Tissue photo-bonding using biopolymer crosslinked with rose bengal

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INTRODUCTION: Visible light-activated photo-bonding of tissues presents an attractive alternative to surgical suturing for closing of dermal wounds. The advantages of photo-bonding include reduced inflammation and less scarring. However, the materials currently used for light-activated wound closure allow for only a limited, if any, ability to modulate the biological and mechanical properties of the resulting bonded tissue. Particularly, the micrometric void within dermal wounds presents another obstacle for the photo-bonding materials, since collagen structures are required for the photobonding to occur. Therefore, developing a light-activated biomaterial glue that can overcome these limitations would represent an important advance in translational potential. To this end, we have developed a new generation of photo-bonding materials based on vinyl-modified collagen and rose Bengal that are crosslinkable using visible light.

METHODS: Different formulations of hydrogels were prepared from vinyl-modified collagen mixed with positively charged amino acids, and rose Bengal, which is used as a photoinitiator, so that the gel can be cross-linked by green light illumination. Different conditions of illumination were used to produce scaffolds with varying physical and biological properties.

RESULTS: The optimal illumination parameters were determined by measuring the bleaching of the photoinitiators with increasing illumination time and subsequent differential scanning calorimetry experiments to determine denaturation temperature. Gels containing rose Bengal bleach most significantly within 5 min, after which the denaturation temperature of the gels was ≤ 40°C, while 10 min of irradiation produced materials with denaturation temperatures of about 48°C. The swelling properties of the gels were examined in saline solution at 37°C. The gels exhibited weight loss associated with water displacement from the matrix, which was partially rescued by amine containing amino acids. Finally, we demonstrated successful photo-bonding properties of the photo-crosslinkable hydrogel; it was able to bond a biopolymer as well as samples of mouse skin *ex vivo*. Different compositions of the hydrogel resulted in different mechanical properties of the photo-bonded system (Table 1).

Table 1. Mechanical properties of a biopolymer and mouse skin photo-bonded using different variations of the light-activated hydrogel. MC – modified collagen, RB – rose Bengal.

Hydrogel composition	Modulus (MPa)	Breaking strain (%)
Biopolymer (control)	**2.4**	**6.1**
MC+RB	1.6	5.8
MC+RB+Arg	1.4	5.4
MC+RB+0.025% Lys	0.3	8.9
MC+RB+0.05% Lys	0.2	4.4
Skin (control)	**0.6**	**35.2**
MC+RB	0.1	17.2

DISCUSSION & CONCLUSIONS: Using the visible light-excited photoinitiator rose Bengal, we produced vinyl-modified collagen scaffolds with tunable properties. Scaffolds illuminated for 10 min are stably crosslinked within the physiological temperature range. Gels exhibit weight loss associated with water expulsion, which was partially prevented by adding positively charged amino acids. The hydrogel was capable of bonding a biopolymer and mouse skin tissue *ex vivo*, but further *in vivo* experiments are needed to characterize its suitability for use in dermal wound closure. In summary, this new photo-crosslinkable hydrogel presents attractive properties for future clinical translation in tissue photo-bonding.

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