2014

Synthesis of Cisplatin & biological testing of the complex, compared to Triplatin (BBR3464)

Heba Dawood
Virginia Commonwealth University

Synthesis of **Cisplatin** & biological testing of the complex, compared to **Triplatin (BBR3464)**

Heba Dawood, Dr. Nicholas Farrell

Abstract

Two chemotherapeutic drugs were studied; one of them is Cisplatin that is currently used to fight cancer and the other is Triplatin (BBR3464) that was developed by Dr. Farrell. Cisplatin was synthesized and many different experiments were conducted such as: Recrystallization, Infrared Spectroscopy, UV-VIS, Melting Point, and Fluorescence experiment. After synthesizing the drug, it was tested in biology lab; we tested the effects of the drug on ovary cancer cells and its ability to kill cancer cells. A Cisplatin MTT ASSAY experiment was done and another MTT for Triplatin was done. Results from both of the experiments were compared and it was concluded that Triplatin is able to kill cancer cells more effectively and at lower concentrations than Cisplatin.

Introduction

Cisplatin is an anti-cancer drug that is currently being used to treat cancer patients. It binds to DNA, bends it and changes the shape of it. However, it has some side effects such as Nephrotoxicity. Therefore, there is a need to develop other drugs

Triplatin (BBR3464) is a drug developed by Dr. Farrell to treat cancer; such as ovary cancer, colon cancer, lung cancer. The drug reached Phase II human clinical trials with evidence of activity - some patients were given three years of extra life. Side effects were not like Cisplatin and dose limiting toxicity (DLT) was diarrhea and extreme tiredness.

Methods

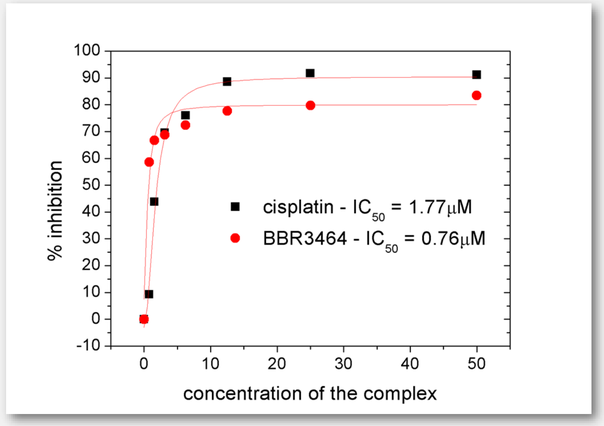
Many experiments were conducted:
For Cisplatin: Synthesis, Filteration, Elemental Analysis, Infrared, Spectroscopy (IR), UV-VIS, Melting Point and Fluorescence Experiment)
Then, biological testing for Cisplatin and Triplatin; (Cisplatin MTT ASSAY experiment MTT ASSAY for Triplatin)

Methods for MTT ASSAY:

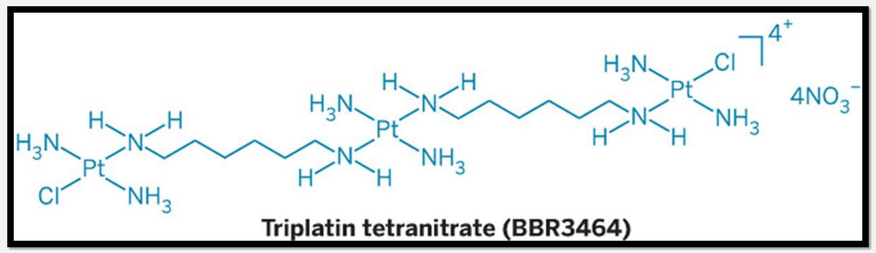
- 1st day: change cell's media, count cells, do the calculations, incubate cells for 24 hours
- 2nd day: prepare the drug samples, give them to cells, incubate for 72 hours
- Lastly; give the cells the MTT compound, wait 3 hours, then solubilization solution.

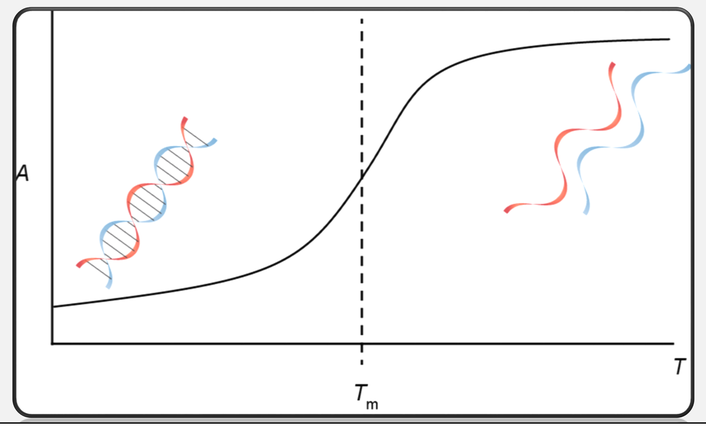
Results/Discussion

Cisplatin-IC_{50}=1.77µM
Triplatin (BBR3464)-IC_{50}=0.76µM
These results show that it takes less amount of Triplatin to kill cancer cells than Cisplatin; we only need 0.76µM of Triplatin to kill about 50% of the cancer cells



Different concentrations needed for specific % Inhibition

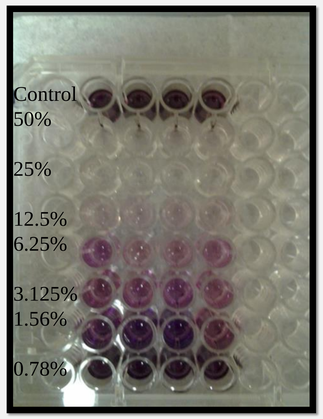


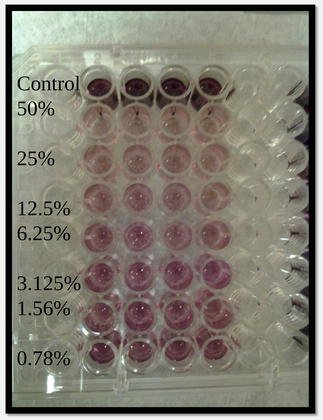


When it is heated; the double stranded DNA becomes a single stranded DNA. The temperature of the melting point at which that occurs is related to the drug that is used

Conclusion

Cisplatin is a good chemotherapeutic drug but it has side effects and therefore Dr. Farrell developed a new chemotherapeutic drug that is Triplatin. Also, Killing cancer cells using Triplatin requires only a small amount of it compared to Cisplatin





Key: Dark color= cancer cells Clear= no cancer cells
Comparison on the amount needed to kill specific % of cancer cells between Triplatin (Left) and Cisplatin (Right)

Works Consulted

Kukushkin, Kukushkin. "Facile Synthesis of isomerically pure cis-dichlorodiammineplatinum(II), cisplatin." Inorganic Syntheses. 32. (1998): 142. Print.

Farrell, NP: Progress in Platinum-Derived Drug Development. *Drugs of The Future*. 37:795-806 (2012).

Smith, Andri . "Cisplatin: The Invention of an Anticancer Drug." *General Chemistry Curriculum Supplement: Cisplatin*. National Science Foundation, 22 June 2005. Web. 30 May 2013. <http://chemcases.com/cisplat/index.htm>.

Hambley, Trevor W., Matthew Hall, Alderden Rebecca, and George Kauffman. "The Discovery and Development of Cisplatin." *Journal of Chemical Education* 83 (5): 728. Print.

Tsotsoros, S.D., Bate, A.B., Dows M.G., Spell, S.R. and Farrell, N.P.: Modulation of the stacking interaction of MN_4 (M= Pt, Pd, Au) complexes with tryptophan through N-heterocyclic ligands. J. Inorg. Biochem. 132:2-5 (2014)

Acknowledgements

Dr. Nicholas Farrell
Biology lab manager:
Erica Peterson
Graduate students:
Daniel Lee
Samantha Tsotsoros
Bruno Dario
Carolina Cardoso
Sarah Spell
Dr. Smith-Mason
Mr. Woods
HSURP program