Prophylactic Drug Delivery System for COVID-19
Heather Sheardown, AIMBE Class of 2019

The Heather Sheardown lab (McMaster University, Canada) is home to an interdisciplinary team of scientists and trainees with expertise in ophthalmology, polymer and biomaterial engineering, chemistry, pharmaceutical formulation and drug delivery, animal/ex-vivo/in-vitro models of disease and drug delivery, early stage material design and synthesis, and synthetic method scalability optimization.

As the availability of a SARS-CoV-2 vaccine is still far off, there is an immediate global need for prophylactic prevention strategies, particularly for vulnerable populations including seniors and frontline workers. The Sheardown lab has developed a mucoadhesive polymeric micelle that allows for the encapsulation of a range of therapeutics, providing local, controlled delivery to mucosal surfaces. This technology overcomes traditional solubility concerns, allowing formulations at higher drug concentrations. Its mucosal binding significantly reduces dosing frequency, increases local bioavailability and improves clinical efficacy. Developed and validated for safety and efficacy in the eye, this system is now being repurposed for the mucosa of the respiratory tract, formulated as a nasal spray or inhaled aerosol, incorporating two treatments that are currently under study internationally: hydroxychloroquine (HCQ) and remdisivir.

Patented Micelle Technology for Targeted Drug Delivery:
Investigators in the Sheardown lab have patented a series of poly(L-lactide)-b-poly(methacrylic acid-co-phenylboronic acid) copolymer micelles with varying amounts of the mucoadhesive phenylboronic acid (PBA). The micelle size is dependent on the type of drug loaded, ranging between 50 nm and 400 nm as determined by dynamic light scattering. Transmission electron micrographs reveal the spherical shape of the micelles. The mucoadhesive properties have been demonstrated by radioactively labelling the micelles with I125, and treating rabbit corneal surfaces once with the labelled micelles. Significant amounts of PBA-micelle continued to be observed on the cornea after 7-days when compared to non-PBA-micelle. Furthermore, the radioactive counts of PBA-micelle were observed to be the same at 3-days and 7-days post-incubating showing the strong interaction of PBA-micelle with corneal surface mucins. A number of drugs including latanoprost, an intraocular pressure reducing drug, and HCQ have been successfully loaded into the micelles.

Research is exploring the mucoadhesive property of the micelle in the organs of the pulmonary system i.e. intranasal cavity, nasopharynx, trachea and the lungs by using radioactively labelled micelles. Pharmacokinetic (pk) studies are being conducted to determine the bioavailability of the drug and validate the sustained release of the drug from the micelle-drug formulation. Due to the sustained drug release property of our polymer, we speculate a significant reduction in dose required to prevent the infection by SARS-CoV-2 that would ultimately reduce the amount of drug required, as well as reduce the incidence of systemic side effects.
The Sheardown lab technology is currently being tested with HCQ and Remdesivir as well as with steroids for intra-lung delivery.

**Industry Partner:** The Sheardown lab has an ongoing partnership with Mannin Research Inc. ([http://mannin.ca/](http://mannin.ca/)), a Canadian biotechnology company. In addition to providing us with an experimental drug from their repertoire, Mannin will assist by manufacturing scalable GMP batches of the micelles that will be used for Investigational New Drug (USA) and Clinical Trial Application (CTA) (Canada) enabling toxicology studies to allow rapid translation to market. By utilizing approved compounds with demonstrated efficacy for COVID-19, an abbreviated regulatory path is possible. The goal is ultimately to reduce the devastating health and economic impacts of the pandemic and decrease the potential impact of the inevitable second wave.