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Biocompatible Self-Healing Hydrogel for Nephron-Sparing Surgery Applications

Ahmed Patel*

Division of Nephrology, King's College London, London, UK

Corresponding author: Ahmed Patel, Division of Nephrology, King's College London, London, UK, E-mail: Patel_A@gmail.com

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Description

Renal Cell Carcinoma (RCC) is a prevalent type of tumor affecting the urinary system globally, with increasing incidence and mortality rates each year. Advances in preoperative assessments and surgical techniques have made nephron-sparing surgery the primary approach for treating clinical T1a patients. However, ischemia/reperfusion injury during temporary blood flow blockage (known as warm ischemia) hinders the preservation of postoperative renal function in RCC patients. Surgeons aim to minimize Warm Ischemia Time (WIT) through techniques like non-clamping partial nephrectomy or intraoperative renal hypothermia, but these are typically available only in advanced medical centers with skilled surgeons and modern equipment. Therefore, the development of hemostatic materials that can stabilize blood clotting and reduce WIT could simplify the surgical process and enhance RCC outcomes. Although Polyethylene Glycol (PEG)-based hydrogels were once used in nephron-sparing surgery, they were found to promote tissue adhesion, exhibit poor adherence to wet tumor beds and lack tissue repair properties. Biomaterials meeting hemostatic requirements for open or laparoscopic nephron-sparing surgery are rarely reported. In nephron-sparing surgery, kidney defect healing typically involves hemostasis, precise closure of the collecting system and covering the wound with fat tissue or peritoneum. This sequence demands a stable surgical environment, crucial for postoperative recovery assessment. The sutured wound is often intentionally covered by perinephric tissues to promote adhesion, preventing urine/blood leakage and accelerating wound healing. However, adhesion can lead to secondary intra-abdominal tissue adhesion. Rapid wound repair may shorten peritoneal drainage time and reduce complications such as abdominal drain-related infections. Therefore, there is a pressing need to develop hemostatic biomaterials with improved wound healing properties for effective management of nephron-sparing surgery.

Hemostasis maintenance

Moreover, patients undergoing open surgery due to complex tumor location or anatomy face potential complications from adhesions between viscera and peritoneum, including chronic abdominal pain, intestinal obstruction and female infertility [1-4]. Adhesiolysis remains the primary strategy for removing postoperative tissue adhesions, despite its tendency to recur. Current research on materials to prevent postoperative tissue adhesion emphasizes reducing inflammatory cell infiltration, fibrin dissolution and obstructing organ interactions to minimize or delay adhesion occurrence [5]. However, challenges persist, such as susceptibility to oxidation, short retention time, weak mechanical properties and re-adhesion. Developing biomaterials for nephron-sparing surgery that promote hemostasis maintenance and wound management while addressing postoperative adhesion prevention is crucial, yet research in this area remains limited. Commercially available hemostatic agents like tissue adhesives, hemostatic cryogels, zeolite-based quick clot, fibrin bandages and gelatin sponges have been explored, but they struggle to meet the needs of wound healing and anti-adhesion after nephron-sparing surgery [6]. Hydrogels, used as dressings, can quickly crosslink with tissue around the wound site through *in situ* gelation, sealing leaks for rapid hemostasis (Scheme 1d1–d2) and creating a suitable microenvironment for promoting rapid wound healing (Scheme 1d3).

Mechanical properties

This study developed a series of versatile and biocompatible hydrogels using free-radical polymerization of the monomers acryloyl-6-Aminocaproic Acid (AA) and N-Acryloyl 2-Glycine (NAG), along with ionic coordination involving Ca^{2+} and the abundant carboxyl groups. The resulting AA/NAG/Ca hydrogels exhibit well-integrated mechanical properties, self-healing capabilities, adhesion and hemostatic effects. They function effectively as hemostats, sealants and barriers to achieve hemostasis, manage postoperative wounds and prevent postoperative tissue adhesions [7-10]. The rheological, mechanical and adhesive properties of AA/NAG/Ca hydrogels were comprehensively analyzed. Additionally, there *in vitro* blood clotting ability and biocompatibility were assessed. The study then demonstrated the hydrogels' hemostatic ability *in vivo* using various liver injury models, as well as in rat and rabbit nephron-sparing surgery models. Furthermore, the wound-healing properties of the AA/NAG/Ca hydrogel were evaluated in a rat nephron-sparing surgery model and its anti-adhesion efficacy was tested in a rat abdomen–caecum model. In conclusion, these adhesive hydrogels exhibit promising clinical potential for achieving hemostasis, managing postoperative wounds and preventing postoperative tissue adhesions in nephron-sparing surgery.

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