



Research article

Prescription system to calculate precise doses of Chinese herbal medicine to avoid toxic effects

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ABSTRACT

Background and objectives: Traditional Chinese Medicine (TCM) is a therapeutic system which has been practiced for thousands of years. Although for much of its history the decoction of medicinal herbs was the most common method of consuming the herbal treatments, TCM prescriptions are now primarily prepared using concentrated Chinese herbal extracts (CCH) in powder or granular form. However, determining the precise dose of each single Chinese herbal constituent within a prescription creates a challenge in clinical practice due to the potential risk of toxicity. To alleviate this, we invented the Chinese Intelligence Prescription System (CIPS) to calculate the exact dose of each single herb within an individual prescription.

Methods: In this study, we applied CIPS in a real-world setting to analyze clinical prescriptions collected and prepared at the TCM Pharmacy of China Medical University Hospital (CMUH).

Results: Our investigation revealed that 3% of all prescriptions filled in a 1-month period contained inexact dosages, suggesting that more than 170,000 prescriptions filled in Taiwan in a given month may contain potentially toxic components. We further analyzed the data to determine the excess dosages and outline the possible associated side effects.

Conclusions: In conclusion, CIPS offers TCM practitioners the ability to prepare exact Chinese herbal medicine (CHM) prescriptions in order to avoid toxic effects, thereby ensuring patient safety.

Abbreviations: TCM, Traditional Chinese Medicine; CCH, Chinese herbal extracts; CIPS, Chinese Intelligence Prescription System; CMUH, China Medical University Hospital; ROS, Reactive oxygen species; MOHW, Ministry of Health and Welfare; CHM, Chinese herbal medicine.

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1. Introduction

Traditional Chinese Medicine (TCM) is an empirical, science-based system of therapeutics focused on maintaining the natural rhythmic balance of Yin and Yang which has been practiced for thousands of years [1]. One of the fundamental characteristics of TCM is the application of herbs in different combinations and quantities, which are applied to elicit diverse effects for individualized treatments.

For the ancient Chinese, herbal decoctions prepared using boiling water were the most common method of consuming Chinese herbal medicine (CHM). In this way, a personalized treatment could be prescribed using exact dosages of various herbal species associated with specific therapeutic functions. Nowadays, however, concentrated Chinese herbal extracts (CCHE) in powder or granular form are the preferred choice for clinical prescriptions due to their ease of preparation and consumption. The use of CCHE in contemporary TCM has several advantages which make them suitable for modern society, including convenience in terms of purchase, consumption, and storage. Additionally, systems controlling the authenticity of herbal species, processing methods and concentration ratios for CCHE manufactured by GMP companies have been audited and standardized.

There are two distinct forms of CCHE manufactured by GMP pharmaceutical companies, single herb medicines and compound herbal formulas. Compound formulas are prepared with specific herbs combined in the fixed ratios recorded in ancient TCM textbooks. The herbs constituting the compound formulas are cooked according to manufacturer processing methods, the resulting herbal granules are then mixed with starch and dried at the specific ratio for a given formula [2]. While some single herbs are prepared using the aforementioned process, others may be prepared by direct grinding of the crude herbal materials.

There are, however, several problems with regards to the prescription of CCHE in clinical practice [3]. For instance, as compound formulas consist of herbs mixed in a fixed ratio at a production facility, it is difficult to modify the herbal composition or ratio. Thus, if a TCM practitioner would like to adjust the composition and/or ratio of the herbal formula, a separate single herb or compound formula would need to be added to the prescription. Furthermore, the precise ratio of herbs constituting a given formula may vary among pharmaceutical companies, and potentially among different batches of the same formula, making it extremely difficult to calculate the exact amount of each herbal constituent within the prescription. Such issues related to compound formula composition inevitably lead to questions regarding the safety of CCHE prescriptions. More specifically, TCM practitioners must ensure that the actual dosages of each single herb are within a safe range to negate any possibility of a toxic effect.

To resolve the risks associated with the above issues, we have designed the Chinese Intelligence Prescription System (CIPS) [Taiwan Utility Model Patent M617562]. The system automatically analyzes the composition of each formula by using an algorithm which calculates the exact dose of each single herb within a prescription. In this study, we applied the system in a real-world clinical setting to analyze the prescriptions collected from the Traditional Chinese Medicine Pharmacy at China Medical University Hospital (CMUH). We used CIPS to evaluate the precise amount and composition ratio of each herb found in TCM prescriptions, and to investigate the number of prescriptions containing inexact dosages of herbal constituents which could be associated with toxic effects.

2. Materials and methods

2.1. Data collection

The data were collected from the TCM Pharmacy at CMUH in May 2019. We randomly selected the prescriptions dispensed by a pharmacist within a 1-month period. A total of 2467 prescriptions were initially included, while 270 prescriptions were subsequently excluded due to being either crude or homemade Chinese herbal medicine. After the exclusion criteria were applied, a total of 2197 prescriptions composed of CCHE were included in this study. Fig. 1 presents a flowchart of the selection process.

2.2. Analysis of the composition of each prescription

Each prescription contained herbal formulas composed of several single Chinese herbs. According to the records of the composition

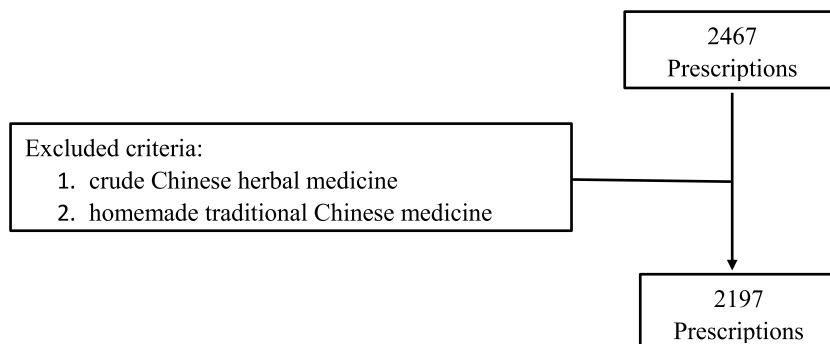


Fig. 1. Flow chart of the selection processes.

and concentration ratios of each herb and herbal formula provided by the Department of Chinese Medicine and Pharmacy, Ministry of Health and Welfare [4], we separated each formula into its single herb constituents and then calculated the actual weight of each herb using CIPS to determine the exact amount of each single herb. The details of the conversion equation and a sample of the separation process are demonstrated in Figs. 2 and 3.

For the sample of the separation and analytical process, we used Ge Gen Tang. As a combination of single Chinese herbs, the original Ge Gen Tang weighed 28 g. During the concentrated extraction process at a ratio of 7:1, 4 g of fluid extract were obtained. The fluid extract was then mixed with an excipient (3.5 g of starch) in a spray-drying process. The initial 28 g of Ge Gen Tang rendered 7.5 g of powder. The 7.5 g of Ge Gen Tang powder contained 6.0 g of *Pueraria lobata*; hence, every gram of Ge Gen Tang contained 0.8 g of *Pueraria lobata*.

2.3. Evaluating a safe dose of Chinese herbs

Through the above process, the exact weight of each constituent herb within a formula may be obtained. By using the data provided in the Du Yao Ben Cao text [5] which indicates the safe dose range to avoid toxic effects, CIPS can automatically identify the single herbs within each prescription which are beyond the range of safety, thereby alerting the TCM practitioner or pharmacist in a clinical setting to the risk of toxicity.

Single herbs can be transformed and impacted on various levels due to the processing method, which could result in altered properties or toxicity levels. The processing method may effectively render a distinct herbal medicine. Therefore, CIPS can identify the toxic effect after the various processing methods and compare the processed herb with the original herb.

3. Results

In one particular clinical prescription, the TCM practitioner prescribed 2.5 g of Ma-Zi-Ren-Wan (麻子仁丸), 5 g of Chia-Wei-Hsiao-Yao-San (加味逍遙散), 2 g of *Corydalis yanhusuo* (延胡索), 1.5 g of *Houttuynia cordata* (魚腥草), 1 g of *Hedyotis diffusa* (白花蛇舌草), 1.5 g of *Magnolia liliiflora* (辛夷), and 1 g of *Lilium* (百合) in a single day.

The separation process revealed that the Ma-Zi-Ren-Wan formula was composed of *Houpoea officinalis* (厚朴), *Rheum officinale* (大黃), *Citrus aurantium* (枳實), *Cannabis sativa* (火麻仁), *Prunus armeniaca* (杏仁), and *Paeonia lactiflora* (白芍).

Using CIPS to analyze the formula based on the data provided by the Sun-Ten Pharmaceutical company, each gram of Ma-Zi-Ren-Wan formula was processed at the point of manufacture to contain 0.25 g of *Houpoea officinalis*, 0.5 g of *Rheum officinale*, 0.25 g of *Citrus aurantium*, 0.625 g of *Cannabis sativa*, 0.25 g of *Prunus armeniaca*, and 0.25 g of *Paeonia lactiflora* (Table 1A).

A similar process was performed for Chia-Wei-Hsiao-Yao-San formula to reveal a composition of *Paeonia suffruticosa* (丹皮), *Gardenia jasminoides* (梔子), *Bupleurum chinense* (柴胡), *Glycyrrhiza uralensis* (甘草), *Angelica sinensis* (當歸), *Paeonia lactiflora* (白芍), *Atractylodes macrocephala* (白朮), *Wolfiporia extensa* (茯苓), *Mentha canadensis* (薄荷), *Zingiber officinale* (生薑) (Table 1B).

The separation process determined the exact amount of each single Chinese herb (The results are shown in Table 1. Medicament licenses are summarized in Supplementary Table 1.).

As shown in Table 1, by using the CIPS algorithm we determined that the exact amount of *Corydalis yanhusuo* in this prescription was 10.94 g (Table 1C). This amount exceeds its maximum recommended dosage (9 g, shown in Table 3), hence the TCM practitioner or pharmacist would be alerted by CIPS as to the risk of side effects to the patient.

We identified a total of 66 out of 2197 (3.00%) prescriptions filled at the TCM pharmacy of CMUH in a 1-month period containing amounts of one or more single Chinese herb exceeding a safe range. The top ten single Chinese herbs in excess amounts as identified by CIPS are demonstrated in Table 2, including Gin Seng (*Panax ginseng*), Tian Hua Fen (*Trichosanthes kirilowii*), Yan Hu Suo (*Corydalis yanhusuo*), Chang Er Zi (*Xanthium strumarium*), Bai Zhi (*Angelica dahurica*), Bin Lang (*Pinellia ternata*), Da Huang (*Rheum rhabarbarum*), Mar Bo (*Calvatia craniiformis*), Shing Ren (*Prunus armeniaca*), Shi Shin (*Asarum sieboldii*), and Shui Zhi (*Whitmania pigra*).

Based on the 2019 data from CMUH, a single pharmacist operating at the TCM pharmacy filled a total of 1408 prescriptions in an average month; therefore, our results indicate that 42 prescriptions containing excess amounts of a Chinese herbal constituent could be filled by a single pharmacist within a given month. According to data obtained from the Ministry of Health and Welfare (MOHW), in August 2021 there were approximately 4100 TCM departments/clinics in Taiwan [6]. By applying the data from CMUH, one may infer that if every TCM clinic has one pharmacist, then 1408 prescriptions may be filled per TCM clinic per month, indicating that a total of 5,772,800 prescriptions filled in Taiwan in the average month may include 173,184 prescriptions containing one or more Chinese

Combined formula (CF) is made up of n single Chinese herbs (A_n)	1
Items of Chinese herbs: $A_1, A_2, A_3, \dots, A_n$	
Dose of each single Chinese herb (gram): $B_1, B_2, B_3, \dots, B_n$	2
C grams of CF contained: $A_1 * B_1 + A_2 * B_2 + A_3 * B_3 \dots A_n * B_n$	3
CF per gram contains: $A_1 * B_1 / C + A_2 * B_2 / C + A_3 * B_3 / C \dots A_n * B_n / C$	4

Fig. 2. Conversion Equation of a combined formula.

<i>Pueraria lobata</i> (葛根): 6.0g
<i>Ephedra sinica</i> (麻黄): 4.5g
<i>Cinnamomum cassia</i> (桂枝) 3.0g
<i>Paeonia lactiflora</i> (白芍): 3.0g
<i>Glycyrrhiza uralensis</i> (炙甘草): 3.0g
<i>Zingiber officinale</i> (生薑): 4.5g
<i>Ziziphus jujuba</i> (大棗): 4.0g
Extract ratio: 7:1
Starch: 3.5g
Total amounts in Ge Gen Tang: 6.0+4.5+3.0+3.0+3.0+4.5+4.0=28.0g
Ge Gen Tang fluid extract: 4.0 g
Ge Gen Tang powders: 4.0g (extract fluid) + 3.5g (starch)=7.5g
Thus, one gram of Ge Gen Tang extract contains: <i>Pueraria lobata</i> : 6.0/7.5 =0.8g

Fig. 3. Ge Gen Tang as an example (KODA Pharmaceutical Company).

Table 1A

Composition of Ma-Zi-Ren-Wan formula as calculated by CIPS.

Ma-Zi-Ren-Wan formula		
single Chinese herb	per gram	per 2.5 g
<i>Houpoea officinalis</i> (厚朴)	0.25	0.625
<i>Rheum officinale</i> (大黄)	0.5	1.25
<i>Citrus aurantium</i> L. (枳實)	0.25	0.625
<i>Cannabis sativa</i> . (火麻仁)	0.625	1.5625
<i>Prunus armeniaca</i> (杏仁)	0.25	0.625
<i>Paeonia lactiflora</i> (白芍)	0.25	0.625

Table 1B

Composition of Chia-Wei-Hsiao-Yao-San formula as calculated by CIPS.

Chia-Wei-Hsiao-Yao-San formula		
single Chinese herb	per gram	per 5.0 g
<i>Gardenia jasminoides</i> (梔子)	0.167	0.835
<i>Bupleurum chinense</i> (柴胡)	0.267	1.335
<i>Glycyrrhiza uralensis</i> (甘草)	0.133	0.665
<i>Zingiber officinale</i> (生薑)	0.267	1.335
<i>Paeonia suffruticosa</i> (丹皮)	0.167	0.835
<i>Angelica sinensis</i> (當歸)	0.267	1.335
<i>Atractylodes macrocephala</i> (白朮)	0.267	1.335
<i>Paeonia lactiflora</i> (白芍)	0.267	1.335
<i>Wolfiporia extensa</i> (茯苓)	0.267	1.335
<i>Mentha Canadensis</i> (薄荷)	0.133	0.665

Table 1C

The exact amount of each single Chinese herb in a prescription as calculated by CIPS.

Composition of Prescription	2.5g of Ma-Zi-Ren-Wan formula	5.0g of Chia-Wei-Hsiao-Yao-San formula	Others single Chinese herbs	Total Amounts (g)
Composition of each compound formula	<i>Houpoea officinalis</i> (厚朴)			0.625
	<i>Rheum officinale</i> (大黄)			1.25
	<i>Citrus aurantium</i> (枳實)			0.625
	<i>Cannabis sativa</i> (火麻仁)			1.5625
	<i>Prunus armeniaca</i> (杏仁)			0.625
	<i>Paeonia</i>	<i>Paeonia lactiflora</i> (白芍)		1.96
	<i>Lactiflora</i> (白芍)			
		<i>Gardenia jasminoides</i> (梔子)		0.835
		<i>Bupleurum chinense</i> (柴胡)		1.335
		<i>Glycyrrhiza uralensis</i> (甘草)		0.665
		<i>Zingiber officinale</i> (生薑)		1.335
		<i>Paeonia suffruticosa</i> (丹皮)		0.835
		<i>Angelica</i>		1.335
		<i>Sinensis</i> (當歸)		
		<i>Atractylodes macrocephala</i> (白朮)		1.335
		<i>Wolfiporia</i>		1.335
		<i>Extensa</i> (茯苓)		
		<i>Mentha</i>		0.665
		<i>Canadensis</i> (薄荷)		
			<i>Corydalis yanhusuo</i> (延胡索)	10.94
		<i>Houttuynia cordata</i> (魚腥草)	3.99	
		<i>Hedyotis diffusa</i> (白花蛇舌草)	4.0	
		<i>Magnolia liliiflora</i> (辛夷)	4.125	
		<i>Lilium brownii</i> (百合)	2.67	

Table 2

Top ten single Chinese herbs in excess amounts.

Single Chinese Herb	Number of Cases of Excess	Percentage	^a Recommended Maximum Dosage (g)	Average Excess Dosage (g)
Gin Seng	20	27%	9	1.63
Tian Hua Fen	18	25%	12	1.37
Yan Hu Suo	13	18%	9	2.29
Chang Er Zi	4	5%	10	3.02
Bai Zhi	4	5%	15	4.58
Ban Shiah	4	5%	12	0.89
Bin Lang	3	4%	9	0.68
Da Huang	2	3%	12	10.94
Mar Bo	1	1%	3	42.12
Shing Ren	1	1%	9	0.50
Shi Shin	1	1%	6	0.67
Shui Zhi	1	1%	3	0.89

^a The recommended dosage for original herbs.

herbal constituents beyond the range of a safe dosage.

4. Discussion

Due to convenience, availability and standardized quality, CCHE have become the primary form of TCM clinical prescriptions of CHM. However, the actual herbal composition of each CCHE, and the varying concentration ratios used by different pharmaceutical companies, present distinct challenges to TCM clinics. The CHM currently used in clinical practice are non-toxic or present low levels of toxicity. However, one cannot ignore the possible side effects induced by herbs due to individual constitutions. Considering this, our team designed CIPS as an analytic algorithm to overcome the challenges associated with imprecise prescription dosages. Our system can calculate the exact amount of each single Chinese herb contained within every prescription, and then compare this figure with the recommended dosage provided in the Du Yao Ben Cao text [5] to identify Chinese herbs occurring in potentially unsafe amounts.

Based on individual constitutions, herbs exceeding the safe dose range may or may not cause toxic effects; nevertheless, such risks must be considered, however minor they may be. Thus, the CIPS software will issue a screen alert to notify the TCM pharmacist or practitioner as to possible side effects associated with an excess dosage of a particular herb. The top ten single Chinese herbs identified in our study found to be in excess, their toxic ingredients, and possible related clinical side effects are summarized in Table 3.

According to our findings, Gin Seng (*Panax ginseng*) was the primary herbal ingredient noted in excess amounts. Its toxic ingredients

Table 3
Common single Chinese herbs found in excess amounts.

Chinese medicinal	Identification of Origin	Recommended Dosage	Toxic Ingredient	Clinical Side Effects	Ref
Gin Seng	Root/ <i>Panax ginseng</i>	3–9 g	Ginsenosides Panaxin Sapogenin	Roseola infantum, Itching, Headache, Dizziness, Fever, Bleeding tendency, Hypotension	[5] [7–13]
Tian Hua Fen	Root/ <i>Trichosanthes kirilowii</i>	9–12 g	Trichosanthin	Nausea, Vomiting, Diarrhea, Fever, Headache, Rash, Sore throat, Stiff neck, Angioedema, Arrhythmia, Hypotension, Bleeding tendency, Miscarriage, Hepatosplenomegaly, Anaphylaxis, Pulmonary edema, Intracerebral hemorrhage	[5] [24,25]
Yan Hu Suo	Tuber/ <i>Corydalis yanhusuo</i>	4.5–9 g	Tetra-hydropalmatine	Dizziness, Lethargy, General weakness, Dyspnea, Convulsion, Hypotension, Heart failure, Liver damage	[5] [26]
Chang Er Zi	Fruit/ <i>Xanthium strumarium</i>	4.5–10 g	Atractyloside, Carboxy-atractyloside, 4'-Disulphate-atractyloside	Fatigue, Headache, Dizziness, Poor appetite, Nausea, Vomiting, Constipation, Diarrhea, Irritable, Lethargy, Tachycardia, Jaundice, Hepatomegaly, Hypotension, Shallow breathing, Kidney failure	[5] [27]
Bai Zhi	Root/ <i>Angelica dahurica</i>	9–15 g	Imperatorin	Dizziness, Nausea, Vomiting, Shortness of breath, Irritable, Hypertension, Seizure attack	[5] [28]
Ban Shiah	Tuber/ <i>Pinellia ternata</i>	6–12 g	Homogentisic acid	Mucosa irritation, Numbness of the tongue, Respiratory paralysis, Nausea and vomiting, Convulsion	[5] [29]
Bin Lang	Seed/ <i>Areca catechu</i>	3–9 g/30–60 g (powder)	Arecoline	Salivation, Nausea, Vomiting, Abdominal fullness, Palpitation, Dizziness, Lethargy, Convulsion	[5] [30]
Da Huang	Root, Stem/ <i>Rheum rhabarbarum</i>	3–12 g	Anthraquinone Chrysophanol, Rheumodin, Sennoside, Chrysophanein	Nausea, Vomiting, Diarrhea, Jaundice, Dizziness, Abdominal cramping pain, Liver cirrhosis, Electrolyte imbalance	[5] [14–17]
Mar Bo	Fruiting body/ Calvatia craniiformis	1.5–3 g	Calvatic acid, Gemmatein	Allergic response, Dizziness, Swollen throat, Chest tightness, Skin itching	[5]
Shing Ren	Seed/ <i>Prunus armeniaca</i>	4.5–9 g	Amygdalin	Salivation, Dizziness, Nausea, Vomiting, Abdominal pain, Diarrhea, Irritation, Nervous, Palpitation, General weakness, Chest tightness, Shortness of breath, Conscious disturbance, Hypotension, Mydriasis, Seizure, Convulsion, Respiratory paralysis, Shock	[5] [31]
Shi Shin	Root/ <i>Asarum sieboldii</i>	3–6 g	Safrole, methyleugenol	Headache, Vomiting, Sweating, Shortness of breath, Irritation, Neck stiffness, Elevated body temperature, Tachycardia, Respiratory paralysis, Inhibition of cardiomyocytes and smooth muscle cells	[5] [18–23]
Shui Zhi	<i>Whitmania pigra</i>	1–3 g	Hirudin	Nausea, Vomiting, Bleeding tendency (stomach, uterus), Hematuria, Severe abdominal pain, Muscle spasm, Conscious disturbance, Heart failure	[5] [32]

include ginsenosides, panaxin, and sapogenin. Gin Seng (*Panax ginseng*) is considered by some in the field of TCM as “lord of the herbs”, offering several beneficial effects for a variety of diseases [7]. In clinical studies, Ginseng has been reported to improve physical and mental well-being, decrease fatigue [8], and enhance cognitive function [9,10]. The possible mechanisms underlying these effects include reducing reactive oxygen species (ROS) and lipid peroxidation, and increasing reduced glutathione in the human body [8]. The recommended dosage of Gin Seng is 3–9 g; meanwhile, side effects such as itchiness, headache, dizziness, and bleeding may occur with dosages exceeding the safe range. In addition, Gin Seng has been reported to have several adverse side effects, including insomnia, headache, gastrointestinal disorder, tachycardia, hypertension, and vaginal bleeding [11]. Furthermore, the LD₅₀ for *Panax ginseng* reportedly varies from 750 to 5000 mg/kg in rats, and 200–1000 mg/kg in mice [11,12]. Indeed, previous animal studies have noted that ginsenosides may cause embryotoxic and teratogenic effects in rodents [13].

Several investigations have revealed the therapeutic and toxic effects of the single Chinese herbs identified in this study both *in vitro* and *in vivo*. For example, Da Huang (*Rheum rhabarbarum*) is a common Chinese herb used to treat a variety of conditions, including gastritis, gastrointestinal pain, liver and spleen disorders, and pulmonary system dysfunction [14]. The major functional ingredient in Da Huang is *Anthraquinone*, which can improve the blood lipid profile, reduce sugar absorption, and offer hepatoprotective effects [15]. However, excessive dosages of *Rheum rhabarbarum* may lead to side effects such as abdominal cramping pain, nausea, vomiting, and diarrhea. Moreover, it could lead to electrolyte imbalances and liver cirrhosis [16]; indeed, elevated concentrations of emodin, which is rich in *Rheum rhabarbarum* (a subtype of *Anthraquinone*), have been shown to cause liver cell damage and apoptosis in a rat model [17].

Shi Shin (*Asarum sieboldii*) is an important Chinese herb used to treat nasal allergies, general edema, raynaud’s syndrome, and can serve as a local anesthesia for toothache. The main toxic ingredient of Shi Shin is the essential oil; thus, it requires an extended cooking time during the preparation process in order to remove the volatile components [18]. Additionally, the flower of *Asarum sieboldii* contains a relatively high amount of aristolochic acid, which may induce nephrotoxicity [19]. Another volatile oil found in Shi Shin is safrole, which has been shown to cause liver cell damage and induce hepatocellular carcinoma [20]. Safrole is also a major component

involved in oral squamous cell carcinoma development via generating ROS and inhibiting anti-oxidative enzyme activity [21]. Although, studies have also revealed that safrole could modulate calcium influx leading to cancer cell apoptosis *in vivo* [22,23]. Thus, *Asarum sieboldii* offers therapeutic benefits and can be effectively applied in safe dosages and with a suitable decoction process.

Based on our analysis and statistics from MOHW, more than 170,000 prescriptions per month in Taiwan could contain one or more single Chinese herb exceeding the recommended maximum dosage. This presents a significant challenge in clinical practice as the TCM practitioner may be unaware of the exact amount of each herb within a given prescription. The TCM practitioner or pharmacist would thus be unable to provide a patient with the necessary information with regards to the potential side effects of a given medicine, thereby placing a patient's health and safety at risk. To limit or negate this risk, CIPS should be integrated with existing clinical computer systems to provide alerts when necessary, and to offer TCM practitioners and pharmacists the opportunity to adjust the prescription prior to it being issued to the patient.

There are limitations to the present study. First, the data used in the study were limited in scope, being obtained from the pharmacy of a single institution during a 1-month period. The data would be more accurate if we could integrate the utilization rates of TCM at different hospitals and clinics in a variety of regions. Second, due to the limited amount of research and literature on the toxic effects of CHM, CIPS uses the recommended safe dosage ranges noted in the "Du Yao Ben Cao" as a reference, more standardized criteria from different database sources could further improve the validity of future studies. Third, herbal interactions are currently not considered in the CIPS software. While there are indeed several studies reporting on interactions between certain drugs [32,33], the data are not sufficient for a full-scale integration. Our team will upgrade CIPS in the future by integrating more data resources as they become available.

5. Conclusion

In this study, we applied CIPS to analyze the prescriptions from the TCM pharmacy at CMUH. The risks associated with the consumption of CHM beyond the recommended dose should be a primary concern for clinical services. By using CIPS, TCM practitioners and pharmacists can identify the exact amount of each Chinese herb within a given prescription and be alerted to cases of excess dosage, thereby limiting the risks of dangerous side effects and toxicity.

Author contribution statement

Wei-Te Huang: Conceived and designed the experiments; Performed the experiments; Wrote the paper.

Sheng-Teng Huang: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Ching-Wen Chang, Hui-Chun Hung: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Dai-Ying Lin: Performed the experiments; Wrote the paper.

Yu-Chuan Lin, Hao-Hsiu Hung, Shi-Chen Ou, Chin-Wei Chang, Hung-En Lin, Ting-Yen Lin: Performed the experiments.

Additional information

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Data availability statement

Data are available from the Traditional Chinese Medicine Pharmacy at China Medical University Hospital. Based on the legal restrictions, "Personal Information Protection Act", imposed by the government of Taiwan, detailed data cannot be made publicly available. The datasets generated for this study are only available on request to the corresponding authors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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