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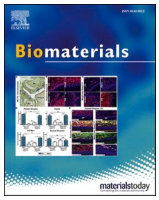

Peptide/glycyrrhizic acid supramolecular polymer: An emerging medical adhesive for dural sealing and repairing

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ABSTRACT

Medical adhesives have emerged as potential materials for sealing, hemostasis and wound repairing in modern clinical surgery. However, most of existing medical adhesives are still far away from the clinical requirements for simultaneously meeting desirable tissue adhesion, safety, biodegradability, anti-swelling property, and convenient operability. Here, we present an entirely new kind of peptide-based underwater adhesives, which are constructed via cross-linked supramolecular copolymerization between cationic short peptides and glycyrrhizic acid (GA) in an aqueous solution. We revealed the unique molecular mechanism of the peptide/GA supramolecular polymers and underlined the importance of arginine residues in the enhancement of the bulk cohesion of the peptide/GA adhesive. We thus concluded a design guideline that the peptide sequence has to be encoded with multiple arginine termini and hydrophobic residues. The resulting adhesives exhibited effective tissue adhesion, robust cohesion, low cell cytotoxicity, acceptable hemocompatibility, inappreciable inflammation response, appropriate biodegradability, and excellent anti-swelling property. More attractively, the dried peptide/GA powder was able to rapidly self-gel into adhesives by absorbing water, suggesting conveniently clinical operability. Animal experiments showed that the peptide/GA supramolecular polymers could be utilized as reliable medical adhesives for dural sealing and repairing.

1. Introduction

Medical adhesives commanded the focus of clinicians, materials scientists and chemists because these artificial materials have the ability to offer reliably mechanical support for preventing the leakage of the body fluids and accelerating the wound healing [1–4]. Furthermore, the use of the medical adhesives can reduce the additional trauma, and minimize patient pain [5,6]. For the dural defect occurred in neurosurgery (spinal surgery complication, traumas or the removal of intradural tumors), the medical adhesives are especially desired for inhibiting the leakage of cerebrospinal fluid and avoiding the emergency of the low intracranial pressure headache, neuroinflammation, meningitis, and other related complications [7–9]. However, most of the existing polymer adhesives or protein adhesives [10–14] are still far away from the clinical requirements due to the following fact. Semi-synthetic polymer adhesives derived from alginate, gelatin, chitosan, and poly (ethylene glycol) are biocompatible, but the adhesion formation on the wet surface of the tissues is a slow process under wet conditions [15–19]. Synthetic polymer adhesives can achieve fast adhesion but their biocompatibility and biodegradability are poor [20,21]. Additionally, inflammatory responses, poor anti-swelling behavior, and time-consuming preparation are unsolved problems [20,21]. Recombinant protein adhesives rarely cause apparent fibrosis, inflammation, or necrosis [22–24]. However, the synthesis of the recombinant proteins often involves some limitations, such as long synthetic term, complicated purifying process, low yield, and poor cost-efficiency [25,26]. Fibrin containing fibrinogen and thrombin from the animal blood plasma is a commercially available adhesives, but it shows weak binding capability to tissues, complicated clinical operability, and carries a risk of infectious transmission from the blood plasma donor [18,19]. Thus, it is indeed a formidable challenge in the exploration of new medical adhesives simultaneously combining the excellent tissue adhesion, safety,

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