

# Study on the wound healing, anti-inflammation and anti-bacterial activities of Jinjianling cream: A Chinese herbal compound

Wu Zhao, Rongrong Zhang, Cuixia Ma, Mingyang Qiu, Peihan Gong, Yuting Liu, Shuai Shao, Mingming Yan\* and Daqing Zhao

Changchun University of Chinese Medicine, Changchun, People's Republic of China

**Abstract:** The aim of the present study was the healing effect and anti-inflammatory effect of Jinjianling cream on skin lesions and to investigate the antibacterial activity *in vitro*, which proved that the preparation is safe and effective. The mouse scald model was established to observe the wound healing time and wound healing rate of mice, serum levels of TNF- $\alpha$  and IL-1 were measured by the ELISA method. The model of eczema in mice was induced by DNCB, and the degree of ear swelling in mice was calculated. The hematoxylin-eosin (HE) staining was used to make pathological sections and count inflammatory cells, and the change of serum IL-2 level was determined by the ELISA method. The bacteriostasis rate was determined by pour plate method, the diameter of inhibition zone (DIZ) was determined by filter paper diffusion method and the minimum inhibitory concentration (MIC) was determined by double dilution method. After treatment, the effect of Jinjianling cream groups on the healing of damaged skin in scalded mice was significant. The serum levels of TNF- $\alpha$  and IL-1 decreased, which were lower than those in the model group ( $p < 0.05$ ,  $p < 0.01$ ). In the mouse eczema model, the degree of ear swelling improved significantly, serum IL-2 level was decreased, and inflammatory cell count was significantly lower than the model group ( $p < 0.05$ ,  $p < 0.01$ ). The results of antibacterial experiments showed that bacteriostasis rate was positively correlated with drug concentration. DIZ values of bacteriostatic circle on *Staphylococcus aureus* and *Escherichia coli* were 17.25mm and 25.62mm. Moreover, the MIC values of two kinds of bacteria all were 64 $\mu$ g/mL. Jinjianling cream can promote the healing ability of damaged skin and reduce inflammation of the wound. It also has a strong inhibitory effect on wound pathogenic bacteria, can significantly improve wound healing and effectively treat dermatitis, eczema and other skin diseases.

**Keywords:** Chinese herbal compound, promote healing, anti-inflammatory, anti-bacterial.

## INTRODUCTION

Skin is the largest organ of the body, always involved in the body's functional activities, as the first physiological defense of human body, which protects various tissues and organs from physical, mechanical, chemical and pathogenic microbial invasion. Therefore, the skin bears the threats of multiple factors *in vivo* and *in vitro*, resulting in skin damage and causing various skin diseases. Scald is one of the most common cutaneous lesions in the routine life and its incidence rate is rising year by year (Wang *et al.*, 2013). And the process of wound healing is characterized by hemostasis phase, inflammatory phase, the epithelial and proliferative phase, and the tissue remodeling phase (Gosain *et al.*, 2004; Suguna *et al.*, 2002). Wound healing is a complex and biological process involving two main roles, namely fight against infection and repair of tissue (Guo *et al.*, 2010). The healing mechanism is related to many cytokines, including inflammatory cytokines interleukin-1 (IL-1), interleukin-6 (IL-6), etc. In addition, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) also plays an important role in the inflammatory response and participates in the whole process (Fry, 2000). Atopic dermatitis (AD) is a common recurrent inflammatory skin

disease that frequently presents with symptoms such as itching, erythema and eczema (Flohr *et al.*, 2000), the skin will be damaged seriously, and resulting in inflammatory reaction including the release of inflammatory media and Th1 cells, such as interleukin-2 (IL-2), which plays an important regulatory role throughout the reaction (Gao *et al.*, 2004; Furue *et al.*, 2004). Moreover, the proliferation of CD4<sup>+</sup> T cells is observed in AD patient (Bradding *et al.*, 1993; Mican *et al.*, 1992; Laborel *et al.*, 2015). At different stages of AD, the number of inflammatory cells will change significantly (Wan *et al.*, 2016).

In these respects, various Chinese medicinal herbs have been reported in the treatment of trauma. *Coptis chinensis* Franch contains a large number of alkaloids such as berberine and coptisine. It has broad-spectrum antiviral and antibacterial effects, and has certain anti-inflammatory and analgesic effects. *Phellodendron amurense* Rupr. mainly contains berberine and phellodendrine, which has anti-inflammatory and anti-fungal effects. It also has a strong inhibitory effect on various cocci and bacilli. Curcumin is the main component of *Rhizoma Curcumae Longae*, which can improve microcirculation and promote blood circulation. The active ingredient of *Angelica sinensis* is ferulic acid,

\*Corresponding author: e-mail: 386759102@qq.com

which can improve local microcirculation, inhibits platelet adhesion, analgesic, anti-inflammatory and antibacterial activities *in vitro*.

The main ingredient of *Rehmannia glutinosa* is Catalpol, which has the functions of diuresis, hemostasis, anti hepatitis virus and so on, and it can reduce blood sugar level.

Like many Chinese herbal medicines, "Jinjianling cream" is also a mixture of natural product complexes. Its recipe is first described in one ancient Chinese book of medicine, The Golden Mirror of Medicine, published in 1742. This study was based on the Chinese herbal medicine of this prescription, including *Coptis chinensis*, *Phellodendron*, turmeric, Chinese angelica and *Rehmannia glutinosa* and the innovation and optimization of preparation process were carried out, developed a kind of external preparations of traditional Chinese medicine. Through the establishment of mouse scald model and mouse eczema model, skin injury was investigated, then investigated antibacterial activity *in vitro*. The results of this paper are intended to provide a theoretical basis for the application and development of external preparations of traditional Chinese medicine and assist the clinical pharmacological studies.

## MATERIALS AND METHODS

### Experimental materials

Sodiumsulfide,2,4-Dinitrochlorobenzene (DNCB) was bought from Sigma, America; Sulfadiazine silver cream was bought from Kunming torch Pharmaceutical (Group) Co., Ltd.; Compound dexamethasone acetate cream was bought from Shenzhen China Resources Gosun Pharmaceutical Co. Ltd., TNF- $\alpha$ , IL-1 and IL-2 were bought from BD, America; *Escherichia coli* strain (ATCC8739) and *Staphylococcus aureus* strain (ATCC6538) were purchased from Jilin University Laboratory; All other chemicals and reagents used in this study were of analytical grade.

### Animals

BALB/c mice were purchased from Hongda Biological Technology Co. Ltd., all male, at the beginning of the study, all were about 6 weeks, they were maintained at 23 $\pm$ 1 $^{\circ}$ C, with a relative humidity of 45-55% and 12:12h dark/light cycle with free access to standard rodent food and water. The animals were treated in accordance with the current national guidelines on animal care and use.

### Extraction process

According to the pre-experiment, the optimal parameters of the extraction process were optimized to get the best extraction scheme, *Coptis chinensis* 32.5g, *Phellodendron* 48.8g, turmeric 48.8g, added with 10 times weight of 70% ethanol to extract 3 times, each time 1h, the filtrate was collected, concentrated and dried. After the medicinal

herbal residues were dried, mixed with Angelica 32.5g and *Rehmannia glutinosa* 195g, added with 8 times weight distilled water to extract 3 times, each time 1h, the filtrate was collected and concentrated to dryness.

### Formability process

Stearic acid 100g, monoglyceride 50g, white petrolatum 50g and liquid paraffin 50g, heated to melt, in addition, 150g of glycerin and 500mL of distilled water were heated to 85 $^{\circ}$ C, added with 10g of sodium lauryl sulfate and 2g of ethylparaben to dissolve, put the extract in it and mixed well, the aqueous phase was slowly added to the oil phase, stirring until fully emulsified to condense.

### Group and therapy of scald models

24 hours before the experiment, 100 mice were depilated with 10% sodium sulfide solution on the back and injected with 1% pentobarbital (0.5ml/10g) intraperitoneally before modeling. The 50g weight was placed in boiling water for 10 min, quickly placed on the back of the mouse skin for 8s. That can form an area of 2 cm $\times$ 2 cm deep second degree scald model. The mice were randomly divided into five groups of twenty animals each (n=20), as follows:

Model group: mice treated with 0.9% saline. Positive control group: mice treated with compound sulfadiazine silver cream 0.1g. Low dose group: equivalent 178.8g/kg dosage, mice treated with Jinjianling cream 0.1g. Medium dose group: Equivalent 357.6g/kg, mice treated with Jinjianling cream 0.1g. High dose group: equivalent 715.2 g/kg, mice treated with Jinjianling cream 0.1g. Each group was dosed twice daily, continuous administration for 28 days. (Wound healing standards: the wound scab off and the epithelial new formation. 28 days unhealed were recorded for 28 days) Wound healing rate: 1, 7, 14, 21 days after scald with a sulfuric acid transparent paper to describe the wound, Cut and weigh, replacing the area with quality. Wound healing rate (%)= (Original burns area- the area that did not heal at each time point) / Original burns area $\times$ 100 Cytokines: At 24 and 48h after scalded, mice were sacrificed by cervical dislocation, the samples were centrifuged at 3500r/min for 15min and the supernatant was taken at below minus 20 centigrade for preservation. The serum levels of TNF-a and IL-1 were determined by the ELISA method and the specific procedures were operated according to the kit instructions.

### Group and therapy of eczema model

A schematic procedure of the topical application of Jinjianling cream to mice is shown in fig. 1. One day before the experiment, 60 mice were depilated with 10% sodium sulfide solution, then formed the area with area of 2cm $\times$ 2 cm on the back skin. After 24 hours, 7% DNCB 100 $\mu$ L was coated on the depilated skin of each mice for sensitization, sensitized once a day, continuing for 3 days,

after 5 days, 0.1% DNCB 10 $\mu$ L were coated in the interior right ears to challenge and sensitize, once every 3 days, totally for 4 times (except for the blank group). Each time after stimulation of 24h, 48 h and 72h, each group was coated with drugs in the interior right ear of mice, administration in the morning and afternoon everyday. The mice were randomly divided into six groups of ten animals each (n=10), as follows:

Blank group: mice treated with vehicle cream 0.1g. Model group: Mice treated with vehicle cream 0.1g. Positive control group: Mice treated with compound dexamethasone acetate 0.1g. Low dose group: (equivalent 178.8g/kg dosage), mice treated with Jinjianling cream 0.1g. Medium dose group: (equivalent 357.6g/kg dosage), mice treated with Jinjianling cream 0.1g. High dose group: (equivalent 715.2g/kg dosage), mice treated with Jinjianling cream 0.1g.

Swelling degree: 1 day of medication withdrawal after the end of the treatment, mice were sacrificed by cervical dislocation. Tissues (holes with the diameter of 0.8mm) were punched at the same positions on each ear by the puncher. Weight difference between their left ears and right ears were calculated.

Inhibition rate (%) = (model group - drug group)/model group  $\times$  100 Cytokine: 1 day after medication withdrawal, mice were sacrificed by cervical dislocation, the samples were centrifuged at 3500 r/min for 15 min, and the supernatant was taken at below minus 20 centigrade for preservation. The serum levels of IL-2 were determined by the ELISA method, and the specific procedures were operated according to the kit instructions.

Inflammatory cell infiltration: 1 day after medication withdrawal, 5 mice in each group were randomly selected, and the right ear tissue was made into pathological sections, the number of infiltrating inflammatory cells was counted by HE staining, and the average was calculated (Kim *et al.*, 2012).

#### ***Antibacterial experiment in vitro colony count***

The experimental group was divided into the low dose group (equivalent 178.8g/kg dosage), medium dose group (equivalent 357.6g/kg dosage), high dose group (equivalent 715.2g/kg dosage). Each group was weighed with a specimen (cut into 1.0cm $\times$ 1.0cm size), evenly coated with drug 0.1g, the sample was placed in 250ml triangle bottle, adding 70mL PBS and 5mL bacteria suspension respectively, that the concentration of bacterial suspension in PBS was 1 $\times$ 10<sup>4</sup>~9 $\times$ 10<sup>4</sup>cfu/mL. The conical flask was fixed on a shaker, 300 r/min, shaking for 1h.

The 0.5mL sample solution was added to PBS for appropriate dilution and cultured with agar plate, then counted colony.

Bacteriostasis rate (%) = (A-B)/A $\times$ 100 A represents the average number of colonies before shaking; B represents the average number of colonies after shaking.

#### ***Diameter of inhibition zone (DIZ) measurement***

The filter paper was punched into a 5mm diameter disc, poured into the appropriate amount (about 4mm thick) sterilized medium (temperature about 45 $^{\circ}$ C), gently rotated the Petri dish, set aside to set the plate, set aside to concrete. The cultured bacteria were made into a suspension with a certain concentration. 1mL of the bacterial suspension was added to the sterilized Petri dish and daubed equably. The filter paper that coated with the quantitative drug (0.1g) was placed on the surface of a Petri dish. The diameter of the inhibition zone was measured with vernier caliper after culture at 37 $^{\circ}$ C for 24 h (Yum *et al.*, 2017).

#### ***Minimum inhibitory concentration (MIC) determination***

The samples were diluted into a series of double concentration gradients (0.5, 1, 2, 4, 8, 16, 32, 64, 128, 256 $\mu$ g/mL) by double dilution method, the samples were added to the test tubes, which containing 10mL medium, then added with 50 $\mu$ L of bacteria solution to each test tube and mixed thoroughly. All test tubes were cultured at 37 $^{\circ}$ C for 24h and maintained at the speed of 220r/pm for shaking. The minimum concentration of invisible turbidity by naked eyes in the test tube was MIC (Saha *et al.*, 2016).

#### ***Ethics approval***

The handle of experimental animals in the study was according to the Guide for the Care and Use of Laboratory Animal of the National Institute of Health as well as Guide of the Animal Welfare Act and approved by the Animal Ethics Committee of Changchun University of Chinese Medicine (approval No. SCXK 2017032).

## **STATISTICAL ANALYSIS**

All statistical comparisons were conducted using Student's t-test. SigmaPlot version 12.0 (SYSTAT software, USA) was used for statistical analysis. The results were expressed as mean  $\pm$  standard deviation. Differences between means were considered significant at P values of less than 0.05.

## **RESULTS**

#### ***Effect on scald model mice***

The healing performance of mice in each group was shown in fig. 2. All mice were cured within 28 days. The positive control group had the best healing effect, medium dose group and the high dose group also had a good therapeutic effect. The scar on the back of the mice became smaller and smaller with time until disappeared. The exposed skin on the back began to grow new hair and

**Table 1:** Wound healing rate and healing time of mice in each group (Mean ± SD)

Group	Dose (g/kg)	Healing rate (%)				Healing time (d)
		1 d	7 d	14 d	21 d	
Model	—	7.68±8.25	25.68±5.17	50.57±6.32	71.28±5.85	27.14±2.47
Positive control	—	15.16±6.84*	61.84±7.26**	83.78±6.93*	95.70±3.27**	19.26±1.62**
Low dose	178.8	8.79±2.32	38.69±2.88*	58.21±3.58	78.36±4.65	24.87±2.18
Medium dose	357.6	11.21±2.87*	42.23±4.64*	65.84±9.12*	82.67±5.67*	22.65±1.94*
High dose	751.2	14.28±3.68**	55.87±8.82**	74.24±3.67**	90.36±6.53**	18.12±2.36**

**Table 2:** TNF-α and IL-1 level of mice in each group (Mean ± SD)

Group	Dose (g/kg)	TNF-α (ng/L)		IL-1 (pg/L)	
		24h	48h	24h	48h
Model	—	545.18±70.14	410.50±90.17	2610.65±498.50	2270.48±189.30
Positive control	—	400.28±89.21*	268.35±78.88*	2055.48±159.25*	1578.64±358.55*
Low dose	178.8	461.20±65.68*	318.78±53.26*	2201.08±518.34	1889.58±378.26
Medium dose	357.6	408.35±105.57*	305.86±110.28**	2145.33±480.68	1650.78±405.28*
High dose	751.2	378.26±85.84**	238.63±102.32**	2058.25±360.26	1428.26±467.82*

**Table 3:** Degree of ear swelling of different mouse eczema model (Mean ± SD)

Group	Dose (g/kg)	Swelling degree (mg)	Inhibition rate (%)
Blank	—	0.13±0.09	—
Model	—	12.87±0.58	—
Positive control	—	4.62±0.63**	64.10±0.85
Low dose	178.8	9.21±0.27	28.43±0.48
Medium dose	357.6	7.38±0.55*	42.65±0.58
High dose	751.2	6.76±0.71**	47.47±0.75

**Table 4:** Cytokines and inflammatory cell of different groups (Mean ± SD)

Group	Dose (g/kg)	IL-2 (pg/mL)	Cell count (n)
Blank	—	12.44±0.32	0
Model	—	33.25±0.28	3.1±0.62
Positive control	—	16.64±0.35**	1.9±1.25*
Low dose	178.8	28.82±0.74	2.8±0.83
Medium dose	357.6	23.63±0.36*	1.9±0.75*
High dose	751.2	20.35±0.83*	1.5±0.14**

\*p<0.05, \*\*p<0.01 compared with model groups

**Table 5:** Bacteriostasis rate in each experimental group (Mean ± SD)

Group	Escherichia coli (%)	Staphylococcus aureus (%)
Low dose	64.28±2.48	64.54±3.66
Medium dose	76.47±0.87*	68.11±1.42
High dose	78.88±3.16*	83.32±1.54*

\*p<0.05, \*\*p<0.01 compared with low dose group

**Table 6:** The DIZ and MIC values of two kind bacteria

Group	DIZ (mm)	MIC (μg/mL)
<i>Escherichia coli</i>	17±1	64
<i>Staphylococcus aureus</i>	25±1	64



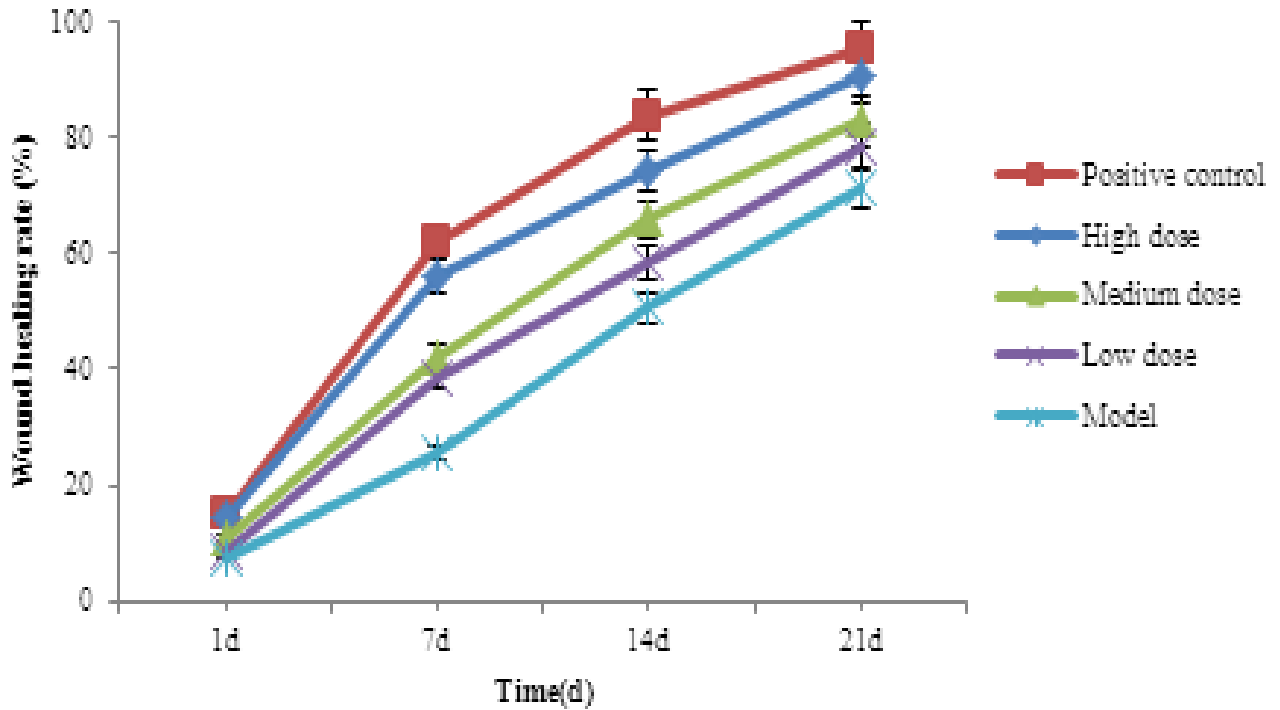


Fig. 3: Wound healing rate of mice in different groups

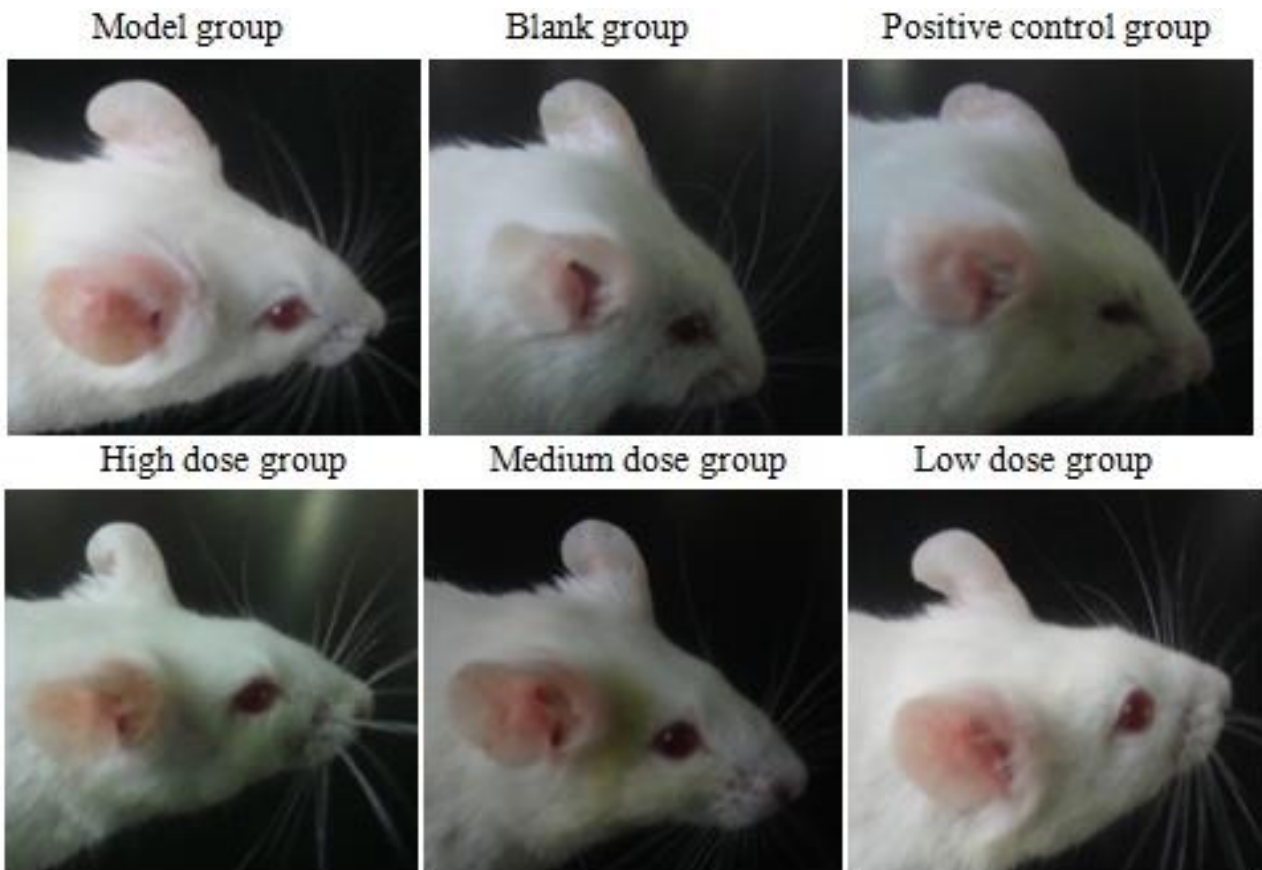


Fig. 4: The results of the treatment in each group of mice

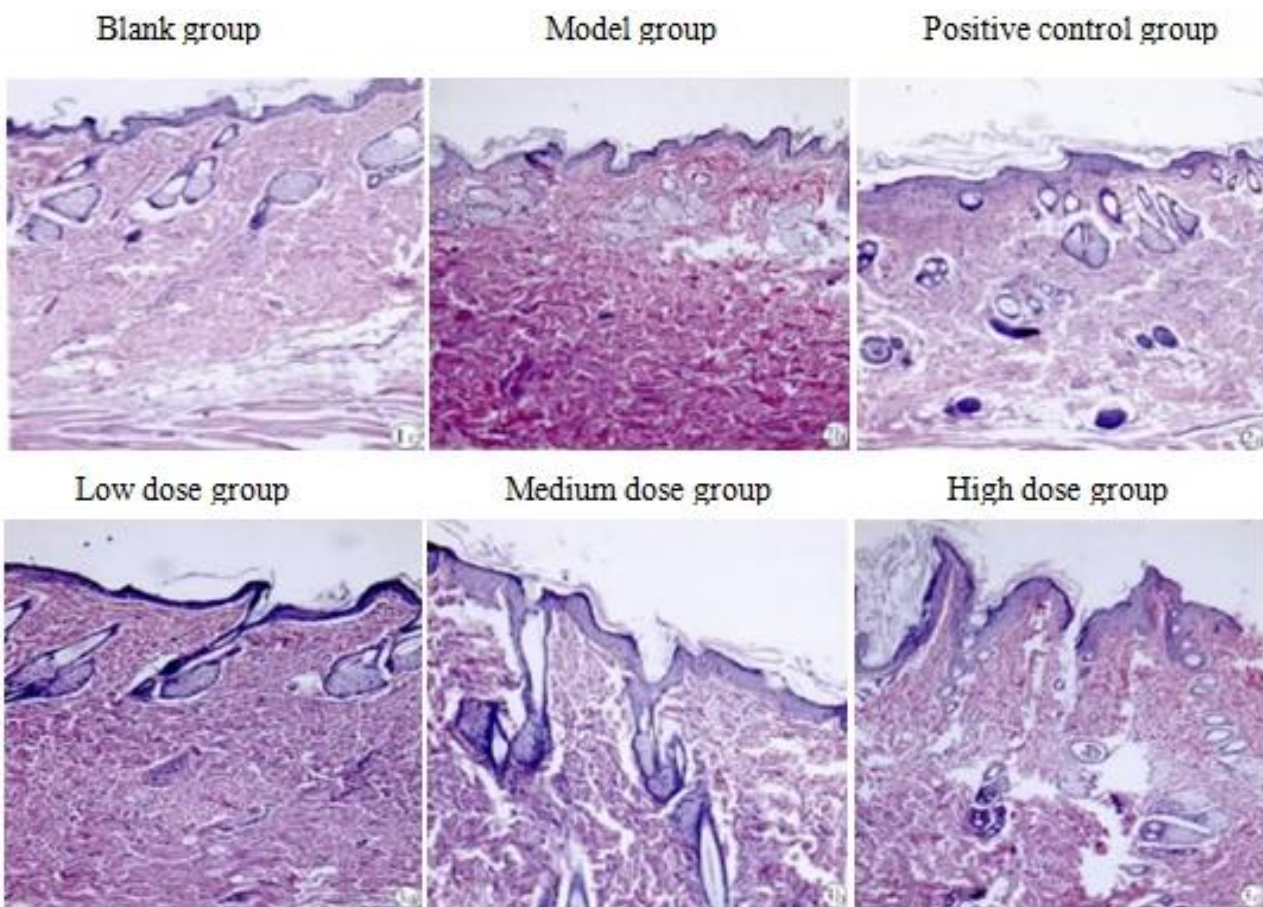


Fig. 5: Pathological sections of mice in each group (HE×200)

**Staphylococcus aureus:**



**Escherichia coli:**

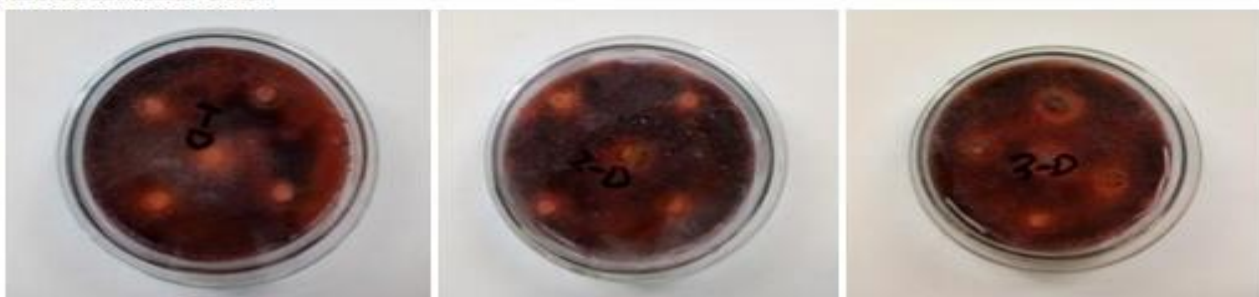


Fig. 6: Bacteriostatic effect of Jinjianling cream

became thick until covered the affected area. It was shown in table 1 that, compared with model group, the healing rate and healing time of positive control group, medium dose group and high dose group had the significant difference ( $p < 0.05$ ,  $p < 0.01$ ); and compared with positive control group, the difference of high dose group was not significant, that is consistent with the trend of healing in each group of mice as shown in fig. 3.

Cytokine changes of mice in each group were shown in table 2. 24, 48h after scald, compared with model group, the TNF- $\alpha$  level of positive control group and three dose groups decreased significantly ( $p < 0.05$ ,  $p < 0.01$ ); and 48 h after scald, the IL-1 level of positive control group, medium dose group and high dose group decreased obviously, compared with model group, they had the significant difference ( $p < 0.05$ ,  $p < 0.01$ ). The results showed that the Chinese medicine cream can inhibit the release of inflammatory mediators, reduce the inflammatory reaction of wound and promote wound healing.

#### **Effect on eczema model mice**

The results of the treatment in each group of mice were shown in fig. 4. Intuitively, different concentrations of drugs have significant differences in the treatment of mice. Ear swelling of mice in each group was shown in table 3. Generally, the degree of ear swelling was believed to reflect the reaction degree of the inflammation, compared with model group, the degree of ear swelling of positive control group and high dose group decreased significantly ( $p < 0.01$ ); and medium dose group could also improve the ear swelling of mice ( $p < 0.05$ ).

Cytokines and inflammatory cell changes of mice in different groups were shown in table 4. The results showed that the positive control group, medium dose group and the high dose group could significantly decrease the count of inflammatory cell ( $p < 0.05$ ,  $p < 0.01$ ), and the effect of high dose group was better than positive control group. Compared with model group, the IL-2 level of positive control group, medium dose group and high dose group decreased significantly ( $p < 0.05$ ,  $p < 0.01$ ).

Pathological tissue of mice in each group was shown in fig. 5. Compared with blank group, the epidermis of model group thickened obviously, edema and vascular dilatation were formed. Meanwhile, a large number of lymphocytes infiltrated, that showed the model was built successfully. Edema symptoms of the positive control group and each concentration group were relieved, the thickening degree of skin decreased obviously, the number of dermal lymphocytes decreased in different degrees.

#### **Effect on antibacterial experiment in vitro**

Bacteriostasis rate in each experimental group was shown

in table 5. Compared with low dose group, the high dose group had significant influence on the bacteriostasis effect of *Staphylococcus aureus* ( $p < 0.05$ ), in addition, the bacteriostasis rate of *Escherichia coli* medium in medium dose group and high dose group increased significantly ( $p < 0.05$ ).

DIZ and MIC of the experimental group were shown in table 6. DIZ values of bacteriostatic circle on *Staphylococcus aureus* and *Escherichia coli* were 17.25 mm and 25.62mm. Moreover, the MIC values of two kinds of bacteria all were 64 $\mu$ g/mL. As shown in fig. 6, Jinjianling cream had the good bacteriostatic effect on two kinds of bacteria. It is noteworthy that the tolerance of Jinjianling cream on *Escherichia coli* was superior than that of *Staphylococcus aureus*, that may be due to the presence of double layer membrane structure in gram negative bacteria (*E. coli*) (Zhao, 2013), that was more resistant to drug invasion than the monolayer structure of gram positive bacteria (*Staphylococcus aureus*).

## **DISCUSSION**

The wound will undergo a series of complicated reactions during recovery after the skin damaged, such as the healing process and inflammatory reaction. Each process has a corresponding mechanism for regulation. Related studies show that, at the different stages of wound healing, the differences are mostly manifested in the changes of cytokines and metabolite levels (Schwacha *et al.*, 2003; Spyrou *et al.*, 2002). Inflammatory reaction is considered to be an important step in the process of wound healing, which may delay wound healing (Arajo *et al.*, 2010). Therefore, it is possible to regulate the inflammatory response by regulating the release of pro-inflammatory cytokines such as IL-1, TNF- $\alpha$  and IL-10 (Dos *et al.*, 2016). The results showed that the concentrations of IL-1, TNF- $\alpha$  and IL-2 increased after the skin injury. After treatment, the above inflammatory factors decreased to some extent, indicating that the preparation seemed to prevent the over expression of the inflammatory reaction and accelerate the formation of wound epithelium. Furthermore, stimulation of epithelial cell proliferations is vital for wound healing to take place. Wound epithelialization is a process whereby there is epithelial regeneration post wounding with the epithelial cells proliferating and migrating over the wound bed, thereby providing a protective cover for the freshly formed tissues (Gurtner *et al.*, 2008; Schreml *et al.*, 2010). There are a lot of pathogenic microbes on the surface of the skin. When the skin is damaged, the wound is easy to infect the pathogenic bacteria and affect the treatment (Lim *et al.*, 2016). *Escherichia coli* and *Staphylococcus aureus* are the most common pathogenic bacteria with the strong pathogenicity (Yagdiran *et al.*, 2016). Antibacterial experiments found that Jinjianling cream had the strong inhibitory effect on pathogenic

bacteria of wound. Antibacterial ability was positively correlated with the concentration of drug, and the inhibition effect on *Staphylococcus aureus* was stronger than that of *Escherichia coli*. In the present study, the observed decrease of wound surfaces provides further evidence in support for the Jinjianling cream in wound healing. The wound area reduction could be attributed to the biological activities of alkaloids, these include the cicatrization, the anti-microbial and anti-inflammatory activities (Rehman *et al.*, 2017). Curcumin is also the main active ingredient in the cream. It has obvious antibacterial and anti-oxidant activities (Gunes *et al.*, 2017; Xie *et al.*, 2015), which plays a synergistic therapeutic role with alkaloids.

Mouse and rat, these animal models, are considered as a good tool to assess wound healing efficiency of medicinal derivatives, its experimental use allow the findings transposition to human beings, since they are the closest human relatives (Ben *et al.*, 2016). We used the classic scald model and mouse eczema model for the experiments. Preliminary results of experiments proved that Jinjianling cream could promote the healing of damaged skin and reduce the inflammatory reaction of wound. Its antibacterial activity was also proved by antibacterial experiment. In addition, we have conducted skin irritation experiments at the beginning of the experiment. The result of pre-experiment showed that Jinjianling cream had no irritation on the skin of mice, indicating that the preparation could be applied to human skin safely. The continuous search for new medicinal derivatives with wound healing activity still a challenging task for the pharmaceutical industry and academia. In this paper, the results are intended to provide a safe and effective topical preparation for the treatment of common skin diseases such as dermatitis and eczema. This provides a scientific rationale to account for the clinical application of Jinjianling cream. We hope this work is helpful for the development of Chinese herbal compound preparation.

## CONCLUSION

To sum up, this suggests that the Chinese herbal compound cream can be widely used in the prevention and treatment of traumatic infection, can significantly improve wound healing, and further extended to the clinical treatment of dermatitis, eczema, psoriasis and other common skin diseases. The results showed that Jinjianling cream also had strong antioxidant activity *in vitro*, which may be related to its anti-inflammatory effect (Fu *et al.*, 2013), the fundamental cause of inflammatory response is oxidative stress, inflammation is only one manifestation of the organism after oxidation. Thus it can be seen that, there is a complex relation between inflammation oxidation in the body, this can serve as a new direction in our research.

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