

Biodegradable Medical SuperGlue of α -Lipoic Acid for Soft Tissue Repair

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Statement of Purpose: New materials advances enable the application of adhesives in many fields. The development of wet adhesives greatly influences the medical field, as virtually all clinical adhesion and sealing procedures are performed on wet tissues. Medical-grade superglues (cyanoacrylates) have been widely used for external wound closure due to their rapid cure, high strength, and good infection barrier properties.^{1,2} While cyanoacrylate superglues are approved and widely used for external wound closure, they have not been approved by the FDA for many internal uses due to high cytotoxicity and the inability to degrade.³ Whereas a number of hydrogel-based medical adhesives, such as fibrin glue, albumin glue and PEG-based glues, are approved for internal procedures; however, this category of adhesives suffers from poor mechanical strength- often an order of magnitude or more weaker than superglues.⁴ As a consequence of the limitations described above, there is an enormous gap between superglues and hydrogel-based internal adhesives. A novel medical adhesive that has the features of a superglue (rapid curing, high mechanical strength, barrier properties) combined with high biocompatibility and degradability, is highly desirable.

Methods & Results: The R-isomer of α -lipoic acid (α LA) is an essential cofactor for aerobic metabolism in animals; however, a racemic mixture of α LA is considered safe and has been widely used as a nutritional supplement. However, practical utilization of polymer of α LA was obstructed over decades due to spontaneous depolymerization.^{5,6} Recently, we developed versatile underwater polymerization methods for α LA that inhibits depolymerization through chain end stabilization with activated esters of α LA or other carbonyl electrophiles.^{7,8} These methods allows ultrafast polymerization in contact with wet surfaces, thus mimicking the feature of cyanoacrylate superglues. The versatility of the chemical stabilization strategy enabled the development of adhesives that can be tailored for a variety of medical or nonmedical uses and recycled in a closed-loop manner. The developed method's high modularity allows the application of the adhesive as a spray, powder, or patch. The adhesive shows instant and robust adhesion to metallic, polymeric, and wet tissue surfaces. In vitro studies confirmed the excellent biocompatibility and high bacteria barrier properties, a unique feature of topical medical adhesives. Moreover, the developed surgical superglue successfully sealed murine amniotic sac ruptures, increasing fetal survival from 0% to 100% in a critical-size defect.

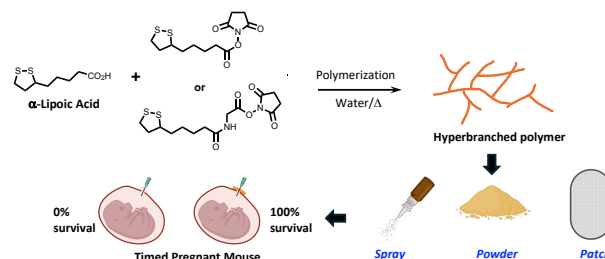


Figure 1. Overview of α -Lipoic Acid Superglue Platform

Conclusions: We have developed ultrafast polymerization protocols for α LA, enabling instant polymerization in contact with water or wet tissue surfaces. The method exploits the stabilization of poly(α -lipoic acid) by the NHS ester of α -lipoic acid, enabling the use of the adhesive in multiple form factors. The adhesive exhibits many of the features of superglue, i.e. superfast polymerization, high adhesion strength to tissue, high bacterial fouling, and barrier property. Besides, the adhesive is biocompatible and biodegradable, thereby unlocking the possibility of both internal and topical applications.

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