Prescription Patterns of Chinese Medicinal Herbs in Switzerland

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Keywords

Chinese herbal medicine · Prescription patterns · Traditional Chinese Medicine, TCM

Summary

Introduction: Chinese medicine is increasingly popular in Switzerland and is often used complementarily to conventional medicine. However, little is known about the habits of prescription of Chinese medicinal herbs in Switzerland. **Material and Methods:** A random sample of 1,053 prescriptions was drawn from the database of Lian Chinaherb AG, Switzerland, and analysed according to the most frequently used individual herbs and classical formulas (all ingredients are referred to as herbs for reasons of simplicity, although not all products are parts of plants). Average number of single herbs and daily dosage of granules (the most popular pharmaceutical form) per prescription were calculated. Cluster analysis was applied to identify common combinations of herbs. **Results:** The herbs dang gui (*Angelicae Sinensis Radix*), fu ling (*Poria*), bai shao (*Paeoniae Radix Alba*), and gan cao (*Glycyrrhizae Radix et Rhizoma*) as well as the formulas gui pi tang (Restore the Spleen Decoction) and xiao yao san (Rambling Powder) were used most frequently. The average number of herbs per prescription was 12, and the average daily dosage of granules was 8.7 g. Cluster analysis confirmed the usage of known herb pairs, e.g. ban xia (*Pinelliae Rhizoma*) and chen pi (*Citri Reticulatae Pericarpium*), and identified combinations of herbs in known formulas. **Discussion:** This study provides a first overview of the application of traditional Chinese medicinal herbs and prescriptions in Switzerland. Future studies may aim to evaluate the simultaneous use of conventional drugs and Chinese medicinal herbs in order to increase knowledge about their safety.

Schlüsselwörter

Chinesische Arzneitherapie · Verschreibungsmuster · Traditionelle Chinesische Medizin, TCM

Zusammenfassung

Verschreibungsmuster chinesischer Arzneien in der Schweiz

Hintergrund: Die Chinesische Medizin erfährt eine zunehmende Beliebtheit in der Schweiz und wird häufig komplementär zur konventionellen Medizin angewandt. Allerdings ist wenig über die Praxis der Verschreibung chinesischer Arzneimittel in der Schweiz bekannt. **Material und Methoden:** Eine zufällige Stichprobe von 1053 Verschreibungen wurde aus der Datenbank der Lian Chinaherb AG, Schweiz, gezogen und auf die am häufigsten verwendeten Arzneien und Rezepturen hin analysiert. Die durchschnittliche Anzahl von Einzelarzneien und die Tagesdosis an Granulat (der beliebtesten Darreichungsform) pro Verschreibung wurden berechnet. Mittels Clusteranalyse wurden gebräuchliche Arzneikombinationen identifiziert. **Ergebnisse:** Am häufigsten wurden die Arzneien dang gui (*Angelicae Sinensis Radix*), fu ling (*Poria*), bai shao (*Paeoniae Radix Alba*) und gan cao (*Glycyrrhizae Radix et Rhizoma*) sowie die Rezepturen gui pi tang (Dekokt, das die Milz wiederherstellt) und xiao yao san (Umherstreifen-Pulver) verwendet. Die durchschnittliche Anzahl Arzneien pro Verschreibung betrug 12, die durchschnittliche Tagesdosis an Granulat 8,7 g. Die Clusteranalyse bestätigte die Verwendung bekannter Arzneipare, wie z.B. ban xia (*Pinelliae Rhizoma*) und chen pi (*Citri Reticulatae Pericarpium*), und ermittelte Elemente bekannter Rezepturen. **Diskussion:** Diese Studie gibt einen ersten Überblick über die Anwendung traditioneller chinesischer Arzneien und Verschreibungen in der Schweiz. In zukünftigen Studien kann die gleichzeitige Verwendung von konventionellen Medikamenten und chinesischen Arzneien untersucht werden, um das Wissen über die Sicherheit solcher Kombinationen zu vergrössern.

Introduction

In May 2009, two-thirds of the Swiss people voted to include complementary medicine in the Swiss constitution. This demonstrates the popularity of complementary and alternative medicine (CAM) in Switzerland [1]. Moreover, voluntary health insurances, which about 65% of the population have, pay for most forms of CAM, and 14% of the physicians in primary care are qualified in at least one CAM discipline [2].

Since a revision in the Swiss medicinal act in 2001, CAM substances including Chinese herbs and homoeopathic remedies have been officially classified as medicinal substances. Therefore, the Swiss Agency for Therapeutic Products, Swissmedic, is now responsible for their quality and safety, and all Chinese medicines sold in Switzerland must fulfil quality requirements for medicinal substances defined by Swissmedic [3]. Even though these quality requirements put much pressure on companies and pharmacies selling Chinese medicines, they are also responsible for raising the quality level of Chinese medicines in Switzerland to one of the best worldwide and thus making Chinese medicine safer (for safety assessment report, see [4]).

The standard prescriptive methodology of Chinese medicine is the individualised patient prescription (for introduction, see [5]). Currently, around 4,000–5,000 individual prescriptions are issued weekly by the estimated 500 medical and non-medical practitioners with specific training in Chinese herbal medicine. At present, there are no registered Chinese medicinal products that can be sold over the counter. Single substances are combined according to a special framework to compose such individual prescriptions. Standard prescription combinations, so-called classical formulas, which have been composed by famous doctors in the past, serve as starting points and as guidelines [6]. Well-trained medical or non-medical herbal practitioners in Switzerland know and work with around 250–350 individual medicinal products and around 100–200 classical formulas.

The traditional form of application is the decoction, which is prepared by cooking a mixture of crude drugs. Because the preparation of such decoctions is time-consuming, new forms of application have been developed. Today, the most popular of these ‘modern’ forms is dried extract powder, commonly referred to as granules [7], which were developed in Taiwan approximately 50 years ago. In Switzerland, an estimated 80% of all Chinese herbal medicine prescriptions are taken in granular form [8].

The benefit of granules is due to the fact that all individual medicinal substances are available as single granules and, similarly to crude drugs, can thus be combined to compose individualised prescriptions. This enables practitioners to issue patient-tailored prescriptions. Further-

more, besides single substances, classical formulas can also be prepared in granular form by cooking the crude herbal ingredients of the classical formula together and preparing granular extracts from such decoctions. Hence, both single substances as well as classical formulas are available in granular form. As is demonstrated below, single herbs and classical formulas are often combined in clinical practice.

Other forms of application of Chinese medicine in Switzerland are crude drugs and so-called hydrophilic tinctures. Hydrophilic tinctures are prepared from alcohol tinctures in which the alcohol is replaced by glycerine. Their benefit in comparison to the crude drug decoctions and the granules is their ease of administration due to their relatively sweet taste. In contrast, the taste of crude herb decoctions and granules is generally quite unpalatable and thus influences compliance.

So far, the habits of prescription in regard to Chinese herbal medicines in Switzerland have not been looked at. It is not clear if the medical and non-medical practitioners of Chinese medicine prescribe primarily individualised prescriptions composed entirely of single substances or if classical prescriptions, with or without modifications, are more commonly applied. Furthermore, there are no studies that investigate which medicinal substances are most commonly applied or what the average daily dosage for granules is.

Material and Methods

Data

A random sample of 998 orders including 1,053 prescriptions for human patients dating between July 2008 and June 2009 was drawn from about 50,000 orders in the database of Lian Chinaherb AG, Wollerau, one of the largest pharmacies of Chinese herbs in Switzerland. The following information was used: product numbers of single herbs and formulas, their respective amount (weight), dosage instructions, the gender of the patient, and the country of origin of the practitioner.

Formulas were split up into their single ingredients for calculations of numbers of herbs per prescription and further analysis. The daily dosage was stated for most of the granular prescriptions. The duration of intake was deduced from the total amount of the prescription.

The origin of the practitioner was coded as Asian or non-Asian according to the name. Naturally, not every practitioner of Asian origin had completed their training in Asia, and not every Swiss or European practitioner had completed their training outside Asia; however, this was found to be true for the majority (>90%), as estimated from a sample of 45 non-Asian and 36 Asian practitioners.

Cluster Analysis

The presence or absence of a herb in a prescription was coded as 1 or 0, respectively, resulting in a binary data set. The Jaccard similarity coefficient and complete linkage method were used to combine single herbs (total occurrence in all prescriptions ≥ 10) into clusters.

Nomenclature

Names of herbs and composition of formulas are used according to Bensky [6, 9]. For herbs, the Chinese (Pinyin) and Latin names are listed, for formulas the Chinese (Pinyin) and English notations. All ingredients are referred to as herbs for reasons of simplicity, although not all products are parts of plants, but some are fungi, minerals, or of animal origin.

Software

For statistical analysis, SPSS Statistics 17.0 (SPSS, Zurich, Switzerland) and R 2.5.1 (www.r-project.org) were used.

Results

Prescriptions, Patients, and Practitioners

The data set consisted of 998 orders including 1,053 prescriptions. Thus, most orders consisted of one prescription. When several prescriptions were ordered for the same patient, it was indicated that they were meant to be taken or used: a) one in the first and one in the second part of the menstrual cycle, b) one internally and one externally, c) one in the morning, one at noon, and one in the evening, or d) one regularly and one for acute conditions.

47.4% of the orders (499) were placed by practitioners of Asian origin and 52.6% (554) by those of non-Asian origin. 74.3% (782) were prescribed for female patients, 24.8% (261) for male patients (for the remaining 10 or 0.9% the gender was unknown). The indications for which the herbs were used could not be analysed since they did not have to be stated by the practitioners during the time period in which data was collected.

Composition of Prescriptions

96.7% of the prescriptions (1,018) were composed of granules and 3.3% (35) were composed of crude herbs. 1.8% (19) were packed in capsules, and 1.3% (14) were specifically marked for external use. 46.8% of the prescriptions (493) were composed of single herbs only while 53.2% (560) were composed of pre-made classical formulas in granular form (with or without the addition of single herbs). It has to be noted that it is possible to add herbs to a pre-made formula, but when a practitioner wants to take out a herb, they have to compose the diminished formula from single herbs as it is not possible to remove individual herbs from a pre-made classical prescription. 427 prescriptions were based on one pre-made classical formula, but combinations of several formulas were also found: 118 prescriptions contained two formulas, 13 three formulas, and 2 four formulas.

The average number of herbs per prescription was 12 (minimum 1, maximum 37, median 12; fig. 1). The average daily dosage for granules – calculated on the basis of 944

prescriptions for which dosages were stated – was 8.7 g (minimum 1 g, maximum 24 g, median 9 g). On average, the granular prescription was dosed to last for 13.9 days (minimum 1, maximum 115, median 12.5 days).

A linear regression model showed that the average daily dosage depended on the origin of the practitioner, the gender of the patient, and the number of herbs in the prescription (table 1). Asian practitioners prescribed higher dosages than non-Asians, male patients received higher dosages than females, and the larger the number of herbs in one prescription, the higher was the daily dosage.

Most Frequently Used Herbs and Formulas

Table 2 shows the most frequently used herbs. More than one-third of the prescriptions contained dang gui (*Angelicae Sinensis Radix*), fu ling (*Poria*), bai shao (*Paeoniae Radix Alba*), or gan cao (*Glycyrrhizae Radix et Rhizoma*). When prescriptions based only on single herbs and prescriptions based on formulas were compared, the most frequently used herbs were basically the same, except for hong shen (*Ginseng Radix et Rhizoma Rubra*) which was frequently included in pre-made formulas but not in prescriptions based on single herbs, in which dang shen (*Codonopsis Radix*) was often used.

Fig. 1. Number of herbs per prescription (formulas were split up into their respective single herbs).

Table 1. Linear regression model for the daily dosage^a

Parameter	Regression coefficient	95% confidence interval		Significance
		lower	upper	
Constant term	7.797	7.191	8.402	0.000
Origin of practitioner ^b	-0.772	-1.149	-0.395	0.000
Gender of patient ^c	0.650	0.216	1.085	0.003
Number of herbs in prescription	0.091	0.049	0.133	0.000

^aOn the basis of 935 cases, r-square 0.047.

^bPractitioner Asian = 0, non-Asian = 1.

^cPatient female = 0, male = 1.

Table 2.

Most commonly used herbs (top 30 in 1,053 prescriptions)

Herb	Frequency	Percentage, %	Category: herbs that ...
dang gui (<i>Angelicae Sinensis Radix</i>)	498	47.3	tonify blood
fu ling (<i>Poria</i>)	473	44.9	drain dampness
bai shao (<i>Paeoniae Radix Alba</i>)	436	41.4	tonify blood
gan cao (<i>Glycyrrhizae Radix et Rhizoma</i>)	371	35.2	tonify qi
bai zhu (<i>Atractylodis Macrocephalae Rhizoma</i>)	346	32.9	tonify qi
chai hu (<i>Bupleuri Radix</i>)	305	29.0	release the exterior
chuan xiong (<i>Chuanxiong Rhizoma</i>)	285	27.1	invigorate the blood
zhi gan cao (<i>Glycyrrhizae Radix et Rhizoma Praeparata</i>)	265	25.2	tonify qi
huang qi (<i>Astragali Radix</i>)	244	23.2	tonify qi
shu di huang (<i>Rehmanniae Radix Praeparata</i>)	213	20.2	tonify blood
sheng di huang (<i>Rehmanniae Radix</i>)	207	19.7	cool blood
sheng jiang (<i>Zingiberis Rhizoma Recens</i>)	204	19.4	release the exterior
chen pi (<i>Citri Reticulatae Pericarpium</i>)	188	17.9	regulate qi
huang qin (<i>Scutellariae Radix</i>)	186	17.7	clear heat and dry dampness
da zao (<i>Jujubae Fructus</i>)	180	17.1	tonify qi
hong shen (<i>Ginseng Radix et Rhizoma Rubra</i>)	174	16.5	tonify qi
mu dan pi (<i>Moutan Cortex</i>)	162	15.4	cool blood
shan yao (<i>Dioscoreae Rhizoma</i>)	150	14.2	tonify qi
suan zao ren (<i>Ziziphi Spinosae Semen</i>)	149	14.2	nourish the heart and calm the spirit
fang feng (<i>Saposhnikoviae Radix</i>)	142	13.5	release the exterior
shan zhu yu (<i>Corni Fructus</i>)	140	13.3	stabilise and bind
gou qi zi (<i>Lycii Fructus</i>)	139	13.2	tonify blood
xiang fu (<i>Cyperi Rhizoma</i>)	137	13.0	regulate qi
bo he (<i>Menthae Herba</i>)	129	12.3	release the exterior
ban xia (<i>Pinelliae Rhizoma</i>)	128	12.2	transform phlegm-cold
jie geng (<i>Platycodonis Radix</i>)	128	12.2	transform phlegm-cold
ze xie (<i>Alismatis Rhizoma</i>)	122	11.6	drain dampness
dan shen (<i>Salviae Miltiorrhizae Radix et Rhizoma</i>)	121	11.5	invigorate the blood
mai men dong (<i>Ophiopogonis Radix</i>)	116	11.0	tonify yin
gui zhi (<i>Cinnamomi Ramulus</i>)	113	10.7	release the exterior

Table 3.

Most commonly used formulas (2.5% or more frequent in 560 prescriptions based on formulas)

Formula	Frequency	Percentage, %	Category: formulas that ...
gui pi tang (Restore the Spleen Decoction)	35	6.3	tonify qi and blood
xiao yao san (Rambling Powder)	31	5.5	regulate and harmonise liver and spleen
liu wei di huang wan (Six Ingredient Pill with <i>Rehmannia</i>)	26	4.6	tonify yin
jia wei xiao yao san (Augmented Rambling Powder)	25	4.5	regulate and harmonise liver and spleen
yu ping feng san (Jade Windscreen Powder)	23	4.1	stabilise the exterior and the lungs
du huo ji sheng tang (<i>Angelica Pubescens</i> and <i>Sangjisheng</i> Decoction)	17	3.0	dispel wind-dampness
tian wang bu xin dan (Emperor of Heaven's Special Pill to Tonify the Heart)	16	2.9	nourish the heart and calm the spirit
suan zao ren tang (Sour Jujube Decoction)	16	2.9	nourish the heart and calm the spirit
yin qiao san (<i>Honeysuckle</i> and <i>Forsythia</i> Powder)	16	2.9	release exterior wind-heat
chai hu shu gan san (<i>Bupleurum</i> Powder to Spread the Liver)	15	2.7	regulate and harmonise liver and spleen
bu zhong yi qi tang (Tonify the Middle and Augment the Qi Decoction)	14	2.5	tonify qi
tao hong si wu tang (Four Substance Decoction with <i>Safflower</i> and <i>Peach Pit</i>)	14	2.5	tonify blood
xue fu zhu yu tang (Drive Out Stasis in the Mansion of Blood Decoction)	14	2.5	invigorate the blood and dispel blood stasis

Table 3 lists the most commonly used formulas. Gui pi tang (Restore the Spleen Decoction) was used most frequently, unless the two similar prescriptions xiao yao san (Rambling Powder) and jia wei xiao yao san (Augmented Rambling Powder) are counted together.

Combinations of Herbs

Cluster analysis of 177 herbs resulted in combination of known couples of herbs, e.g. tao ren (*Persicae Semen*) and hong hua (*Carthami Flos*), mu li (*Ostreae Concha*) and long gu (*Fossilia Ovis Mastodi*), mo yao (*Myrrha*) and ru xiang (*Olibanum*), ban xia (*Pinelliae Rhizoma*) and chen pi (*Citri*

Fig. 2. Partial results of the cluster analysis. **A** Clustering of herbs related to food stagnation. **B** Clustering of herbs that release the exterior, clear heat, or drain fire.

Reticulatae Pericarpium), and huang bo (Phellodendri Chinensis Cortex) and zhi mu (Anemarrhenae Rhizoma). Later steps in the analysis revealed combinations from classical formulas, e.g. shou wu teng (Polygoni Multiflori Caulis), gou teng (Uncariae Ramulus cum Uncis), tian ma (Gastrodiae Rhizoma), and shi jue ming (Haliotidis Concha), part of the formula tian ma gou teng yin (Gastrodia and Uncaria Decoction), or shu di huang (Rehmanniae Radix Praeparata), mu dan pi (Moutan Cortex), shan yao (Dioscoreae Rhizoma), shan zhu yu (Corni Fructus), and ze xie (Alismatis Rhizoma), part of liu wei di huang wan (Six Ingredient Pill with Rehmannia), and related formulas. Figure 2 shows two examples of branches of the dendrogram (the complete dendrogram contains 177 herbs). In figure 2A, herbs were clustered that are related to food stagnation, and in figure 2B herbs that mostly release the exterior and clear heat or drain fire.

Discussion

The aim of this analysis was to give an initial overview of the most frequently used Chinese single herbs within individual prescriptions and the most commonly prescribed classical formulas as well as an insight into the prescriptive habits of Chinese medical practitioners in Switzerland. It shall serve as a starting point for discussion and as a base for further studies.

In order to investigate the prescription methodology of Chinese medicinal herbs, data from health insurances that reimburse the costs for the treatment, individual practitioners, and pharmacies selling Chinese herbs could be

used. Insurance companies may be a poor data source since not all patients have an insurance covering Chinese medicine and data may be difficult to access. Analysing prescriptions of practitioners may result in describing an individual practitioner's preferences for certain herbs or formulas instead of giving an overview of prescription patterns in Switzerland. We therefore chose to analyse a sample of orders placed at one of the largest pharmacies selling Chinese herbs. Some pharmacies specialise in certain preparations that are not included in our sample, e.g. hydrophilic solutions; therefore, we cannot make any statements about the frequency of usage of other pharmaceutical forms than granules. Obviously, only herbs that are available can be ordered, and there may be a slight variation in the choice of rare herbs in different pharmacies. Thus, we mainly concentrated on the usage of the most common single herbs and formulas.

The average number of herbs per prescription in our sample was 12, with a maximum of 37, which seems to be a rather large number. A study investigating the composition of 11,810 formulas from 13 medical classics, however, found that about 92% contained 1–13 herbs and that the maximum was 40 herbs in one formula [10]. Herb pairs are used for mutual enhancement, assistance, and restraint, and they display special features which distinguish them from random pairs [11]. Using cluster analysis, we investigated which herbs were often combined in prescriptions. Herbs in our sample were clustered to well-known couples and groups [6, 12].

The average daily dosage of granules prescribed was 8.7 g, corresponding to a medium dosage [8]. In clinical studies in Japan, where granules are commonly used, dosages of 6.0–9.0 g were applied [13–16]. The daily dosage in our sample was higher when the practitioner was of Asian origin compared to non-Asian origin. This could either reflect differences in the education of the practitioners in regard to dosing of granules or differences in patients, e.g. patients with certain conditions could preferably choose to visit a Chinese medical centre. However, since the country in which practitioners had actually received their education as well as the diagnosis of the patients were not definitely known, we abstained from further analysis of this aspect.

Prescriptions of Chinese herbs are often investigated for special groups, e.g. patients with rhinitis [17], menopause [18, 19], or patients in a certain hospital [20]. The diagnoses for the recipients of the prescriptions in our analysis are unknown, which makes comparisons with most studies difficult. However, one study from Taiwan that analysed data from the national health insurance reimbursement database also found jia wei xiao yao san (Augmented Rambling Powder), yin qiao san (Honeysuckle and Forsythia Powder), suan zao ren tang (Sour Jujube Decoction),

and tian wang bu xin dan (Emperor of Heaven's Special Pill to Tonify the Heart) amongst the most frequently used formulas [21]. 7 out of the top 10 herbs in our sample were from the tonifying category and are present in many formulas. A similar result regarding the most frequently used herbs was found when the treatment of drug addiction with Chinese medicine was investigated [22].

Apart from prescriptions composed of single herbs or based on one classic herbal formula, we also found prescriptions composed of several formulas. Combinations (of small formulas) have a long tradition, e.g. ba zhen tang (Eight Treasure Decoction) is composed of the two smaller classical formulas si jun zi tang (Four Gentlemen Decoction) and si wu tang (Four Substance Decoction). Furthermore, even though the composition of patient prescriptions from classical formulas is not documented well in standard textbooks on Chinese medicine, this method of prescribing Chinese medicine is being practiced in Taiwan [7, 21].

Patients in countries dominated by a western healthcare system consider Chinese medicine to be a complementary rather than an alternative form of treatment [23, 24]. Since the majority of patients even in countries like Japan and Malaysia do not tell their physician that they are using CAM including herbal medicine [25, 26], we may expect a similar situation in Switzerland. For the patients' safety, it will be important to identify the commonly combined conventional drugs and Chinese herbs in order to study possible interactions of their respective ingredients. Some of the research on Chinese herbal medicine has already started to focus on this topic [27–29].

Disclosure Statement

SK, who initiated the study, collected, and analysed the data, and DZ, who participated in the analysis, received no financial support for this work. SB, who wrote the introduction and contributed to the discussion, has a part-time job (30%) at Lian Chinaherb AG.

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