CytoSorbents

A Platform of Sorbent Therapies to Empower Military Resilience and Readiness

An Oral Sorbent for TRAVELER'S DIARRHEA

Traveler's diarrhea (TD), caused by a variety of enteric bacterial pathogens, is the number one infectious disease **threat to warfighter readiness**. Symptoms are caused by the toxins secreted by the bacteria, as well as the resulting gut inflammation. TD can be highly debilitating and can easily spread throughout an entire unit.

Current treatment approaches include over-the-counter anti-diarrheals, which often have limited success at treating symptoms, antibiotics, which can promote resistance, and vaccines, which are often pathogen specific and, to date, have not been proven successful.

SOLUTION

Enterica™ is a novel, orally administered sorbent that can directly remove a **broad array of enteric toxins** as well as a variety of inflammatory mediators at the site of infection in the gut. The sorbent is dry and lightweight and can be carried in single-dose packets that can be mixed with water for **easy oral administration**. Once in the gut, Enterica binds the toxins and is eliminated in the feces. Used prophylactically, Enterica can prevent the onset of symptoms, ensuring **sustained operational readiness**.

Inflammatory Mediator	MW	% Removal
IL-8	8 kDa	100
IL-1Ra	17 kDa	100
IL-1α	17 kDa	100
IL-10	18 kDa	85
IL-6	26 kDa	87
HMGB1	30 kDa	80
TNF-α trimer	51 kDa	55

Toxin	MW	% Removal
CTX	84 kDa	98
STX-1	69 kDa	99
STX-2	69 kDa	99
CPE	35 kDa	93
SEA/B	23-29 kDa	99
Ricin	65 kDa	99
LT Toxin	85 kDa	95

Table 1. *In-vitro* testing demonstrates over 90% adsorption of inflammatory mediators and toxins, including Enterotoxigenic E. coli (ETEC) heat-labile toxin. CTX, cholera toxin; STX-1 and -2, Shiga toxins 1 and 2; CPE, C. *perfringens* enterotoxin; SEA/B, S. *aureus* enterotoxin A and B.

Designed to Meet Military Needs

Stored dry, making it lightweight and stable at temperature extremes, Enterica can be **easily stockpiled**. Fine-tuned to adsorb a broad array of toxins, Enterica acts on a variety of TD causative agents. As it does not remove antibodies, Enterica **does not interfere with vaccine-induced or natural immunity**.

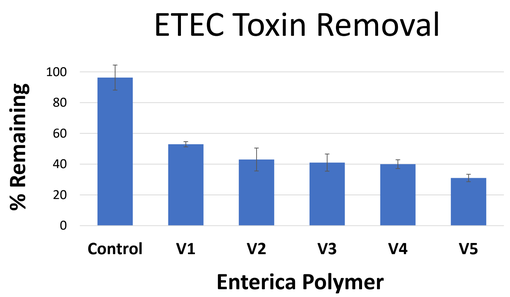


Figure 2. *Enterica design improvements have increased toxin removal capabilities. Experiments conducted in Simulated Intestinal Fluid with excess competing protein. Adsorption was achieved in just three hours. N=3; mean± SE*

Current DoD Studies

CytoSorbents is working with **Naval Medical Research Unit South** in Lima, Peru. Enterica is being evaluated in a highly translationally relevant **non-human primate model** of TD. Pilot studies indicate that Enterica exhibits no adverse effects and that the sorbent is **reliably eliminated** in the feces.

Next Steps

Planned next steps include:

- *In vitro* testing on clinical isolates from a variety of TD-causing pathogens and strains
- *In vivo* studies in NAMRU-South's non-human primate model of TD
  - Efficacy studies on effects of Enterica on severity and duration of diarrhea, toxin levels, and inflammation
  - Long-term tolerability studies using endoscopy to assess adverse events associated with long-term prophylactic use

We are actively seeking advocates within the DoD to support this work.

An Injectable Sorbent for JOINT INJURY

Joint injuries, whether sustained during training or in the field, are a major source of **lost duty days**. The immediate effects are severe pain, swelling, and inflammation. If left unchecked, this can lead to cartilage degradation within days to weeks, potentially causing **long-term disability**.

Current treatment approaches include NSAIDs, which cannot mitigate long-term cartilage damage, and steroid injections, which temporarily relieve symptoms by completely suppressing the immune response, interfering with healing. Further, repeated injections can actually cause damage to cartilage and weakening or rupture of tendons.

SOLUTION

CytoSorbents has developed a novel nanoparticle sorbent (NPS) that, when injected to an injured joint, can bind a **broad range of cytokines and cartilage-degrading** proteases, reducing inflammation, pain and swelling and helping prevent cartilage degradation. It resides in the joint for weeks to months, providing **prolonged effectiveness.**

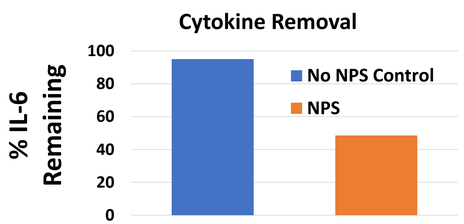


Figure 3. *Significant removal of IL-6, a key inflammatory mediator in joint injury, was achieved by our NPS in* ***just three hours****.*

Next steps

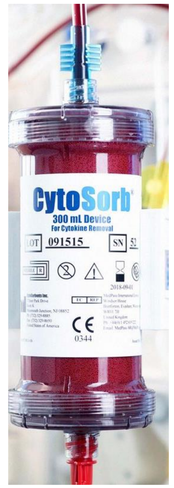
- *In vitro* validation that cytokine and protease sequestration can minimize subsequent cartilage damage
- *In vivo* studies in a large animal model of joint injury to demonstrate that our NPS can reduce pain and prevent cartilage damage, yielding short-term (**return to duty**) and long-term **(prevent permanent disability**) benefits.

We are actively seeking advocates within the DoD and throughout the federal government to support this work.

An Extracorporeal Sorbent for TBI

Severe traumatic brain injury (TBI) is a life-threatening injury that initiates dysregulated inflammation, leading to neuroinflammation and neuronal injury. Even when patients survive, these downstream effects result in poorer neurologic and cognitive outcomes. Currently, there are **no therapeutic treatments** to slow the progression of this inflammation-driven secondary brain injury.

SOLUTION



CytoSorb® is an extracorporeal blood purification device that can treat hyperinflammation (e.g., sepsis) by adsorbing cytokines. It has proven safe and effective in 205,000 human uses.

CytoSorb represents a **promising new therapy** for TBI. By dampening hyperinflammation, it can help reduce the secondary neurodegenerative brain injury and cerebral edema that can lead to permanent neurocognitive deficits and death, thus **improving survival** as well as preserving long-term **cognitive and neurological function**.

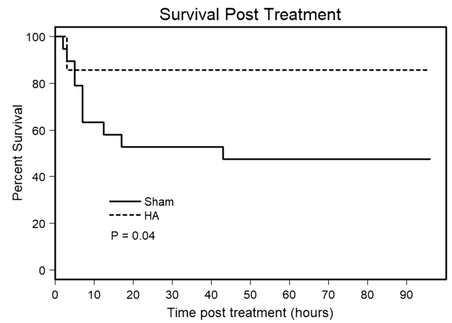


Figure 4. *Rats subjected to polytrauma (severe TBI plus hemorrhagic shock) had a significant increase in 4-day survival when treated with hemoadsorption (HA) with CytoSorb compared to control (sham).*

Next steps

Planned next steps include a large animal study assessing 30-day **cognitive and neurological function** after 72-hour CytoSorb treatment post-TBI.

We are actively seeking collaborators with an appropriate animal model system of severe TBI to assess not just survival, but cognitive outcomes.

We also seek advocates within the DoD and throughout the federal government to support this work.

Correspondence: Aphurvikaa Manivannan Email: amanivannan@cytosorbents.com