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Physiological Effects of Light

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The destructive effects produced in living systems by ultraviolet light are in many cases quite similar to effects produced by visible light in living systems sensitized by dyes (photodynamic action). As examples may be cited: the hemolysis of red blood cells; the production of erythema, pigmentation, and destructive lesions of the skin of mammals; muscle responses, etc. These similarities suggest a common causal mechanism.

The writer[1] has called attention to the fact that the photodynamic and ultraviolet effects can be differentiated, in so far as they have been studied, by the fact that the former take place only in the presence of oxygen, whereas the latter take place quite readily in the absence of oxygen. Nevertheless the thermodynamic considerations given below indicate the possibility of a common mechanism.

In investigations of the photochemical reactions of fluorescein dyes in this laboratory it has been found that hydrogen peroxide is formed when aqueous solutions of these dyes are irradiated with visible light in the presence of molecular oxygen, and as has been shown by the writer,[2] it is most probable that the production of peroxide is a step in the destruction of living systems sensitized by these dyes.

The principal reaction involved would appear to be:

(1) $2\,H_2O\,(l.) + O_2 = 2\,H_2O_2\,(aq.)$; $\Delta F_{298} = 50180$ cals.; $\Delta H = 46000$ cals.[3]

Obviously this reaction cannot proceed very far in the direction indicated, and at equilibrium the concentration of H_2O_2 present would be approximately 10^{-18} M. Since in the above mentioned experiments H_2O_2 was produced in concentrations up to 10^{-3} M, it is obvious that we are not dealing with a thermal reaction, the rate of which is increased by the action of light, but one in which the energy is supplied directly by the light.

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[1] Blum, H. F., *Physiol. Rev.*, 1932, **12**, 23.

[2] Blum, H. F., *Biol. Bull.*, 1930, **58**, 224; **59**, 81.

[3] The data for the calculation of ΔF and ΔH in this paper were obtained from *Thermodynamics*, Lewis and Randal (1923), McGraw Hill, New York; and *International Critical Tables*. The values of ΔH are taken to the nearest 1000 cal., which is sufficient for our purposes.

We may represent the reaction as follows:

$$(2)\quad D + h\nu = D'$$

Where D is the dye molecule, D′ an activated molecule, and $h\nu$ the light quantum.

$$(3)\quad D' + H_2O = D + H_2O'; \text{ or } D' + O_2 = O_2' + D$$

Indicating the transference of the energy of activation from D′ to O_2 or H_2O.

$$(4)\quad 2\,H_2O + O_2' = 2\,H_2O_2$$

It is possible that an intermediate peroxide of the dye may be formed, but if so, our experiments would indicate that it must proceed very rapidly to H_2O_2 and dye.

$\Delta H/N$ ($N =$ Avagadro's number) is in this case the energy which must be supplied per molecule by light or the minimum value for the quantum which is capable of bringing about this type of reaction.

Under such conditions:

$$\frac{\Delta H}{N} = h\nu$$

when h is Planck's constant and ν the frequency of the radiation, and since

$$\nu = \frac{c}{\lambda}$$

where λ is the wave length and c the velocity of light

$$\lambda_{max} = \frac{c\,h\,N}{\Delta H}$$

λ_{max} representing the maximum wave length which would supply sufficient energy for the reaction.

$\Delta H = 46000$ cals. for reaction (1) and, substituting the proper numerical values:

$$\lambda_{max} = \frac{3 \times 10^{10} \times 6.56 \times 10^{-27} \times 6.06 \times 10^{23}}{46000 \times 4.185 \times 10^{7}} = 6.195 \times 10^{-5} \text{ cm.} = 6195\text{Å}$$

Thus it will be seen that light of wave lengths less than 6200Å is capable of bringing about reaction (1), but not light of longer wave lengths. Most of the visible spectrum and all the absorption spectra of the fluorescein dyes are included below this value so that reaction (1) is possible as the chemical mechanism for the production of the photodynamic effects.

The reaction:

$$(5)\quad 2\,H^+ + O_2 = H_2O_2\,(aq.);\ \Delta F = -31470 \text{ cals.}$$

has a large negative free energy but could not account for the concentration of H_2O_2 formed in our experiments, since the concentration of H^+ limits the concentration of H_2O_2 which can be formed to 10^{-14} M.

The mechanism:

$$(6)\ D' + O_2 = 2\,O + D;\ \Delta H = 150{,}000 \text{ cals.}$$
$$(7)\ H_2O + O = H_2O_2$$

is ruled out since reaction (6) would require 150,000 cals., which represents a maximum wave length far below the visible region.

Assuming the possibility that ultraviolet effects, like the photodynamic effects, are due to the production of H_2O_2 the following reactions are possible:

$$(8)\ 2\,H_2O\ (1.) = H_2O_2\ (aq.) + H_2;\ \Delta F_{298} = 81650 \text{ cals.};\ \Delta H = 91000 \text{ cals.}$$
$$\text{or } (9)\ 2\,H_2O\ (1.) = H_2O_2\ (aq.) + 2\,H^+$$

These reactions do not involve molecular oxygen, as is required by the experimental evidence. $\Delta H = 91000$ cals. and calculating as above we find 3205 Å as the longest wave length at which this reaction can occur.

It may be considered highly suggestive that the value of 3200 Å very closely approximates the upper limit for the known destructive ultraviolet effects in living systems. Interestingly enough, it also includes below it the region of anti-rachitic effects and that for the activation of ergosterol.

In reaction (8) it might be expected that the H_2 molecule, if formed, would combine with a hydrogen acceptor in the tissues. Since water does not absorb very strongly above 2000 Å, the mechanism would probably necessitate a sensitizer which we must assume as some compound present in the tissue; this compound might also serve as the hydrogen acceptor.

The reactions:

$$3\,OH^- = HO_2^- + H_2O\ (1.);\ \Delta F_{298} = 40195 \text{ cals.};\ \Delta H = 61000 \text{ cals.}$$
$$\text{and } 2\,OH^- = H_2O_2\ (aq.);\ \Delta F_{298} = 59300 \text{ cals.};\ \Delta H = 65000 \text{ cals.}$$

could occur up to 4700 Å and 4400 Å respectively. However, the probability of an activated sensitizer molecule colliding with an H_2O molecule as against its collision with an OH^- ion might be expected to be about 55×10^7. In any event the concentration would be limited by the concentration of OH^- ion, so that these reactions could probably not account for H_2O_2 production in effective concentrations.

The above reactions are offered to call attention to an interesting possibility. Whether there is a definite relation between photodynamic and ultraviolet effects and whether H_2O_2 is or is not an immediate causal factor in the latter can only be determined by further experimental study. Since the photodynamic effects are probably the resultants of 2 mechanisms, a photo and a dark reaction (see Blum[2]), certain discrepancies in the photodynamic and ultraviolet effects are to be expected. Numerous other mechanisms for ultraviolet effects are, of course, possible, and the mechanism suggested can only be considered as a working hypothesis. Experiments are in progress in this laboratory to test the point.

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Electromigration of Iodobismuthite in Colloidal Systems.

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Electromigration of the complex ion (BiI_5) of sodium iodobismuthite (Na_2BiI_5) in colloidal systems is of interest in connection with the absorption and cerebrospinal penetration of this electronegative bismuth in antisyphilitic medication.[1] The red (BiI_5) ion migrates to the anode in aqueous, alcoholic and glycolic media.[2] The question of cerebral and spinal fluid penetration hinges, partly at least, on another question, whether the unchanged complex ion (BiI_5) can migrate in colloidal systems analogous to those of the body, such as serum and a gel. Direct test of migratibility in living tissue and blood is practically impossible. Therefore, a special electrolytic cell, which also acted as a model, containing serum, agar-gel, and iodobismuthite was used.

The anionic character of the bismuth in iodobismuthite was originally demonstrated with bare platinum electrodes.[2] However, such electrodes require constant attention in order to avoid decomposition of the labile complex (BiI_5) ion. Therefore, the use of KCl-agar bridges in the anode and cathode chambers was suggested, since their use would prevent loss of the electrical charge on, and consequent decomposition of, the complex (BiI_5) ion. This arrangement also made it practically feasible to test the migration, if any, of the (BiI_5) ion in colloidal systems, *i. e.,* into serum and from serum into the agar-gel. The analogy to conditions prevailing in the intramuscular administration of iodobismuthite (iodobismitol) was al-

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[1] Hanzlik, Mehrtens, Gurchot and Johnson, *J. Am. Med. Assn.,* 1932, **98**, 537; Hanzlik and Spaulding, *Am. J. Syph.,* 1932, **16**, 335; Hanzlik, Mehrtens and Spaulding, *Am. J. Syph.,* 1932, **16**, 350.

[2] Hanzlik and Spaulding, PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 847; Gurchot, Hanzlik and Spaulding, *J. Pharm. Exp. Therap.,* 1931, **45**, 427.