Advances in Clinical Research on Prevention and Treatment of Diabetic Nephropathy by Jingfang of Promoting Blood Circulation and Removing Blood Stasis

Xiaobing Li1,*, Wen Liu2,†, Xiao Wang1,*, Mingming Huang3,†, Qing Shi3,†, Tian Wang4,*, Qian Xue1,*, Yuanyuan Cao4,*, Danhua Zhang5,*, Donghao Yin6,†, Mengjie Yang1,†, Junchao Duan5,†, Bingqian Li1,*, Manman Yao1,† and Xiaoxue Li1,†

1Henan University of Traditional Chinese Medicine, Zhengzhou, China
2Nanjing University of Chinese Medicine, Jiangsu Province Hospital of Chinese Medicine, Nanjing, China
3Beijing University of Chinese Medicine, Dongzhimen Hospital, Beijing, China
4Shanghai University of Traditional Chinese Medicine affiliated Shuguang, Shanghai, China
5The first affiliated Hospital of Henan University of Traditional Chinese Medicine, Zhengzhou, China
6Children's Hospital affiliated to Capital Medical University, Beijing, China
7Xinjiang Medical University, Xinjiang, China

*Corresponding author e-mail: baishaoyao@163.com, *15538188836@163.com, †suyi111@126.com, ‡hmm15538188905@163.com, §shiqing3357@163.com, ¶wangtian918@126.com, ¶¶936462319@163.com, ¶¶¶caoyuanyuan213@126.com, ¶¶¶¶huai8236776024@163.com, ¶¶¶¶liuqinzho996@163.com, ¶¶¶¶a15239180933@163.com, ¶¶¶¶¶18337136340@163.com, ¶¶¶¶¶li1976211667@163.com, ¶¶¶¶¶¶¶¶1779175488@126.com, ¶¶¶¶¶¶¶¶¶xiaoxue945@163.com

Abstract. Promoting Blood Circulation and Removing Blood Stasis is key to prevent and treat diabetic nephropathy (DN). After a long-term practice, some JingFang of promoting blood circulation and removing blood stasis (PBCRBS) have been proved to be effective in clinic, which reviewed in this article can regulate the disorder of glucose and lipid metabolism, inhibiting the inflammation as well as oxidative stress of diabetic nephropathy, accordingly reducing renal fibrosis and delaying the degree of DN lesions. The author reviews the research progress of preventing and treating DN by JingFang of PBCRBS in the clinic.

1. Introduction
Diabetic nephropathy is one of the most serious complications of diabetes and the leading cause of death in type 1 diabetes. In type 2 diabetes, it is only second to cardiovascular and cerebrovascular diseases in endpoint events.

There are different levels of glucose and lipid metabolism disorders in DN patients, which have a positive correlation with renal dysfunction as well as a systemic and local inflammatory response [1].
Proteinuria, edema, and progressive renal dysfunction are the main clinical features of DN. "Blood Syndrome" says: "Blood stasis can form water, which can also lead to edema. So it is not only a blood disease but also a water disease." The bad state of the blood system may cause an abnormal condition of water transformation and transportation. PBCRBS is an effective method to treat edema. The author has sorted out the related clinical research on the treatment of DN in recent years, which will provide references for the clinical application of JingFang of PBCRBS in DN.

2. References analysis

Frequency analysis of clinical research on DN-related PBCRBS syndrome: 43 relevant high-quality works of literature are selected by keywords such as "diabetic nephropathy", "promote blood circulation and remove blood stasis" "Jingfang", "clinical research" and "basic research" for frequency statistics, and are reviewed by four other researchers in the research group.

The results show that there are 22 clinical studies and 21 basic studies on diabetic nephropathy, and the frequency of the two is quite similar. This shows that the basic research and clinical research on DN are currently comparable. This paper will focus on analyzing clinical research. In the clinical study of diabetic nephropathy, there are 18 studies related to promoting blood circulation to remove blood stasis "Jingfang", "clinical research" and "basic research" for frequency statistics, and are reviewed by four other researchers in the research group.

The results show that there are 22 clinical studies and 21 basic studies on diabetic nephropathy, and the frequency of the two is quite similar. This shows that the basic research and clinical research on DN are currently comparable. This paper will focus on analyzing clinical research. In the clinical study of diabetic nephropathy, there are 18 studies related to promoting blood circulation to remove blood stasis classical prescription, and 2 cases of non-classical prescription. All the treatment effects are ideal (Tab 1). The research-based on Danggui Shaoyao San (DSS), Guizhi Fuling Pill (GFP), Taohe Chengqi Decoction (TCD), Dahuang Zhechong Pill (DZP), and Didang Decoction (DD) is 4 articles, 4 articles, 5 articles, 2 articles, 4 articles respectively (Fig. 1), among which DSS, GFP, TCD, and DD have a similar research frequency, but the DZP is the least.

| References | The treatment group | The Control group | The result of treatment group (Effective or ineffective) |
|------------|---------------------|-------------------|-----------------------------------------------------|
| Zhou Qiang, Tong Xiaolin.2011 | DSS | N/A | Effective |
| Guo Jianzhong, Lu N et, al.2016 | DSS | N/A | Effective |
| Li Xiaobing, Xie Zhongli et al.2013 | Modified DSS and Irbesartan | Oral Irbesartan Tablets | Effective |
| Guo Jianzhong, Qiu Quan et, al.2016 | DSS and Fangji Huangqi Tang | Oral Benazepril Hydrochloride Tablets | Effective |
| Huang Jie, Cui Yunzhu.2014 | GFP | N/A | Effective |
| Liu Siyuan.2010. | Modified GFP | Oral Pills-Shen Shuai Ning | Effective |
| Li Feng, Fan Xiangyu et al.2017 | Modified GFP | N/A | Effective |
| Jiao Angui.2014 | Modified GFP | N/A | Effective |
| Huang Jie, Cui Yunzhu.2014 | TCD | N/A | Effective |
| Xiong Longnian, Yang Hui.2015 | TCD | N/A | Effective |
| Zou Jianping, Chen Ying.2016 | Modified TCD | Oral Metformin Tablets | Effective |
| Sun Xia, Wang Xinghua.2013 | TCD | N/A | Effective |
| Liang Lige.2016 | TCD and Shenqi Dihuang Decoction | Oral Irbesartan Tablets | Effective |
| Qi Hui, Tan Siming.2016 | Modified DZP | Alprostadil Injection | Effective |
| Wu Jian, Zhang Zhenzhong.2017 | DZP and Bailing Capsule | Basic treatment of western medicine | Effective |
| Tian Jiaxing, Zhao Linhua, et al.2012 | Modified DD | Not have | Effective |
| Duan Gong, Shi Caiyun, et al.2015 | Modified DD | Basic treatment of western medicine | Effective |
| Wu Moujun, Peng Long. 2011 | Modified DD | Basic treatment of western medicine | Effective |
| Huang Liuying, Zhang Mingyu, et al.2018 | DD | Basic treatment of western medicine | Effective |
3. Etiology and pathogenesis

Traditional Chinese medicine believes that the related viscera of DN are kidney, spleen, lung, heart, and liver, mainly in the kidney, called ShenXiao, namely diabetic nephropathy.

Symptoms and signs of diabetic nephropathy belong to the concept of diabetes, edema, urine turbid and other notions in traditional Chinese medicine, which are characterized by asthenia in origin and sthenia in superficiality. The asthenia in origin is a deficiency of both qi and yin. When it comes to late-stage, spleen and kidney deficiency or yin and yang deficiency will emerge. Sthenia in superficiality is a substantial pathogenic factor in renal collaterals, such as stagnation of blood, turbid phlegm and pathogenic dampness, which can also be mixed [2]. In the "Huangdi Neijing-LingShu.WuBian pian", it is recorded that "the blood and qi are reversed so that the blood is not able to pass. And it accumulates the heat which is used to burn muscles, so it is diabetes." It shows that blood countercurrent is the cause of diabetes, and the blood can not run normal leads to blood stasis. If the blood runs poorly, it forms water. The water is not normally transported, then edema forms [3]. Zhou Qiang et al. believe that when applying the method of promoting blood circulation for removing blood stasis to diabetes, this therapy is suitable for patients with no proteinuria or intermittent proteinuria in an early stage. Accordingly, the method of dredging collaterals, eliminating blood stasis to promote new blood to make the choroid patency, which suitable for patients with persistent proteinuria [4]. Zhang Panke et al. believe that in the course of DN, obstruction of collaterals by blood stasis runs through all the time. Blood stasis is the pathological product first and then becomes a causative factor, which leads to a vicious cycle and makes the condition more difficult to cure [5].

4. Effect of promoting blood circulation and removing blood stasis on clinic research

4.1. Danggui Shaoyao San

Danggui Shaoyao San (DSS) is a prescription in" Synopsis of the Golden Chamber" which recorded that "Danggui Shaoyao San can be prescribed for a pregnant woman with chronic abdominal pain and contractions "and "Danggui Shaoyao San is effective in curing abdominal pain caused by various gynopathies ".

DSS is the famous formula of Zhang Zhongjing's therapy of PBCRBS. In the prescription, Angelicae Sinensis Radix is used to promote blood circulation and nourish the blood and activate blood circulation for dissipating blood stasis, Paeoniae Radix Alba is used to nourish yin for

Figure 1. Frequency of Clinical Research on Diabetic Nephropathy treated by PBCRBS.
harmonizing Yingfen and soften liver for relieving pain; Chuanxiong Rhizom is used to activate qi for relieving qi stagnation and disperse stagnated liver qi for relieving pain; Atractylodis Macrocephalae Rhizoma, Poria cocos and Alismatis Rhizome are used to invigorate spleen for eliminating dampness. Li Xiaobing et al. reported that irbesartan combined with the Modified Danggui Shaoyao San can reduce the levels of IL-6, TNF-α, and IL-18 in patients with DN, which has a delayed effect on the progression of DN. And the treatment group plays a better role than Western medicine alone [6]. Professor Li Fazhi believes that the pathogenesis of DN is qi deficiency, blood stasis, and water retention, this syndrome type is suitable for using the DSS. This prescription which combined with Fangji Huangqi Decoction for the treatment of DN can benefit qi for strengthening the spleen and remove blood stasis for alleviating water retention, and it has achieved good clinical results [7]. Huang Keji et al. reported that the Modified Danggui Shaoyao San can reduce BUN and Scr, increasing the levels of Hb and Alb. Besides, It improved the disordered state of TG, LDL-c, and HDL-c, ameliorating clinical symptoms in patients with end-stage diabetic nephropathy (ESDN) [8]. Guo Jianzhong et al. used Danggui Shaoyao San combined with Fangji Huangqi Decoction to treat DN patients, which can reduce the levels of BUN and Scr and significantly reduce the levels of urinary β2-MG and UAER. The decrease was more significant in the treatment group than in the control group (the difference was statistically significant), indicating that this prescription can effectively delay renal fibrosis in patients with diabetic nephropathy [9].

4.2. Guizhi Fuling Pill
Guizhi Fuling Pill (GFP) comes from "Synopsis of Golden Chamber" which says, "A women patient who originally suffered from Zheng disease ceases menstruating for less than three months, but continues to suffer from mild chronic bloody vaginal discharges. She also feels a quickening in the abdomen above the navel, which is caused by Zheng disease. If menstruation is normal for three months before conception and if the patient feels the quickening during the sixth month after conception, the fetus will be normal. In case menstruation ceases for three months and is followed by mild chronic bloody vaginal discharge, blood stasis will result. The bloody discharge does not cease because Zheng has not yet subsided. Stasis should be removed with Guizhi Fuling Pill." Ramulus Cinnamoni is the king medicine, which can warm blood vessels, eliminating blood stasis and dispersing stagnation; Semon Persicae is the minister medicine, which can assist the king medicine in removing blood stasis and removing symptoms; Cortex Moutan Radicis can cool serum heat and promote blood circulation and dissipate blood stasis; Radix Paeoniae can relieve pain and dampness; Poria can remove dampness by promoting diuresis and replenish Qi to invigorate the spleen. Huang Jie et al. believe that patients with diabetic nephropathy are prone to blood stasis and water-damp stagnation due to microcirculatory disturbances. GFP may be able to improve renal blood perfusion and disturbance of water metabolism caused by this condition, thereby improving patients' clinical symptoms. Therefore, all the pathogenesis which is formed by blood stasis, cold and dampness stagnation can be treated by Guizhi Fuling Pill [2]. Liu Siyuan's research has shown that the application of GFP in the CRF stage of patients with diabetic nephropathy can improve Chinese medical syndrome and significantly reduce Scr, BUN and 24h urine protein [10]. The study of Li Feng et al. have observed that GFP can regulate VEGF and urine microalbumin excretion in patients with diabetic nephropathy [11]. Jiao Angui's clinical research showed that the application of GFP in treating diabetic nephropathy can improve Chinese medical syndrome and reduce urinary albumin excretion. Its effect is better than Western medicine treatment group [12].

4.3. Taohe Chengqi Decoction
Taohe Chengqi Decoction is from"Treatise on Febrile Diseases". The provision is"Before the taiyang disease is gone, pathogenic heat congeals in the urinary bladder, the patient behaves in a manic way. The blood is coming out, people are healed. Before the exterior syndrome is dispersed, we can’t use the purgative method, but relieving the exterior.
When the exterior syndrome is dispersed, but people feeling uneasy in the abdomen, we can use Taohe Chengqi Decoction."Taohe Chengqi Decoction beneficial effect on lower jiao blood amassment. In this prescription, the Peach kernel can promote blood circulation and remove blood stasis, Rhubarb can purge away the heat and remove stasis. When these were used in combination, the heat and stasis can be treated together. Cinnamon Twig's property and taste are warm and acrid, which can dredge blood vessels. Sodium Sulfate's property and taste are cold and salty, which can assist Rhubarb to purge away the heat and remove stasis. Licorice can harmonize the stomach and subdue the taste and property of the herb. Taohe Chengqi Decoction has the function of promoting blood circulation, removing blood stasis, purging away the heat and promoting purification, which is applied to diseases with blood stasis blocking in various clinical departments. Professor Huang Wenzheng combined this Prescription with Shenqi Dihuang decoction to treat diabetic nephropathy and achieve a notable curative effect. He advocates removing Sodium Sulfate, adding ground beetle, leech and other insect medicines to promote blood circulation and remove blood stasis when there are serious proteinuria and complications [13]. Studies have shown that Modified Taohe Chengqi Decoction can improve the renal function of diabetic patients. The levels of UTP, BUN, and Scr are lower than those of the control group (P<0.05) after treatment of patients with heat stagnation and blood stasis syndrome, reducing renal oxidative damage degree [14]. The study of Sun Xia has demonstrated that the addition and subtraction of Taohe Chengqi Decoction can improve the "the state of polydipsia, polyphagia, and polyuria" symptoms of diabetes patients, ameliorating hemodynamic abnormalities and microcirculatory disorders and reducing the levels of blood glucose and lipid [15]. Liang Lige's clinical research reported that Taohe Chengqi Decoction and Shenqi Dihuang Decoction had a good curative effect on diabetic nephropathy, which could effectively reduce fasting blood glucose (FPG), postprandial two-hour blood glucose (2 h PG), blood lipids as well as UAER in patients with DN. Besides, the levels of UTP, Scr, urinary α1-MG, and β2-MG were also significantly reduced [16].

4.4. Dahuang Zhechong Pill
Dahuang Zhechong Pill (DZP) is a classical formula in" Synopsis of the Golden Chamber" which was written by Zhang Zhongjing. It says that "The patient is extremely feeble and thin and suffers from the five strains, with abdominal distention and anorexia.

This is caused by unregulated eating and drinking, melancholy, hunger and overexertion in sexual activity or physical labor. Channels and collaterals, Nutrient Essence, Vital Resistance and Vital Energy are all impaired. In such cases, blood stasis will result. The patient's skin is scaly, with rings around the eyes. The therapy aims to harmonize and ease the Interior and replenish the Deficiency. Pills of Dahuang Zhechong are efficacious". The formula consists of Auhubarb, Leech, Scutellaria, Peach Kernel, Bitter Almond, Ground Beetle, Grub, Gadfly Insect, White Peony Root, Dried Lacquer, Prepared Radix Rehmanniae, Glycyrrhiza and other traditional Chinese medicines. Its effectiveness is reflected in removing blood stasis in promoting tissue regeneration and deficiency elimination in blood-stasis. One clinical research revealed that Sanchong Decoction, a Chinese herbal compound of DZP, can reduce the levels of inflammatory factors IL-6 and TNF-α as well as levels of Scr, BUN, urinary β2-MG and 24-hour urine protein, improving renal function in diabetic patients with nephropathy [17]. Wu Jian et al. clinically observed that the addition of DZP based on western medicine could effectively reduce the levels of high-sensitivity C-reactive protein, the early β2 microglobulin, urinary microalbumin as well as 24-hour urinary protein excretion rate and increase serum albumin in DN patients. The decrease of the protein excretion rate proves that the DZP has an effect of strengthening body resistance and eliminating evil, which can lead to effective treatment of diabetic nephropathy [18].

4.5. Didang Decoction
Didang Decoction comes from "Treatise on Febrile Diseases", which shows that "Initial Yang syndrome, sixth or seventh days, when the exterior syndrome remains and the pulse is feeble and deep, the patient does not suffer a blocked-up chest, but behaves in a manic way.
This is because the pathogenic Heat congealed at the Lower Portion of the Body Cavity and formed a hard abdominal distention. To resolve the blood stasis when urination is normal will be the cure. The pathology of the syndrome is that the pathogenic Heat intrudes into the Interior along the Initial Yang Channel. Didang Decoction is a proper curative”. It majors in the syndrome of heat stagnation and blood stasis syndrome in lower energizer. In the decoction, the leech is good at sucking blood and relieves blood stasis; the gadfly is salty in taste, so it can soft firm dissipating and resolving hard lump; the peach kernel’s property and taste are acrid and sweet whereby it relieve blood stasis; the rhubarb, which property and taste are cold and bitter, has the function of breaking stagnant and eliminating blood stasis. Wu Moujun et al. have observed that Modified Didang Decoction can effectively reduce HbA1c, urinary microalbumin and the deterioration of renal function in patients with diabetic nephropathy [19]. Tian Jiaxing et al. have observed that the addition and subtraction of the Didang Decoction may be able to reduce microalbuminuria in diabetic nephropathy, ameliorate insulin resistance, and lower the level of blood glucose, blood pressure as well as blood lipid [20]. Duan Gong et al. reported that when they treated the type 2 diabetic nephropathy with phlegm and blood stasis type by using the addition and subtraction of this decoction, compared with the control group which used insulin treatment solely, the treatment group played a better role [21]. Huang Liuqi et al. found that Didang decoction had a good intervention effect on DN patients in the early stage. It significantly shortens the R-value (time of thromboplastin production) and K value (absolute coagulation time) in the thrombus elasticity test of patients with blood stasis type of DN. On the contrary, it can also enhance angle value (speed of thrombin formation), MA value (maximum thrombus intensity) and CI value (coagulation comprehensive index) significantly [22].

5. Evaluation and Outlook

In conclusion, modern medicine considers the influencing factors of DN mainly include glucose and lipid metabolism disorder, hemodynamic abnormalities, oxidative stress, inflammatory medium, cytokines, signal path activation and so on, among which the degree of the inflammatory response and oxidative stress is a reliable means for early diagnosis and treatment of DN.

Therefore, actively looking for drugs to prevent the activation and expression of inflammatory cells is expected to delay the progress of diabetic nephropathy and better prevent and treat DN. Chinese medicine has an advantage in the treatment of DN. And there are more clinical studies and less basic research. Currently, in terms of basic research, we tend to study single traditional Chinese medicine, while the classical prescription compound is difficult to study due to its complex composition. The basic research on JingFang or traditional Chinese medical compound, which has relatively few researches on diabetic nephropathy, mainly focuses on the observation of inflammatory cytokines and other phenomena, and there are few reports on more in-depth research on signal pathways. Future research on the mechanism of JingFang of PBCRBS in the treatment of DN from the cellular, molecular and gene levels will open up a new path for the clinical prevention and treatment of diabetic nephropathy and the development of proprietary Chinese medicine.

Acknowledgments

Supported by a project grant from The National Natural Science Foundation of China (Grand No.81603527), Science and technology project of Henan Province (Grand No.162102310466), Key scientific research projects of Henan Province College sand Universities (Grand No.16A360010), Henan University of Traditional Chinese Medicine Scientific and technological innovation talent support program (Grand No.2015XCRRC05). Science and technology project of Zhengzhou City (Grand No.20150310), The Young Core Teacher of Henan Province (Grant No. 2016GGJS-080).

References

[1] Li Lan, Li Jianwei. Glucose and lipid metabolism of diabetic nephropathy patients and their relationship with Renal function, Inflammation [J]. Journal of Hainan Medical College, 2017, 23 (10): 1341-1343.
[2] Huang Jie, Cui Yunzhu. Research on the treatment of diabetic nephropathy by Jingfang [J]. Shaanxi Journal of Traditional Chinese Medicine, 2014, 35 (6): 768-769.

[3] Xu Yunsheng, Huang Yanqin. Discuss the Pathogenesis of Diabetes Microvascular Disease Treating by Bushen Huoxue Methods [J]. Chinese Medicine Forum, 2011, 13 (3): 10-12.

[4] Zhou Qiang, Tong Xiaolin. The application of Classical Prescriptions in the treatment of diabetic kidney disease [J]. Journal of Traditional Chinese Medicine, 2011, 52 (17): 1459-1462.

[5] Zhang Panke, Wang Fang. Efficacy Observation of Diabetic Nephropathy Treated with Ginkgo-Damole Injection [J]. World Journal of Integrated Traditional and Western Medicine, 2011, 6 (1); 54-55.

[6] Li Xiaobing, Xie Zhongli, Zhao Yunfang. Effect of Modified Angelica Peony Powder on Inflammatory Cytokine in Patients with Early Diabetic Nephropathy[J]. Shizhen Guo Yi Guo Yao, 2013, 24 (6): 1447-1448.

[7] Guo Jianzhong, Lu Na, Han Yingping. Professor Li Fazhi's Experience in Treating Diabetes Complications with Danggui Shaoyao San in the Golden Chamber [J]. TCM research, 2016, 29 (6): 36-39.

[8] Huang Keji, Sun Yunsong, Liu Xianying, et al. Efficacy of renal collaterals methods in the treatment of diabetic nephropathy of end-stage and its influence on the experimental indexes [J]. China Medical Herald, 2016, 13 (30): 189-191.

[9] Guo Jianzhong, Qiu Wei, Han Yingping. Effects of Benefiting qi for removing blood stasis and diuresis on Serum Creatinine, Urea Nitrogen, Urinary Microalbumin and β2 Microglobulin in Patients with Diabetic Nephropathy [J]. Henan Medical Research, 2016, 25(8): 1385-1387.

[10] Liu Siyuan. Clinical observation of Guizhi Fuling bolus Jia Wei in the treatment of chronic renal failure of decompensation period of blood stasis and obstruction [D]. Heilongjiang: Master's thesis of Heilongjiang Academy of Traditional Chinese Medicine, 2010.

[11] Li Feng, Fan Xiangyu, Zheng Fang, et al. Wu Songhe. Research Progress on Correlation Between VEGF and Mechanism of Removing Blood Stasis and Dredging Collaterals for Traditional Chinese Medicine [J]. Chinese Journal of Traditional Chinese Medicine and Pharmacy, 2017, 35 (9).

[12] Jiao Angui. Clinical observation of 30 cases of diabetic nephropathy treated with Modified Guizhi Fuling Pill [J]. Sichuan Journal of Traditional Chinese Medicine, 2014, 32 (8): 102-103.

[13] Xiong Longnian, Yang Hui, Wang Yaoguang. Professor Huang Wen-zheng’s experience on the treatment of kidney disease applying Taohe Chengqi Decoction [J]. Chinese Journal of Traditional Chinese Medicine, 2015, 30 (8): 2811-2813.

[14] Zou Jianping, Chen Ying. Observation on the Antioxidative Stress and Renal Function Protection of Modified Taohe Chengqi Decoction [J]. Journal of New Chinese Medicine. 2016, 48 (11): 46-48.

[15] Sun Xia, Wang Xinghua. Application of classical prescriptions in treating diabetes and its complications [J]. Journal of Changchun University of Traditional Chinese Medicine, 2013, 29 (2): 353-355.

[16] Liang Lige. Treating Qi-Yin Deficiency and Blood Stasis Blocking Meridians Syndrome Diabetic Nephropathy Patients with Shenqi Dihuang Decoction and Taohe Chengqi Decoction [J]. Liaoning Journal of Traditional Chinese Medicine, 2016, 43 (10): 2115-2117.

[17] Qi Hui, Tan Siming. The Clinical Research into Early-Stage Diabetic Nephropathy Treated with Three Worms Decoction [J]. Henan Traditional Chinese Medicine, 2016, 36 (11): 1965-1967.

[18] Wu Jian, Zhang Zhenzhong, Liu Ningzhou, et al. Clinical Observation of Bailing Capsule and Dahuang Zhechong Pill Combined with Basic Treatment for Proteinuria of Early Diabetic Nephropathy [J]. Information on Traditional Chinese Medicine, 2017, 34 (6): 107-110.
Decoction [J]. Hunan Journal of Traditional Chinese Medicine, 2011, 27 (6): 57-58.

[20] Tian Jiaxing, Zhao Linhua, et al. Retrospective analysis on modified Didang Tang for treating microalbuminuria of diabetic nephropathy [J]. Journal of Beijing University of Traditional Chinese Medicine (Chinese medicine clinical edition) 2012, 19 (6): 7-10.

[21] Duan Gong, Shi Caiyun, Chen Yucui, et al. Clinical observation of modified Didang decoction on the treatment of type 2 diabetes with blood stasis-phlegm type [J]. Hebei Traditional Chinese Medicine, 2015, 37 (11): 1667-1669.

[22] Huang Liuzhen, Zhang Mingyu, Chen Yaxi, et al. Effect of Zhongjing Dangdang Decoction on Thrombus Elasticity Test in Patients with Blood Stasis Type of Early Diabetic Nephropathy [J]. Strait Pharmaceutical Journal, 2018, 30 (11): 132-133.