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Development of a Liquid Bandage Containing Rhubarb and Borneol

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Abstract: To address the limitations of traditional adhesive bandages such as poor air permeability, insufficient adaptability, and single function, this study developed a novel liquid bandage using rhubarb and borneol as core raw materials, polyvinyl butyral as the film-forming matrix, combined with glycerol and diethyl phthalate. The preparation process was optimized via $L_9(3^4)$ orthogonal experiment, with film-forming time, film adhesion, and 24-hour emodin dissolution rate as evaluation indicators to determine the optimal process parameters. The product's film-forming performance, antibacterial activity, skin safety, and wound healing-promoting effect were systematically investigated. Results showed that the optimal process parameters were: rhubarb extract concentration of 12%, borneol concentration of 1.5%, and film-forming temperature of 45 °C. Under these conditions, the product had a film-forming time of 3.2 ± 0.3 min, film adhesion of 3.8 ± 0.2 N, and 24-hour emodin dissolution rate of 86.7 ± 1.6%. Performance evaluation indicated that the product exhibited excellent water resistance, antibacterial activity, hemostatic effect, and high stability. This liquid bandage achieves efficient integration of traditional Chinese medicine efficacy and modern film-forming technology, holding promising application prospects in the field of wound care.

Keywords: Liquid bandage; Rhubarb; Borneol; Orthogonal experiment; Wound healing

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1. Introduction

As a core material for daily trauma care, bandages have long dominated the household care market due to their portability, simplicity of operation, and low cost [1,2]. However, traditional adhesive bandages have three core limitations: first, poor air permeability easily leads to wound moisture and bacterial growth, triggering secondary infections; second, insufficient adaptability causes easy detachment during limb movement, failing to form a continuous protective barrier; third, single function only achieves physical isolation, lacking active antibacterial, anti-inflammatory, and healing-promoting therapeutic effects, which is difficult to meet the care needs of complex wounds [3,4]. As a new type of wound care material, liquid bandage rapidly forms a transparent film after spraying or smearing on the wound, integrating both physical protection and drug therapy, effectively making up for the defects of traditional products. Moreover, it can adaptively extend with skin deformation, perfectly fitting movable parts such as joints [4].

Traditional Chinese medicine (TCM) has inherent advantages of "multi-component and multi-target" in wound care: rhubarb is rich in anthraquinone compounds such as emodin and rhein, and modern pharmacological studies have confirmed that its inhibition rate against common wound pathogens such as *Staphylococcus aureus* and *Escherichia coli* can reach more than 85%, reducing wound redness and swelling; borneol can expand transdermal absorption channels and alleviate wound pain and discomfort [5,6]. Some previously reported TCM liquid bandages have obvious wound stinging sensation due to high ethanol content, affecting user experience [7]. Based on this, this study used polyvinyl butyral as the film-forming matrix and glycerol as the plasticizer, optimizing the compound ratio of rhubarb and borneol and the preparation process via orthogonal experiment, aiming to develop a novel liquid bandage with rapid film formation, safety, painlessness, efficient antibacterial activity, and healing-promoting function.

2. Materials and methods

2.1. Experimental materials

2.1.1. Medicinal materials and reagents

(a) Rhubarb
Purchased from Beijing Tongrentang (Group) Co., Ltd., Batch No. 2023100;

(b) Borneol
Purchased from Shanghai Pharmaceutical Group Co., Ltd., Batch No. 20231002;

(c) Polyvinyl butyral
Purchased from Sinopharm Chemical Reagent Co., Ltd.;

(d) Glycerol, diethyl phthalate
Purchased from Jiangsu Yurun Biomedical Co., Ltd.

2.1.2. Instruments and equipment

(a) Electronic balance (ME204E)
Mettler Toledo Instruments (Shanghai) Co., Ltd.;

(b) Constant temperature water bath (HH-S4)
Shanghai Yiheng Scientific Instruments Co., Ltd.;

(c) Rotary evaporator (RE-52AA)
Shanghai Yarong Biochemical Instrument Factory.

2.2. Experimental methods

2.2.1. Preparation of rhubarb extract

The ethanol reflux extraction method was used to optimize the extraction process of active components from rhubarb: rhubarb medicinal materials were crushed and passed through a 40-mesh sieve; 10.0 g was accurately weighed, and 70% ethanol was added at a solid-liquid ratio of 1:10. The mixture was placed in a round-bottom flask and reflux extracted in a constant temperature water bath at 60 °C for 2 h, then filtered while hot with double-layer qualitative filter paper to remove residues [8]. The filtrate was concentrated to a relative density of 1.20 using a rotary evaporator to obtain the rhubarb extract.

The emodin content in the extract was determined by HPLC: chromatographic column was Agilent ZORBAX SB-C18; mobile phase was methanol 0.1% phosphoric acid solution (85:15, v/v); detection wavelength was 254 nm; column temperature was 30 ℃; flow rate was 1.0 mL/min; injection volume was 10 μL. Results showed that the emodin content in the rhubarb extract was 1.12 mg/mL.

2.2.2. Preparation of borneol solution

10.0 g of borneol was accurately weighed, dissolved in anhydrous ethanol to a constant volume of 100 mL, and stirred at room temperature on a magnetic stirrer for 15 min until completely dissolved, preparing a 10% (w/v) borneol ethanol solution [9].

2.2.3. Preparation of film-forming matrix

Raw materials were weighed according to the basic formula: polyvinyl butyral 15%, glycerol 2%, diethyl phthalate 0.5%, and purified water 82.5%. Polyvinyl butyral was slowly added to purified water, stirred in a constant temperature magnetic stirrer at 50 ℃ for 2 h until completely dissolved to form a transparent viscous solution; glycerol and diethyl phthalate were then added, and stirring was continued for 30 min to mix uniformly; the mixture was left to stand at room temperature for 30 min to remove bubbles, obtaining the film-forming matrix.

2.2.4. Compound process of rhubarb-borneol liquid bandage

Rhubarb extract and borneol solution were added to the film-forming matrix at a ratio of 3:1, stirred on a magnetic stirrer at room temperature; the mixture was filtered through a 0.22 μm microporous membrane and dispensed into brown light-proof spray bottles to obtain liquid bandage samples.

2.2.5. Optimization design of preparation process

Based on single-factor preliminary experiments, three key influencing factors were selected, and the process was optimized using $L_9(3^4)$ orthogonal experimental design, with 3 levels set for each factor. The experimental design and levels were shown in **Table 1**. Film-forming time (Y_1, min), film adhesion (Y_2, N), and 24-hour emodin dissolution rate (Y_3, %) were used as evaluation indicators. Each experimental point was repeated 3 times, and the average value was used for data analysis.

Table 1. Factors and levels of L9 (34) orthogonal experiment

Level	Factor A: Rhubarb extract concentration (%)	Factor B: Borneol concentration (%)	Factor C: Film-forming temperature (℃)
1	8	1.0	35
2	10	1.5	45
3	12	2.0	55

2.2.6. Determination methods of evaluation indicators

(1) Film-forming time determination

A clean glass slide was taken, and 50 μL of sample was accurately pipetted and uniformly spread on the slide surface. The slide was placed in a constant temperature and humidity chamber with set temperature and 50% relative humidity, and a stopwatch was used to record the time from completion of smearing to complete drying of the film [10].

(2) Film adhesion determination

Fresh pigskin was taken, and the sample was uniformly spread on the pigskin surface, then dried to form a film at the corresponding film-forming temperature; a digital display tensile testing machine was used to determine the 180° peel strength between the film and pigskin, with a tensile speed of 10 mm/min and a sensor range of 10 N. The maximum force during peeling was taken as the film adhesion [11].

(3) 24-hour emodin dissolution rate determination

The dialysis bag method was used to simulate the in vivo drug release process. 2 mL of sample was accurately pipetted into a dialysis bag, sealed and immersed in 50 mL of PBS, and oscillated in a constant temperature water bath at 37 °C; 5 mL of sample was taken at 1, 2, 4, 6, 8, 12, and 24 h respectively. After filtering through a 0.22 μm membrane, the emodin concentration was determined by HPLC, and the 24-hour dissolution rate was calculated.

(4) Dissolution rate calculation formula

24-hour emodin dissolution rate (%) = (Total cumulative emodin dissolved within 24 h / Initial total emodin in sample) × 100%

2.2.7. Product performance evaluation

(1) Physical performance evaluation

Appearance: The color, clarity, and film transparency of the sample were observed with the naked eye; pH value: The pH value of the sample was determined with a pH meter, repeated 3 times in parallel; Stability: Samples were stored at 4 °C, 25 °C, and 40 °C for 30 d, observed every 5 d to record whether stratification, precipitation, or discoloration occurred.

(2) Wound healing-promoting experiment

Two healthy SD rats were selected, and wounds were created on their tails. Three groups were set: blank control group (normal saline) and sample group (this study's product). Wounds were cleaned with sterile normal saline and hemostasis was performed. Treatment methods for each group including blank control group: 0.1 mL of normal saline was applied with a sterile cotton swab daily; sample group: 0.1 mL of the product was applied with a sterile cotton swab daily. Then, wounds were photographed with a camera after medication to record the repair effect.

3. Results and analysis

3.1. Optimization results of preparation process

3.1.1. Orthogonal experiment results and range analysis

The results and range analysis of the $L_9(3^4)$ orthogonal experiment was shown in **Table 2**. Range analysis indicated that the order of influence of each factor on film-forming time (Y_1) was: C (film-forming temperature) > A (rhubarb extract concentration) > B (borneol concentration). Comprehensive consideration of the three evaluation indicators determined the optimal process parameters as $A_3B_2C_2$, i.e., rhubarb extract concentration of 12%, borneol concentration of 1.5%, and film-forming temperature of 45 °C.

Table 2. Results and range analysis of L9(34) orthogonal experiment

Experiment No.	A	B	C	D	Film-forming time Y_1 (min)	Film adhesion Y_2 (N)	Emodin dissolution rate Y_3 (%)
1	1	1	1	1	4.8 ± 0.4	3.2 ± 0.2	75.3 ± 1.8
2	1	2	2	2	3.9 ± 0.3	3.4 ± 0.2	81.5 ± 1.6
3	1	3	3	3	3.1 ± 0.2	3.5 ± 0.2	83.2 ± 1.5
4	2	1	2	3	3.7 ± 0.3	3.5 ± 0.2	78.6 ± 1.7
5	2	2	3	1	2.9 ± 0.2	3.7 ± 0.2	85.4 ± 1.4
6	2	3	1	2	4.5 ± 0.3	3.6 ± 0.2	82.1 ± 1.6
7	3	1	3	2	3.0 ± 0.2	3.7 ± 0.2	80.2 ± 1.5
8	3	2	1	3	4.2 ± 0.3	3.9 ± 0.2	84.5 ± 1.3
9	3	3	2	1	2.8 ± 0.2	3.8 ± 0.2	87.1 ± 1.4
K_1	3.93	3.83	4.50	5.45	-	-	-
K_2	3.17	3.67	3.47	4.64	-	-	-
K_3	3.33	3.13	2.93	3.11	-	-	-
R	0.76	0.70	1.57	2.34	-	-	-

Note: K is the average value of indicators at the same level of each factor; R is the difference between the maximum and minimum K values under the same indicator.

3.1.2. Verification experiment

To verify the reliability of the optimal process, 3 batches of samples were prepared according to the $A_3B_2C_2$ parameters, and film-forming time, film adhesion, and 24-hour emodin dissolution rate were determined. Results showed that the film-forming time of the 3 batches of samples was (3.2 ± 0.3) min, film adhesion was (3.8 ± 0.2) N, and 24-hour emodin dissolution rate was (86.7 ± 1.6%), with relative standard deviation (RSD) < 5%, indicating stable and reliable process with good repeatability.

3.2. Product performance evaluation results

3.2.1. Physical performance

(a) Appearance and film thickness

The sample was a pale-yellow transparent liquid without turbidity or precipitation; after drying, it formed a uniform and transparent film with a smooth surface free of pores or spots (**Figure 1**).

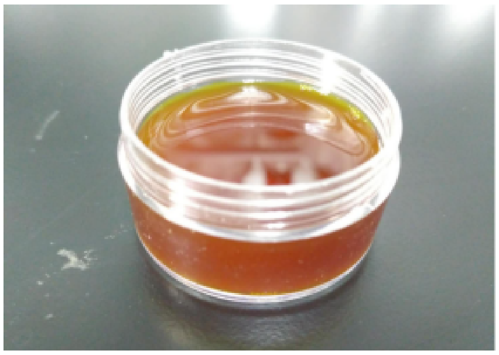

Figure 1. Rhubarb-borneol liquid bandage sample.

(b) pH value

The pH value of the sample was (6.8 ± 0.2), which was within the skin tolerance range (6.0–7.5), reducing irritation to the wound.

(c) Stability

Samples stored at 4 °C and 25 °C for 30 d showed no stratification, precipitation, or discoloration; the film-forming time change rate was 8.5%, and the film adhesion change rate was 7.2%, both ≤ 10%; slight stratification occurred after storage at 40 °C for 15 d, indicating that the sample should be stored at room temperature or refrigerated to avoid high temperatures.

3.2.2. Wound healing-promoting effect

Figures 2a1 and **2a2** were hemostasis photos of mice treated with normal saline; it was seen from **Figure 2a2** that blood still flowed out after applying normal saline to mice with tail injuries. **Figures 2b1** and **2b2** were hemostasis photos of mice treated with the rhubarb-borneol liquid bandage; it can be seen that bleeding stopped after applying the product to mice with tail injuries. This indicates that the rhubarb-borneol liquid bandage has a good hemostatic effect and can promote wound healing.

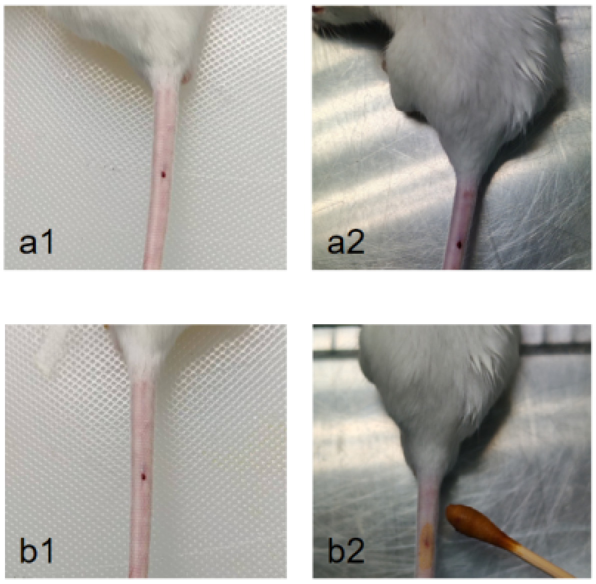

Figure 2. Hemostasis photos of the rhubarb-borneol liquid bandage.

4. Discussion

4.1. Film-forming mechanism

As the film-forming matrix, polyvinyl butyral can form a three-dimensional network structure through hydrogen bonds between hydroxyl groups on its molecular chain, forming a continuous and transparent film [11]. Glycerol, as a plasticizer, can insert between polyvinyl butyral molecular chains, weakening intermolecular forces, reducing the glass transition temperature of the film, and improving flexibility; diethyl phthalate further enhances film ductility by forming ester bonds with polyvinyl butyral, avoiding film breakage during joint movement [12].

4.2. Synergistic mechanism of rhubarb and borneol

The synergistic effect of rhubarb and borneol is the core of the product's function.

(1) Antibacterial synergy

Emodin destroys bacterial cell membrane integrity, causing leakage of intracellular substances; borneol enhances bacterial cell membrane permeability, promoting emodin entry into bacteria, together improving bactericidal efficiency. Experiments showed that the compound antibacterial rate was 15–20% higher than that of rhubarb alone.

(2) Penetration-promoting synergy

D-borneol in borneol changes the lipid arrangement of the skin stratum corneum, forming "temporary channels" to promote transdermal absorption of emodin

(3) Anti-inflammatory and analgesic synergy

Emodin reduces wound redness and swelling by inhibiting the release of inflammatory factors; borneol activates skin cold receptors, producing a cool sensation to mask wound pain and improve user comfort [13,14].

4.3. Advantage comparison with traditional bandages

Compared with traditional adhesive bandages, the rhubarb-borneol liquid bandage developed in this study has significant advantages.

(1) Better adaptability

The film can adaptively extend with skin deformation, achieving higher coverage on irregular parts such as finger joints and finger gaps

(2) More comprehensive functions

Integrating physical protection and drug therapy, while traditional bandages only achieve physical protection

(3) Higher safety

No adhesive, avoiding allergic reactions, suitable for people with sensitive skin

(4) Better user experience

The transparent film does not affect appearance, has good air permeability, and avoids wound moisture [15]

4.4. Research limitations and improvement directions

This study has the following limitations

(1) The stability study only lasted 30 d, and the impact of long-term storage (> 3 months) on components and performance needs further investigation

(2) The wound healing-promoting experiment only used rat models, and the applicability to human wounds (such as diabetic foot ulcers and pressure ulcers) requires clinical research verification

(3) The inhibitory effect of the product on fungi was not investigated, failing to cover the care needs of fungal wounds

Future research can be improved from three aspects

(1) Adding antioxidants and stabilizers to extend the product shelf life

(2) Conducting multi-center clinical trials to verify the product's efficacy in different types of human wounds

(3) Introducing antifungal components to expand the product's application range

5. Conclusion

In this study, a novel rhubarb-borneol liquid bandage was successfully developed using polyvinyl butyral as the film-forming matrix, and rhubarb and borneol as core active components. The preparation process was optimized via $L_9(3^4)$ orthogonal experiment. The optimal process parameters were rhubarb extract concentration of 12%, borneol concentration of 1.5%, and film-forming temperature of 45 °C. Under these conditions, the product had rapid film formation (3.2 ± 0.3 min), good film adhesion (3.8 ± 0.2 N), and high emodin dissolution rate (86.7 ± 1.6%).

This study achieves effective integration of traditional Chinese medicine and modern film-forming technology, providing a practical scheme for the innovation of wound care materials. The product has wide raw material sources, simple preparation process, and controllable cost, with industrialization potential. It is expected to become an upgraded alternative to traditional bandages, offering a new choice for clinical trauma care and family health management.

Disclosure statement

The authors declare no conflict of interest.

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