Synthesis of Disulfide Linked Covalent-Organic Frameworks for the Delivery and Release of Chemotherapeutics

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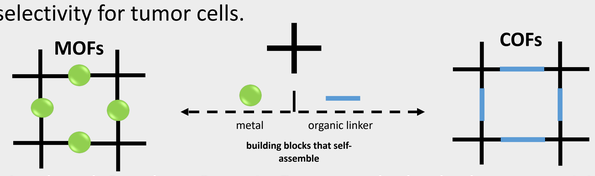
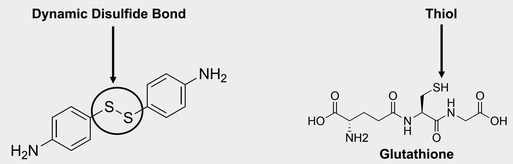
Introduction

Cancer remains one of the leading causes of death worldwide, with an estimated 2 million new cases expected in the United States this year alone. Cancer involves the unchecked and rapid process of mitosis and cell division, which can lead to the formation of a tumor. Treatment options for cancer include chemotherapy, radiation, hormonal therapy, and surgery. While these treatments can be effective, they each come with limitations, such as their cost, their invasiveness, and their poor selectivity for tumor cells.



Metal and Covalent-Organic Frameworks both show promising potential for drug delivery applications. Along with their ability to self assemble, These complex crystalline nanocarriers made up of organic building blocks can be highly functionalized to respond to stimuli. This high tunability factor can be utilized for design of a drug delivery system with a selectivity for proteins found in cancer cells.



Our objective is to deliver chemotherapeutics with disulfide linked Covalent-Organic Frameworks to induce apoptosis in cancer cells.

Experimental Methods

The investigation of redox-responsive disulfide bonds as drug delivery systems has gained traction due to tumor-specific physiological triggers. Under oxidative conditions, these bonds can be broken by cellular free thiols such as glutathione (GSH), which is 100 to 1000 times more concentrated in cancer cells. The COF should degrade in these conditions without harming any healthy cells.

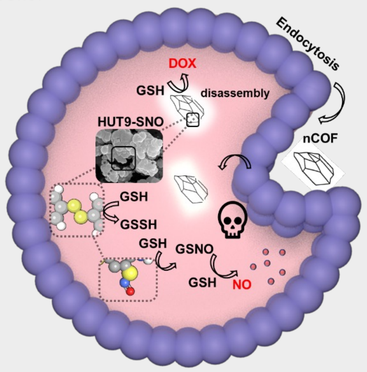
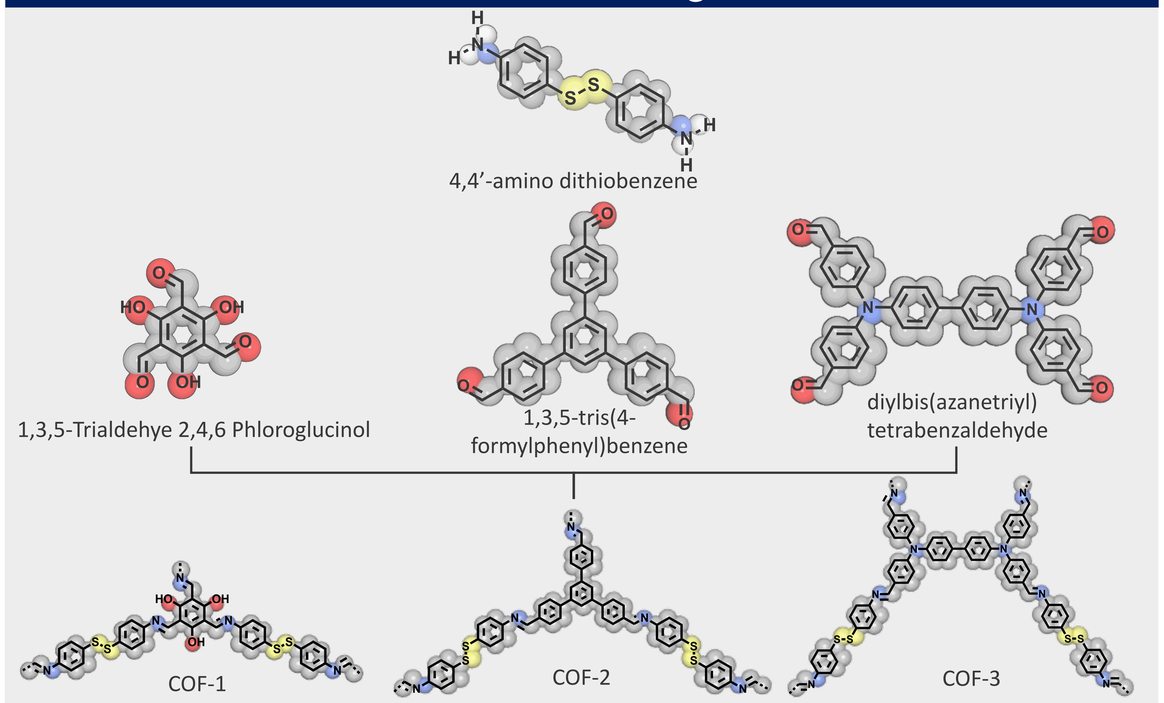


Figure 1. *Endocytosis of nCOF to facilitate the release of chemotherapeutics doxorubicin (DOX) and reactive oxygen species (ROS)*

Molecular Design



Scanning Electron Microscopy

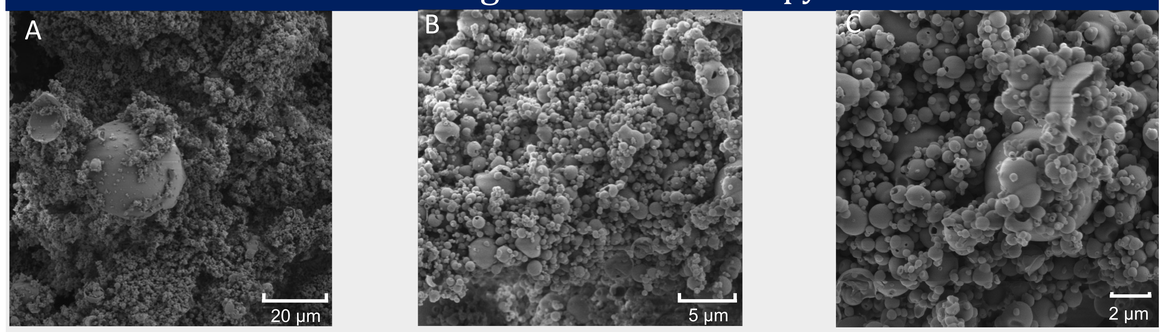


Figure 2. *Scanning Electron Microscopy (SEM) Imaging of COF-3 product at three magnifications 20 µm (A), 5 µm (B), and 2 µm (C) showing similar spherical morphology.*

Powder X-Ray Diffraction and Fourier-Transform Infrared Spectroscopy

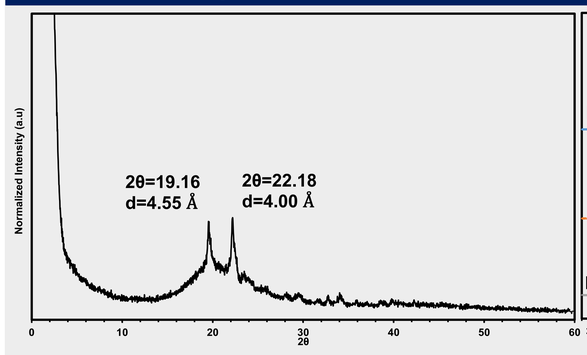


Figure 3. *Powder X-Ray Diffraction (pXRD) pattern of COF-2 product showing evidence of pi stacking*

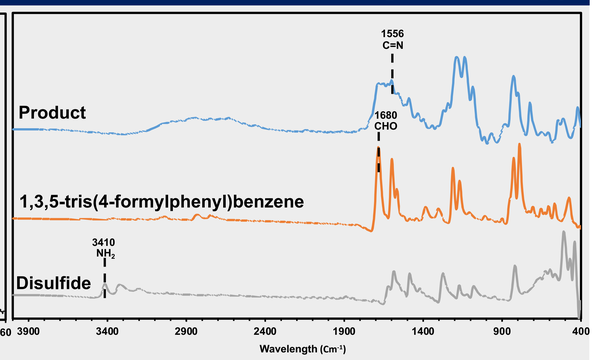
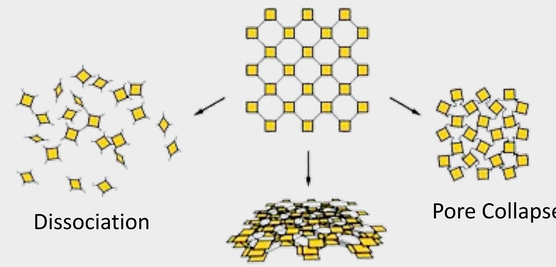


Figure 4. *Infrared (IR) Spectroscopy analysis of COF-2 product and starting materials showing dynamic bond formation*

Future Work

While there is evidence of dynamic Imine formation, Improvements still need to be made on the crystallinity factor of the system. The data collected from pXRD shows evidence of pi stacking, which can be a sign of crystal degradation.



As crystallinity improves, drug loading studies will be taken to test the absorption factor of each synthesized COF. Using fluorescence spectroscopy, the concentration of chemotherapeutics absorbed can be tracked until an effective dose is reached. Once a proper amount of chemotherapeutics is loaded into the synthesized COFs, then we can begin to run preliminary cellular studies. In these studies, we will be able to test the full selective nature of the COF delivery systems and design a product which can induce apoptosis in cancer cells.

Drug Loading Studies

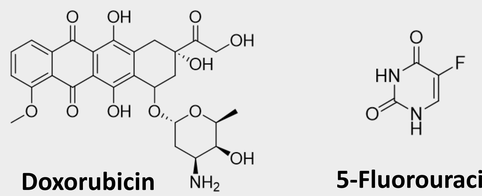


Figure 7. *Doxorubicin and 5-Fluorouracil are two chemotherapy drugs that will be loaded into the COF to target and treat cancer.*

Acknowledgements

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