

RESEARCH ARTICLE

Drug-loaded PLGA-mPEG microparticles as treatment for atopic dermatitis-like skin lesions in BALB/c mice model

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Abstract

This study evaluated the feasibility of mizolastine-loaded microparticles as therapy for atopic dermatitis. Microparticles have been researched for decades as a controlled-release drug delivery system, but seldom been used as treatment for skin disease. In this research, we induced dermatitis in BALB/c mice model by repeated topical application of dinitrofluorobenzene and compared the mizolastine microparticles injection and daily mizolastine injection treatment. The results showed that the mizolastine microparticles treatments significantly inhibited ear thickness and dermatitis index in dermatitis model compared with the dermatitis mice without treatment, showing a similar curative effect compared with daily mizolastine injection treatment, and the improvement continued for several days. Inflammatory cells infiltration into the ears and the plasma level of immunoglobulin E were also suppressed by mizolastine microparticles according to the histopathology analysis. In conclusion, the results suggested that drug-loaded microparticles could be a proper candidate for the treatment of skin diseases.

Keywords

Biomaterial, controlled release, dermatitis, microspheres

History

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Introduction

Atopic dermatitis, or atopic eczema, is a common chronic and relapsing inflammatory skin disease (Dibildox, 2001; Boguniewicz and Leung, 2006; Kim et al., 2012). Population studies suggest that atopic dermatitis affects 10–20% of all children during childhood and 1–3% adults in most countries, and the prevalence of atopic dermatitis shows a continuous increase in frequency over the past 30–40 years (Leung et al., 2004). Current treatments for atopic dermatitis rely on topical steroids and immunosuppressive agents, and these treatments are not always effective (Barzegar and Pradalier, 2002; Boguniewicz et al., 2003), patients need to receive treatment frequently, even several times a day, which cause great inconvenience. New drugs have been tried for this disease in animal model, such as aloperine (Yuan et al., 2011), tacrolimus (Kim et al., 2012; Pople and Singh, 2012), red ginseng (Samukawa et al., 2012) and silymarin (Kang et al., 2008), and they show significant effects dealing with the disease, but the drugs still need to be taken daily.

The frequency of treatment can be decreased by the use of controlled release vehicles, which is very beneficial for patients who require daily and long-term treatment. Polyester microparticles have been researched for decades as a controlled-release drug delivery system (Yeh and Chiang, 2004; Jay and Saltzman, 2009; Park et al., 2009; Bjorses et al., 2011; Patel et al., 2012). Biodegradable polyesters such as PLA, PCL, PLGA and poly(dl-lactide-co-glycolide)-methoxypoly(ethyleneglycol) (PLGA-mPEG) are widely used as carriers in controlled-release

delivery systems due to their biocompatibility (Yang et al., 2001; Lecaroz et al., 2006; Karal-Yilmaz et al., 2011; Makadia and Siegel, 2011). Drug-loaded microparticles provide complementary benefits, especially reduced side effects, greater convenience and facilitated compliance of the treatments. Microparticles have been reported to have good performance in dealing with hyperglycemia (Al-Qadi et al., 2012), cancer (Yang et al., 2011; Na et al., 2012) and other diseases (Hazekawa et al., 2012). Applying microparticles to skin diseases, however, very few researches had been conducted. Rosado et al. have done some researches about the feasibility of nanoparticles for the treatment of acne and atopic dermatitis (Rosado et al., 2013; Reis et al., 2014), and they focused on the *in vitro* studies. In this research, we take microparticles encapsulating mizolastine into treating atopic dermatitis in BALB/c mice model.

Mizolastine is a well-tolerated antihistamine agent with antiallergic properties and proven to be effective and safe in the treatment of allergic rhinitis and chronic urticaria (Bachert and Maspero, 2011). It also has the ability to inhibit the mediators of inflammation. The clinical trials indicated that mizolastine is more effective in treating acute urticaria than other antihistamine agent. Atopic dermatitis mice model can be established by repeated painting of dinitrofluorobenzene (DNFB) in ears (Terakawa et al., 2008), which cause a significant swelling and erythema of ears. Several types of inflammatory cell infiltrate into skin lesion, such as lymphocytes, eosinophil (Koo et al., 1998; Hochhaus, 2008). Mast cells that express high-affinity receptor for immunoglobulin E (IgE) are significantly increased in the skin of atopic dermatitis. Atopic dermatitis also associates with high level of serum IgE. These symptoms are used to evaluate the severity of dermatitis and tell us if the drug-loaded microparticles have worked on the dermatitis.

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Materials and methods

Materials

PLGA-mPEG ($M_{W(mPEG)}$:5000, $M_{W(PLGA)}$: 15 000, LA:GA = 3:1) was synthesised by our laboratory as described in our previous work (Zou et al., 2012). Mizolastine was purchased from Kang Bao Tai Fine Chemical Co., Ltd. (Wuhan, China).

BALB/c mice (6–8 weeks old, female) were purchased from Xingjian Company (Wuhan, China). All animals were healthy and housed in 12 mice per cage and fed a laboratory diet and water. All animal experiments were conducted in accordance with the National Institutes of Health Guide for Care and Use for Laboratory Animals and under Institutional Animal Care and Use Committee-approved protocols.

Microparticles preparation

Mizolastine microparticles (Mizolastine MP) were prepared using the oil-in-water (O/W) emulsification-solvent evaporation method (Rosca et al., 2004; Hernan Perez de la Ossa et al., 2012; Jhunjhunwala et al., 2012). A quantity of 5.5 mg of mizolastine was added to 3 ml of dichloromethane containing 120 mg PLGA-mPEG. The solution was then mixed with 10 ml 1% polyvinyl alcohol (PVA, polymerisation degree ~ 1700 and hydrolysis degree $\sim 99\%$, molecular weight 70 kDa $\sim$ 80 kDa) under homogenisation at 8000 rpm for 30 s to obtain O/W emulsion. This emulsion was then added to 100 ml of 0.1% PVA solution and stirred continuously for 2 h at 600 rpm to evaporate the dichloromethane completely. The resulting mizolastine MP were then centrifuged for two minutes at 3500 rpm under room temperature and washed three times with water, freeze-dried overnight and stored at -20°C .

Characterisation of the microparticles

Morphology and size distribution of the microparticles

Scanning electron micrographs of the microparticles were taken using a scanning electron microscope (SEM; Quanta 200 FEI, Holland, the Netherlands). Microparticles were mounted onto metal stubs using a double-sided adhesive tape. After vacuum-coating with a thin layer of gold, the microparticles were examined by SEM at 15 kV. For the mean size and size distribution analysis, three-hundred microparticles were randomly chosen from the SEM micrograph, and the software (Nano Measurer 1. 2) was applied to counting the mean size and size distribution.

Drug encapsulation efficiency

High-performance liquid chromatography (HPLC) was used for the quantification of mizolastine in the microparticles. The mobile phase of acetonitrile:0.02 M ammonium acetate (40:60) at a flow rate of 1 ml/min was used for mizolastine. Samples of 20 μl were injected and detected at 220 nm. The analytical method was validated according to the ICHQ2 (R1) guideline. The retention time of mizolastine was 6 min, and total run time of HPLC analysis was 10 min.

To determine the amount of mizolastine encapsulated into the microparticles, 10 mg of drug-loaded microparticles were dissolved in 1 ml of methylene chloride and then added 50 ml of HPLC mobile phase and stirred for 1 h. The resulting mixtures were filtered through 0.45 μm nylon filters and analysed by HPLC. The entrapment efficiency was calculated using Equation (1).

$$\text{EE (\%)} = \frac{(\text{actual drug in PLGA} - \text{mPEG})}{(\text{Initial drug in PLGA} - \text{mPEG})} \times 100 \quad (1)$$

All measurements were conducted in triplicate.

In vitro release of drugs from microparticles

Briefly, 15 mg of mizolastine-loaded microparticles were suspended in 30 ml of pH 7.4 PBS buffer supplemented with 0.1 wv% Tween 80 and 0.05 wt% sodium azide (in triplicate). These samples were incubated in a thermostated shaking water bath (Ronghua SHA-C, Zhejiang, China) at 37°C with continuous agitation (50 strokes/min). Sink conditions were maintained during the study. At regular time intervals, sample tubes were centrifuged for three minutes at 3500 rpm under room temperature and 28 ml of the supernatants were withdrawn, filtered through 0.45 μm nylon filters and analysed for drug content by HPLC. The withdrawn volume was immediately replaced with an equal volume of fresh and pre-warmed medium.

Groups and treatment

The experiment mice were randomly divided into five groups ($n=12$) and received induction of atopic dermatitis except group one. Atopic dermatitis was induced by repeated topical application of DNFB according to a published method (Yuan et al., 2011) with a minor modification. Briefly, 40 μl of 0.5% DNFB in acetone/olive oil (3:1) was applied topically to inner and outer sides of right ears of BALB/c mice on day 1, day 2 and day 6. On the 11th day, 10 μl 0.1% DNFB was applied to the ears of mice again to yield extensive disease. The first group (control) was normal mice without any treatment. The second group (dermatitis) received DNFB-repeated application but no drug treatment. The third group (dermatitis with mizolastine MP injection) received DNFB-repeated application and mizolastine MP (5 mg microparticles in 0.4 ml normal saline each mice) suspension treatment once by tail vein injection on the sixth day. The fourth group (dermatitis with blank MP injection) received DNFB-repeated application and blank MP (5 mg blank microparticles in 0.4 ml normal saline each mice) injection on the sixth day. The fifth group (dermatitis with mizolastine) received DNFB-repeated application and daily mizolastine injection (0.77 mg/kg/day, 0.4 ml/d) from days 6 to 14, and the total amount of mizolastine injected is equal to that in mizolastine MP group.

On the 9th, 11th, 13th, 15th day, three mice in each group were sacrificed randomly for evaluating the severity of dermatitis; 5 mm of the ears in the same region was punched and fixed with 10% formaldehyde, embedded in paraffin and thin sections were made and photoed by microscope. Samples were stained with hematoxylin–eosin for observation of lymphocytes and eosinophils infiltration. For measurement of infiltration of mast cells, samples were stained with toluidine blue. To all of the sacrificed mice, blood was collected in ethylenediaminetetraacetic acid tubes and spun for 10 min at 3000 rpm. Plasma was pipetted out and stored under -80°C for analysis of IgE.

Ear thickness and the score of dermatitis

The ear thickness and the score of dermatitis were used as an evaluation of the atopic dermatitis severity. On the 9th, 11th, 13th and 15th day, three mice in each group were sacrificed, and 5 mm of the ears in the same region was punched. In order to measure the ear thickness, thin ear section was made and photoed by microscope. Total score of dermatitis severity was defined as the sum of the individual scores graded as 0 (none), 1 (mild), 2 (moderate) and 3 (severe) for each of five signs and symptoms (itch, erythema/haemorrhage, oedema, excoriation/erosion and scaling/dryness).

Histopathology

Skin sections of ear samples were stained with hematoxylin and eosin for the measurement of eosinophils and lymphocytes infiltration. The microscopic examination was carried out and examined by a board-certified veterinary pathologist unaware of the treatment of the samples being evaluated. For analysis of mast cell infiltration, skin sections were stained with toluidine blue, and the number of mast cell in five sites chosen at random was counted. The microscopic examination was carried out and examined by a board-certified veterinary pathologist unaware of the treatment of the samples being evaluated.

Analysis of total IgE production in blood samples

Total IgE production in blood samples were measured by enzyme-linked immunosorbent assay (ELISA). Serums were separated immediately after mice were sacrificed, and IgE concentrations were quantified using IgE ELISA kits (RB, Saint Louis, MO) according to the manufacturer's instruction.

Statistical analysis

All data were presented as mean $\pm$ SD. Comparisons among groups were made using one-way analysis of variance followed by Dunnett's *t* test. The *p* values less than 0.05 were considered significant.

Results

Microparticle characterisation

Mizolastine MP was prepared using the O/W emulsification solvent evaporation method. Microparticle morphology examined by scanning electron micrographs revealed spherical and smooth particles homogeneous in size, as shown in Figure 1. Three-hundred microparticles were randomly chosen from the SEM micrograph for the size analysis, and the result showed a mean particle size of approximately 5.9 μ m. HPLC was used for the quantification of mizolastine in the microparticles, and the result showed that the encapsulation efficiency of mizolastine was quite high ($92.44 \pm 5.04\%$).

The release profiles of mizolastine from microparticles as function of time was shown in Figure 2. The *in vitro* release of mizolastine exhibited an apparent triphasic release pattern: an initial burst release, followed by a lag period and subsequently a constant release. A burst release around 20% of entrapped drug

was detected during the first day and after that, only 16% of mizolastine was released within the following four days at a relative slow rate. At the end of the sixth day, the drug release accelerated, till the 90% of mizolastine release after 12 days of incubation.

Effects of drug-loaded microparticles on ear thickness and the score of dermatitis

The therapeutical effect of drug-loaded MPs was investigated in BALB/c mice and compared with daily mizolastine injection. Ear samples were taken every two days from the ninth day, and ear thickness was measured by taking micrograph of the ear sections, as shown in Figure 3. Repeated topical application of DNFB obviously increased ear thickness in BALB/c mice compared with control group on the ninth day ($p < 0.01$, shown in Figure 3), and the symptom deteriorated over time. For the groups with treatment of mizolastine MP, ear swelling was significantly inhibited on the ninth day ($p < 0.05$), and this improvement continued over time, showing a similar curative effect compared with daily mizolastine injection group. The mice dealing with mizolastine MP and daily mizolastine injection were almost recovered of ear swelling on the 15th day (both $p < 0.01$). The mice dealing with blank MP showed no improvement compared with that in dermatitis group.

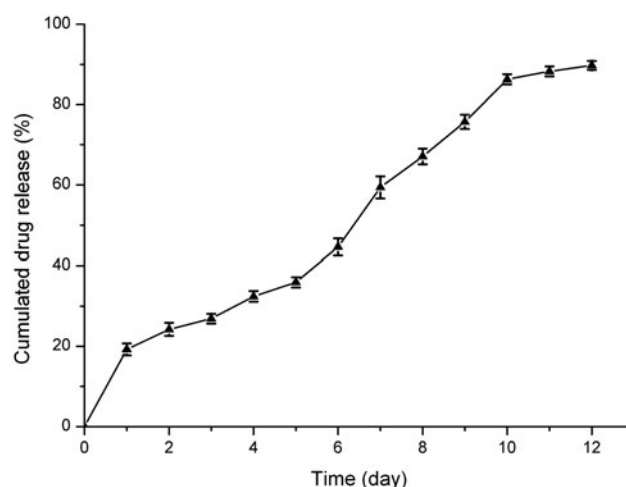


Figure 2. *In vitro* release profile of mizolastine microparticles. Means $\pm$ SDs ($n = 3$).

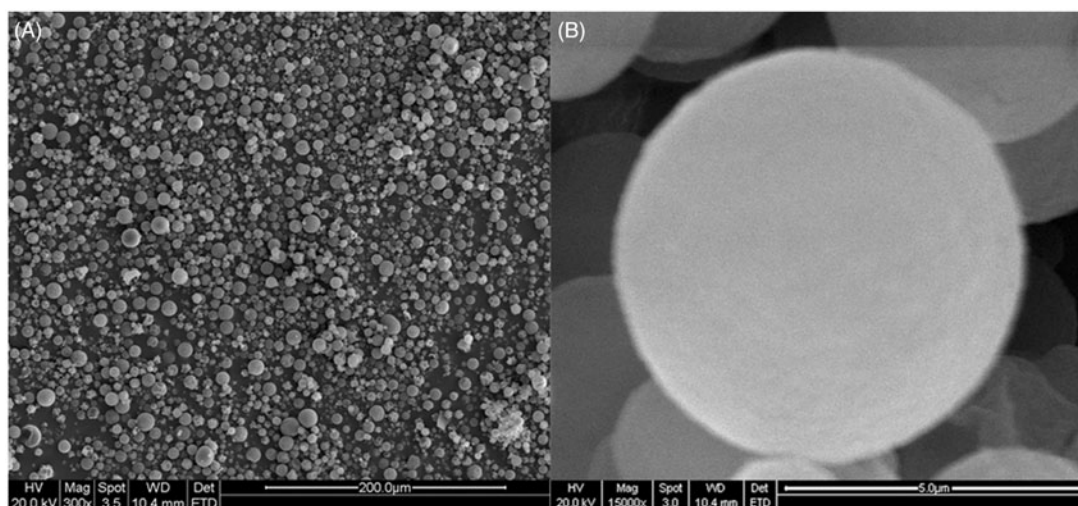


Figure 1. Scanning electron micrographs of mizolastine microparticles at different magnification: (A) 300 $\times$ and (B) 15 000 $\times$.

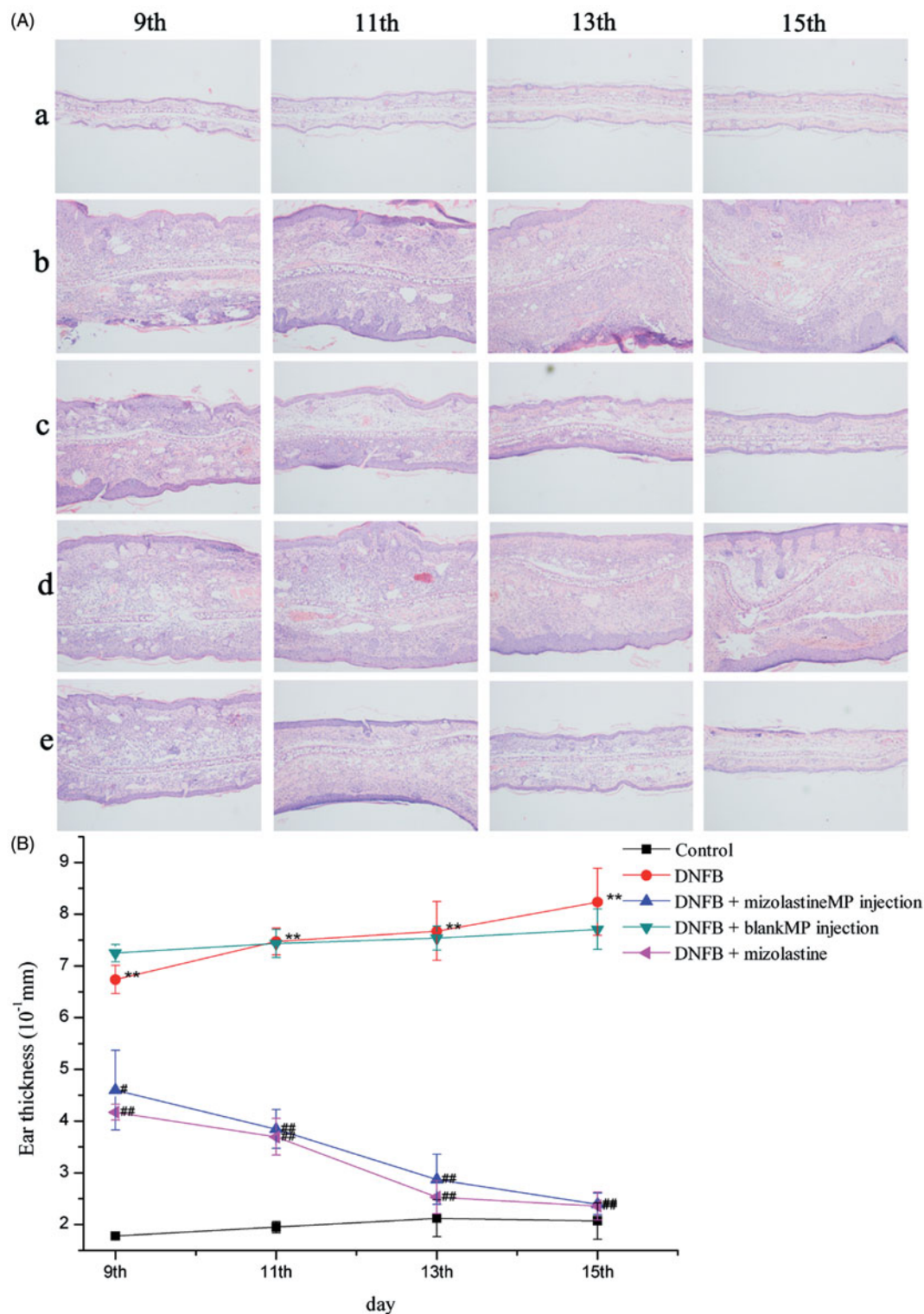


Figure 3. Effects of mizolastine microparticles on ear thickness in dermatitis model induced by repeated painting with DNFB. (A) Typical micrographs of ear section in each group taken on 9th, 11th, 13th and 15th day. (a) Control, (b) dermatitis, (c) dermatitis with mizolastine microparticles injection, (d) dermatitis with blank microparticles injection and (e) dermatitis with daily mizolastine injection. (B) Statistical analysis of ear thickness in each group taken on 9th, 11th, 13th and 15th day. Means $\pm$ SDs ($n = 3$). ** $p < 0.01$, as compared with the control group; # $p < 0.05$ and ## $p < 0.01$, as compared with the DNFB group.

Total score of dermatitis severity was defined as the sum of the individual scores graded as 0 (none), 1 (mild), 2 (moderate) and 3 (severe) for each of five signs and symptoms (itch, erythema/haemorrhage, oedema, excoriation/erosion and scaling/dryness) (Yuan et al., 2011). We took ear pictures and observed scratching behaviour of mice in each group in order to evaluate the severity

of the dermatitis. As the pictures were too many, we just show those taken on the 9th and 15th day (Figure 4A and B). Atopic dermatitis group and blank MP-treated groups showed moderate ear swelling and erythema on the ninth day, but these symptoms got suppressed in groups dealing with mizolastine MP and daily mizolastine injection. On the 15th day, ear swelling and erythema

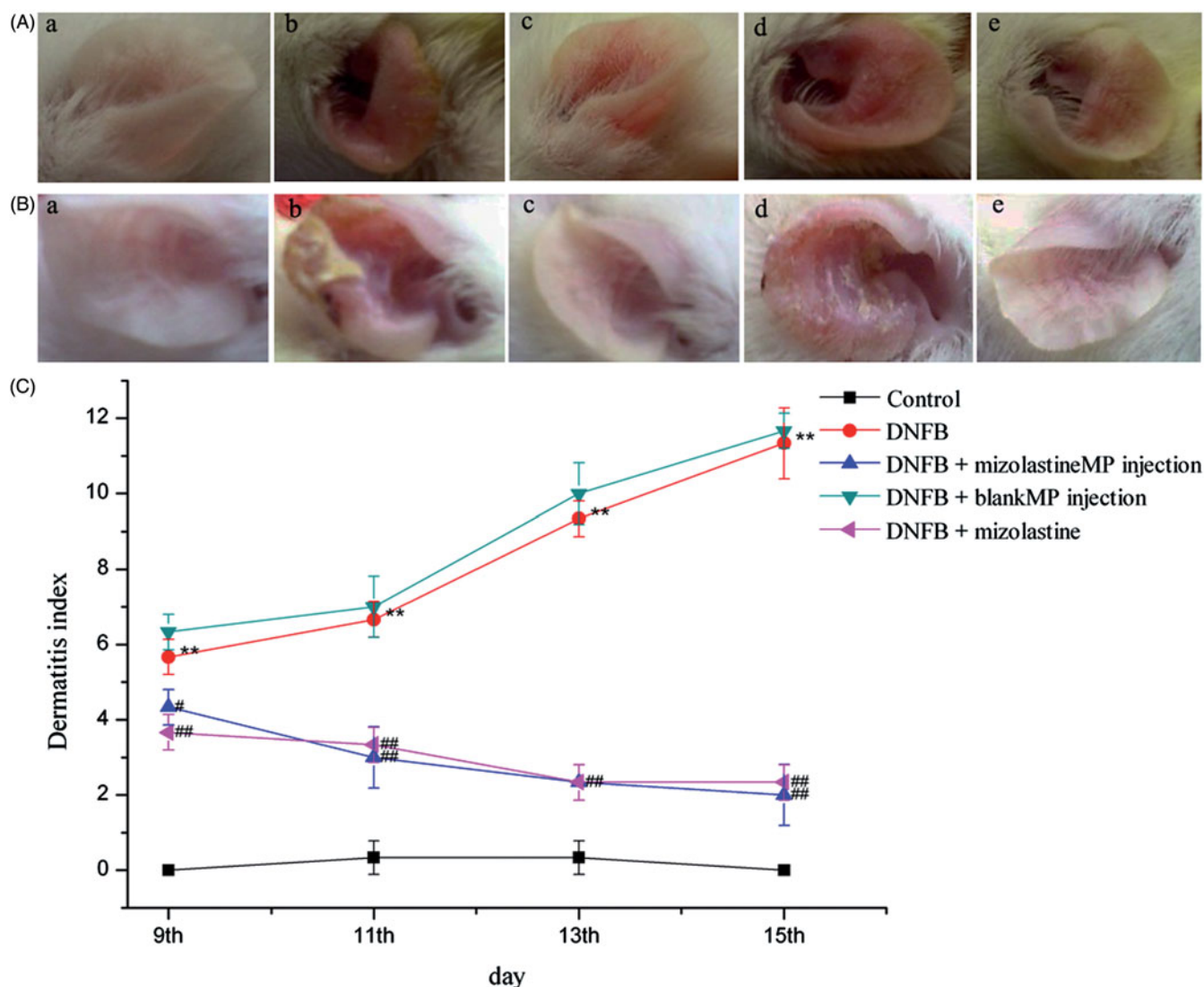


Figure 4. Ear pictures taken on (A) 9th day and (B) 15th day. (a) Control, (b) dermatitis, (c) dermatitis with mizolastine microparticles injection, (d) dermatitis with blank microparticles injection and (e) dermatitis with daily mizolastine injection. (C) Effect of mizolastine microparticles on dermatitis index in dermatitis model. Means $\pm$ SDs ($n = 3$). ** $p < 0.01$, as compared with the control group; # $p < 0.05$ and ## $p < 0.01$, as compared with the DNFB group.

of mice in dermatitis group and blank MP-treated group became severe and we observed some new symptoms – haemorrhage, excoriation and scaling, caused by constant scratching behaviour of mice, whereas, the ear swelling and erythema of mice in groups dealing with mizolastine MP and daily mizolastine injection were almost recovered, as shown in Figure 4(B). The total score of dermatitis severity as a function of time in each group is similar to ear thickness, shown in Figure 4(C). In dermatitis group, the score of dermatitis (5.7 points in the ninth day) is higher than control (0 point in the 9th day) ($p < 0.01$), and the score got higher over time (11.3 points in the 15th day) as some new symptoms appeared, which also happened in groups dealing with blank MP (11.7 points in the 15th day). Groups dealing with mizolastine MP injection showed a relative low score of dermatitis (4.3 points in the ninth day), and this score got lower over time (2 points in the 15th day) ($p < 0.01$ after 11th day), showing a similar inhibition effect compared with daily mizolastine injection group.

Effects of drug-loaded microparticles on inflammatory cell accumulation

Repeated DNFB painting had been known to accumulate inflammatory cells in the inflamed dermis (Nagai et al., 1997).

To evaluate the effects of drug-loaded microparticles on inflammatory cell accumulation, three mice in each group were sacrificed randomly at predetermined time intervals (9th, 11th, 13th and 15th day), and ears in the same region of each mice was punched and stained with hematoxylin–eosin and toluidine blue. As the histopathological pictures were too many, only those taken on the 15th day were demonstrated.

Histopathological pictures on the 15th day demonstrated that excessive lymphocytes and eosinophils infiltration into the dermis were observed in dermatitis group, while lymphocytes and eosinophils infiltration were reduced in groups treating with mizolastine MP and daily mizolastine injection, as shown in Figure 5. This improvement could also be seen in histopathological pictures taken on the 9th, 11th and 13th day. In accordance with expectation, mice treated with blank MP showed no difference with that in dermatitis group during the experiment.

The infiltration of mast cells was also significantly increased in dermatitis group, higher than those in control (Figure 6A). We chose five site of each stained section at random in 10 high-power fields ($\times 400$ for count) and counted mast cells numbers (Figure 6B). Mizolastine MP and daily mizolastine injection inhibited the mast cells infiltration (both $p < 0.05$ after 11th day),

Figure 5. Effect of mizolastine microparticles on lymphocytes and eosinophils infiltration in dermatitis model induced by repeated painting with DNFB. (A) Control, (B) dermatitis, (C) dermatitis with mizolastine microparticles injection, (D) dermatitis with blank microparticles injection and (E) dermatitis with daily mizolastine injection. Sections were stained with haematoxylin–eosin, micrograph at 100 $\times$. Sections shown are representatives of more than five observations.

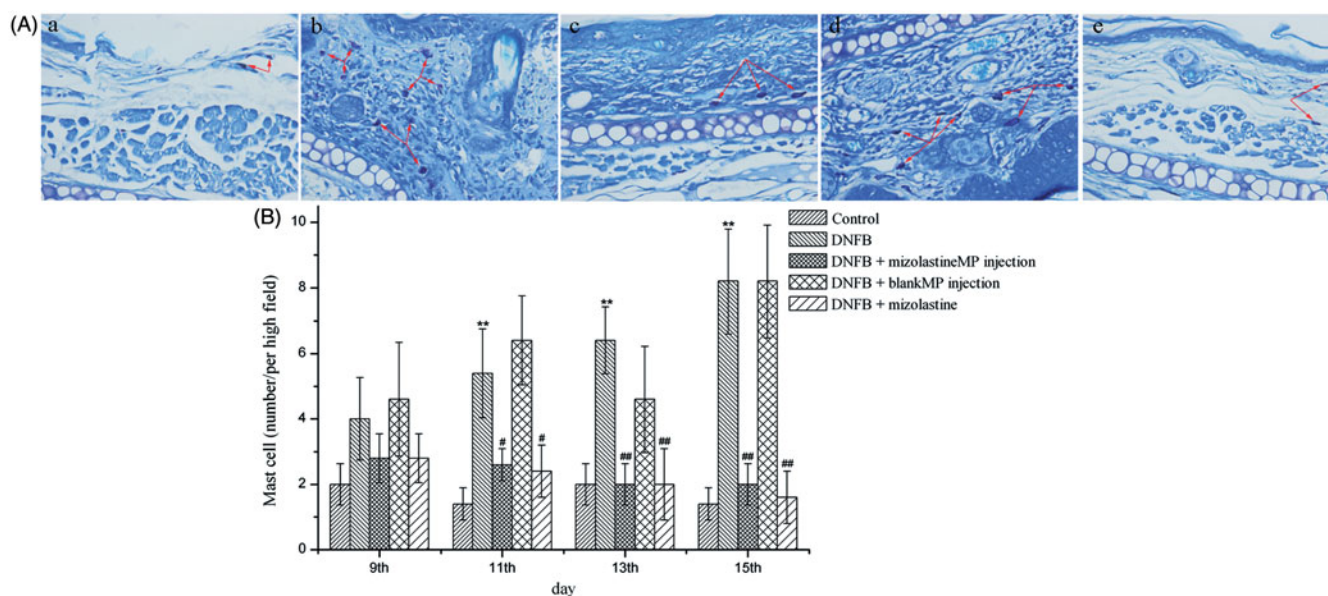
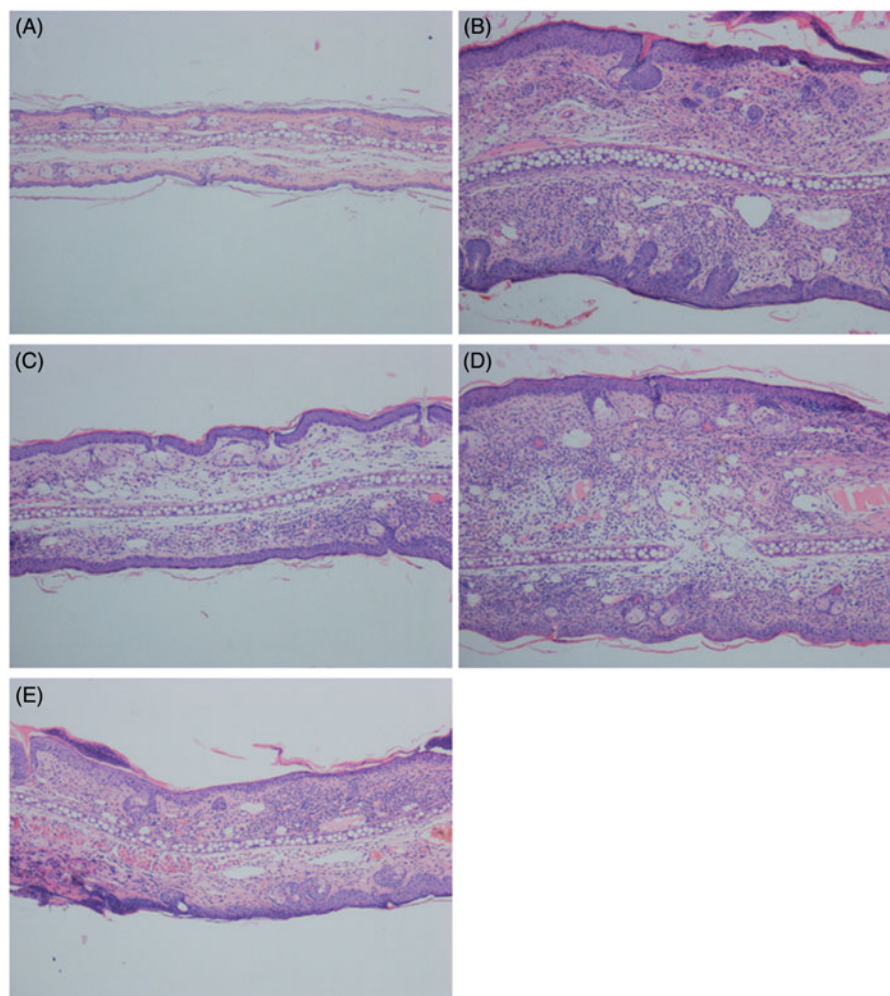


Figure 6. Effect of mizolastine microparticles on mast cells infiltration in dermatitis model induced by repeated painting with DNFB. (A) The ear in group of (a) Control, (b) dermatitis, (c) dermatitis with mizolastine microparticles injection, (d) dermatitis with blank microparticles injection and (e) dermatitis with daily mizolastine injection. Sections were stained with toluidine blue, micrograph at 400 $\times$. Sections shown are representatives of more than five observations. (B) The number of mast cells in five sites chosen at random was counted. Data were presented as means $\pm$ SD ($n = 5$). ** $p < 0.01$, as compared with the control group; # $p < 0.05$ and ## $p < 0.01$, as compared with the DNFB group.

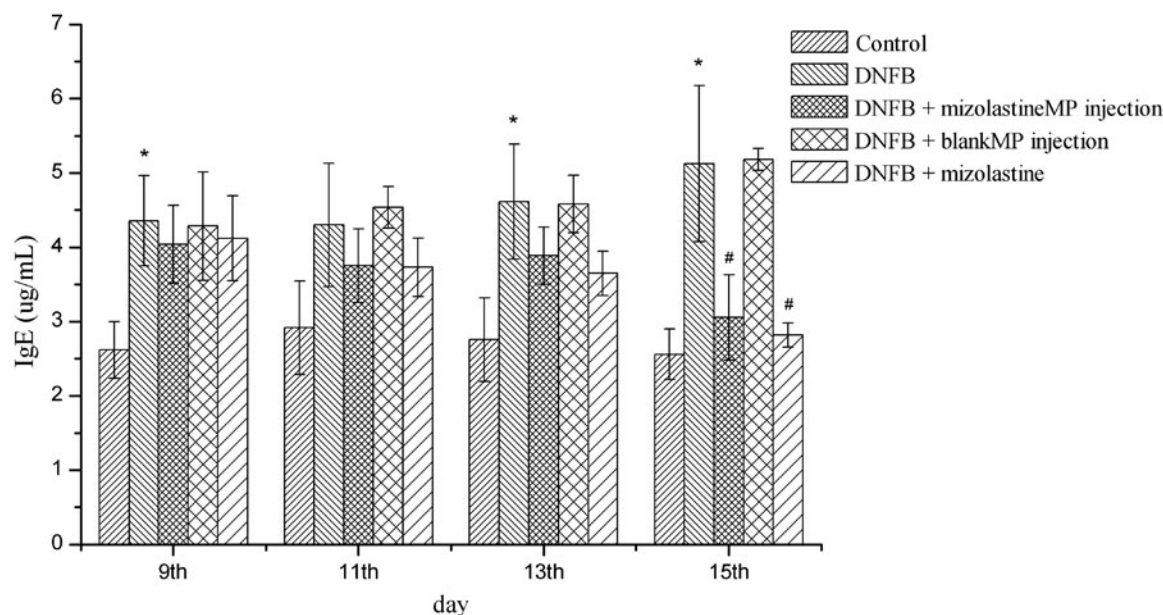


Figure 7. Effects of drug-loaded microparticles on serum plasma level of IgE in dermatitis model induced by repeated painting with DNFB. Data were presented as means $\pm$ SD ($n = 3$). * $p < 0.05$, as compared with the control group; # $p < 0.05$, as compared with the DNFB group.

while blank MP treatment did not inhibit the infiltration, according to the histopathological pictures and data.

Effects of drug-loaded microparticles on serum plasma level of IgE

An important characteristic for atopic dermatitis is the high levels of IgE in serum plasma (Yuan et al., 2011). As shown in Figure 7, mice in dermatitis group got a higher plasma level of IgE than those in the control group, and as the dermatitis got more serious, the level of IgE got higher in general. To the mice dealing with mizolastine MP, the secretion of IgE got suppressed compared with those in dermatitis group, especially in day 15 (both $p < 0.05$). Both the mizolastine MP injection and daily mizolastine injection therapy made the IgE level reduce gradually over time, from $4.04 \pm 0.52 \mu\text{g/ml}$ (mizolastine MP injection) and $4.12 \pm 0.57 \mu\text{g/ml}$ (daily mizolastine injection) on the 9th day to $3.06 \pm 0.57 \mu\text{g/ml}$ (mizolastine MP injection) and $2.82 \pm 0.16 \mu\text{g/ml}$ (daily mizolastine injection) on the 15th day. Blank MP still failed to show effect in reducing the IgE level, just like the results in ear swelling, dermatitis index and inflammatory cells infiltration.

Discussion

Atopic dermatitis is a common chronic inflammatory skin disease, and patients need to receive treatment frequently, which cause great inconvenience. A sustained-release and long-acting formulation may solve this problem. Biodegradable polyesters have been successfully employed to design drug delivery system, such as implants, scaffolds, microparticles and nanoparticles. An ideal microparticle formulation should have reasonably high drug encapsulation efficiency, loading capacity and sustained release of the loading drug. In this study, we demonstrated that application of drug-loaded microparticles suppressing DNFB-induced atopic dermatitis-like skin lesion in mouse model.

Mizolastine-loaded microparticles were prepared through O/W emulsification solvent evaporation method. The microparticles revealed an encapsulation efficiency around 90%, which is in agreement with earlier reports of high encapsulation efficiency of hydrophobic drugs (Hernan Perez de la Ossa et al., 2012; Lee and Feijen, 2012). This could be attributed to the lipophilic nature of

mizolastine, thus the drugs tended to remain entrapped into the microparticles instead of partitioning into the external aqueous phase during the preparation process. *In vitro* release experiment was conducted in pH 7.4 PBS buffer, which better mimic *in vivo* environment and eliminated the interference caused by pH difference between *in vitro* and *in vivo* (Li et al., 2008b). The release profiles of mizolastine from microparticles as function of time exhibited a typical triphasic release pattern. The burst release during the first day was largely due to the dissolution and diffusion of drugs placed on the most superficial part of the microparticles (Rosca et al., 2004; Hernan Perez de la Ossa et al., 2012). The lag period, which involved slow mizolastine release until day 5, should be the result of continuous diffusion from the microparticles. The later rapid release from days 5 to 10 was believed to be due to polymer erosion-induced diffusion of mizolastine. At the end of the release, almost all of the mizolastine were detected. A similar research reported (Li et al., 2008a) the methotrexate ($M_w = 454.44$) release behaviour from PLGA-mPEG microparticle, revealing a similar release pattern to mizolastine, but a much longer release time, which should be ascribed to its higher PLGA-mPEG molecular weight ($M_w(\text{mPEG})$: 3000, $M_w(\text{PLGA})$: 50 000, LA:GA = 3:1) and larger particle size (50–60 μm), according to the research by Avgoustakis et al. (2002).

Mizolastine were administrated through mizolastine MP injection and daily mizolastine injection, respectively. Burst release from mizolastine MP would cause a higher dosage than expected and may cause some side effects. The most common side effects reported for the mizolastine are drowsiness, fatigue and dry mouth (Leynadier et al., 1996; Bachert et al., 2001). While, during the whole experiment, such side effects were not obvious, and all the mice were lively without any other adverse reactions; what is more? These side effects did not affect the mizolastine therapy for dermatitis according to the results. So, in this experiment, we did not discuss the side effects caused by the mizolastine. In this study, we demonstrated the symptom difference between mice with and without treatment. Ear swelling and dermatitis score were important index to evaluate the severity of dermatitis. Therefore, we measured the mice ear thickness according to ear section pictures and observed the dermatitis symptoms and took photos of ears at regular intervals. The results

revealed that the ear swelling and dermatitis score of mice treated with mizolastine MP injection, and daily mizolastine injection got relieved over time compared with that in groups without drug treatment or blank MP treatment, which proved that mizolastine was under controlled release from microparticles *in vivo* and got a similar curative effect compared with the daily mizolastine treatment, indicating that drug-loaded microparticles could be a proper candidate for dermatitis. The effect of drug-loaded microparticle on atopic dermatitis was further supported by histopathological and IgE concentration analysis. The skins of atopic patients are pathologically characterised by the infiltration of inflammatory cells and mast cells degranulation (Fujii et al., 2009). Mast cells are known as key effector cells in IgE-mediated allergic disorders and activated by cross-linking of a high affinity IgE receptor (Fujimoto et al., 2009). Matsuoka et al. (2003) reported that the infiltration of mast cells into the dermis is a necessary factor to define an appropriate animal model for atopic dermatitis. In this research, we demonstrated that repeated application of DNFB resulted in eosinophils and mast cell infiltration into the dermis in the ears of BALB/c mice. Application of drug-loaded microparticles inhibited the DNFB-induced infiltration of eosinophils and mast cell continually as drug released constantly from microparticles. The results revealed that the mizolastine MP injection and daily mizolastine injection also got a similar effect on inhibiting the mast cells infiltration. The upregulation of total serum IgE was a hallmark of atopic dermatitis, and elevated serum IgE had several effects on skin inflammation (Inagaki et al., 2006; Belloni et al., 2011). In this study, we found that total serum IgE were increased in DNFB-treated mice and mizolastine MP inhibited the upregulation over time ($p < 0.05$ on the 15th day). The histopathological and IgE concentration analysis results also indicating that the drug-loaded microparticles could be used for chronic and relapsing skin disease, relieving the inconvenience of patient.

Conclusion

In this research, we offered the interesting report on treatment of atopic dermatitis-like skin lesions on BALB/c mice with PLGA-mPEG microparticles encapsulating mizolastine. Drug-loaded microparticle was prepared by O/W emulsification solvent evaporation method and showed high encapsulation efficiency and controlled release up to 12 days. Animal experimental results showed that mizolastine MP injection got a similar curative effect on inhibiting the ear swelling, dermatitis score, inflammatory cell infiltration and concentration of IgE compared with daily mizolastine injection treatment, indicating that drug-loaded microparticles treatment could provide an effective alternative therapy for the management of atopic dermatitis, which can fairly well solve the inconvenience of daily treatment. In general, this study suggested that drug-loaded microparticles could be a promising candidate for dermatitis-suffering patients who required daily and long-term treatments.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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