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Discussions of Medication Rule of Chief Physician Xu Jianqin in the Treatment of Bi Disease Based on Data Mining

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Abstract: Objective: To provide new ideas for clinical diagnosis and treatment of arthralopathy through data mining of professor Xu Jianqin's characteristics of Traditional Chinese Medicine (TCM) drug use in the treatment of arthralopathy, in order to provide data support for the inheritance of famous TCM experience. ***Methods:*** The effective prescriptions of professor Xu Jianqin of Changan Mi school in outpatient department for the treatment of Bi disease from April 1, 2019 to March 31, 2021 were collected, and standardized input was conducted by the TCM inheritance auxiliary platform system (V2.5), and the frequency of medication, the meridian, sexual and flavors, and the rule of prescription composition were analyzed. ***Results:*** A total of 102 prescriptions of Bi disease were included, involving 117 TCMs. Among them, the first 8 TCMs were Salt eucommia ulmoides, Vinegar corydalis yanhusuo, Dioscorea collettii, Salt semen plantaginis, Acorus tatarinowii, Lindera aggregate, Smilax glabra, Ground beeltle. The proportion of warm drugs and sweet taste drugs was higher, and the main channels of TCM frequency > 300 were foot Jue Yin liver meridian (26.50%), foot Shaoyin kidney meridian (18.33%), foot taiyin spleen meridian (13.36%), hand taiyin lung meridian (9.12%). Four core TCM combinations and two new prescriptions were obtained. ***Conclusion:*** The application of TCM inheritance auxiliary platform software to explore and analyze professor Xu Jianqin's TCM characteristic experience in treating Bi disease. This research demonstrates professor Xu Jianqin's scientific treatment of Bi disease from two aspects of TCM inheritance theory and modern pharmacology, and provides a research basis for clinical differentiation, treatment of arthralgia, optimization of diagnosis, treatment scheme, research and development of new drugs.

1. Introduction

Bi disease is a common clinical disease, covering a wide range of diseases, various doctors have different understanding of this disease, it mainly includes visceral arthralgia and limb arthralgia. The arthralgia mentioned in this article mainly refers to limb arthralgia, in traditional Chinese medicine, rheumatoid arthritis, gout, ankylosing spondylitis and other muscular joint diseases all belong to the

category of "limb paralysis"[1]. Limb paralysis refers to a kind of disease general term which is caused by congenital deficiency, deficiency of vital gas, and phlegm, dampness, gore blocking the meridians and collaterals, leading to pain and swelling of limb joints, muscles and bones, muscles, severe numbness and (or) adverse joint flexion and extension and other symptoms[2, 3]. With the aid of the TCM inheritance auxiliary platform, this study deeply explored and analyzed the law of TCM characteristic drug use in the treatment of Bi disease by Professor Xu Jianqin, summarized and analyzed the characteristics and experience of TCM characteristic drug use in the treatment of Bi disease by Professor Xu Jianqin, in order to provide effective theoretical basis for the diagnosis and treatment of clinicians and the research of new prescriptions and new drugs.

2. Data and Methods

2.1 Sources of prescription

Medical records of professor Xu Jianqin's outpatient treatment of bi disease from April 1, 2019 to March 31, 2021 were collected (68 cases of gout and 33 cases of rheumatoid arthritis), 102 prescriptions were selected, a total of 117 drugs.

2.2 Prescription screening

2.2.1 Inclusion criteria

Meet the TCM diagnostic criteria of Bi disease (refer to "TCM Internal Medicine"), all medical records are selected from professor Xu Jianqin's outpatient medical records for diagnosis and treatment of Bi disease. All the information, composition of prescription, taking method and drug dose of the medical records are required to be completely recorded, and the TCM decoction is mainly taken internally. Western medicine diagnostic criteria (refer to "Practical Internal Medicine"), all medical records in accordance with the national western medicine diagnostic criteria to standardize the name of the disease.

2.2.2 Exclusion criteria

Medical records that do not meet the diagnostic criteria of TCM for Bi disease; Incomplete records of medical records (including only describing the name of the prescription and not showing the composition and dosage of prescription); Medical cases mainly treated with non-TCM decoction; Medical records of Bi disease complicated with other serious complications.

2.3 Specification of TCM

The name, flavor and meridian tropism, function and indications of TCM were recorded according to the standard of <Traditional Chinese Medicine>, due to different planting methods, regions and environments, the names of TCM in prescriptions are unified, such as yuan shen unified records for the xuan shen as such, in order to avoid too low drug frequency, prepared glycyrrhiza and glycyrrhiza were recorded as glycyrrhiz, fried and raw Atractylodes macrocephala were recorded as the original prescription.

2.4 Data Entry

After being screened and confirmed by two outpatient physicians in strict accordance with the inclusion and exclusion criteria, the medical records were recorded by using the TCM inheritance Auxiliary platform system (V2.5), data entry and collation are carried out by two people, and the

input of TCM terms should be standardized to ensure the authenticity and accuracy of data.

2.5 Data Analysis

The TCM Inheritance auxiliary platform system (V2.5) was used for data input and in-depth analysis of drug use rules. For drugs with frequency > 15% and frequency > 8, the Apriori algorithm was used for analysis, and the association between drugs was analyzed with association rule method.

3. Results

3.1 Statistics of TCM frequency of Bi disease the prescription

By analyzing the application frequency of the input data, 102 prescriptions and 117 drugs were included, with a total of 1473 drug frequencies. The TCM with drug frequency ≥9 were sequentially arranged in descending order, and a total of 46 high-frequency drugs were obtained. The first 8 TCMs were Salt eucommia ulmoides, Vinegar corydalis yanhusuo, Dioscorea collettii, Salt semen plantaginis, Acorus tatarinowii, Lindera aggregate, Smilax glabra, Ground beeltle, see table 1.

Table 1: Bi disease prescription high frequency TCM frequency

The serial number	TCM name	Frequency	The serial number	TCM name	Frequency
1	Salt eucommia ulmoides	70	24	Centipede	20
2	Vinegar corydalis yanhusuo	70	25	Caulis spatholobi	19
3	Dioscorea collettii	62	26	Spatholobus suberectus	18
4	Salt semen plantaginis	59	27	Rehmanniae	17
5	Acorus tatarinowii	59	28	Yam	17
6	Lindera aggregate	56	29	Polygonum cuspidatum	16
7	Smilax glabra	56	30	Fried atractylodes	15
8	Ground beeltle	53	31	Codonopsis pilosula	15
9	Clematis root	49	32	Fried bombyx batryticatus	14
10	Radix dipsaci	45	33	Main licorice	14
11	Money grass	44	34	Fried peach kernels	14
12	Mulberry parasitism	42	35	Astragalus membranaceus	13
13	Wine rhubarb	39	36	Herba siegesbeckiae	13
14	Wine wu shao snake	38	37	Cortex moutan	12
15	Wine radix cyathulae	33	38	Alisma orientale	12
16	Semen coicis	30	39	Cinnamon	11
17	Fructus alpiniae oxyphyllae	30	40	Notopterygium	11
18	Poria cocos	29	41	Papaya	10
19	Scorpion	26	42	Cassia twig	10
20	Angelicae pubescentis	23	43	Wine fructus corni	10
21	Radix paeoniae alba	21	44	Phellodendron	9
22	Angelica sinensis	21	45	Bupleurum chinense	9
23	Ligusticum chuanxiong hort	21	46	Passepartout	9

3.2 Statistical analysis of drug flavor and meridian tropism

Among 117 drugs included, table 2 shows the statistics of four gas: The proportion of warm drugs was the highest, accounting for 48%, followed by cold drugs and flat drugs, accounting for 24% respectively, cool drugs and heat drugs were less, accounting for 3% and 1% respectively. Table 3

shows the statistics of five flavors: sweet drugs accounted for 32%, spicy drugs accounted for 28%, bitter drugs accounted for 28%, salty drugs accounted for 6%, sour drugs accounted for 3%, and astringency drugs accounted for 3%. Table 4 shows the statistics of TCM meridian, for drug frequency > 300, the meridian of liver (26.50%), kidney (18.33%), spleen (13.36%) and lung (9.12%).

Table 2: Statistical analysis of four gas of bi disease drugs

Four gas	Frequency	Proportion (%)
Warm	651	48%
Cold	334	24%
Flat	333	24%
Cool	39	3%
Heat	13	1%

Table 3: Statistical analysis of five flavors of bi disease drugs

Five flavors	Frequency	Proportion (%)
Sweet	658	32%
Spicy	580	28%
Bitter	571	28%
Salty	118	6%
Sour	67	3%
Astringency	61	3%

Table 4: Statistical analysis of meridian of bi disease drugs

Meridian	Frequency	Proportion (%)
liver	895	26.50%
kidney	619	18.33%
spleen	451	13.36%
lung	308	9.12%
stomach	286	8.47%
heart	283	8.38%
bladder	240	7.11%
bravery	104	3.08%
large intestine	87	2.58%
small intestine	62	1.84%
Pericardium	40	1.18%
triple energizer	2	0.06%

3.3 Association rules

3.3.1 TCM combination analysis

According to the actual situation, the number of support degree is set as 48, the confidence is 0.6, and 56 TCM combinations are involved, among the included Bi disease prescriptions, there were 19 drug combinations with frequency > 51, see table 5.

Table 5: TCM combination analysis

The serial number	Drug combination	Frequency	The serial number	Drug combination	Frequency
1	Dioscorea collettii, Smilax glabra	57	11	Smilax glabra, Salt eucommia ulmoides	54
2	Dioscorea collettii, Ground beeltle	57	12	Smilax glabra, Salt semen plantaginis	53
3	Dioscorea collettii, Lindera aggregate	56	13	Ground beeltle, Lindera aggregate	53
4	Dioscorea collettii, Acorus tatarinowii	56	14	Ground beeltle, Acorus tatarinowii	53
5	Dioscorea collettii, Vinegar corydalis yanhusuo	55	15	Ground beeltl, Salt semen plantaginis	53
6	Dioscorea collettii, Salt eucommia ulmoides	55	16	Lindera aggregate, Acorus tatarinowii	52
7	Dioscorea collettii, Salt semen plantaginis	55	17	Lindera aggregate, Vinegar corydalis yanhusuo	52
8	Smilax glabra, Lindera aggregate	55	18	Lindera aggregate, Salt eucommia ulmoides	52
9	Smilax glabra, Acorus tatarinowii	54	19	Lindera aggregate, Salt semen plantaginis	52
10	Smilax glabra, Vinegar corydalis yanhusuo	54			

3.3.2 Drug combinations under association rules

Set the number of support degrees to 53, confidence degree to 0.9, a total of 39 association rules were extracted by descending order of confidence degree, and 22 combinations of TCM with confidence degree > 0.95 were extracted, see table 6. At the same time, the network display diagram of drug combination association rule analysis is shown, as shown in Figure 1.

Table 6: Association rule analysis of TCM combination

The serial number	Rule	Confidence degree	The serial number	Rule	Confidence degree
1	Smilax glabra -> Dioscorea collettii	1	12	Lindera aggregate -> Salt semen plantaginis	0.96
2	Lindera aggregate -> Dioscorea collettii	1	13	Salt semen plantaginis -> Acorus tatarinowii	0.96
3	Dioscorea collettii -> Lindera aggregate	1	14	Acorus tatarinowii -> Salt semen plantaginis	0.96
4	Acorus tatarinowii -> Dioscorea collettii	1	15	Lindera aggregate, Acorus tatarinowii -> Dioscorea collettii	0.96
5	Dioscorea collettii -> Acorus tatarinowii	0.98	16	Dioscorea collettii, Acorus tatarinowii -> Lindera aggregate	0.96
6	Salt semen plantaginis -> Dioscorea collettii	0.98	17	Dioscorea collettii, Lindera aggregate -> Acorus tatarinowii	0.96
7	Dioscorea collettii -> Salt semen plantaginis	0.98	18	Acorus tatarinowii -> Dioscorea collettii, Lindera aggregate	0.96
8	Smilax glabra -> Acorus tatarinowii	0.98	19	Lindera aggregate -> Dioscorea collettii, Acorus tatarinowii	0.96
9	Acorus tatarinowii -> Lindera aggregate	0.98	20	Lindera aggregate, Salt semen plantaginis -> Dioscorea collettii	0.96
10	Lindera aggregate -> Acorus tatarinowii	0.96	21	Dioscorea collettii, Salt semen plantaginis -> Lindera aggregate	0.96
11	Salt semen plantaginis -> Lindera aggregate	0.96	22	Dioscorea collettii, Lindera aggregate -> Salt semen plantaginis	0.96

3.4 Analysis of formation law based on entropy clustering

Based on the association degree analysis between drugs, set the relevance degree to 5, set the punishment degree to 2, unsupervised entropy layer clustering analysis was carried out, the

association degree of 117 drugs in Professor Xu Jianqin's prescription for treating Bi disease was obtained. Only the drug pairs with association coefficient > 0.2 were listed in Table 7, and there were 19 drug pairs in total. Based on unsupervised entropy clustering analysis, set relevance as 5 and punishment as 2, and the evolution results in 4 core drug combinations, see table 8. At the same time, the network diagram of core drug combination is shown, as shown in Figure 2. Two new prescriptions were derived on the basis of the core drug pairs, see table 9.

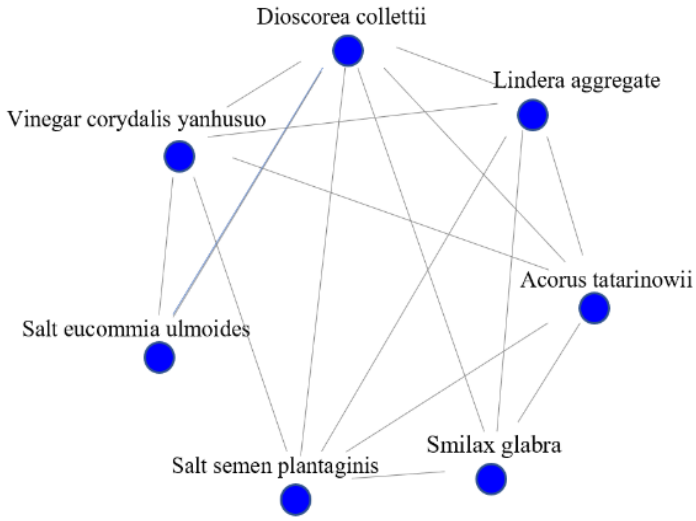

Figure 1: Network display diagram of drug combination association rule analysis

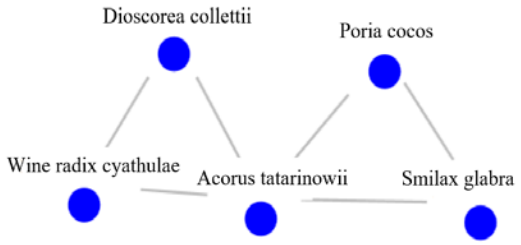

Figure 2: Network diagram of core drug combination

Table 7: Drug combination analysis based on entropy clustering

The serial number	Drug pairs	Association coefficient	The serial number	Drug pairs	Association coefficient
1	Lindera aggregate, Money grass	0.29	11	Acorus tatarinowii, Money grass	0.21
2	Acorus tatarinowii, Ground beeltle	0.25	12	Dioscorea collettii, Ground beeltle	0.21
3	Salt semen plantaginis, Money grass	0.25	13	Dioscorea collettii, Wine rhubarb	0.21
4	Smilax glabra, Money grass	0.25	14	Poria cocos, Money grass	0.20
5	Smilax glabra, Ground beeltle	0.23	15	Acorus tatarinowii, Fructus alpiniae oxyphyllae	0.20
6	Ground beeltle, Dioscorea collettii	0.23	16	Salt semen plantaginis, Fructus alpiniae oxyphyllae	0.20
7	Salt semen plantaginis, Wine radix cyathulae	0.22	17	Lindera aggregate, Ligusticum chuanxiong hort	0.20
8	Lindera aggregate, Fructus alpiniae oxyphyllae	0.22	18	Smilax glabra, Ligusticum chuanxiong hort	0.20
9	Smilax glabra, Spatholobus suberectus	0.22	19	Salt semen plantaginis, Wine rhubarb	0.20
10	Dioscorea collettii, Money grass	0.22			

Table 8: Core drug combination

The serial number	Core drug combination	The serial number	Core drug combination
1	Lindera aggregate, Smilax glabra, Poria cocos	3	Smilax glabra, Poria cocos, Acorus tatarinowii
2	Poria cocos, Acorus tatarinowii, Wine radix cyathulae	4	Dioscorea collettii, Acorus tatarinowii, Wine radix cyathulae

Table 9: New prescription

The serial number	New prescription
0	Lindera aggregate, Smilax glabra, Poria cocos, Acorus tatarinowii
1	Poria cocos, Acorus tatarinowii, Wine radix cyathulae, Dioscorea collettii

4. Discussion

Bi disease, a systemic disease involving multiple organs and tissues, is a kind of disease with the main symptoms of limb or joint pain, swelling, gravity, numbness or accompanied by movement disorders, its etiology is concerned with constitution, climate, diet and living habits more[4].

The etiology and pathogenesis of Bi disease originated from the combination of wind, cold and dampness, which was put forward in "Su Wen · Arthralgia", generations of physicians followed the theory and emphasized the feeling of external evil as the main cause. Professor Xu Jianqin, through years of clinical observation, emphasizes that this disease is based on liver and kidney deficiency, damp-heat accumulation, congestion blocking collateral as the standard [5]. Patients with congenital deficiency or poor work and rest, resulting in liver blood deficiency, kidney essence is insufficient, TCM emphasizes liver advocate muscle, kidney advocate bone, liver and kidney deficiency sends muscles and bones to lose nourishment, then muscles and bones waist and knees wither, joint injury, gas and blood operation is not free, long sends gore, gore blocks the meridians, not general pain, it have the disease. Modern doctor Wang Chengde[6] proposed that "Bi must contain dampness", emphasizing that Bi disease starts from dampness and changes from dampness. Therefore, dampness evil is the key in treating Bi disease. A total of 102 prescriptions and 117 drugs for Bi disease were included in this study. The top 8 places in frequency of TCM use were: Salt eucommia ulmoides, Vinegar corydalis yanhusuo, Dioscorea collettii, Salt semen plantaginis, Acorus tatarinowii, Lindera aggregate, Smilax glabra, Ground beeltle. High-frequency TCM combinations were as follows: Dioscorea collettii, Smilax glabra; Dioscorea collettii, Ground beeltle; Dioscorea collettii, Lindera aggregate; Dioscorea collettii, Acorus tatarinowii; Dioscorea collettii, Vinegar corydalis yanhusuo; Dioscorea collettii, Salt eucommia ulmoides; Dioscorea collettii, Salt semen plantaginis.

Eucommia ulmoides is sweet and slightly pungent, enters the liver and kidney meridians, has the efficacy of tonifying liver and kidney, strengthening muscles and bones. In the shennong Bencao Jing, it was recorded to Eucommia ulmoides, "Attending waist and knee pain... strengthening bones and muscles... Long-term use can make the body light, resistant to aging. [7]" Contemporary pharmacological studies have shown that the extracts of eumoides ulmoides, such as clove terpene, kaempferol, β -sitosterol and quercetin, have different degrees of regulation of osteoblast formation and anti-inflammatory effects[8]. Corydalis yanhusuo is pungent and bitter in taste, warm in nature, enters the liver and spleen meridians, has the functions of activating blood circulation, relieving pain, and promoting gas. Modern pharmacological studies have found that tetrahydropalmatine A and hexine extracted from Corydalis yanhusuo, reflect good analgesic effect [9], and vinegar Corydalis yanhusuo has better analgesic effect than Corydalis yanhusuo. Dioscorea collettii is bitter in taste, which enters to kidney and stomach meridians, has the effects of eliminating arthralgia, dampness

and turbidity. The Dioscorea collettii B, C and three lignans, components of Dioscorea collettii, can regulate bone metabolism[10]. Researcher Guangliang et al. [11] found that total saponins of Dioscorea collettii can improve the degree of joint and surrounding tissue lesions in gout arthritis model rats by inhibiting inflammatory factors. Semen plantaginis is sweet in taste, cold in nature, into the liver, kidney, lung and small intestine meridians, function of clearing dampness and heat, facilitating urination, stopping diarrhea. Zhang Zhongjing said: "The syndrome of dampness, ... but you should facilitate urinate." The modern physician Jin Mingxiu[12] believes that there is no paralysis without dampness, and commonly used dampness-clearing drugs include Alisma orientale, Semen plantaginis, etc, and the effect is remarkable. Modern pharmacological studies have shown that extracts from different parts of Semen plantaginis can reduce the level of uric acid in gout model mice at a given dose [13] and have certain anti-inflammatory effects [14]. Acorus tatarinowii is hot, bitter in taste, lukewarm in nature, has the effects of clearing dampness, promoting blood circulation and appetizing. Studies have shown that microwave water extract of Acorus tatarinowii can significantly inhibit auricle and toe swelling in mice [15]. Lindera aggregate is spicy and warm, which belongs to the lung, spleen, kidney and bladder meridians, and has the effects of stopping arthralgia and warming kidney Yang. Modern network pharmacology studies have found that Liubaosine and neocarpine, the representative components of Lindera aggregate generated alkali, can act alone on four signaling pathways such as tyrosine metabolism and calcium signaling pathway, and then inhibit the center and play anti-inflammatory and analgesic effects[16]. Noriporidine, a component of Lindera aggregate, can treat Bi disease by weakening the differentiation of osteoclasts [17]. Smilax glabra is sweet, light in taste, flat in nature, mainly enters the liver and stomach meridians, with the effects of detoxifying and dehumidifying, and promoting joints. Clinically, it is often used in combination with Dioscorea collettii to enhance the effect of dampness. Some researchers have found that astilbin, the extract of Smilax glabra, can obviously inhibit the development of gouty arthritis and improve toe swelling in model rats [18], and both it and Smilax glabra polysaccharide can inhibit the expression of TNF-α mRNA and iNOS inflammatory genes, inhibit the secretion of inflammatory factor NO, and finally play an analgesic role by inhibiting the excessive response of macrophages [19, 20]. Ground beeltle is salty in taste, and cold in nature, enters liver meridians, have the function of removing congestion, stopping arthralgia. Modern pharmacological studies have shown that the water-decocted extracts of Ground beeltle has analgesic effects [21]. The above eight herbs are treated from three aspects: deficiency, evil, and extravasated blood, playing a total of the functions of tonifying the liver and kidney, eliminating dampness evil, and clearing extravasated blood. Dioscorea collettii and Smilax glabra combined with detoxification and dehumidification synergistically enhanced; Dioscorea colletti and Ground beeltle combined with dehumidification and blood circulation; Dioscorea colletti and Lindera aggregate combined with removing dampness and arthralgia, warming kidney and dispersing cold; Dioscorea collettii clears dampness and reduces turbidity, Acorus tatarinowii appetizes and disperses dampness, the combination of the two can eliminate dampness in the middle and lower coke; Dioscorea collettii and Corydalis yanhusuo are used together to disperse dampness and at the same time promote blood circulation and relieve pain; Dioscorea collettii and Salt eucommia ulmoides are combined to dehumidify and at the same time tonify liver and kidney, strengthen muscles and bones; Dioscorea collettii and Salt semen plantaginis are combined to strengthen the clearing of dampness and heat in the lower coke. Through the theory of TCM and modern pharmacology, the scientificity of Professor Xu Jianqin in the treatment of Bi disease was demonstrated. Professor Xu Jianqin emphasizes that the disease is mainly characterized by "deficiency, evil and extravasated blood ", which is based on deficiency of liver and kidney, dampness and heat accumulation, and extravasated blood blocking collaterals. On the treatment, the main prescription for treatment of Bi disease is Chubi Zhitong Decoction, Duhuo Jisheng Decoction and Liuwei Dihuang Decoction, etc.

This study conducted an in-depth analysis of the medication rules of Bi disease from the aspects of TCM theory and modern pharmacology through the TCM inheritance auxiliary platform system, and demonstrated the scientific nature of Professor Xu Jianqin's treatment of Bi disease. Through unsupervised entropy layer clustering analysis, four groups of core drug combinations were obtained and the data were deeply mined, so as to conclude that Professor Xu Jianqin's new prescription combinations for treating Bi disease were obtained as follows: The combination of Lindera aggregate, Smilax glabra, Poria cocos and Acorus tatarinowii can warm kidney and spleen, remove dampness and detoxify; The other combination of Poria cocos, Acorus tatarinowii, Wine radix cyathulae and Dioscorea collettii can tonify the spleen and dampness, Invigorate the kidney and promote blood Circulation. Based on Professor Xu Jianqin's thinking in diagnosing and treating Bi disease, the new prescription makes a dialectical analysis, pays attention to the characteristics of the disease, and combines syndrome differentiation with disease differentiation as an important clinical supplement.

To sum up, this study conducted an in-depth analysis of Professor Xu Jianqin's medication experience and regularity in the treatment of Bi disease through the TCM inheritance auxiliary platform, providing an important reference for the clinical application of differentiation and treatment of Bi disease and the development of new drugs. However, the core drug combinations and new prescriptions obtained after the above analysis and evolution still need to be evaluated through near-real experimental studies and clinical studies. The purpose of this study is to explore and analyze Professor Xu Jianqin's characteristic medication rules, broaden TCM clinical thinking and medication thinking for clinical prevention and treatment of Bi disease, and provide important data support for the inheritance of famous doctors' experiences.

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