

NEW JERSEY INSTITUTE OF TECHNOLOGY

Chit02-Clot

Project Description

George Ulsh
Dung Le
Jennifer Moy
Maxwell McDermott

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Our product ChitO₂-Clot™ aims to stem uncontrolled blood loss on the battlefield. Nearly a quarter of the 4,596 combat deaths in Iraq and Afghanistan between 2001 and 2011 were “potentially survivable.” [1]. Uncontrolled blood loss was the leading cause of death in 90% of the potentially survivable battlefield cases [1]. That’s over a thousand sons and daughters who never came back to their families. Our product intends to reduce that number significantly. Our goal was to create a cost effective, chitosan based wound dressing material with inherent microbicidal properties and oxygen releasing capability to create a non-toxic protective barrier with greatly enhanced bacterial and fungal resistance. Our design is intended to replace existing traditional cotton gauzes and current hemostatic gauzes, used for traumatic injuries, as well as all other bandage material. Our product is used in the same fashion as these current alternatives. The appearance of our material is even similar to that of cotton substrates (Figure 1). This was done purposely to increase ease of use for the end user. ChitO₂-Clot™ is packed into a wound, it stops bleeding by rapidly swelling and forming a gelatinous clot. ChitO₂-Clot™ initiates clot formation rapidly via the common pathway [11] and the chitosan within ChitO₂-Clot™ also causes the agglutination of platelets and swells into a gelatinous matrix that form fits the wound dimensions. The current market leader’s product, Combat Gauze, only initiates clotting via the extrinsic pathway and has minimal swelling because it’s composed primarily of non-woven cotton. Because of our common pathway activation coupled with chitosan’s inherent ability to cause platelets to undergo

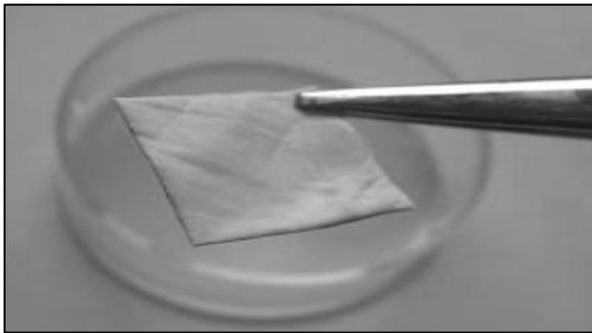


Figure 1: Electrospun chitosan nano-fiber mat

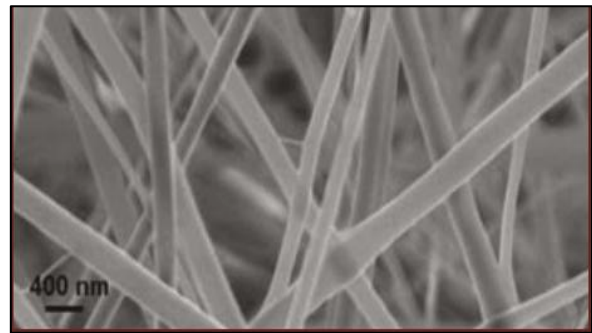


Figure 2: SEM image of Figure 1

agglutination and swell to form fit the wound, ChitO₂-Clot’s™ clot rate formation and clot strength we project will far exceed that of our competitors. These claims will be proven or disproven with animal models and eventually clinical trials. ChitO₂-Clot™ is unique in that it is the first ever oxygen releasing wound dressing. The benefits of oxygen in the wound are described in more detail below. ChitO₂-Clot™ can be removed, if needed, by medical personal. If remnants of ChitO₂-Clot™ remain in the patient there is no cause for alarm because chitosan eventually breaks down into sugars and is reabsorbed into the body, while the Perfluorocarbon (PFC) is expelled via the renal system. ChitO₂-Clot™ is literally safe enough to eat, although this is not recommended. We have electrospun chitosan to form the bulk structure of our substrate. Chitosan is naturally hemostatic, microbicidal, and bioresorbable lending itself to be a perfect wound healing material [4]. The chitosan causes increased permeability and rupture of bacterial and fungal membranes. We chose to electrospin chitosan into a micro/nano-fiber mat (Figure 2) because it allowed us to optimize surface area for platelet adhesion and in turn, clotting [5]. Our novelty comes from our incorporation of an oxygen carrier, PFC (specifically

perfluorotributylamine, PFTBA). The high surface area of the electrospun chitosan provides a large area of interface for oxygen release. PFCs readily complex with oxygen and can completely release oxygen in the presence of a concentration gradient [6]. By diffusing oxygen into the wound, our gauze will increase cell viability around the damaged tissue and increase wound closure rate [6]. Secondly we anticipate that a negative oxygen ion will elicit an immune response furthering our functionality [7]. Higher levels of oxygen at the wound site have shown a rapid increase in wound closure rate and a decrease in scar formation. The scars that form with these increased levels of oxygen are more aesthetically pleasing to the eye and still maintain optimal functionality [8]. ChitO₂-Clot™ will be competitive in the marketplace because of our common pathway activation clotting response, agglutination of platelets, increase in clot strength, and increase in tissue viability and wound closure via oxygen release, and most importantly ChitO₂-Clot's™ safety. Our main competitor Z-Medica's Combat gauze has to be surgically removed and leaves behind kaolin particles that build up in the kidneys and liver. In the short term this can cause allergic reaction, inflammation, and even neutralize certain heart medications. The long term ramifications of this are not yet known. We are currently producing ChitO₂-Clot™ in small scale batches via laboratory electrospinning for validation testing and demonstrations. Electrospinning is very time intensive and produces small amounts of material. While we are using electrospinning to produce our early prototypes, force-spinning is anticipated as the technique to produce large spools of the product for commercialization. At the moment we are stock piling large quantities of ChitO₂-Clot™ to prepare for animal testing which is currently underway. We have completed a blood clot simulation using porcine blood to demonstrate rapid clot formation and the preliminary effectiveness of ChitO₂-Clot™ as a hemostatic agent. An oxygen titration using the Winkler method was performed that showed oxygen being released. And live culture study was performed demonstrating the microbicidal effectiveness of the dressing. These test although preliminary validated our claims of being hemostatic, oxygen releasing, and microbicidal.

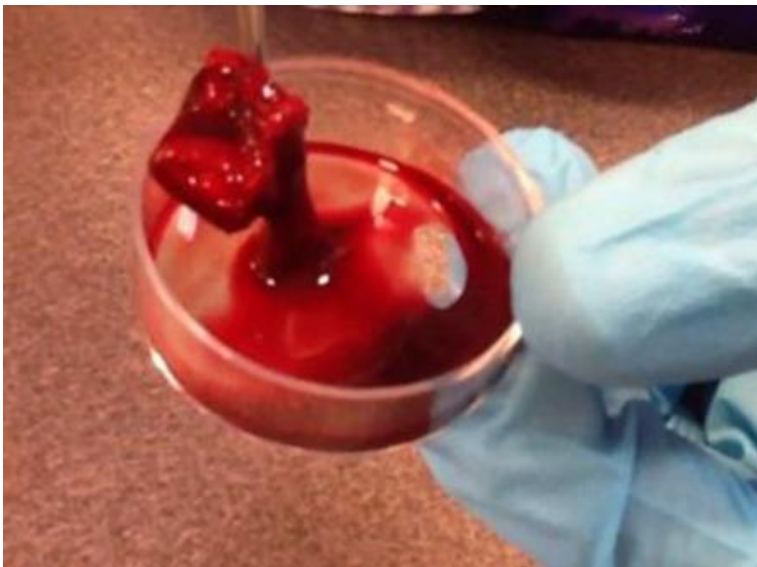


Figure 3: Blood clot simulation in-vitro



Figure 4: Oxygen titration precipitate

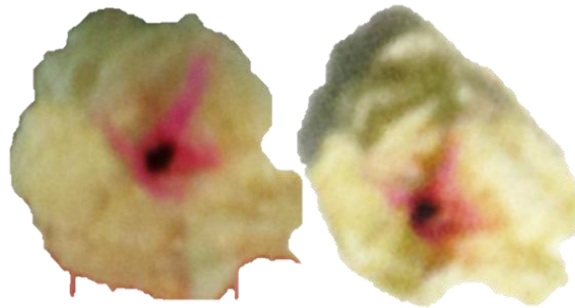


Figure 5: Live culture study over a period of 2 weeks

Both chitosan and PFTBA have separately been used extensively in other applications and are both approved by the FDA for internal and external use. Our device is a Class I device, our product falls under PART 878 -- GENERAL AND PLASTIC SURGERY DEVICES, Subpart E--Surgical Devices, Sec. 878.4450 Nonabsorbable gauze for internal use, the device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter,9. Since ChitO2-Clot is a consumable that is mainly used in a single instance, we do not expect it to be reimbursable by Medicare/Medicaid. The only situation we could see it being reimbursable by Medicare/Medicaid was if it was being used for the treatment of diabetic sores/lesions or pressure sores related obesity or prosthesis use. Anyone that bleeds can use this product. This makes our market quite expansive. In order to develop a more manageable approach, we have broken this down into three segments, because of the nature of traumatic injuries there is some overlap between segments. ChitO₂-Clot[™] usage is not just limited to traumatic injuries, it can be applied to any injury where bleeding occurs regardless of severity. Whether it is shrapnel from an IED or a scraped knee ChitO₂-Clot[™] should be used most indefinitely. The first segment (Packing Gauze Substitute) customers would include the military and subsidiaries, law enforcement both state & local, and emergency medical services. Customers also include the international version of these entities. The end users of ChitO₂-Clot for this segment will consist of soldiers, government field agents (FBI, CIA, ATF, etc.), police officers, paramedics and emergency medical technicians (EMT). EMT's ability to administer the product will be state specific. The benefit of using ChitO₂-Clot is increasing the survival rate of the end user. This is accomplished by causing rapid clotting, releasing oxygen to damaged tissue and preventing infection. Within the second segment (Orthopedic Bandage), the customers shift primarily to the health care industry and a few in the private sector. The end users in this case are patients undergoing a surgical procedure or recovering from a traumatic injury. Much like the first segment, the benefit of using ChitO₂-Clot is increasing the survival rate of the end user, but in this segment the situation of the end user is less dire. And preventing infection becomes paramount, preventing infection saves lives number one but also saves the hospital or health care facility exuberant amounts of money. The third and final market segment (Normal Bandage) customers

are you and me, the public sector. In this case the customer is normally the end user or the person administering the product to the end user. The benefit here lies in preventing infection, a rapid increase in wound closure rate and a decrease in scar formation [8]. ChitO2-Clot achieves these benefits without the use of antibiotics. Each of these markets will require a different entry and growth strategy. For the first segment we will attack two fronts. Since gaining CE approval is a much faster process than gaining FDA approval, we first obtain CE and while waiting for the FDA we will market and sell ChitO2-Clot to Germany's military and law enforcement agencies. Over time Germany has shown its willingness to adapt to new technology rapidly and also sets the standard for many other nations. Once we receive FDA approval we will turn our focus to obtaining a contract with the DOD and other military subsidiaries. If we can demonstrate our effectiveness in the US and Germany, other countries will follow suit. Law Enforcement in the US is split between state and local governments. We will target states/cities with high crime rates. For the second market there is a lack of competition, making market entry easier. We would target hospitals in areas with a high volume of traumatic injuries and number of surgeries. The normal bandage sector has a huge amount of competition, however, no current product can provide a similar level of clot formation, prevent infection, increase in wound closure, and decrease in scar tissue. These factors set us apart from the competition. So to penetrate this market will we have to sell at a cost to distributors that allow our product to be initially competitive. Licensing may be the best alternative in this market for building a customer base.

The first segment has a large market size and very few competitors, because it seems to be entirely contract based. As stated above the market consists of military, emergency services, police both state and local, and the international versions of these entities. The largest contract lies with the military and its subsidiaries. More specifically, the Department of Defense (DOD). The DOD's contract entails all branches of the armed forces and other agencies that carry firearms. The current DOD contract holder 2008 – Present is Z-Medica and their product is Combat Gauze. The previous contract holder 2004 – 2008 was Hemcon and their product was Chitogauze, the initial contract value was \$29,600,000. A deciding factor between the changes in the contract holder was that Hemcon was sued for patent infringement. The main competition in this segment is from the previously mentioned contract and former contract holders. These contracts are reviewed and challenged by other products routinely. Combat Gauze activates the clotting cascade via the extrinsic pathway by exposing kaolin to blood. Chitogauze does the opposite, by activating the clotting cascade intrinsically. Our product contains both chitosan and oxygen, and will activate the common pathway [11], which in theory should give us a much faster rate of clot formation and clot strength. Both Combat Gauze and Chitogauze use non-woven cotton backing that must be surgically removed after use, which is why both products have an x-ray detectable strip. Our product is completely reabsorbed into the body and broken down into sugar, which makes it far less invasive because surgical removal is not needed. Our product is used in the same fashion as these current alternatives. The appearance of our material is even similar to that of cotton substrates. This was done purposely to preserve the ease of use for the end user. Technically you could safely consume our dressing with no adverse effects other than the taste. The innovation of our dressing is that it also releases oxygen, which aids in healing and can sustain damaged tissue whose blood

supply has been disrupted. It also has microbicidal properties. These additional factors allow our product to far outperform the competition, while still being cost effective and a safer alternative to similar traditional products. The cost of Chitogauze is \$88.00 per dressing, and Combat Gauze is \$30.00. The raw material costs of ChitO2-Clot are \$1.50 for a dressing of the same size (25grams). A standard military dressing is 25 grams. Of course the cost of ChitO2-Clots costs will increase when including processing, manufacturing, and distribution costs but with such a low raw material cost we plan to undercut our competition or come in at a cost of \$30.00. The reason our raw material costs are so low is because our main component chitosan is derived from the shells of crustaceans like shrimp and also from fungi membranes. These shells and fungi membranes are normally discarded and seen as a waste product, hence their low cost. And our other active ingredient PFTBA is extremely cheap when purchased in bulk.

The second market segment is moderate in size; however it provides us with an opportunity to become a niche product. The target market would be the private sector, and the health care industry. However we are going to also focus on professional athletics. In boxing, and mixed martial arts bleeding occurs frequently, if one of the participants is bleeding too quickly or too much the fight will be called. These decisions carry enormous weight financially for the participant, but even more so for the gambling industry. Hundreds of millions of dollars can be lost on a few drops of blood. Our product meets the standards of the Mixed Martial Arts and World Boxing Council for use within their events. Our product is not only used for clotting, it also is able to combat and prevent methicillin-resistant staphylococcus aureus (MRSA) and other harmful bacteria. MRSA is extremely costly to hospitals and patients. MRSA causes 17,000 deaths annually [9]. It is the most common hospital acquired infection (HAI) [9]. It is very expensive to rid a facility of MRSA, because of its ability to grow on most surfaces [9]. Most reported cases also incur malpractice and wrongful death suits and because of this, many cases go unreported. A high profile case of MRSA recently arose from the sports world. Ryan Howard of the Philadelphia Phillies tore his Achilles tendon at the end of the 2011 season. His recovery was delayed by 3 months from MRSA complications which cost the Phillies organization just under 7 million dollars and a slim shot at the playoffs. There is one possible competitor that can offer similar results. The 3M Tegaderm Ag Mesh Dressing [10] provides similar results. However it is marketed solely for burn treatments and diabetic ulcers. The problem with the mesh is that it contains silver sulfides. Silver can cause damage to native tissue and builds up in the kidneys. While the sulfides carry a high risk of allergic reaction. Our product is hypoallergenic and carries no heavy or ionic metals.

The third and final market segment is the largest but also the most competitive. This market was estimated to be worth 28.3 billion dollars in revenue in 2010. The largest competitors here are Johnson & Johnson, Proctor & Gamble, and 3M. Normal bandages have been used for quite a long time without any drastic changes in design or function. Our product is radically different and because of our oxygen releasing properties, natural microbicidal properties, and rapid clot rate formation, we can provide faster wound closure with minimal scarring and prevent infection making the overall

wound healing process accelerate to levels not yet seen in industry today. With our product there is also no need for the use of antibiotics or disinfectants at the wound site.

During our design process we talked to state and local police, FBI field agents, former and currently military personnel, as well as clinicians. Their opinions and suggestions helped shape our final design. We were shocked to discover that law enforcement personnel have no hemostatic agents or anything to handle a traumatic injury on their person, and a very minimal medical kit in the trunk of their vehicle. When a police officer is injured it is almost always traumatic in nature, and if you have just been shot how are you supposed to get back to your car and then open the trunk before bleeding out? The other issue that all of the law enforcement personnel interviewed had was a lack of belt space. From this we decided that vacuum packaging is a must for this market segment as well as a Z-fold design to conserve space while maximizes the amount of material in the package. These packaging constraints were affirmed by the military and FBI personnel interviewed. The military personnel also discussed how the current military contract holder, Z-Medica is not preferred and often not used if an alternative is available, even when the alternative does not offer the same hemostatic benefits. The reason for Z-Medica's poor reputation was their first product iteration before Combat Gauze. Their first iteration Quik Clot used a mineral known as zeolite as its hemostatic agent. The problem was when zeolite is exposed to blood it causes an immense exothermic reaction which is excruciatingly painful especially after being shot or suffering a traumatic injury. Clinician opinions focused on shelf-life and when the product would be offered. The pediatricians and orthopedic surgeons interviewed were especially interested in the microbicidal properties of ChitO2-Clot because it would minimize or eliminate the need for antibiotics. The large scale impact of our innovation is to increase first responder's capabilities to save both their lives and the lives of others. Increase survival rates of those in traumatic injuries, while at the scene and in route to a medical center. Decrease the number of amputations needed. Decrease the number of families struck by tragedy.

We expect to form a for-profit or a joint venture in NJIT's Enterprise & Development Center. However, we are currently in talks with five companies about potential licensing agreements the three largest listed here: Covidien, EMD Chemicals, and Johnson & Johnson. Licensing can lessen the burden of bringing Chito2-clot to market while maximizing NJIT's return. That being said to further these agreements we must complete our animal testing in a timely manner. Our intellectual property rights are intact and backed by our university NJIT. We have a patent on our technology. While we are using electrospinning to produce our early prototypes, force spinning is anticipated as the technique to produce large spools of the product can be produced quickly. These spools then would be cut in a die on an assembly line, and then they can be sent to packaging. By using a company like M&C Specialties, Inc. we would have basically our own facility. The force spinning could be done on their premises and sent straight through the assembly line and packaging line in one seamless process. M&C Specialties, Inc. also has an expansive distribution network. The amount of capital being saved by having everything in one facility can give us a competitive edge.

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