Discovery and Development of Seprafilm; a Unique Surgical Adjunct

James W. Burns, Ph.D.
Drug and Biomaterial R&D
Genzyme Corporation
Waltham, MA

Seprafilm bioabsorbable membrane was developed to reduce formation of the undesired fibrous connections between tissues that form following most surgical procedures. In 1996, Seprafilm was approved by the FDA for preventing adhesions following open general abdominal and gynecologic surgical procedures. To date Seprafilm has been used in over 2 million surgical patients world wide, and it is the only adhesion prevention product with the distinction of being FDA approved for use in more than one type of surgical procedure. The idea for a bioabsorbable membrane to prevent adhesions originated from the desire to find uses for the naturally occurring biopolymer, hyaluronic acid (HA). As a viscoelastic solution, HA was already having an enormous impact on cataract surgery where it greatly facilitated intraocular lens insertion without damaging the corneal endothelium. And there was much early work on HA's application as a synovial fluid replacement for treating pain associated with osteoarthritis. Solutions of HA were also being studied in animal models of orthopaedic surgery for preventing adhesions, which was one of our original product development interests. Our analysis of the field following review of the literature and extensive discussions with leaders from the various surgical disciplines convinced us that post-surgical adhesions were a significant clinical problem that adversely impacted patients, surgeons, the health care system, and that it was possible to develop products to reduce their formation. Our approach to developing a successful product was based on trying to understand the answers to four questions: (1) How do adhesions form? (2) What type of surgical procedures should we focus our efforts on? (3) What is the best way to prevent adhesions amongst the many possibilities? And (4) How do we prove adhesion prevention clinically?

It became quickly obvious to us that we should focus our efforts on surgical procedures in the peritoneal cavity. Most of the research on the biology of surgical wound repair and adhesion development was conducted on the peritoneum of animals, and this was the surgical area with the only reasonable chance of directly measuring adhesion development in human surgery. An understanding of the literature indicated that peritoneal adhesions start to form almost immediately after surgery, but if they hadn't formed by about 2-4 days, they would likely never form. We therefore decided to design a bioabsorbable barrier that could be applied directly to a site of surgical trauma and keep it separated from surrounding tissue for the initial few days after surgery when adhesions develop. The formulation that we ultimately developed, Seprafilm, is comprised of a 2:1 ratio of HA and carboxymethylcellulose (CMC). The HA and CMC in Seprafilm are chemically modified to impart a positive charge to a portion of the carboxyl groups. This allows an ionic interaction to occur that slows down the degradation of the resulting complex compared to their unmodified form. This material when formed into a sheet lasts in the body about 5-7 days, the ideal period for preventing peritoneal adhesions.

The safety and efficacy of Seprafilm was initially evaluated in a colo-rectal surgical procedure and in female patients undergoing myomectomy. These procedures were chosen because they provided an opportunity for the surgeon to determine whether adhesions formed at a planned second surgery. In both trials Seprafilm was found to be safe and it significantly reduced the incidence of adhesions leading to its approval by the FDA, in Europe, and Japan. Since these initial trials, Seprafilm has been evaluated in over 40 published human trials, which have consistently shown its effectiveness in preventing adhesions including reducing adhesive small bowel obstruction.

An extensive and highly accomplished team of scientists, engineers, clinical scientists, regulatory, and operations personnel are responsible for the development and success of Seprafilm. This team worked incredibly well together over an extended period of time and ultimately brought a new kind of product to surgeons that has helped millions of patients throughout the world.

References:

(Becker JM. J Am Coll Surg. 1996;183,4: 297-306)
(Diamond MP. Fertil Steril. 1996; 66,6: 904-910)
(Fazio VW. Dis Colon Rectum. 2005;49:1-1)

©2011 Society For Biomaterials