Amination of N3-Alkylamide-2-amino-quinazolinone scaffold

Daniel Tolas, Yen-Po Huang, Haleigh Rzonca, Kelly E Kim.

The focus of our research has been on the tropical disease known as Chagas Disease which is caused by the parasite *Trypanosoma Cruzi.*The parasite's vector of transmission is the *Triatominae* (Kissing bug). Chagas disease is most commonly found in south and central America, the prevalence of Chagas disease in this region is described by Padilla and Rodriguez to be estimated that there are 20,000 new cases of Chagas disease per year, and that 10 million people are currently infected with an additional 100 million living in areas with high risk of transmission (Padilla, Rodriguez 2014). Currently there are two drugs on the market to treat chagas disease Benznidazole and Nifurtimox but neither of these drugs provide an ideal solution to Chagas disease as they both have limitations in their accessibility and effectiveness. With regards to the previously mentioned drugs accessibility, Both Nifurtimox and Benznidazole require long treatment regiments making it harder for people to afford treatment and the mild toxicity of the drugs makes it harder to prescribe to patients who might be drug sensitive. The largest shortcoming of the previously mentioned drugs is their effectiveness, they are only effective in treating the acute phase of Chagas disease (Padilla, Rodriguez 2014), they only act to treat patients in the acute and early chronic stages of Chagas disease and don't convey any preventative benefits or chronic stage treatment. Recent research from the drugs for neglected diseases initiative found N3-Alkylamide-2-amino-quinazolinone to posses antiparasitic activity (Rassi Lancet, 2010). Which could be a major breakthrough in the treatment and furthermore the prevention of chagas disease as it would target the parasite responsible for chagas disease. The goal of our project was to further expand the chemical library of the aforementioned quinazolinone as well as improve methods for synthesizing certain derivatives of the initial quinazolinone. The way our team set out to achieve this goal was through testing various types of amines in an amination reaction while using thin layer chromatography TLC to measure reaction progress before eventually collecting an NMR sample and weighing our final product in order to calculate a yield. Our results were inconclusive as we consistently had low yields across the different types of amines and NMR samples that were contaminated with excess starting material. Based on these rather inconclusive results more time should be invested in testing other amines as we were limited to what amines were readily available to our group before any investigation into new methods surrounding the animation step be explored.

References:

Padilla J A, Rodriguez A. High throughput screening for Anti-Trypanosoma Cruzi Drug Discovery. PLOS, 2014. 8 (50). page 1-6.

Rassi A, Rassi A, Marin-Neto JA. 2010. Chagas disease. The Lancet. 375(9723):1388–1402. doi:10.1016/s0140-6736(10)60061-x.