IN SITU MODIFICATION OF ALGINATE

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to a material which can be placed into intra-articular spaces to serve primarily as a space occupier for post-operative intra-articular adhesions. More specifically, it relates to a biocompatible and biodegradable material which is modified while in the intra-articular space (in situ) to prevent adhesions formed post-operatively.

2. Description of the Prior Art

Alginic acid was first purified from seaweed in 1896 (British Patent No. 11,538), and was subsequently commercialized in 1954 by Kelco (Advan. Chem. Ser. No. 11., American Chemical Society, Washington, D.C., pp. 68–82). Alginic acid, the polysaccharide extracted from the seaweed, is composed of segments of D-mannuronic acid units, L-guluronic units, and segments of alternating mannuronic and guluronic units. This polysaccharide is most commonly used to thicken solutions, stabilize suspensions and emulsions, gel various mixtures, and form films on various surfaces. Although alginic acid is water insoluble, the sodium salt of alginic acid, sodium alginate, is water soluble.

One of the most desirable properties of sodium alginate is its ability to complex and form strong gels with divalent cations such as calcium. Calcium alginate gels are water insoluble. There is a correlation between the strength of the calcium alginate gel and the guluronic acid content of the sodium alginate. Because of this characteristic, alginate has been established as a versatile biopolymer for use in various biomedical applications. Commercially available wound dressings, such as Kaltostat (BritCair Ltd.) and Sorbsan (Steriseal Ltd.), have been manufactured from fibers of calcium alginate. Extensive research is being conducted in the area of creating artificial organs by entrapping cells within calcium alginate beads and implanting them in the body. This same technology has been utilized in the drug delivery field. A good example of the use of this encapsulation technology is outlined in U.S. Pat. No. 4,744,933 by Rha in 1988. As early as 1947, George Blaine presented the idea of using calcium alginate as a method of preventing adhesions in the surgery of nerves and tendons (Blaine, The Medical Press, Aug. 20, 1947, p. 166). Subsequently, sodium alginate solution was shown to be effective in prevention of adhesions in the peritoneal cavity following laparotomy procedures (Japanese Patent SH057-167919). More recently, ester derivatives of sodium alginate have been developed and mentioned as potential anti-adhesions materials (European Patent Application 0 251 905). However, none of these patents or studies teach a simple in situ method of complexing alginate to prevent intra-articular adhesions and other intra-articular complications.

Adhesions result from the organization of fibrinous exudate on tissue surfaces due to the infliction of trauma or inflammation. Vital tissues such as blood vessels, or organs including the kidney, liver, and intestines are coated with mucous or serous membranes so that they can function independently of each other. Examples of these mucous or serous membranes are the body wall pleura and the organ pleura in the thoracic cavity and the parietal peritoneum and mesentery in the abdominal cavity, each protecting the corresponding organs. Surgical trauma or inflammation in those portions of the body coated with serous membranes may result in the build up of fibrinous exudate regardless of the size of the affected part. This ultimately causes the creation of organized fibrin many times referred to as scarring or adhesions. Such adhesions between these tissues may be observed in all tissues of the body, not just those mentioned above. Fibrinous adhesions between tissues can lead to severe pain, decreased function, and even permanent loss of motility.

In the orthopaedics field, conditions such as acute or chronic arthritis (e.g. suppurative arthritis, rheumatoid arthritis, gonorrheal arthritis, tuberculous arthritis), or traumatic injuries at the joint (e.g. fracture, sprain) would result in ankylotic diseases wherein the surface of the bones constituting the joint adhere to each other and thereby restrict the mobility of the joint. Congenital radioulnar syntosis wherein a spoke bone and an ulna adhere together is difficult to remedy by a surgical operation, since the separated bones would frequently re-adhere.

Adhesions are also prominent in tendon surgery. In this instance, there is a general tendency towards adhesion between the tendon and the surrounding sheath or other surrounding tissue during an immobilization period following the operation (P. Matthews et al, JBJS vol. 58B, no. 2, p. 230, 1976, Matthews, The Hand, vol. 11, no. 3, p. 233, 1979, Gelberman et al, Hand Clinics, vol. 1, no. 1, p. 35, 1985).

Recently, there has been a resurgence of interest in the prevention of the "laminectomy membrane" which forms following spinal laminectomy procedures. The laminectomy membrane is a well organized mass of fibrinous tissue which replaces the bone that was removed at the laminectomy. This fibrinous mass binds the dura to the overlying muscles (H. LaRocca and I. McNab, JBJS, vol. 56B, no. 3. p. 545, 1974) and causes narrowing of the spinal canal which places pressure on the cauda equina or nerve roots. This scar tissue formation may require reoperation which is tedious and dangerous, leading to the possibility of dural tears and damage to the emergent nerve roots resulting in motor weakness, sensory change and painful paresthesia.

The present invention also addresses the prevention of adhesions in the intra-articular spaces. While complications of the patello-femoral joint following total knee replacement are rare, the dysfunction of the patello-femoral articulation has been found secondary to intra-articular fibrinous bands (Thorpe et al, JBJS vol. 72A, no. 6, p. 811, 1990). Intra-articular fibrosis in anterior cruciate ligament (ACL) reconstruction has also been identified as a problem (Shelbourne et al, Am. J. Sports Med., vol. 19, no. 4, p. 332, 1991).

The prior art teaches various treatments to prevent scar tissue build up. Treatments such as liquid paraffin, camphor oil, chondroitin sulfate, and urea exhibit an insufficient effect since they function only temporarily. Other prophylactic treatments such as silicone membranes, gutta percha, or poly(tetrafluoroethylene) membranes have been used to serve as barriers to adhesion formation. However, these materials are inert and will, therefore, remain in the body and many times be recognized as a foreign body. Therefore, a second operation may be necessary to remove the barrier material.

Chitosan and xanthan gum (U.S. Pat. Nos. 5,093,319 and 4,994,277) respectively, owned by the assignee of the present invention, also teach methods of preventing adhesions with polysaccharides. Neither of these pa-