Study On Drug Combination Rules of Hypertension Treating By Traditional Chinese Medicine

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Abstract

Objective: The author studied the drug using modes of hypertension with yin deficiency and yang excess syndrome in Chinese medicine with the Traditional Chinese Medicine inheritance auxiliary system software.

Method: The author collected all of the literatures about hypertension with yin deficiency and yang excess syndrome in Chinese medicine in China National Knowledge Infrastructure (CNKI) to build a prescription database, and then analyzed the drug using modes for networked show.

Result: The author chose 110 pieces of prescriptions to set up the database, and then obtained the using condition of prescriptions, frequency of drugs, drug combination patterns, and networked show of drugs association.

Conclusion: (1) There are three drug using modes for hypertension with yin deficiency and yang excess syndrome in Chinese medicine: calming liver and suppressing yang combination patterns, tonifying yin and replenishing kidney combination patterns, and neutral supplementation combination patterns. (2) The drug using modes could be analyzed and networked showed better by the Traditional Chinese Medicine inheritance auxiliary system software.

Key words: hypertension; yin deficiency and yang excess syndrome; Drug using mode; Networked presence

Hypertension is a common clinical frequently-occurring disease, and " Traditional Chinese Medicine (TCM) evidence-based clinical practice guidelines ·TCM internal medicine" points out that generally it can be divided into several types: liver-yang hyperactivity syndrome, yin deficiency and yang excess syndrome, liver and kidney yin deficiency , Yin and Yang deficiency , syndrome-complex of wind-phlegm , and symptom of blood stasis and channel blockage, etc. In this paper, the author use the Traditional Chinese Medicine inheritance auxiliary system software to research the drug using modes of hypertension with yin deficiency syndrome yang excess syndrome and make a networked show, in order to understanding the current drugs using condition of it in TCM. The report is as follows.

I. literature materials

1. 1 Materials Source

The author entered into the retrieval page in CNKI, chose the primary retrieval, and chose the "high blood pressure" as key words. Search term：title；matching term：fuzzy；ranking term: time; retrieval time limitation term: 2000 to 2011; others: default. 69927 pieces of literatures about hypertension were obtained in the end.

1. 2. 1 Accepted Standard

The author chose literatures about hypertension treatment in TCM and integration of traditional Chinese and Western medicine, and articles of experts' experience, which include therapy with syndrome differentiation and prescriptions about hypertension with yin deficiency and yang excess syndrome.

1. 2. 2 Exclusion Standards

(1) People who were definitely diagnosed as hypertension with complication (such as hypertensive nephropathy) or secondary hypertension (such as hypertension of pregnancy) were rejected.

(2) Literature review, experiment research, popular science literature and repeated articles were rejected.

1. 3 Settle Results

Based on the above selection standard, 110 pieces of literatures, meeting the research standard, consisting of prescriptions, were selected from the related 69927 literatures.

1.4 Standard of Names for Chinese Medicinal

Names of Chinese Medicine in literatures were standardized according to the "pharmacopoeia of the People's Republic of China · 2005 edition", such as HangBaiJu, BaiJuHua, and HuangJuHua were collectively called as JuHua; ShengHangShao and BaiShao were collectively called as BaiShao; HeShouWu, ShouWu, and ZhiShouWu were collectively called as HeShouWu; ShanZhiZi and ShanZhi were collectively called as ZhiZi; Qiguo and GouQi were collectively called as GouQiZi; ShengLongMu was called as ShengLongGu and ShengMuLi respectively; DanPi was called as MuDanPi; CaoJueMing was called as JueMingZi; etc.

II. Establishment of Database and Data Analysis

There is a "prescription management" in the Data Manager Module of the Traditional Chinese Medicine inheritance auxiliary system software, and the author recorded the prescription data into it to establish the prescription database of hypertension with yin deficiency and yang excess syndrome. Then the author made a statistical analysis through the "prescription analysis" in the Data Analysis Module of the Traditional Chinese Medicine inheritance auxiliary system software.

III. Result

3.1 General Situation Analyses

3. 1. 1 Prescription Using Situation

In the accepted 110 pieces of prescriptions, there were 55 pieces self-made prescriptions, 26 pieces of TianMa GouTeng decoction with its modification (including 3 pieces of TianMa GouTeng decoction with Qi Ju DiHuang pill), 10 pieces of calming liver wind soup with its modification, 10 pieces of Qi Ju DiHuang soup with its modification (including 1 piece of Qi Ju DiHuang soup with calming liver wind soup), 3 pieces of LingJiao GouTeng soup with its modification, 2 pieces of JianLing soup with its modification, and 4 other prescriptions. (Figure 1)
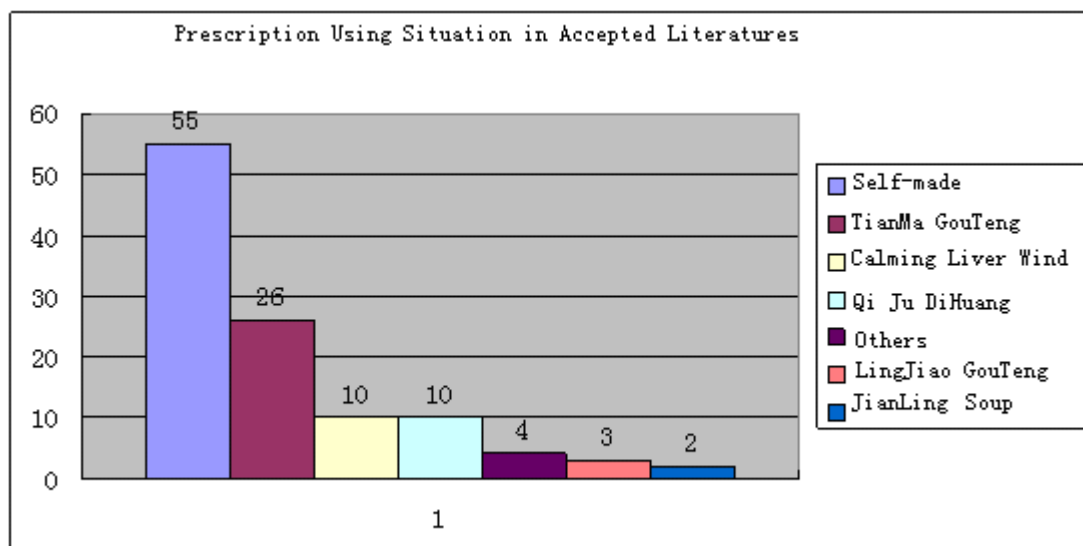
Figure 1   Prescription Using Situation

3. 1. 2 Drug Using Situation

Frequency statistics of drugs in the accepted 110 pieces of prescriptions about hypertension with yin deficiency and yang excess syndrome had been worked out to obtain the frequency of 112 kinds of drugs from high to low. There were 38 kinds of Chinese medicinal whose frequency were more than 10 times in Table 1.

Table 1   38 kinds of Chinese medicinal whose frequency were more than 10 times

No	Medicine	Rate	No	Medicine	Rate	No	Medicine	Rate	No	Medicine	Rate
1	Gou Teng	82	11	Ze Xie	32	21	Shu dihuang	23	31	DiLong	14
2	Tian Ma	68	12	Gou Qizi	30	22	Xuan shen	23	32	Bai Jili	14
3	Chuan Niuxi	53	13	Fu Ling	28	23	Dan Shen	22	33	Tian dong	13
4	Ju hua	49	14	Gui Jia	27	24	Huai Niuxi	22	34	Ge Gen	12
5	Sheng Dihuang	48	15	Shan Zhuyu	27	25	Zhi zi	20	35	Yin Chen	11
6	Bai Shao	47	16	Mu Danpi	27	26	Shan Yao	20	36	Fu Shen	10
7	Shi Jueming	47	17	Huang Qin	27	27	Yi Mucao	20	37	Jue Mingzi	10
8	Sheng Muli	35	18	Xi Kucao	27	28	Dai Zheshi	17	38	Chuan Xiong	10
9	Sang Jisheng	33	19	Sheng Longgu	26	29	Sheng Gancao	17			
10	du Zhong	33	20	Ye JiaoTeng	25	30	Nu zhenzi	15			

3.2 Drug Using Modes and Networked Presence Based on Association Rule

On the analysis interface of the Traditional Chinese Medicine inheritance auxiliary system software, when the number of Minimal Support was 33(about 30% of the whole data), and the confidence coefficient   was 0.9, there were 9 pieces of data, meaning 9 kinds of drug combination modes (Table 2), including 6 kinds of Chinese medicinal, including TianMa, GouTeng, ChuanNiuXi, ShiJueMing, ShengDiHuang, JuHua. Choose "networked presence" button to make a networked display. (Figure 2)

Table 2 Drug Using Modes Based on Association Rule (Support Degree was 30%)

No	Drug Mode	Rate	No	Drug Mode	Rate
1	Tian Ma，Gou Teng	64	6	Gou Teng，Sheng Dihuang	39
2	Chuan Niuxi，Gou Teng	48	7	Gou Teng，Ju hua	38
3	Shi Jueming，Gou Teng	45	8	Tian Ma，Gou Teng，Shi Jueming	41
4	Tian Ma，Shi Jueming	42	9	Tian Ma，Gou Teng，Chuan Niuxi	40
5	Tian Ma，Chuan Niuxi	40			
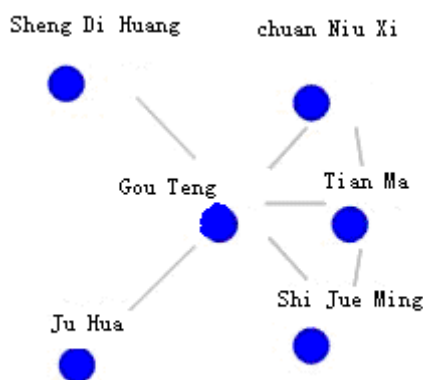
Figure 2 Networked Presence Based on Association Rule (Support Degree was 30%)

On the analysis interface of the Traditional Chinese Medicine inheritance auxiliary system software, when the number of Minimal Support was 22(about 20% of the whole data), and the confidence coefficient was 0.9, there were 59 pieces of data, meaning 59 kinds of drug combination modes (Table 3), including 15 kinds of Chinese medicinal, including TianMa, GouTeng, ChuanNiuXi, ShiJueMing, ShengDiHuang, JuHua, DuZhong, BaiShao, YeJiaoTeng, SangJiSheng, ShengMuLi, ShengLongGu, HuangQin, FuLing, ZeXie. Choose "networked presence" button to make a networked display. (Figure 3)

Table 3 Drug Using Modes Based on Association Rule (Support Degree was 20%)

No	Drug Mode	Rate	No	Drug Mode	Rate
1	Tian Ma，Gou Teng	64	31	Bai Shao， Sheng Muli	23
2	Chuan Niuxi， Gou Teng	48	32	Tian Ma， Huang Qin	22
3	Shi Jueming， Gou Teng	45	33	Tian Ma， Ye JiaoTeng	22
4	Tian Ma ， Shi Jueming	42	34	Tian Ma， Fu Ling	22
5	Chuan Niuxi，Tian Ma	40	35	Shi Jueming， Sang Jisheng	22
6	Gou Teng， Sheng Dihuang	39	36	Tian Ma， Shi Jueming， Gou Teng	41
7	Gou Teng， Ju hua	38	37	Chuan Niuxi， Tian Ma， Gou Teng	40
8	Bai Shao ， Gou Teng	32	38	Chuan Niuxi， Shi Jueming， Gou Teng	31
9	Chuan Niuxi， Shi Jueming	31	39	Chuan Niuxi， Tian Ma， Shi Jueming	30
10	Tian Ma ， Sheng Dihuang	31	40	Tian Ma， du Zhong， Gou Teng	29
11	Tian Ma，du Zhong	30	41	Tian Ma， Gou Teng， Sheng Dihuang	28
12	du Zhong ， Gou Teng	30	42	Tian Ma， Gou Teng， Ju hua	28
13	Gou Teng ， Sang Jisheng	30	43	Chuan Niuxi， Gou Teng ， Sheng Dihuang	25
14	Tian Ma， Ju hua	29	44	Shi Jueming， du Zhong， Gou Teng	25
15	Chuan Niuxi ， Sheng Dihuang	28	45	Chuan Niuxi， Gou Teng， Ju hua	24
16	Bai Shao， Sheng Dihuang	28	46	Tian Ma， Shi Jueming， du Zhong	24
17	Chuan Niuxi， Ju hua	27	47	Shi Jueming， Gou Teng， Ju hua	24
18	Ze Xie， Gou Teng	27	48	Bai Shao， Gou Teng， Sheng Dihuang	24
19	Ju hua ， Sheng Dihuang	27	49	Gou Teng， Ju hua， Sheng Dihuang	24

20	Tian Ma，Bai Shao	25	50	Chuan Niuxi，Tian Ma，du Zhong	23
21	Shi Jueming，du Zhong	25	51	Chuan Niuxi，du Zhong，Gou Teng	23
22	Sheng Muli，Sheng Longgu	25	52	Tian Ma，Gou Teng，Sang Jisheng	23
23	Chuan Niuxi，du Zhong	24	53	Tian Ma，Gou Teng，Huang Qin	22
24	Shi Jueming，Ju hua	24	54	Tian Ma，Gou Teng，Ye JiaoTeng	22
25	Gou Teng，Huang Qin	24	55	Tian Ma，Bai Shao，Gou Teng	22
26	Gou Teng，Ye JiaoTeng	24	56	Tian Ma，Fu Ling，Gou Teng	22
27	Bai Shao，Ju hua	24	57	Chuan Niuxi，Tian Ma，Shi Jueming，Gou Teng	30
28	Tian Ma，Sang Jisheng	23	58	Tian Ma，Shi Jueming，du Zhong，Gou Teng	24
29	Gou Teng，Sheng Muli	23	59	Chuan Niuxi，Tian Ma，du Zhong，Gou Teng	23
30	Fu Ling，Gou Teng	23			

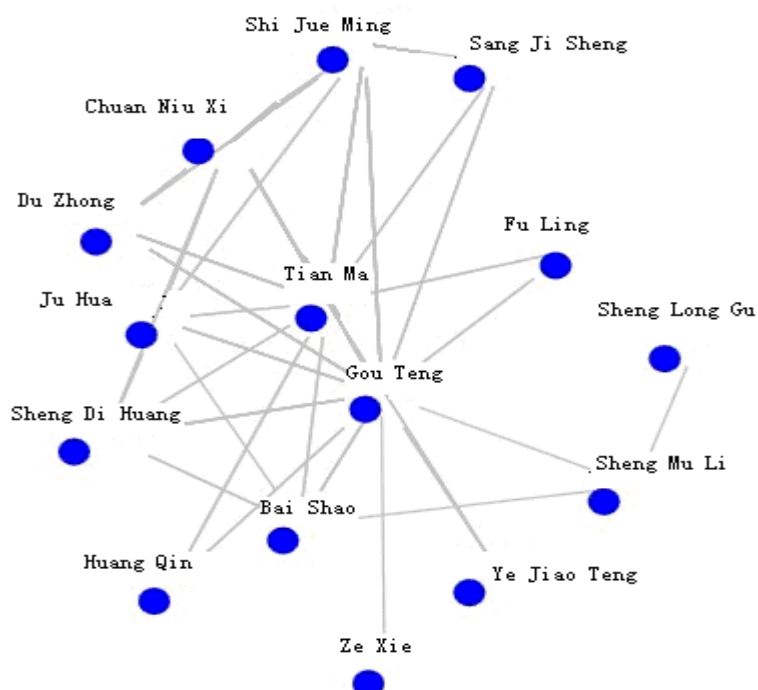**Figure 3 Networked Presence Based on Association Rule (Support Degree was 20%)**

IV. Discussion

Traditional Chinese Medicine inheritance auxiliary system software is an analyzing and processing software for Traditional Chinese Medicine data, which has consulted related researches(JX Chen et al., 2012a; JX Chen et al., 2007; JX Chen et al., 2010; JX Chen et al., 2011a;). Jian Li (Jian Li et al., 2012) thinks that this software includes functions of Data Entry, Data Management, Data Query, Data Analysis and visible networked presence, and it can be used in fields of inheriting experience of famous veteran doctors of TCM, summarizing individual experience, analyzing prescription and discovering new prescriptions, etc. Zhigeng Li,Jian Li and Jingchang Sun(Zhigeng Li et al., 2012; Jian Li et al., 2012 ; Jingchang Su et al., 2012) have got good results by using the software to analyze the inherent relationships between herbs in prescriptions of influenza,atrophic lung disease and edema. In other fields, it can order some researches(JX Chen et al., 2012b; JX Chen et al., 2012c; JX Chen et al., 2011b). This study selected hypertension with yin deficiency and yang excess syndrome as the research object, mainly through the unsupervised data mining method in Traditional Chinese Medicine inheritance auxiliary system software, to detect its drug using modes and make a networked presence.

Based on the prescriptions using situation, it could be concluded that self-made prescription took up the largest proportion, about 50%, and TianMa GouTeng decoction, largest in effective prescriptions, about 23.6%. These prescriptions were fit for the etiology of hypertension with yin deficiency syndrome yang excess syndrome. Frequency of the top 10 drugs were GouTeng, TianMa, ChuanNiuXi, JuHua, ShengDiHuang, BaiShao, ShiJueMing, ShengMuLi, SangJiSheng and DuZhong, which belonged to drug types with calming liver and suppressing yang, tonifying liver and kidney. If ShengDiHuang and ShuDiHuang were collectively called as DiHuang, its frequency would take up the second position.

Based on the data analysis, when the number of support degree was 33, there were 9 drug combination patterns. 7 of them had 2 kinds of drugs and 2 of them had 3 kinds of drugs, which were the foundation of the drug using mode. Serial number 1, 4, and 5 were respectively corresponding to TianMa with GouTeng, TianMa with ShiJueMing and TianMa with ChuanNiuXi, which could enhance the effect of calming liver and suppressing yang, and especially the combination of TianMa with GouTeng appeared up to 64 times. Serial number 1, 2, 3, 6 and 7 were respectively corresponding to GouTeng with TianMa, GouTeng with ChuanNiuXi, GouTeng with ShiJueMing, GouTeng with ShengDiHuang and GouTeng with JuHua, which were also proper compatibility of medicines. GouTeng with ShengDiHuang, one clears heat and calms liver, and another one cools blood and nourishes Yin, which aimed at the pathogenesis of hypertension with yin deficiency and yang excess syndrome. The model of 3 kinds of drugs were respectively TianMa, GouTeng plus ShiJueMing with effect of calming liver and suppressing yang, clearing liver and improving vision or TianMa, GouTeng plus ChuanNiuXi with effect of activating blood circulation to dissipate, tonifying liver and kidney and ensuring proper downward flow of the blood, which were great drug using modes, and these drugs were all in the proved prescription(Hongxian Wang 2008; Jingyun Yin 2012; Xueni Mo et al., 2012; Chunfu Wang and Xuefeng Wang 2009; Lin Huang 2009; Zhikai Zhu 2011).

When the support degree was 22, drug combination modes and types of drugs started to increase, which were due to reduction of the demand conditions and the frequencyof drug combination in the overall data model. At this time, drug combination modes of 2 drugs were 35, 3 drugs, 21, and 4 drugs, 3. The 9 new kinds of traditional Chinese medicine were Duzhong, BaiShao, TeJiaoTeng, SangJiSheng, ShengMuLi, ShengLongGu, HuangQin, FuLing and ZeXie.

In the involved 15 kinds of drugs only ShengDiHuang and BaiShao tended to nourish Yin, when the support degree reduced , such as 17, some drugs, such as GouQiZi, GuiJia and ShanZhuYu, would appear, which indicated that doctors tend to use the drugs with calming liver and suppressing yang than drugs with nourishing Yin. Drug combination modes can be classified as three types: 1.calming liver and suppressing yang

combination, such as 1, 3, 4, 7, 14, 22, 24, 36, 42 and 47, such combination mode could enhance the effect of li calming liver and suppressing yang combination; 2. tonifying yin and kidney combination, such as 15, 16 and 23, such combination mode could enhance the effect of tonifying yin and kidney; 3. neutral supplementation combination , such as 2, 5, 6 , 8 ~ 13, 17 ,19 ~21, 24, 27, 28, 31, 35, 37 ~39, 40, 41, 43 ~46, 48 ~ 52, 55, 57 ~ 59, such was the most combination model, caring both inside and outside, to restore balance of Yin and Yang.

In conclusion, there are three drug using modes for hypertension with yin deficiency and yang excess syndrome in Chinese medicine: calming liver and suppressing yang combination patterns, tonifying yin and replenishing kidney combination patterns, and neutral supplementation combination patterns. The drug using modes could be analyzed and networked showed perfectly by the Traditional Chinese Medicine inheritance auxiliary system software.

V. Acknowledgment

Reference

[1]   China Academy of the Chinese Medical Sciences. "Traditional Chinese Medicine evidence-based clinical practice guidelines · TCM internal medicine" [M]. Beijing: China Chinese medicine press, 2011:233

[2]   Jianxin Chen, Peng Lu, Xiaohan Zuo, Qi Shi, Huihui Zhao, Liangtao Luo, Jianqiang Yi, Chenglong Zheng, Yi Yang andWeiWang. Clinical Data Mining of Phenotypic Network in Angina Pectoris of Coronary Heart Disease. Afr. J. Pharm. Pharmaco. Volume 2012, Article ID 546230, 8 pages.

[3].   JIANXIN CHEN∗ , GUANGCHENG XI, JING CHEN (2007). An unsupervised pattern (syndrome in traditional Chinese medicine) discovery algorithm based on association delineated by revised mutual information in chronic renal failure data.   J. Biol. Syst. 15(4):   435–451.

[4].   JIANXIN CHEN, ZHENHUA JIA, XIANGCHUN WU, GUOQIANG YUAN, CONG WEI, CHENGLONG ZHENG, JIANQIANG YI, YILING WU   (2010). Selecting biomarkers for primary hyperlipidemia and unstable angina in the context of neuro-endocrine-immune network by feature selection methods.   J. Biol. Syst. 18(3): 605–619.

[5].   Jianxin Chen, Xueling Ma, Huihui Zhao, Ying Yang, Jing Han, Shuzhen Guo, Bing Liu, Jian Ni,Wei Wang* (2011). Biological effects based quality control of a traditional Chinese medicine.   J. Med. Plants. Res.   5(31): 6895-6906.

[6]   Jian Li, Peng Lu, ShiHuan Tang, et al. Analysis of pulmonary abscess prescriptions Based on Traditional Chinese Medicine inheritance auxiliary system software [J]. China Journal of experimental traditional medical formulate, 2012, 18 (2): 254 ~ 257.

[7]   Zhigeng Li, Yan Feng,Shihuan Tang. Analysis on Inherent Relationships between Herbs in Prescriptions for Flu Prevention and Treatment by Using Traditional Chinese Medicine Inheritance System [J], China Journal of experimental traditional medical formulate,2012,18(14):13~17

[8]   Jian Li,Peng Lu,Ruixian Zhang, Furong Xin,Jianxin Chen,Shihuan Tang,Hongjun Yang.Analysis on composition principles of prescriptions for atrophic lung disease in the book of <the prescription of traditional chinese medicine dictionary>,China Journal of experimental traditional medical formulate,2012,18(10):1~5

[9]   Jingchang Sun,Yanping Wang. Analysis on composition principles of prescriptions for edema by using traditional chinese medicine inheritance support system, China Journal of experimental traditional medical formulate,2012,18(10):11~16

[10].   Jianxin Chen, Huihui Zhao, Liangtao Luo, Chenglong Zheng, Fugang Wang, Qi Shi, Bing Liu, Wei Wang* (2012). Pharmacokinetics of oral administration of 2, 3, 5, 4'-tetrahydroxystilbene-2-O-β-d-glucoside from Polygonum multiflorum in beagle dogs. Afr. J. Pharm. Pharmaco. 6(14): 1022 – 1025.

[11]   Jianxin Chen, Huihui Zhao, XuelingMa, Xiao Han, Liangtao Luo, LuyaWang, Jing Han, Bing Liu, WeiWang (2012). The Effects of Jiang-Zhi-Ning and ItsMain Components on CholesterolMetabolism. Evid-based. Compl. Alt. Volume 2012, Article ID 928234, 10 pages

[12].   Jianxin Chen,Huihui Zhao,Ying Yang,Bing Liu,Jian Ni,Wei Wang (2011). Lipid-lowering and antioxidant activities of Jiang-Zhi-Ning in Traditional Chinese Medicine. J.Ethnopharmacol. 134 (2011): 919–930

[13]   Hongxian Wang.Clinical study of effect on essential hypertension treated byTianmaGoutengYin, chinese archives of traditional chinese medicine,2008,26(2):338~340

[14]   Jingyun Yin.Effect of TianmaGoutengYin in treatment of stage Ⅰ and Ⅱ hypertension 60 cases, Modern Journal of Integrated Traditional Chinese and Western Medicine,2012,21(4):407~408

[15]   Xueni Mo,Yibao Yang,Shaoxiang Huang,Junchao Liu.Effect of TianmaGoutengYin on vascular remodeling in hypertensive rats, Chinese Journal of Experimental Traditional Medical Formulae,2011,17(9):149~152

[16]   Chunfu Wang,Xuefeng Wang.Effect of modified TianmaGoutengYin to treating 50 cases of primary hypertension,HuNan journal of traditional chinese medicine,2009,2(2):58~60

[17]   Lin Huang.Curative effect observation of TianmaGoutengYin in treatment of primary hypertension,HeNan journal of traditional chinese medicine,2009,29(2):186~187

[18]   Zhikai Zhu.Clinical observation of TianmaGoutengYin in treating hypertension with Yin Deficiency and Yang Excess Syndrome,ShanXi journal of traditional chinese medicine,2011,27(4):20~21