Supplementary Information

Combining Dietary Phenolic Antioxidants with Polyvinylpyrrolidone: Transparent Biopolymer Films based on *p*-Coumaric Acid for Controlled Release

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Transparency analysis

To determine the transparency of the films, UV-VIS spectra were recorded in the range from 400 to 800 nm. As representative examples, the UV-VIS spectra of PVP/PCA 1:0, 2:1, 5:1, and 10:1 are shown in Figure S1A. Minimum values of absorbance were observed for PVP/PCA 1:0 in the analyzed range, while the samples containing PCA exhibited higher values. From these spectra, transparency was calculated according to the ASTM 1746 by normalizing the values for 50 µm thickness[1], Figure S1B. In general, transparency values were high, typical of transparent materials, and ranged from ~72% for PVP/PCA 2:1 to ~82% for PVP/PCA 10:1 and 7.5:1.

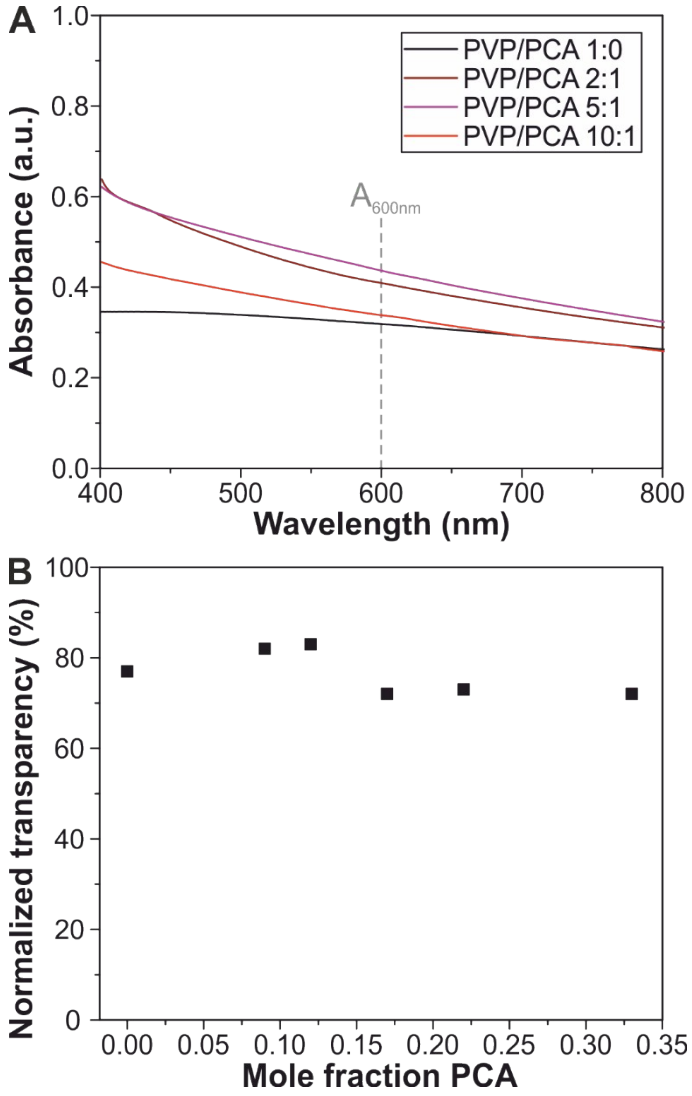

Figure S1. A, UV-VIS- spectra in the range 400-800 nm for PVP/PCA 1:0, 2:1, 5:1 and 10:1 samples. **B**, normalized transmittance as a function of the mole fraction of PCA.

Morphological Analysis

The cross-section of the PVP/PCA 10:1 and 2:1 samples were obtained by cutting cross-section slices with Leica UCS ultramicrotome equipped with a glass knife. After, the samples were coated with a thin layer of gold and SEM imaging was performed using SEM JEOL-JSM 6490 operating with an acceleration voltage of 10 kV. The obtained images are reported in Figure 2 A-B.

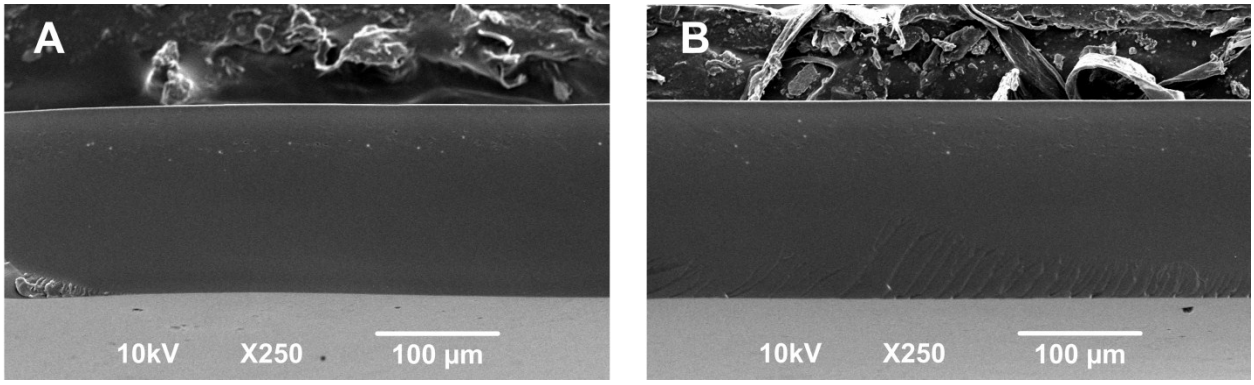

Figure S2. A, **B**, Cross-section SEM images of the PVP/PCA 10:1 and 2:1 samples, respectively.

Nuclear Magnetic Resonance (NMR) analysis

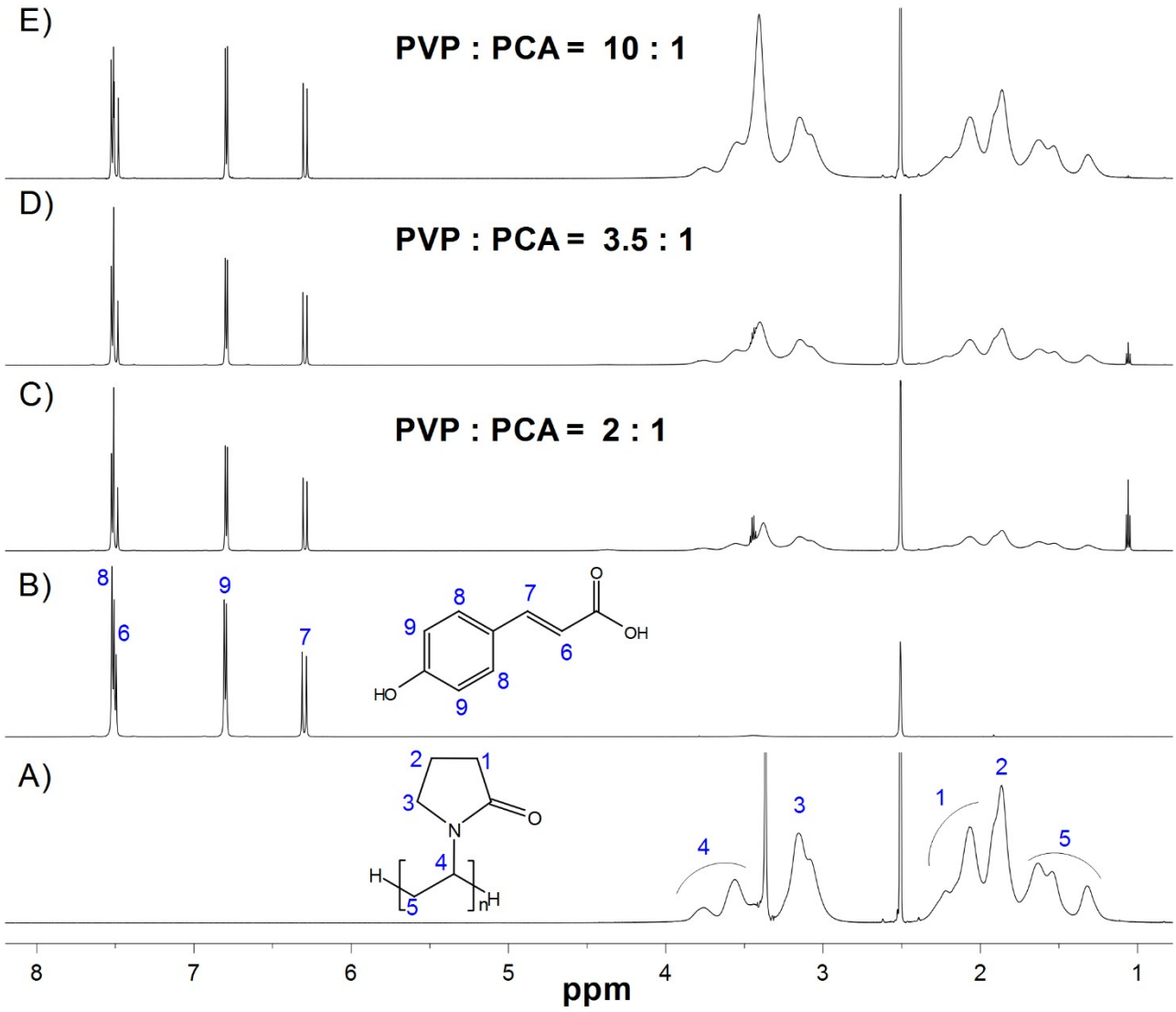

Figure S3. ^{1}H NMR in DMSO-d6 of A) PVP, B) PCA, C) PVP/PCA 2:1, D) PVP/PCA 3.5:1, E) PVP/PCA 10:1.

The ^{1}H NMR spectrum of PVP shows signals between 1 and 4 ppm whose assignments are reported in **Figure S3A.** Such signals are broad and with unresolved fine structure, characteristic of polymers (with short T_2, the transversal correlation time). On the contrary, signals between 6.26 and 7.53 ppm are sharp and with a recognizable multiplicity, typical of small molecules (with long T_2 time)[2]. Assignments, in such a region, reported in **Figure S3B**, are attributed to the *p*-coumaric acid moiety (region of double bonds and aromatic ^{1}H). Such signals remain

substantially unaffected by applying a 1D-CPMG[3] acquisition scheme **Figure S4** while the broad signals belonging to the PVP moiety are reduced in intensity down to the baseline. We can thus exclude that the *p*-coumaric acid is chemically bound to the PVP.

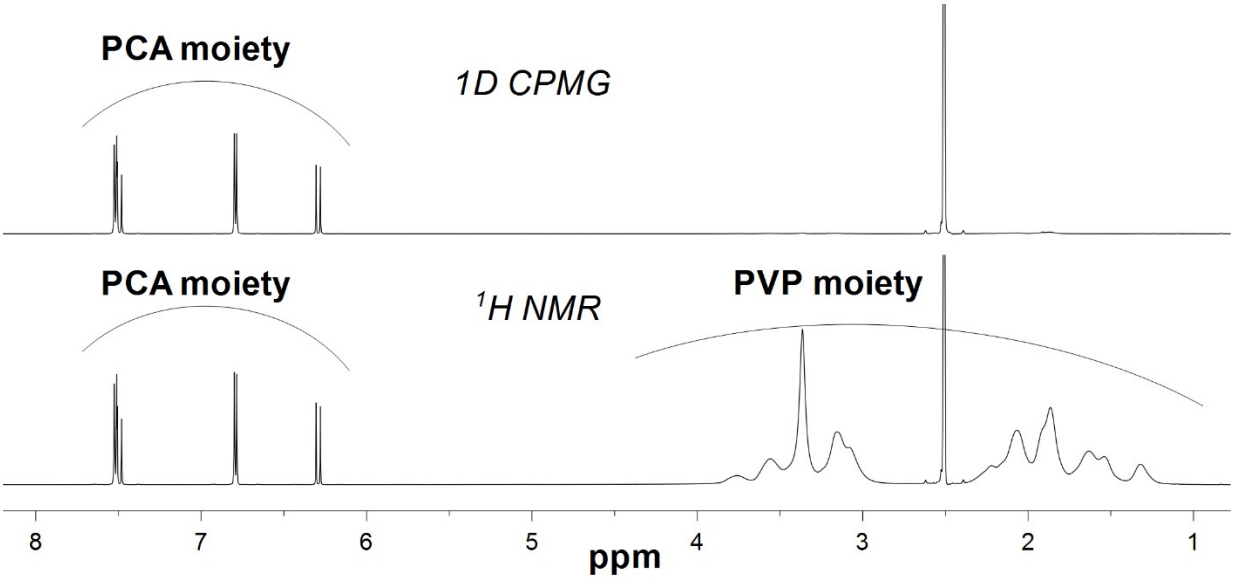

Figure S4. ^{1}H NMR and 1D-CPMG of the PVP/PCA 10:1 sample in DMSO-d6. The PVP signals are suppressed after the application of a 1D CPMG acquisition scheme, while the signals of PCA are only slightly decrease in intensity (due to their intrinsic T_2 resonance decay). Analogous results were obtained with all the samples.

Kinetics data

From the drug release data showed in Figures 6A,B the apparent rate constants were calculated, Figure S5. The increase of cumulative percentages was empirically best fitted to a $ln(1-P) = -kt$ first-order kinetic law, where P is the fraction of PCA released at time t and k is the apparent rate constant. As an example, the fittings of PVP/PCA 10:1 and 2:1 are displayed in Figure S5A. Rate constants were reduced with the PCA content, ranging from ~1.10 h^{-1} for PVP/PCA 10:1 to

to ~0.04 h^{-1} for PVP/PCA 2:1, Figure S5B. An important drop in the value of *k* was observed between PVP/PCA 7.5:1 and 3.5:1. This phenomenon can be related to a PCA content-dependent formation of H-bonds, as described in the infrared characterization.

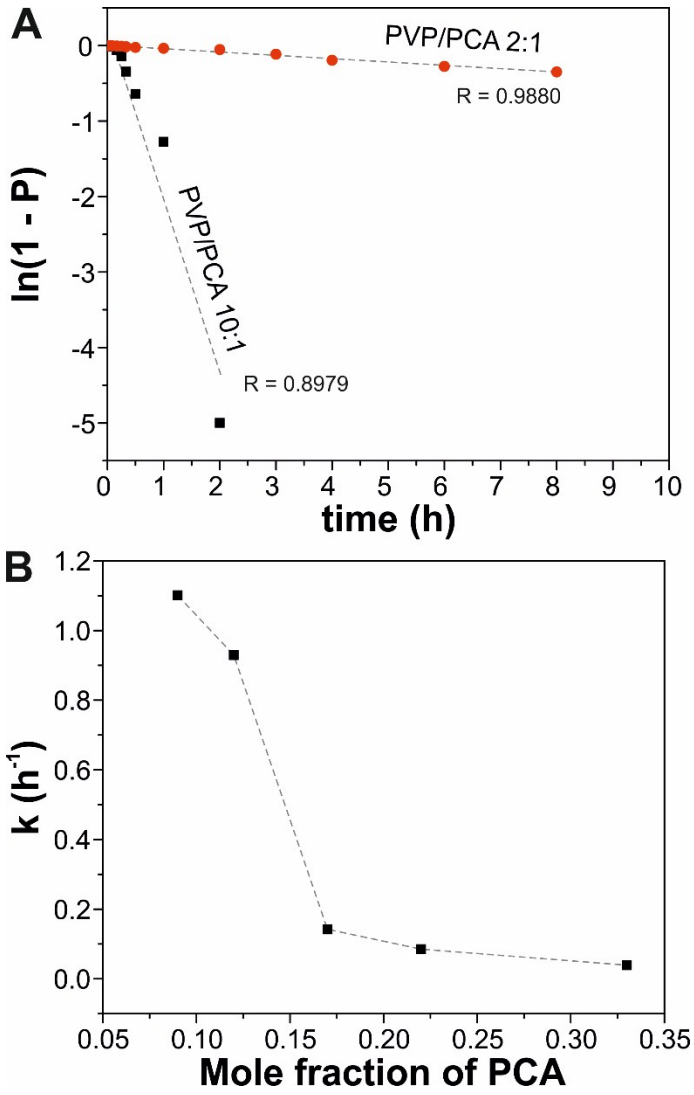

Figure S5. A, first-order fitting of drug release experiments for PVP/PCA 10:1 and 2:1. The correlation factor R is included. **B**, calculated kinetic constants as a function of the mole fraction of PCA.

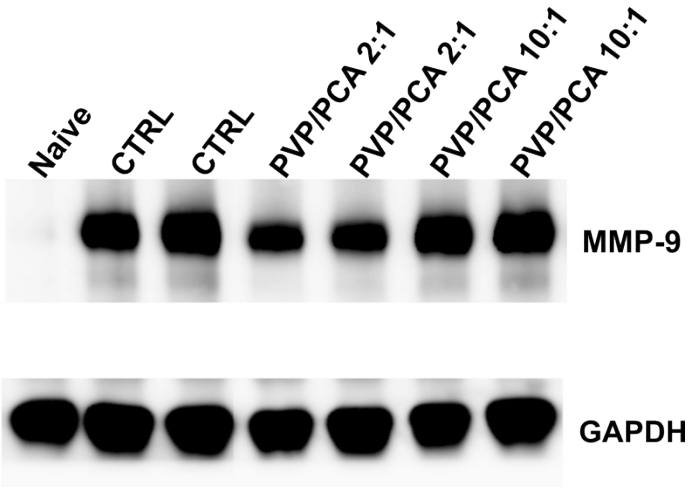

Figure S6. Western blot analysis of MMP-9 protein in naïve, sham, PVP/PCA 2:1 and PVP/PCA 10:1 mice. The blot is representative of 3 different analyses and illustrates the MMP-9 protein expression in mouse wounded skin. GAPDH was used as internal control. Protein weights are expressed in kDa.

References

(1) ASTM D1746-15, Standard Test Method for Transparency of Plastic Sheeting. ASTM International: West Conshohocken.

(2) Bloembergen, N.; Purcell, E. M.; Pound, R. V. Relaxation effects in nuclear magnetic resonance absorption. *Physical review* **1948**, *73*, 679.

(3) Carr, H. Y.; Purcell, E. M. Effects of diffusion on free precession in nuclear magnetic resonance experiments. *Physical review* **1954**, *94*, 630.