Topical Astragaloside IV-Releasing Hydrogel Improves Healing of Skin Wounds in Vivo

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Topical delivery of therapeutic agents at the time of injury to accelerate skin repair and prevent the formation of scars during the wound healing process has received increasing attention and represents a novel regenerative and prophylactic strategy for wound treatment. The aim of this study was to investigate, for the first time, the influence of topical astragaloside IV-releasing hydrogel on the wound repair and regeneration. Using the sodium alginate-gelatin as a hydrogel vehicle, the astragaloside IV was incorporated into the topical carrier and kept releasing with a sustained manner at the wound site. With the rat skin excision model, regulation of the astragaloside IV hydrogel on the wound repair and regeneration were investigated. It was found that the astragaloside IV hydrogel was effective in the skin wound repair, leading to a significant improvement on the wound closure, collagen synthesis and skin tensile strength recovery. Meanwhile, for the first time, that functions of astragaloside IV hydrogel in activating the skin appendages regeneration and increasing the transforming growth factor-β1 (TGF-β1) level in serum were shown. Results of this study provided evidence for the alginate-gelatin hydrogel as efficient carrier for the topical delivery of bioactive molecules to the injured site. The astragaloside IV releasing hydrogel was shown a promising therapeutic formulation for wound healing, as well as its regenerative feature and underlying mechanism contribute to the skin regeneration were disclaimed.

Key words astragaloside IV; hydrogel; wound healing

Wounds represent a major health burden and drain on resources. In the context of the increasing number of patients with wounds, defining the role of various wound treatments represents the next challenge.1) Topical treatment of wounds has many advantages including decreased cost and increased ease of application, compared with the systemic treatments.2) Increasing studies have demonstrated that faster rates of wound closure could be achieved when an agent was serially delivered over a prolonged period.3–5) Sodium alginate, fibrin, gelatin, chitosan, collagen are popular biomaterial for quicker wound healing.6) Especially, sodium alginate is the sodium salt of alginic acid, a polysaccharide comprising mannuronic and guluronic acid units. In contact with body fluids, alginates are known to break down to simple monosaccharide-type residues that will be totally absorbed and the sodium salt which can facilitate the removal of the residual by dissolution.7) The functions of alginate materials for wound treatment are well known, including: 1) high absorbency to form gels upon contact with wound exudates, which limits wound secretions and minimises bacterial contamination; 2) the moist environment produced by alginate gel leads to rapid granulation and reepithelialization and prevents the formation of scab9); 3) alginate increased proliferation of fibroblasts but not their motility10); 4) the ease of biodegradation.11) Gelatin is a denatured collagen and its biosafety has been proven through long clinical applications.12) Other advantages of gelatin include the usability of materials with different charges and the easiness of chemical modification.13) Additionally, increasing studies have demonstrated that the combination of natural polymers shown better results, than when used alone in most topical therapy.14)

Astragaloside IV is one of the major compounds contained in the Astragali Radix (AR), which is a popular herb used in Chinese medicine for promoting the repair and recovery of tissues and organs. The promoting effects of AR in diabetic foot ulcers healing in animals and patients through the mechanisms of regeneration enhancement, pro-angiogenesis and anti-inflammation have been reported that AR crude extract could enhance the closure of acute wounds in rats.15–18) Taking into account these evidences, it was hypothesized that the chief component of AR, astragalosides IV may have the therapeutic potential for wounds which deserves much more studies. Recently, we have demonstrated the significant stimulation of the astragalosides IV on wound repair and regeneration, which reminded the great potential of this compound on clinical wound treatment.19) In present study, astragalosides IV-sustained releasing hydrogel was designed to decrease the degradability of astragalosides IV to the elements of heat, acid, etc. in the wound pathological environment upon topical application. Accordingly, the influence of the astragalosides IV-solution and astragalosides IV-hydrogel on wound healing were investigated and compared.

Wound healing process may be divided into four continuous phases, namely inflammation, proliferation and maturation or remodeling. Among which, the proliferation phase is mainly responsible for the wound closure and lesion. In this phase, re-epithelialization starts few hours after the injury, including the movement of cells, especially the keratinocytes coming from the margins and the epidermal appendices; and the new blood vessels formed from pre-existing vessels, namely angiogenesis. Both of which are important activities determining the wound lesion. The remodeling phase is marked by maturation of elements and affections to the extracellular matrix. It is an attempt to recover the normal tissue structure.20) Wound healing is also a complex process regulated by an equally complex signaling network involving numerous growth factors, cytokines and chemokines.21) Especially, transforming growth factor-β1 (TGF-β1) is well known cytokine to initiate the sequent wound healing phases of inflammation, angiogenesis, reepithelialization, and connective tissue regeneration.
It is closely involved in the remodeling phase with function of stimulating the collagen synthesis and disposition by the sustained activation of fibroblasts. TGF-β1 can up-regulate the angiogenic growth factor vascular endothelial growth factor (VEGF) and is also a potent inhibitor of metalloproteinase MMP-1, MMP-3, and MMP-9 and a promoter of tissue inhibitor of metalloproteinase (TIMP)-1 synthesis, thus inhibiting collagen breakdown.22)

In this study, the hydrogel made from the blended materials of sodium alginate and gelatin was prepared and characterized. Saturated with the astragaloside IV, the effects of the topically applied astragalosides IV-releasing hydrogel for wound repair and regeneration was investigated, with the aims to testify the efficacy of natural polymer based hydrogel as a topical drug delivery vehicle for wound treatment, as well as to investigate the potential of astragalosides IV as a therapeutic agent for wound therapy.

MATERIALS AND METHODS

Astragaloside IV was purchased from Zhejiang Institute of Food and Drug Control (purity above 99.3%, HPLC). Gelatin obtained from acid-treated pork skin and sodium alginate were kindly supplied by the Laboratory of Professor Yasuhiko Tabata (Kyoto University, Japan) and Delong glue, Co., Ltd. (Shanghai, China), respectively. The molecular weight of the sodium alginate was 198.11 and its viscosity (1% solution, 20°C) is ≥0.02. Transforming growth factor-β1 (TGF-β1) mouse monoclonal antibody was purchased from Santa Cruz Biotechnology, Inc. (Santa Cruz, CA, U.S.A.). Horseradish peroxidase (HRP) labeled goat anti-mouse immunoglobulin G (IgG) antibody was purchased from Boster, Inc. (Wuhan, China). Masson’s trichrome staining kit was purchased from Nanjing Keygen, Inc. (Nanjing, China). Chlormal hydrate was purchased from China National Medicines, Inc. (Beijing, China). 4% buffered paraformaldehyde was purchased from Boster, Inc. (Wuhan, China). The pictures of masson’s trichrome staining were photographed by Leica image analyzing system (Leica, Germany). The wound tensile strength was measured by the BLD-200N tensometer (Labthink, China). Dialysis bag MD44 (8000–14000) was purchased from BaiSai Biological Products Company, Shanghai.

Preparation of Sodium Alginate-Gelatin Hydrogel To prepare gelatin solution, 0.6 g gelatin was added to 20 mL distilled water and the mixture was stirred at 60°C. One and a half grams sodium alginate solution was added to 30 mL distilled water and the mixture was stirred at 60°C. The sodium alginate solution was then poured into the gelatin solution, mixed with stirring at 60°C for 2 h. Astragaloside IV was dissolved in dimethylsulfoxide (DMSO) before addition to the hydrogel (DMSO to gelatin was below 1:100 v/v). The appropriate volume of freshly prepared astragaloside IV-DMSO solution was added to the hydrogel solution with stirring at room temperature for homogenization. Control hydrogel without drug incorporated was prepared by the same procedure, using DMSO alone in the place of astragaloside IV solution. The hydrogels were used immediately after preparation.

Characterization of Sodium Alginate-Gelatin Hydrogel The hydrogel loaded with astragaloside IV was characterization for the following physicalchemical properties. The pH was measured using pH meter of a glass electrode (Shenzhen Kedida Electronics Co., Ltd.). The hydrogel was centrifuged at 3000rpm for 30 min and was observed for the change of texture and turbidity. Viscosity was measured with rotary viscometer at 25°C (Model NDJ-1, GuoWang Chemical Limited Company, Shanghai, China). Before the viscosity measurement, the samples of hydrogel were placed on a thermostated (25±0.1°C) viscometer plate for 30 min to reach the temperature equilibrium. The smallest rotor was selected with rotation rate maintained at 80 rpm. Color and turbidity were assessed visually against white sheet in standardized conditions of lightning (2000–3500lux). Any apparent change of gel color, texture, turbidity, water absorption and pH were recorded during the whole study. The water sorption capacities of hydrogel were determined gravimetrically after immersing these samples into milliQ water. The resulting swollen gels were removed from water and then weighted after removing the surface water. The water sorption capacity was calculated when the gel weight was stable, as the ratio between sample weight and sample initial dry weight. Each assay was triplicated and the corresponding average value was taken as the capacity for each sample.

Release Profile of Astragaloside IV Diffusion measurement of astragaloside IV from the hydrogel carrier was performed using a modified vertical diffusion cell, based on the Franz cell model. This cell had a donor and a receptor compartment separated by a Dialysis membrane, with cutoff at 5 kDa. The donor compartment was filled with 0.5 g hydrogel contained 0.25 mg astragaloside IV. The receptor compartment was filled with 7.0 mL phosphate-buffered saline (PBS) solution, pH 7.4, and was kept immersed in water in a thermostatic bath at 37°C with magnetic stirring. The release investigation was carried out under sink conditions, keeping drug concentration below its solubility limit. Sampling was performed by withdrawing aliquots of 30 µL from the receptor compartment with a syringe at time intervals of 1, 2, 3, 4, 9 and 24 h. An equal volume of PBS replacing solution was introduced into the receptor compartment after each sampling. Astragaloside IV concentration in the samples was measured by HPLC (Beckman, U.S.A.) analysis. A calibration curve was obtained with standard astragaloside IV solutions. Each measurement was performed in duplicate.

Animal Experiments and Ethics Eight-week-old Sprague-Dawley (SD) female rats (200–250 g) were supplied by Zhejiang University Experimental Animal Center, China. All animals were maintained under constant conditions (temperature 25±1°C) and had free access to a standard diet and drinking water. All of the animal experimental procedures were in accordance with the Zhejiang University guidelines for the welfare of experimental animals. Animal experimentation ethics approval number: Zju2010-1-02-015. 36 SD male rats aged 8 weeks were used in this study and were divided into four groups: blank control group, gel control group, astragaloside IV solution treated group and astragaloside IV gel group. The animals were anesthetized with 10% chloral hydrate. The hair on the back was clipped, and the skin washed with povidone-iodine solution and wiped with sterile water. The 1×1 cm² full-thickness skin excision wounds were made. Animals were separated into four groups (n=6 in each group), including (a) blank control group, the animal was undisturbed without any handling after the wound; (b) hydrogel control group, in which the 0.5 mg hydrogel without astragaloside IV...
was topically applied daily on the wound bed, from the day of lesion until day 7 and day 14 post-wounding; (c) astragaloside IV solution treated group, in which 0.5 mg astragaloside IV-containing solution was topically applied daily to the wound bed from the day of lesion until the day 7 and day 14 post-wounding; (d) astragaloside IV hydrogel treated group, in which 0.5 mg astragaloside IV-containing hydrogel was topically applied daily to the wound bed from the day of lesion until the day 7 and day 14 post-wounding. The animals were housed in individual cages with free access to food and water. Checking of any postsurgery pain, distress, or complications was done 24 h after surgery and daily afterward. On postoperative day 7 and day 14, rats in each group were euthanized and the reconstituted skin was harvested for assays.

Wound Closure Rates The wound closure percentage was measured everyday from day 1–8 and on day 10 and day 14, by copying the wounds with filter papers and calculating the weight percentage of filter papers at different time points post-wounding. Wound closure percentage (%) = \[
\frac{\text{area on day } 0 - \text{open area on day } n}{\text{area on day } 0} \times 100.
\]

Skin Tensile Strength Measurement The reconstituted skin was cut and excised for tensile strength determinations at day 7 and 14 post-wounding. Every strip of the new formed skin was removed from each tested animal, and the cross-sectional area of each strip was determined with calipers within 10 min of the harvest. The skin strips were individually mounted on a tensometer (Labthink Co., Ltd., China) with a cross head speed of 25 mm/min, and the wound tensile strength was determined.\(^{24}\) The resulting tensile strength values for three strips of each wound were averaged to arrive at a mean determination for each animal.

Transforming Growth Factor-β1 (TGF-β1) Production Five milliliters venous blood sample was taken from each rat on the day 7 and day 14 post-wounding. Serum was separated, aliquoted, and stored at −20°C till being used to assay TGF-β1 level by (Bio Source International, Inc., Multispecies TGF-β1 kit, U.S.A.). The results were analyzed according to the manufacturer’s instructions, by using a graph paper, the absorbance of the standards was blotted against the standard concentration to construct the standard curve. The TGF-β1 concentrations for the unknown extracted samples and controls were read from the standard curve, and then multiplied by a factor of 40 to reach the actual TGF-β1 concentration in pg/mL.\(^{25}\)

Masson’s Trichrome Staining and Histological Analysis The wound specimens at day 7 and day 14 post-wounding including full thickness skin layers (epidermis, dermis, and hypodermis) were fixed in 4% buffered paraformaldehyde and processed according to the routine light microscope tissue processing methods, and the processed tissues were embedded in paraffin. Eight micrometers tissue sections with masson’s trichrome staining were examined and photographed by Leica image analyzing system.\(^{26}\)

Statistical Analysis All values are expressed as mean± S.D. Student’s paired t-test was performed for comparison of data of paired samples, and analysis of variance was used for multiple group comparisons. A probability (\(p\)) value <0.05 was considered significant.

RESULTS

Physicochemical Properties of the Sodium Alginate-Gelatin (SAG) Hydrogel Carrier The physicochemical properties of the hydrogel vehicle were listed in Table 1. The prepared hydrogel was light yellow with even texture. Its pH was 7.2±0.2 and the viscosity was 6.5±0.3 Pa·s. It can be spread easily and removed completely upon water wash. Its water absorptivity is around 137% and the water mass loss can be kept <5%. No major variations of pH, colour, viscosity and turbidity were observed of the used hydrogel during the whole study.

Release Profiles of Astragaloside IV from Hydrogel In this study, the bioactive astragaloside IV (see structure as Fig. 1A) were investigated to testify the releasing property of the hydrogel carrier. Figure 1B was the release profile of

![A](image1.png)  
![B](image2.png)

Fig. 1. (A) Chemical Structure of Astragaloside IV; (B) Diffusion of Astragaloside IV from Hydrogel over 24h at 37°C

Table 1. Physicochemical Properties of the SAG Hydrogel Vehicle

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Descriptions/values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Light yellow, transparent, even texture</td>
</tr>
<tr>
<td>Solubility</td>
<td>Water soluble and can be removed completely upon water wash</td>
</tr>
<tr>
<td>Spreadability</td>
<td>Good spreadability</td>
</tr>
<tr>
<td>pH</td>
<td>7.2±0.2</td>
</tr>
<tr>
<td>Viscosity</td>
<td>6.5±0.3 Pa·s</td>
</tr>
<tr>
<td>Water absorptivity</td>
<td>137±2.5%</td>
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astragaloside IV from the hydrogel over 24 h at 37°C. It was shown that the astragaloside IV was released with the sustained manner within 24 h and no burst release existed. The accumulative release percentages of in 12 h and 24 h were 99.1 ± 3.2% (13.9 mg) and 97.8 ± 6.2% (13.7 mg), respectively. Accordingly, astragaloside IV action was supposed to be present during the 24-hour application period in which the wounds remained coated with the hydrogel.

**In Vivo Wound Healing Effects** No postoperative adverse effects, e.g. infection, pyogenesis, and body fluid effusion occurred in any animals throughout the experimental periods. Diet, drinking, and defecation were normal. All animals survived until the completion of the study with the stable body weights. The wound status was evaluated for the closure rates, recovery of skin tensile strength recovery and histology, as well as the growth factor (TGF-β1) secretion after treatments with different formulations at day 7 and 14 post-wounding.

**Wound Closure Rates** Figure 2 showed the wound macroscopic changes in the wound sites after the different treatments. Each wound was observed at day 3, 6, 9, and 12 post-operation. It was shown that up to the 12d post-operation, the majority of the wounds appeared to be healed over 90%. Figure 3 illustrated the closure rates of wound in each group by determining the percentage of wound surface covered by regenerated skin. It was shown that, up to day 3, there was no significant difference in wound size among the tested group. The astragaloside IV solution and blank gel didn’t exhibit significant acceleration on the wound closure in the whole study, despite that a trend of wound closure acceleration was shown by these two groups. In contrast, compared with the blank control, the astragaloside IV gel was shown to be effective in accelerating wound contraction/epithelialization of the acute wounds in the present rat skin incision model used among the 14d post-wounding, with 1.0–1.3 folds of increase ($p < 0.05$ or 0.01). With the blank gel as a control, the astragaloside IV gel expressed promotion at day 7 and day 8 with around 1.2 folds of increase ($p < 0.05$). Difference of astragaloside IV gel and astragaloside IV solution was observed at day 14 ($p < 0.05$).

**Skin Wound Tensile Strength Recovery** From the Fig. 4A, besides the astragaloside IV solution showed a significant enhancement for the skin tensile strength recovery at the day 14, all the other tested group expressed the trend to enhance the tensile strength recovery in contrast to the blank control, despite that no statistical significance existed. Moreover, despite that there was no difference between the biomechanical strength of most tested group and that of blank control, there was no significant difference of tensile strength between the tested groups and that of normal skin group. Since after the skin injury, the normal collagen will be replaced by the newly formed collagen and the connective tissue would not regain the original highly organized structure of collagen at a short period, the fact that the healed skin of other groups until the 14th day post-wounding is significantly lower in tensile strength than that of normal skin is thought as a feasible phenomenon. The significant enhancement of astragaloside IV or gel matrix on the skin tensile strength recovery might be received at longer time points post-wounding.

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**Fig. 2. Scheme Summarizing Macroscopic Lesions Aspects of the Experimental Wounds Healing of Different Groups at Day 0–12**

(A) Blank control group; (B) SAG hydrogel control group; (C) astragaloside IV solution treated group; (D) astragaloside IV hydrogel treated group.
Transforming Growth Factor-β1 (TGF-β1) Production

From Fig. 4B, on day 7 post-wounding, only the astragaloside IV gel expressed a significant stimulation on the TGF-β1 secretion with 2.4 folds (*p<0.05), compared with the blank control. 2.3-fold enhancement was also expressed by the astragaloside IV gel than astragaloside IV solution group (*p<0.05). However, after 14d, the strong stimulation on the production of TGF-β1 was expressed in all the blank gel matrix, astragaloside IV solution and astragaloside IV gel treated groups with similar 1.6 folds (**p<0.01).

Masson’s Trichrome Staining and Collagen Synthesis

From the Fig. 5, up to the day 7 post-wounding, no apparent histological difference was observed in most tested groups. Most of them expressed the scar tissue displayed most areas of dense dermis devoid of skin appendages and characteristic of scar formation (Figs. 5a–c), except for some skin appendages with blood vessels like structure (indicated by yellow arrows) (Fig. 5d) were observed in the astragaloside IV gel treated group. However, at the day 14, more collagen could be seen in the gel matrix (Fig. 5g), astragaloside IV solution (Fig. 5h), and astragaloside IV gel (Fig. 5i) treated groups.

It was also found that skin appendages with blood vessels like structure appeared in the astragaloside IV gel/solution treated groups (Figs. 5h,i). Compared with other groups, the constructed skins in the astragaloside IV gel treated group was much more closer to that of normal rat skin, in terms of the histological characteristics and skin appendages involvement, which reflected the regenerative features of the topical applied astragaloside IV hydrogel.

DISCUSSION

Local drug delivery to promote cell migration, proliferation and differentiation is an enormous tool to improve the required time and quality of tissue regeneration.
Three-dimensional template, e.g. scaffold, gel matrix were frequently used for tissue in growth by mimicking the extracellular matrix (ECM) for cell adhesion and proliferation. Moreover, the inclusion of bioactive molecules in these ECMs like carriers for cell adhesion, cell signaling and drug or gene delivery is a major consideration in wound topical treatment.28) This is really important contribution, especially when the incorporated bioactive constituents have well approved regenerative and wound healing activities. Ideally, the vehicle of wound treatment should enhance the topical drug delivery, be nonirritating and be easy to use. Therefore, in the present study, the hydrogel made from the highly absorbent, gel-forming materials with controlled drug release features were prepared and characterized as topical drug delivery systems for the applications in skin repair. Particularly, as both gelatin and alginate have been reported as components of wound dressings, the beneficial effects of hydrogels composed of gelatin29) and sodium alginate30) for wound treatment were investigated in this study. The effects of hydrogels composed of gelatin and sodium alginate was prepared, characterized and investigated for its regulation in wound healing. Compared with the blank control, results of this study definitely showed the gelatin and sodium alginate based gel matrix can promote the collagen synthesis and stimulating the TGF-β1 secretion in skin wounds. Although the clear mechanism has hitherto not been fully disclaimed, their values for wound healing may be contributed to be their activities in 1) initiating hemostasis in conjunction with maintaining a moist environment; 2) activating wound healing with the mechanism of creating an macrophages resulting in the elevated levels of inflammatory cytokines including TNF-α and IL-6; 3) improving the skin elasticity and biomechanics, as the isolated hydrolyzed collagen.31–33) With the sodium alginate-gelatin as a topical vehicle, the astragaloside IV was incorporated into a hydrogel and kept being released with a sustained manner to the wound site. As a result, the apparent enhancement of the astragaloside IV hydrogel in wound repair was observed, which agreed with our report that astragalosides IV could promote the wound re-epithelialization, improve the recovery of the wound skin tensile strength, as well as induce the skin appendages regeneration.34) On the other hand, compared with the astragalosides IV solution, the hydrogel with drug sustained releasing property was demonstrated for its superiority in the topical delivery of astragalosides IV. The astragalosides IV-hydrogel was demonstrated for its increased efficiency in wound re-epithelialization, TGF-β1 secretion, and skin appendages new formation, which indicated both the therapeutic potential and improved adaptability of astragalosides IV-hydrogel in clinical wound treatment.

It is known that the restoration of epidermal barrier through wound re-epithelialization is essential to wound healing, of which, the proliferation and migration of keratinocytes are the central activities and defects in these functions resulted in most clinical non/delayed healing cases. These results demonstrated the superiority of the prepared hydrogel loaded with astragaloside IV over the hydrogel vehicle alone and the astragaloside IV solution. The stimulating effects of astragaloside IV hydrogel on collagen synthesis was also demonstrated with the masson’s staining, in which, much more collagen and increased skin tensile strength have been received after the astragaloside IV hydrogel treatment.

It was reported that overexpression of TGF-β1 increases the proliferative phenotype of keratinocytes particularly during the late stages of wound healing.35) This study firstly found the topical application of sodium alginate-gelatin hydrogel and/or astragaloside IV at wound sites could significantly increase the TGF-β1 level of serum, which provided the novel evidence for the enhancement healing feature of these biomaterials and natural product. The promotion of SAG gel matrix, astragaloside IV solution or hydrogel on TGF-β1 secretion suggested their interference in the later phase of wound healing and the skin extracellular matrix remodeling. Especially, the stimulation of alginate-gelatin hydrogel or astragaloside IV on the TGF-β1 secretion may be one of the major reasons for their collagen synthesis enhancement effect, considering that TGF-β1 is centrally involved in collagen production.

Another interesting result received lies in that the activation of astragaloside IV hydrogel on skin appendages formation was identified, which displayed the regenerative potential of astragaloside IV hydrogel on tissue repair. Compared with the astragaloside IV solution and hydrogel controls, astragaloside IV incorporated hydrogel was demonstrated to be a promising agent with the strongest healing efficacy and the characteristic for wound repair and skin appendages regeneration. Furthermore, in our preliminary study, compared with the blank control, it was found that the topical application of astragaloside
IV solution on rat wounds can significantly promote the regeneration of blood vessels in wound site. In present study, in contrast to the wide areas of dense dermis devoid of skin appendage with the characteristics of scar in blank control and gel control, the appendages (indicated in the white arrows) in the healed skins with the structures of blood vessels were identified in both the astragaloside IV solution and hydrogel treated groups.

CONCLUSIONS

Results of the present study provided the novel evidence for the local effect of astragaloside IV on wound healing upon topical application. The great potential of alginate blended gelatin based carrier as the topical drug delivery vehicle with good biocompatibility and healing feature for wound healing, as well as the regenerative effects of astragaloside IV incorporated hydrogel for wound healing were firstly demonstrated, which provided the proofs for their applications in the tissue repair and regeneration. For the first time, the stimulation of sodium alginate and gelatin based hydrogel and/or the astragaloside IV in the TGF-β1 secretion were reported, which deserve further investigation from molecular level.

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REFERENCES


