

## Relationship Between Exposurt to Ultraviolet Radiation in Sunlight and Incidence of Skin Cancer

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### I. INTRODUCTION

The sun is the source of warmth, of light by which we see, and of the energy with which life continues on earth. It is a mixture of visible light, and infrared radiation, both invisible. Of these ultraviolet radiation has special interest because of its relatively high photon energy as compared to other types. This could lead to considerable variation in biological response.

The known effects of ultraviolet radiation (UVR) exposure on man may be beneficial or harmful, depending on a number of circumstances. On the one hand the best known beneficial effect is the production of vitamin D<sub>3</sub>, which is necessary for the prevention of rickets in man. On the other hand, it is well known that UVR produces detrimental effects. These may be acute or chronic. These may take place in the eyes and skin. Our concern, however, will be confined to the effects on skin.

The acute effects on the skin consist of UVR erythema, that is sunburn. If severe enough, it may result in blistering and destruction of the surface of skin with secondary infection and systemic effects, similar to a first or second degree heat burn.

Chronic skin changes due to UVR consist of aging (solar elastosis), and of induction of premalignant changes (actinic keratoses) and malignant skin cancers. In regard to these chronic effects this case study will concentrate on the carcinogenesis of UVR, Although the obvious mechanisms have not been known so far, it is now generally believed through the prevalence data that UVR may be the carcinogenesis of skin cancer.

Sunlight is not the sole cause of skin cancer. There are a variety of factors that may develop skin cancer. Thus, the aim of this case study is to study the relationship between the incidence of skin cancer and exposure to UVR in sunlight through a review of the existing literature.

One of the important points of concerned here is the dose-response relationship in which the effects depend on the product of the light intensity and the duration of exposure.

### II. PROPERTIES AND MEASUREMENT OF UVR

#### 1. PROPERTIES OF UVR

The sun, being essentially a very hot black body radiator, emits radiation within a wide range

of wavelengths. Sunlight is a mixture of visible light, and ultraviolet and infrared radiation, both invisible. The UVR is that part of electromagnetic spectrum lying between the softest ionizing radiation on the one side and visible radiation on the other.

Because of differences in physical properties and in biological effects, the UVR can be divided into three major regions. Although the dividing way of the UVR regions varies somewhat, this study uses the British Standard : UV-A covers from 400nm to 315nm, which is called long wave UVR, near UVR or "black light". UV-B extends from 315nm to 280nm, which is known as middle UVR or "erythema" (sunburn radiation). UV-C covers between 280nm and 100nm, which is called short wave, far UVR, or "germicidal radiation". Of these it is generally accepted that the UV-B region is the most biologically active and potentially harmful to the skin.

UVR is not only present in the direct solar beam, but also reaches the earth's surface as diffuse radiation, or the solar UVR being scattered within the atmosphere. The path length traversed in the atmosphere by UVR determines the intensity of the radiation at the surface of the earth. It is affected by geographical latitude, altitude above sea level and season (Paltridge & Barton, 1978).

## 2. MEASUREMENT OF UVR

The principle for the measurement of UVR may be divided into two classes : chemical and biological.

### 2.1. *Biological Detection*

A biologically effective irradiance could be determined, either by measuring the spectral irradiance at the point of interests and combining it with the effectiveness of the wavelengths present in the source for producing the required biological effect (action spectrum), or by using a detector whose spectral response matched the biological action spectrum.

Measurement of spectral irradiance can be achieved in two different ways : directly or indirectly. In direct measurement the total irradiance at the point of interest is simply equal to the integral of spectral irradiance over all wavelengths emitted by the source. The relative spectral intensity, or spectral power distribution for the total irradiance is measured by a detector which has a uniform spectral response over the wavelength range of the source, and preferably a 180 degrees field of view with a cosine-weighted response so that measurements can be performed on extended, linear sources (Diffey, 1982).

In addition to the above two methods a third method has been reported. This method employs a detector whose spectral response matches the action spectrum of the appropriate biological effect. The best known acute biological effect in man following exposure to ultraviolet radiation is erythema (Giese, 1976).

## 2.2. Chemical Detection

The degree of blackening of photographic films is a measure of radiation intensity. The principle is to relate the degree of deterioration of the films, usually in terms of changes in their optical properties, to the incident UVR dose.

The principal advantage of this method is that it is a simple means of integrating UVR exposure continuously with a high degree of accuracy under carefully controlled conditions of exposure and development. A polysulphone film is available as a personal UVR dosimeter.

On the other hand some measurable change of chemicals on exposure to UVR is used for the measurement of radiant exposure (WHO, 1979). The most widely used detector has been the actonemethylene blue reaction. Moreover, the systems based on the rate of photochemical decomposition of oxalic acid in the presence of uranyl acetate and on the photolysis of iron(III)oxalate have been reported. This method is relatively simple, but is slow and requires laborious analysis. They are sensitive to temperature and to small amounts of impurities.

## III. UVR AND SKIN CANCER

There are no firm data on the relationship between incidence of skin cancer and UVR exposure. However, it is widely believed that it is possible to demonstrate a correlation between them. This belief is based on three sources : results of experiments in animal photocarcinogenesis observations on the geographical distribution of non-melanoma skin cancer in man and the hypothesis that the molecule deoxyribonucleic acid (DNA) is the target for UVR-induced carcinogenesis.

### 1. FACTORS RELATED TO SKIN CANCER

The cause of skin cancer may depend upon numerous factors. Sunlight is not the sole cause of the skin cancer. It is significant to study these causal factors which could influence strongly the onset of skin cancer.

#### 1.1. Environmental Factors

The relative intensities of UVR that reach the earth's surface depend on, to a considerable extent, an attenuation by the atmosphere because of absorption and scattering. In the stratosphere, the spectral irradiance of the sun is mainly absorbed by ozone (Giese, 1976).

UVR is not only present in the direct solar beam, but also can be reflected, scattered and attenuated by clouds, haze, and smog near the ground. Under the hazy and cloudy conditions this component can be very important (Paltridge et al, 1978).

The path length traversed in the atmosphere by the UVR determines the intensity of the radiation at the surface of the earth. But it is also affected by geographical latitude, altitude above sea level and time of year. From the numerous measurements, it is apparent that there

are daily fluctuations, throughout the year, at each location.

Some studies have shown that high winds and high humidity significantly increase tumour incidence (WHO, 1979).

It is generally accepted that a portion of sunlight spectrum is carcinogenic, even in the absence of an exogenous photosensitizer. Many widely distributed natural or artificial chemicals (pesticides, halocarbons, etc.) can be altered by UVR, resulting in photoproducts that may be less or more biologically effective than the parent compound.

Furthermore, many chemicals can be activated by UVR in situ in biological systems and this activation may elicit a biological effect which neither the chemical nor the radiation alone exhibits (Psoralens).

At the current rate of introduction of new compounds into the environment, it has become increasingly important to determine whether a readily demonstrable property, such as phototoxicity, can be used to predict compounds or treatment regimes that could enhance photocarcinogenesis (WHO, 1979).

The relative enhancing effects on carcinogenesis of two widely recognized photoactive compounds, 8-methylpsoralen(8 MOP) and anthracene were studied by Forbes et al (WHO, 1979).

### 1.2. Individual Factors

It is generally known that erythema (sunburn) and skin cancer arise in the same tissue, and UVR causes erythema. It is also accepted that those who are more susceptible to skin cancer sunburn more easily.

Numerous studies have shown that, in fair-skinned people, skin cancer arise primarily on sites exposed to sunlight. Among races with dark skin, in which pigment filters UVR, there is very little skin cancer and the disease does not occur predominantly in areas of the skin exposed to the sun.

People suffering from the skin disease, Xeroderma pigmentosum(XP), due to an hereditary defect, show abnormal pigmentation and high incidence of skin cancer initiated by exposure to solar UVR. Reduction of DNA repair in XP patients could very plausibly be related to carcinogenesis.

In several carefully controlled studies comparing patients with non-melanoma and melanotic skin cancer to age-sex matched controls from the same populations, a distinct association was found between skin cancer and light coloured eyes, fair complexion, light hair colour, poor ability to tan, ease of sunburning and a history of repeated severe sunburn (Marks & Selwood, 1985).

It is widely accepted that persons who are much exposed to solar UVR because of occupation are more likely to get skin cancer. Thus, farmers, fishermen, sailors, and others such as road workers, roofers, policemen, and postmen, have a high incidence of skin cancer than office and factory workers (Giese, 1976 : Diffey, 1982 : WHO, 1979).

It is essential to educate the general public and workers concerning the profound importa-

nce of sunlight and the possibilities of either UVR deprivation or of acute and chronic UVR injury.

It is also necessary to overcome the concept that, if something is natural, it must be totally beneficial and safe.

## 2. MECHANISM OF UVR CARCINOGENESIS

### 2.1. *Cause of cancer*

A cancer (or tumour) is a group of cells that divides to give a rather loosely organized mass of cells. At the present there is no real answer for the mechanisms that cause normal cells to become cancerous. It seems true to say that until there is further understanding of the control mechanisms of normal cell division, there is little chance of a better understanding of the cancer cells, which is essentially a cell dividing out of turn.

Despite the lack of data, there are some theories that could help us to understand the mechanism of carcinogenesis.

Most theories concentrate on the fact the alteration of a normal cell involves its inability to integrate with its neighbouring cells. The somatic mutation theory and the viral theory received the most support (WHO, 1979).

### 2.2. *Effects of UVR*

A certain human disease such as Xeroderma pigmentosa (XP) in which the patients are predisposed to develop cancer, shows instability in their chromosomes and varying degrees of deficiency for DNA repair capacity.

This example can be a strong support for the somatic mutation theory. The somatic mutation theory of cancer suggested that the DNA of a cell becomes altered or mutated so that its information content is changed. The mutation might take the form of an invisible gene mutation, or an actual breakage or loss of a chromosome might occur. The deficiency for DNA repair capacity provides the best evidence for a causal link between cancer and damage to gene structure and/or function in somatic cells of the body.

Solar keratoses are common on light-exposed areas of fair-skinned persons in hot, sunny climates. They are believed to be the premalignant stage of the development of nonmelanotic skin cancer, particularly squamous cell carcinoma (Marks and Selwood, 1985). This study also supports the somatic mutation theory.

Although many viruses are known to be associated with cancer cells and with an increased incidence of cancer, the scientific literature is insufficient to give any definite conclusion in relation of solar UVR.

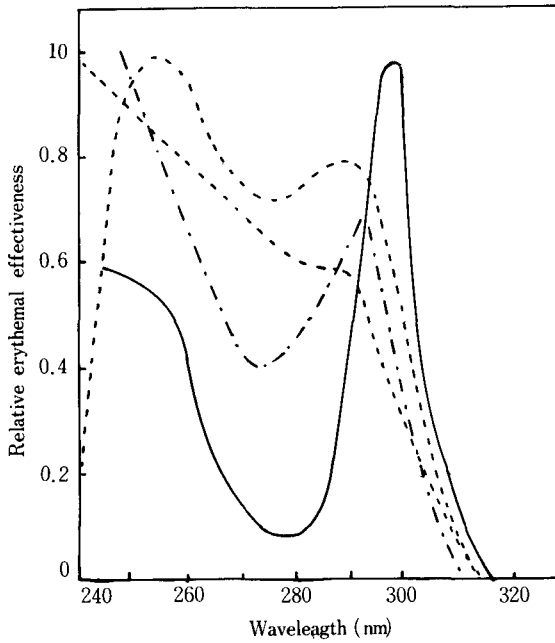


Figure 1. Comparison of the standard erythema curve (ICI 1935) with the erythema action spectra determined by Everett et al (1965), Freeman et al (1966), and Cripps and Ramsay (1970) : full curve, standard erythema curve : broken curve, Everett et al : dotted curve, Freeman et al : and chain curve, Cripps and Ramsay.

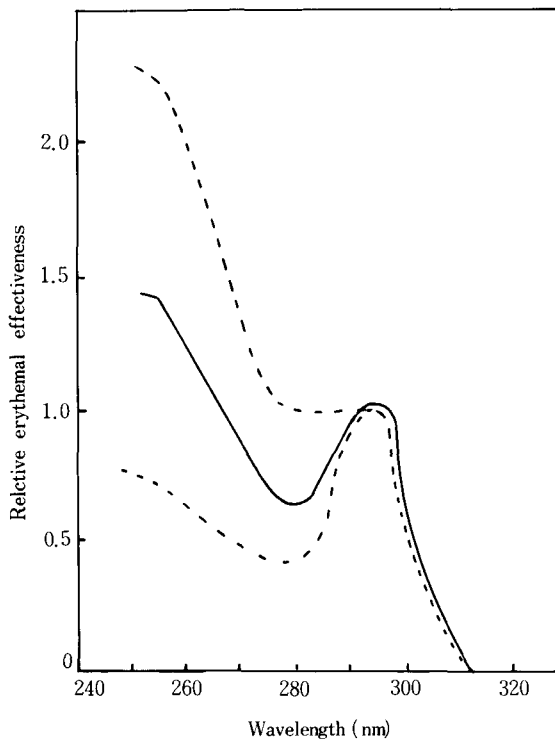


Figure 2. Action spectrum for human skin according to different criteria (from Berger et al 1968) : broken curve, 8h MED : full curve, 24h MED : and dotted curve, 24h moderate erythema.

### 3. ACTION SPECTRUM

The effectiveness of UVR to produce damaging effects in human skin is a complex function of wavelengths.

When the effectiveness of a beam as a function of wavelengths is to be evaluated, it is necessary to know the relative response of wavelengths.

The biological effectiveness of a beam of UVR depends on the photon flux and on the relative efficiency of the photon energy to produce a particular biological effect. An action spectrum indicates the wavelengths that are most capable of producing a given effect.

Thus the effect of UVR from a source may be assessed by comparing the appropriate action spectrum with the absorption spectrum of the source.

In simple physical system, the action spectrum may be similar as the absorption spectrum in the tissue materials. However, shielding and other factors which are not fully understood, the identities of the absorption and action spectrum become less definite, and the result to be drawn may be that there is no simple relationship between the absorption spectrum and the action spectrum.

It is not possible to determine experimentally the action spectrum for skin carcinogenesis in man because of the effects of cancer-induced factors other than UVR. Nevertheless, it is widely believed that action spectrum of erythema can be used to provide a low limit for the cancer induction.

The action spectrum for erythema has long been the subject of controversy. The first precise determination of the action spectrum was reported in 1922. It exhibited a major peak of activity at 297nm, a minimum at 280nm, and a second but less peak at 250nm. Related studies carried out in the 1920s and 1930s showed close agreement from approximately 270nm to 310nm. From these reports a standard erythema curve was adopted by the International Commission on Illumination (ICI) in 1935. This double-peaked curve was accepted as standard for many years. Some works in the 1960s and 1970s suggest a curve with increasing amplitude as the wavelength becomes shorter, with a shoulder at about 300–280nm. The next figure compares the ICI action spectrum with other estimates.

The great effect of time after irradiation and of choice of degree of redness on the action spectrum of human skin is shown in the next figure. From 297nm on, there appears to be remarkably good agreement between most published figures.

Unfortunately, in the absence of knowledge of biological mechanism there is no better way of comparing the effectiveness of sources of different UVR composition than the present method of calculating the skin erythema effectiveness of UV-B. Despite the controversy and problems, it is generally agreed that only those wavelengths less than 315nm are responsible for skin carcinogenesis (Wong and Fleming, 1984).

#### 4. DOSE-RESPONSE RELATIONSHIP

Excessive amounts of UVR can be very damaging to human skin. A question which is arising here is whether erythema or skin cancer depends on the total UVR dose. Most of the existing evidence is consistent with the concepts that the development of skin cancer is a stochastic effect, and that there is no threshold.

A recent report suggests that most non-melanotic skin cancer appears to be related to cumulative sunexposure, and is most prevalent among the elderly, while short-term exposure to unusually intense sunlight seems to have a considerable part in the development of melanotic skin cancer (Elwood et al, 1985).

Green et al(1976) and Fears et al(1977) have correlated epidemiological skin cancer data with both measured and calculated estimates of the UVR environment. In both instances the age-adjusted data have been modelled (Diffey, 1982) by a power law relationship of the form

skin cancer incidence  $\propto$  (annual UVR dose).

A power law representation of age-adjusted incidence data versus UVR dose has the convenience that the power index  $p$  serves as a constant biological amplification factor in the sense that

$$p = (dI/I) / (dD/D),$$

where  $I$  is skin cancer incidence and  $D$  is annual UVR dose.

While it is evident that the uncertainties of these studies are large, the best accepted model data to date suggest that a 5% increase in erythemally effective global UVR may result in a 15% (range 7.5–25%) increase in skin cancer in a susceptible population after about 60 years, when a steady state has been reached (WHO, 1979; Diffey, 1982).

#### IV. GUIDELINES FOR HEALTH PROTECTION

At the present there are no guidelines for evaluation of the risk of skin cancer development of solar UVR. The reasons why it is extremely difficult to develop the criteria, for both upper and lower limits of exposure to UVR, are:

- (a) the variation in UVR effects of different wavelengths;
- (b) the considerable differences in the spectral composition of sunlight at different latitudes;
- (c) the great differences in cutaneous sensitivity to UVR due to genetic, environmental, and the considerable variation in sensitivity in the same person at different times; and
- (d) the difficulty of differentiating between the necessary dose of UVR compatible with the upkeep of life, and the lowest dose that results in serious detrimental effects (Diffey, 1982).

However, the limits which could be used in the preparation of guidelines for occupational exposure to UVR, have been proposed by the National Institute of Occupational Safety and



Health in the United States. This standard has also been adopted as a voluntary standard in the United Kingdom.

The proposed exposure limits for occupational exposure levels can be summarized as follows (NIOSH, 1975).

Summary of Dose limits			
UV-A (400–315) nm			
Organ	Duration of exposure	Effective irradiance	
unprotected eyes & skin	> 100sec	10W/m <sup>2</sup>	
	< 1000sec	1000J/m <sup>2</sup>	
UV-B and UV-C (315–200nm)			
Organ	Wavelength(nm)	MPE(J/m <sup>2</sup> )	RSE, S( $\lambda$ )
unprotected eyes & skin	200	1000	0.03
	210	400	0.075
	220	250	0.12
	230	160	0.19
	240	100	0.30
	250	70	0.43
	254	60	0.5
	260	46	0.65
	270	30	1.0
	280	34	0.88
	290	47	0.64
	300	100	0.30
	305	500	0.06
	310	2000	0.015
315	10000	0.003	

MPE : Maximum permissible exposure for 8 hours

RSE : Relative spectral effectiveness

## V. CONCLUSION

In this day and age of technological advances, individuals are obliged to live in a complicated ecophysiological balance with solar UVR. Geographic location, customs, life-styles and chosen professions determine to a great extent one's sun exposure habits. For many, sunlight is a part of their everyday routine and for many, outdoor activities in the sun are essential to sustain a normal, healthy life.

Generally the appearance of erythema is taken as a sign for the skin cancer development. The action spectrum for erythema has been found to drop off at around 315nm as the wavelength of the radiation increases.

At the present there are no firm data on relationship between UVR exposure in sunlight and the incidence of skin cancer. But the numerous studies have shown that UVR exposure plays an important part in the risk of development of skin cancer.

A variety of risk factors have been discussed. In particular individual risk factors have drawn more interest in most reports. Lots of studies have reported that fair-haired people,

and those having either preexisting pigmented nevi, a history of melanoma in family members, or sun-sensitive skin are a greater risk for the development of skin cancer (Hicks et al, 1985).

Statistical measurement shows that the incidence of skin cancer increases with the  $p$ th power of the annual UVR dose where  $p$  is an empirical parameter to be determined.

To better understand the effects of UVR of sunlight on man, and in particular the relationship between solar UVR and skin cancer, measurements of UVR should be accurately performed. One of major problems in measuring the solar UVR is the accurate spectral discrimination at the shortest end of the solar spectrum (Wong and Fleming, 1984).

The uncertainty of the shape of the action spectrum for skin carcinogenesis should be unveiled. Although the general direction and approximate limits of action spectrum seems to parallel those for skin erythema, the fine structure of the carcinogenesis action spectrum is not known.

A strong recommendation was put forth to develop and deploy personal UVR dosimeter to acquire data on occupational and recreational exposure levels (WHO, 1979). Personal dosimeters and portable instruments have already been available (Fanselow et al, 1983 : Diffey et al, 1984). Massive and comprehensive studies should be performed using these available devices to collect data for the goals described above.

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