NOVEL PLATINUM-CHLORIN COMPLEXES AS POTENTIAL PHOTODYNAMIC AND CHEMOTHERAPEUTIC ANTICANCER AGENTS

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I. Introduction.

Photodynamic therapy is a method of treatment for various cancers. In this treatment, a photosensitizing agent is activated via a light source. This allows the excited agent to transfer its energy to oxygen, creating singlet oxygen that is capable of reacting with numerous biological compounds.[1] Cisplatin is a common chemotherapy drug that works by binding with a cell's DNA, preventing replication, and causing apoptosis. However, this drug suffers many drawbacks due to its ability to damage any cell within the body causing many side effects.[3] The combination of these two drugs have been studied in the past and show promising results.[4]

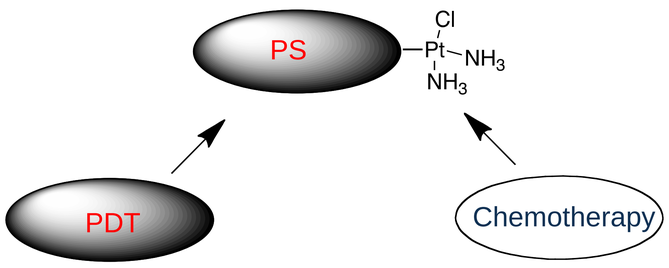


Fig 1. Showing the combination of two modes of treatment.

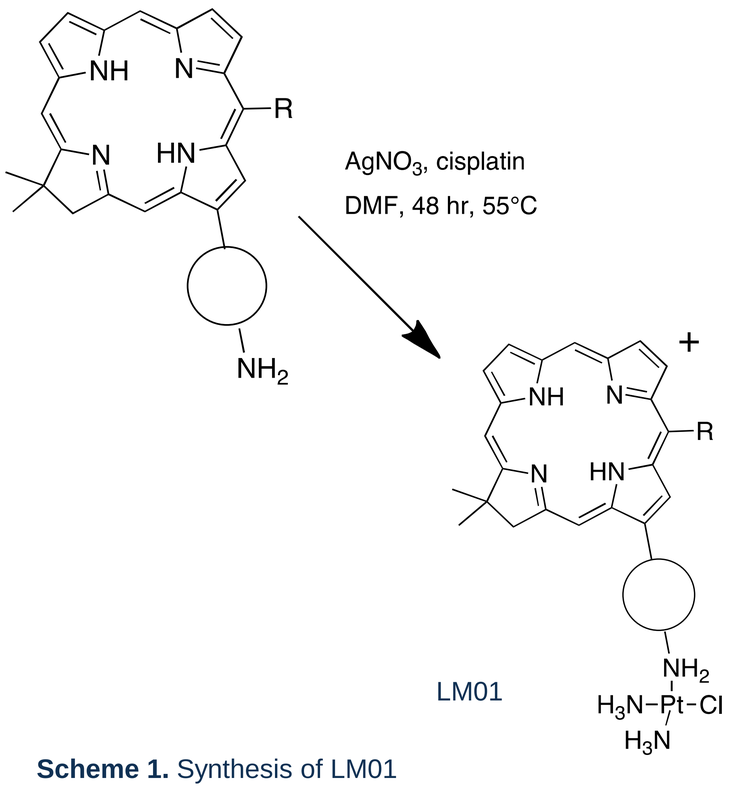
I.1 Goal.

The goal of this project is to determine whether the addition of cisplatin to a photosensitizer (PS) would allow for combining both photodynamic and chemotherapeutic modalities in one agent. Two new molecules were created by conjugating them with cisplatin in order to determine the changes in their structural and photochemical properties with the addition of cisplatin. The creation of these molecules allows for the possibility of dual action photosensitizing agents via high production of singlet oxygen, as well as the ability of these molecules to bind to DNA via the cisplatin constituent.

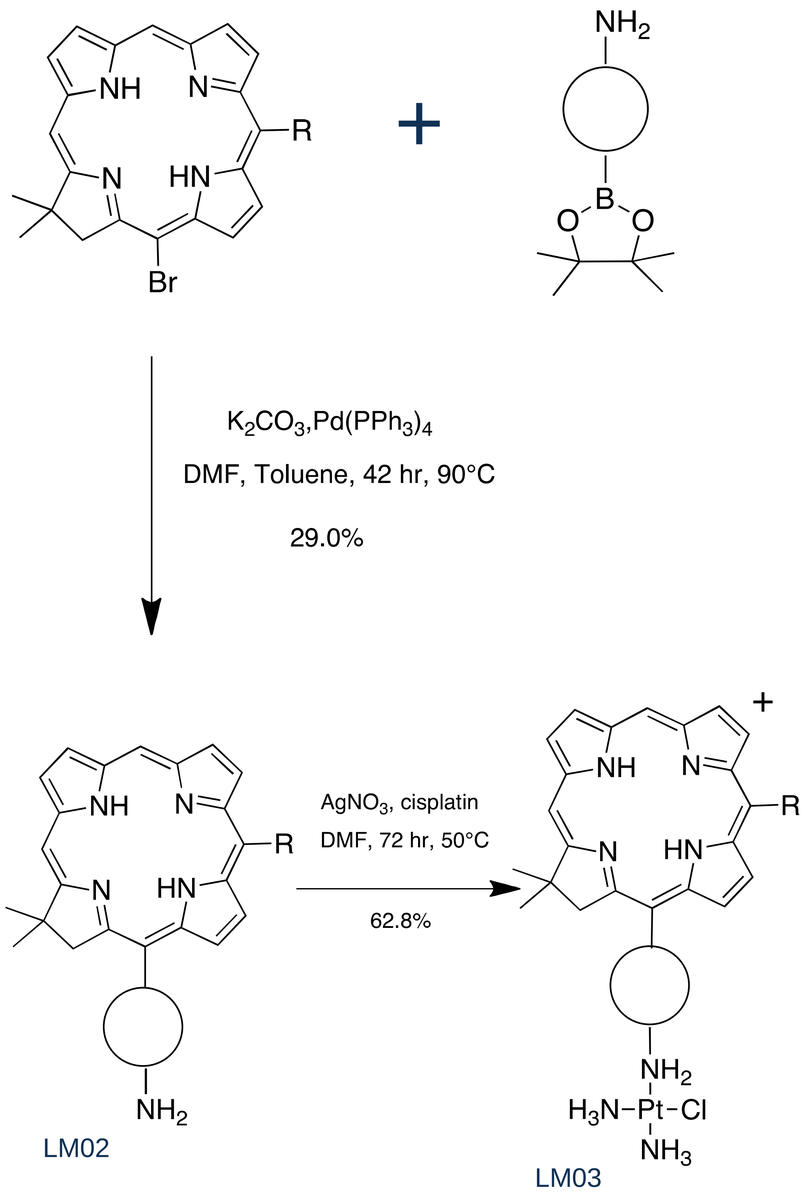
II. Results.

II.1 Molecular Design and Synthesis.

The synthesis of the target molecules are described below. The development of various precursors are detailed in previous publications by this group. LM02 was a new precursor to be synthesized, and thus its characteristics were taken.



Scheme 1. Synthesis of LM01



Scheme 2. Synthesis of LM02 and LM03

II.2 Absorbance, Emissions, and $^1O_2$ Production.

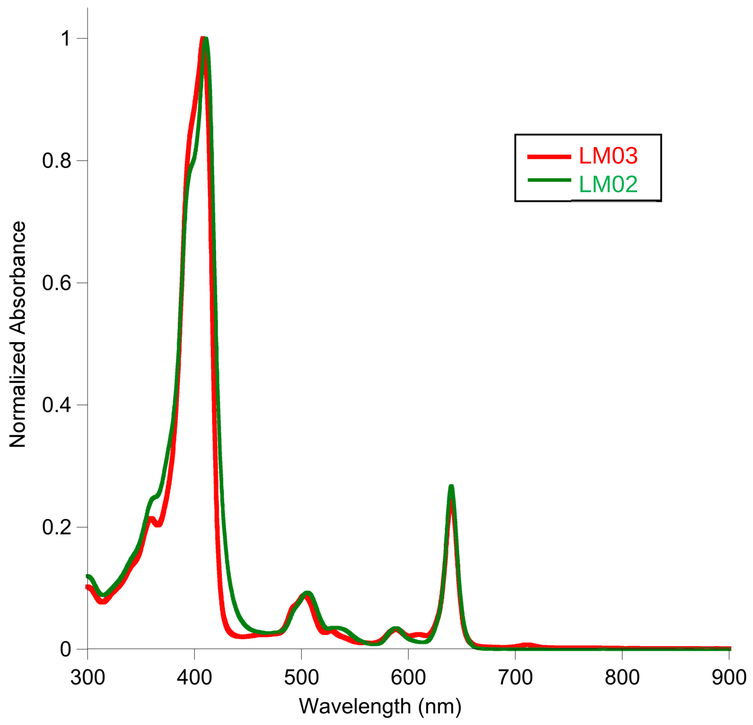


Fig 2. Absorbance spectrum for LM02 and LM03.

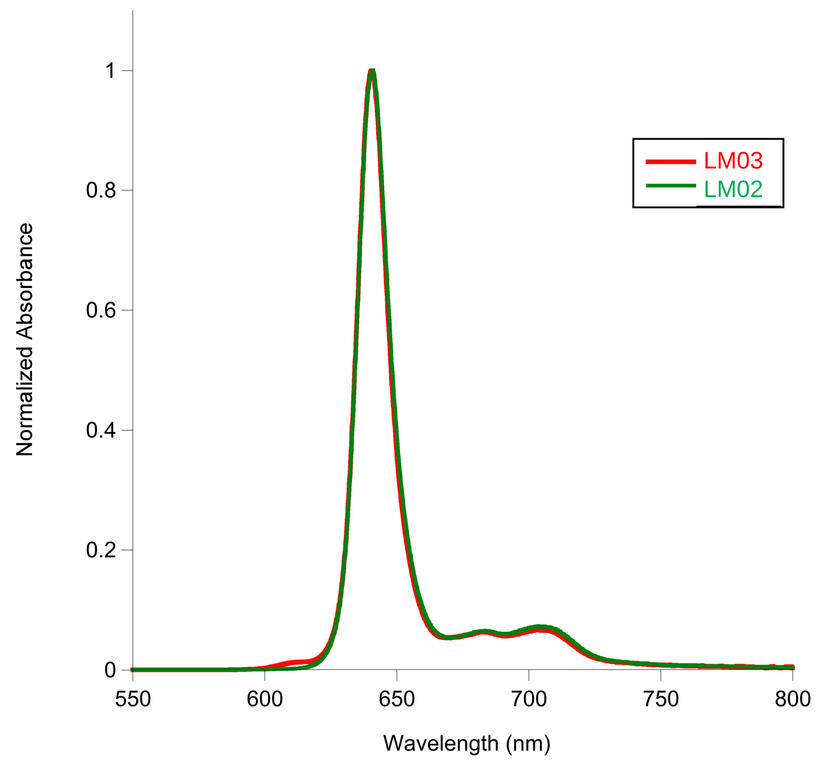


Fig 3. Emission spectrum for LM02 and LM03

Compound	Emission yield	Singlet oxygen ratio*
TPP	N/A	1
LM02	0.20	1.2
LM03	0.18	1.0

Table 1. Results showing the quantum yield of emissions and singlet oxygen photosensitization compared to reference tetraphenylporphyrin (in CH_2Cl_2).

III. Conclusions.

The synthesized molecules were found to possess the desirable characteristics that make promising photosensitizing agent. That is they absorb readily at 640 nm, fluoresces at around 645 nm, and high singlet oxygen production. Future experiments are to be conducted to determine the compounds ability to enter through a cells membrane, bind to the DNA within the nucleus of a cell, and take effective action against that cell when subjected to light and in dark conditions. These tests will be able to determine the compounds potential as an effective dual mode photosensitizing agent for use in photodynamic therapy.

IV. References.

1. Dolman, D., Fukumura, D., Jain, R. Photodynamic Therapy for Cancer. *Nat. Rev. Cancers*, **2003**, *3*, 380-387
2. Krumova, K.; Cosa, G.; Chapter 1 : Overview of Reactive Oxygen Species, in Singlet Oxygen: Applications in Biosciences and Nanosciences, Volume 1, **2016**, *1*, pp. 1-21.
3. Dasari, S.; Tchounwou, P.; Cisplatin in cancer therapy: molecular mechanisms of action. *Euro. Journ. Of Pharm.* **2014**, *0*, 364-378.
4. Naik, A.; Rubbiani, R.; Gasser, G.; Spingler, B. Visible-Light-Induced Annihilation of Tumor Cells with Platinum–Porphyrin Conjugates. Angew. *Chem. Int. Ed.*, **2014**, *53,* 6938–6941.

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