The effect of light activated complexes on skin cancer

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Cancer and its treatments

Malignant neoplasm: Unregulated cell growth invading nearby parts of the body.

Treatments:

Surgery – Excise the tumor, microscopic metastasis limits effectiveness.

Radiation Therapy – Ionizing radiation damages tumor DNA killing the cells. Hypoxic cancer cells are more resistant.

Chemotherapy – Drugs designed to kill cells that divide rapidly also kill normal cells which is the main cause of negative side effects.
Skin cancer is the most commonly diagnosed form of cancer with 3.5 million new cases diagnosed annually in the United States.

Three types: Basal Cell Carcinoma, Squamous Cell Carcinoma, and Melanoma

Basal cell carcinoma is most common and most easily treated

Squamous cell carcinoma is the second most common form of skin cancer generally treated with topical chemotherapy

Melanoma is the least common form of skin cancer but the most deadly causing 75% of the deaths related to skin cancer. It is typically non-responsive to chemo and radiation therapy
Photodynamic Action: The damage or destruction of living tissue in the presence of light, a photosensitizer and molecular oxygen.

Photosensitizers

Acridine Orange

\[(\text{CH}_3)_2\text{N} - \text{N} - (\text{CH}_3)_2\]

Methylene Blue

\[\text{Cl}^-\]

Tetra-phenylporphyrin

Advantages of Macrocycles As PDT agents
- Intense absorption in visible
- Stable
- Low toxicity in dark
Photodynamic Therapy

1. Photosensitizer
2. Light source
3. Oxygen
New Ruthenium Porphyrins

- Affinity for tumor sites
- Efficient photosensitizer
- Intercalates into DNA
- Adds water solubility
- Stable in aqueous media
- Fluorinated phenyl groups extend the excited state lifetime
- Fluorines provide a reactive position for altering the porphyrin structure

M = 2H⁺, Ni²⁺, Cu²⁺, Zn²⁺

I-IV
Modes of Binding to DNA

- **Covalent Binding:** Coordination to bases
- **Surface Binding:** H-bonding interaction. Small molecules favor small groove.
- **Intercalation:** Insertion between base-pairs favored by aromatic groups.
- **External Binding:** Electrostatic interaction.


Our complexes gave binding constants in the millions (10^6) suggesting Intercalation is the mode of binding.
Photocleavage of DNA
Migration dictated by
charge and shape

Neg 104 V Pos
Gel electrophoresis of circular plasmid DNA (pUC18) in the absence (lanes 1-9) and presence (lanes 10-18) of complex I at a 5:1 base pair to complex ratio. Samples were irradiated with a 100 W mercury arc lamp equipped with a long pass filter, cutting off wavelengths below 400 nm. Samples were taken at 15 minute intervals.
Photocleavage of DNA
Cell Studies

Normal cells in the dark

Melanoma cells in the dark

Normal cells plus complex in the dark

Melanoma cells plus complex in the dark
Cell studies irradiated with a 60 W tungsten bulb for 30 minutes, 3 micromolar solutions of complex
Cell studies irradiated with a 60 W tungsten bulb for 60 minutes, 10 micromolar solutions of complex

Normal Cells

Melanoma Cells

Visible light
Cell studies irradiated with a 60 W tungsten bulb for 30 minutes, 5-10 micromolar solutions

Normal Cells
Cell studies irradiated with a 60 W tungsten bulb for 30 minutes, 5-10 micromolar solutions
Synthesized a new series of ruthenium metal centered porphyrins.
All of the complexes bind to DNA through intercalation.
The free base porphyrin photocleaves DNA after only 2 minutes of irradiation.
The copper and nickel porphyrins photonick DNA but do not cause bond cleavage.
The zinc porphyrin photocleaves DNA after 30 minutes of irradiation.
All of the complexes are nontoxic to cells in the dark.
The free base porphyrin kills both normal and melanoma cells.
The copper and nickel porphyrins show no toxicity to normal or melanoma cells when irradiated for one hour.
The zinc porphyrin is non-toxic to normal cells when irradiated but kills melanoma cells.
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