Exploring the pattern of identification and use of drugs in the treatment of menstrual disorders by Yang Jialin based on data mining

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Abstract: The objective of the paper is to use the Chinese medicine inheritance auxiliary platform (V2.5) to explore the rules of medication used by Professor Yang Jialin, a national famous veteran Chinese medicine practitioner, in the treatment of menstrual disorders. The method applied in this paper is to read and collect the prescriptions of 'China's Modern Hundred Chinese Medicine Clinicians-Yang Jialin' for the treatment of menstrual diseases, to establish a database of prescriptions by using the Chinese Medicine Inheritance Auxiliary Platform (V2.5), and to carry out the statistics and analysis of the data by frequency counting analysis, correlation rules, and clustering analysis. A total of 18 formulas were selected from the book, 71 flavours of drugs were used, and the total number of times they were used was 206. The top ten most frequently used drugs were, in descending order, white peony, angelica sinensis, wolfberry, ligusticum chuanxiong, chickweed vine, cuscuta, chaihu, ripened diclofenac, motherwort, and cimicifuga; the drug meridians were liver meridian, followed by spleen and kidney meridians; the four qi of the drug were cold and warm, followed by flatness; and the flavours of the drug were sweet and bitter, followed by pungent and acidic flavours. Twenty-three drug combinations were obtained by association rule analysis; six core drug groups and three new prescriptions were obtained by cluster analysis. The conclusion of this thesis is that the academic characteristics of Professor Yang Jialin's treatment of menstrual disorders are: emphasis on the liver, spleen and kidneys, and treatment according to different age groups; classification of menstrual disorders as either too much or too little, and either passage or regulation according to the menstrual cycle; and the use of medication based on the Four Substance Soup, with a great deal of emphasis on qi and blood.

Menstruation is a common gynecological disease, and it is the first of the gynecological diseases, which can be followed by other gynecological diseases and seriously affect women's physical and mental health and quality of life. Therefore, gynaecologists have always attached great importance to regulating menstruation, as pointed out in the 'Complete Recipes for Women': 'Any doctor who treats women must first regulate menstruation'.

Professor Yang Jialin, as a national famous old Chinese medicine expert, has been studying Chinese medicine for dozens of years, inheriting the theory and method of the sages, learning from the modern new knowledge, academic self-contained system, took the lead in proposing that an important link in the production of menstruation is the axis of 'Kidney - Tiankai - Chongren - Cytotropic Uterus' [1], pioneering the theoretical study of the regulation and control of the reproductive axis of menstruation; researching and developing menstrual regulating series of prescriptions, ingenious and therapeutic. He has made outstanding contributions to the development of Chinese gynaecology with his unique design and precise therapeutic effect. The book 'China's Modern Hundred Chinese Medicine Clinicians - Yang Jialin'[2](hereinafter referred to as 'Yang Jialin') is a collection of clinical essence of Professor Yang. In this study, we mainly used the frequency analysis, association rules and cluster analysis of the Traditional Chinese Medicine (TCM) inheritance assistance platform V2.5 to excavate the rules of medication for menstrual disorders in the Yang Jialin, and we will present the results as follows.

1. Data and Methods

1.1 Source of Data

Read the contents related to the treatment of menstrual diseases in the section of 'Yang Jialin' , which is a collection of commonly used clinical prescriptions, to select prescriptions used for the treatment of menstrual diseases, and the efficacy of this category of prescriptions includes regulating menstruation, stopping bleeding, and relieving pain. The statistical content of Yangjialin in the following section only includes the above selected contents.

1.2 Data standardisation

Based on the 2020 edition of the Pharmacopoeia of the People's Republic of China [3] and the 14th Five-Year Plan textbook of Traditional Chinese Medicine [4], prescriptions and drug names were standardised. For example, 'Dampy' was changed to 'Mudanpi', 'Yuanhu' was changed to 'Yanhusuo', The name 'Xian Ling Spleen' was changed to 'Epimedium', and the name 'Squid Bone' was changed to 'Cuttlebone', 'Faxia' was changed to "Fagaxia", and "Silkworm Sand" was changed to "Silkworm Sand". The standardised data were then entered by two persons and checked with each other to ensure the accuracy of the data.

1.3 Analysis Methods Through

The function of 'Statistical Analysis' in the Chinese Medicine Inheritance Auxiliary Platform (V2.5), the frequency of the use of medicines and their flavours and attributes were counted. Through the 'association rules' and 'cluster analysis', we analysed the pattern of formulae and explored the core drugs and potential new formulae. The data were reviewed several times to ensure their accuracy.

2. Results

2.1 High-frequency Drugs

The content related to regulation of menstruation in the section of 'Yang Jialin' involves 18 prescriptions, 71 flavours of drugs, and a total of 206 times. The top ten most frequently used medicines were, in order: Paeonia lactiflora, Radix Angelicae Sinensis, Fructus Lycii, Rhizoma

Ligustici Chuanxiong, Rhizoma Polygonati Odorati, Semen Cuscutae, Radix Rehmanniae Praeparata, Rhizoma Polygonati Odorati, Radix et Rhizoma Polygonati Odorati and Radix et Rhizoma Polygonati.

Table 1: Top 30 drugs in terms of frequency of use

Herbs Frequency	Herbs Frequency	Herbs Frequency	Herbs Frequency	Herbs Frequency	Herbs requency
Baishao 14	tusizi 7	diyu 5	Shengdi 4	xiangfu 4	zhishi 3
danggui 9	chaihu 6	huangqi 4	Dangshen 4	maidong 3	xiakucao 3
gouqizi 7	shudi 6	fuling 4	digupi 4	puhuang 3	yiyiren 3
chuanxiong 7	yimucao 6	yanhusuo 4	chuanlianzi 4	hanliancao 3	huangbai 3
jixueteng 7	qiancao 5	gancao 4	Danshen 4	Fupenzi 3	baizhu 3

2.2 Drug Character

The 'four qi' of the drug were analysed, in the order of cold (77 times), warm (73 times), flat (46 times) and cool (8 times). See Table 2-3.The 'five flavours' of the drug were analysed, in order of bitterness (117 times), sweetness (109 times), pungency (75 times), acidity (3 times), astringency (8 times) and saltiness (7 times). See Table 3.

Table 2: Four qi distribution

Four qi Frequency	Four qi Frequency
cold 77	peaceable 46
warm 73	cool 8

Table 3: Distribution of the five flavours

Fiveflavors Frequency	Fiveflavors Frequency
bitter, 117	sour 35
sweet 109	rough 8
pungent 75	salty 7

2.3 Commonly used drug combinations

The prescriptions of Yangjialin for treating menstrual diseases were analysed by drug association rules, and the support degree was set to 5, which yielded 23 drug combinations, which were sorted according to the frequency and sorted according to the support degree (see Tables 4-6 for details). The confidence level was set to 0.75, and 21 sets of association rules were obtained after analysis, as

shown in Table 7.The correlations between drugs were displayed through networking, as shown in Figure 2.

Table 4: Analysis of dosing pattern of 2-flavour drug combinations

Herbalmodel	Frequency	Herbalmodel	Frequency
danggui,baishao	7	diyu, qiancao	5
Chuanxiong,danggui	7	baishao, gouqizi	5
shudihuang, danggui	6	chuanxiong, baishao	5
shudihuang, baishao	6	tusizi, tusizi	5
jixueteng, baishao	6	danggui, gouqizi	5
baishao, chaihu	6	shudihuang, chuanxiong	5
tusizi, danggui	6	tusizi, chuanxiong	5
jixueteng,danggui	6		

Table 5: Analysis of dosing pattern of 3-flavour drug combinations

Herbalmodel Frequency
shudi, danggui,baishao 6
shudi, chuanxiong,baishao 5
chuanxiong,danggui,baishao 5
jixueteng,danggui,baishao 5
tusizi,danggui,gouqizi 5
shudi,chuanxiong,danggui 5
tusizi,chuanxiong,danggui 5

Table 6: Analysis of dosing pattern of 4-flavour drug combinations

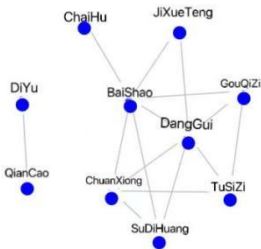| Herbalmodel Frequency |
|---|
| shudi,chuanxiong,danggui,baishao 5 |

Figure 2: Display of drug association rule network

Table 7: Results of association rule analysis (confidence level ≥ 0.75)

Rule Level	Confidence	Rule Confidence Level
shudi -> baishao	1	Shudi,baishao->chuanxiong 0.8333
chaihu -> baishao	1	Jixueteng,baishao->danggui 0.8333
shudi -> danggui	1	Jixueteng,danggui->baishao 0.8333
chuanxiong ->danggui	1	tusizi,danggui ->tusizi 0.8333
shudi,baishao-> danggui	1	Shudi,danggui->chuanxiong 0.8333
shudi,danggui-> baishao	1	Tusizi,danggui->chuanxiong 0.8333
shudi -> danggui,baishao	1	shudi,danggui,baishao -> chuanxiong 0.8333
jixueteng->baishao 0.8571		Shudi-> chuanxiong 0.8333
tusizi -> danggui 0.8571		Danggui->baishao 0.7778
jixueteng ->danggui 0.8571		
Danggui,baishao-> shudi 0.8571		Danggui->chuanxiong 0.7778

2.4 Drug core combinations and new prescriptions

Clustering analysis of the drugs in the *Yang Jia Lin*, with the correlation set to 5 and the penalty set to 1. A total of 63 eligible records were finally obtained, resulting in 6 core drug groups, see Table 8. 3 new prescriptions were obtained by applying the unsupervised entropy hierarchical clustering algorithm based on the extracted core combinations. See Table 9.

Table 8: Core drug analysis portfolio

serialnumber herbal	serialnumber herbal
1digupi-nvzhenzi-maidong	4cangzhu-huangbai-yiyiren
2cangzhu-huangbai-muxiang	5cangzhu-yiyiren-guanzhong
3gancao-chuanlianzi-gouqi	6gancao-gouqizi-yanhusuo

Table 9: New formula combinations

serialnumber	herbal
1	digupi-nvzhenzi-maidong-cangzhu-huangbai-yiyiren
2	cangzhu-huangbai-muxiang-yiyiren-guanzhong
3	gancao-chuanlianzi-gouqizi-yanhusuo

3. Discussion

A comparison of the frequency of high-frequency drugs in the Yang Jialin formula for regulating menstruation (see Table 1) shows that the drugs used more frequently are mainly tonic drugs, including those that tonify the whole body as a whole, such as Paeonia lactiflora, Radix Angelicae Sinensis, Radix Rehmanniae Praeparata, and Fructus Lycii. There are also motherwort, chickweed, and celandine, which are aimed at regulating menstruation and directly affecting the uterus. We can see Professor Yang's comprehensive and holistic understanding of menstrual diseases and her precise grasp of the targeting of Chinese medicine.

Professor Yang divided menstrual diseases into two categories: too much menstruation and too little menstruation. Professor Yang's treatment of too much menstruation is mostly cold, sour and bitter, such as Huangbai which is used to clear heat and diarrhoea and reduce deficiency heat, combined with Zhimu for treating yin deficiency and fire exuberance; Xiaku Cao is bitter and pungent in taste and clears the liver fire; Shengdihuang is the top product for clearing heat and cooling the blood, nourishing yin and generating body fluids; Dibongpi has a sweet and cold effect in the yin, which cools the blood and stops bleeding. ... to remove the fire in the cell'; white peony nourishes blood and astringent yin, "Tang Materia Medica" said it can "benefit women's blood". For the treatment of menstrual disorders, most of the medicines used are warm and hot in nature, pungent and sweet in taste, such as Cuscuta chinensis, which tonifies yin and helps yang, and has the specific ability to tonify the spleen, liver and kidneys; Schizandra chinensis warms and tonifies the kidney yang and astringes the yin and benefits the qi; Chinese wolfberry and Radix Rehmanniae Praeparata tonify the liver and kidneys, and benefit the vitality of the essence and blood; Angelica sinensis and Rhizoma Ligusticum Chuanxiong tonify and nourish the blood and regulate the menstruation with the blood; Nansha Ginseng and Astragali benefit the vitality and strengthen the spleen to assist in the production of vitality.

The attributed meridians are mainly the liver, spleen and kidney meridians(see Figure 1), which corresponds to Professor Yang's academic view that menstrual disorders are mainly pathogenic in terms of the internal organs, which are blamed on the liver, spleen and kidneys. Moreover, Professor Yang believes that with the different stages of women's age, the clinical treatment focuses on the liver, spleen and kidneys differently: during puberty, the kidney qi is in full bloom and the kidney essence is not yet solid, so it is necessary to tonify the kidneys to assist in the establishment of a regular cycle; during the middle-age period, the kidney qi is even, but due to menstruation, pregnancy, childbirth and breastfeeding, the liver and blood are depleted, and the liver blood is depleted, losing the moistening and draining, and the disorders of excretion are caused by the disorders of the menstrual cycle. During menopause, when the kidney qi starts to decline, the decadal period is gradually depleted, the Chong Ren is weakened, and the imbalance of yin and yang leads to irregular menstruation. Therefore, the clinical examination of the disease mechanism, speculation on the nature of the drug flavour and meridian, targeted selection of drugs, so that the band leads all the medicines, the power of the drug can be directed to the disease, to enhance the accuracy of the use of drugs to improve the clinical efficacy of the important significance.

After analysing the association rules of medicines for regulating menstruation in Yang Jialin, the results are: the two medicines with the highest degree of support are Chuanxiong - Angelica sinensis, Angelica sinensis - Paeonia lactiflora, Radix et rhizoma Rhei - Paeonia lactiflora, Radix et rhizoma Rhei - Angelica sinensis, Cuscuta sinensis - Angelica sinensis, Cynomorium henselae - Angelica sinensis, three medicines are Radix et rhizoma Rhei - Angelica sinensis - Paeonia lactiflora, and four are Radix et rhizoma Rhei - Rhizoma Ligustici Chuanxiong - Angelica sinensis - Paeonia lactiflora. It can be seen that Professor Yang's treatment of menstrual diseases is based on the Four Substances Tang, which is flexibly applied according to the physiological characteristics of women at different

times or the development of the disease, with additions and subtractions.
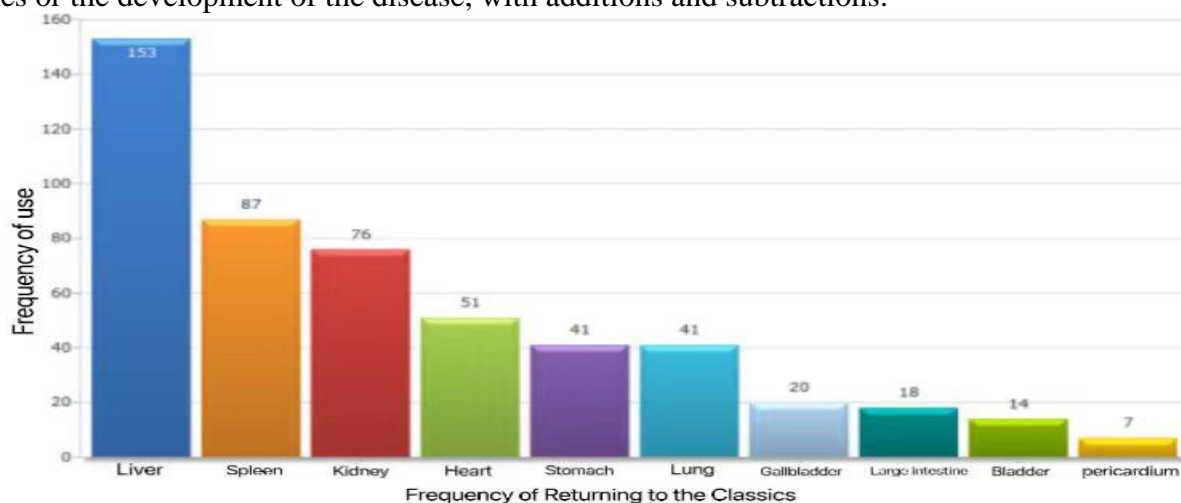

Figure 1: Statistical chart of the frequency of use of the attributed sutra

Modern research has proved that Si Wu Tang has the effect of regulating menstruation. Li Jie et al. studied the mechanism of action of Siwu Tang to regulate menstruation through network pharmacology technology, predicted 16 components and 16 target proteins, and initially found that Siwu Tang's may treat primary dysmenorrhoea through the mechanisms of regulating hormones, diastolic uterine smooth muscle, central analgesia, and anti-inflammation [3] Zhu Min et al. found through animal experiments that Siwu Tang has a bidirectional regulatory effect on uterine smooth muscle, which can be used in small doses to inhibit the contraction of blood vessels and uterine myometrium, safeguard the uterine blood supply, and alleviate the response to dysmenorrhoea [4]. Siwu Tang also has phytoestrogenic activity [5], which promotes endometrial development, promotes ovulation, rapidly reduces the abnormal elevation of estrogen, regulates and balances the levels of various hormones, and achieves therapeutic purposes such as regulating menstruation and resuming menstruation.

Finally, three new prescriptions were obtained based on the analysis function of unsupervised entropy hierarchical clustering. The new formulas are in line with Professor Yang's treatment concept of 'tonifying with tonifying, and tonifying with tonifying'. New Formulas 1 and 2, excluding the spleen and yin tonic, contain Ermiao Pill, 'Cangzhu is good for drying dampness, and Huangbai is good for removing heat' (Examination of Medical Formulas). Professor Yang believes that the treatment of disease should be combined with the local climatic characteristics, the Sichuan Basin, the rivers and rivers, wet and foggy, diffuse water, dampness can not be ignored, and then combined with the specific physiological period, different diseases, the formulation of the 'treatment of dampness, five methods', will be the three causes of the best in which the best in the appropriate way. New formula 1 can be used to treat Yin deficiency and Damp-Heat, while new formula 2 is used to treat Damp-Heat obstruction. New Formula 3 contains Chinese wolfberry to tonify the kidney and nourish yin, and liquorice to tonify qi and relieve urgency; neem and yanhuisuo are used together to activate blood circulation and relieve pain. Therefore, the new formula 3 can be used to treat the syndrome of kidney deficiency and liver depression by adding and subtracting according to the symptoms.

4. Summary

Through the collation and data mining of the prescriptions for menstrual diseases in the book 'Yang Jialin', we explored the pattern of their medication. Ultimately, the results of this paper show

that Professor Yang Jialin treats menstrual diseases from a holistic perspective, focusing on the liver, spleen and kidneys. She grasps the development of the disease and treats it by age. She is good at identifying the evidence and treating the disease by treating too much and too little. She is well versed in the properties of herbs in the menstrual cycle, and is able to regulate menstruation for a period of time. Taking care of the blood as the key and the four substances as the foundation, this study provides ideas for identifying and treating menstrual diseases, and unearths new formulas to provide references for clinical dialectic and administration of medicines.

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