Study on the preparation technology of Sanqi Shangyao gel plasters for percutaneous absorption

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Abstract: Objective: To optimize the preparation technology and matrix ratio of Sanqi Shangyao gel plasters. Methods: The effects of sodium polyacrylate, gelatin and sodium carboxymethyl cellulose on the matrix formability of gel plasters were investigated by L_9 (3^3) orthogonal test, and the optimum ratio of matrix was optimized by examining the formability, appearance of the dosage form, heat resistance, initial viscosity and human body sense. Results: Through the analysis of the orthogonal test and the results, Sanqi Shangyao gel plasters was superior with sodium polyacrylate 4g, sodium carboxymethyl cellulose 3g, gelatin 4g when the proportion of other matrix is fixed. Conclusion: Sanqi Shangyao gel plasters is stable, easy to adhere and no discomfort during strippingaccording to the technology and matrix ratio determined by orthogonal test.

1. Introduction

Gel plasters refer to the adhesive plasters prepared by mixing the extract, fine powder of decoction pieces and chemicals with appropriate hydrophilic matrix and coating on the backing material. It has the following characteristics: (1) It displays high drug loading; (2) In the preparation, the drug release performance is good and the gastrointestinal irritation is small; (3) The dosage is accurate, the blood concentration is balanced, and the side effects are small; (4) It is easy to use and can be stopped at any time and applied repeatedly [1]. However, there is no report about the gel plasters changed from Sanqi Shangyao tablet, so the research group chose to study it in order to expand the way of administration.

2. Methods and results

2.1. Prescription Optimization

2.1.1. Single factor test.

(1) Add sodium carboxymethyl cellulose to the purified water to fully swell; (2) Add gelatin to a proper amount of purified water and put it on a 55℃water bath until until it was completely dissolved; (3) Disperse sodium polyacrylate in appropriate amount of propylene glycol. Mix (1) (2) (3) and mix well. Take an appropriate amount of Sanqi Shangyao extract dissolved in water and add the matrix to stir evenly, then apply it on the non-woven cloth and cover with embossed membrane.The research group carried out a number of single-factor experiments and obtained the approximate formula ratio of gel plasters matrix. The effect was better when sodium polyacrylate was 3-4g, sodium carboxymethyl cellulose was 1-3g and gelatin was 2-6g. According to the results of pre-test to determine the matrix dosage range of the orthogonal test.

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2.1.2. Orthogonal test design.

On the basis of pre-test, L_9 (3^3) test is used to design the level table of orthogonal factors. The levels and factors of orthogonal test were shown Table 1.

Table.1. Factors and levels of orthogonal test

Levels	Factors		
	Sodium polyacrylate (g) A	Sodium carboxymethyl cellulose (g) B	Gelatin (g) C
1	3	1	2
2	4	2	4
3	5	3	6

2.1.3. Quality evaluation and scoring standards

2.1.3.1. Formability

One piece of the sample was taken and placed in a constant temperature and humidity box of 64% relative humidity at 37℃ for 30 minutes. After it was taken out, the sample was fixed on a flat steel plate with a clamp, the inclination angle between the steel plate and the horizontal plane was 60°, and it was placed for 24 hours [2]. Score according to the phenomenon and degree of flow on the surface of the gel plasters. The full score was 20 points.

2.1.3.2. Appearance

The paste of the gel plasters should be coated evenly, and the paste surface should be smooth and clean, and consistent of color, and the paste should not remove the paste and lose adhesion; The backing should be flat, clean and no leakage of ointment. Score according to the above situation and its degree. The full score was 20 points.

2.1.3.3. Heat resistance

Take two pieces of sample and remove the cover lining and heat it at 60 ℃ for 2 hours. After cooling, the backing should have no oil leakage; The paste surface should be shiny, and the finger touch test should still be sticky. Score according to the above situation and its degree. The full score was 20 points.

2.1.3.4. Initial adhesion [2]

It was measured by slope rolling ball. The stainless steel ball was rolled over the adhesive surface of the test sample placed on the inclined 30° plate, and the initial adhesion was evaluated according to the largest steel ball which the viscous surface could stick. The total score was 20 points. In three pieces of samples, two or more pieces should be able to stick the steel ball in the test section. If one piece could not stick, it should be able to stick with a smaller steel ball for test. If only one piece could stick to the steel ball, and the other two pieces could only stick to the smaller steel ball, another three pieces should be taken for retest, and all three pieces samples could stick to the steel ball,then the quality of the product was considered to be in conformity with the regulations.

2.1.3.5. Human senses

It could adhere to the skin surface independently, the adhesive force should be within the acceptable range of the human body, and there should be no residue and discomfort after stripping [3]. The full score was 20 points.

2.2. Results of orthogonal test

Table.2. Results of orthogonal test

Serial number	A	B	C	Total score
1	3	1	2	46
2	3	2	4	64
3	3	3	6	60
4	4	1	4	84
5	4	2	6	80
6	4	3	2	92
7	5	1	6	64
8	5	2	2	52
9	5	3	4	62
K_1	170	194	190	
K_2	256	196	210	
K_3	178	214	204	
k_1	56.67	64.67	63.33	G=604 CT=40535.11
k_2	85.33	65.33	70	
k_3	59.33	71.33	68	
R	28.66	6.67	6.67	

2.3. Analysis of variance results

Table.3. Analysis of variance results

Source of variance	Sum of squares from mean deviation	Degree of freedom	Variance	F	P
A	1504.89	2	752.44	21.43	< 0.05
B	80.89	2	40.44	1.15	
C	70.22	2	35.11		
Error (e=C)					

$F_{0.05}(2,2)=19.00$ $F_{0.01}(2,2)=99.00$

The results of analysis of variance results showed that only factor A, that is, the amount of sodium polyacrylate had a significant effect on the test results, while factor B and factor C, namely the amount of sodium carboxymethyl cellulose and gelatin, had no significant effect on the test results. However, the analysis of variance results showed that although factor B did not have a significant impact on the test results, its influence ability was still obvious in the analysis. Combined with the analysis of the results of orthogonal test, the best process combination for the preparation of Sanqi Shangyao gel plasters is $A_2B_3C_2$, that is, 4g sodium polyacrylate, 3g sodium carboxymethyl cellulose, 4g gelatin. Factor B and factor C could be adjusted according to the actual situation.

3. Verification test

Three batches of gel plasters matrix are prepared according to the optimum matrix ratio, and then an appropriate amount of medicine is mixed evenly to get Sanqi Shangyao gel plasters, and the gel plasters are evaluated as a whole. It is proved that it is basically consistent with the technology selected by orthogonal test in the aspects of formability, appearance of dosage form, heat resistance, initial adhesion, human senses and so on.

4. Conclusion

Compared with the traditional black plaster, gel plasters have the following advantages: (1) It displays high drug loading, and it is especially suitable for traditional Chinese medicine extract; (2) It

has good biocompatibility with skin, breathability, perspiration resistance, non sensitization and non irritation; (3) It is easy to use, no pollution to clothes, easy to wash, and sticky repeatedly, and so on. It has many advantages compared with traditional black plaster, but also has its shortcomings: (1) There is no clear and stable process for the preparation of gel plasters of traditional Chinese medicine to follow. Therefore, it is necessary to explore and select the appropriate preparation process according to the nature of traditional Chinese medicine; (2) There is no effective method to eliminate the material loss caused by its viscosity in the preparation of gel plasters matrix. Matrix and penetration enhancer are also the key factors in the formation of gel plasters, so the research on gel plasters matrix and penetration enhancer should be more in-depth and extensive.

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References

[1] Fu CM.Pharmaceutics of Chinese Materia Medica [M].Beijing. China Medical Science and Technology Press, 2014: 207.

[2] Zhang SJ, Liu L, Guo JB, et al. Preparation of TCM Cataplasms of Cross-linkded Hydrogel Matrix [J]. Modern Chinese Medicine, 2015, 17 (6): 587-589.

[3] Zhu DF, Yang DK. Study on Preparation of Xiaoyan Zhentong Cataplasm [J]. Chinese Journal of Experimental Traditional Medical Formulae, 2010, 16 (10): 26-29.