

Nano Non-Steroidal Anti-Inflammatory Devices (_nNSAIDs) for the treatment / prevention of shock

- Designed for integration into the existing *Tactical Combat Casualty Care Guidelines* as part of the *Basic Management Plan for Tactical Field Care* (28 October 2013).
- Intended to be used as a “value added” adjuvant to complement, not replace, the use Tranexamic Acid (TXA) and Hextend for fluid resuscitation.
- Technology Readiness Level = 5

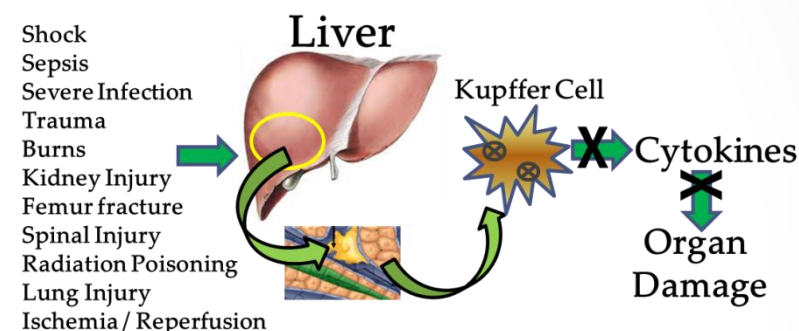
Technical Highlights






- **Decreased mortality to lethal insult: 1600% increase in animal survivability in following lethal shock stimulus**
- **Stand-alone treatment.** One time injection (0.1 – 0.5 mg/kg). Does not require antibiotics, vasopressors, fluid resuscitation or other supportive care
- **Material does not need refrigeration, likely stable over wide range of temperatures (-100 to +100 °C)** in powder or in liquid form for years.
- **No toxicity:** Long term (3 months) toxicity studies suggest that the compound is non-toxic. “Generally Considered Safe”
- **Mechanism of action: Known.** Comprehensive *in vivo* / *in vitro* testing already performed to determine mechanism of action.
- **Compound could be used to treatment:** severe trauma, hemorrhage-induced tissue damage, burns, acute kidney injury, chest trauma, femoral fracture, sepsis, spinal injury, radiation exposure, acute respiratory distress syndrome, and ischemia / reperfusion.
- **Could be used as a prophylactic to protect against subsequent insult.**
- **Manufacture:** Facile large-scale sterile manufacture in one-step synthesis process using existing technology.

Mechanism of Action

First ever nanotechnology based device for anti-inflammatory applications.

Nanoparticle treatment (⊗) targeting the liver Kupffer cells prevents cellular activation and the release of damaging cytokines



	Circulatory	↓ Systemic capillary permeability, ↓ Generalized edema																												
	Cardiac	↑ Diastolic and systolic function																												
	Pulmonary	↓ Pulmonary damage ↓ Neutrophil infiltration																												
	Renal	↑ Cystatin (GFR) ↓ BUN ↓ Creatinine ↓ AST																												
	Systemic makers	<table border="0"> <tbody> <tr> <td>↓ TNF-α</td> <td>↓ IL-6</td> </tr> <tr> <td>↓ NO</td> <td>↓ Total ROS</td> </tr> <tr> <td>↓ HMGB1</td> <td>↓ MIP-2</td> </tr> <tr> <td>↓ MDC</td> <td>↓ CGP-2</td> </tr> <tr> <td>↓ Eotaxin</td> <td>↓ VEGF-A</td> </tr> <tr> <td>↓ β-microglobulin</td> <td>↓ Myoglobin</td> </tr> <tr> <td>↓ GST-mu</td> <td>↓ GST-α</td> </tr> <tr> <td>↓ KIM-1</td> <td>↓ Osteopontin</td> </tr> <tr> <td>↓ Leptin</td> <td>↓ VEGF</td> </tr> <tr> <td>↓ Growth hormone</td> <td></td> </tr> <tr> <td>↓ Superoxide (ROS)</td> <td></td> </tr> <tr> <td>↓ iNOS/COX-2/ nitric oxide</td> <td></td> </tr> <tr> <td>↓ p38-MAPK/NF-kB → NF-kB binding to DNA</td> <td></td> </tr> <tr> <td>Anti-bacterial and anti-inflammatory</td> <td></td> </tr> </tbody> </table>	↓ TNF-α	↓ IL-6	↓ NO	↓ Total ROS	↓ HMGB1	↓ MIP-2	↓ MDC	↓ CGP-2	↓ Eotaxin	↓ VEGF-A	↓ β-microglobulin	↓ Myoglobin	↓ GST-mu	↓ GST-α	↓ KIM-1	↓ Osteopontin	↓ Leptin	↓ VEGF	↓ Growth hormone		↓ Superoxide (ROS)		↓ iNOS/COX-2/ nitric oxide		↓ p38-MAPK/NF-kB → NF-kB binding to DNA		Anti-bacterial and anti-inflammatory	
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