SoftSeal®-STF
Hemostatic Pad
Technology Description

Prepared by Chitogen Inc.

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Introduction

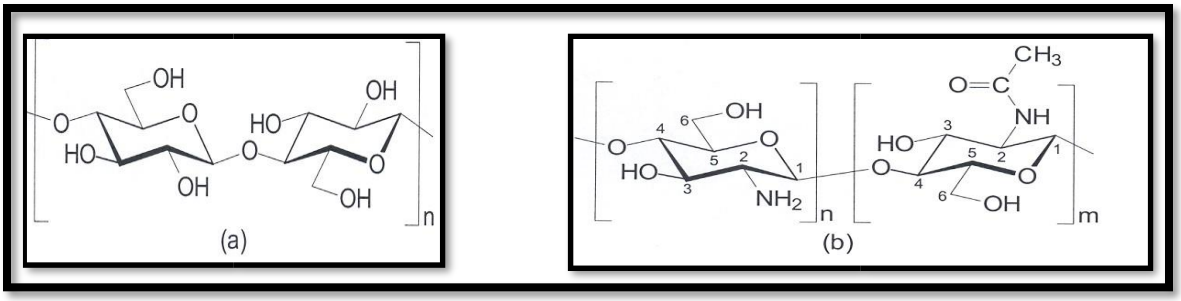
The SoftSeal®-STF Hemostatic Pad, produced by Chitogen Inc., is a nonwoven fleece pad that offers a significant improvement in hemostatic performance, ease of use, and patient comfort. Chitogen has developed the unique and proprietary chitosan structure and formulation that forms a technology platform for a family of products both on the market and under development.

SoftSeal®-STF and Chitosan

The SoftSeal-STF pad is made of a proprietary formulation of chitosan (poly-D glucosamine and poly-N-acetyl glucosamine). The natural biological properties of this material give the SoftSeal-STF an advantage as an effective hemostat while providing for an optimal wound-healing environment. The STF (Surface Treated Fiber) process further enhances the performance. The SoftSeal-STF is a non-woven pad composed of chitosan fibers attached to a thin polypropylene backing material. The pad is intended to be used as an aid in the management of topical bleeding wounds such as vascular access sites and lacerations.

Several biomedical applications of chitosan have been reported on the safety and use of these materials. Chitosan has many advantageous properties as a wound dressing, such as biocompatibility, biodegradability, hemostatic activity, and anti-infective activity. Chitosan is a positively charged polymer that forms strong associations with the negative charges found on tissue and blood components. The resulting bioadhesion is believed to be a major component in the effectiveness of chitosan as a hemostatic agent.

Chitosan is a water-soluble polymer made from chitin by chemical treatment. Chitin is an abundant natural product that is the primary structural material in the shells of crustaceans. Chitin's structural role in shells is similar to the role of cellulose in plants. Both chitin and cellulose are high molecular weight polymers containing glucose molecules linked together to form long, linear polysaccharide chains.



Chemical structures of Cellulose (left) and Chitin – Chitosan (right)

Chitin is recovered from the crab shell by treatment with acid to remove the minerals and with alkali to remove protein. After these treatments, purified chitin remains as thin, white sheets that are further processed into chitosan. Chitosan is made by heating purified chitin with strong alkali to remove acetyl groups from the polymer chains. These exposed amino groups have a positive charge in water or dilute acid. When 50% or more of the amino groups have been exposed the material becomes soluble in water or dilute acid due to the repulsion of the charged groups along the polymer chain. Thus, chitosan is defined as a derivative of chitin in which 50% or more of the amino groups are deacetylated.

SoftSeal®-STF Pads

The Chitogen FDA approved labeling for the SoftSeal-STF Hemostatic Pad does not contain an allergy warning due to the extensive chemical processes used to create the chitosan polymer. The U.S. Army endorsed the use of chitosan containing hemostatic dressings and they published results confirming that the product did not illicit an allergenic response in people who were known to be allergic to shellfish.

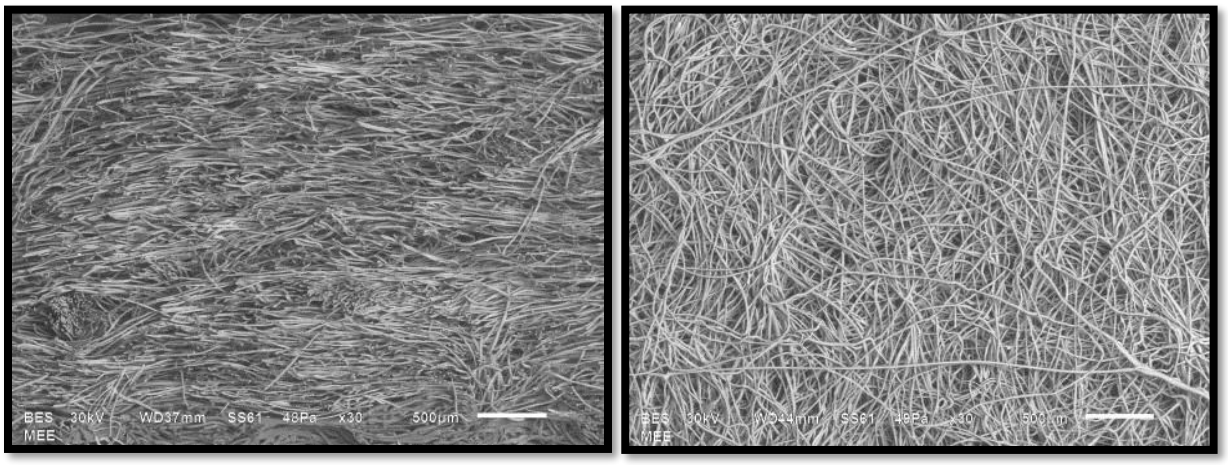
The principle of operation of SoftSeal-STF is believed to result from bioadhesion between the chitosan polymer chains (positive charge) and blood and tissue components (negative charge) as well as pressure related tamponade. The charge density and uniformity of the positive charge is enhanced by the surface treated fiber (STF) process.

SoftSeal®-STF structure

The SoftSeal-STF structure is unique. The pad is soft, pliable and easily conforms to the patient's wound site. The non-woven structure (fleece) is unlike other hemostatic pads that are lyophilized (freeze-dried), dried flake, or prepared as a gel. Freeze dried pads are brittle and less pliable when first applied and only soften when exposed to blood. The SoftSeal-STF pad is covered by world-wide patents and patent applications.

The soft, fleece-like pad consists of fine (10 to 100 micrometer) chitosan fibers spun from high molecular weight chitosan. The unique SoftSeal-STF fleece structure promotes adherence to bleeding tissues and the number of fibers increases the available chitosan surface area to promote stable clot formation. The pad retains its overall structure with a portion of the pad contacting blood changing to a gel-like structure forming a synthetic clot.

The surface treated fiber (STF) process, in addition to the nonwoven structure, enhances the hemostatic properties by creating a more uniform electric charge that is providing a more consistently charged matrix. The positively charged surface attracts negatively charged biological molecules such as red blood cells to promote adherence and clotting.



SoftSeal-STF structure using scanning electron microscopy (SEM at 30X). Discrete and small fibers can be seen on edge view (left) and top of pad (right).

Manufacturing and Quality Systems

The Chitogen supply chain is reliable and cost effective. The product is manufactured using equipment designed and owned by Chitogen. Chitogen has implemented its own quality system consistent with the Quality System Regulations of the Food & Drug Administration (FDA) and the ISO Quality System. Chitogen received its Certification of Compliance with the ISO standards in 2015.

Final packaging is done by an FDA audited and ISO certified manufacturer. The SoftSeal-STF pad is packaged in a metalized / plastic film barrier pouch, heat sealed, and terminally sterilized by Cobalt-60 gamma irradiation. The product is ready-to-use and requires no out of package preparations.

Sample of SoftSeal®-STF Clinical Studies and Evaluations

At Wheaton Memorial, a Chitogen sponsored clinical evaluation investigated the use of SoftSeal pads for femoral access. The Principal Investigator concluded that safety was enhanced with

hematoma incidence eliminated in this pilot study, at a $p < 0.05$ level. Moreover, reduced hold time was achieved, and a 6-minute protocol was found to be effective without increased bleeding. The benefit of reduced bed rest by a factor of over 200% after the procedure was also observed and this too was statistically valid, at the $p < 0.01$ level.

At the 2017 American College of Cardiology Annual Meeting, Dr. Machernis reported on a large study of 1,348 patients at St. Luke's, Milwaukee, WI. The SoftSeal group had an average hold time of less than 8 minutes versus the traditional manual compression (TMC) group that had a hold time of 20 minutes in femoral access patients. Complications were statistically equivalent for both groups.

SoftSeal-STF pads were studied on transradial cardiac access procedures in the catheter lab at Alleghany General Hospital, Pittsburgh, PA. The staff was able to move the patient to the recovery room for the hold time and more quickly begin preparing the lab for the next procedure. The average hold time was 13.3 minutes for a 6 Fr introducer and the ACT average was 223 (173 to 306). The change in procedure was enabled due to the effectiveness of the SoftSeal hemostatic pad to quickly control bleeding without vascular complications.

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