**Highlights**

Silk fibroin/gelatin composite hydrogel loaded artemisinin was developed.

Silk fibroin/gelatin/artemisinin hydrogel shows good flexibility and ductility.

Silk fibroin/gelatin/artemisinin hydrogel shortens the inflammatory process and accelerates wound healing.

Silk fibroin/gelatin/artemisinin can significantly inhibit the tumor growth in vivo.

**Table S1 RSM-designed formula and experimental response results**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Run** | **Factor 1****A-concentration of silk fibroin (%)** | **Factor 2****B-concentration of gelatin (%)** | **Factor 3****C-****ratio of crosslinking** | **Response****24h sustained-release rate (%)** |
| **1** | 6 (-1) | 10 (1) | 125:1 (0) | 20.3747 |
| **2** | 6 (-1) | 6 (-1) | 125:1 (0) | 45.7501 |
| **3** | 6 (-1) | 8 (0) | 200:1 (1) | 22.6101 |
| **4** | 8 (0) | 6 (-1) | 200:1 (1) | 43.9213 |
| **5** | 8 (0) | 8 (0) | 125:1 (0) | 51.0796 |
| **6** | 8 (0) | 8 (0) | 125:1 (0) | 49.7403 |
| **7** | 8 (0) | 8 (0) | 125:1 (0) | 53.942 |
| **8** | 10 (1) | 10 (1) | 125:1 (0) | 30.0414 |
| **9** | 10 (1) | 8 (0) | 200:1 (1) | 41.8081 |
| **10** | 8 (0) | 6 (-1) | 50:1 (-1) | 67.4792 |
| **11** | 6 (-1) | 8 (0) | 50:1 (-1) | 44.2623 |
| **12** | 8 (0) | 8 (0) | 125:1 (0) | 52.942 |
| **13** | 10 (1) | 8 (0) | 50:1 (-1) | 54.2344 |
| **14** | 8 (0) | 10 (1) | 200:1 (1) | 22.4744 |
| **15** | 8 (0) | 8 (0) | 125:1 (0) | 45.6945 |
| **16** | 8 (0) | 10 (1) | 50:1 (-1) | 27.1034 |
| **17** | 10 (1) | 6 (-1) | 125:1 (0) | 72.287 |

**Table S2 ANOVA data for response surface quadratic model for 24h sustained-release rate**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Source** | **Sum of squares** | **Df** | **Mean square** | **F value** | **P value prof>F** | **Significant/not significant** |
| **Model** | 3631.55 | 9 | 403.51 | 50.10 | <0.0001 | Significant |
| **A- concentration of SF** | 534.22 | 1 | 534.22 | 66.33 | <0.0001 |  |
| **B- concentration of G** | 2094.46 | 1 | 2094.46 | 260.04 | <0.0001 |  |
| **C-ratio of crosslinking** | 484.62 | 1 | 484.62 | 60.17 | 0.0001 |  |
| **AB** | 71.15 | 1 | 71.15 | 8.83 | 0.0207 |  |
| **AC** | 21.28 | 1 | 21.28 | 2.64 | 0.1481 | Not significant |
| **BC** | 89.58 | 1 | 89.58 | 11.12 | 0.0125 |  |
| **A2** | 68.76 | 1 | 68.76 | 8.54 | 0.0223 |  |
| **B2** | 86.22 | 1 | 86.22 | 10.71 | 0.0136 |  |
| **C2** | 147.06 | 1 | 147.06 | 18.26 | 0.0037 |  |
| **Residual** | 56.38 | 7 | 8.05 |  |  |  |
| ***Lack of Fit*** | *14.73* | *3* | *4.91* | *0.47* | *0.7186* | *Not significant* |

Notes: R2=0.9847, R2Adj=0.9651.



Fig.S1 a) The correspondence figure between the residuals and the prediction of the equation. b) The correspondence figure between the predicted value and the actual experimental.



Fig.S2 Two-dimensional contour maps and three-dimensional response surface maps of influence of each factor and interaction on the dependent variable. a-b) concentration of silk fibroin-concentration of gelatin. c-d) concentration of silk fibroin-crosslinking degree. e-f) concentration of gelatin-crosslinking degree.

**Table S3 Model fitting results of ART release**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **pH** | **Time/h** | **Zero-order kinetic equation/Q=a*t*-b** | **First-order kinetic equation/Q=a(1-e-b*t*)** | **Higuchi equation/Q=a*t*1/2+b** | **Ritger-Peppas equation/Q=a*t*n** |
| **A** | **b** | **R2** | **a** | **b** | **R2** | **a** | **b** | **R2** | **a** | **n** | **R2** |
| **3.2** | **24** | 70.63 | 0.64 | 0.2111 | 79.38 | 0.84 | 0.9926 | 10.52 | 43.78 | 0.4963 | 63.84 | 0.096 | 0.5599 |
| **24~120** | 79.93 | 0.075 | 0.9505 | Non-convergence | 1.31 | 74.50 | 0.9431 | 65.73 | 0.062 | 0.9073 |
| **4.5** | **24** | 48.52 | 1.84 | 0.2754 | 77.48 | 0.80 | 0.9975 | 10.36 | 41.83 | 0.4495 | 45.32 | 0.23 | 0.7053 |
| **24~120** | 76.39 | 0.069 | 0.9124 | Non-convergence | 1.17 | 71.59 | 0.9046 | 63.51 | 0.059 | 0.8837 |
| **6.0** | **24** | 59.72 | 0.94 | 0.1265 | 74.61 | 0.76 | 0.9975 | 10.33 | 38.92 | 0.4674 | 53.28 | 0.15 | 0.5442 |
| **24~120** | 73.51 | 0.082 | 0.9587 | Non-convergence | 1.44 | 67.53 | 0.9467 | 58.23 | 0.074 | 0.9253 |
| **7.4** | **24** | 27.17 | 2.55 | 0.5333 | 68.89 | 0.71 | 0.9789 | 1054 | 33.02 | 0.5929 | 31.39 | 0.31 | 0.8415 |
| **24~120** | 70.27 | 0.10 | 0.9755 | Non-convergence | 1.63 | 63.78 | 0.9683 | 53.84 | 0.086 | 0.9422 |