Supplementary Information

ECM-oligourethane-silica hydrogels as local drug release system of dexamethasone for stimulating macrophages

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1. Scheme of the loading of dexamethasone in the biocomposite hydrogels

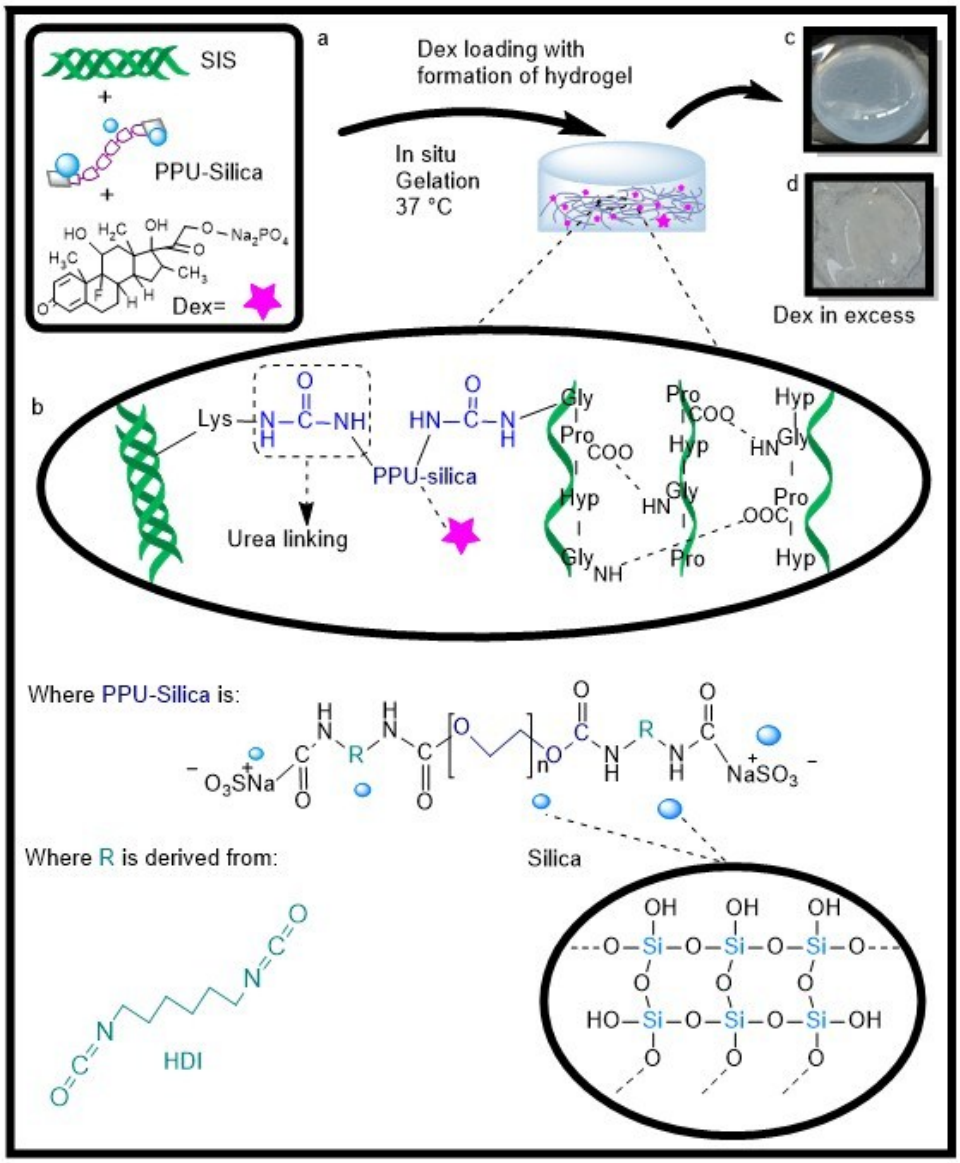

Figure S1. (a) Schematic description of the simultaneous process of Dex-loading and formation of composite hydrogels. (b) Outline of the collagen crosslinking by urea linkages produced by oligourethanes. Representative images of the composite hydrogels loaded with 400 (c) or 500 (d) μg of Dex per each hydrogel.

2. SEM and TEM images

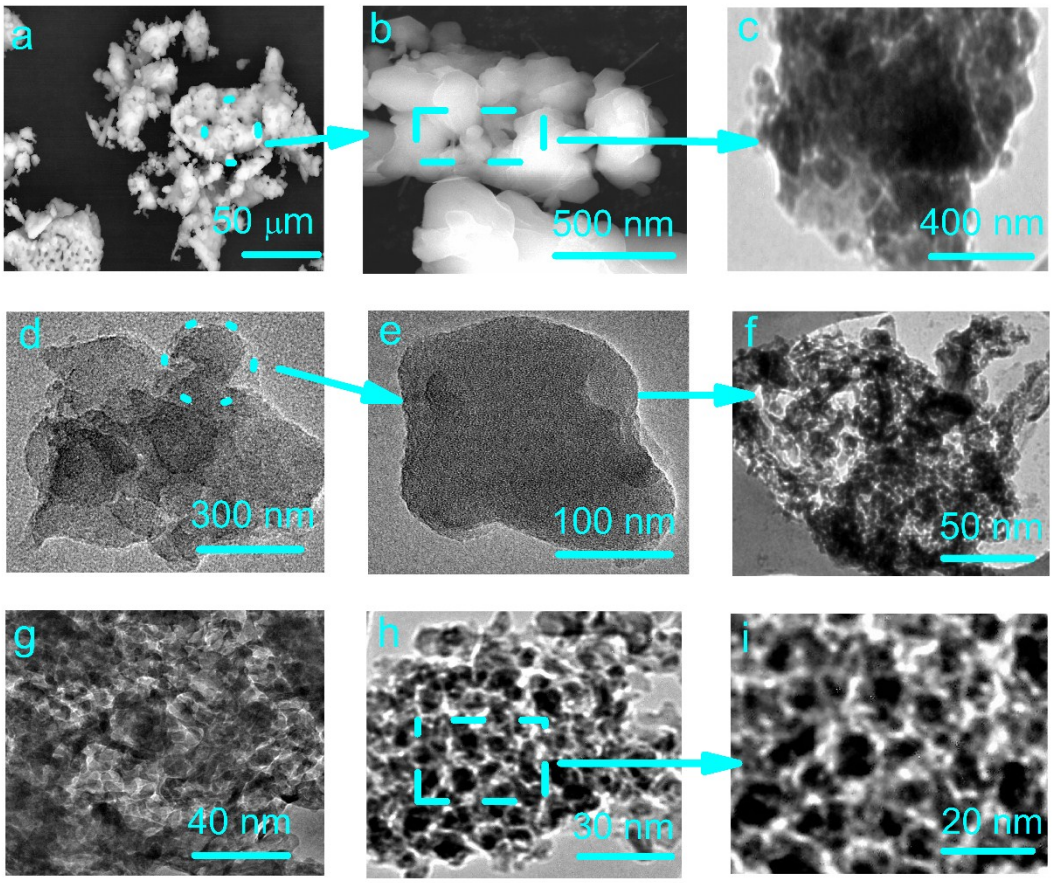

Figure S2. SEM micrographs showing the silica particles deposited on composite hydrogels (Fig. a-b). The collagen fibers are covered by silica particles with irregular morphology. TEM micrographs indicating the ultrastructure, size and porosity of SiP dispersed in the biocomposites (figure c-i). All SiP are semispherical and they form agglomerates and they have similar particle sizes of around 86-98 nm. The mesoporous structure of the particles can be clearly observed from the TEM images and pore sizes were found to be around 5-19 nm.

3. Quantification of the dexamethasone release

The determination of Dex released from composite hydrogels was carried out spectrophotometrically, measuring the abs values corresponding to Dex in PBS at 297 nm, as shown in figure S2a. Changes to Abs or released amount over time are shown in figures S2b and S2c, respectively. The data were translated to cumulative release using the equation S1:

$$Q = \sum_{t=0}^{t} \frac{M_t}{M_0} \qquad (S1)$$

Where Q is the cumulative release in percentage, Mt is the cumulative amount released at each sampling time and M0 is the initial mass of Dex loaded in the sample. The figure S3d shows the cumulative Dex release with respect to time.

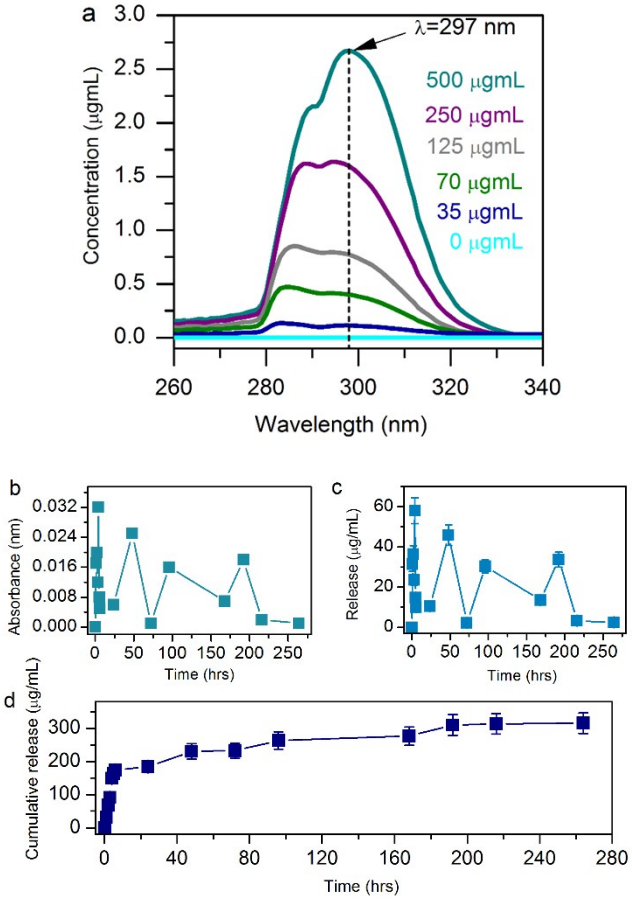

Figure S3. Methodology for the determination of the Dex release. Calibration curve of dexamethasone (a). Dexamethasone release profiles from SIS P15 indicating: Absorbance vs time (b) Dex Release vs time (c) and Cumulative Dex release vs time (d).

4. Macrophages cultured with material-conditioned medium

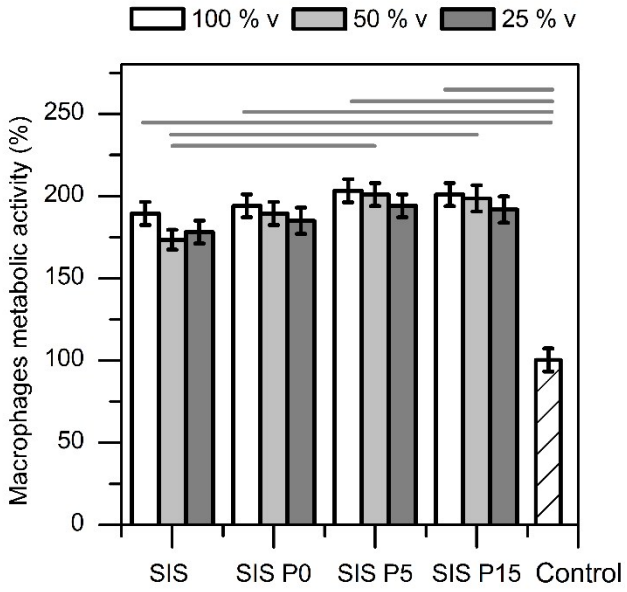

Figure S4. The metabolic activity of macrophages was checked in media conditioned with biocomposite hydrogels, either concentrated (100%) or diluted to 50 or 25% with fresh culture medium. The number of viable macrophages cultured on standard polystyrene wells (without materials, as control) for 1 day was $23.5 \pm 5.7 \times 10^4$. Data are expressed as mean values ± SD, n=3. The difference of the means is significant ($p<0.05$) between all marked groups002E