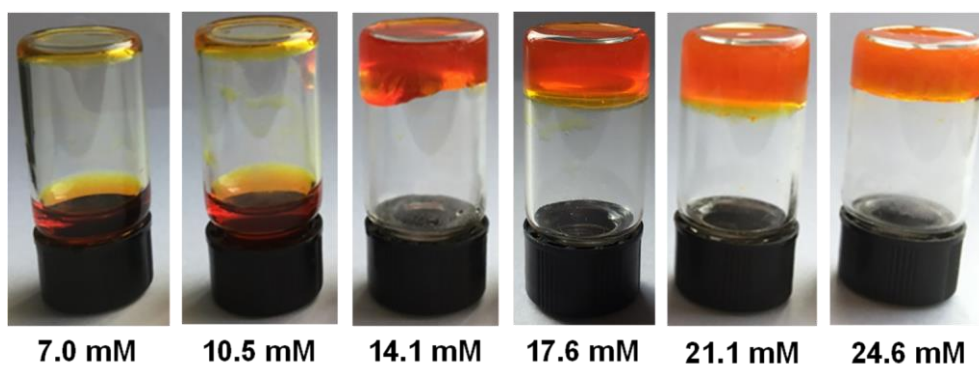


Supplementary Information

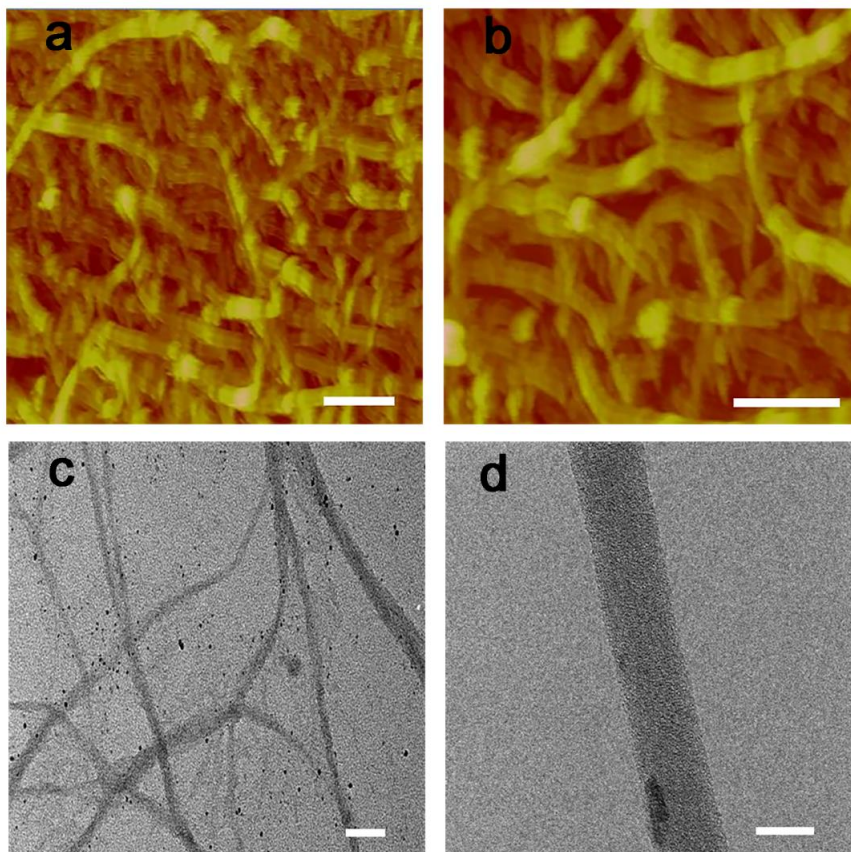
Direct self-assembly hydrogel of herbal small molecules towards a natural medicine

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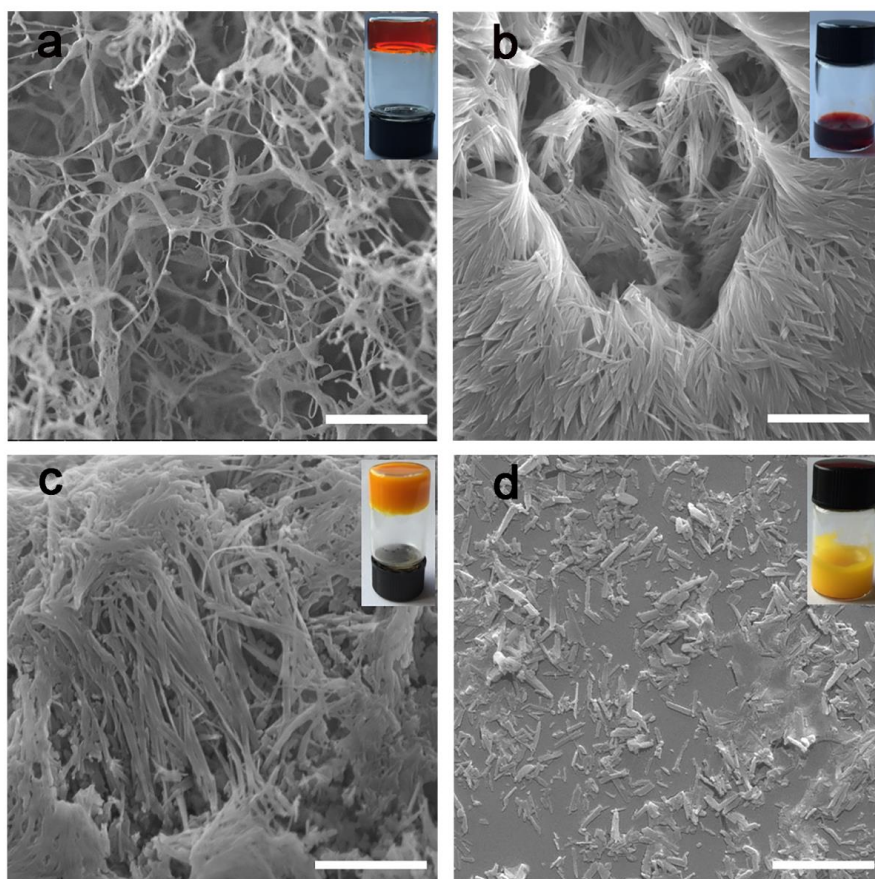
Supplementary Figures



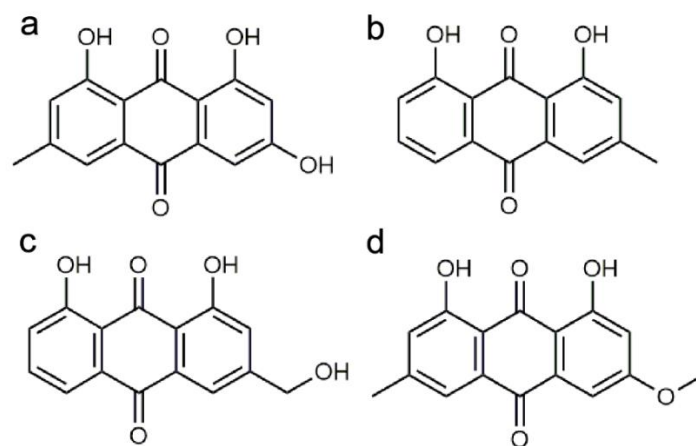
Supplementary Figure 1. Digital images of critical gelation concentration test.



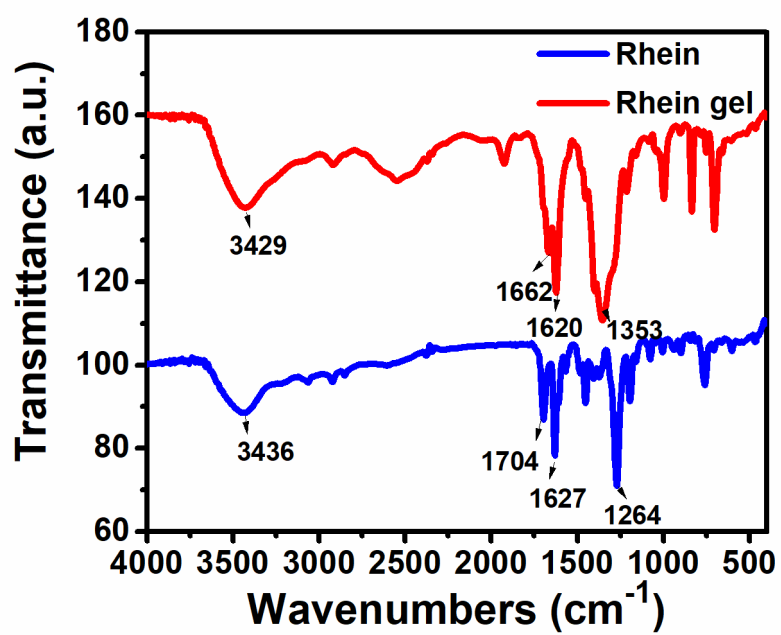
Supplementary Figure 2. Morphological characterization of the rhein hydrogel. **(a)** AFM image of the rhein hydrogel, scale bar, 500 nm. **(b)** Local amplification of a. scale bar: 500 nm. **(c)** TEM image of rhein hydrogel, scale bar: 100 nm. **(d)** Local amplification of c, scale bar: 20 nm.



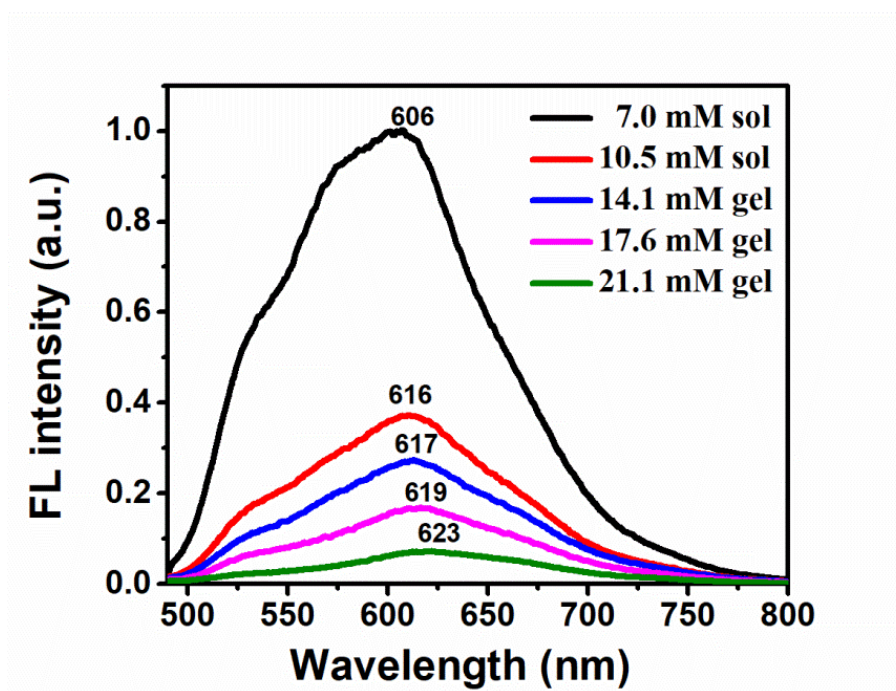
Supplementary Figure 3. SEM images of rhein at different pH values. (a) pH=8.3, (b) pH=10.2, (c) pH=7.4, (d) pH=6.5. All the rhein concentrations are 5 mg mL^{-1} (17.6 mM), scale bar: $5 \text{ }\mu\text{m}$.



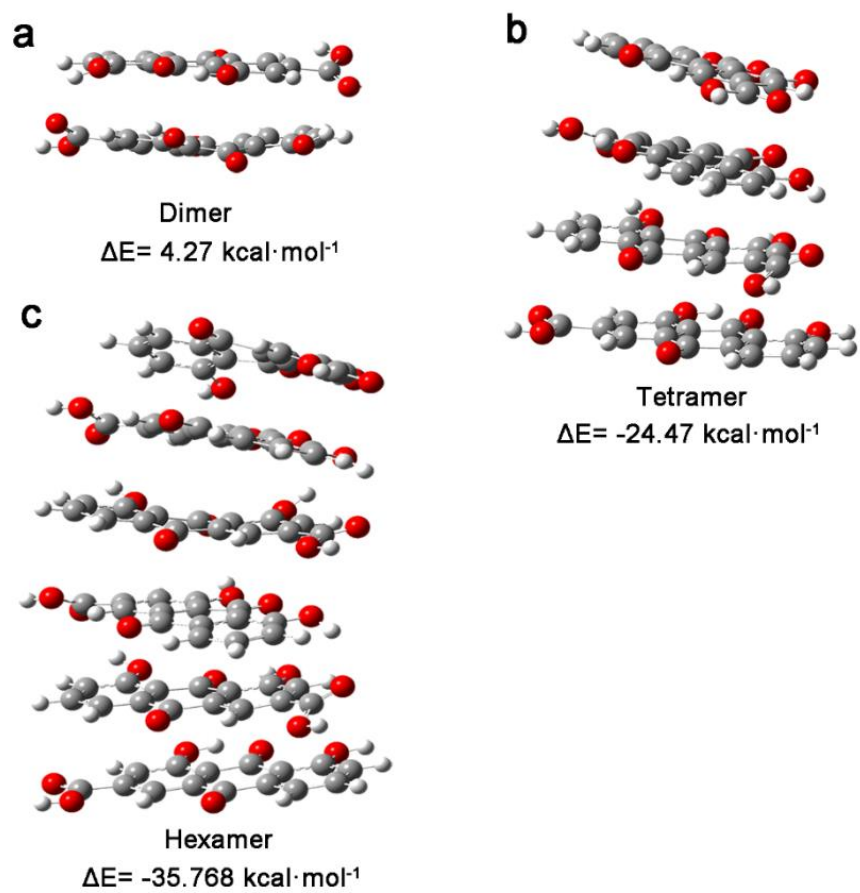
Supplementary Figure 4. The structural formula of (a) emodin, (b) chrysophanol, (c) aloë-emodin and (d) physcion.



Supplementary Figure 5. FT-IR of the rhein and rhein hydrogel. Samples were prepared at a concentration of 4 mg mL^{-1} , scanned between 4000 and 400 cm^{-1} .

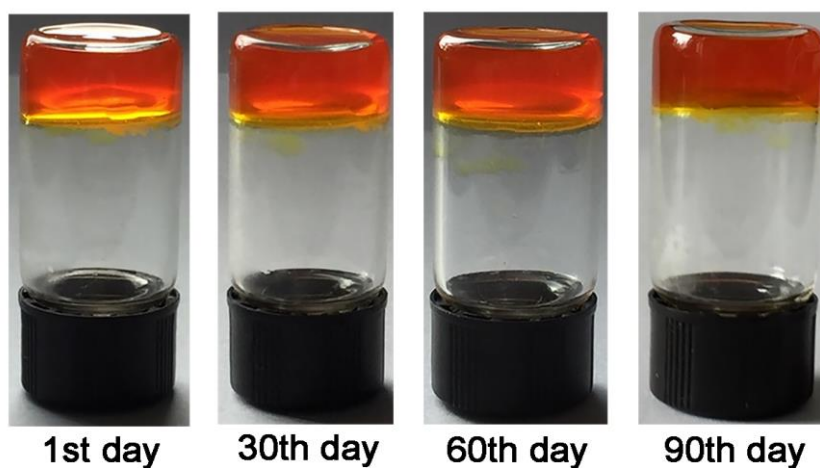


Supplementary Figure 6. The fluorescence emission spectrum of the rhein hydrogel.

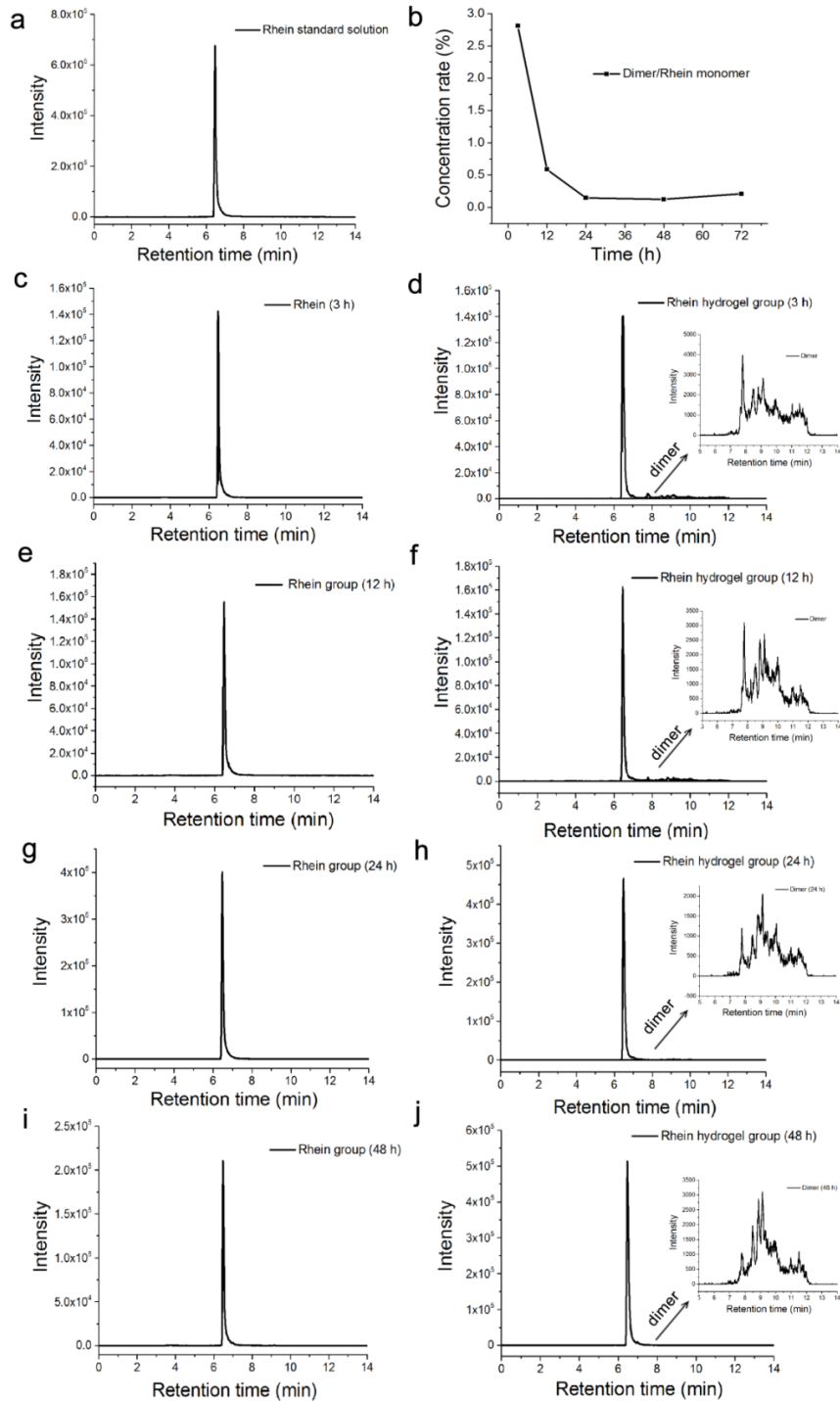


Supplementary Figure 7. Configuration and energy value of the rhodium aggregates. **(a)**

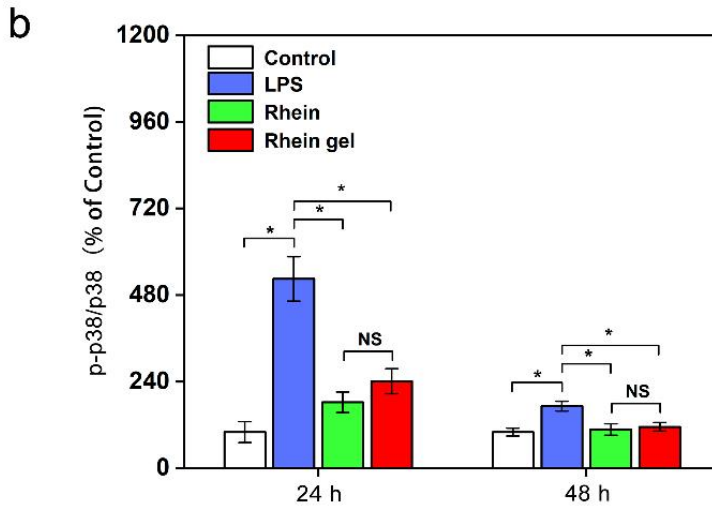
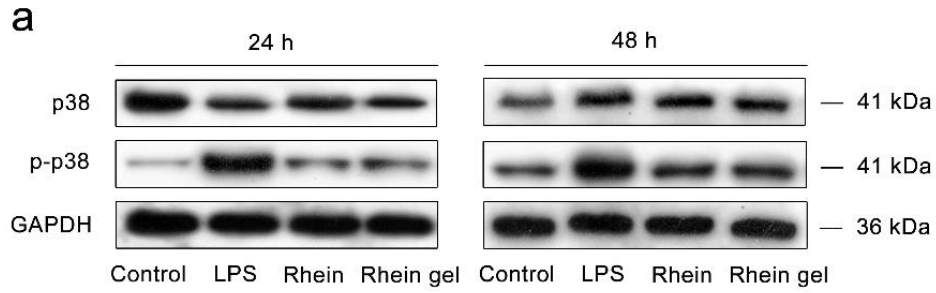
Dimer, **(b)** Tetramer and **(c)** Hexamer, respectively.



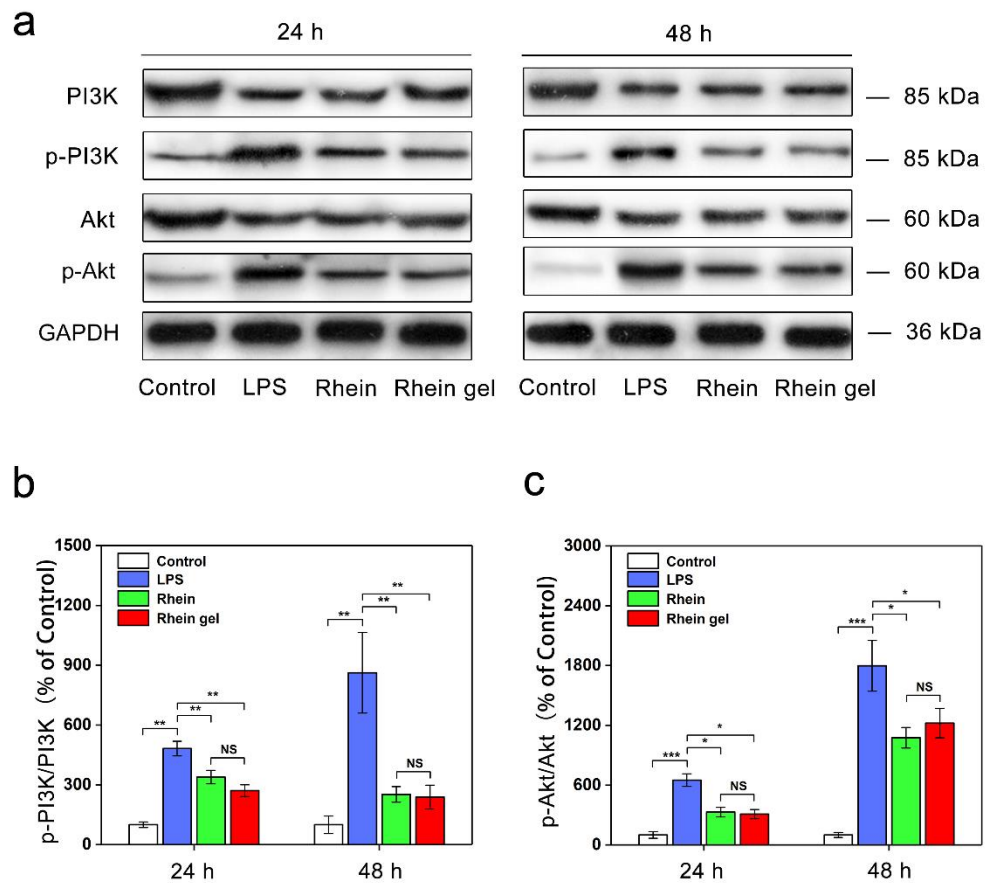
Supplementary Figure 8. The digital photos of rhein hydrogel at different time points. The concentration of hydrogel was 4 mg mL^{-1} (17.6 mM).



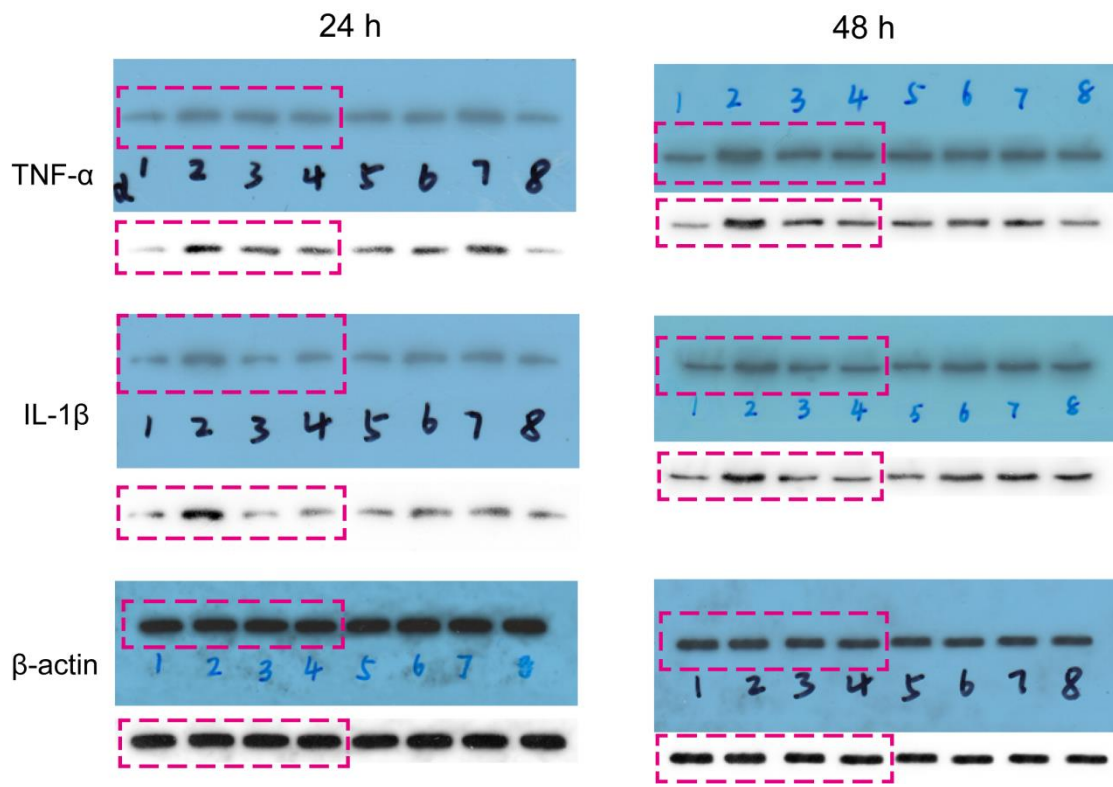
Supplementary Figure 9. LC-MS analysis of rhein and dimer in BV2 cells. (a) Rhein standard solution (b) Concentration ratio of dimer to rhein monomer in cells cultured with hydrogel. (c) Rhein group at 3 h. (d) Rhein hydrogel group at 3 h. (e) Rhein group at 12 h, (f) Rhein hydrogel group at 12 h, (g) Rhein group at 24 h. (h) Rhein hydrogel group at 24 h. (i) Rhein group at 48 h. (j) Rhein hydrogel group at 48 h.



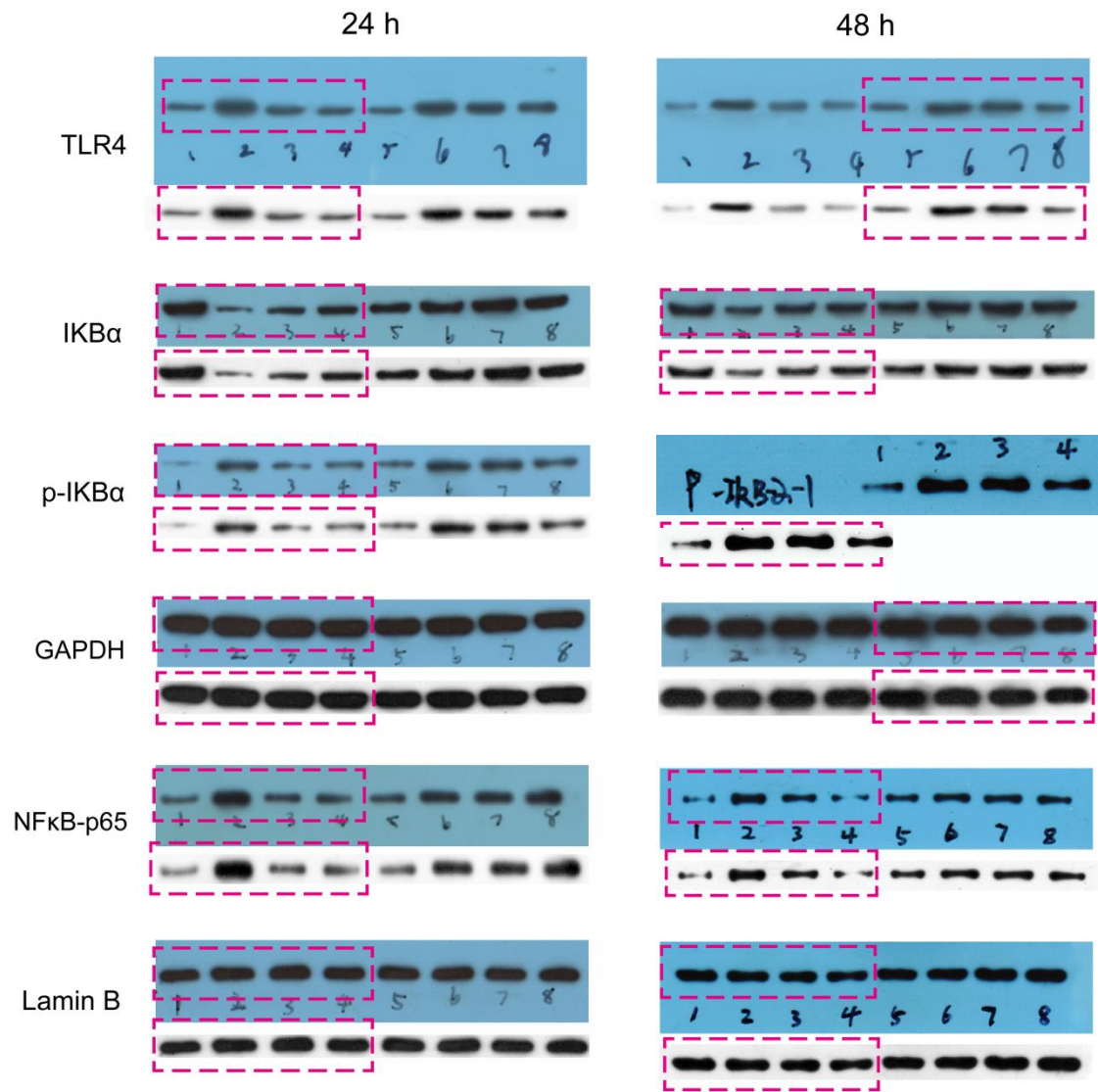
Supplementary Figure 10. Rhein and its hydrogel blocked p38 pathway. **(a)** Representative western blots of p38 after treatment of rhein and its hydrogel for 24 h and 48 h. **(b)** Quantification of p38 according to densitometric analysis. Values are expressed as the means \pm SEM ($n = 3$). One-way ANOVA with Tukey's post hoc test. * $p < 0.05$. Error bars represent SEM.



Supplementary Figure 11. Rhein and its hydrogel blocked PI3K/Akt pathway. **(a)** Representative western blots of PI3K, p- PI3K, Akt and p-Akt after treatment of rhein or rhein hydrogel for 24h and 48h. **(b, c)**, Quantification of p-PI3K/PI3K **(b)** and p-Akt/Akt **(c)** according to densitometric analysis. Values are expressed as the means \pm SEM (n = 3). One-way ANOVA with Tukey's post hoc test. *p < 0.05, **p < 0.01, ***p < 0.001. Error bars represent SEM.



Supplementary Figure 12. Uncropped blots scans of all blots in Fig. 5b.



Supplementary Figure 13. Uncropped blots scans of all blots in Fig. 6b (Correction; 48h p-IkBa has been replaced with correct blots at authors request).