Nano Today (2014) 9, 574—589

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/nanotoday

REVIEW

Surgical materials: Current challenges and nano-enabled solutions

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Received 18 May 2014; received in revised form 28 July 2014; accepted 1 September 2014
Available online 1 November 2014

KEYWORDS
Nano-enabled surgical materials;
Sealants;
Tissue adhesives;
Hemostatic agents;
Antibacterial bioadhesives

Abstract Surgical adhesive biomaterials have emerged as substitutes to sutures and staples in many clinical applications. Nano-enabled materials containing nanoparticles or having a distinct nanotopography have been utilized for generation of a new class of surgical materials with enhanced functionality. In this review, the state of the art in the development of conventional surgical adhesive biomaterials is critically reviewed and their shortcomings are outlined. Recent advancements in generation of nano-enabled surgical materials with their potential future applications are discussed. This review will open new avenues for the innovative development of the next generation of tissue adhesives, hemostats, and sealants with enhanced functionality for various surgical applications.

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http://dx.doi.org/10.1016/j.nantod.2014.09.006
1748-0132/

Introduction

Reconnection of injured tissues after surgery is essential to restore their structure and function. Sutures, wires, and staples are widely used for this purpose, *i.e.*, mostly to hold the tissues in close proximity for fast healing, to resist applied mechanical loads, and to stop body fluid leakages after surgery. Despite their common use in clinic, these methods are not suitable for many procedures, in particular for applications that require preventing body fluid and air leakages. In addition, complete sealing of incisions by sutures generally requires high level of training of surgeons and is particularly challenging for minimally invasive surgeries. In addition, it is challenging to accurately apply sutures and staples in the regions of body that are not easy-to-access. The incision closure procedures using sutures and staples may also induce additional damage in the surrounding tissues in the surgery site. Surgical adhesive biomaterials have emerged as attractive alternatives to stapling and suturing due to their easy application and versatility. These materials can close the incision site more quickly and effectively compared to sutures, which reduces the risk of infection and blood loss by the patient [1,2].

Biomaterials can be used for various surgical operations as tissue adhesives, sealants, and hemostats [3]. Much success has been achieved in hard- and soft-tissue adhesives with the availability of many commercially available bioadhesive systems [4]. Tissue adhesives are surgical materials which can be used to adhere two tissues together, hemostats are mainly used to control bleeding, and sealants act as a barrier to liquid or air [2]. Surgical materials should be biocompatible, easy-to-apply, biodegradable, and inexpensive. They should also possess appropriate mechanical strength and adhesion properties as well as fast curing capability [5]. Commercially available surgical materials are formed from natural or synthetic sources, or a combination of both in the form of composites [6]. Commonly used natural materials for surgical applications include fibrin [7,8], collagen [9], gelatin [10], and polysaccharides [11] and their mixtures. Cyanoacrylates [12,13], various dendrimers [14], polyurethanes (PUs) [15], and poly(ethylene glycol) (PEG) [16] are examples of synthetic surgical materials. Various composite surgical materials have been also formed by using both natural and synthetic polymers such as gelatin-resorcinol-formaldehyde (GRF) [17], albumin/PEG (Progel, Bard Inc.) [18], dextran/(2-hydroxyethyl methacrylate) [19], chitosan/polylysine [20], and PEG/dextran [21].

High cost, limited availability, pro-inflammatory potential, and immunogenicity are some of the limitations associated with naturally derived surgical materials, which limit their use in some surgical procedures. Despite having higher mechanical strength and tissue-bonding properties, synthetic and composite surgical materials have several disadvantages including cytotoxicity, chronic inflammation, low adherence to the wet tissues and, in some cases, long curing time [6].

Recently, extensive research efforts have been made to incorporate nanoscale structures and materials in the design of surgical materials to overcome the aforementioned challenges and provide the next generation of surgical adhesives. For example, it has been demonstrated that aqueous solution of nanoparticles can be used to introduce strong bonding between the tissues without the need for complex *in situ* polymerization or crosslinking reactions [22]. These particle solutions absorb on the surfaces of tissues and act as a connector between the tissues. Nanoparticle solutions can be also used as hemostatic materials to stop internal bleeding with no requirement for specific preparation or control on polymerization reactions as needed for polymer-based hemostatic agent [23]. In addition, various types of nanomaterials have been incorporated into polymer matrices to introduce new functionalities such as providing antibacterial activity. In addition, nanoparticles loaded into surgical materials can improve their adhesion strength and mechanical properties. In general, the use of nanomaterials in the design of tissue adhesive has eliminated the requirement for complex *in vivo* polymerization or crosslinking reactions and led to the development of easy-to-use tissue adhesives and hemostats with improved functionalities for clinical applications. Nanomaterial-incorporated tissue adhesives can address many limitations of currently available tissue adhesives such as toxicity, extensive swelling, insufficient strength, and complex polymerization process. They have the potential to be used instead of sutures and staples in clinical practice, particularly in invasive surgeries to minimize tissue damage.

More recently, an active area of research has focused on developing surgical tissue adhesive with specific nanotopography to engineer biomimetic structures inspired by nature. Nanotopography is deemed as the specific spatiotemporal coordination and distribution of molecular structures that provides detailed and desirable structures. The employed nanotopography can enhance the adhesion force through the augmentation of contact area and the adhesive van der Waals and capillary forces. Moreover, these nanopatterns can be used for creating mechanical interlocking to increase the required detachment forces [24].

In this work, conventional surgical materials made of natural and synthetic polymers are critically reviewed along with their advantages and limitations for surgical applications. Recent developments in synthesis and characterization of nanomaterial incorporated surgical materials with hemostatic and antibacterial properties are discussed. In addition, emerging technologies for generating micro- and nanoscale topography in tissue adhesives to improve their adhesion strength are highlighted.

Conventional surgical materials

Wound closure is a key step in the success of various surgical procedures. Each procedure carries specific risk factors, which should be addressed by utilization of functional bioadhesive that meet these criteria. For example, during vascular anastomosis preoperative bleeding from the surgery site and blood coagulation are among the key risk factors [25]. Thus, the employed tissue adhesives should be hemostatic, while possess sufficient mechanical properties to hold the tissue together. Ease of application and the minimal need for utilization of external devices during the crosslinking process are also important for closing internal surgery lacerations during operation. However, for treating traumatic injuries, the wound closure procedure