Original Article

# Characteristics of traditional Chinese medicine users and prescription analysis for paediatric atopic dermatitis

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**Abstract**

***Background:*** Traditional Chinese medicine is commonly used to treat children with atopic dermatitis. This research study reviewed patients with atopic dermatitis, recorded in Taiwan's National Health Insurance Research Database, to investigate the characteristics and prescriptions of traditional Chinese medicine (TCM) so as to propose the use of TCM for a broader societal application.

***Objective:*** The aim of this study is to determine the application mode of TCM in children with atopic dermatitis, specifically the combination of Chinese herbal medicines (CHMs) used.

***Methods:*** The database reported atopic dermatitis-diagnosed children aged 5 to 12. TCM users documented data relate to age, diagnostic code, residence area and the use of corticosteroids. An analysis of the medications used for atopic dermatitis was achieved through a review of examining the association of various factors.

***Results:*** A total of 13,646 children with atopic dermatitis, and treated using TCM, were sampled from different area of Taiwan. The use of TCM is associated with use by women (male: OR 0.83), adolescence (OR: 10.0, 95% CI: 8.88-11.15) and allergic rhinitis (OR: 2.44; 95 % CI: 2.10-2.85). Fewer TCM users than non-users receive corticosteroid therapy (35.8% of all users receive TCM). Still, the percentage of TCM users who use long-lasting corticosteroid therapy is greater than TCM non-users (10.6% of TCM users and 2.0% of TCM non-users). In total, 36,398 CHM prescriptions were used by 93.7% of Chinese medicine users. There was a total of 5.62 types CHM types used. Relationships between the Chinese herbal medicine forms network, where Xiao fengsan is the primary treatment for atopic dermatitis.

***Conclusions:*** The article describes features of children with atopic dermatitis who are treated with Chinese medicine. Xiao fengsan is the most common CHM used to treat atopic dermatitis in children. Further research on the safety and efficiency of this treatment is still required. [*Ethiop. J. Health Dev.* 2020; 34(4):253-261]

***Key words:*** Traditional Chinese medicine, atopic dermatitis, paediatrics, Chinese herbal medicine

## Introduction

Allergic disorders, including atopic dermatitis, asthma and allergies, have risen considerably over the past few decades, not only in China but across the globe (1-4). In 2013, the World Allergy Organization reported that 30% to 40% of the world's population had one or more allergies, including eczema, asthma, rhinitis, and allergic and food-related disorders (5). The increased incidence of allergic diseases has substantial economic, medical and social implications.

Western medicines used to treat allergies (6,7) include antihistamines, corticosteroids, leukotriene modifiers, and ß2 and anticholinergic agonists. However, Western medicines can only relieve symptoms; they have no therapeutic effect. On the other hand, traditional Chinese medicine (TCM) offers an alternative approach to treating allergies.

TCM consists of various forms of herbal medicines, as well as cupping therapy, acupuncture, qigong, guasha, exercise, massage (tui-na), bone setting (die-da), and dietary therapy. TCM also has fewer side-effects compared to Western medicine(8). Furthermore, Western medicine is partially successful in treating allergy sufferers, which largely explains why they pursue supplementary and complementary therapies (9). TCM has been used for thousands of years in Asia, in particular in China, Japan, South Korea and Taiwan.

Atopic dermatitis in children is a severe chronic inflammatory skin disease (10,11). Age and level of a condition, Purulent vesicle erosion, and lichenification of the skin, are the clinical signs of atopic dermatitis. Severe skin itching, particularly during the night, affects the quality of life of children with atopic dermatitis, often resulting in insomnia and chronic fatigue (10,12).

In the UK, annual atopic dermatitis spending stands at around £465 million (5); in the USA, the national direct costs range from US$3.64 billion to US$3.8 billion (13). In Australia, annual personal financial costs per sufferer range from AUD$330 to AUD$1,255 (14). Atopic dermatitis affects the day-to-day life of sufferers, and places financial strain on many patients, their families, and the medical profession (15-17).

It should come as no surprise that in Western countries, patients pursue therapeutic alternatives, such as CHM (18). In day-to-day clinical practice, the features of children who use Chinese medicine are not yet apparent. Most dermatologists in the USA use 'orthodox' therapies – treatment methods approved by the Food and Drug Administration (DA) and generally accepted in mainstream medical literature, in particular in English-language literature. However, as noted above, a substantial number of dissatisfied patients opt for alternatives to conventional medicine. In a recent study, Fleischer and colleagues found that 5% of psoriasis patients use alternative therapies without the use of sunlight and solariums. These therapies included food discipline, herbal therapy and vitamin therapy (19).

Alternative therapy, including TCM, is becoming increasingly popular in the Western world. For those administering TCM, however, it is important to carry out a thorough assessment of the potential side-effects they may have in patients. In practice, many Western

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dermatologists have misconceptions about Chinese medicine because of their ignorance of the field. For example, some dermatologists may not know about TCM studies carried out in the West, such as two UK-based double-blind, placebo-controlled Chinese medicine trials, one involving children and one among adults (20,21).

A related misconception is that the mechanism of action of Chinese medicine has never been studied in depth by scientists. On the contrary, a number of countries, including China, have published scientific publications on Chinese medicines' proposed mechanism of action and further research is ongoing (21).

A further misconception is that the TCM do not have any side-effects. Many people (even some doctors) hold this view on the misunderstanding that because CHMs are 'natural' they are therefore 'mild'.
The goal of this study is to establish how TCM treats atopic dermatitis in children, and assess the most widely used CHMs that treat the condition. We also try to determine the major combinations of CHMs in order to determine the network of these CHMs, and to assess the characteristics of TCM users. The information should serve as a good reference for clinicians and medical students.

**Materials and methods**

*Source of data:* This study uses data from Taiwan's National Health Insurance Research Database (NHIRD). Given the high coverage rate for the National Health Insurance (NHI) scheme (> 98.3% of the overall population) and the reimbursement of all medical expenditures, including medication, acupuncture and care, this database is especially useful for research into epidemiology (22). Detailed patient profiles, diagnosis and care information is provided by NHIRD. The Clinical Alteration Code of the International Classification of Diseases (9th edition) (ICD-9-CM) is used to check the diagnosis of a patient (23,24). NHIRD has been utilized as a source of evidence for many of the epidemiology and prescription reviews of TCM (25).

***TCM regulations****:* Data on Chinese medicine formulations that can be used for research purposes are given by NHIRD. All CHM components can be found in this database, apart from acupuncture and manual therapy. While Taiwan reimburses the herbal formula (HF) and basic herbal (SH) recipes for two kinds of CHM – HF includes SH with fixed components based only on traditional TCM, and every HF can be joined with other HF or SH components. Both CHMs should be manufactured in China by the pharmaceutical industry, in line with good manufacturing practices, and it is strictly prohibited to use pesticides and heavy metals.

***Plan and subject of study:*** In this manuscript we use sex, age and number of allergic combinations of disease available. We focused on the basic difference between those who use Chinese medicine and those who do not. An increased sample size may have improved the quality of the analysis, but we have tried to get the most accurate conclusion with the available data. Patients from 0 to 12 years old who had been diagnosed and ICD-9-CM codes, 691.8 and 692.x applied for atopic dermatitis were recruited. TCM users were classified as those who used TCM from 1 January 2015 to 31 December 2015 for at least one type of treatment, and non-TCM users that never used TCM in this time period (26). Atopic dermatitis is usually diagnosed on the basis of clinical symptoms such as scratching, bruises, suppuration, erythema and lichen formation. Enrolled patients age limit was limits up to 12 years as occurrence of atopic dermatitis is high in pre-adolescence (27). Those with incomplete data were not included in the final report.

***Variables for analysis:*** We used sex, age and number of allergic combinations of diseases, residential climate, urbanization level and the use of corticosteroids to determine the differences between those who use TCM and those who do not – odds ratio covariate. Comorbidities were recognized by the ICD-9-CM codes, 477.0, 477.1 477.2 and 477.8, for allergic rhinitis; 491.x for chronic bronchitis, and 493.x for asthma. Since atopic dermatitis has a clear relation to the place of residence of a patient, geographical location and urbanization are seen as covariates. In China, the level of urbanization can be split into seven stages of urbanization, of which level 1 is the highest and level 7 the lowest. In this analysis, levels 4 to 7 were all included in level 4 because of the relatively limited number of children living in these zones. Because the key treatment for atopic dermatitis is corticosteroids and the use of corticosteroids is a factor that determines the use of alternatives, discrepancies in the use of corticosteroids between TCM users and non-TCM users were also studied. The rate, time, and prescription frequency of corticosteroids over the previous year were analyzed in order to determine the corticosteroid use of each patient. In defining the widely used CHMs, the average daily dose and prevalence of CHM were used.

***Assessment of variance:*** In this analysis, the referral bias and selection reduce since NHI covers nearly all regions of China. In addition, the data is more comprehensive than that of hospitals. Moreover, as the ICD-9-CM codes are used to classify diseases accurately, registration errors have effectively been removed.

***Statistical analysis:*** We explain the characteristics of Chinese medicine users using descriptive statistics and using an independent t-test used for differentiate the continuous variable and chi-square test to analyze the disparity between TCM and non-users between categorical variables. We use the binary logistic regression approach to differentiate the characteristics of people who use TCM and not used the TCM, and used adjusted odds ratios (aOR) for covariates. All findings were considered statistically relevant, with double-side p-values below 0.05.

**Results**

*TCM users' characteristics;* A total of 13,646 children attended Chinese atopic dermatitis medicine clinics from 1 January 2015 to 31 December 2015. We also added 28,457 patients as the control group, who have not been in charge of the TCM database. The demographics for TCM users are listed in Table 1. Female patients are marginally more likely to use Chinese medicine than non-Chinese men (OR: 0.83, 95% CI: 0.79-0.86, p<0.001). Moreover, older children use TCM more often than younger children (OR: 10.0% for school-age children, 95% CI: 8.88-11.14, p<0.001), and most TCM users are school children (all TCD users are 69%). TCM treatment is more common (1.34 times the number of non-Chinese users) in children with co-existing allergic diseases. Chinese medication is 2.44 times more than for children with atopic dermatitis and allergic rhinitis (95% CI: 2.10% to 2.85). In comparison, the use of TCM is less likely for children with atopic dermatitis and respiratory diseases. Moreover, Chinese medicine is used more frequently by children living in urbanized areas.

**Table 1:** Demographic features of traditional Chinese medicine (TCM) users and non TCM users for pediatric atopic dermatitis

| Demographic features | TCM users *n* = 13,646 | Non-TCM users *n* = 28,457 | aOR | 95% CI | *p*-value |
|---|---|---|---|---|---|
| Sex | | | | | |
| Female (%) | 6,973 (51.1) | 13,292 (46.7) | 1 | | |
| Male (%) | 6,673 (48.9) | 15,165 (53.3) | 0.83 | 0.79-0.86 | <0.001 |
| Age (mean (SD)) | 7.81 (3.4) | 5.00 (3.7) | | | <0.001 |
| Infants, <1 (%) | 348 (2.6) | 4,986 (17.5) | 1 | | |
| Toddlers, 1-2 (%) | 1,230 (9.0) | 6,396 (22.5) | 2.78 | 2.45-3.16 | <0.001 |
| Pre-school, 3-5 (%) | 2,657 (19.5) | 6,036 (21.2) | 5.57 | 4.94-6.29 | <0.001 |
| School age, 6-12 (%) | 9,411 (69.0) | 11,039 (38.8) | 10.0 | 8.88-11.15 | <0.001 |
| Combined allergic diseases | | | | | |
| Asthma (%) | 1,381 (10.1) | 2,057 (7.2) | 0.87 | 0.77-0.99 | 0.041 |
| Allergic rhinitis (%) | 4,565 (33.5) | 3,877 (13.6) | 2.44 | 2.10-2.85 | <0.001 |
| Bronchitis (%) | 4,604 (33.7) | 12,220 (42.9) | 0.53 | 0.45-0.62 | <0.001 |
| Number of combined allergic diseases | | | | | |
| 0 | 6,293 (46.1) | 14,604 (51.3) | 1 | | |
| 1 | 4,774 (35.0) | 10,418 (36.6) | 1.33 | 1.14-1.55 | <0.001 |
| ≥ 2 | 2,579 (18.9) | 3,435 (12.0) | 1.34 | 1.02-1.90 | 0.039 |
| Geo-location | | | | | |
| Northern area | 6,144 (45.0) | 14,191 (49.9) | 1 | | |
| Middle area | 3,624 (26.6) | 5,413 (19.0) | 1.77 | 1.67-1.89 | <0.001 |
| South area | 3,648 (26.7) | 8,281 (29.1) | 1.12 | 1.06-1.19 | <0.001 |
| East area | 230 (1.7) | 572 (2.0) | 1.03 | 0.87-1.22 | 0.718 |
| Urbanization level | | | | | |
| 1 (most urbanization) | 4,218 (30.9) | 8,586 (30.2) | 1 | | |
| 2 (more urbanization) | 4,418 (32.4) | 8,411 (29.6) | 1.05 | 0.99-1.11 | 0.109 |
| 3 (middle urbanization) | 2,306 (16.9) | 4,855 (17.1) | 0.90 | 0.83-0.96 | <0.001 |
| 4 (least urbanization) | 2,704 (19.8) | 6,605 (23.2) | 0.75 | 0.70-0.81 | <0.001 |

*Use of corticosteroids by Chinese medicine users:* Prior to the use of TCM, corticosteroids had been used by just 35.8% of TCM users, compared to two-thirds of TCM users (see Table 2). The most widely used medications are topical corticosteroids, with most children being treated for less than 14 days. But longer-term (over 14 days) topical glucocorticoid therapy was given to TCM consumers. Although approximately 10% of children in both groups received systemic atopic dermatitis corticosteroids, the share of TCM users who had been using systemic corticosteroids was greater than non-TCM users (see Table 2).

| **Utilization patterns of corticosteroids** | **TCM users *n*=13,646(%)** | **Non-TCM users *n*=28,457(%)** | ***p*-value** |
|---|---|---|---|
| Exposure to steroids | | | |
| Any steroids | 4,886 (35.8) | 19,334 (67.9) | <0.001 |
| Topical steroids | 4,763 (34.9) | 18,062 (63.5) | <0.001 |
| Systemic steroids | 1,235 (9.1) | 2,807 (9.9) | 0.004 |
| Prescribed duration of steroids | | | |
| Topical steroids | | | <0.001 |
| Never used | 8,883 (65.1) | 10,397 (36.5) | |
| Short term (<14 days) | 3,315 (24.3) | 17,492 (61.5) | |
| Long term (≥14 days) | 1,448 (10.6) | 568 (2.0) | |
| Systemic steroids | | | <0.001 |
| Never used | 12,411 (90.9) | 25,650 (90.1) | |
| Short term (<14 days) | 906 (6.6) | 2,730 (9.6) | |
| Long term (≥14 days) | 329 (2.4) | 77 (0.3) | |
| Frequency of visits for steroids | | | |
| Topical steroids | | | <0.001 |
| 0 | 8,883 (65.1) | 10,395 (36.5) | |
| 1-3 | 3,807 (27.9) | 18,060 (63.5) | |
| ≥ 4 | 956 (7.0) | 2 (.0) | |
| Systemic steroids | | | <0.001 |
| 0 | 12,411 (90.9) | 25,650 (90.1) | |
| 1–3 | 1,068 (7.8) | 2,807 (9.9) | |

Table 2: **Differences in use of corticosteroid use among TCM users and non-users with pediatric atopic dermatitis (p value obtained from logistics regression analysis TCM user's data and NON-TCM user's data)**

| | | |
|---|---|---|
| ≥ 4 | 167 (1.2) | - (-) |

***Use of** CHM in children with atopic dermatitis:* For children with atopic dermatitis, CHM is the most popular type of Chinese medicine. Overall, CHM was used by 12,790 children (93.7%) in 2015, totaling 36,398 prescriptions. Over 600 CHMs, with an average of 5.6 CHMs, were used during this time. With compared to CHM, Xiao fengsan (XFS), followed by Xingfang baidushan (10.6%) and Xinyiqing feitang (8,9%) (see Table 3) were the most widely used HFs (31.6% of all recipes). While the other herbal formulas are Zhen-Ren-Huo-Ming-Yin, Long-Dan-Xie-Gan-Tang also used in the treatment. The most frequently used SH was *Glycyrrhiza uralensis* (16.7%) with *Dictamnus dasycarpus* (13.4%) and *Cryptotympana pustulata* (13.3%) (see Table 4 and Figure 1). XFS with *Dictamnus dasycarpus* is the most frequently used combination of CHM (6.7%), and the link among commonly used CHMs forms a network of CHM. The network clearly demonstrates that XFS is the primary CHM used in children with atopic dermatitis: XFS is the most common single CHM, and, more significantly, XFS involves the simultaneous use of other CHMs.

Table 3: **The top 5 commonly prescribed herbal formulas (HFs) used for paediatric atopic dermatitis during 2015 (Total prescriptions = 36,398)**

| Herbal formulas | Ingredients | Dosage (gm/day) | Number of prescriptions (%) |
|---|---|---|---|
| Xiao fengsan (XFS) | *Saposhnikovia divaricata*<br>*Atractylodes lancea*<br>*Schizonepeta tenuifolia*<br>*Arctium lappa*<br>*Glycyrrhiza uralensis*<br>*Rehmannia glutinosa*<br>*Gypsum fibrosum*<br>*Clematis armandii*<br>*Anemarrhena asphodeloides*<br>*Angelica sinensis*<br>*Cryptotympana pustulata*<br>*Sesamum indicum*<br>*Sophora flavescens*<br>*Notopterygium incisum* | 3.4 | 15,676 (31.6) |
| Xingfang baidushan | *Angelica biserrata*<br>*Ligusticum chuanxiong*<br>*Bupleurum chinense*<br>*Peucedanum praeruptorum*<br>*Citrus aurantium*<br>Platycodon grandiflorus<br>*Panax ginseng*<br>*Poria cocos* | 2.9 | 3,841 (10.6) |
| Xinyiqing feitang | *Glycyrrhiza uralensis*<br>*Magnolia biondii*<br>*Scutellaria baicalensis* | 3.0 | 3,254 (8.9) |

| | | | |
|---|---|---|---|
| | *Gardenia jasminoides*<br>*Ophiopogon japonicus*<br>*Lilium brownii*<br>*Gypsum fibrosum*<br>*Anemarrhena asphodeloides*<br>*Glycyrrhiza uralensis*<br>*Eriobotrya japonica*<br>*Cimicifuga heracleifolia*<br>*Lonicera japonica*<br>*Saposhnikovia divaricata*<br>*Angelica dahurica*<br>*Angelica sinensis*<br>*Paeonia lactiflora*<br>*Boswellia carterii*<br>*Commiphora myrrha*<br>*Fritillaria thunbergii*<br>*Trichosanthes kirilowii*<br>*Gleditsia sinensis*<br>*Citrus reticulata* | | |
| Zhen-Ren-Huo-Ming-Yin | *Glycyrrhiza uralensis*<br>*Gentiana scabra*<br>*Scutellaria baicalensis*<br>*Gardenia jasminoides*<br>*Alisma plantago-aquatica*<br>*Caulis clematidis armandii*<br>*Plantago asiatica*<br>*Angelica sinensis*<br>*Rehmannia glutinosa*<br>*Bupleurum chinense*<br>*Glycyrrhiza uralensis* | 3.0 | 2,803 (7.7) |
| Long-Dan-Xie-Gan-Tang | | 2.7 | 2,540 (7.0) |

Table 4: **The top 10 commonly used single herbs (SHs) used for paediatric atopic dermatitis (Total prescriptions = 36,398) (2015)**

| Name | Dosage (gm/day) | Number of prescriptions |
|---|---|---|
| *Glycyrrhiza uralensis* | 0.9 | 6,076 |
| *Dictamnus dasycarpus* | 0.9 | 4,876 |
| *Cryptotympana pustulata* | 0.9 | 4,846 |
| *Lonicera japonica* | 1.1 | 4,204 |
| *Forsythia suspensa* | 1.1 | 4,141 |
| *Coix lacryma-jobi* | 1.2 | 3,588 |
| *Paeonia suffruticosa* | 1.1 | 3,520 |
| *Kochia scoparia* | 0.9 | 3,461 |
| *Angelica dahurica* | 1.4 | 2,234 |
| *Schizonepeta tenuifolia* | 1.0 | 2,186 |

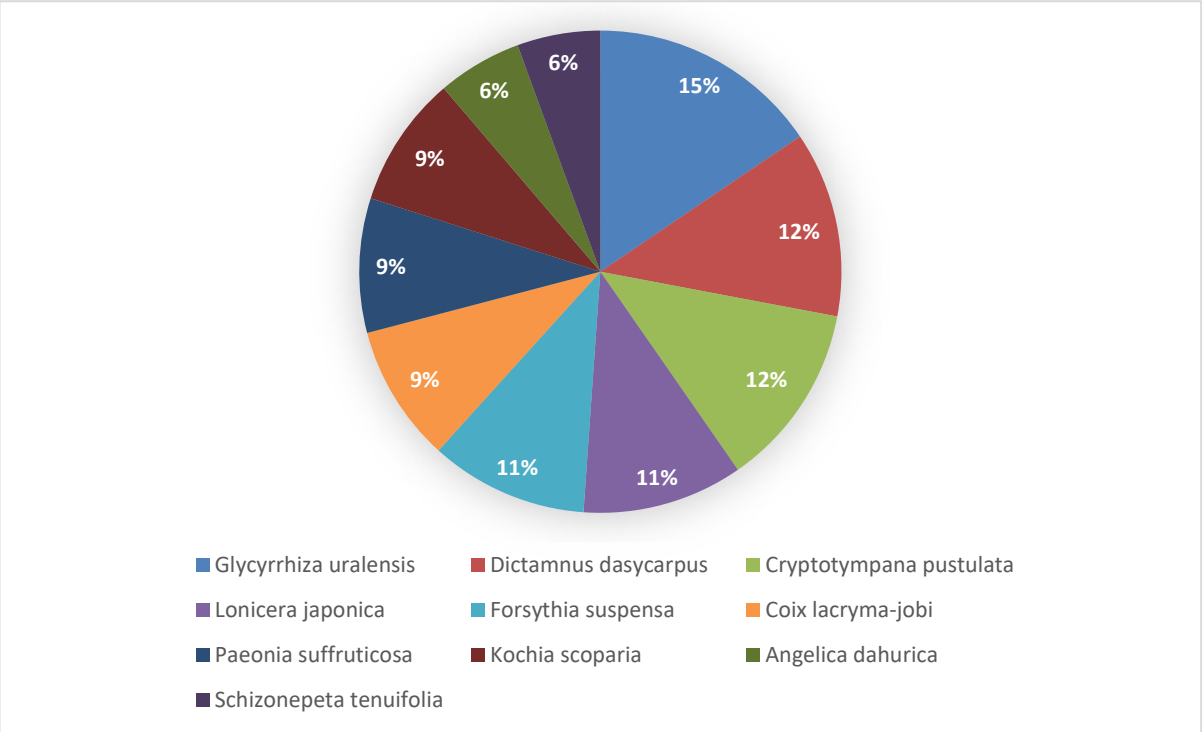


Figure 1: **Top 10 commonly used single herbs**

**Discussion**

As far as we know, this is the first broad study to explain variations in the disposition of children who may or may not use TCM to treat atopic dermatitis. We focused mainly on patients with this disease only, but we observed that patients with co-morbidities or who were critically ill can easily be treated CTM for atopic dermatitis. Moreover, CTMs are mainly plant derivatives or herbal products. According to our study, allopathic medicines are not proven significantly effective than Traditional Chinese medicine in treating atopic dermatitis, though there are limited data on this observation. More frequently, older boys and girls, particularly children suffering from allergic rhinitis and various allergic diseases, use TCM. Atopic dermatitis develops is typically around age of 5, while in older children have less control over atopic dermatitis by using medication.

Unhappiness with established Western therapy may lead to older children being treated with TCM, and this pattern is similar to that of the population as a whole (22,28). Children with allergies usually use CTM, particularly children with both neuro-dermatitis and allergic rhinitis. This may also explain why children living in urban areas, where allergic conditions are more common, use TCM (29). For example, children suffering from more serious allergic diseases have significantly increased use of Western medicine. Increase the antihistamine dosage or use various antihistamine forms or even corticosteroids concurrently. Western high-dose medication may raise the risk of side-effects, which could cause parents to consider using TCM. In our study we found that TCM has similar effect in treating atopic dermatitis as modern drugs. Though this research is based only on the sample available to us, like many other herbal medicines TCM has fewer side effects noted. This is purely herbal product where no artificial steroid has been used. Corticosteroid is used to lower the inflammation of the body but can easily be avoided for its side-effects. No post-medicinal reaction has been registered in modern research nor seen in our observation too. Plant extracts are safer than steroids because less side effect has been seen or registered in the research available or in our observations. Only a prescription and minimal side-effects will allow the use of herbal medicines to enhance sneezing and skin propitiation (30).Chinese medicine generally takes the whole human population into account when administering a drug and attempting to manage the effects with a single medication, contrary to the treatment of certain disease conditions (31). Moreover, the use of corticosteroids varies widely from one individual to the next. In general, corticosteroid usage was relatively low in TCM users prior to treatment with TCM, whereas corticosteroid use was relatively high in long-term users.

Long-term use of topical corticosteroids may cause skin atrophy, telangiectasia, as well as corticosteroid systemic endocrine disorders (32,33). Concern regarding the use of corticosteroids is, therefore, one of the main factors in sufferers turning to TCM to treat symptoms (28). Also, children using Western medicines appear to have more serious symptoms, and turn to Chinese medicines to enhance symptom control (34). CHM was screened for possible contaminants (including steroids) in four previous studies (20,30,35,36), while hochu-ekki-to, an immunity enhancing herbal medicine of China, was made by a accredited company (16). Three of the five research

studies that recorded adverse incidents showed substantial differences. The aspartate amino transferase had one case of temporary elevation, which was reversed in 8 weeks after treatment was terminated (35). Elevated levels of aspartate aminotransferase can be caused by many factors, including alcohol misuse, and medicaments, such as antihistamines and non-steroidal anti-inflammatory drugs and some herbs (37). There was no additional information to determine the potential correlation between the elevation and the test protocol. The atopic dermatitis, according to TCM, results in a congenitally poor composition that contributes to predisposition to atopic dermatitis and susceptibility to external and internal pathogens, such as wind, humidity and heat (38). However, the same TCM diagnosis might be shared in such dermatological conditions as psoriasis. Of the studies included, only two were TCM distinguished, the rest used a standardized formula of CHM. Nonetheless the atopic dermatitis effects of any formulation were reduced, the quality of life increased, and/or the need for topical corticosteroids reduced(39). To find out the characteristics of the traditional Chinese medicine user and prescription analysis for pediatric dermatitis, and also correct immunological dysfunction, and alter physical function rather than control local illness (40,41) after the whole we find out more than 90% patients in china and Taiwan uses the Chinese medicine. The traditional Chinese medicine is found the same effectivity as western medicine from the statistical analysis of the obtained data. So, use of the corticosteroid can be limited while the treatment of atopic dermatitis (30,35,39).

**Conclusion**

Atopic dermatitis along with allergic rhinitis comorbid children, living in the urban area, more uses traditional Chinese medicine. TCM is used extensively in many parts of China and beyond for the treatment of atopic dermatitis. TCM has anti-inflammatory, anti-allergic and anti-oxidant effects that are crucial in treating atopic dermatitis. The most commonly used CHM is XFS formula. Further clinical trials and mechanism studies are needed to clarify the issues of safety and efficacy

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