Photochemotherapeutic Agents
A New Role for the Inorganic Chemist

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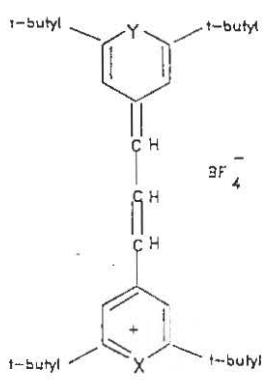
In the last five years there has been a tremendous growth in the field of photochemotherapy, a technique that uses light activated molecules to destroy cancer cells. The established methods of cancer treatment, such as radiation, do not always work in every case, and thus has spurred interest in this area. In order for this technique to be beneficial in the treatment of cancer, it must follow several guidelines [1]. Effective photochemotherapeutic (PCT) agents should: 1) generate singlet oxygen, 2) be non-mutagenic, 3) be excreted from the body after treatment, 4) be preferentially located in the cancer cell. In addition the light used must penetrate to the cancer cell through the "biological window". The absorbance of light by PCT agents generates singlet oxygen which destroys the cell presumably by inhibiting cytochrome c oxidase in the mitochondria.

The biological window is especially important in the administration of light to the cancer cell. The window, for maximum light transmittance, is believed to be between 700-900 nm [2]. This wavelength of light can be produced with commercially available lasers for fiber optic systems. Shorter wavelength light is absorbed by the cellular membranes and by the hemoglobin and myoglobin in the circulatory system.

The first type of PCT agents developed were substituted psoralen [3] and substituted angelicin [4]. They showed moderate success in treating cancer. These organic systems absorb light in the range of 350-400 nm. Their major drawback is that they can intercalate in DNA strands. With the exposure to light, the DNA cross-links, leading to irreparable damage [5]. This is still an area of debate, but the likelihood that these agents will be used clinically appears slim.

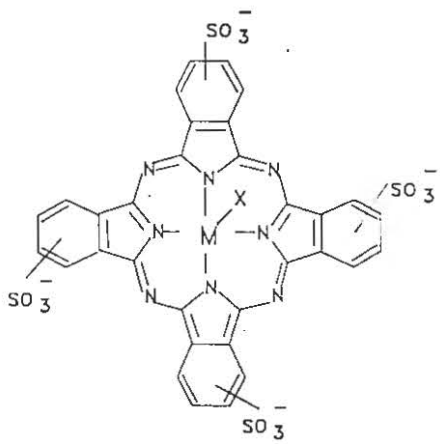
The second type of PCT agents to be developed were the porphyrins. Various chlorins [6] and tetrasulfonatophenylporphyrin [7] have received attention, but their alpha and beta bands in the 500-600 nm range are slightly outside the biological window. In spite of this, hematoporphyrin (HPD) [8] has made it to the clinical stage of cancer treatment. The absorbance of light at 630 nm by HPD and its preferential uptake into cancer cells has resulted in complete recovery in some human patients [9]. None of these PCT agents meet all the requirements for an effective PCT agent.

Chalcogenapyrylium Dyes



Y,X=Te,Se,S,O

Metal Phthalocyanine Tetrasulfonates



M=Al, Zn X=Cl

Metal phthalocyanine tetrasulfonates and chalcogenapyrylium dyes have potential as cancer treatment drugs and are currently under study. The metal phthalocyanines have an absorption in the 670-700 nm range [10], whereas the chalcogenapyrylium dyes have an absorption in the 700-800 nm range [11]. The tellurapyrylium dye is easily oxidized compared to the other chalcogen dyes, thus making it more susceptible to singlet oxygen attack. The chalogenapyrylium dye with a tellurium and selenium has been shown to destroy cancer cells [12]. The wavelength of the absorbance in the chalcogenapyrylium dyes can be modified by changing the conjugation network or the chalcogen atom. The analogous dye where oxygen atoms have replaced the tellurium atoms does not effectively generate singlet oxygen, thus the tellurium atoms are essential to the dyes potential as a PCT agent. This ability to modify the electronic structure of the molecules is a tool that an inorganic chemist can exploit. With this information, dyes and metal phthalocyanines can be synthesized to meet the requirements for photochemistry.

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