Amphiphilic Neomycin Derivative

UtahStateUniversity
Department of Chemistry & Biochemistry

Taylor Shepherd

[1] Department of Biology, Utah State University, Logan, UT
[2] Department of Chemistry and Biochemistry, Utah State University, Logan, UT

OFFICE of RESEARCH and GRADUATE STUDIES
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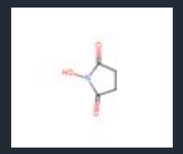
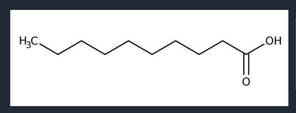
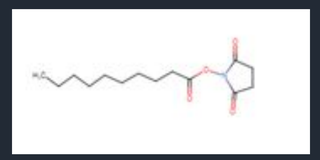
Introduction

Neomycin is an aminoglycoside antibiotic that is used to inhibit protein synthesis by binding to the bacterial ribosome. Bacteria have become more resistant to these treatments, so in previous years researchers have looked for other methods. Recently, researchers have reported amphiphilic neomycin which is selective toward bacteria. Our goal is to use amphiphilic neomycin and, through a series of reactions, attach a 12-carbon chain to amphiphilic neomycin. We will use this new compound on microbes to test for antimicrobial activity. We will then use the same methodology on 8 and 10 carbon chains. If found successful, this may lead to new medications for treating fungal and bacterial infections.

Creating Decanoic Acid into a usable form.

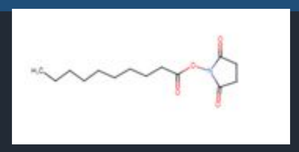


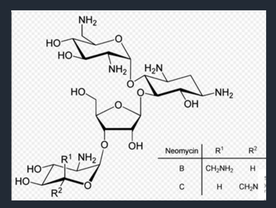




DCC, Anhydride DCM

Addition of Decanoic Acid to Neomycin





K2CO3, H2O, DMF

Above shows the first steps of creating a usable form of Decanoic acid by connecting it to N-Hydroxysuccinimide. Once we have a usable form, we can connect this 10 Carbon chain onto Neomycin which is the 2nd process shown. The reason there is a question mark is we are unsure where on Neomycin it will connect.

Methods

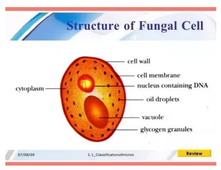
1. 1st Process to Create Decanoic Acid

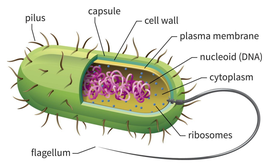
In order to create the usable form of decanoic acid we combined .516 g. of decanoic acid and dissolved it in 20 mL of DCM. Then .518 g. of NHS was added slowly to this previous reaction and stirred for 15 minutes. Lastly, we slowly added .928 g of DCC (over 15 minutes) to the reaction. This reaction was then stirred together for 48 hours. Then we vacuum filtrated this reaction. We then added 30 mL of DCM and stirred, and vacuum filtrated once again. After this step, we took the filtrate and put it on the rota-vap. We then took proton NMR of this which gave us a clear reading, indicating that we had the pure form of NHS connected to the decanoic acid.

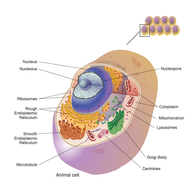
2. 2nd Process add Decanoic Acid to Neomycin

In order to get the neomycin and the 10 carbon chain attached to it, we took .5 g of neomycin sulphate and .276 g of K2CO3 and added them to 10 mL of water. We then took .26 g of NHS and dissolved it in 10 mL of DMF. Then we divided this mixture into 4 portions and added one portion of this to the SM and K2CO3 flask every hour for 4 hours. We let this dry for 72 hours by having air slowly blow dry it. We washed what was left 3 times with 10 mL of DCM via vacuum filtration. Then, with the residue, we dissolved it in 5% AcOH (acetic acid) 3 times, using 10 mL each time. Then we air dried this and it became our final product. We checked this by H NMR.

3. Currently What We Are Doing



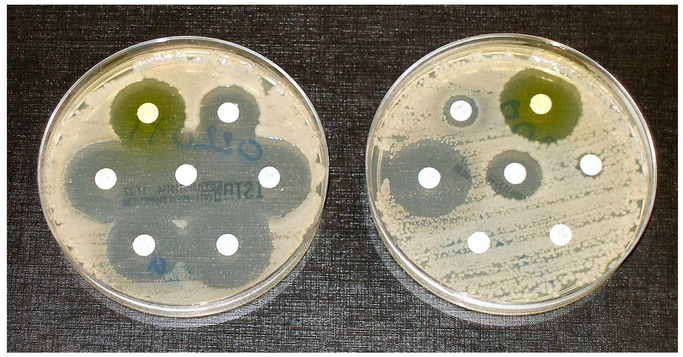




We have a pure carbon 10 chain connected to Neomycin. Now we are in the process of making a 12, 8 and 14 carbon chain. We have run into a few complications because they aren't purifying the same way that the carbon 10 chain did. So, once we figure out how to purify them, we will then try test all of them on different cultures of bacterial and fungal microbes.

Testing the Final Product

We will be testing them by growing cultures of different bacteria and fungi. We will have some control groups and then we will add some of our chemical into the cultures to see if they inhibit growth. This is a very simple way to tell if it is working. If it does, then we can do more specific testing to see if the chemicals actually kill the bacteria or fungus



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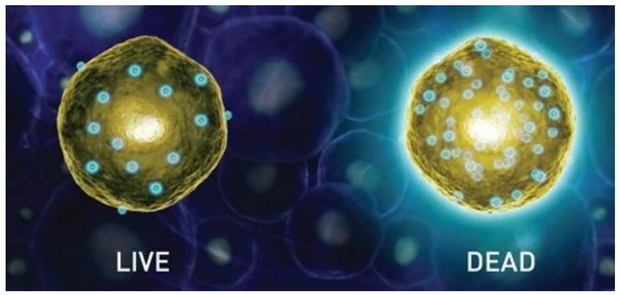

One way to tell if it is working would be a live vs dead cell stain.

Conclusions

If our project is successful, further experiments would need to be conducted.

If we can get any of these to work and see that they have antimicrobial effects, then further testing and comparisons would need to be done to see how they work, and if they are safe.

If everything turns out successful, this could lead to a new type of drug that bacteria or fungus aren't resistant to because they have never encountered something like this.