

Effect of a Chinese herbal formula, Shi-Bi-Lin, on an experimental model of allergic rhinitis

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Background: *Jia Wei Cang Er Zi San*, a traditional Chinese herbal formula, has been used to treat allergic rhinitis (AR) for several centuries. However, its effect on experimental animal models and its therapeutic mechanism remain unclear.

Objective: To study the effect of Shu-Bi-Lin, a modified *Jia Wei Cang Er Zi San*, on an animal model of AR.

Methods: Shu-Bi-Lin was administered to the guinea pig model of AR. Meanwhile, an antihistamine-treated group for the treatment control, an ovalbumin-sensitized and untreated group for the positive control, and a sham-sensitized, sham-challenged group for the sham control were studied in parallel. Symptomatic and some pathophysiologic variables were evaluated.

Results: Sneezing and nasal scratching after challenges were significantly ameliorated in the Shu-Bi-Lin-treated group compared with the ovalbumin-sensitized and untreated group, but rhinorrhea volume was not reduced. Shu-Bi-Lin significantly suppressed the production of IgG1 in the passive cutaneous anaphylaxis test. The thromboxane B₂ level in nasal lavage fluid was significantly decreased in the Shu-Bi-Lin-treated group; however, the reduction in histamine and peptide leukotriene levels did not reach statistical significance. In addition, eosinophil infiltration and endothelial nitric oxide synthase immunoreactivity in the nasal tissues were reduced in the Shu-Bi-Lin-treated group.

Conclusions: Shu-Bi-Lin could alleviate the nasal symptoms of AR, and its mechanism might be related to its inhibitory effect on type I anaphylaxis reactions and eosinophil infiltration in the nasal tissues, as well as the inhibition of some mediators related to AR.

Ann Allergy Asthma Immunol. 2006;96:844–850.

INTRODUCTION

Allergic rhinitis (AR) has emerged as a major public health problem worldwide, with an increasing prevalence in recent years.¹ Traditional Chinese medicine has been used for centuries and has been demonstrated to be effective in the control of allergic diseases. Recent studies showed that it had an immunomodulatory effect on the regulation of T_H1/T_H2 pathways,² the suppression of IgE production,³ and the promotion of the activities of natural killing cells and macrophages.⁴ Some classic herbal formulas have been demonstrated to be effective in clinical trials for AR, and their mechanisms have also been partially studied in recent years.⁵ *Jia Wei Cang Er Zi San* (*JWCEZS*) is a traditional herbal formula that has been used for the treatment of AR, the common cold, and paranasal sinusitis for centuries. Although *JWCEZS* was claimed to be clinically effective for AR, we did not find sufficient evidence about its efficacy based on well-controlled scientific research. To our knowledge, no clinical trial using the principles of evidence-based medicine has ever been performed on it. Shu-Bi-Lin is a modified *JWCEZS* that has been developed and used in the Prince of Wales Hospital, Hong Kong. An in vitro study and a multicenter, randomized, double-blind, placebo-controlled clinical trial of Shu-Bi-

Lin are being performed by our group. However, the mechanism by which it exerts its action in improving patients' symptoms remains unclear. In the present study, the extract of the formula was given to the guinea pig model of AR, and the possible antiallergic effect and the mechanism were investigated.

MATERIALS AND METHODS

Animals

Eight- to 12-week-old Hartley guinea pigs (weighing 400–650 g) were purchased from the Animal House of the Chinese University of Hong Kong and housed under a specific allergen-free environment in an air-conditioned room. A standard laboratory diet and water were given ad libitum. The sensitization was started 1 week after the animals were settled. All experimental procedures in the present study complied with the standards specified by the Animal Experimentation Ethics Committee of Hong Kong.

Preparation of the Extract of Shu-Bi-Lin

Sixty grams of Shu-Bi-Lin was prepared with a mixture of 6 herbs, including *Fructus Xanthii*, 7.5 g; *Radix Angelicae Dahuricae*, 20 g; *Radix Saposhnikoviae*, 7.5 g; *Flos Magnoliae*, 15 g; *Radix Gentianae*, 5 g; and *Herba Verbenae*, 5 g. These plant materials were purchased from an herbal supplier (Anguo, Hebei province, China). Authentication was performed at the Institute of Chinese Medicine, Chinese University of Hong Kong, and their voucher specimens were deposited at the Clinical Center of the Institute of Chinese Medicine, Chinese University of Hong Kong. The main

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Accepted for publication in revised form October 31, 2005.

Table 1. Composition of Shu-Bi-Lin and the Main Pharmacologic Components of Each Herb in the Formula*

Crude ingredient	Dose in the formula, g	Main active pharmacologic components
<i>Fructus Xanthii</i>	7.5	Xanthostrumarin, stigmasterol, and ceryl alcohol
<i>Radix Angelicae Dahuricae</i>	20	Byak-angelicin, scopoletin, angenomalin, and anomalin
<i>Radix Gentianae</i>	5	Gentiopicroside, C ₁₆ H ₂₀ O ₃ , swertiamarin, sweroside, gentisin, and gentianose C ₁₆ H ₃₂ O ₁₆
<i>Herba Verbenae</i>	5	Verbenalin, hastatoside, β -caryophyllene, and verbenalol
<i>Radix Saposhnikovia</i>	7.5	Ovatodiolide, anisofolinA, tetracosane, anisomelic acid, and anisomelin
<i>Flos Magnoliae</i>	15	Citral, eugenol, and 1,8-cineole

* Data are from the *Chinese Herbal Medicine Database* [book on CD-ROM]. Beijing, China: Beijing Zhongyanxin; 2000.

active pharmacologic components of each herb contained in the formula of Shu-Bi-Lin are given in Table 1. None of the herbs contain a glucocorticoid-like component. Extract of Shu-Bi-Lin was prepared by decocting the dried prescription of herbs with boiling distilled water for 3 hours. After being filtered and condensed with a rotary evaporator, the decoction was lyophilized and the final freeze-dried powder was the extract of the formula, with 12.4% of the original weight of the raw materials. The doses mentioned in the text refer to the weight of the powdered extract.

Animal Model Establishment and Drug Administration

Animals were randomly divided into 4 groups. Group 1 was the Shu-Bi-Lin-treated group. Animals were sensitized and challenged, followed by daily Shu-Bi-Lin treatment at a dose of 1.5 g/kg for the duration of challenge. Group 2 was the antihistamine treatment control group. Animals were sensitized and challenged, followed by daily treatment with 1.5 mg/kg of desloratadine (Shering-Plough Corp, Brussels, Belgium), a second-generation H₁-receptor antagonist, for the duration of challenge. Group 3 was the ovalbumin (grade V)-sensitized (Sigma-Aldrich Corp, St Louis, MO) and un-

treated group. Animals were sensitized and challenged, and saline was given as the sham treatment. Group 4 was the sham control group. Animals were sham sensitized and sham challenged, followed by sham treatment with saline.

The protocol of sensitization and challenge was described in a previous study,⁶ with modifications (Fig 1). Ovalbumin was given as an antigen, which was absorbed on the freshly prepared aluminum hydroxide gel. The dosage of the sensitization was 20 μ g of ovalbumin/0.5 mg of aluminum hydroxide gel per 100 μ L of saline per nostril given twice a day for 10 consecutive days. The sham control group was sham sensitized with 0.5 mg of aluminum hydroxide gel/100 μ L of saline per nostril. After 5 days, the animals were challenged 11 times with 1% ovalbumin saline solution, 100 to 150 μ L per nostril once every 3 days. The sham control group was sham challenged with saline instead of the 1% ovalbumin solution.

Sneezing and Nasal Scratching Frequencies and Rhinorrhea Volume

The animals' activities were recorded using a DigitalCam (model 420E; Sony, Shanghai, China), and the sneezing and nasal scratching events were counted during the first, second, and third 10-minute intervals after each challenge. An inde-

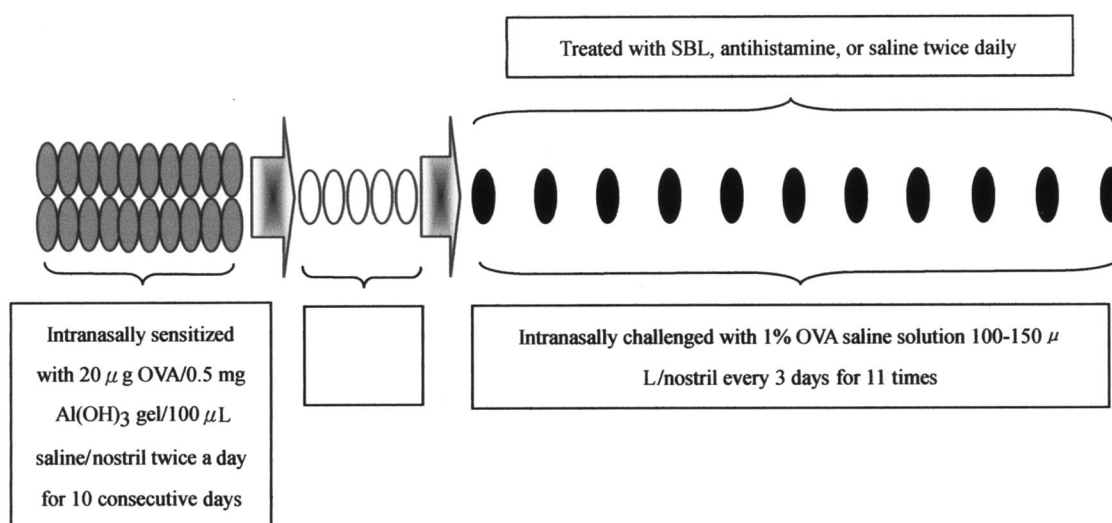


Figure 1. Protocol of the development of the animal model and treatment schedule. The sham control group was sham sensitized by aluminum hydroxide (Al[OH]₃) solution, followed by sham challenge with saline after 5 days. Ova indicates ovalbumin; SBL, Shu-Bi-Lin.

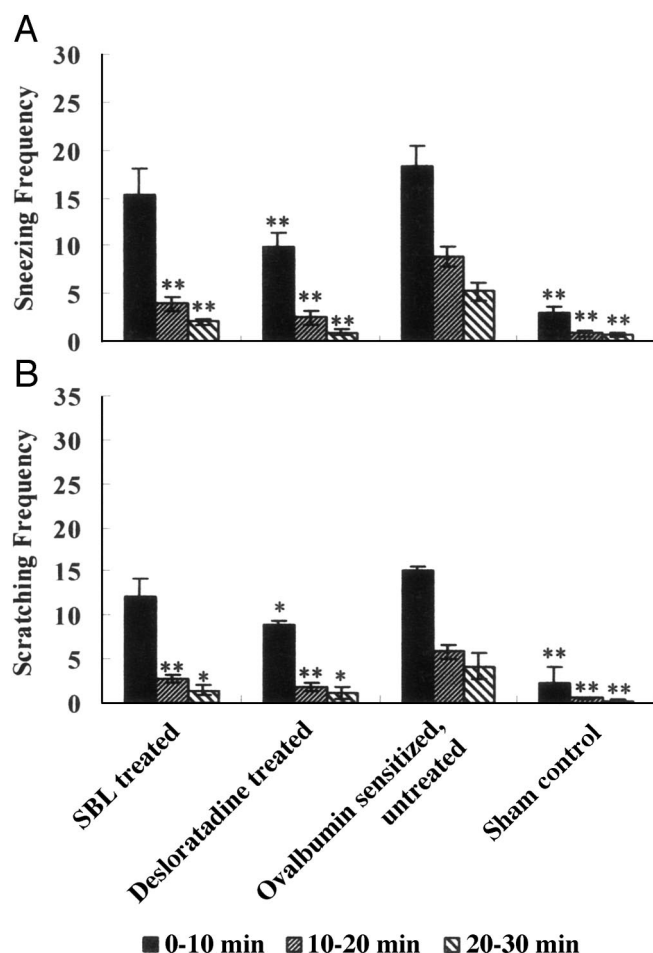


Figure 2. Time course changes in sneezing (A) and nasal scratching (B) frequencies during the first, second, and third 10-minute intervals after the fifth challenge in each group of guinea pigs. Each column represents the mean of 10 to 14 guinea pigs for 10 minutes. SBL indicates Shu-Bi-Lin; asterisk, $P < .05$ vs the ovalbumin-sensitized and untreated group; double asterisk, $P < .01$ vs the ovalbumin-sensitized and untreated group. Error bars represent SEM.

pendent observer who was not involved in the research performed the counting from the tape. Nasal secretion was measured using the filter paper technique.⁷ Ten minutes after the challenges, the secretion was continuously wiped off, using the preweighed paper, during the second 10-minute interval after the challenges. The gained weight of the filter paper after the wiping was the indication of the quantity of secretion.

Passive Cutaneous Anaphylaxis Test

The IgG1 is the main antibody in type I anaphylaxis reactions in guinea pigs instead of IgE. Four-hour and 7-day passive cutaneous anaphylaxis (PCA) tests were performed to evaluate the titers of IgG1 and IgE according to the method of Levine et al.⁸ The test serum samples were collected 5 hours after the challenges.

Measurement of Histamine, Thromboxane B₂, and Peptide Leukotriene Levels in Nasal Lavage Fluid

Nasal lavage fluid (NLF) samples were collected according to the method previously reported.⁹ Five hours after the tenth challenge, the NLF sample for this assay was collected and stored in a tube containing indomethacin (10 μ mol/L), AA-861 (1 μ mol/L), and EDTA (7.7 mmol/L). The histamine level in NLF was measured using the *o*-phthalaldehyde spectrofluorometric procedure according to the method previously described.¹⁰ After extraction of the samples as previously introduced,¹¹ the thromboxane B₂ (TXB₂) and peptide leukotriene (p-LT) levels in NLF were measured by enzyme immunoassay using the TXB₂ and LTC₄/LTD₄/LTE₄ enzyme immunoassay systems (Amersham Pharmacia Biotech, Buckinghamshire, England) according to the manufacturer's instructions.

Pathologic Observations

After the last challenge, the animals were humanely killed. The nasal tissue was harvested and fixed in 4% paraformaldehyde for 48 hours, followed by decalcification with 5% formic acid. The tissue slides were prepared for hematoxylin-eosin and immunohistochemical staining. In hematoxylin-eosin staining, infiltrating eosinophils in the nasal mucosa were observed, and the intensity of eosinophil infiltration in the nasal mucosa was semiquantitatively graded using an arbitrary scale¹²: grade 0, not present or not found; grade 1, mild; grade 2, moderate; and grade 3, severe. To avoid bias, all the slides were coded and blindly read by the observer. The trachea and lung tissues were also observed to identify whether the allergic reaction also happened in the lower airway.

Immunohistochemical Staining of Nitric Oxide Synthase and Image Analysis

The nitric oxide synthase (NOS) immunohistochemical staining protocol was performed according to the avidin-biotinylated horseradish peroxidase complex method. The primary rabbit polyclonal antibodies of inducible NOS (iNOS) (1:1,000) (Biotech Inc, Santa Cruz, CA) and endothelial NOS (eNOS) (1:200) (Biotech Inc) were applied, and the negative control was provided with normal rabbit IgG instead of the primary antibody. Slides were examined using a microscope (DM RXA2; Leica, Wetzlar, Germany). Images of the nasal tissue slides were acquired, using a Leica DC500 camera, from 9 consecutive fields for each slide (magnification $\times 400$). The semiquantitative image analysis was performed using a computer (Dell Inc, Round Rock, TX) and the MetaMorph Imaging System software (Universal Imaging Corp, West Chester, PA). All analyses were performed blind to the observers.

Statistical Analyses

The results are given as mean $\pm$ SEM. Statistical analyses were performed using the Wilcoxon signed rank test or 1-way analysis of variance. Statistical calculation was performed

using a software program (SPSS 10.0; SPSS Inc, Chicago, IL). $P < .05$ was considered statistically significant.

RESULTS

Time Course Changes in Sneezing and Nasal Scratching Frequencies and Rhinorrhea Volume

Sneezing and nasal scratching frequencies after the fifth challenge were demonstrated to be representative of the first, third, seventh, and ninth postchallenges, which were similar to each other (Fig 2). The animals started to sneeze frequently immediately after the challenge, and the peak frequency was observed during the first 10 minutes. During the second 10 minutes, the frequencies decreased rapidly, and sneezing was only occasional during the third 10 minutes. The Shu-Bi-Lin-treated group had lower frequencies of sneezing during the second and third 10 minutes ($P = .009$ for both), although no significant difference was shown during the first 10 minutes compared with the ovalbumin-sensitized and untreated group ($P = .21$). Desloratadine seemed to have a stronger effect than Shu-Bi-Lin on alleviating the sneezing symptom, especially during the first 10 minutes after challenge, with significant difference ($P = .008$). The nasal scratching frequencies followed a similar pattern as the sneezing frequencies.

The volume of rhinorrhea in the ovalbumin-sensitized and untreated group was higher than that in the negative sham control group ($P = .009$, $.002$, and $.002$ in the second, sixth, and tenth challenges, respectively) and the antihistamine-treated group ($P = .02$ in both the sixth and tenth challenges), but no significant reduction was found in the Shu-Bi-Lin-treated group ($P = .69$, $.65$, and $.70$ in the second, sixth, and tenth challenges, respectively). The sham control group had minimal rhinorrhea volume (data not shown).

PCA Test

The titers of ovalbumin specific IgG1 antibody in the ovalbumin-sensitized and untreated group, as indicated by the 4-hour PCA test results, ranged from 1:2 to 1:64 at the sixth challenge and from 1:16 to 1:128 at the tenth challenge; the sham control group showed no increase at all (Table 2). Meanwhile, the level of IgE assayed by the 7-day PCA test was modestly increased, ranging from negative to 1:8 at the sixth challenge and from 1:1 to 1:32 at the tenth challenge;

the sham control group also showed no increase. Shu-Bi-Lin treatment inhibited the increase of IgG1 at the sixth ($P = .03$) and tenth ($P = .009$) challenges but had no effect on the IgE level. However, desloratadine did not inhibit the IgG1 level at the sixth challenge, whereas it exerted an inhibition effect on IgE increase.

Histamine, TXB₂, and p-LT Levels in NLF

The level of TXB₂ in the NLF of the ovalbumin-sensitized and untreated group was higher than that in the antihistamine-treated group ($P = .009$), the sham control group ($P = .007$), and the Shu-Bi-Lin-treated group ($P = .01$) (Table 3). However, Shu-Bi-Lin treatment did not lead to significant inhibition of the p-LT level ($P = .06$), although the level was lower than that in the ovalbumin-sensitized and untreated group. The ovalbumin-sensitized and untreated group had a higher histamine level than the other 3 groups, and the difference was significant compared with the sham control and antihistamine-treated groups ($P = .03$ for both). No significant difference was detected between the ovalbumin-sensitized and untreated group and the Shu-Bi-Lin-treated group ($P = .09$). However, a tendency toward decrease in the Shu-Bi-Lin-treated group was observed.

Eosinophil Infiltration in Nasal Tissue

The pathological observations showed that eosinophil infiltration dominantly occurred in the ovalbumin-sensitized and untreated group but much less in the Shu-Bi-Lin-treated group ($P = .04$) and the antihistamine-treated group ($P = .04$) (Table 4 and Fig 3). Eosinophil infiltration was modest in the sham control group ($P = .007$). In addition, no eosinophil infiltration was found in the lower airway tissues (data not shown).

NOS Immunoreactivities in Nasal Tissues

The immunoreactivity of eNOS was clearly observed in the nasal mucosa of the ovalbumin-sensitized and untreated group and the antihistamine-treated group, whereas in the Shu-Bi-Lin-treated group and the sham control group, it was weakly stained, with significant difference ($P = .009$ and $.008$, respectively) (Table 4 and Fig 3). However, the iNOS immunoreactivity showed no differences among groups ($P >$

Table 2. IgG1 (4-Hour) and IgE (7-Day) Titers of Serum Samples From Each Group of Guinea Pigs in the Passive Cutaneous Anaphylaxis Test*

	IgG1			IgE		
	Second	Sixth	Tenth	Second	Sixth	Tenth
SBL treated		3.8 ± 3.6†	18.1 ± 11.6‡	1.4 ± 0.7	8.1 ± 5.2	
Desloratadine treated		6.4 ± 1.0	9.0 ± 2.4‡		2.2 ± 0.6†	
Ovalbumin sensitized and untreated		6.6 ± 4.5	42.7 ± 11.4	2.2 ± 1.0	6.0 ± 2.5	
Sham control						

Abbreviation: SBL, Shu-Bi-Lin.

* Serum samples were drawn on the second, sixth, and tenth challenges. Titers are given as geometric mean ± SEM. Significant difference was compared with the ovalbumin-sensitized and untreated group.

† $P < .05$.

‡ $P < .01$.

Table 3. TXB₂, p-LT, and Histamine Levels in Nasal Lavage Fluid After the 10th Challenge in Each Group of Guinea Pigs*

	TXB ₂ , pg/mL	p-LT, pg/mL	Histamine, ng/mL
SBL treated	163.4 ± 23.3†	76.5 ± 18.8	9.6 ± 2.2
Desloratadine treated	156.4 ± 34.0‡	66.0 ± 16.7†	6.8 ± 1.1†
Ovalbumin sensitized and untreated	271.8 ± 36.5	114.5 ± 40.0	11.7 ± 2.4
Sham control	62.1 ± 1.6‡	12.4 ± 2.3‡	6.8 ± 1.3†

Abbreviations: p-LT, peptide leukotriene; SBL, Shu-Bi-Lin; TXB₂, thromboxane B₂.

* Values are given as the mean ± SEM from 10 to 14 guinea pigs (magnification ×400).

† *P* < .05 vs the ovalbumin-sensitized and untreated group.

‡ *P* < .01 vs the ovalbumin-sensitized and untreated group.

Table 4. Results of Semiquantitative Image Analysis for eNOS and iNOS Expression by Immunohistochemical Staining and Eosinophil Infiltration by Hematoxylin-Eosin Staining in Sections of Nasal Tissue From Each Group After the Last Challenge*

	SBL treated	Antihistamine treated	Ovalbumin sensitized and untreated	Sham control
eNOS, area %	12.4 ± 1.5†	17.7 ± 2.4	20.1 ± 2.1	11.5 ± 1.5†
iNOS, area %	12.4 ± 1.9	10.9 ± 1.7	11.5 ± 1.9	11.3 ± 2.5
Eosinophil, grade	1.6 ± 0.2‡	1.8 ± 0.2‡	2.6 ± 0.2	0.8 ± 0.2†

Abbreviations: eNOS, endothelial nitric oxide synthase; iNOS, inducible nitric oxide synthase; SBL, Shu-Bi-Lin.

* Data are given as the mean ± SEM from 10 to 14 guinea pigs.

† *P* < .01 vs the ovalbumin-sensitized and untreated group.

‡ *P* < .05 vs the ovalbumin-sensitized and untreated group.

.05 for all). Endothelial NOS was also strongly stained in goblet cells in addition to the distribution area of iNOS.

DISCUSSION

The symptomatic observations are the most direct variables to evaluate the effect of Shu-Bi-Lin. In the present study, although Shu-Bi-Lin could not significantly reduce the frequency of sneezing and nasal scratching during the first 10 minutes after challenge, it reduced the frequency during the second and third 10 minutes. However, unlike desloratadine, Shu-Bi-Lin seemed to have no effect on the reduction of nasal discharge. Allergic rhinitis is a type I anaphylaxis reaction that is mediated by IgE in human patients and in rat models. The level of serum IgE corresponds to the severity of nasal symptoms. In contrast, IgG1, instead of IgE, plays a major role in the guinea pig model of AR. Increased IgG1 titers can aggravate nasal allergy-like symptoms. In the present model, after exposure to ovalbumin for several weeks, the titers increased dramatically in the sensitized groups but not in the sham control group, and desloratadine reduced the increase in the titers. This phenomenon was consistent with other AR models of rat and guinea pig, as well as in human patients.^{13–15} Shu-Bi-Lin could also significantly inhibit the increase in IgG1. This result indicated that Shu-Bi-Lin might have a potent immunomodulatory effect on type I anaphylaxis reactions, which might contribute toward its therapeutic mechanism in the treatment of AR. The effect of Shu-Bi-Lin resembled that of antihistamine, which could suppress the PCA reaction.^{14,15}

Increases in TXA₂, p-LT, and histamine levels have been observed in the NLF of allergic patients after antigen chal-

lenge,¹⁶ and the role of these mediators in the pathogenesis of early and late phases of nasal blockage were demonstrated in an experimental AR model.¹¹ Recent studies^{17,18} suggested that TXA₂ and p-LTs increased the permeability of nasal mucosa blood vessels to induce nasal congestion and blockage. Thromboxane A₂ and p-LTs were also thought to contribute to antigen-induced eosinophilia in the guinea pig model of AR.¹⁹ Eosinophilia is a distinctive feature of AR and is associated with the development of nasal symptoms. Thromboxane B₂, the stable breakdown product of TXA₂, has been detected in the NLF of other animal models and in patients with AR.^{12,16} In the present study, the levels of TXB₂, p-LT, and histamine in the NLF were significantly higher in the sensitized groups than in the sham control group, and such an increase could be partly suppressed by Shu-Bi-Lin and desloratadine, which probably contributed to the relief of the nasal symptoms. The decrease in TXB₂, p-LT, and histamine levels, especially TXB₂, is speculated to be related to the effect of Shu-Bi-Lin on the relief of nasal symptoms in the animals. The levels of p-LTs and histamine in the NLF decreased in the Shu-Bi-Lin-treated group; although no significant differences compared with the ovalbumin-sensitized and untreated group were detected, a tendency toward decreased levels in the Shu-Bi-Lin-treated group was observed.

Eosinophil infiltration in the nasal tissues is one of the characteristic results of AR. In allergic asthmatic patients and sensitized animals, delivery of antigen into the airways resulted in early neutrophil recruitment, which led to goblet cell degranulation and later eosinophil recruitment.⁴ Furthermore, the activated eosinophils can release various cytotoxic granule proteins and lipid mediators.²⁰ Therefore, eosinophils have been the sub-

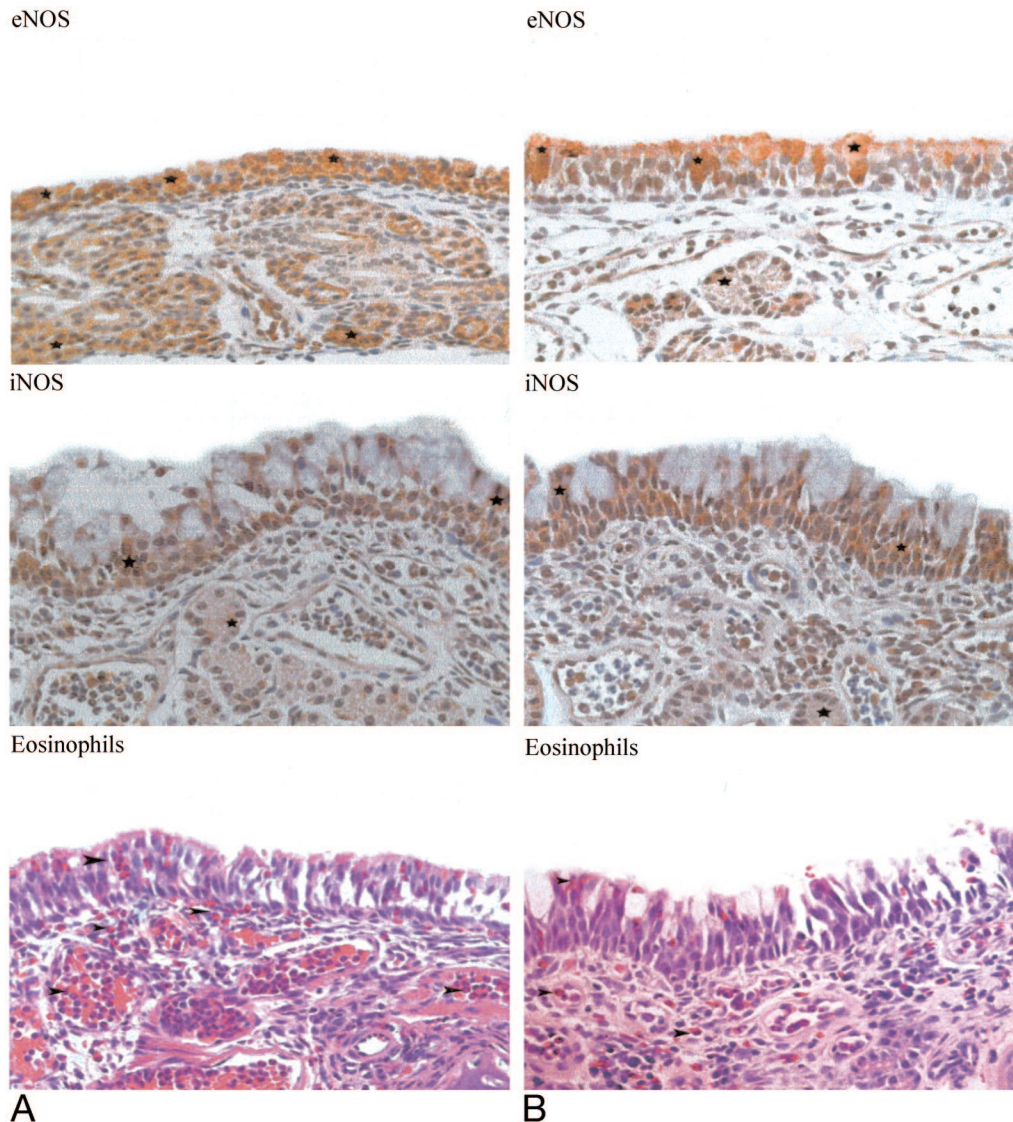


Figure 3. Light photomicrographs of hematoxylin-eosin and nitric oxide synthase (NOS) immunohistochemical-stained sections of nasal tissues selected from the ovalbumin-sensitized and untreated group (A) and the Shu-Bi-Lin-treated group (B) of guinea pigs after the last challenge. Slides show eosinophil infiltration in the nasal mucosa (arrowheads). Endothelial NOS (eNOS) and inducible NOS (iNOS) were found in the cytoplasm of the submucosal glandular cells and epithelium. Endothelial NOS was also expressed strongly in goblet cells (stars), whereas iNOS was not expressed in goblet cells. The differences in eosinophil infiltration and eNOS expression between the 2 groups are also shown (original magnification $\times 400$).

ject of numerous studies as one of the most interesting effector cells associated with AR. In the present study, similar to desloratadine treatment, eosinophil infiltration in the nasal tissues was significantly inhibited by Shu-Bi-Lin. The reduction in eosinophil infiltration might be associated with the decrease in TXB_2 and p-LT levels in the NLF followed by treatment with Shu-Bi-Lin and desloratadine.

Nitric oxide plays an important role in the regulation of upper airway function and is considered an important inflammatory mediator.²¹ Nitric oxide is produced by NOS, which is believed to induce the vessel dilatation and hyperfunction of

submucosal glands and, therefore, leads to nasal congestion and discharge. Increased iNOS and eNOS expression has been observed in the nasal epithelium of patients with AR.²² In the present study, eNOS and iNOS were detected in the nasal tissues. Endothelial NOS, rather than iNOS, seemed to be the pathogenetic isoform in this model, which was similar to another guinea pig model.²³ Parallel to alleviation of the symptoms of AR, Shu-Bi-Lin treatment significantly inhibited the expression of eNOS. It was, therefore, speculated that the reduction in eNOS expression contributed, at least in part, to the therapeutic mechanism of Shu-Bi-Lin. In addition,

eNOS was found to be strongly expressed in goblet cells. This result suggested that eNOS might play a role in the regulation of goblet cell function, by which the rhinorrhea volume of allergic guinea pigs might be altered. However, the fact that the rhinorrhea was not reduced by Shu-Bi-Lin treatment suggested that factors other than eNOS were also involved in the secretion process.

The formula of Shu-Bi-Lin, modified from *JWCEZS*, demonstrated its efficacy in the animal model in the present study. A clinical trial is being performed on patients with AR by our group that should provide its real efficacy in the therapy of AR in human beings. The results of the present animal study and our previous *in vitro* study²⁴ gave good support for the therapeutic justification of the formula.

In conclusion, this study showed that Shu-Bi-Lin was effective in relieving the symptoms of sneezing and nasal scratching, except rhinorrhea, in the AR model of guinea pigs. The anti-allergic mechanisms and the main targets in the pharmacologic pathway of Shu-Bi-Lin might be attributed to its inhibitory effects on PCA reaction and the inhibition of eosinophil infiltration in nasal tissues. Its inhibitory effects on eNOS expression and the release of TXB₂ might also be associated with its therapeutic mechanism. Although desloratadine, in some cases, was better at inhibiting mediators and inflammatory markers than Shu-Bi-Lin, Shu-Bi-Lin seemed to be a valuable alternative medicine as well. This is the first study, to our knowledge, that applied a scientific method to test the efficacy of *JWCEZS*. However, further study of the mechanism of action of the formula in the treatment of AR remains to be performed.

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