Chinese herbal bath therapy for the treatment of Atopic dermatitis in children

A meta-analysis and systematic review

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Abstract

Background: To conduct a systematic review of the efficacy of Chinese herbal bath therapy on children with Atopic dermatitis.

Methods: We searched Chinese databases (CNKI, VIP, and Wanfang) and English databases (PubMed, Embase, Web of science, Cochrane library) for studies from the establishment of the database to September 2022. The included literature was randomized control studies investigating the treatment of Atopic dermatitis in children by Chinese herbal bath therapy. The outcomes included the cure rate, scoring atopic dermatitis (SCORAD) index, adverse reactions and recurrence rate. RevMan 5.4 was used to analyze the extracted data.

Results: A total of 8 related studies were included containing 854 cases. The meta-analysis showed that Chinese herbal bath therapy group was superior to control group in terms of cure rate, SCORAD index, adverse reactions and recurrence rate in children with Atopic dermatitis [RR = 1.11, 95%(1.02, 1.21), P = .01; SMD = –0.77, 95%(-0.99, -0.55), P < .00001; RR = 0.44, 95%C(0.28,0.67), P = .0002; RR = 0.25, 95%C(0.10, 0.59), P = .0002].

Conclusion: The present study shows that Chinese herbal bath therapy is an effective treatment for children with Atopic dermatitis in China.

Abbreviations: AD = atopic dermatitis, RCT = randomized controlled trial, SCORAD = scoring atopic dermatitis.

Keywords: atopic dermatitis, children, Chinese herbal bath therapy, meta-analysis

1. Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by intense itching and recurrent eczema-like lesions. Since the 1970s, the incidence of AD in industrialized countries has increased by 2 to 3 times, affecting about 15% to 20% of children and 1% to 3% of adults, becoming one of the most common skin diseases in children.[1–3] AD onset is the most common to 3 and 6 months of age, with approximately 60% of patients developing the eruption in the first year of life and 90% by 5 years of age.[4] Twenty percent of children who develop AD before the age of 2 will have persistent symptoms; 17% of people have intermittent symptoms by age 7, and only 16.8% of AD patients develop after puberty.[5] The etiology and pathogenesis of atopic dermatitis have not been clarified, but current studies have shown that they are closely related to family genetics, environmental factors, modern lifestyles, environmental exposure and psychological factors.[6] The symptoms of itching and sleep disorders caused by recurrent episodes of AD seriously affect the growth and development of the child, while affecting the quality of daily life and causing other psychosocial problems.[7,8] It also brings a heavy financial burden on the families and societies.[3] Therefore, there is an urgent need to conduct research evaluations to find more effective treatment strategies for AD in children.

According to the guidelines of care for the management of atopic dermatitis developed by the American Academy of Dermatology in 2014, the treatment of AD usually includes 5 parts: topical therapy, phototherapy, systemic medication, prevention of disease onset, and adjuvant therapy.[5,9–11] Pharmacotherapy is still the first choice in the current treatment plan, such as glucocorticoids, antihistamines, immunosuppressants, etc. However, none of these drugs can completely cure AD. Moreover, long-term use of these drugs will have greater side effects and high recurrence rates, which are unacceptable to patients.[12] As a result, many researchers are looking for other effective treatments from complementary and alternative medicine therapies.

Chinese herbal bath therapy is an important part of traditional Chinese medicine and has a long history as a traditional...
diagnosis/treatment method of complementary and alternative medicine therapy. According to the theory of traditional Chinese medicine, Chinese herbal bath therapy can achieve a satisfactory effect by penetrating the drugs with warm effect into the skin, meridian points and blood vessels. At the same time, it can play an important role in regulating the function of the internal organs and helping to correct and dispel evil. Modern medical research has found that Chinese herbal solutions can not only play antibacterial and anti-inflammatory effects directly on the surface of the body, but also can be absorbed by sweat glands, mucous membranes, capillaries, etc., to produce local or systemic therapeutic effects.[13,14] In addition, the nerve endings receptors under the skin can reflexively regulate the functioning of nerves, body fluids and circulation after being stimulated by Chinese herbal liquids, thereby improving the body’s disease resistance and repair ability.[15] In recent years, Chinese herbal bath therapy has been widely used in the treatment of children’s atopic dermatitis. By combining traditional Chinese medicine decoction with bathing, the drug plays a role in reducing inflammation, improving microcirculation, and promoting the resolution of skin lesions by acting on the skin, and achieving a relatively satisfactory effect.[16–17]

Previous studies have shown that Chinese herbal bath therapy has a good therapeutic effect on AD. From the perspective of safety and comfort, it is more suitable for children than other treatment methods.[18–20] However, there are no systematic review studies specifically for the treatment of AD in children with Chinese herbal bath therapy. Therefore, we conducted systematic reviews and meta-analyses of Chinese herbal bath therapy for the treatment of AD in children to evaluate its efficacy and safety. Our goal is to fill this research gap by seeking the latest evidence available to researchers, physicians and patients.

2. Methods

2.1. Ethics statement

Our study protocol has been registered in the PROSPERO and the registration number is CRD42022359138. As all analyses in our article were based on previously published studies, no ethical approval or patient consent was required.

2.2. Literature search

The Cochrane and grading of recommendations, assessment, development and evaluation approaches[21,22] were used to guide the conduct of this review. This review was prospectively registered (PROSPERO CRD42022359138). This study was reported in accordance to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. Scientific databases (PubMed, Embase, Web of Science, Cochrane library, VIP, CNKI, Wanfang) were comprehensively searched to identify relevant literature without language restriction. Relevant keywords, medical terms and titles include Dermatitis, Atopic, children, bath, hydrotherapy, and randomized controlled trials. The search results included original research papers published in online journals. Specific search method, Appendix 1, Supplemental Digital Content, http://links.lww.com/MD/H990.

2.3. Inclusion and exclusion criteria

According to the aims of the study, the inclusion criteria were as follows: the included population should meet the diagnostic criteria for AD[5]; age < 18 years old; Chinese herbal bath therapy intervention is the main therapeutic approach; randomized controlled trials; complete original data.

Exclusion criteria were as follows: conference abstracts and systematic reviews; repeated publications; animal experiments or non-clinical experiments; articles with unreasonable experimental design; full text was not available.

2.4. Data selection and data extraction

First, all literature was screened using End-Note 9.0 software according to the preset inclusion/exclusion criteria, and any duplicated literature from different databases was removed. Then, any obviously irrelevant literature was excluded based on the title and abstract. Finally, the full text of all remaining literature was read intensively, and those papers conforming to the requirements were included (Fig. 1). The data were extracted independently by 2 investigators; a cross-check was made. Any disagreement was settled through discussion or the arbitration of a third investigator.

The following data were extracted from each eligible study: first author, year, study types, country, number of participants, age, gender, course, intervention, period of treatment, follow-up time, cure rate, scoring atopic dermatitis (SCORAD) index, adverse reactions and recurrence rate.

2.5. Risk of bias assessment

The Cochrane Risk of Bias tool[23] was applied to assess the quality of the included randomized controlled trial (RCTs), including sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other potential threats to validity. Studies were rated on each variable as low risk, high risk, or unclear risk of bias. If a study received “high risk” judgment in any 1 domain, it would be classified as “high risk of bias.” Two independent assessors conducted quality assessment, and any disagreement was settled by reaching a consensus or consulting a third researcher.

2.6. Statistical analysis

RevMan 5.4 supplied by the Cochrane net was used in this meta-analysis. The pooled enumeration data was expressed as relative risk (RR) and 95% confidence interval (CI). The pooled continuous variables were expressed as mean standard deviation (MD) and 95% CI Operation. P < .05 was used as the standard to determine the difference to be statistically significant. Q test (P value) and chi-square test (F) were used to determine the heterogeneity. If the test results indicated that there was no significant heterogeneity (P ≥ .1, I² < 50%), the fixed-effects model was used for analysis. When there is statistical heterogeneity between studies (P < .1, I² > 50%), a random-effect model is used, and a sensitivity analysis is performed to exclude studies that can cause heterogeneity, and then a meta-analysis is performed. When the included literature > 10, a funnel plot was used to test for publication bias.

3. Results

3.1. Literature search and screening

A total of 1076 articles were initially retrieved, and 761 articles were selected after removing duplicated publication. A total of 176 articles were removed by reading the title and abstract. After reading the full text, 12 articles were removed due to incomplete results, unavailable data, and low quality of the literature, and 8 articles were finally involved in this analysis[24–31] with a total of 854 patients. The flow chart of literature search is shown in Figure 1:

The trial group was treated with Chinese herbal bath, which contained a total of 28 kinds of Chinese herbal medicines, and each prescription ranged from 4 to 14 kinds. The Chinese herbal medicines and functions commonly used in the 8 Chinese
3.3. Meta-analysis results

3.3.1. Cure rate. There were 8 studies\cite{24,25,27-31} mentioning the cure rate of the 2 groups which was presented as dichotomous variables. The random-effects model ($P = 63\%$, $P = .009$) was used to pool the effect size. The pooled results showed that the difference between the 2 groups was statistically significant ($RR = 1.11, 95\%CI (1.02, 1.21), P = .01$) (Fig. 3A). However, the heterogeneity between groups was obvious for the effective meta-analysis. We correspondingly excluded individual documents 1 by 1 for a sensitivity analysis. The results showed that the heterogeneity was significantly reduced ($P = .07, 12 = 48\%$) while Huang Wenhui’s literature was deleted. Though, this paper was stripped out when analyzing efficiency and the fixed-effects model was used to pool the effect size. Finally, the results of the meta-analysis were not affected [$RR = 1.14, 95\% (1.04, 1.24)$, $P = .004$] (Fig. 3B). The meta-analysis results presented that the effect of Chinese herbal bath therapy was significantly superior to the control group in AD. Since the number of documents is $< 10$, we did not make funnel charts for analysis.

3.3.2. Severity scoring of AD. A total of 6 papers\cite{24,25,27-30} reported improvements in AD severity score. Five of the studies evaluated AD severity by SCORAD index, involving a total of 632 samples, of which 311 were in the trial group and 321 in the control group. One study\cite{27} evaluated the severity of AD by eczema area and severity index score, involving a total of 102 samples, of which 68 were in the trial group and 34 in the control group. Because there was only 1 document using eczema area and severity index as the evaluation indicator, the data were insufficient, so only 5 articles with SCORAD index as criteria were meta-analyzed. The random-effects model ($P = 31\%, P = .21$) was used to pool the effect size. The pooled results showed that the difference between the 2 groups was statistically significant [$SMD = -0.77, 95\%CI(-0.99, -0.55), P < .00001$] (Fig. 4). The meta-analysis results presented that the effect of Chinese herbal bath therapy was significantly superior to that of the control group in improving SCORAD index.

3.3.3. Adverse reactions. In the included articles, 5 studies\cite{24,27-30} mentioned the occurrence of adverse reactions, which reported the number of adverse reactions and specific symptoms of adverse reactions in the trial and control groups, such as burning sensation, mild tingling, papules and dry skin. All literature reported on the incidence of adverse reactions was expressed as dichotomous variables. The fixed-effects
model ($I^2 = 33\%$, $P = .20$) was used to pool the effect size. The pooled results showed that the difference between the 2 groups was statistically significant [RR = 0.44, 95%CI(0.28,0.67), $P = .0002$] (Fig. 5). The meta-analysis results presented that the effect of Chinese herbal bath therapy was significantly superior to that of the control group in adverse reactions.

3.3.4. Recurrence rate. A total of 3 studies[27–29] reported recurrence rates as an outcome indicator. All literature reported on the recurrence was expressed as dichotomous variables. The fixed-effects model ($F = 0\%$, $P = .63$) was used to pool the effect size. The pooled results showed that the difference between the 2 groups was statistically significant [RR = 0.25, 95%CI(0.10,0.59), $P = .0002$] (Fig. 6). The meta-analysis results presented that the effect of Chinese herbal bath therapy was significantly superior to that of the control group in recurrence rate.

4. Discussion

This first systemic review and meta-analysis of 8 RCTs in 854 individuals indicate that Chinese herbal bath therapy has greater beneficial effects than control group treatment for AD in children. Overall, Chinese herbal bath therapy appears to be safe and effective for children who suffer with AD. The etiology and pathogenesis of atopic dermatitis are complex and have not been fully elucidated but are closely related to various factors such as genetics, immunity, environment, and infection. Pharmacological treatment of AD includes systemic drugs (antihistamines and anti-inflammatory mediators, anti-infective drugs, glucocorticoids, immunosuppressants, traditional Chinese medicine, etc.) and topical drugs (moisturizers, glucocorticoids, calcineurin inhibitors, antimicrobial preparations, antipruritics, etc.), the main purpose is to reduce recurrence and relieve clinical symptoms such as pruritus. Some of these treatments have the disadvantages of high side effects, slow onset, and high price, such as long-term topical glucocorticoid preparations that can lead to local skin atrophy and telangiectasia.[32,33]

Due to the risk of long-term medication coupled with the recurrence of the disease, the patient’s compliance and confidence in curing the disease is greatly reduced. At present, although the mechanism of action of Chinese herbal bath therapy in the treatment of AD has not been elucidated, it has the characteristics of hyperthermia and medicinal therapy, which can accelerate blood circulation by dilating capillaries, thereby promoting the transcutaneous absorption of drugs directly on the site of the lesion and giving full play to the therapeutic role.[14] Most of the Chinese herbal medicines selected in Chinese herbal bath therapy have anti-inflammatory, anti-allergic and immunomodulatory effects, and work synergistically through multiple targets and multiple pathways. Studies have confirmed that Chinese medicine can play a therapeutic role by acting on immune response, skin barrier function, neuro-endocrine-immune system, microfloral flora, etc.[15–36]

This article systematically reviews the clinical efficacy and safety of Chinese herbal bath therapy in the treatment of AD in children. Eight studies were selected to evaluate the clinical efficacy from multiple perspectives, such as cure rate, recurrence rate, incidence of adverse reactions, and AD severity score (SCORAD). The results showed that the effective rate of Chinese herb bath therapy was higher than that of conventional treatment. While performing the efficiency analysis, there was significant heterogeneity between studies. Therefore, the method of excluding documents 1 by 1 was adopted to perform a sensitivity analysis, and homogeneity between studies was significantly increased while removing the research.
Table 2
Basic information of the included literature.

| Number | Year  | Author         | Study Types | Country | Cases | Ages (mean ± sd) | Gender (Male/female) | Course | Intervention                                                                 | Period of treatment | Follow-up |
|--------|-------|----------------|-------------|---------|-------|------------------|----------------------|--------|-------------------------------------------------------------------------------|---------------------|-----------|
|        |       |                |             |         |       | T C              | T C                  | T C    |中文中药治疗基础上的外用0.03%他克莫司软膏。 |                      |           |
| 1      | 2019  | Li Pengying    | RCT         | China   | 35    | 6.6 ± 1.1 yr     | 6.4 ± 1.3 yr         | 22/13 | 1.6 ± 0.3 yr                                                                 | 4 w                 |           |
| 2      | 2017  | Xu Jianqing    | RCT         | China   | 53    | 6.5 ± 2.3 yr     | 7.1 ± 1.9 yr         | 38/15 | 0.9 ± 0.3 yr                                                                 | 2 mon               |           |
| 3      | 2012  | Yang Lijun     | RCT         | China   | 60    | 1.2 ± 0.09 yr    | 1.1 ± 0.1 yr         | 31/29 | 17 ± 0.45 d                                                                  | 3d, 15d             |           |
| 4      | 2016  | Huang Wenhu    | RCT         | China   | 34/34 | 6.3 ± 2.26.5 ± 2 yr | 6.6 ± 2.3 yr         | 19/15 | -                                                                           | 3 w                 | 3 mon     |
| 5      | 2021  | Huang Wenxin   | RCT         | China   | 30    | 10.6 ± 2.51 yr   | 9.33 ± 2.8 yr        | 18/12 | -                                                                           | 2-3 mon             |           |
| 6      | 2013  | Han Haijun     | RCT         | China   | 22    | 10 ± 2.56 yr     | 9.61 ± 2.64 yr       | 12/10 | -                                                                           | 4 w                 | 3 mon     |
| 7      | 2021  | Chen Hanqiang  | RCT         | China   | 31    | 15.89 ± 2.1 yr   | 16.12 ± 2.05 yr      | 21/10 | -                                                                           | 4 w                 |           |
| 8      | 2020  | Zhu Jie        | RCT         | China   | 140   | 5.95 ± 0.75 yr   | 5.44 ± 0.62 yr       | 94/46 | -                                                                           | 2 w                 |           |

RCT = randomized controlled trial.
of Huang Wenhui. At this time, the cure rate of the Chinese herb bath group was still significantly higher than that of the control group. The reason this article affects homogeneity may be that this study had 2 control groups with different treatment and 2 sets of data were merged together after we re-read Huang Wenhui's research. In addition, the SCORAD index, recurrence rate and incidence of adverse reactions of Chinese herb bath therapy group are significantly lower than control group. According to the available evidence, Chinese herbal bath therapy can significantly improve the symptoms of skin lesions, itching and other symptoms, reduce the number of AD attacks, and can avoid the side effects of oral drugs on the body to a certain extent. However, in most studies, the intervention of experimental group was Chinese herbal bath therapy based on conventional treatment. Therefore, the available evidence suggests that Chinese herbal bath can only be used as an adjunct therapy, and cannot yet be used as a monotherapy for AD.

It is important to note that our study still had certain limitations: The included literature was of low quality; the generation of random allocation sequences and the concealment of randomization protocols were not reported in some studies; the conditions of dropout and withdrawal from the study were not described in detail; These studies were short-term, whose treatment did not exceed 8 weeks; therefore, longer duration of follow-ups is needed in the future research; The publication bias, which was caused by all the studies being published in China, may exaggerate the efficacy of Chinese herbal bath therapy to some extent; The included RCTs were all single-center studies, and the sample size of the experimental studies was relatively small, which made the research results lack reliability; There were some discrepancies in the interventions of the control groups in the trials. Consequently, the efficacy of Chinese herbal bath therapy for AD needs to be further confirmed by more well-designed, large-scale clinical trials.

5. Conclusion
The present study shows that Chinese herbal bath therapy is an effective treatment for children with AD in China, especially in relieving clinical symptoms and reducing recurrence. Due to the limitations of the study, further research should be conducted in the future with rigorous design, large sample size, sham/placebo control or blank/waiting control, and accurate report to
### Figure 3. Forest plot and sensitivity analysis of meta-analysis on Cure rate.

| Study or Subgroup | Events | Control | Events | Total | Weight | Risk Ratio M-H. Random, 95% CI | Risk Ratio M-H. Random, 95% CI |
|-------------------|--------|---------|--------|-------|--------|-------------------------------|-------------------------------|
| Chen Hanzheng2021 | 26     | 31      | 21     | 35    | 5.7%   | 1.40 [1.02, 1.91]             |                               |
| Han Hailin2013    | 23     | 23      | 22     | 45    | 13.4%  | 1.10 [0.94, 1.28]             |                               |
| Huang Wenxiu2016  | 30     | 31      | 60     | 62    | 19.8%  | 1.00 [0.92, 1.08]             |                               |
| Huang Wenxiu2021  | 35     | 38      | 22     | 30    | 8.6%   | 1.29 [1.03, 1.62]             |                               |
| Li Pengying2019   | 29     | 35      | 21     | 35    | 5.7%   | 1.38 [1.01, 1.88]             |                               |
| Xu Jiaojing2017   | 50     | 54      | 41     | 53    | 12.6%  | 1.20 [1.02, 1.41]             |                               |
| Yang Liu2012      | 47     | 56      | 47     | 54    | 13.4%  | 0.86 [0.63, 1.12]             |                               |
| Zhu Jie 2020      | 134    | 140     | 124    | 140   | 20.6%  | 1.08 [1.01, 1.16]             |                               |
| Total (95% CI)    | 408    | 431     | 399    | 439   | 100%   | 1.11 [1.02, 1.21]             |                               |
| Total events      | 375    | 396     |        |       |        |                               |                               |
| Heterogeneity: Tau² = 0.01; Chi² = 18.89, df = 7 (P = 0.009); I² = 63% |
| Test for overall effect: Z = 2.45 (P = 0.01) |

### Figure 4. Forest plot of meta-analysis on SCORAD index. SCORAD = scoring atopic dermatitis.

| Study or Subgroup | Events | Control | Events | Total | Weight | Std. Mean Difference IV. Random, 95% CI | Std. Mean Difference IV. Random, 95% CI |
|-------------------|--------|---------|--------|-------|--------|---------------------------------------|---------------------------------------|
| Han Hailin2013    | 23     | 23      | 22     | 45    | 13.4%  | -0.69 [-1.28, -0.09]                   | -0.69 [-1.28, -0.09]                   |
| Huang Wenxiu2016  | 30     | 31      | 60     | 62    | 19.8%  | -0.64 [-1.13, -0.15]                   | -0.64 [-1.13, -0.15]                   |
| Li Pengying2019   | 29     | 35      | 21     | 35    | 5.7%   | -0.58 [-0.94, -0.2]                   | -0.58 [-0.94, -0.2]                   |
| Xu Jiaojing2017   | 50     | 54      | 41     | 53    | 12.6%  | -0.56 [-0.94, -0.17]                   | -0.56 [-0.94, -0.17]                   |
| Zhu Jie 2020      | 47     | 56      | 47     | 54    | 16.6%  | -1.04 [-1.29, -0.79]                   | -1.04 [-1.29, -0.79]                   |
| Total (95% CI)    | 377    | 369     | 369    | 377   | 100%   | 0.14 [0.04, 0.24]                     | 0.14 [0.04, 0.24]                     |
| Total events      | 345    | 306     |        |       |        |                                        |                                        |
| Heterogeneity: Tau² = 0.01; Chi² = 11.57, df = 6 (P = 0.07); I² = 48% |
| Test for overall effect: Z = 2.85 (P = 0.004) |

### Figure 5. Forest plot of meta-analysis on adverse reactions.

| Study or Subgroup | Events | Control | Events | Total | Weight | Risk Ratio M-H. Fixed, 95% CI | Risk Ratio M-H. Fixed, 95% CI |
|-------------------|--------|---------|--------|-------|--------|-------------------------------|-------------------------------|
| Chen Hanzheng2021 | 1      | 31      | 5      | 35    | 9.8%   | 0.20 [0.02, 1.61]             |                               |
| Han Hailin2013    | 11     | 23      | 16     | 42    | 32.5%  | 0.66 [0.40, 1.08]             |                               |
| Huang Wenxiu2016  | 4      | 31      | 25     | 65    | 32.1%  | 0.34 [0.13, 0.88]             |                               |
| Huang Wenxiu2021  | 1      | 38      | 7      | 45    | 15.5%  | 0.11 [0.01, 0.87]             |                               |
| Li Pengying2019   | 4      | 35      | 5      | 35    | 9.9%   | 0.80 [0.23, 2.73]             |                               |
| Total (95% CI)    | 158    | 183     | 100%   | 100%  | 0.44 [0.28, 0.67]             |                               |
| Total events      | 21     | 58      |        |       |        |                               |                               |
| Heterogeneity: Chi² = 6.01, df = 4 (P = 0.20); I² = 33% |
| Test for overall effect: Z = 3.76 (P = 0.0002) |

### Figure 6. Forest plot of meta-analysis on recurrence rate.

| Study or Subgroup | Events | Control | Events | Total | Weight | Risk Ratio M-H. Fixed, 95% CI | Risk Ratio M-H. Fixed, 95% CI |
|-------------------|--------|---------|--------|-------|--------|-------------------------------|-------------------------------|
| Han Hailin2013    | 2      | 23      | 4      | 28    | 16.0%  | 0.49 [0.10, 2.35]             |                               |
| Huang Wenxiu2016  | 4      | 31      | 14     | 45    | 37.2%  | 0.15 [0.02, 1.09]             |                               |
| Huang Wenxiu2021  | 3      | 38      | 10     | 48    | 46.0%  | 0.24 [0.07, 0.78]             |                               |
| Total (95% CI)    | 92     | 117     | 100%   | 100%  | 0.25 [0.10, 0.65]             |                               |
| Total events      | 0      | 28      |        |       |        |                               |                               |
| Heterogeneity: Chi² = 0.92, df = 2 (P = 0.63); I² = 0% |
| Test for overall effect: Z = 3.15 (P = 0.002) |
support the evidence of Chinese herbal bath therapy of AD in children.

Author contributions

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