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Detection of consensuses and treatment principles of diabetic nephropathy in traditional Chinese medicine: A new approach

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Abstract *Objective:* To propose and test a new approach based on community detection in the field of social computing for uncovering consensuses and treatment principles in traditional Chinese medicine (TCM).
Methods: Three Chinese databases (CNKI, VIP, and Wan Fang Data) were searched for published articles on TCM treatment of diabetic nephropathy (DN) from their inception until September 31, 2014. Zheng classification and herb data were extracted from included articles and used to construct a Zheng classification and treatment of diabetic nephropathy (DNZCT) network with nodes denoting Zhengs and herbs and edges denoting corresponding treating relationships among them. Community detection was applied to the DNZCT and detected community structures were analyzed.
Results: A network of 201 nodes and 743 edges were constructed and six communities were detected. Nodes clustered in the same community captured the same semantic topic; different communities had unique characteristics, and indicated different treatment principles. Large communities usually represented similar points of view or consensuses on common Zheng diagnoses and herb prescriptions; small communities might help to indicate unusual Zhengs and herbs.
Conclusion: The results suggest that the community detection-based approach is useful and feasible for uncovering consensuses and treatment principles of DN treatment in TCM, and could be used to address other similar problems in TCM.

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Introduction

In complex network theory, a social network is a social structure made of nodes (individuals or organizations) connected by edges to exemplify various relationships such as friendship, affiliation, or cooperation. Community detection is one of the fundamental tasks in social network analysis. It solves problems by studying groups rather than individuals. Finding a community in a social network is a function of identifying a group of nodes that interact with each other more frequently than with nodes outside the group.[1] The real-world significance of identifying such communities are, for example, that friends in the same group share more similar interests and interact with each other more frequently[2]; that community analysis has uncovered thematic clusters on the Internet[3]; and, in biochemical or neural networks, that communities may be functional modules.[4] Nowadays, social computing research has gradually shifted from its traditional research fields such as computer science and engineering to other fields such as health services and communications.[5] He[6] et al and Chang[7] et al extended social cooperation networks to the field of traditional Chinese medicine (TCM) based on a theory that different herbs work together in a complementary manner to treat a disease. Their research also presented a traditional Chinese herbal prescription formulation network (TCHPFN).

In China, TCM herbal formulas have been widely used to treat many diseases. Zheng classification and treatment (ZCT, *bian zheng lun zhi,* in Chinese) is a unique feature of TCM, and use of TCM herbal formulas must follow ZCT. Many studies have been conducted to illustrate that treatment based on Zheng classification can improve specificity and efficiency in both TCM and Western medicine.[8–10] However, Zheng classification depends mostly on the observations, knowledge, and clinical experience of TCM practitioners.[11] Zheng diagnosis always varies from practitioners, leading to different formulas, although with equivalent efficacy. There might be underlying consensuses and treatment principles among TCM practitioners to guide their treatments. Therefore, we proposed a community detection-based approach to uncover the underlying consensuses and treatment principles, and tested the approach by applying it to the Zheng classification and treatment of diabetic nephropathy (DNZCT) data. We present the DNZCT network as a social cooperation network of different Zhengs and herbs, and analyze the potential communities in the DNZCT.

Materials and methods

Search strategy

Databases searched include the China National Knowledge Infrastructure Database (CNKI), the Chongqing VIP Chinese Science and Technology Periodical Database (VIP), and Wan Fang Data from their inception to September 31, 2014. The following search terms were used individually or combined: "DN", "diabetic nephropathy", "*xiao ke* (in Chinese)", "*xiao ke shen bing* (in Chinese)", "traditional Chinese medicine", "Chinese herbal medicine", "herb", "Zheng", "*bian zheng lun zhi*in Chinese".

Inclusion criteria

We included those articles that focused on the Zheng classification and treatment of DN and that contained specific information on ZCT and herbs.

Exclusion criteria

We excluded: (1) reviews without Zheng and herb information; (2) articles on animal or cell experiments; (3) meta-analyses and articles on safety and effect evaluation; (4) studies on data mining or bibliometrics; (5) news; and (6) studies with unclear data.

Article selection proceeded as shown in Fig. 1.

Data extraction

Data were extracted using a predesigned data extraction table. The extracted data included Zheng classification, herbs, and ZCT details.

Quality control

Two authors conducted the literature search (TX, XQY), study selection (TX, XQY), data extraction (TX, XQY), and data processing (TX, XQY) independently. Disagreements were resolved by discussion and reaching consensus through third-party (MQG) intervention.

Two-mode network

In TCM practice, the practitioner examines the patient through four diagnostic methods (looking, listening and smelling, asking, and touching) and also uses certain biochemical tests results to reach a Zheng diagnosis. Then the practitioner prescribes a customized TCM herbal formula comprising several herbs to heal the patient. Each herb is prescribed to treat the Zheng. In graph theory, a two-mode network is also called a bipartite graph,[12] in which the nodes are divided into two disjoint sets, U and V. Each edge connects a node in U to a node in V. In our study, the relationships between herbs and Zhengs can be modeled as a two-mode network. The herb node is one mode, and the Zheng node is the other. Each treating relationship between herb and a Zheng is an edge. Fig. 2 shows the relationships in this two-mode network. Edges only exist between herb nodes and Zheng nodes, and there are no edges within the mode.

We classified the data we collected into a node list and an edge list. The node list comprised two sets of nodes; one was a list of all Zhengs, and the other was a list of all herbs. The edge list was a list of edges that connected all Zhengs and herbs. The two-mode network was therefore constructed by the node list and the edge list.

Community detection

Our task was to analyze a two-mode network as described above. Many researchers have used the projection method to transform a two-mode network into a one-mode

network. This projection-based transition may lose some properties of the network structure.[13] In our study, we used a spectral co-clustering algorithm that extended spectral analysis to a two-mode network. We denoted a two-mode network $G_{n,m}$ with n rows and m columns. Mode u had n entities while mode t had m entities. Its adjacency matrix is as follows:

$$A_{n,m}=\begin{bmatrix} u_1t_1 & u_1t_2 & \cdots & u_1t_{m-1} & u_1t_m \\ u_2t_1 & u_2t_2 & \cdots & u_2t_{m-1} & u_2t_m \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ u_nt_1 & u_nt_2 & \cdots & u_nt_{m-1} & u_nt_m \end{bmatrix} \quad (1)$$

where

$$u_nt_m=\begin{cases} 1 & \text{if an edge connected } u_n \text{ and } t_m \\ 0 & \text{if no edge connected } u_n \text{ and } t_m \end{cases} \quad (2)$$

For mode u, its degree matrix was:

$$D_u=\begin{bmatrix} Deg(u_1) & 0 & \cdots & 0 & 0 \\ 0 & Deg(u_2) & \cdots & 0 & 0 \\ 0 & 0 & \cdots & Deg(u_{n-1}) & 0 \\ 0 & 0 & \cdots & 0 & Deg(u_n) \end{bmatrix} \quad (3)$$

For mode t, its degree matrix was:

$$D_t=\begin{bmatrix} Deg(t_1) & 0 & \cdots & 0 & 0 \\ 0 & Deg(t_2) & \cdots & 0 & 0 \\ 0 & 0 & \cdots & Deg(t_{m-1}) & 0 \\ 0 & 0 & \cdots & 0 & Deg(t_m) \end{bmatrix} \quad (4)$$

Hence, we could normalize the adjacency matrix as:

$$\tilde{A}=D_u^{-1/2}AD_t^{-1/2} \quad (5)$$

The matrix $\tilde{A}$ was then decomposed by the singular value decomposition (SVD) method, obtaining:

$$\tilde{A}=U\sum V^T \quad (6)$$

where $\sum$ was a diagonal matrix that consisted of singular values of matrix $\tilde{A}$. If the expected number of communities in the two-mode network was k, then let $S^{(u)}=U_{1:k}$, $S^{(t)}=V_{1:k}$. The community detection results could be obtained by applying the k-means clustering method to the joint soft community indicator Z, which consisted of $S^{(u)}$ and $S^{(t)}$:

$$Z=\begin{bmatrix} D_u^{-1/2} & S^{(u)} \\ D_t^{-1/2} & S^{(t)} \end{bmatrix} \quad (7)$$

Evaluation of community

As the number and sizes of potential communities were unknown in advance, there had to be a measure for the possible results of community detection. For one-mode networks, modularity Q has been widely accepted as a measure for communities.[14] Modularity Q was introduced by Newman and Girvan as follows[15]:

$$Q=\frac{1}{2m}\sum_{i,j}(A_{ij}-P_{ij})\delta(v_i,v_j) \quad (8)$$

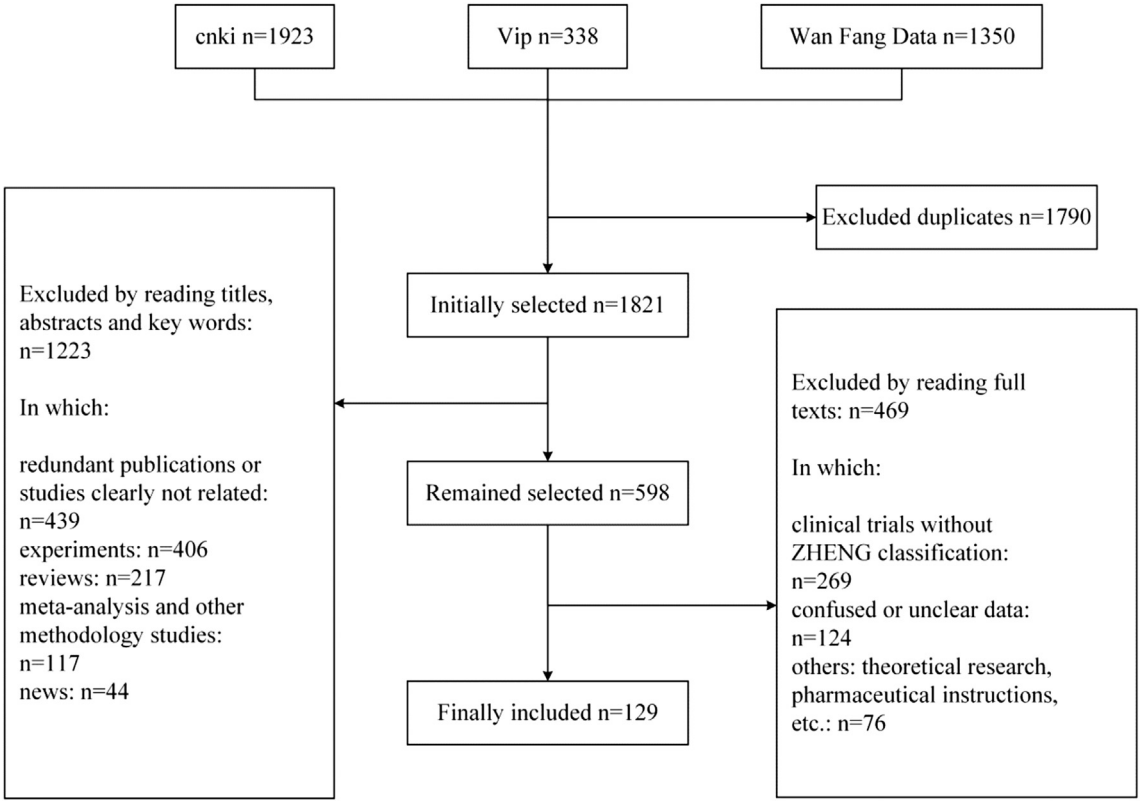

Figure 1 Flow diagram of study selection.

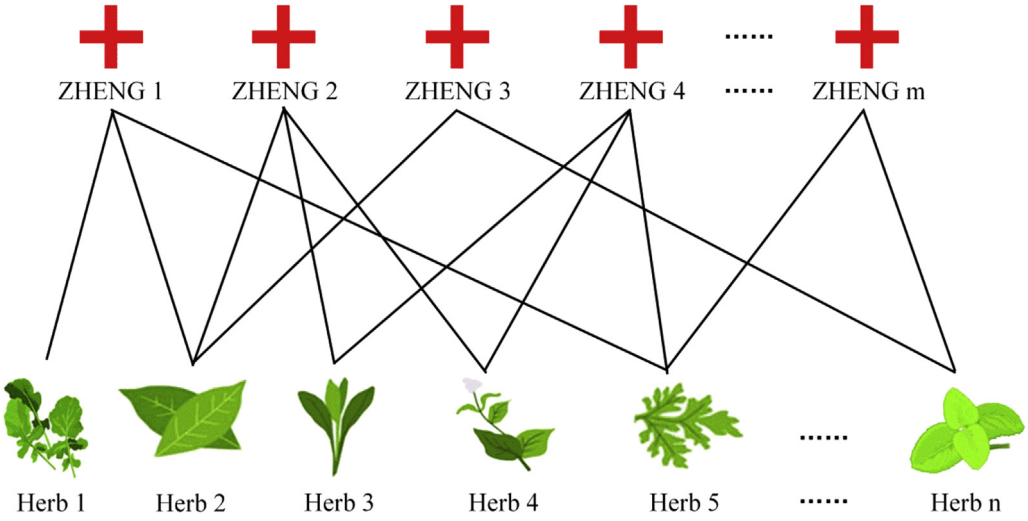

Figure 2 A simple illustration of a two-mode network of Zhengs and herbs.

where $P_{ij}=d_i d_j/2m$ is the expectation of edges between node v_i and v_j, and d_i and d_j are the degrees of node v_i and v_j, respectively. $\delta(v_i, v_j)$ was defined as:

$$\delta(v_i, v_j)=\begin{cases}1 & v_i \text{ and } v_j \text{ are in the same community}\\ 0 & \text{others}\end{cases} \tag{9}$$

This index provides a quantitative measurement to decide the best division of networks. The larger the value of Q, the more accurate the network partitioning. For the two-mode network in our study, we applied the bipartite modularity, which was more appropriate and proposed by Barber as an extension of Newman's work.[16] The bipartite modularity was introduced as:

$$Q=\frac{1}{m}\sum_{i=1}^{p}\sum_{j=1}^{q}(A_{ij}-P_{ij})\delta(u_i, v_j) \tag{10}$$

where $P_{ij}=d_i d_j/m$ is the expectation of the possibility of connection between node u_i, and v_j, d_i and d_j are the degrees of node u_i and v_j, respectively. $\delta(u_i, v_j)$ was defined as:

$$\delta(u_i, v_j)=\begin{cases}1 & u_i \text{ and } v_j \text{ are in the same community}\\ 0 & \text{others}\end{cases} \tag{11}$$

Therefore we sought to find a partition with a higher bipartite modularity Q without a pre-determined k value.

Quantitative definition of community

In topology, a community is a group of nodes that interact with each other more frequently than with those outside of the group. In practical applications, we needed additional non-topological information on the nature of the network to understand which of the network groups had real significance.[17] Radicchi[17] et al gave a precise quantitative definition, and if the detected group did not meet the criterion, the group isolated from the network was not a community. The definition was described as follows.

For the definition of community in a strong sense, the subgraph V is a community in a strong sense if

$$k_i^{in}(V) > k_i^{out}(V), \quad \forall i \in V. \tag{12}$$

In a strong community, each node has more connections within the community than with the rest of the graph. For the definition of community in a weak sense, the subgraph V is a community in a weak sense if

$$\sum_{i\in V} k_i^{in}(V) > \sum_{i\in V} k_i^{out}(V). \tag{13}$$

In a weak community, the sum of all degrees within V is larger than the sum of all degrees within the rest of the network.

Inspired by the comparative definition of one-mode networks, Poon[18] et al proposed a comparative definition of community in bipartite networks that we used in our study.

For the definition of community in a strong sense, the subgraph V is a community in a strong sense if

$$\sum_{j\in V, a\in\omega} A_{ia}\times A_{ja}^T > \sum_{j\in G-V, a\in\omega} A_{ia}\times A_{ja}^T, \quad \forall i \in V. \tag{14}$$

For the definition of community in a weak sense, the subgraph V is a community in a weak sense if

$$\sum_{i\in V}\sum_{j\in V, a\in\omega} A_{ia}\times A_{ja}^T > \sum_{i\in V}\sum_{j\in G-V, a\in\omega} A_{ia}\times A_{ja}^T. \tag{15}$$

where ω is the set of nodes different from node i and j, and node a is an element in it. $A_{ia}\times A_{ja}^T$ represents the number of nodes i and j sharing node a.

Proposed approach

We started by classifying the collected DN treatment data into a node list and an edge list. A two-mode network DNZCT was constructed by the node list and edge list. Then a spectral co-clustering algorithm was applied to the DNZCT

to identify potential communities. The bipartite modularity Q and quantitative definition were used to evaluate the best Zheng—herb community results. Fig. 3 depicts the overall approach.

Results

Overview of the DNZCT network

From the processed data, we created a node list of 201 nodes and an edge list of 743 edges. We constructed a DNZCT network with 64 Zheng nodes, 137 herb nodes, and 743 edges. Fig. 4 provides an overview of the DNZCT network. Nodes denote Zhengs and herbs (red for Zhengs, blue for herbs), whereas edges denote treating relationships between Zheng nodes and herb nodes. We represented the frequency of Zhengs or herbs recorded in included articles as the size of a node; for example, a more frequently used herb in articles could be visualized as a herb node that is larger as well as having a larger label word. For clarity of display, each herb and Zheng was assigned a number, and is represented by that number in the following figures. The numbers are given in Appendix A and B. H is short for herb, and Z is short for ZHENG.

In the center of the DNZCT network were several significantly larger nodes, indicating their high frequency in clinical practice. The top 11 high-frequency herbs are visualized in Fig. 5.

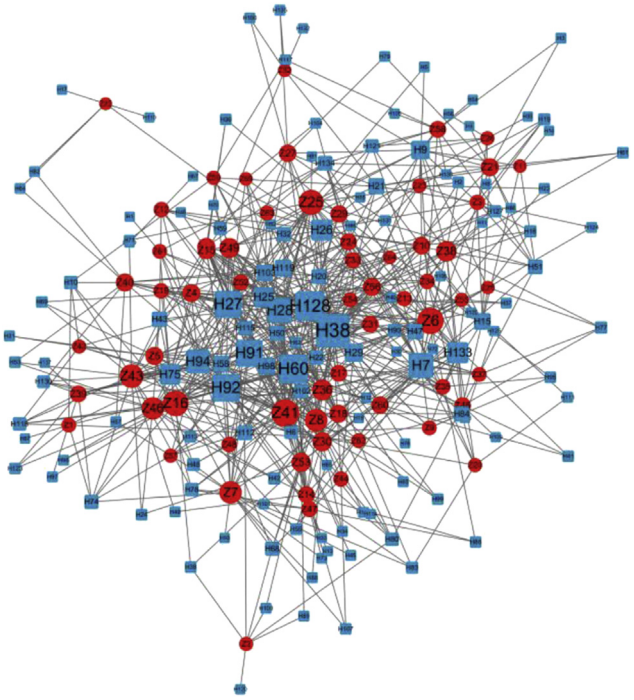

Figure 4 Overview network of the DNZCT.

Detected communities

We finally identified six communities of varying sizes after community detection and evaluation (Fig. 6).

Community 1

For clarity, each community is depicted individually in the following figures. Community 1 (Fig. 7) comprised 60 nodes and 138 edges. Zheng nodes included qi deficiency and blood stasis (Zheng number and Chinese—English translations are given in Appendix B), qi stagnation and blood stasis, and blood stasis obstructing the collaterals. All Zheng nodes shared the "blood stasis" topic. Herb nodes in community 1 included danshen root (*Salvia miltiorrhiza Bge.*) (herb number and translation are given in Appendix A), Chinese angelica [*Angelica Sinensis (Oliv.) Diele*], and peach seed [*Prunus persica (L.)Batsch*]. Most of the herbs have the effect of invigorating blood circulation, promoting the circulation of qi, and dredging collaterals.

Community 2

Community 2 (Fig. 8) comprised 24 nodes and 54 edges. Zheng nodes included qi and yin deficiency (early stage, middle stage, and stage unknown), yin deficiency and dryness-heat (stage unknown), and yin deficiency in the lung and kidney (early stage). Early-stage Zhengs accounted for the most. All the Zheng nodes shared the topic of "qi deficiency" and "yin deficiency". Herb nodes in community 2 included coastal glehnia root (*Glehnia littoralis Fr. Schmidt ex Miq.*), Chinese wolfberry root/bark (*Lycium chinense Mill.*), and dwarf lilyturf tuber [*Ophiopogon japonicas(L.f.)Ker-Gawl.*]. All of the herbs are cold and cool, attributed to the lung, stomach and kidney meridians, and function to replenish yin, clear heat, reinforce qi, and moisten dryness.

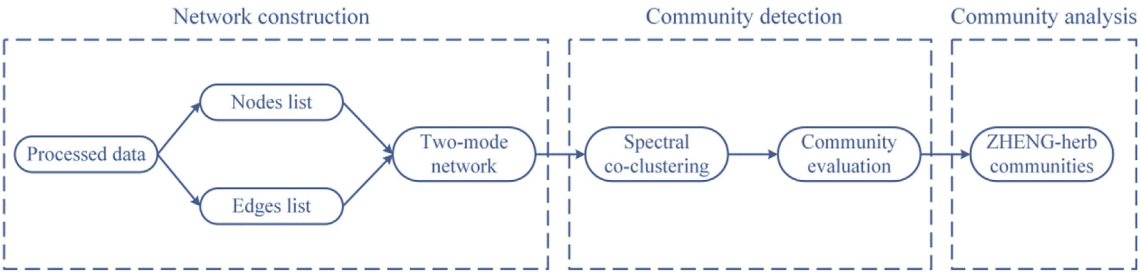

Figure 3 Overall approach.

Figure 5 Word cloud of top 11 high-frequency herbs. Note: font size is proportional to the frequency of herbs.

Community 3

Community 3 (Fig. 9) comprised 18 nodes and 32 edges. Zheng nodes in community 3 included blockage and repulsion due to constipation, excessive dampness due to deficiency in the spleen, and internal retention of dampness-heat. Characteristics of the pathogenesis of these Zhengs were pathological substances retention and disordered qi activity. Herb nodes in community 3 included pinellia tuber [*Pinellia ternate(Thunb.)Breit.*], atractylodes rhizome [*Atractylodes lancea(Thunb.)DC.*], and dried tangerine peel (*Citrus reticulate Blanco*). These herbs are either aromatic or warm and dry, and show efficacy in resolving dampness, removing turbid substances, and restoring qi activity.

Community 4

Community 4 is shown in Fig. 10. The Zheng node in community 4 was stirring of internal wind due to dampness-heat, and corresponding herb nodes were Cicada Slough (*Cryptotympana pustulata Fabricius*), Stiff Silkworm (*Bombyx mori L.*), Scorpion (*Buthus martensii Karsch*), and Centipede (*Scolopendra subspinipes mutilans L. Koch*). They are all insects and believed to have the medicinal effect of expelling wind, dredging deep collaterals, and activating local blood circulation to relief pain.

Community 5

Community 5 is shown in Fig. 11. The Zheng node in community 5 was blockage and repulsion due to dampness-heat (late stage). Herbs used to treat this Zheng were perilla stem [*Perilla frutescens(L.)Britt*], immature orange fruit (*Citrus aurantium L.*), bamboo shavings (*Bambusa tuldoides Munro*), which are with the efficacy of bringing down adverse flow of qi and clearing heat to relieve vomiting.

Community 6

Community 6 (Fig. 12) comprised five nodes and four edges. The Zheng node was dysfunction in essence storage. Herbs

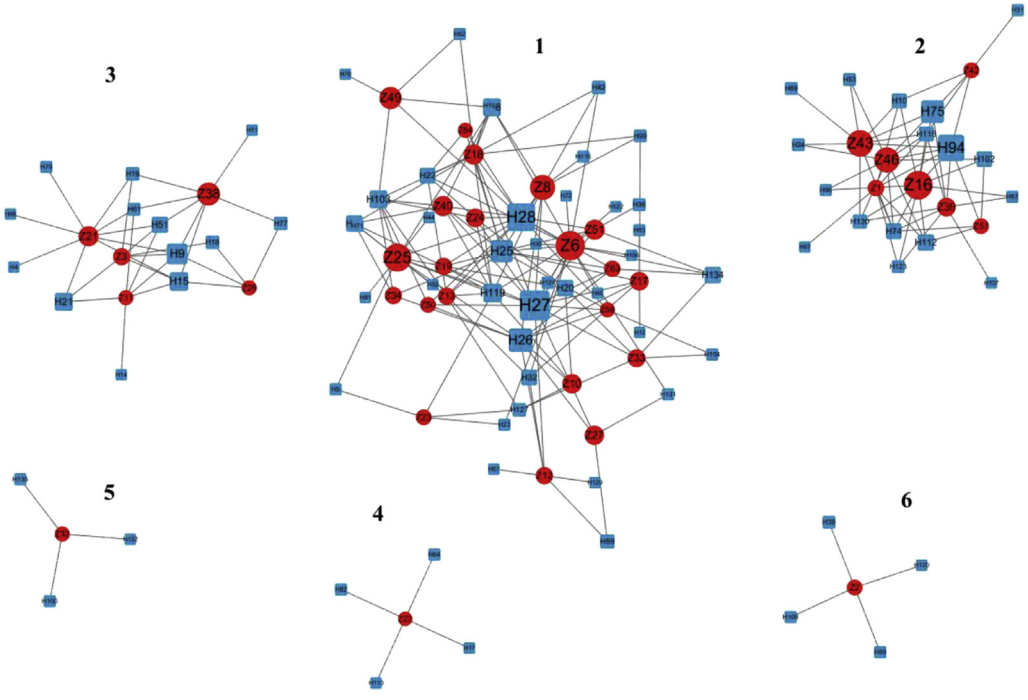

Figure 6 Six detected communities in the DNZCT.

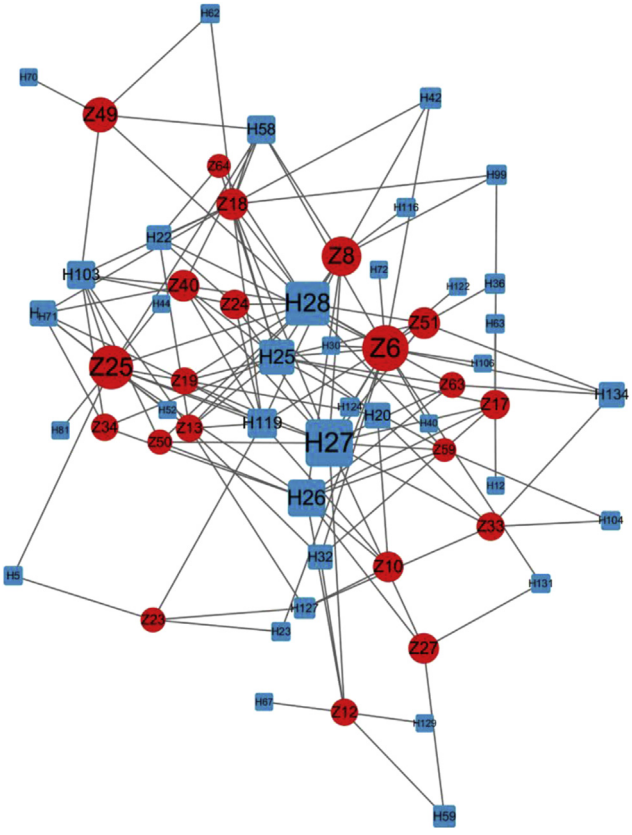

Figure 7 Community 1.

used were palmleaf raspberry fruit (*Rubus chingii Hu*), mantis egg-case (*Tenodera sinensis Saussure*), sharpleaf glangal fruit (*Alpnia oxyphylla Miq.*), and smoked plum

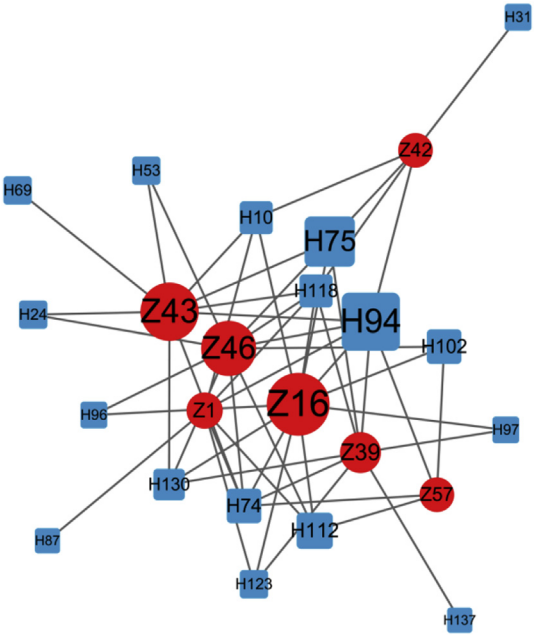

Figure 8 Community 2.

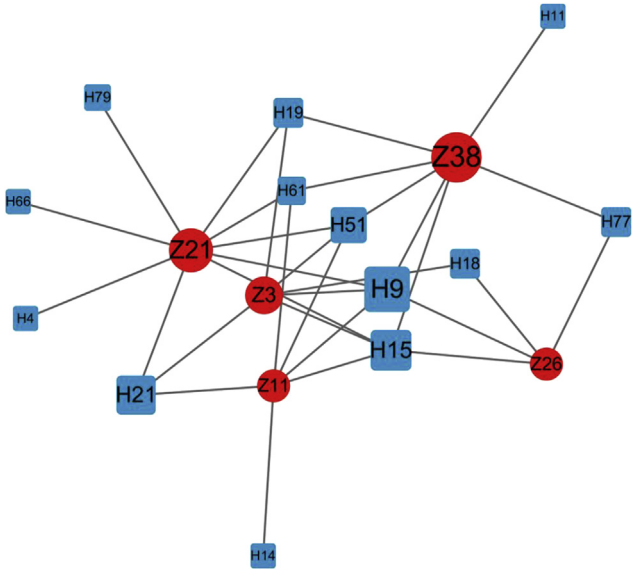

Figure 9 Community 3.

[*Prunus mume (Sieb.) et Zucc*]. They tonify the kidney and secure and replenish essences.

Discussion

We first constructed a DNZCT network with herb nodes, Zheng nodes, and edges denoting the corresponding treating relationships between Zhengs and herbs. In previous work,[6,7] TCHPFN network was constructed with a herb node connecting with another herb node from the same herbal formula to present which herbs work together to treat a diseases. This one-mode network is concise to understand and easy to analyze. However, we cannot get more

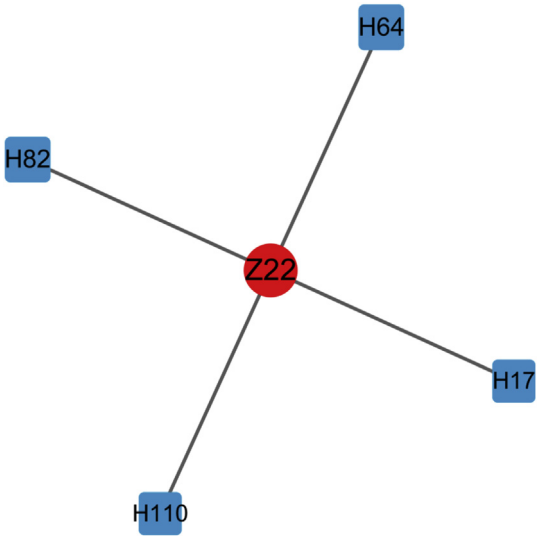

Figure 10 Community 4.

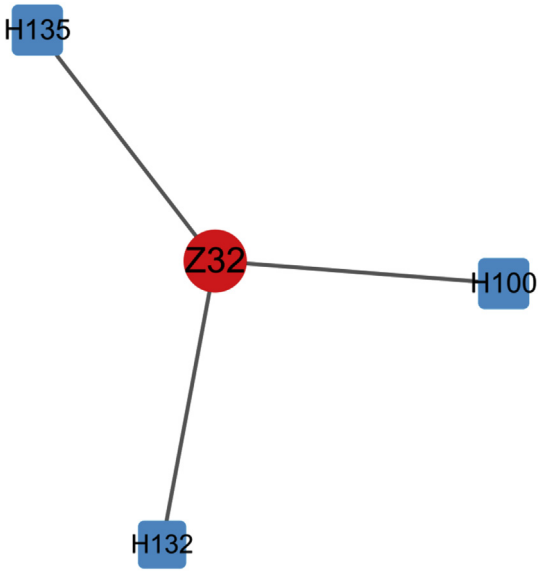

Figure 11 Community 5.

information regarding treatment from it. In DNZCT, all Zhengs, herbs, and corresponding treating relationships came from scholarly articles published by different TCM practitioners, therefore the DNZCT network could be regarded as a social cooperation network in which different Zhengs and herbs are connected with each other to exemplify how TCM practitioners treat DN. And the DNZCT network could be used to represent views and perceptions of TCM practitioners regarding the ZCT of DN.

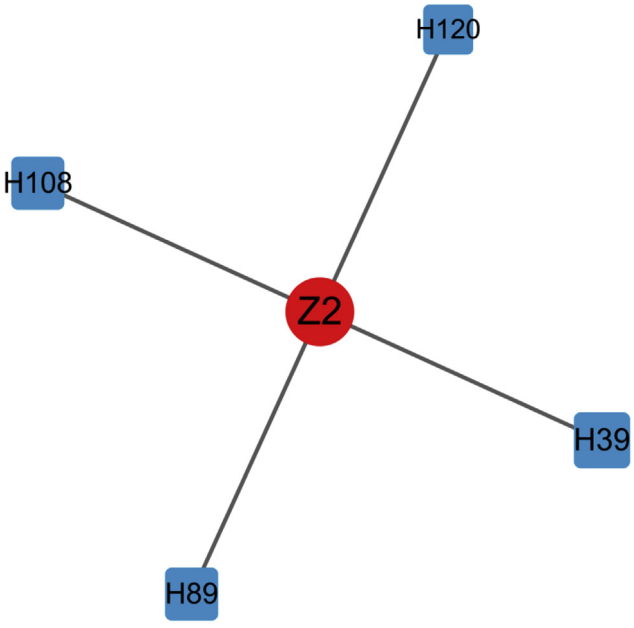

Figure 12 Community 6.

Among the top 11 high-frequency herbs in the DNZCT, we found six herbs—prepared rehmannia root (*Rehmannia glutinosa Libosch*), asiatic cornelian cherry fruit (*Cornus officinalis Sieb.et Zucc.*), common yam rhizome (*Dioscorea opposite Thunb.*), tree peony bark (*Paeonia suffruticosa Andr.*), Indian bread [*Poria cocos (Schw.) Wolf*], oriental waterplantain rhizome [*Alisma orientalis (Sam.)Juzep.*]—that are the composition of the famous formula *Liu Wei Di Huang Wan*, which is commonly used in TCM to treat patients with diabetes.[19] This suggests that there might be a consensus of using *Liu Wei Di Huang Wan* as a basic prescription to treat DN among TCM practitioners.

As mentioned previously, a community is a group of nodes that interact with each other more frequently than with those outside of the group; in other words, edges within a community are denser than those outside of it.[20] Edges in the DNZCT represented treating relationships prescribed by practitioners; therefore, communities could be considered as representing consensuses among different practitioners for the treatment of DN.

Previous research has shown that communities in networks with semantics, in which nodes and edges represent attributes or semantics, can be evaluated by checking for consistency with the semantics.[1] We found that the identified communities in the DNZCT network all showed their own features in semantics and medicine. For example, two detected communities, community 1 and community 2, contained a topic in common. Nodes and edges in community 1 shared the topic of "blood stasis", while nodes and edges in community 2 shared the topic of "qi deficiency and yin deficiency". This result justifies applicability of the bicluster algorithm for community detection in a two-mode network from the perspective of community evaluation; moreover, each community's shared topic, represented by Zhengs and corresponding treating herbs, in turn represented treatment principles and experience of DN treatment from various practitioners. Each community in the DNZCT indicated a different category of Zhengs and gave corresponding treatment principles and herbs. For instance, community 3 indicated a consensus on Zheng diagnoses regarding dampness retention and disordered qi activity, with the corresponding treatment principle of resolving dampness, removing turbid substances, and restoring qi activity.

Large herb nodes indicated their high frequency of use in clinical practice, and large Zheng nodes in the network indicated commonly diagnosed Zhengs among DN patients. By contrast, small nodes indicated infrequently used herbs and seldom diagnosed Zhengs. We also found that large nodes were usually clustered into large communities. Community 1, for example, was relatively large and had comparatively large nodes. It indicated "blood stasis"—one of the most common Zhengs in TCM clinical practice for treating DN, which is often investigated by TCM practitioners with regard to its removal. In fact, in TCM theory "blood stasis" is a vital pathologic factor in the development of DN.[21] Therefore, large communities might tell us that the majority of practitioners are likely to have similar

points of view or consensuses on common Zheng diagnoses and herb prescriptions. We also found that small nodes tended to be clustered into small communities. Nodes in communities 4, 5, and 6 were smaller and fewer than in others, and there was only one small Zheng node and three or four herb nodes in each community. This indicated that Zhengs such as stirring of internal wind, blockage and repulsion due to dampness-heat, and dysfunction in essence storage were not as common as they were in large communities, with herbs also not as frequently used as they were in large communities. Therefore, small communities might help us find unusual Zhengs and herbs and elucidate the experience of a minority of practitioners. However, another explanation regarding the meaning of small communities is that because Zhengs of stirring of internal wind, blockage and repulsion, and dysfunction in essence storage were all in the late stage of DN, those Zhengs are not usually treated by TCM herbal formulas because dialysis and other replacement treatments are invariably needed as these patients' conditions deteriorate.

Compared with communities 1, 2, and 3, communities 4, 5, and 6 were smaller, and Zhengs in those communities were usually late-stage Zhengs with smaller nodes. In large communities such as community 1, early- and middle-stage Zhengs were represented the most. The size differences of communities and nodes indicate that DN treatment in TCM is often aimed at early and middle stages. This coincides with the clinical understanding that treatment of early-stage DN can effectively prevent disease progression, thus improving quality of life and reducing mortality.[21,22]

Our study has a few limitations. Because all data came from published articles, publication bias cannot be avoided. Also, overlapping communities may exist in this network, whereas the community detection algorithm we used could only identify non-overlapping communities.

Conclusion

The community detection-based approach proposed in our study has shown good performance and promising results. The results suggest that this approach is useful and feasible for uncovering consensuses and treatment principles of DN treatment. It could be expanded and used to address other problems in TCM.

Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgments

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Appendix

Appendix A: Herb number and translation

Number	Herb	Translation
	Chinese/Chinese *pinyin*	Latin/English
H1	阿胶 [Ejiao]	Donkeyhide Glue (*Equus asinus L.*)
H2	巴戟天 [Bajitian]	Morinda Root (*Morinda officinalis How*)
H3	白豆蔻 [Baidoukou]	Round Cardamon Fruit (*Amomum kravanh Pierre ex Gagnep*)
H4	白花蛇舌草 [Baihuasheshecao]	Spreading Hedyotis Herb (*Oldenlandia diffusa (Willd.) Roxb.*)
H5	白茅根 [Baimaogen]	Lalang Grass Rhizoma (*Imperata cylindrical Beauv. Var. major (Nees) C. E. Hubb*)
H6	白芍 [Baishao]	White Peony Root (*Paeonia lactiflora Pall*)
H7	白术 [Baizhu]	Largehead Atractylodes Rhizome (*Atractylodes macrocephala Koidz*)
H8	败酱草 [Baijiangcao]	Dahurian Patrinia Herb (*Patrinia scabiosaefolia Fisch. Ex Link.*)
H9	半夏 [Banxia]	Pinellia Tuber (*Pinellia ternate(Thunb.)Breit.*)
H10	北沙参 [Beishashen]	Coastal Glehnia Root (*Glehnia littoralis Fr. Schmidt ex Miq.*)
H11	白扁豆 [Baibiandou]	White Hyacinth Bean (*Dolichos lablab L.*)
H12	鳖甲 [Biejia]	Turtle Carapace (*Trionyx sinensis Wiegmann*)
H13	补骨脂 [Buguzhi]	Malaytea Scurfpea Fruit (*Psoralea corylifolia L.*)
H14	蚕沙 [cansha]	silkworm excrement (*Bombyx mori Linnaeus*)
H15	苍术 [cangzhu]	Atractylodes Rhizome (*Atractylodes lancea(Thunb.) DC.*)
H16	柴胡 [Chaihu]	Chinese Thorowax Root (*Bupleurum chinense DC.*)
H17	蝉蜕 [chantui]	Cicada Slough (*Cryptotympana pustulata Fabricius*)
H18	石菖蒲 [shichangpu]	Grassleaf Sweetflag Rhizome (*Acorus tatarinowii Schott*)
H19	车前草 [Cheqiancao]	Plantain Herb (*Plantago asiatica L.*)
H20	车前子 [Cheqianzi]	Plantain Seed (*Plantago asiatica L.*)
H21	陈皮 [Chenpi]	Dried Tangerine Peel (*Citrus reticulate Blanco*)
H22	赤芍 [Chishao]	Red Peony Root (*Paeonia lactiflora Pall.*)
H23	赤小豆 [Chixiaodou]	Rice Bean (*Vigna umbeuata Ohwi et Ohashi*)
H24	川牛膝 [chuanniuxi]	Medicinal Cyathula Root (*Cyathula officinalis Kuan*)

(*continued*)

Number	Herb	Translation
	Chinese/Chinese *pinyin*	Latin/English
H25	川芎 [chuanxiong]	Szechwan Lovage Rhizome (*Ligusticum chuanxiong Hort.*)
H26	大黄 [Dahuang]	Rhubarb (*Rheum palmatum L.*)
H27	丹参 [danshen]	Danshen Root (*Salvia Miltiorrhiza Bge.*)
H28	当归 [danggui]	Chinese Angelica (*Angelica Sinensis (Oliv.) Diele*)
H29	党参 [Dangshen]	Tangshen (*Codonopsis pilosula (Franch.) Nannuf.*)
H30	倒扣草 [Daokoucao]	Common Achyranthes Herb (*Achyranthes aspera L.*)
H31	地骨皮 [digupi]	Chinese Wolfberry Root-bark (*Lycium chinense Mill.*)
H32	地龙 [Dilong]	Earthworm (*Pheretima aspergillum (E. Perrier)*)
H33	冬虫夏草 [Dongchongxiacao]	Chinese Caterpillar Fungus (*Cordyceps sinensis (Berk.) Sacc.*)
H34	杜仲 [Duzhong]	Eucommia Bark (*Eucommia ulmoides Oliv.*)
H35	煅牡蛎 [Duanmuli]	Calcined Oyster Shell (*Ostrea gigas Thunberg*)
H36	莪术 [Ezhu]	Zedoray Rhizome (*Curcuma phaeocaulis Val.*)
H37	防己 [Fangji]	Fourstamen Stephania Root (*Stephania terandra S. Moore*)
H38	茯苓 [fuling]	Indian Bread (*Poria cocos (Schw.) Wolf*)
H39	覆盆子 [fupenzi]	Palmleaf Raspberry Fruit (*Rubus chingii Hu*)
H40	甘草 [Gancao]	Liquorice Root (*Glycyrrhiza uralensis Fisch.*)
H41	干姜 [Ganjiang]	Zingiber/Dried Ginger (*Zingiber officinale Rosc*)
H42	葛根 [Gegen]	Kudzuvine Root (*Pueraria lobate (Willd.) Ohwi*)
H43	枸杞子 [gouqizi]	Barbary Wolfberry Fruit (*Lycium barbarum L.*)
H44	瓜蒌 [Gualou]	Snakegourd Fruit (*Trichosanthes kirilowii Maxim.*)
H45	龟板胶 [Guijia]	Tortoise Carapace and plastron (*Chinemys reevesii (Gray)*)
H46	鬼箭羽 [Guijianyu]	Winged Euonymus Twig (*Euonymusalatus (Thunb.) Sieb.*)
H47	桂枝 [Guizhi]	Cassia Twig (*Cinnamomum cassia Presl*)
H48	旱莲草 [Mohanlian]	Yerbadetajo Herb (*Eclipta prostrata*)
H49	何首乌 [Heshouwu]	Fleeceflower Root (*Polygonum multiflorum Thunb.*)
H50	红花 [honghua]	Saffloeer (*Carthamus tinctorius L.*)
H51	厚朴 [houpu]	Officinal Magnolia Bark (*Magnolia officinalis Rehd. Et Wils.*)
H52	葫芦瓢 [Hulupiao]	Bottle Gourd Peel (*Lagenaria siceraria (Molina) Standl.*)
H53	天花粉 [tianhuafen]	Snakegourd Root (*Trichosanthes kirilowii Maxim*)
H54	滑石 [Huashi]	Talcum ($Mg_3(Si_4O_{10})(OH)_2$)
H55	怀牛膝 [Niuxi]	Twotoothed Achyranthes Root (*Achyranthes bidentate Bl.*)
H56	槐花 [Huaihua]	Pagodatree Flower (*Sophora japonica L.*)
H57	黄柏 [Huangbai]	Chinese Cork-tree (*Phellodendron amurense Rupr.*)
H58	黄精 [Huangjing]	Solomonseal Rhizome (*Polygonatum kinganum Coll et Hemsl.*)
H59	黄连 [Huanglian]	Golden Thread (*Coptis chinensis Franch.*)
H60	黄芪 [Huangqi]	Milkvetch Root (*Astragalus membranaceus (Fisch) Bge.*)
H61	藿香 [huoxiang]	Cablin Patehouli Herb (*Pogostemon cablin (Blanco) Benth*)
H62	鸡血藤 [Jixueteng]	Suberect Spatholobus Stem (*Spatholobus suberectus Dunn*)
H63	积雪草 [Jixuecao]	Asiatic Pennywort Herb (*Centella asiatica (L.) Urban*)
H64	僵蚕 [jiangcan]	Stiff Silkworm (*Bombyx mori L.*)
H65	降香 [Jiangxiang]	Rosewood (*Dalbergia odorifera T. Chen*)
H66	金钱草 [Jinqiancao]	Christina Loosestrife (*Lysimachia christinae Hance*)
H67	金银花 [Jinyinhua]	Japanese Honeysuckle Flower (*Lonicera japonica Thunb.*)
H68	金樱子 [Jinyingzi]	Cherokee Rose Fruit (*Rosa laevigata Michx.*)
H69	菊花 [juhua]	Chrysanthemum Flower (*Chrysanthemum morifolium Ramat.*)
H70	橘红 [Juhong]	Red Tangerine Seed (*Citrus maxima (Burm.) Merr. cv. Tomentosa*)

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Number	Herb	Translation
	Chinese/Chinese *pinyin*	Latin/English
H71	决明子 [Juemingzi]	Cassia Seed (*Cassia obtusifolia L.*)
H72	灵芝 [Lingzhi]	Glossy Ganoderma (*Ganoderma lucidum Karst.*)
H73	鹿角胶 [Lujiao]	Deer Horn/Antler (*Colla cornus cervi*)
H74	麦冬 [maidong]	Dwarf Lilyturf Tuber (*Ophiopogon japonicas(L.f.) Ker-Gawl.*)
H75	牡丹皮 [mudanpi]	Tree Peony Bark (*Paeonia suffruticosa Andr.*)
H76	木瓜 [Mugua]	Common Floweringqince Fruit (*Chaenomeles speciosa (Sweet) Nakai*)
H77	木香 [muxiang]	Common Aucklandia Root (*Aucklandia lappa Decne*)
H78	女贞子 [Nvzhenzi]	Glossy Privet Fruit (*Ligustrum lucidum Ait.*)
H79	佩兰 [peilan]	Fortune Eupatorium Herb (*Eupatorium fortunei Turcz.*)
H80	芡实 [Qianshi]	Gordon Euryale Seed (*Euryale ferox Salisb.*)
H81	茜草 [Qiancao]	Indian Madder Root (*Rubia cordifolia L.*)
H82	全蝎 [quanxie]	Scorpion (*Buthus martensii Karsch*)
H83	肉苁蓉 [Roucongrong]	Desertliving Cistanche (*Cistanche deserticola Y. C. Ma*)
H84	肉桂 [Rougui]	Cassia Bark (*Cinnamomum cassia Presl*)
H85	三棱 [Sanleng]	Common Burreed Tuber (*Sparganium stoloniferum Buch.*)
H86	三七 [sanqi]	Sanchi (*Panax notoginseng (Burk.) F. H. Chen*)
H87	桑白皮 [sangbaipi]	White Mulberry Root-bark (*Morus alba L.*)
H88	桑寄生 [Sangjisheng]	Chinese Taxillus Herb (*Taxillus chinensis (DC.) Danser*)
H89	桑螵蛸 [Sangpiaoxiao]	Mantis Egg-Case (*Tenodera sinensis Saussure*)
H90	砂仁 [Sharen]	Villous Amomum Fruit (*Amomum villosum Lour.*)
H91	山药 [shanyao]	Common Yam Rhizome (*Dioscorea opposite Thunb.*)
H92	山茱萸 [shanzhuyu]	Asiatic Cornelian Cherry Fruit (*Cornus officinalis Sieb.et Zucc.*)
H93	升麻 [Shengma]	Largetrifoliolious Bugbane Rhizome (*Cimicifuga heracleifolia Kom.*)
H94	生地 [shengdihuang]	Rehmannia Root (*Rehmannia glutinosa Libosch.*)
H95	生姜 [Shengjiang]	Fresh Ginger (*Zingiber officinale Rosc.*)
H96	石膏 [shigao]	Gypsum ($CaSO_4$)
H97	石斛 [shihu]	Dendrobium (*Dendrobium loddigesis Rolfe.*)
H98	熟地 [shudihuang]	Prepared Rehmannia Root (*Rhemannia glutinosa Libosch*)
H99	水蛭 [Shuizhi]	Leech (*Whitemania pigra Whitman*)
H100	苏梗 [sugeng]	Perilla Stem (*Perilla frutescens(L.)Britt*)
H101	苏木 [Sumu]	Sappan Wood (*Caesalpinia sappan L.*)
H102	太子参 [taizishen]	Heterophylly Falsestarwort Root (*Pseudostellaria heterophylla (Miq.) Pax ex Pax et Hoffm.*)
H103	桃仁 [taoren]	Peach Seed (*Prunus persica (L.) Batsch*)
H104	葶苈子 [Tinglizi]	Pepperweed Seed/ Tansymustard Seed (*Lepidium apetalum Willd.*)
H105	通草 [Tongcao]	Ricepaperplant Pith (*Tetrapanax papyriferus*)
H106	土茯苓 [Tufuling]	Glabrous Greenbrier Rhizome (*Smilax glabra Roxb.*)
H107	菟丝子 [Tusizi]	Dodder Seed (*Cuscuta chinensis Lam.*)
H108	乌梅 [Wumei]	Smoked Plum (*Prunus mume (Sieb.) et Zucc*)
H109	吴茱萸 [Wuzhuyu]	Medicinal Evodia Fruit (*Evodia rutaecarpa (Juss.) Benth.*)
H110	蜈蚣 [wugong]	Centipede (*Scolopendra subspinipes mutilans L. Koch*)
H111	五加皮 [Wujiapi]	Slenderstyle Acanthopanax Bark (*Acanthopanax gracilistylus W. W. Smith*)
H112	五味子 [wuweizi]	Chinese Magnoliavine Fruit (*Schisandra chinensis (Turcz.) Baill*)
H113	西洋参 [Xiyangshen]	American Ginseng (*Panax quinquefolium L.*)
H114	仙鹤草 [xianhecao]	Hairyvein Agrimonia Herb (*Agrimonia pilosa Ledeb.*)
H115	仙灵脾 [Xianlingpi]	Epimedium Herb (*Epimedium brevicornum Maxim.*)
H116	仙茅 [Xianmao]	Common Curculigo Rhizome (*Curculigo orchioides*)

(*continued*)

Number	Herb	Translation
	Chinese/Chinese *pinyin*	Latin/English
H117	杏仁 [Xingren]	Bitter Apricot Seed (*Amygdalus communis Vas.*)
H118	玄参 [xuanshen]	Figwort Root (*Scrophularia ningpoensis Hemsl.*)
H119	益母草 [Yimucao]	Motherword Herb (*Leonurus heterophyllus Houtt.*)
H120	益智仁 [Yizhiren]	Sharpleaf Glangal Fruit (*Alpnia oxyphylla Miq.*)
H121	薏苡仁 [Yiyiren]	Coix Seed (*Coix lacryma — jobi L. var. ma — yuen (Roman.) Stapf*)
H122	玉米须 [Yumixu]	Corn Stigma (*Zea mays L.*)
H123	玉竹 [yuzhu]	Fragrant Solomonseal Rhizome (*Polygonatum odoratum (mill.) Druce*)
H124	郁金 [Yujin]	Turmeric Root Tuber (*Curcuma wenyujin Y.H. Chen et C. Ling*)
H125	远志 [Yuanzhi]	Thinleaf Milkwort Root (*Polygala tenuifolia Willd.*)
H126	酸枣仁 [Suanaoren]	Spine Date Seed (*Ziziphus jujube Mill. Var. spinose (Bunge) Hu ex H. F. Chou*)
H127	泽兰 [Zelan]	Hirsute Shiny Bugleweed Herb (*Eupatorium japonicum Thunb.*)
H128	泽泻 [zexie]	Oroental Waterplantain Rhizome (*Alisma orientalis (Sam.) Juzep.*)
H129	榛花 [Zhenhua]	Hazel's Flower (*Corylus heterophylla Fisch. Ex Bess.*)
H130	知母 [zhimu]	Common Anemarrhena Rhizome (*Anemarrhena asphodeloides Bge.*)
H131	枳壳 [Zhiqiao]	Orange Fruit (*Citrus aurantium L.*)
H132	枳实 [zhishi]	Immature Orange Fruit (*Citrus aurantium L.*)
H133	制附片 [Zhifupian]	Prepared Common Monkshood Daughter Root (*Aconitum carmichaelii*)
H134	猪苓 [Zhuling]	Chuling (*Polyporus umbellatus*)
H135	竹茹 [zhuru]	Bamboo Shavings (*Bambusa tuldoides Munro*)
H136	竹叶 [Zhuye]	Lophatherum Herb (*Phyllostachys nigra (Lodd.) Munro var. henonis (Mitf.) Stapf ex Rendle*)
H137	紫苑 [Ziyuan]	Tatarian Aster Root (*Aster tataricus L. f.*)

Appendix B: ZHENG number and translation

Number	ZHENG	Translation
Z1	肺胃两虚	Deficiency in the lung and stomach
Z2	封藏失职	Dysfunction in essence storage
Z3	腑实关格	Block and repulsion due to constipation
Z4	肝肾气阴两虚，肾络瘀滞	*Qi* and *yin* deficiency of the liver and kidney, and blood stasis obstructing the kidney collaterals
Z5	肝肾阴虚	*Yin* deficiency of the liver and kidney
Z6	脾肾亏虚，浊瘀内停	Deficiency in the spleen and kidney, and internal retention of turbid substances and blood stasis
Z7	脾肾两虚	Deficiency in the spleen and kidney
Z8	脾肾两虚，肾络瘀阻	Deficiency in the spleen and kidney, and blood stasis obstructing the kidney collaterals
Z9	脾肾阳虚	*Yang* deficiency of the spleen and kidney
Z10	脾肾阳虚，浊毒内蕴	*Yang* deficiency of the spleen and kidney, and internal retention of turbid substances
Z11	脾虚湿困	Spleen being fettered by dampness
Z12	脾胰失调，毒损肾络	Dysfunction of spleen and pancreas, and poison damaging kidney collaterals
Z13	气虚血瘀	Blood stasis due to *qi* deficiency
Z14	气血两虚	Deficiency of both *qi* and blood
Z15	气血阴阳俱虚，肾络瘀结	Deficiency of *qi*, blood, *yin* and *yang*, and blood stasis obstructing the kidney collaterals
Z16	气阴两虚	Deficiency of both *qi* and *yin*
Z17	气阴两虚，瘀血阻络	Deficiency of both *qi* and *yin*, and blood stasis obstructing the collaterals
Z18	气滞血瘀	*Qi* stagnation with blood stasis
Z19	肾虚血瘀	Deficiency in the kidney with blood stasis
Z20	肾阳亏虚	Deficiency of kidney *yang*
Z21	湿热胶着	Internal retention of dampness-heat
Z22	湿热生风	Stirring of internal wind due to dampness-heat
Z23	水湿停聚	Internal retention of dampness
Z24	水瘀互结	Union of water and blood stasis
Z25	水湿痰浊夹瘀	Union of water, dampness, phlegm, and blood stasis

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(*continued*)

Number	ZHENG	Translation
Z26	晚期寒湿关格	Block and repulsion due to dampness-cold (late stage)
Z27	晚期脾肾亏虚，湿热内蕴	Deficiency in the spleen and kidney, and internal retention of dampness-heat (late stage)
Z28	晚期脾肾亏虚，瘀浊毒留	Deficiency in the spleen and kidney, and internal retention of turbid substances and blood stasis (late stage)
Z29	晚期脾肾阳虚，浊瘀阻络	*Yang* deficiency of the spleen and kidney, and turbid substances and blood stasis obstructing the collaterals (late stage)
Z30	晚期脾肾阴阳俱虚，痰湿瘀血内阻	*Yin* and *yang* deficiency of the spleen and kidney, and internal retention of phlegm, dampness, and blood stasis (late stage)
Z31	晚期脾肾阴阳两虚	*Yin* and *yang* deficiency of the spleen and kidney (late stage)
Z32	晚期湿热关格	Block and repulsion due to dampness-heat (late stage)
Z33	晚期心阳不足，瘀水内停	*Yang* deficiency of the heart, and internal retention of water and blood stasis (late stage)
Z34	晚期阳衰浊毒瘀阻	*Yang* deficiency and internal retention of turbid substances and blood stasis (late stage)
Z35	晚期阳虚水泛	Edema due to *yang* deficiency (late stage)
Z36	晚期阴阳俱虚	Deficiency of both *yin* and *yang* (late stage)
Z37	心脾两虚	Deficiency in the heart and spleen
Z38	阳虚水泛	Edema due to *yang* deficiency
Z39	阴虚燥热	Dryness-heat due to *yin* deficiency
Z40	阴虚血瘀	*Yin* deficiency with blood stasis
Z41	阴阳两虚	Deficiency of both *yin* and *yang*
Z42	早期肺肾阴虚	*Yin* deficiency of the lung and kidney (early stage)
Z43	早期肝肾阴虚	*Yin* deficiency of the liver and kidney (early stage)
Z44	中期脾肾气虚	*Qi* deficiency of the spleen and kidney (middle stage)
Z45	中期脾肾阳虚	*Yang* deficiency of the spleen and kidney (middle stage)
Z46	早期气阴两虚	Deficiency of both *qi* and *yin* (early stage)
Z47	早期气阴两虚，肾络瘀阻	Deficiency of both *qi* and *yin*, and blood stasis obstructing the kidney collaterals (early stage)
Z48	早期气阴两虚，肾虚不固	Deficiency of both *qi* and *yin*, and deficiency in the kidney (early stage)
Z49	早期气阴两虚，痰湿内蕴	Deficiency of both *qi* and *yin*, and internal retention of phlegm and dampness (early stage)
Z50	中期肺肾气虚，浊毒内留	*Qi* deficiency of the lung and kidney, and internal retention of turbid substances (middle stage)
Z51	中期脾肾两虚，水瘀互结	Deficiency in the spleen and kidney, and union of water and blood stasis (middle stage)
Z52	中期脾肾两虚，痰湿内蕴	Deficiency in the spleen and kidney, and internal retention of phlegm and dampness (middle stage)
Z53	中期脾肾阳虚，肾失封藏	*Yang* deficiency of the spleen and kidney, and dysfunction in essence storage (middle stage)
Z54	中期脾肾阳虚，水邪泛滥	*Yang* deficiency of the spleen and kidney, and excessive water retention (middle stage)
Z55	中期气虚水停	*Qi* deficiency with water retention (middle stage)
Z56	中期气血两虚，浊毒内留	Deficiency of both *qi* and blood, and internal retention of turbid substances (middle stage)
Z57	中期气阴两虚	Deficiency of both *qi* and *yin* (middle stage)
Z58	中期湿热水停	Internal retention of dampness-heat and water (middle stage)
Z59	中期心肾气虚，浊毒内留	*Qi* deficiency of the heart and kidney, and internal retention of turbid substances (middle stage)
Z60	中期阳虚水停	*Yang* deficiency and water retention (middle stage)
Z61	中期阴虚水停	*Yin* deficiency and water retention (middle stage)
Z62	中期阴阳两虚	Deficiency of both *yin* and *yang* (middle stage)
Z63	中期阴阳两虚，浊毒内留	Deficiency of both *yin* and *yang*, and internal retention of turbid substances (middle stage)
Z64	中期瘀血水停	Blood stasis and water retention (middle stage)

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