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Original Article

Investigation of Chinese herbal products prescribed to patients with psoriasis of outpatient service from the National Health Insurance Research Database in Taiwan

Chun-Ting Liu [1, 2], Cheng-Chieh Chang [1, 2], Yao-Hsu Yang [2, 3, 4], Bei-Yu Wu [1, 2], Pau-Chung Chen [4, 5], Shang-Hung Lin [2, 6], Ming-Yen Tsai [1, 2, *]

[1] *Department of Chinese Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan*
[2] *School of Traditional Chinese Medicine, Chang Gung University College of Medicine, Taoyuan, Taiwan*
[3] *Department of Chinese Medicine, Chiayi Chang Gung Memorial Hospital, Chiayi, Taiwan*
[4] *Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University College of Public Health, Taipei, Taiwan*
[5] *Department of Environmental and Occupational Medicine, National Taiwan University Hospital, Taipei Taiwan*
[6] *Department of Dermatology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan*

This study analyzed the prescription patterns of Chinese herbal products (CHPs) in patients with psoriasis based on outpatient service data of National Health Insurance Research in Taiwan and investigated their clinical application. This population-based cohort study was conducted using a randomly sampled cohort of one million patients between 2003 and 2013 selected from the National Health Insurance Research Database in Taiwan. The use of CHPs and the top ten most frequently prescribed formulae and single herbs for treating psoriasis were assessed, including average formula doses and frequency of prescriptions. Demographic characteristics including sex and age were examined. The therapeutic principles and possible mechanisms of CHPs prescriptions are discussed. We identified 1,055 (8.5%) patients with psoriasis who used CHPs during the study period. Patients between 19 and 45 years of age comprised the largest number of those treated (54.6%). Male patients used CHPs for psoriasis more frequently than did female patients (male:female = 1.4:1). The most frequently prescribed herbal formula and single herb for the treatment of psoriasis were Wen-Qing-Yin and Mu Dan Pi, respectively. According to the association rule, the most commonly prescribed two-

***Correspondence authors:** Ming-Yen Tsai, Department of Chinese Medicine, Kaohsiung Chang Gung Memorial Hospital, No. 123, Dapi Rd., Niaosong Dist., Kaohsiung 83301, Taiwan, Tel: +886-7-7317123, ext. 2334; Fax: +886-7-7317123, ext. 2335, Email: missuriae@yahoo.com.tw

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formula CHP combination for treating psoriasis was Wen-Qing-Yin plus Xue-Fu-Zhu-Yu -Tang, while the most commonly prescribed combination of formula CHP and single herb was Xiao-Feng-San plus Tu Fu Ling. Further research is required to fully elucidate the efficacy and safety of these CHPs.

Key words: Chinese herbal products, Psoriasis, Pharmacoepidemiology, National Health Insurance Research Database, Traditional Chinese Medicine

Introduction

Psoriasis is a chronic, complex, relapsing and remitting inflammatory skin disease affecting 1–3% of the world's population [1-3]. An estimated 0.235 % of Taiwanese adults are affected, and the prevalence of psoriasis is higher in men than in women [4]. The clinical features of psoriasis are variable, ranging from one or several cutaneous patches and papules to severe exfoliation involving the entire skin [5]. A major complaint is severe skin itching with silvery scales developing, especially after physiological and psychological stress, and injury of normal-appearing skin corresponds to the so-called Koebner phenomenon [6,7]. The pathogenesis of psoriasis is complicated and not fully understood. Genetic factors, excessive stimulation of keratinocytes, immune dysregulation, dendritic cell activation, and skin infections have all been reported to be highly associated with psoriasis [8]. The numerous management strategies proposed to control the severity include emollients containing corticosteroids, vitamin D analogs, retinoid and calcineurin inhibitors for mild and moderate symptoms, and phototherapy and immunotherapy for severe symptoms [9]. However, in consideration of patient compliance and the potential benefits and adverse effects of the therapies, treatment must be individualized [10,11].

In Taiwan, traditional Chinese medicine (TCM) is commonly used to control the symptoms of psoriasis, and one of the most commonly used modalities of TCM treatment is Chinese herbal products (CHPs) [12]. A previous study by Weng et al. estimated that more than 70% of Taiwanese patients with newly diagnosed psoriasis receive TCM therapy [13], but the average daily dosages of several CHPs mentioned in that study were very high compared with typical clinical practice. A detailed analysis of the characteristics and prescription patterns of CHPs for the treatment of psoriasis would be worthwhile.

Unlike previous studies, which included herbal medicine, acupuncture and traumatology in TCM treatment, this study specifically focused on identifying the usage patterns of CHPs for psoriasis and the most commonly used CHPs by analyzing data from the National Health Insurance Research Database (NHIRD). In addition to the characteristics of the CHP users, we aimed to clarify the most important formula CHPs and single herbs, and thereby the indications of these CHPs. Such information would be a good reference for clinicians and also provide good candidates for further studies, since TCM practitioners usually prescribe several CHPs in combination to treat a disease.

Material and methods

1. Data Source

In March 1995, the Taiwanese government implemented the NHI program, which provides general health insurance coverage to nearly all residents of Taiwan. We used the Longitudinal Health Insurance Database 2005 (LHID 2005), which contains the medical information of 1 million beneficiaries randomly sampled from the registry of all beneficiaries in 2005. The random method of LHID 2005 is described online (http://nhird.nhri.org.tw/date_cohort.html). The database contains all longitudinal reimbursement information about gender, birth date, medications, and diagnosis codes base on the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM). The

sampled patients exhibited no significant differences in age, sex, birth year, or average insured payroll-related amount from the general population. Because the National Health Insurance Research Database (NHIRD) contains de-identified secondary data for research, the requirement of informed consent was waived for the present study.

2. Study Subjects

The psoriasis cohort was selected from a random sample of one million individuals by using the diagnostic variables in the outpatient visit database from the NHIRD. Figure 1 shows the flowchart for

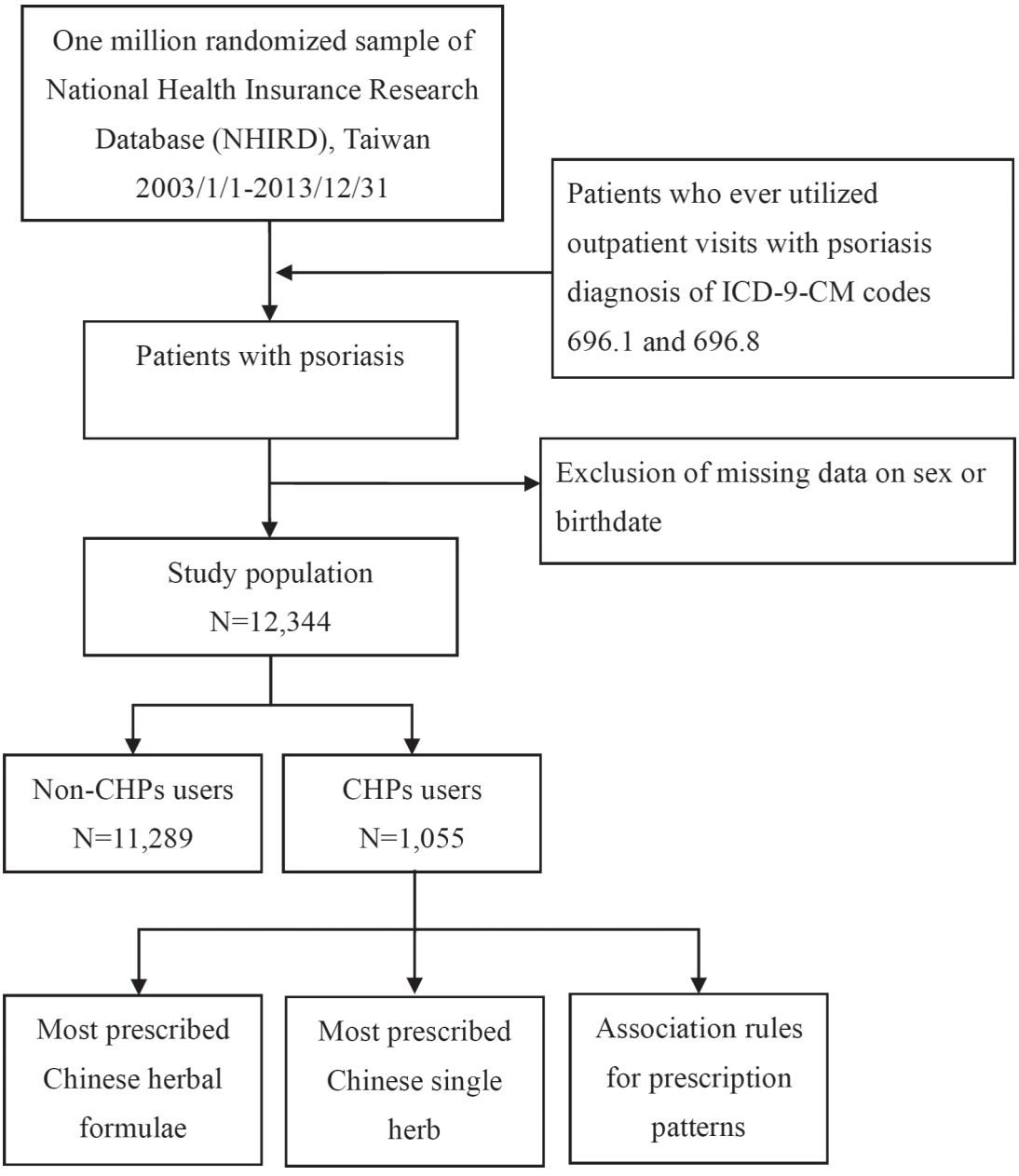

Figure 1. Flow diagram of this study

selecting the study population. Data from 2003 to 2013 were used for the purposes of this study. The ICD-9-CM codes 696.1 (other psoriasis) and 696.8 (other psoriasis and similar disorder) were used for identification of the cohort. Patients who had visited the outpatient department during the study period (from 2003 to 2013) were included in the evaluations. The single or formula CHPs or the 2–3 kinds of combination prescriptions at each visit were analyzed. Patients with missing data on sex or birthdate were excluded.

3. CHPs prescriptions

Currently, the NHI program provides reimbursement for two kinds of Chinese herbal remedies: Chinese single herbs and Chinese herbal formulas. Each Chinese herbal formula is combined with two or more fixed proportions of Chinese single herbs, in strict adherence to TCM theory. The list of CHPs eligible for reimbursement was downloaded from the website of the NHI Bureau. Corresponding drug information on a specific mixture or name was then obtained from the website of the Committee on Chinese Medicine and Pharmacy, including the proportions of each ingredient, the date and period of drug approval, drug names, and manufacturers' codes. For most formula CHPs, daily doses of 6–9 grams are recommended, and for single herbs, 1–2 grams. The average number of doses per day is two or three.

4. Statistical Analysis

Drug registration numbers from the Committee on Chinese Medicine and Pharmacy website were linked to the outpatient visit records of the psoriasis cohort. Most CHPs prescriptions contain one or more herbal formulas combined with several single herbs. The frequencies and percentages of herbal formula and single-herb prescriptions were then analyzed. Daily doses and average prescription durations were calculated for each prescription.

Association rules were applied to evaluate the coprescription patterns of CHPs for psoriasis. Evaluation with association rules, at a basic level, involves the use of machine learning models to analyze data for patterns, or co-occurrence, in a database. The models identify frequent if–then associations, which are called association rules. An association rule has two parts: an antecedent (if) and a consequent (then). An antecedent is an item found within the data. A consequent is an item found in combination with the antecedent. Association rules are created by searching data for frequent if–then patterns and using the criteria support and confidence to identify the most important relationships. Support is an indication of how frequently the items appear in the data. Confidence indicates the number of times the if–then statements are found to be true. In this study, the support factor (the proportion of coprescriptions of medications A and B amongst all prescriptions) was first determined. The confidence factor (the proportion of coprescriptions of medications A and B amongst all prescriptions containing medication A) was then determined. SAS version 9.1 software (SAS Institute Inc., Cary, NC, USA) was used for the data linkage and descriptive statistics on patterns of drug use.

Results

In all, 12,344 of the one million randomly-sampled patients from the NHIRD from 2003 to 2013 had received outpatient treatment for psoriasis (Table 1). Based on age distribution of psoriasis [14], age bracket with four population groups was subclassified as children/adolescents (0-18 years old), young

Table 1 Age-specific and associated comorbidities in patients with psoriasis under National Health Insurance in Taiwan

Variable	Patients with psoriasis (n=12344)	(%)	CHP use (n=1055)	(%)	Crude odds ratio	P value	Adjusted odds ratio	P value
Sex								
Female	5556	45.0%	432	40.9%	REF			
Male	6788	55.0%	623	59.1%	1.20 (1.05–1.36)	0.0056	1.24(1.083–1.41)	0.0021
Age group								
0–18	1366	11.0%	109	10.3%	REF			
19–45	5342	43.3%	576	54.6%	1.39 (1.13–1.73)	0.0024	1.28 (1.03–1.60)	0.0265
46–65	3543	28.7%	280	26.6%	0.99 (0.79–1.25)	0.9291	0.90 (0.70–1.17)	0.4463
> 65	2093	17.0%	90	8.5%	0.52 (0.39-0.69)	< 0.0001	0.51 (0.37–0.70)	< 0.0001

Adjust odds ratio: adjusted for sex and age.

adulthood (19-45 years old), middle age (46-65 years old) and old age (more than 65 years old) in this study. Similar subgroups of population based on disease-prone age and author's expectations was also used and adapted by other studies [15,16]. The largest group of patients with psoriasis was those between 19 and 45 years old (43.3%). The next largest group was patients between 46 and 65 years old (28.7%). More than 70% of the individuals with psoriasis were between 19 and 65 years old. Approximately 8.5% of the patients with psoriasis received CHP therapy. The largest age group of patients who received CHPs treatment was those between 19 and 45 years old (54.6%). Male patients used CHPs for psoriasis more frequently than female patients did (male:female = 1.4:1). After sex and age were analyzed for, CHPs users tended to be males aged 19–45 years.

Table 2 lists the top 10 single and formula CHPs prescribed to patients with psoriasis. Wen-Qing-Yin (WQY) was the most commonly used CHP formula (30.5 % of all prescriptions), followed by Xiao-Feng-San (XFS) (19.0 %). Mu Dan Pi was the most commonly used single CHP (18.7 %), followed by Bai Xian Pi (15.2 %). The most common single and formula CHPs were Mu Dan Pi and WQY, respectively. The average daily dose and prescription duration of WQY were 8.5 grams and 17.3 days, far exceeding those of the other herbal formulas.

Table 3 reveals the most common two-drug combinations of CHPs in a single prescription as determined by association rules. The most common two-formula CHP combination for patients with psoriasis was WQY plus Xue-Fu-Zhu-Yu-Tang (XFZYT). The most common formula CHP and single-herb combination was XFS plus Tu Fu Ling. The most common two-single-CHP combination was Bai Xian Pi plus Tu Fu Ling.

Table 2 The top 10 single and formula CHPs prescribed by TCM practitioners for treating patients with psoriasis in Taiwan

Single CHP (*Latin names*)	Frequency, n (%)	Average daily dose (g)	Average duration per prescription (days)	Formula CHP	Frequency, n (%)	Average daily dose (g)	Average duration per prescription (days)
Mu Dan Pi *(Paeonia suffruticosa Andrews)*	1,622 (18.7)	1.5	13.2	Wen-Qing-Yin (WQY)	2,639 (30.5)	8.5	17.3
Bai Xian Pi *(Dictamnus dasycarpus Turcz.)*	1,318 (15.2)	1.5	12.4	Xiao-Feng-San (XFS)	1,644 (19.0)	5.5	11.8
Jin Yin Hua *(Lonicera japonica Thund.)*	1,052 (12.1)	1.3	11.7	Long-Dan-Xie-Gan-Tang (LDXGT)	861 (9.9)	4.0	12.7
Tu Fu Ling *(Smilax glabra Roxb.)*	1,012 (11.7)	1.9	10.2	Jia-Wei-Xiao-Yao-San (JWXYS)	709 (8.2)	3.8	14.5
Sheng Di Huang *(Rehmannia glutinosa (Gaertn.) Steud.)*	880 (10.2)	1.8	14.2	Dang-Gui-Yin-Zi (DGYZ)	698 (8.1)	4.8	11.4
Zi Cao *(Lithospermum erythrorhizon Sieb. et Zucc.)*	679 (7.8)	1.7	12.9	Xue-Fu-Zhu-Yu-Tang (XFZYT)	674 (7.8)	4.0	15.8
Di Fu Zi *(Kochia scoparia (L.) Schrad.)*	656 (7.6)	1.5	11.3	Huang-Lian-Jie-Du-Tang (HLJDT)	604 (7.0)	3.5	13.1
Lian Qiao *(Forsythia suspensa (Thunb.) Vahl)*	627 (7.2)	1.3	11.4	Xiang-Sha-Liu-Jun-Zi-Tang (XSLJZT)	531 (6.1)	2.4	19.7
Gan Cao *(Glycyrrhiza uralensis Fisch.)*	597 (6.9)	1.0	11.5	Zhi-Bai-Di-Huang-Wan (ZBDHW)	433 (5.0)	4.8	16.2
Dan Shen *(Salvia miltiorrhiza Bunge)*	544 (6.3)	1.5	11.3	Zhen-Ren-Huo-Ming-Yin (ZRHMY)	337 (3.9)	5.4	15.1

Table 3 The most common combinations of CHP pairs for psoriasis.

Herbal associations	Support (%)	Confidence (%)	Transaction count	Association rule
Two-formula CHPs	5.04	14.91	394	Wen-Qing-Yin ➡ Xue-Fu-Zhu-Yu -Tang
	4.93	14.62	386	Wen-Qing-Yin ➡ Xiang-Sha-Liu-Jun-Zi-Tang
	4.36	12.92	341	Wen-Qing-Yin ➡ Xiao-Feng-San
Formula CHP and single herb	6.40	30.49	501	Xiao-Feng-San ➡ Tu Fu Ling
	6.30	18.68	493	Wen-Qing-Yin ➡ Mu Dan Pi
	6.00	28.54	469	Xiao-Feng-San ➡ Bai Xian Pi
Two single CHPs	7.30	56.42	571	Bai Xian Pi ➡ Tu Fu Ling
	7.04	52.33	550	Bai Xian Pi ➡ Jin Yin Hua
	6.49	50.20	508	Tu Fu Ling ➡ Jin Yin Hua

Discussion

Psoriasis is called "white mange" (bai bi) or "dry ringworm" (gan xuan) in Chinese and has been recorded for thousands of years in China. According to TCM theory, psoriasis is attributed to long stagnation of pathogenic wind and heat resulting from exposure to exogenous wind, dampness, or heat, or from internal factors of emotional injury and stagnation of qi, and also to obstruction of the meridians and collaterals leading to qi stagnation and blood stasis [17]. Psoriasis develops from an excess of blood heat stagnating in the skin and then consuming body fluid and yin-blood [17].

The pathogenesis of psoriasis is similar to the immune system “misfiring” and causing excess growth and inflammation of skin cells [18]. As Ainsworth described [19], stressed keratinocytes induce dendritic cells to release many cytokines, such as TNF-α, IL-12, IL-23, IL-17, and IFN-r, resulting in the dead scales characteristic of psoriatic plaques. In addition, prolonged stimulation of these pathways will worsen epidermal thickening and erythema through angiogenesis and vasodilation [20]. The primary characteristic of CHP treatment is that it focuses not only on controlling the local disease but also on modifying the patient’s constitution and correcting immunity disorders. Therefore, it is believed that the therapeutic effect can be enhanced by using topical and oral biomedicines concurrently to relieve psoriatic discomfort from the inside to the outside of the body. Under this model of integrative medicine, patients’ symptoms can be well-controlled and the use of biomedicines can be reduced, as observed in small-scale clinical trials [21].

Based on TCM theory, the various TCM syndromes of psoriasis are often categorized into

dampness-heat, blood heat, blood dryness, blood stasis, and yin deficiency [17]. Therefore, most CHPs prescribed for treating psoriasis are based on these syndromes and their derived morphologies, courses or severities. Blood heat syndrome is the TCM syndrome most or second-most frequently associated with psoriasis [17, 22]. If either body fluids or nutrient blood are stagnated or exhausted by certain factors, it will lead to blood stasis in the skin, joints, or viscera, thereby causing blood dryness and yin deficiency. The treatment principals for blood heat and blood dryness and for yin deficiency are to clear heat and resolve toxins, and to cool and nourish the blood, respectively. Mu Dan Pi and WQY are the core single and formula CHPs for treating psoriasis due to their high utilization and coverage of those TCM syndromes. Much of the research on the frequently used CHPs in our results has pointed to biological activity that can inhibit the specific cytokines responsible for the development of inflammatory immune responses and skin lesions [23-38]. The possible mechanisms of frequently used CHPs for psoriasis are presented in Table 4.

Table 4 Potential effects of the single and formula CHPs contained in the five most common formulae prescribed by CM practitioners for treating psoriasis.

CHPs	Principle of CHPs treatment	Possible pharmacological effects
Single CHP		
Mu Dan Pi *(Paeonia suffruticosa Andrews)*	Clean heat and cool blood	Inhibit beta-hexosaminadase and TNF-α release via inactivation of p38, ERK, Akt, and NF-κB pathways [23]. Inhibit histamine release, reduce IgE-mediated PCA reaction, decrease TNF-α, IL-6, MCP-1, ICAM-1, TGF-β1 and RAGE expression, inhibit NF-κB/IκB-α and phosphorylation of ERK [24].
Sheng Di Huang *(Rehmannia glutinosa (Gaertn.) Steud.)*	Clean heat and cool blood	Inhibit IL-1 and TNF-α, inhibit histamine release, reduce IgE-mediated PCA reaction and systemic anaphylaxis [25].
Jin Yin Hua *(Lonicera japonica Thund.)*	Clean heat and resolve toxicity	Increase IL-10 production and inhibit TNF-α and IL-6 expression, reduce ROS and NO production [26]. Inhibit the expression of various inflammatory mediators regulated by NF-κB and MAPKs that are components of the TLR4 signaling pathway, inhibit phosphorylation of IκB-α, IKKα/β, TAK1, TBK1 and IRAK-1 pathways [27,28].
Bai Xian Pi *(Dictamnus dasycarpus Turcz.)*	Clean heat and dissolve dampness	Diminish epidermal hyperplasia, immune cell infiltration, edema and spongiosis in inflamed tissues, inhibit ICAM-1, TNF-α, IFN-γ, histamine, β-hexosaminidase IL-6, IL-8, MIG, MCP-1 and RANTES release, inhibit p38 MAPK pathway, NF-κB pathway and Th1 skewing reactions, inhibit the proliferation of T cells [29].

CHPs	Principle of CHPs treatment	Possible pharmacological effects
Tu Fu Ling *(Smilax glabra Roxb.)*	Dissolve damp and detoxify	Inhibit NO, iNOS and TNF-α, ameliorate keratinocytes proliferation and infiltration of CD3+ cells, reduce circulating CD4+ and CD8+ T cells and inflammatory cytokines, inhibit Th17 cell differentiation, IL-17 secretion, Jak/Stat3 signaling in Th17 cells [30].
Formula CHP		
Wen-Qing-Yin (WQY)	Drain fire, cool the blood, and resolve toxicity	Inhibit allergic reactions and suppress the induction phase but not the effector phase of the cellular immune response [31].
Xiao-Feng-San (XFS)	Disperse wind, eliminate dampness, and clear heat	Act as an immunomodulatory agent to correct the Th1/Th2 balance, increase IL-4 mRNA expression, and decrease IFN-r mRNA expression [32,33]. Inhibit IgE dependent histamine release from cultured mast cells [34].
Long-Dan-Xie-Gan-Tang (LDXGT)	Drain excess heat and dampness from the liver and gallbladder	Reduce the expression of proinflammatory cytokines, including IFN γ, IL-6, IL-17 and TNF- α [35].
Jia-Wei-Xiao-Yao-San (JWXYS)	Strengthen the spleen, nourish the blood, and harmonize the liver and spleen	Inhibit the LPS-induced production of NO, PGE2, TNF-α, and IL-6. Downregulate the expression of iNOS and COX-2 mRNA induced by LPS. Suppress the LPS-induced activation of NF-κB and MAPKs such as p38, extracellular signal-regulated kinase (ERK), and c-Jun N-terminal kinase (JNK) [36].
Dang-Gui-Yin-Zi (DGYZ)	Nourish blood, moisten dryness, dispel wind, and relieve itching	Enhance the expression of Filaggrin and Caspase-14 gene and protein of skin lesions in psoriatic animal model [37]. Promote the proliferation, regulate peripheral T cell function and inhibit leukotriene B4 [38].

Notes: **WQY Constituents:** *Rz. Coptidis, Rx. Scutellariae, Cx. Phellodendri, Fr. Gardeniae, Rx. Rehmanniae Preparata, Rz. Chuanxiong, Rx. Angelicae Sinensis, Rx. Paeoniae Alba.* **XFS Constituents:** *Hb. Schizonepetae, Rx. Saposhnikoviae, Fr. Arctii, Periostracum Cicadae, Rz. Atractylodis, Rx. Sophorae Flavescentis, Caulis Akebiae, Gypsum Fibrosum, Rx. Anemarrhenae, Rx. Rehmanniae, Rx. Angelicae Sinensis, Sm. Cannabis, Rx. Glycyrrhizae.* **LDXGT Constituents:** *Rx. Gentianae, Rx. Scutellariae, Fr. Gardeniae, Caulis Akebiae, Sm. Plantaginis, Rz. Alismatis, Rx. Bupleuri, Rx. Rehmanniae, Extremitas Radicis Angelicae Sinensis, Rx. Glycyrrhizae.* **JWXYS Constituents:** *Rx. Bupleuri, Rx. Angelicae Sinensis, Rx. Paeoniae Alba, Rz. Atractylodis Macrocephalae, Poria, Rx. Glycyrrhizae Preparata, Hb. Menthae Haplocalycis, Rz. Zingiberis Recens, Fr. Gardeniae, Cortex Moutan.* **DGYZ Constituents:** *Rx. Rehmanniae, Rx. Angelicae Sinensis, Rx. Paeoniae Alba, Rz. Chuanxiong, Dry-fried Fr. Tribuli, Hb. Schizonepetae, Rx. Saposhnikoviae, Rx. Astragali, Rx. Polygoni Multiflori, Rx. Glycyrrhizae, Rz. Zingiberis Recens.*

When managing patients with psoriasis, it is important for TCM practitioners to take complete medical histories to screen for these comorbidities. Since the use of herbal medicine concomitantly with prescription drugs is increasing worldwide, it is important to assess potential herb–drug interactions. Concurrent use of herbs may mimic, magnify, or counteract the effects of drugs [39]. For example, Mu Dan Pi has a wide spectrum of activities, such as anti-inflammatory, antioxidant, anti-tumor, anti-diabetic, neuroprotective and cardiovascular protective effects [40]. Concurrent use of Mu Dan Pi may increase the effects of anti-tumor and anti-diabetic agents. However, some herbs may reduce the efficacy of conventional drugs or increase complications, particularly in the case of concurrent use of herbal medicines in patients receiving cardiovascular pharmacotherapy. Licorice (Gan Cao) has an additive effect on potassium excretion that may reduce the antihypertensive effects of spironolactone and induce hypokalemia when used concurrently with certain diuretics [41]. Dan Shen and Dong Quai may increase the anticoagulant effect, which may increase the risk of bleeding when used concurrently with warfarin [39,41]. Despite increasing reports of herb–drug interactions, many studies have lacked laboratory analysis of suspect drugs and sometimes have produced inconsistent results. For example, Bai Xian Pi, commonly used for skin itching, was reported to cause hepatotoxicity in some case reports [42]. However, a recent study reported that Bai Xian Pi exhibits antioxidative and hepatoprotective activity both *in vitro* and *in vivo* [43]. Herb–drug interactions undoubtedly do occur and may put individuals at risk. However, our present knowledge is incomplete, and more research is urgently needed [44].

Psoriasis is a chronic, complex, relapsing and remitting inflammatory skin disease. Based on TCM theory, chronic illness could cause deficiency of qi, and deficiency of qi over a long period of time may lead to blood stasis. In our study, the most commonly prescribed patterns of two-formula CHP combinations for treating psoriasis were WQY plus XFZYT, followed by WQY plus Xiang-Sha-Liu-Jun-Zi-Tang (XSLJZT). Our results were consistent with TCM theory and clinical practice, in which XFZYT and XSLJZT are typically used for treating blood stasis and deficiency of qi, respectively. We also found that the most commonly prescribed pattern of a formula CHP and single-herb combination for treating psoriasis was XFS plus Tu Fu Ling, followed by WQY plus Mu Dan Pi. According to TCM theory, Tu Fu Ling can increase the effect of XFS to eliminate dampness, and Mu Dan Pi can increase the effect of WQY to clear heat. According to the association rule, the most common combinations of CHPs could be as a TCM clinical guide for treating psoriasis.

Our study results were inconsistent with one previous cohort study reporting that WQY and Bai Xian Pi were the CHPs concomitantly prescribed most frequently in the Taiwanese population [13]. The differences can be ascribed to the years of enrollment for the analysis and the precise ICD-9 codes. Patients with psoriasis with ICD-9-CM codes (696.1 and 696.8) have a chronic illness for which irrelevant diagnoses such as parapsoriasis (696.2), pityriasis rosea (696.3) or other and unspecified pityriasis (696.5) have been ruled out. In addition, the average daily doses of formula and single CHPs analyzed in our study were 4.67g and 1.5g, respectively. This result is inconsistent with a report by Weng et al., found formula CHP doses of 65.4g and single CHP doses 23.5g, which do not conform to our prescription habits [13]. Since no standard

recommended dosages for evaluating the safety and efficacy of CHPs have been established, the therapeutic doses of CHPs tend to vary widely, depending on TCM practitioners' experience or the manufacturers' labels. Generally, the maximal dose is 6g in every package; therefore, the upper limit is 18–24g daily. The contradiction between statistical results and clinical practice needs to be explained reasonably.

The strengths of this study include the immediate availability of a nationwide database, the comprehensiveness of the database, and the statistical power derived from the large sample size, all of which limit the possibility of selection bias and provide exploration of better treatment options. In addition, compared with previous studies, we implemented more stringent standards for the psoriasis cohort to investigate the prescription patterns for treating psoriasis, and the results were reasonable and applicable in clinical practice. Despite these strengths, several limitations should be noted when interpreting the results of the present study. First, the identification of the psoriasis cohort was based on ICD-9-CM codes, and misclassification was a possibility. The times from diagnosis of psoriasis to the initial visit to a TCM outpatient service for treatment of psoriasis, as well as disease severity, were unavailable. Second, the NHI program provides reimbursement only for CHPs prescribed by TCM doctors. Topical TCM ointments, decoctions of raw herbal medicine, health foods containing natural herbs, folk medicine, and direct purchases from TCM herbal pharmacies were not analyzed in this study. The related missing data might have led to underestimation of the usage frequencies and doses of CHPs. The above limitations should be noted when interpreting the results of the present study.

Conclusions

This study explored the prescription patterns and the clinical application of CHPs for treating psoriasis in Taiwan. The most commonly prescribed formula CHP was found to be Wen-Qing-Yin, and the most commonly prescribed single CHP, Mu Dan Pi. The therapeutic effects and safety of these commonly used formula or single CHPs require further examination in clinical studies or well-designed randomized, double-blind, placebo-controlled trials.

Author contributions

YHY and CCC conceptualized the study. YHY and PCC performed the statistical analysis. BYW, CTL, YHY, PCC, and CCC contributed to the interpretation of CHP data. CTL and MYT contributed to the interpretation of pharmacological mechanisms and also drafted and finalized the manuscript.

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原始論文

探討台灣健保資料庫門診乾癬病人之中藥處方分析

劉俊廷[1,2]、張正杰[1,2]、楊曜旭[2,3,4]、吳蓓禹[1,2]、陳保中[4,5]、林尚宏[2,6]、蔡明諺[1,2,*]

[1] 長庚醫療財團法人高雄長庚紀念醫院中醫部，高雄，臺灣
[2] 長庚大學中醫系，桃園，臺灣
[3] 長庚醫療財團法人嘉義長庚紀念醫院中醫科，嘉義，臺灣
[4] 臺大公共衛生學院職業醫學與工業衛生研究所，台北，臺灣
[5] 臺大醫院環境暨職業醫學科，台北，臺灣
[6] 長庚醫療財團法人高雄長庚紀念醫院皮膚科，高雄，臺灣

本研究分析了台灣健保門診資料庫乾癬病人之中藥濃縮製劑的處方模式及其臨床運用探討。這項基於乾癬族群的世代研究是使用 2003 年至 2013 年間，從台灣全民健康保險研究資料庫中選出的 100 萬名患者進行隨機抽樣。評估了中藥濃縮製劑產品中治療乾癬十大最常用複方和單一中藥，包括平均配方劑量和處方頻率。分析了人口統計學特徵，包括性別和年齡。還討論了中藥濃縮製劑處方的施治原則和相關的機制。我們確定了 1,055 名（8.5%）乾癬患者，他們在這段期間曾使用過中藥濃縮製劑。年齡在 19 歲至 45 歲間的患者佔治療人數的最多（54.6%）。男性患者使用中藥濃縮製劑的頻率高於女性患者（男性：女性＝1.4：1）。溫清飲和牡丹皮分別是治療乾癬最常用的複方和單味藥。最常用的治療乾癬的雙中藥複方組合是溫清飲加血府逐瘀湯，而最常用的複方和單味藥的組合是消風散加土茯苓。後續仍需要進一步的研究來充分闡明這些中藥的功效和安全性。

關鍵字：中藥濃縮製劑、乾癬、藥物流行病學、全民健康保險學術資料庫、中醫藥

* **通訊作者：**蔡明諺，長庚醫療財團法人高雄長庚紀念醫院中醫部，地址：83342 高雄市鳥松區大埤路 123 號，電話：07-7317123 分機 2334，傳真：07-7317123 分機 2335，Email：missuriae@yahoo.com.tw

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