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High-Flux Hemofiltration System for Rapid Toxin Removal

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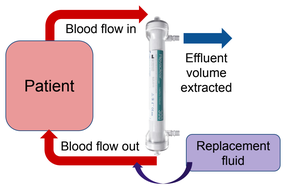
Background and Objectives

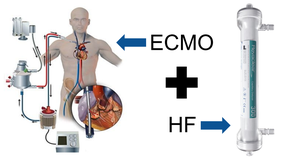
Acute poisonings affect 2.16 million people each year.[1] Unfortunately, traditional removal modalities such as hemofiltration (HF) typically are not useful for toxins that have a high protein binding fraction or volume of distribution. These toxins are termed non-dialyzable (ND), and overdoses frequently result in death.



Toxin	Purpose	Protein Bound	Dialyzable?
Colchicine	Anti-inflammatory	40-50%	No
Flecainide	Anti-arrhythmic	40%	No
Metformin	Anti-diabetic	Negligible	Yes

Left: Hemofiltration process with a single filter.
Above: Candidate non-dialyzable and dialyzable toxins.
Below: High flow design concept combining ECMO flow rate with HF removal modality.[2]

Conventional HF methods are inadequate for ND toxins due to low blood flow rates and an insufficient membrane surface area. Extracorporeal membrane oxygenation (ECMO) is a technology for heart and lung failure that circulates blood at 4-5 L/min.

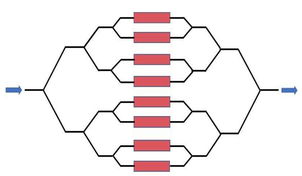


Objective: Develop an **ECMO-compatible hemofiltration system** with an increased surface area to facilitate **rapid acute toxin removal** at high flow rates for the treatment of poisoning victims.

Identify use cases (non-dialyzable toxins) → **Select** a high-flux hemofilter → **Create** a hemofilter circuit prototype → **Test** filtration capacity for toxins of interest, **compare** to HF

Design Specifications

System Design



- ✓ Parallel flow circuit
- ✓ 8 filters
- ✓ 4 L/min total flow
  - 500 mL/min per filter

HF removal: 41 mg/hour

Our design: 1,000 mg/hour

System ultrafiltration 2,437 mL/min

Filter ultrafiltration 305 mL/min

Filter Selection

Baxter Revaclear 300 Capillary Dialyzer[3]

Parameter	Revaclear 300
Blood flow rate > 400 mL/min	500 mL/min
TMP allowance > 400 mm Hg	600 mm Hg
High ultrafiltration coefficient	48 mL/hr*mm Hg
Cost < $600	$219.95 for 24
Middle molecule removal	Yes, 70% β2M

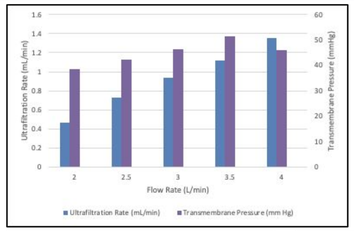
Methods

Parallel Eight Filter System - Seven Y connectors were used on each of the inlet, outlet, and effluent ends of the eight filter group to produce one system inlet, outlet, and effluent tube. The inlet tube is attached to the ECMO pump, while the outlet tube connects to the replacement bag. The effluent tubing is placed into an empty bucket to discard the ultrafiltrate.

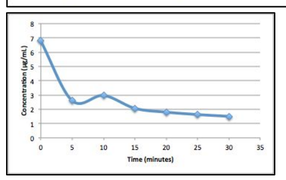
Pressure and Flow Sensors - Flowmetric sensors were attached to the main input, output, and effluent tubing to monitor flow rates. Pressure sensors were attached at the same locations on an individual filter in the system to measure the transmembrane pressure (TMP).

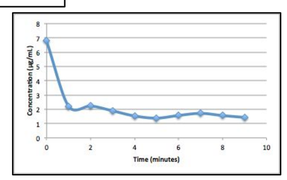
Toxin - Flecainide was used to test the performance of the system because it is non-dialyzable. The initial concentration was the plasma concentration for a 5,000 mg overdose in an 80 kg adult (6.8 μg/mL). Flecainide was dissolved in 5 L of saline. Samples were taken from the effluent outflow and the concentration of flecainide was measured with UV-visible spectroscopy.

Results



Ultrafiltration (effluent) flow rates and transmembrane pressures were measured over several input flow rate increments in the eight filter system. Ultrafiltration rate increased linearly with flow rate. Likewise, transmembrane pressure increased in the same manner as flow rate increased up to 3.5 L/min. At 4 L/min, the transmembrane pressure dropped back to the pressure value observed at 3 L/min.





Eight filters
Effluent flow rates (L/min)
Measured 1.87
Target: 2.44

Flecainide concentration over time is shown in a two filter system with flow rate 1 L/min (above left), and in an eight filter system with flow rate 4 L/min (above right). Mass removal rates over time were then calculated in mg/hr (below). Potential removal rate represents the theoretical rate given addition of an effluent pump to reach the target ultrafiltration rates. The possibility of moderate flecainide adsorption onto the hemofilters may contribute partially to the observed decrease in concentration.

Filter Number	Average removal rate	Initial removal rate	Potential removal rate	Target removal rate	Percent error
2	52.9	115.0	175.0	250	30%
8	178.9	684.4	891.9	1000	10.81%

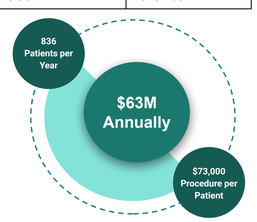
CVVH 41 mg/hr

PT 891.9 mg/hr

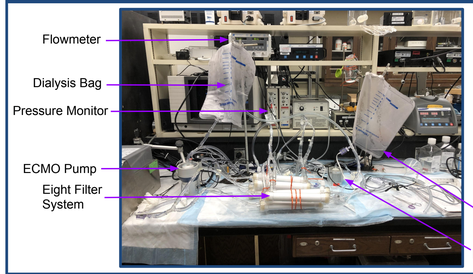
Filtering capacity x **21.6**

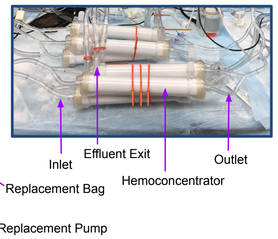
2.16M Poison Exposure Cases

0.0004% require ECMO[4]



Prototype





Ethical Implications

While some poisoning patients may already require ECMO for heart and/or lung failure, others may not. For these patients, the **risks of ECMO** including bleeding, clotting, hemolysis, and air embolism[5] must be **outweighed by the benefits.** Our modality also requires rapid addition of replacement fluid to the blood, which can lead to hemodynamic instability. However, the ECMO system is designed to mitigate this general complication. Regardless, providers must use their best acute judgment to determine whether or not our system will be safe for each individual patient.

Conclusions and Future Work

Developed a ***parallel hemofilter system*** that:

- Supports an **ECMO-compatible** flow rate of 4 L/min
- Removes the toxin flecainide at a **clinically relevant rate** of 684.4 mg/hr, with a potential rate of **891.9 mg/hr** with an effluent pump
  - Demonstrates a potential **21.6-fold increase** in removal rate compared to **conventional hemofiltration**

Clinical contribution: A **robust, time-saving toxin removal modality** for patients who have overdosed on **traditionally non-dialyzable drugs**

Future Work

Test with **effluent pump** and flecainide in **animal blood** → Test multiple toxins in **ECMO circuit** with animal blood → Explore a **modular approach** with different filters → **Patent technology** and explore **animal testing**

We will explore testing with animal blood to further improve clinical relevance. We predict that this will reduce the error between the potential and target removal rates because the filter ultrafiltration coefficient (which was used to calculate target flow rates) was given for blood at 37 °C.

References/Acknowledgments

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