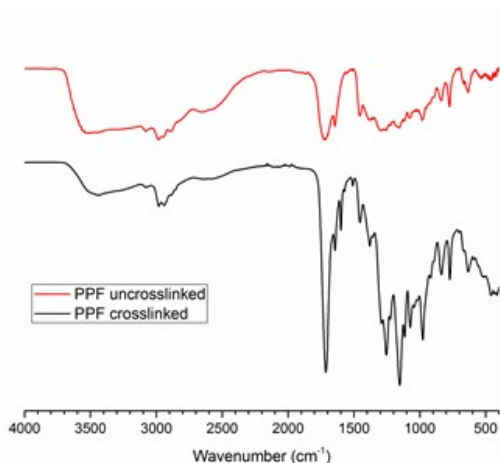


Supplementary

S1. Polypropylene fumarate (PPF): Synthesis and Characterization

Poly(propylene fumarate) (PPF) is a biocompatible, biodegradable, linear polymer which has unsaturated double bonds along its main chain. These double bonds can be crosslinked to form three dimensional network structure. In this study, PPF was synthesized from fumaric acid and propylene glycol (1.5:1.65 moles) in a round bottom flask equipped with stirrer and heater. Hydroquinone was the radical inhibitor and p-toluene sulfonic acid was the catalyst in the reaction that was performed under nitrogen atmosphere at 145°C. The obtained polymer was dissolved in dichloromethane (DCM) and purified by washing with methanol:water (20:80) solution. Molecular weight of the PPF was determined with gel permeation chromatography (GPC) (CTO-10ASVP, Shimadzu, Japan). The chemical structure of the uncrosslinked and crosslinked PPF was analyzed with Fourier Transform Infrared Spectroscopy (FTIR) (Frontier, Perkin Elmer, USA).

The number average molecular weight (M_n), weight average molecular weight (M_w) and PDI value of PPF were found as 1816 g/mol, 2704 g/mol and 1.48, respectively by gel permeation chromatography. Infrared spectra of uncrosslinked and crosslinked PPF are shown in Figure.



The characteristic peak at 1730 cm⁻¹ and 1646 cm⁻¹ corresponded to the ester carbonyl group and unsaturated double bonds in fumarate unit, respectively. Peaks at 1455 cm⁻¹ and 1375 cm⁻¹ correspond to methyl stretching, and the peak at 1296 cm⁻¹ corresponds to the secondary alcohol. These are in a good agreement with literature.^[61]

PPF can be crosslinked with free radical polymerization in the presence of monomers of methyl

methacrylate or N-vinyl pyrrolidinone (NVP) or with photoinitiation process. In the presence of a photoinitiators it is possible to crosslink its fumarate groups using a UV light. Photo crosslinking was preferred in this study since it was a faster method. The FTIR spectra of crosslinked PPF was similar to uncrosslinked one. The absorption peak for -CH=CH- at 1646 cm^{-1} still can be observed for crosslinked PPF proving not all the unsaturated double bonds were used up during crosslinking reaction.

S2. Scores of *in vivo* biocompatibility tests.

a. Irritation scores of PCL, PCL/HAp and PCL/HAp/PPF scaffolds.

Sample	Test Site	Score
PCL (polar)	left anterior site	0
PCL (non-polar)	right anterior site	0.13
Polar solvent control	left posterior site	0
Non-polar solvent control	right posterior site	0
PCL/HAp (polar)	left anterior site	0
PCL/HAp (non-polar)	right anterior site	0.11
Polar solvent control	left posterior site	0
Non-polar solvent control	right posterior site	0
PCL/HAp/PPF (polar)	left anterior site	0
PCL/HAp/PPF (non-polar)	right anterior site	0.20
Polar solvent control	left posterior site	0
Non-polar solvent control	right posterior site	0

Mean severity score based on the following: 0=no erythema/edema, 1=very little erythema/edema (noticed barely), 2=distinguishable erythema/edema, 3=moderate erythema/edema, 4=severe erythema/edema.

b. Implantation scores of PCL, PCL/HAp and PCL/HAp/PPF scaffolds.

Sample	PCL			PCL/HAp			PCL/HAp/PPF											
	Test Sample	Control	Control	Test Sample	Control	Control	Test Sample	Control	Control									
Inflammation	0	0	0	0	0	0	0	0	0	0	0	0						
Polymorphonuclear cells	1	1	1	0	0	1	0	0	0	0	0	0						
Lymphocytes	0	0	0	0	0	0	1	1	1	0	0	1						
Plasma cells	0	0	0	0	0	0	0	0	0	0	0	0						
Macrophages	0	0	0	0	0	0	0	0	0	0	0	0						
Giant cells	0	0	0	0	0	0	0	0	0	0	0	0						
Necrosis	0	0	0	0	0	0	0	0	0	0	0	0						
Sub-Total (x2)	1	1	1	0	0	1	1	1	1	0	1	1						
New angiogenesis	0	1	0	0	0	0	1	0	0	0	0	0						
Fibrosis	1	1	1	0	1	1	1	1	1	0	1	1						
Fatty infiltration	0	0	0	0	0	0	0	0	0	0	0	0						
Sub-Total	1	2	1	0	1	1	2	1	1	0	1	1						
TOTAL	2	3	2	0	1	2	3	2	2	0	1	1						
GROUP TOTAL	2.33			1.00			2.33			0.67			1.67			1.00		

Mean severity score based on the following: 0-2.9=not irritant, 3.0-8.9= low irritant, 9.0-15.0=moderately irritant, >15.0 very irritant.