Optimizing Linear Sialic Acid-Containing Polymer Parameters for Enhanced Influenza Inhibition

Rachel H. Bianculli, Jonathan D. Mase, Matthew Dupree, Michael D. Schulz
Department of Chemistry
Virginia Tech, Blacksburg, VA

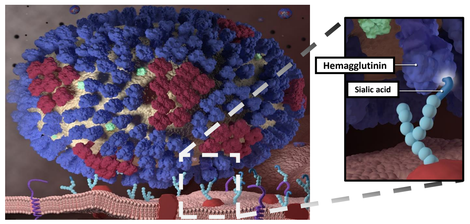
Introduction

Influenza is a major health concern worldwide. Currently, vaccines are the primary means of influenza maintenance, but they suffer from several limitations. Vaccines:

(1) require annual updates due to virus mutations
(2) require specific storage and transport conditions (refrigeration)
(3) are not tolerated by everyone (e.g., patients with specific allergies or compromised immune systems)

Antiviral drugs may also be used to treat influenza infections, but these drugs are often limited by the emergence of resistant virus strains.

Let's make something that is not strain dependent and can withstand various storage conditions.

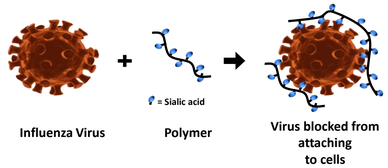


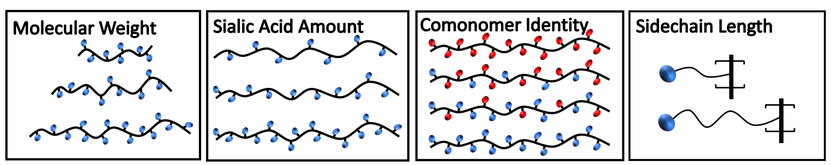
Influenza's replication is initiated by the binding of hemagglutinin (HA) on the viral surface and sialic acid (SA) on the cell surface (depicted above). If we can inhibit this interaction from occurring, we can stop viral replication before it even begins!

The interaction between HA and SA can be mimicked synthetically with polymers containing sialic acid side chains. Multiple SA moieties can then bind to the surface of influenza acting like "Velcro" and effectively blocking the surface from interacting with anything else.

Research Goals

- Synthesize sialic acid-containing polymers with systematically varied parameters (molecular weight, sialic acid amount, sidechain length).
- Measure inhibition against influenza using a hemagglutination inhibition (HAI) assay.

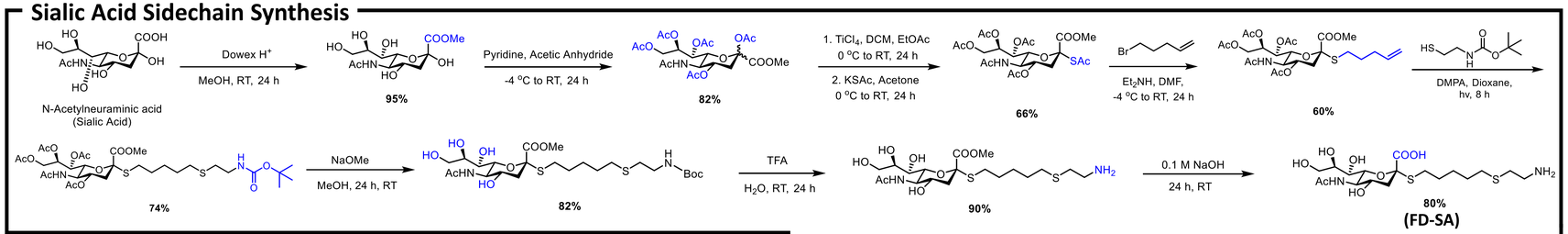




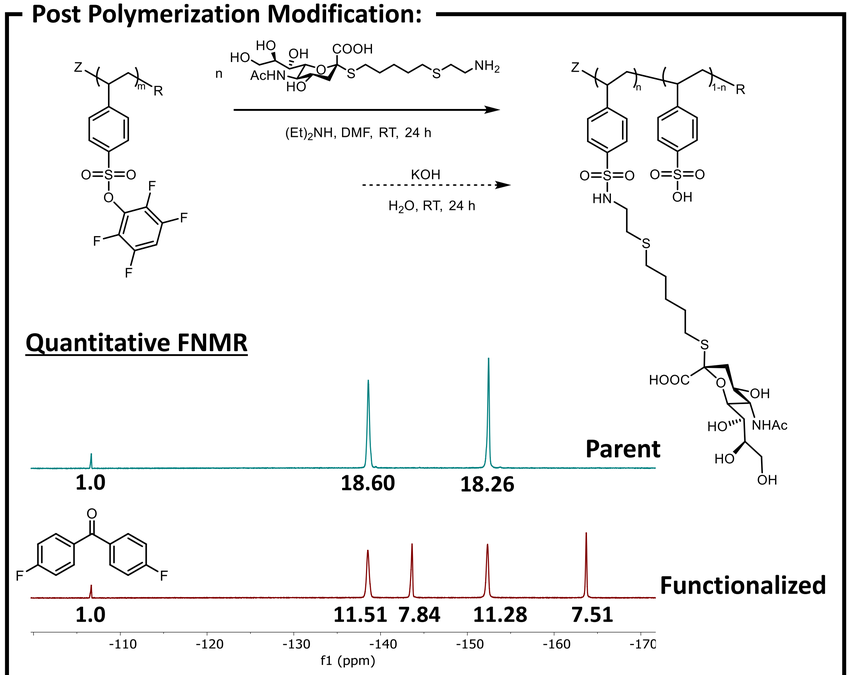
Bianculli, R.H.; Mase, J.D.; Schulz, M.D., Antiviral Polymers: Past Approaches and Future Possibilities, *Macromolecules* 2020, 53, 21, 9158–9186

Design and Synthesis

Sialic Acid Sidechain Synthesis

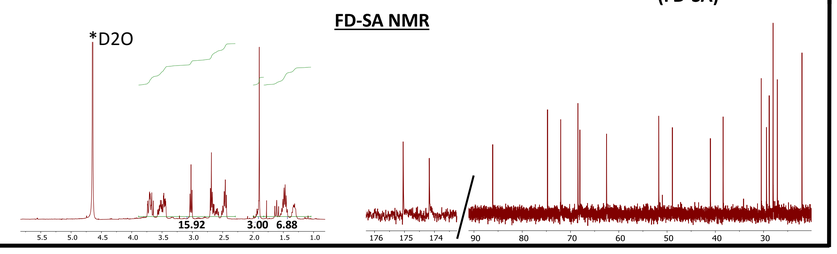


Post Polymerization Modification:

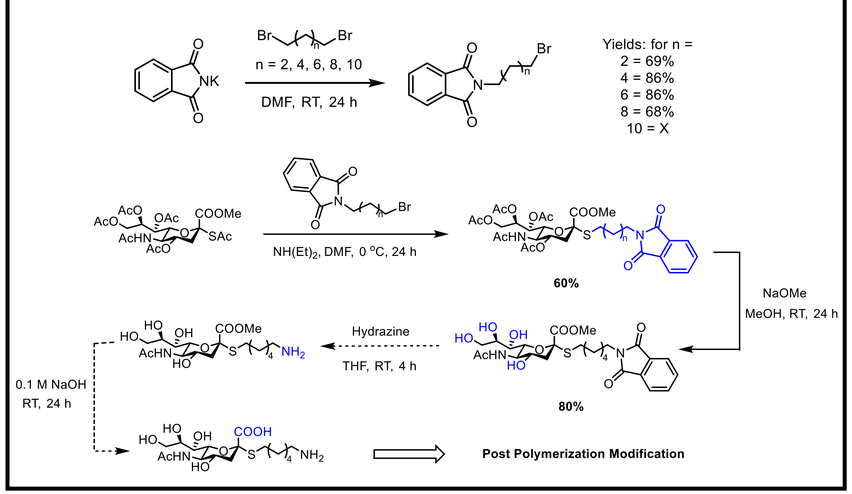


Target = 50% Functionalization | Actual = 42% Functionalization

FD-SA NMR



Sialic Acid Sidechain Length



Future Work

After synthesizing the complete library of systematically varied polymers for sialic acid content and molecular weight, we will measure influenza inhibition using a hemagglutination inhibition (HAI) assay. This data will measure the concentration of polymer and sialic acid needed to inhibit hemagglutination. This data will be used to study structure-property relationships and optimize materials for enhanced inhibition.

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