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PHOTOSENSITIZATION IN BIOLOGICAL SYSTEMS

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Protoplasm, in general, is relatively insensitive to direct effects of visible and near ultraviolet light since most molecules of biological importance do not absorb appreciably in this wavelength range. However, in the presence of an appropriate photosensitizer, cells, organisms and many kinds of biomolecules are damaged and destroyed by light. We usually date the start of the study of photosensitization as an area of photobiology from the observation by Oscar Raab, a medical student in Munich, that acridines sensitize paramecia to killing by light (1). However, on this occasion, we should take note of the earlier work of Arturo Marccaci, a physiologist in Perugia, who reported in 1888 that low concentrations of quinine, which had no effect in the dark on grain germination, the development of amphibian eggs, etc. produced severe damage in the light (2). Photosensitized cells are killed by selective photochemical damage to certain cell organelles, with effects on the organelle resulting from selective alteration of macromolecules in the organelle; alteration of the macromolecule results in turn from selective damage to certain of its subunits. Thus, studies of photosensitization in biology range from an examination of the photophysics and photochemistry of sensitizer molecules to the physiology and pathology of the photosensitized injury and killing of mammals. Several review papers on photosensitization in biological systems are listed in the references (3-9).

The light energy involved in most photosensitized reactions is absorbed by the photosensitizer molecule rather than by the biological system affected. Light of wavelengths greater than approximately 320 nm is generally used in photosensitization studies, since a number of biologically important molecules

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including nucleic acids and proteins absorb at shorter wavelengths. To function as a photosensitizer, a molecule must be capable of more than merely absorbing light of the wavelength involved; in general, it must have the capability to be excited by light into a long-lived energy-rich form, the triplet-state. Many kinds of synthetic and natural molecules can act as photosensitizers.

The majority of the photosensitized reactions in biological systems that have been studied involve molecular oxygen, i.e., they are sensitized photooxidation processes. These reactions in biological systems are often termed "photodynamic action" or "photodynamic" reactions. The sensitizer molecule is typically neither consumed nor destroyed in these reactions, but is used repeatedly in a somewhat "catalytic" fashion. The excited sensitizer in photooxidation reactions can react directly with the substrate (the molecule being oxidized) by an electron or hydrogen transfer process; the resulting semi-reduced substrate can then react with oxygen giving an oxidized form of the substrate. Alternatively, the excited sensitizer can react with molecular oxygen by an energy transfer process giving an excited singlet form of oxygen which then oxidizes the substrate. The relative participation of these different pathways depends on the sensitizer, the substrate, and the reaction conditions. In contrast, some photosensitizers do not require molecular oxygen for their action, and may be consumed in the sensitized reaction.

Our symposium today examines the current status of our knowledge of the photosensitized reactions of nucleic acids and proteins. Significant advances have been made in this area of photobiology since the last international Congress. The first paper will explore the role of molecular oxygen in photosensitized reactions of proteins and nucleic acids. The last three papers are concerned primarily with photosensitized reactions of nucleic acids and their components in which the sensitizer is consumed by bonding covalently with the substrate on irradiation. The best understood reactions of this type are those sensitized by furocoumarins such as 5-methoxypsoralen. These sensitizers show promise in the photochemotherapeutic treatment of proliferative diseases of the skin, such as psoriasis.

It is altogether fitting that this symposium emphasizes the photochemistry and photobiology of the skin-sensitizing psoralens, since much of the fundamental research in this area of photobiology has been carried out in our host country, Italy. (Supported by the U.S. Energy Research and Development Administration under Contract. No. EY-76-S-02-0875.*000).

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