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The Creation of a Next-Generation Cancer Treatment Using Photodynamic Therapy

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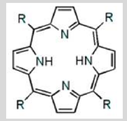
Abstract

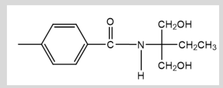
Photodynamic therapy (PDT) is a treatment for various health disorders, including cancer, that uses a photosensitive agent and light. Unlike other cancer treatments, PDT is a focused treatment that kills cancerous cells without harming the surrounding tissues. When a photosensitive agent is administered, it accumulates in the tumor as it binds to low density lipoproteins. When the tumor is exposed to a specific wavelength of light, the photosensitive agent is activated; this results in the release singlet oxygen, which kills the tumor. The objective of this research was to synthesize and characterize a novel photosensitive agent, H_2TPP-2A2E. Purification of the novel be used in the next generation of photodynamic therapy. material was achieved using column chromatography. In addition, IR, UV-vis, and NMR spectroscopies were used to characterize the product, and purity was determined using HPLC. After determining that our product was refined, cytotoxicity testing in light and dark conditions revealed that the novel H_2TPP-2A2E, could potentially be used in the next generation of photodynamic therapy.

Figure 1: Standard Porphyrin Core Structure (Unsubstituted)



A standard poryphrin ring structure, unsubstituted.

Figure 2: R-Group attached to Porphyrin Core



2-Amino-2-ethyl-1,3-propanediol

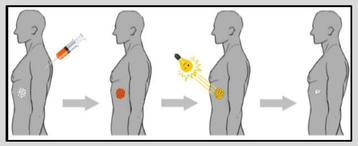
Introduction

A549 Cell Line

- Non-small Cell Lung Cancer Cells
- The most common form of lung cancer
- Constitutes 84% of all lung cancer diagnoses
- 5 year survival rate is 24%

Photodynamic Therapy

- A patient diagnosed with a tumor is injected with a photosensitizer.
- Due to the nature of the photosensitizer, it collects in the tumor over time.
- The tumor is exposed to light for a given amount of time, activating the photosensitizer.
- The tumor is selectively destroyed.



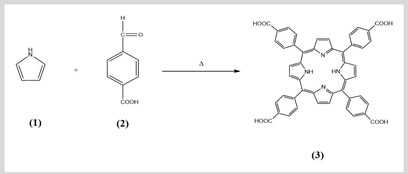
Porphyrins

- A porphyrins' usefulness is largely due to its conjugated structure, light absorbing qualities, and efficacy as photosensitizers.
- Various uses of porphyrins include gene regulation, drug and iron metabolism, hormone synthesis, electron transfer medium (conducting polymers), oxygen transport medium (hemoglobin), solar cell (convert light or chemical energy), metal binder (ligand).
- This research specifically utilizes and tests the light sensitivity of the porphyrins and how they react to cells.

Synthesis

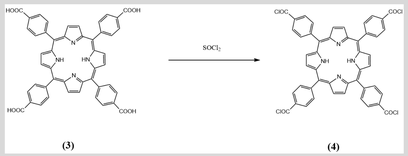
Reaction 1

- 4-formylbenzoic acid (2) reacted with pyrrole (1) in a propionic acid solution to form H_2TPPC (3).



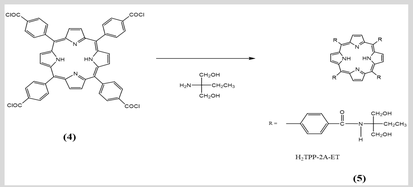
Reaction 2

- H_2TPPC (3) reacts with thionyl chloride in dimethylformamide, forming an acid chloride porphyrin (4).



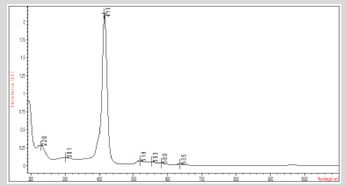
Reaction 3

- The acid chloride porphyrin (4) reacts with diisopropylamine in methanol to form , the final product (5).



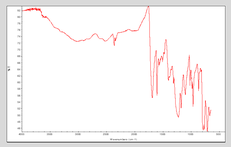
Characterization

UV-vis Spectroscopy

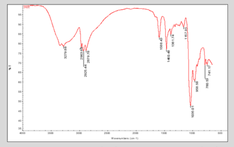


Peaks (nm)	Molar Absorptivity Coefficient, e (cm^{-1} mM^{-1})
415	261.6
518	9.79
555	5.8
581	4.4
636	2.9

Infrared Spectroscopy



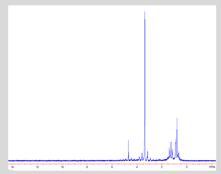
H_2TPPC



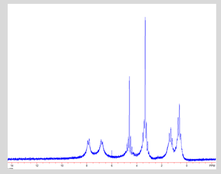
2-Amino-2-ethyl-1,3-propanediol

H_2TPP-2A2E

Nuclear Magnetic Resonance Spectroscopy

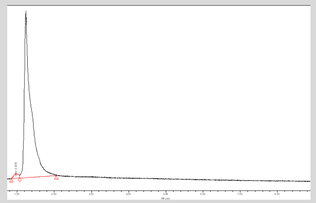


2-Amino-2-ethyl-1,3-propanedio



H_2TPP-2A2E

High Performance Liquid Chromatography



Waters NovaPak C_{18} 3.9 x 150 mm Column

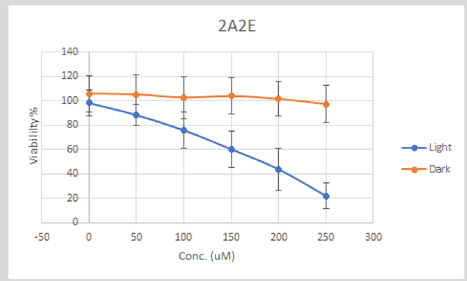
100% Acetonitrile Solvent

98% Purity

MTT Assay

- Light (left) and dark (right)
- H_2TPP-2A2E plated on wells 8-12
- 50 uM, 100 uM, 150 uM, 200 uM, and 250 uM concentrations
- Purple is indicative of living cells.
- Column 12 of the light plate are noticeably lighter in color.

Results



- Correlation between higher concentrations of 2A2E and compound toxicity.
- MTT assay results indicate that the exposure to light significantly decreases cell viability.
- The largest difference in cell viability is found at a concentration of 250 uM, at which cells kept in the dark maintained their original viability compared to those exposed to light which have 22% viability.

Conclusions

- A novel water-soluble porphyrin was successfully synthesized.
- The compound was characterized by UV-vis, IR, and NMR spectroscopies.
- The spectrums indicate that the correct compound has indeed been formed.
- At concentrations of 100 uM and above, light treatment consistently increases cell death, whereas treated cells kept in the dark remained viable.
- Results conclude that at high concentrations, H_2TPP-2A2E is an effective photosensitizer.

Future Direction

- Examine the cytotoxicity of H_2TPP-2A2E among normal cells and other cancer cell lines.
- Synthesize additional novel water-soluble metallic porphyrin derivatives, such as ZnTPP-DIPA, to see if other derivatives are more desirable in killing A549 lung cancer cells and are, therefore, candidates for PDT.

Acknowledgements

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