

ANTI-ADHESION FILMS AND COMPOSITIONS FOR MEDICAL USE

FIELD OF THE INVENTION

This invention relates to the field of thin films and, more particularly, relates to thin films for use in medical application, specifically in the prevention of adhesions. The anti-adhesion films of the present invention comprise at least one layer of substrate material, such as collagen, covalently bonded to a receptive tissue of a patient.

BACKGROUND OF THE INVENTION

The mechanism of adhesion formation represents a variation of the physiological healing process wherein vital tissues, usually different tissues, adhere to one another in an undesirable fashion. See, for example, Pados et al., 1992, *Current Opinion in Obstetrics and Gynecology*, 4:412-18.

For example, increased permeability of blood vessels as a result of a peritoneal injury produces a serosanguinous, proteinaceous exudate that quickly coagulates, forming a fibrinous material that first plugs the defective area, and which is further infiltrated by inflammatory cells. If this fibrinous mass is not dispersed by fibrinolysis, fibroblasts and blood vessels invade, resulting in organization and formation of adhesions.

Pelvic or abdominal adhesions, a frequent occurrence after abdominal surgery and inflammatory processes such as infections and endometriosis, represent a major cause of female infertility. Such adhesions further increase intra-operative complications, constitute a major cause of small bowel obstructions, and have been implicated in the pathogenesis of chronic pelvic pain.

Vital tissues, such as blood vessels or organs including the kidney, liver, and intestines, are coated with mucous membranes or serous membranes so that they can function independently of each other. Surgical operations or inflammation in those portions of the body coated with serous membranes could result in adhesion between these and adjacent tissues.

In the field of orthopedics, acute or chronic arthritis such as suppurative, gonorrheal, tuberculous or rheumatoid arthritis, or traumatic injuries at a joint (such as fractures or sprains) 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 synostosis, wherein the radius and ulna adhere together, is difficult to remedy by a surgical operation, as the separated bones would frequently re-adhere.

When neural spine and spinal cord are removed dorsally by a surgical operation in a vertebral canal cavity in treating myeloma, intervertebral hemia, or adhesive spinal meningitis, it is necessary to prevent adhesion to the body wall.

Suturing of ruptured tendons and tendon transfer would sometimes fail because of the post-operative adhesion of the tendon to the scar in the skin. Furthermore, in the case of rupture of a flexor tendon between a metacarpophalangeal joint and a proximophalangeal joint, the function of the finger would not recover by the intermittent suture of musculus flexor digitorum superficialis and musculus flexor digitorum profundus, as these tendons, if injured simultaneously, would adhere to one other. Therefore, is also necessary to prevent adhesion between the two tendons in this case.

In the field of thoracosurgery, bronchi dilated by primary diseases, such as pulmonary or suppurative diseases, would allow the extension of inflammation over the surrounding pulmonary parenchyma and the formation of a suppurative focus, thereby resulting in adhesion to the pleura. In addition, lung cancer would result in adhesion to the body wall.

In the field of abdosurgery, external damages, such as disjunction or rupture by a severe impact, or morbid damages such as inflammation or tumor in organs in an abdominal cavity, including liver, kidney, pancreas, spleen and intestine, would result in adhesion of organ to each other or of an organ to the abdominal wall. Rupture of the diaphragm or peritoneum caused by severe external closed damage would result in adhesion of an organ to the abdominal wall.

Further, ileus of the small or large intestine, which has the same meaning as intestinal obstruction and generally refers to an acute obstruction, would be mainly caused by adhesive ileus, wherein the intestinal cavity is closed by a crooked or flexed intestinal tract resulting from adhesion in the abdominal cavity, most of which would be formed post-operatively. Therefore, it is necessary to prevent adhesion in the abdominal cavity after the operation to prevent said adhesive ileus. Abdominal abscess could sometimes result in adhesion of peritoneum, diaphragm, or pleura to each other. In addition, adhesion between adjacent organs, or of an organ to the abdominal wall, should be prevented in the case of various diseases or tumors which cannot be removed completely in internal organs.

In the field of obstetrics and gynecology, endometritis, excessive artificial abortions, or intra-uterine curettage would sometimes result in partial or whole adhesion of the placenta to the uterine wall, making separation of the placenta at delivery difficult. Adhesion formation following infertility surgery, such as microsurgery, reconstructive tubal surgery, laparotomy and laparoscopy, remains a significant cause for failure of conception. For example, adhesions which encapsulate the ovary or the distal oviduct, or which distort the normal relationship that exists between the ovary and the oviduct, may interfere with fertility by preventing or impeding ovum pick-up. See, for example, Gomel et al., 1992, *Current Opinion in Obstetrics and Gynecology*, 4:390-99. Furthermore, cancerous tissues found in breast cancer multiply remarkably and may adhere to adjacent skin or a tendon.

In the field of brain surgery, adhesive arachnitis would be induced by chronic or suppurative intracranial inflammation (resulting from an unknown primary cause, syphilis, tuberculosis, or the like), intrathecal injection of medicine in therapy, or myelography.

In addition, adhesions resulting from facial palsy caused by a malignant tumor in the salivary gland would sometimes restrict mobility. A cancerous cervical lymph node adheres to the surrounding tissues to thereby restrict mobility.

In the field of ophthalmology, ocular surgery involving the musculature, ligaments, glands, and nerve tissue may generate post-operative adhesions.

Similarly, periodontal surgery may result in post-operative adhesions between soft and hard tissues of the mouth and throat, such as the palate, gums, teeth, and bone (such as the jawbone).

As described above, adhesion of vital tissues, large or small, may be observed in most of the surgical fields. Adhesion formation may occur for various reasons, including mechanical and chemical stimulation of vital tissues accompanying surgical operations, post-operative bacterial infection, inflammation, or complications. Additional fac-