs per cm^2 of 297nm. This is equivalent to 25,000 $\mu\text{W-sec}$ per cm^2 of 297nm. or its erythema equivalent.

The type of erythema produced depends somewhat on the wavelength. The erythema produced by longer wavelengths develops more slowly than that which is produced by shorter wavelengths. The erythema produced by wavelengths shorter than 270nm. is of a more superficial character than that produced by longer wavelengths. This may be due to the fact that penetration of the shorter wavelengths into the skin is less.

The latent period for erythema produced by solar radiation is somewhat less than for erythema produced by the mercury arc. (D. Langen, Strahlentherapie, 63, 163 (1938)) - The former increases relatively rapidly after exposure and reaches its maximum in about 5-6 hours. The erythema produced by mercury arcs shows a latent period of 2-3 hours after which it increases gradually to its maximum in about 9 hours..

The relation between the degree of erythema and its intensity of irradiation depends upon the wavelength. Equal multiples of the threshold dose at different wavelengths do not produce equal degrees of erythema. The degree of erythema increases much more rapidly with increase in dose of the longer than the shorter wavelengths. Thus Hausser and Vahle found that a small increase in exposure to 302nm. over that required to produce MPE resulted in a more severe erythema than an exposure of several times the threshold value of for 254nm. radiation. Thus an exposure of several times the threshold value of of solar radiation will produce more severe burns than in a similar over-exposure to a germicidal lamp which radiates only in the shorter wavelengths. The extent to which the degree of erythema increases with dose is roughly parallel to the ratio of energy between 280-315nm. to that between 240-280nm.

The degree of erythema produced by exposure to midsummer noonday sun in terms of dose which produces MPE is as follows:

Relative Exposure Time	Degree of Erythema
1	MPE
2.5	Vivid, producing moderate tan.
5	Painful "burn".
10	Blistering.

Erythema is also produced by wavelengths between 320 and 420nm. However, this region requires 500 to 800 times as much energy to produce the same effect as at 300nm.

Pigmentation or Tanning from exposure to ultraviolet becomes noticeable about 48 hours after exposure, and increases gradually for several days. Tanning is in part due to the migration of the pigment melanin, which is already present in the basal cells, to the more superficial layers of the skin where it has a greater effect on the spectrum of reflected light. It is also in part due to the formation of new pigment. The tanning response curve or action spectrum appears to follow the erythema curve in a general way. The type of tanning, however, appears to vary with wavelength, being a deeper brown when produced by longer wavelengths and somewhat more yellowish when produced by shorter wavelengths. Tanning seems to be a mechanism for protecting the skin by screening out the ultraviolet. In addition another result to ultraviolet exposure is a thickening of the stratum corneum or outer layer of the skin so that it screens more effectively.

The formation of pigment involves two separate photobiological processes. They are primary melanization (melanin formation) and pigment darkening. Also it has been shown that pigment darkening (darkening of the already existing melanin as the result of an oxidation reaction) is caused by a broad band of radiation from 300 to 660nm. with a maximum effect between 360 and 440nm. The action spectrum for immediate pigment darkening is shown in Fig.2. This darkening reaches its maximum immediately after irradiation. It fades and can no longer be detected 2 to 3 hours after irradiation. However, 48 to 72 hours after irradiation the exposed areas again become discernible as the result of new pigment formed by the long wave energy.

The formation of pigment by long wave energy is probably more important in the case of exposure to sunlight than to artificial sources. This is because the solar spectrum has a relatively large proportion of its energy in the 320 to 400nm region in comparison to the energy below 320nm. This is not the case for most artificial ultraviolet sources.

Typical exposure limits for exposure tolerance for installations for germicidal lamps - Continuous exposure = 0.1 uW per cm², less than 7 hour exposure day = 0.5 uW per cm². The erythema effectiveness for various sources are listed as follows to obtain MPE on the average untanned skin by average midday midsummer sunlight in efficient reflectors at a distance of 24 inches from the skin:-

		(Values in minutes)
Summer sunlight	20	
Type S1, 400 watts	4	
Type S4, 100 watts	5	
Type RS4, 100 watts	18	
Type RS, 275 watts	6	
F-Sunlamp 40 watts	8	
Quartz mercury arc 360 watts	3	
Germicidal, 4 watt	8	
Germicidal, 30 watt	0.7	
Type AH-6 quartz, 1000 watts	0.05	

At low temperatures the sensitivity of the skin to erythema is decreased. Tests made with artificial ultraviolet show that erythema is affected by the simultaneous irradiation of the skin with infrared radiation. The result of the infrared in most cases is to reduce the erythema threshold and to decrease the latent period.

It is convenient to use the ability of ultraviolet radiation to produce erythema as a unit of measure. As stated, the actual amount of energy required to produce erythema will vary with the wavelength of the radiation.

The Council of Physical Therapy of the American Medical Assn. has adopted 10 uW of homogeneous radiation of wavelength 2967Å (297nm) as the unit of erythema flux or EU. This is also called the E-viton. Thus, 1 E-viton is the radiant flux which will produce the same erythema effect as 10 uW of 297nm. radiation. For example, it can be seen from Fig.1 that the wavelength 260nm. is only 60% as efficient in producing erythema as is 297nm. Accordingly, 16.6 uW at this wavelength would constitute an E-viton.

In order to produce the same effect as 10 uW of 297nm radiation the amount of 260nm. radiation required would be:-

$$\frac{1}{0.6} \times 10 \text{ or } 16.6 \text{ uW.}$$

The E-viton which is radiant energy weighted according to its ability to produce a certain (erythema) effect, is quite analogous to the lumen used in photometry.

The total dose of ultraviolet is the product of E-vitons and time, and can be referred to as E-viton minutes, hours or seconds. One E-viton per cm² has been adopted as the unit of erythema flux intensity and has been called the "Finsen". It requires about 25,000 uW-sec per cm² of wavelength 297nm. or 2,500 E-viton seconds per cm² or 2,500 Finsen seconds to produce a just perceptible erythema on untanned skin.

The use of the erythema unit is possible only because of the reciprocity law, where the effect produced is proportional to the total amount of energy received, that is to the product of the intensity of the radiation and the time of exposure. The same effect is produced by a short exposure to a very high intensity as by a longer exposure to a correspondingly lower intensity. This law does not hold true for very low intensities.

Since the artificial source is not generally monochromatic, the erythema effectiveness depends upon the sum of the effectiveness of the wavelengths which are present. The total effect is calculated in the case of a line spectrum by adding the weighted intensities of the various lines of the source, as shown below:

Wavelength	Intensity uW/cm ²	% Erythema effect	Equiv.297nm. uW/Cm ²
248	16.2	90	13.6
254	55	80	44
257	7	70	4.9
265	4	30	1.2
267	8	15	1.2
275	6	5	0.3
280	18.7	6	1.1
289	9.8	25	2.5
292	3.3	70	2.3
297	27.0	100	27
302	54	50	27
313	122	2	2.4
	331.0		127.5

Above for Quartz mercury arc.

It can be seen, that the erythema effects is due to the 254, 297, and 302 nm. lines. The very strong line at 313nm. contributes very little to the effect. The 254, 297, and 302 nm. lines contribute more than 3/4 of the erythema effect, although they account for only 1/2 of the total energy.

The procedure is quite similar for a continuous spectrum. The ultra-violet portion of the solar spectrum is a good example. In this spectrum some energy is present at all wavelengths in the UV between 290 and 400 nm. If one divides the spectrum into 1.0nm bands and multiply the energy in each band by the relative effectiveness curve (Fig.1) and then add these values we will obtain the equivalent energy of 297nm. wavelength which would produce the same erythema effect.

Solar Radiation:

Wavelength	Intensity $\mu\text{W}/\text{cm}^2/\text{nm}$	Erythema %	Equiv. $\mu\text{W}/\text{cm}^2$ of 297nm.
292	0.3	55	0.165
293	0.4	60	0.24
294	0.6	65	0.39
295	0.8	70	0.56
296	1.0	95	0.95
297	1.1	100	1.10
298	1.6	95	1.52
299	2.0	90	1.80
300	2.9	35	2.47
301	3.6	80	2.88
302	4.5	65	2.93
303	5.4	30	1.62
304	6.0	20	1.20
305	7.1	10	0.71
306	7.8	7	0.54
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44.1			<hr/> 19.56

Referring to the second and fourth columns show that the region between 292 and 302 nm. although accounting for only about 43% of the energy below 306nm. is responsible for 79% of the erythema effect. In this respect the erythema equivalent of any spectral distribution of radiant energy can be calculated and expressed as the equivalent amount of energy of wavelength 297nm. which would produce the same erythema effect as the heterogeneous radiation in question.

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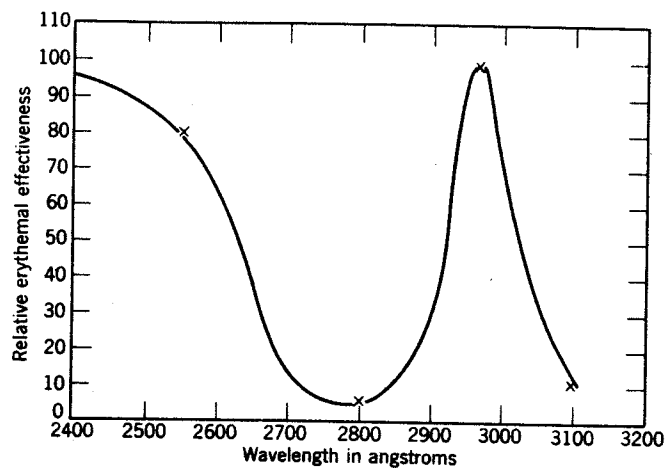


Fig. 1. Relative effectiveness of ultraviolet energy of various wavelengths in producing erythema. (Heavy curve M. Luckiesh and A. H. Taylor, *General Electric Review*, 42, 274 [1939].) Points marked X are recent measurements by Dr. M. A. Pathak, Massachusetts General Hospital.

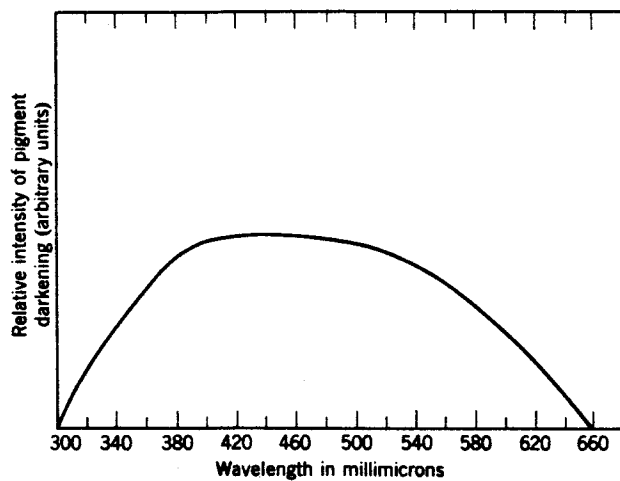


Fig. 2. Action spectrum for "immediate pigment darkening." (After M. A. Pathak, F. C. Riley, and T. B. Fitzpatrick, *J. of Investigative Dermatology*, 39, 435 [1962].)