

lations were rated on a scale of 0 to 3, with a rating of 3 indicating that the formulation was very tacky or had very good form, and a rating of 0 indicating that the formulation had poor tackiness or form.

TABLE 5

Characterization of Collagen-based Bioadhesive Formulations						
Formulation	Temp. (°C.)	pH	Collagen Conc. (mg/ml)	DSG-PEG Conc. (% wt)	Adhesion	Form
DC/DSG-PEG	>40	7	100-150	1	2	2
DC/DSG-PEG	>40	7	100-150	0.1	2	2
MC/DSG-PEG	20	7	60	1	1	1
MC/DSG-PEG	20	7	60	0.1	2	2
MC/DSG-PEG	>40	7	60	1	1	1
MC/DSG-PEG	>40	7	60	0.1	2	3
SC/DSG-PEG	20	7	50	1	3	3
GC/DSG-PEG	20	7	65	1	3	3
GC/DSG-PEG	20	7	65	0.1	3	3
GC/DSG-PEG	20	7	35	1	3	3
GC/DSG-PEG	20	7	35	0.1	3	3

DC = Denatured collagen (i.e., gelatin)

MC = Methylated collagen

SC = Sucrose/collagen

GC = Glycerol/collagen

All of the sucrose/collagen/DSG-PEG and glycerol/collagen/DSG-PEG formulations demonstrated excellent adhesion characteristics and handling properties. The methylated collagen/DSG-PEG formulations did not show quite as good adhesion and handling characteristics, indicating that the ratios of DSG-PEG to methylated collagen used in this experiment were not optimal.

Example 9

(In vivo Evaluation of Solutions of Difunctionally Activated SE-PEG as Bioadhesives on De-epithelialized Rabbit Corneas)

Preformed lenticules were prepared according to the following procedure: Methylated collagen (53 mg/ml collagen concentration) was mixed with 40 mg of difunctionally activated SG-PEG (DSG-PEG, 3800 MW, obtained from Shearwater Polymers, Huntsville, Ala.) and formed into a curved film having a thickness of approximately 250 μ m. Circular lenticules having a diameter of 7-8 mm were cut out of the film. The lenticules were placed in solutions comprising 80 mg DSG-PEG in 2 ml PBS or 2 ml of 0.2% glutaraldehyde and allowed to incubate overnight.

The corneas of several male New Zealand white rabbits were de-epithelialized using a gill knife. A solution comprising 40 mg of difunctionally activated SE-PEG (DSE-PEG, 3800 MW, obtained from Shearwater Polymers, Huntsville, Ala.) in 200 μ l of PBS was applied to the concave portion of the de-epithelialized rabbit corneas. Within 2 minutes, the excess DSE-PEG solution was aspirated out using a pipettor. Preformed collagen lenticules (prepared as described above) were then immediately applied to the surface of the de-epithelialized corneas.

The preformed lenticules were found to adhere well to the de-epithelialized corneal tissue with the DSE-PEG "adhesive". The lenticules could easily be removed by gentle manipulation with a gill knife.

Example 10

(In vivo Evaluation of Solutions of Difunctionally Activated SE-PEG as Bioadhesives on De-epithelialized Rabbit Corneas)

The corneas of several male New Zealand white rabbits were de-epithelialized using a gill knife. Solutions compris-

ing 40, 53, or 66 mg of difunctionally activated SE-PEG (DSE-PEG, 3800 MW, obtained from Shearwater Polymers, Huntsville, Ala.) in 200 μ l of PBS were applied to the concave portion of the de-epithelialized rabbit corneas. Within 2 minutes, the excess DSE-PEG solution was aspirated out using a pipettor. Preformed collagen lenticules (obtained from Imedex, Lyon, France) were then immediately applied to the surface of the de-epithelialized corneas.

The preformed lenticules were found to adhere well to the de-epithelialized corneal tissue with the DSE-PEG "adhesive". The lenticules could easily be removed by gentle manipulation with a gill knife.

After 7 days, the lenticule that had been adhered to a rabbit cornea using the 53 mg/ml DSE-PEG solution was observed. The central portion of this particular lenticule was found to have good adhesion to the cornea; however, the edges of the lenticule were not tightly adhered to the cornea. The central portion of the cornea was observed to be slightly opaque. It is believed that there may have been protein deposition between the lenticule and the cornea and that the DSE-PEG covalently bound to the deposited protein and held it in place on the surface of the cornea, resulting in the observed opacity of the central portion of the eye.

Example 11

(In vivo Evaluation of a Solution of Difunctionally Activated SE-PEG as a Bioadhesive on a De-epithelialized Primate Cornea)

The cornea of a macaque monkey (*Macaca cynomologous*) was de-epithelialized using a gill knife. A solution comprising 40 mg of difunctionally activated SE-PEG (DSE-PEG, 3800 MW, obtained from Shearwater Polymers, Huntsville, Ala.) in PBS was applied to the concave portion of the de-epithelialized macaque cornea. Within 2 minutes, the excess DSE-PEG solution was aspirated out using a pipettor. A preformed collagen lenticule (obtained from Imedex, Lyon, France) was then immediately applied to the surface of the de-epithelialized corneal tissue.

After 3 weeks, the lenticule was found to be firmly attached to the cornea of the monkey. No corneal opacity was observed. Minimal inflammation was observed during the first week following the procedure. The inflammation, however, had subsided by week 2.

The present invention is shown and described herein at what is considered to be the most practical, and preferred embodiments. It is recognized, however, that departures may be made therefrom which are within the scope of the invention and that obvious modifications will occur to one skilled in the art upon reading this disclosure.

What is claimed is:

1. A method for effecting the nonsurgical attachment of a first surface to a second surface, comprising the steps of:
 - providing collagen and a multifunctionally activated synthetic hydrophilic polymer;
 - mixing the collagen and synthetic polymer to initiate crosslinking between the collagen and the synthetic polymer;
 - applying the mixture of collagen and synthetic polymer to a first surface before substantial crosslinking has occurred between the collagen and the synthetic polymer; and
 - contacting the first surface with a second surface to effect adhesion between the first surface and the second surface.