Characterizing New Pharmaceutical Agents Using NMR

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Introduction

We are an undergraduate-only research group so outside collaborations are critical for our work. This data was used in several pharmaceutical agent submissions to the National Institutes of Health, including: **(1) Antibiotics:** Two drugs we developed were accepted for testing by NIH-Division of Microbiology and Infectious Diseases, NIAID for testing against tuberculosis. The first compound (CuCap) did exceedingly well and has advanced to a second round of testing. The second compound is in the first round of testing at this time (CuAmk). NMR was critical in determining the structure of the copper complex (**Figure 1**).

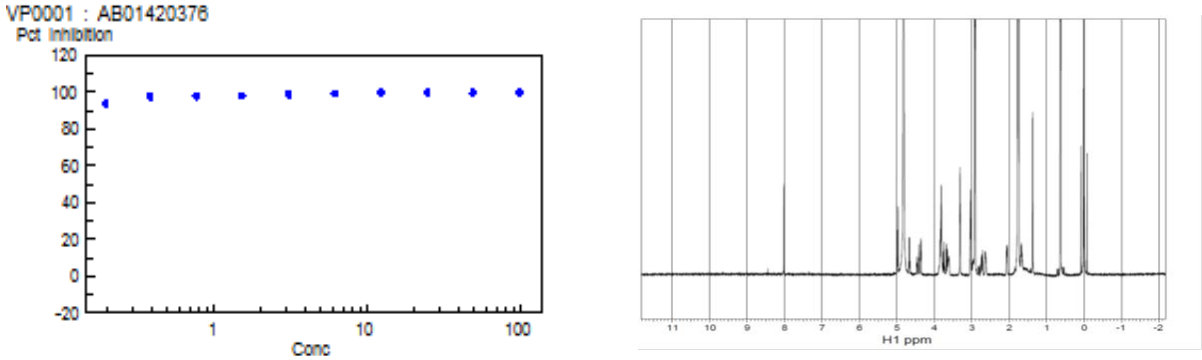
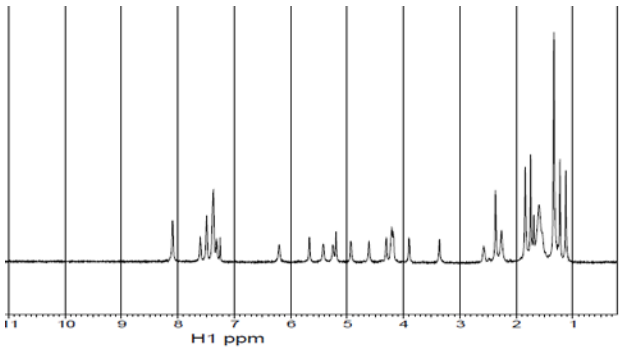


Figure 1. Growth inhibition data of copper complex against Mtb H37Rv (Mycobacterium tuberculosis and NMR spectra of molecule associated with the new Tb drug.

Experimental

(2) Copper-Complex for Cancer Treatment. We developed a copper compound that has been accepted and tested by the National Cancer Institute. It has progressed in stages including; Copper(II)-quinine; Cu(II)-hydrochloroquine; Cu(II)-taxol; Cu(II)-docetaxil; and Cu(II)-hydroxychloroquine-taxol. The goal of this work is to deliver two molecules to a cancer cell at the same time with different mechanisms (mitotic inhibitor, autophagy). The equipment at the NHMFL has been critical in determining the structures of these compounds (**Figure 2**).

Figure 2. NMR has been critical in identifying Cu-taxane and Cu-hydroxychloroquine complexes that have been accepted by NCI for testing against cell line panels.



Results and Discussion

(3) Farm the Ocean: Bryostatin is a well-known marine natural product that has shown activity against cancer, HIV and Alzheimer's but, it is extremely difficult to synthesize. We have developed a synthetic method called *pharmaceutical aquaculture* or farming the ocean. The use of NMR was critical in two areas; identifying matrix interference and identifying a new form of bryostatin.

Conclusions

One paper has been submitted, two are in the final stages of writing and we anticipate two additional papers once all of the data is evaluated. Copies are available upon request.

Acknowledgements

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