

# ***Medication rule of Professor Li Jun in the Treatment of Insomnia Based on Traditional Chinese Medicine Inheritance Auxiliary Platform System***

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**Abstract:** Based on the traditional Chinese Medicine inheritance auxiliary system software, the medical records of Professor Li Jun in the treatment of insomnia were sorted out, and the medication rules of Professor Li Jun in the treatment of insomnia were analyzed. Fifty cases of insomnia treated by Professor Li Jun, a famous TCM doctor in Shaanxi Province, were collected. Through the application of the traditional Chinese medicine inheritance auxiliary platform developed by China Academy of Chinese Medical Sciences, the author analyzed and excavated the medication rules of Professor Li Jun in the treatment of insomnia. Through the software analysis of their frequency, association and clustering, it was found that the top three drugs most frequently used in prescriptions were Fu Shen, Cicada decidua and pueraria root. The top three drug combinations were "Pueraria root, Fu Shen", "Cicada decidua, Fu Shen", "Pueraria root, Cicada decidua". Sixteen core drug combinations and eight new prescriptions were found. Professor Li Jun believes that insomnia is mainly caused by the deficiency of heart and spleen, shyness of heart and spleen, Yin deficiency and fire. The empirical evidence of insomnia is mostly caused by burning heart, liver depression, phlegm and heat internal disturbance, caused by restlessness; And insomnia long illness can be manifested as empty and actual hold clip concurrently, or be caused by stasis. According to the theory of "homology of phlegm and blood stasis", the method of "treating phlegm and blood stasis together, dispelling wind and calming the mind" is often used in the treatment.

## 1. Introduction

Professor Li Jun, the famous professor of traditional Chinese Medicine, chief physician, second-level professor, national famous veteran traditional Chinese medicine, famous traditional Chinese medicine of Shaanxi Province, "New century 35 talent project" talent of Shaanxi Province, postgraduate tutor, national veteran traditional Chinese medicine expert academic experience inheritance guidance teacher. He has been engaged in clinical practice, teaching and scientific research of cardiovascular and cerebrovascular diseases for more than 40 years, with abundant knowledge and experience. Insomnia is a common clinical sleep disorder, sleep time, sleep quality often can not be satisfied for a kind of disease [1]. With environmental pollution, social development and the change of human disease spectrum, the incidence of insomnia gradually increases [2]. Long-term insomnia can bring serious adverse effects to people's normal life and work, and even cause serious accidents [3]. The treatment of insomnia in western medicine is mainly symptomatic treatment, but it is easy to have problems such as unsatisfactory long-term efficacy, easy to form drug dependence and the rebound of drug withdrawal symptoms, which affect its clinical application. Therefore, TCM syndrome differentiation and treatment has great advantages [4]. In this study, 50 cases of insomnia treated by Professor Li Jun, a famous traditional Chinese medicine doctor in Shaanxi Province, were collected. Through the analysis and mining of the traditional Chinese medicine inheritance auxiliary platform, the internal rules of the treatment of insomnia were obtained, and new prescriptions were explored.

## 2. Clinical Data and Research Methods

### 2.1. Clinical Rata Collection

#### 2.1.1. Case Source

The prescriptions were derived from the data of insomnia patients treated in Professor Li Jun's outpatient clinic from 2015 to 2016. The main symptoms of insomnia in the Chinese Guidelines for the Diagnosis and treatment of Insomnia were used as the criteria. A total of 50 prescriptions for insomnia were screened for analysis.

#### 2.1.2. Diagnostic Criteria

The diagnosis of TCM is based on the efficacy criteria for the diagnosis of TCM diseases (Trial Edition of the People's Republic of China). Patients with mild illness have difficulty falling asleep or wake up easily after sleep, and it is difficult to fall asleep after waking up, and patients with more severe illness cannot sleep all night. Often accompanied by headache, dizziness, palpitations, forgetfulness, many dreams and other diseases. No abnormalities were found by the various system and laboratory tests [5].

Western medicine diagnosis was based on the diagnostic criteria of the Chinese Guidelines for the Diagnosis and Treatment of Insomnia (2017). Insomnia is a sleep disorder characterized by frequent and persistent difficulty in falling asleep and/or difficulty in maintaining sleep and causing an unsatisfactory sleep sensation [6].

## 2.2. Data Research Software

The software of "Traditional Chinese Medicine Inheritance Assistance System (V2.5)" was used. This software was provided by the Institute of Chinese Materia Medica, China Academy of Chinese

Medical Sciences. Through the function of "prescription analysis" in the "Data analysis" section of the "Traditional Chinese Medicine Inheritance Assistance System (V2.5)" software, the rules of medication and new prescription were excavated and analyzed.

### **2.3. Record Entry and Check**

The selected prescriptions were entered into the "Traditional Chinese Medicine Inheritance Assistance System (V2.5)" by two data entry staff. After the data entry was completed, the data were checked by the two data clerks to ensure the accuracy of the data.

### **2.4. Data Analysis**

#### **2.4.1. Extracting Data Sources**

In this software, the name of the disease "insomnia" was filled in the item of "western medicine diseases", and all the prescriptions for treating insomnia in the program were extracted through this function.

#### **2.4.2. Frequency Statistical Analysis**

After entering the "data analysis" interface, select the "frequency statistics" function of the software, and arrange the use frequency of each Chinese medicine in the treatment of insomnia from large to small in order to form the "frequency statistics" results and then export them.

#### **2.4.3. Analysis of Traditional Chinese Medicine and Prescription Composition Rules**

In the "frequency statistics", the "number of support degree" was set to 30, and the "confidence degree" was set to 0.9. According to the frequency of the combination of traditional Chinese medicine, the combination was arranged from large to small. Click the "Rule Analysis" option in the program to automatically analyze its internal rules.

#### **2.4.4. Search for New Prescriptions**

The cluster analysis method (the core algorithm includes the improved mutual information method and the complex system entropy clustering method) is used to find new methods. First, set the appropriate degree of correlation and penalty, and then click the "Extract combination" key. The program will automatically screen out new prescriptions (its basic algorithm is unsupervised entropy level clustering) and form a network association graph.

## **3. Results**

### **3.1. Statistical Results of Medication Frequency**

The frequency of drugs in Professor Li Jun's 50 prescriptions for insomnia was analyzed. There were 18 Chinese herbs used more than 20 times, among which the top three were *Poria cocos*, *Cicada slough* and *Radix pueraria*. (Table 1)

Table 1. Statistical Table of Medication Frequency ( $\geq 20$  times)

Sequence	Name of Chinese medicine	Frequency	Sequence	Name of Chinese medicine	Frequency
1	Poria cocos	45	10	Peach kernel	30
2	Cicada slough	44	11	Ginger processed pinellia	29
3	Radix pueraria	44	12	Rehmannia glutinosa	28
4	Gastrodia elata	38	13	Moutan cortex	27
5	Chuanxiong rhizoma	36	14	Turmeric	27
6	Paeoniae radix rubra	34	15	Arisaema cum bile	25
7	Carthamus tinctorius	32	16	Gardenia jasminoides	23
8	Pericarpium citri reticulatae	32	17	Acori tatarinowii rhizoma	20
9	Angelica sinensis	31	18	Salvia miltiorrhiza	20

### 3.2. Research Results of Prescription Rules

The program was ordered according to the frequency of drug combination from high to low, and the top three were "Radix pueraria, Poria cocos", "Cicada slough, Poria cocos", "Radix pueraria, Cicada slough" (Table 2). The association rules of the resulting traditional Chinese medicine combination were analyzed. (Table 3)

Table 2. The combination of traditional Chinese medicine used ( $\geq 30$  times)

Sequence	Traditional Chinese medicine combination	Frequency	Sequence	Traditional Chinese medicine combination	Frequency
1	Radix pueraria, Poria cocos	39	12	Carthamus tinctorius, Chuanxiong rhizoma	31
2	Cicada slough, Poria cocos	39	13	Carthamus tinctorius, Cicada slough	31
3	Radix pueraria, Cicada slough	38	14	Paeoniae radix rubra, Cicada slough	31
4	Radix pueraria, Gastrodia elata	35	15	Radix pueraria, Gastrodia elata, Poria cocos	31
5	Cicada slough, Gastrodia elata	35	16	Paeoniae radix rubra, Chuanxiong rhizoma, Cicada slough	31
6	Paeoniae radix rubra, Chuanxiong rhizoma	34	17	Cicada slough, Gastrodia elata, Poria cocos	31
7	Gastrodia elata, Poria cocos	34	18	Carthamus tinctorius, Peach kernel	30
8	Chuanxiong rhizoma, Cicada slough	33	19	Radix pueraria, Chuanxiong rhizoma	30

9	Radix pueraria, Cicada slough, Poria cocos	33	20	Paeoniae radix rubra, Poria cocos	30
10	Chuanxiong rhizoma, Poria cocos	32	21	Carthamus tinctorius, Chuanxiong rhizoma, Cicada slough	30
11	Radix pueraria, Cicada slough, Gastrodia elata	32	22	Paeoniae radix rubra, Chuanxiong rhizoma, Poria cocos	30

Table 3. Association rules of traditional Chinese medicine combinations (confidence degree>0.9)

Sequence	Regulation	confidence degree	Sequence	Regulation	confidence degree
1	Paeoniae radix rubra-> Chuanxiong rhizoma	1	12	Gastrodia elata -> Radix pueraria	0.92105
2	Paeoniae radix rubra,Cicada slough -> Chuanxiong rhizoma	1	13	Gastrodia elata -> Cicada slough	0.92105
3	Carthamus tinctorius-> Chuanxiong rhizoma	0.96875	14	Chuanxiong rhizoma ->Cicada slough	0.91667
4	Carthamus tinctorius -> Cicada slough	0.96875	15	Cicada slough, Gastrodia elata -> Radix pueraria	0.91429
5	Carthamus tinctorius,Cicada slough -> Chuanxiong rhizoma	0.96774	16	Radix pueraria,Gastrodia elata -> Cicada slough	0.91429
6	Carthamus tinctorius,Chuanxiong rhizoma -> Cicada slough	0.96774	17	Paeoniae radix rubra ->Cicada slough	0.91176
7	Chuanxiong rhizoma->Paeoniae radix rubra	0.94444	18	Gastrodia elata,Poria cocos ->Radix pueraria	0.91176
8	Chuanxiong rhizoma,Cicada slough -> Paeoniae radix rubra	0.93939	19	Paeoniae radix rubra, Chuanxiong rhizoma->Cicada slough	0.91176
9	Carthamus tinctorius->Peach kernel	0.9375	20	Paeoniae radix rubra -> Chuanxiong rhizoma,Cicada slough	0.91176
10	Carthamus tinctorius-> Chuanxiong rhizoma, Cicada slough	0.9375	21	Gastrodia elata,Poria cocos -> Cicada slough	0.91176
11	Chuanxiong rhizoma,Poria cocos -> Paeoniae radix rubra	0.9375	22	Chuanxiong rhizoma,Cicada slough -> Carthamus tinctorius	0.90909

### 3.2.1. Research Results of Formula Formulation Law Based on Entropy Clustering

According to the software usage manual, extract the data and the input quantity, set the correlation to 8 and the penalty is 2. Click the cluster analysis button to form the correlation between the two drugs in the formula, and show the drug pairs with a correlation coefficient above 0.07 (Table 4).

Table 4. Results of the interpair correlation coefficient analysis

Couplet medicines	Correlation coefficient	Couplet medicines	Correlation coefficient
Massa medicata fermentata— Forsythia suspensa	0.1095408	Chuanxiong rhizoma—Stir- baked rhizoma dioscoreae	0.08148517
Angelica sinensis—Fructus leonuri	0.09788057	Carthamus tinctorius—Leech	0.0804792
Massa medicata fermentata— Uncaria rhynchophylla	0.09560853	Peach kernel—Rhizoma corydalis	0.07737917
Chuanxiong rhizoma—Rhizoma anemarrhenae	0.09304309	Poria cocos—Carthamus tinctorius	0.07664299
Chuanxiong rhizoma—Forsythia suspensa	0.09304309	Corni fructus—Ginger processed pinellia	0.07426599
Massa medicata fermentata— Fritillariae thunbergii Bulbus	0.08817258	Arisaema cum bile— Eupolyphaga	0.07398668
Poria cocos—Stir-baked semen raphani	0.08807507	Fructus leonuri—Persimmon calyx	0.07259703
Semen raphani—Moutan cortex	0.08423325	Angelica sinensis—Leech	0.07114804
Processed Epimedium—Dipsacus asperoides	0.08418643	Rehmannia glutinosa—Stir- baked malt	0.07014808
Processed Epimedium—Prepared Radix glycyrrhizae	0.08418643	Rehmannia glutinosa— Common Curculigo Rhizome	0.07014808
Angelica sinensis—Stir-baked semen raphani	0.08320108	Rehmannia glutinosa—Stir- baked semen raphani	0.07014808

### 3.3.2 Analysis results of core drug combination

Based on the results of the above inter-drug correlation analysis, several core combinations composed of three Chinese medicines were developed by correlation and penalty clustering. (Table 5)

Table 5. List of newly discovered core combinations of TCM

Sequence	Core combination	Sequence	Core combination
1	Massa medicata fermentata, Ground beetle, Herba taxilli	9	Massa medicata fermentata, Ground beetle, Panax notoginseng powder
2	Peach kernel, Massa medicata fermentata, Rehmannia glutinosa	10	Peach kernel, Massa medicata fermentata, Stir-baked malt
3	Peach kernel, Stir-baked malt, Paeoniae radix rubra	11	Paeoniae radix rubra, Carthamus tinctorius, Stir-baked semen raphani
4	Euonymus alatus, Ginger processed pinellia, Arisaema cum bile	12	Euonymus alatus, Arisaema cum bile, Radix rehmanniae praeparata
5	Gardenia jasminoides, Radix scrophulariae, Pericarpium citri reticulatae	13	Gardenia jasminoides, Processed epimedium, Polygala
6	Massa medicata fermentata, Stir-baked malt, Carthamus tinctorius	14	Massa medicata fermentata, Carthamus tinctorius, Stir-baked semen raphani
7	Curcuma aromatica, Phellodendron amurense, Semen raphani	15	Phellodendron amurense, Rhizoma anemarrhenae, Stir-baked rhizoma dioscoreae
8	Rhizoma anemarrhenae, Rhizoma alismatis, Chrysanthemum	16	Rhizoma anemarrhenae, Rhizoma alismatis, Stir-baked rhizoma dioscoreae

### 3.3.3. Analysis of New Prescriptions Based on Unsupervised Entropy Hierarchical Clustering

Based on the above drug core combinations, the unsupervised entropy hierarchical clustering algorithm was used to obtain 5 new prescriptions. (Table 6)

Table 6. New prescriptions for treating insomnia

Sequence	New prescriptions
1	Massa medicata fermentata, Ground beetle, Herba taxilli, Panax notoginseng powder
2	Peach kernel, Massa medicata fermentata, Rehmannia glutinosa, Stir-baked malt
3	Peach kernel, Stir-baked malt, Paeoniae radix rubra, Chuanxiong rhizoma, Carthamus tinctorius, Stir-baked semen raphani
4	Euonymus alatus, Ginger processed pinellia, Arisaema cum bile, Radix rehmanniae praeparata
5	Gardenia jasminoides, Radix scrophulariae, Pericarpium citri reticulatae, Processed epimedium, Polygala
6	Massa medicata fermentata, Stir-baked malt, Carthamus tinctorius, Stir-baked semen raphani
7	Curcuma aromatica, Phellodendron amurense, Semen raphani, Rhizoma anemarrhenae, Stir-baked rhizoma dioscoreae
8	Rhizoma anemarrhenae, Rhizoma alismatis, Chrysanthemum, Stir-baked rhizoma dioscoreae

## 4. Discussion

Insomnia, also known in Chinese medicine as "sleepless" in traditional Chinese medicine, "Huangdi Neijing" will insomnia as "do not sleep" "do not lie" [7]. Sleep process is a Yin and Yang, mutual induction process [8]. Classified Treatment in the words "Yang qi automatic and quiet sleep, Yin qi from the static movement on" [9]. If this process is abnormal, it can lead to insomnia. Its pathogenesis belongs to Yang Sheng Yin decline, Yin and Yang do not cross. It is caused by the Yang does not enter the Yin caused by the characteristics of the disease [10]. People

with light symptoms have difficulty in falling asleep, and it is easy to wake up more often. People can not fall asleep after waking up, and sometimes wake up when sleeping. People with serious symptoms can not even fall asleep all night [11].

Professor Li Jun believes that insomnia deficiency diseases are mostly caused by heart and spleen deficiency, heart deficiency and timidity, Yin deficiency and fire flourishing, leading to the loss of anxiety. Insomnia empirical is because the heart fire, liver yu fire, phlegm heat disturbance, resulting in anxiety. However, insomnia for a long time can be manifested as virtual and solid inclusion, or caused by blood stasis. The ancients once said that "long disease more blood stasis", "strange disease more phlegm", according to the theory of "phlegm and stasis homology", the method of "phlegm and stasis treatment, dispel wind and calm god" is used in treatment [12].

This paper adopts the software of "Traditional Chinese Medicine Inheritance auxiliary System", and inputs 50 prescriptions of insomnia diagnosed by Professor Li Jun in the outpatient department, digging out the traditional Chinese medicine commonly used by Professor Li Jun in the clinical treatment of insomnia. Traditional Chinese medicine includes: *Poria cocos*, *Cicada slough*, *Radix pueraria*, *Gastrodia elata*, *Chuanxiong rhizoma*, *Paeoniae radix rubra*, *Carthamus tinctorius*, *Pericarpium citri reticulatae* and so on. *Pericarpium citri reticulatae*: *Radix pueraria* and *Poria cocos*, *Cicada slough* and *Poria cocos*, *Radix pueraria* and *Cicada slough*, *Radix pueraria* and *Gastrodia elata*, *Cicada slough* and *Gastrodia elata*. Through the analysis of the combination of commonly used Chinese medicine and traditional Chinese medicine, most of them are things to dispel wind and remove phlegm and blood stasis, which is consistent with Professor Li Jun's method of "treating phlegm and blood stasis, dispelling wind and calming nerves". Using the clustering algorithm analysis, the common drug pairs include: *Massa medicata fermentata*—*Forsythia suspensa*; *Angelica sinensis*—*Fructus leonuri*; *Massa medicata fermentata*—*Uncaria rhynchophylla*, *Cicada slough*; *Chuanxiong rhizoma*—*Rhizoma anemarrhenae*; *Chuanxiong rhizoma*—*Forsythia suspensa*. Newly discovered drug combinations include: *Massa medicata fermentata*, Ground beetle, *Herba taxilli*; Peach kernel, *Massa medicata fermentata*, *Rehmannia glutinosa*; Peach kernel, Stir-baked malt, *Paeoniae radix rubra*; *Euonymus alatus*, Ginger processed *pinellia*, *Arisaema cum bile*; *Gardenia jasminoides*, *Radix scrophulariae*, *Pericarpium citri reticulatae*. And derive 8 new prescriptions based on entropy hierarchical clustering analysis. New prescription 1 is composed of *massa medicata fermentata*, ground beetle, *herba taxilli*, *panax notoginseng* powder, which has the function of enriching blood and promoting blood circulation, invigorating spleen and kidney. New prescription 2 is composed of peach kernel, *massa medicata fermentata*, *rehmannia glutinosa*, stir-baked malt, which has the function of invigorating spleen and stomach, nourishing Yin and producing jin. New prescription 3 is composed of peach kernel, stir-baked malt, *paeoniae radix rubra*, *chuanxiong rhizoma*, *carthamus tinctorius*, stir-baked *semen raphani*, which has the function of promoting blood circulation and removing blood stasis, invigorating the spleen and stomach. New prescription 4 is composed of *euonymus alatus*, ginger processed *pinellia*, *arisaema cum bile*, *radix rehmanniae praeparata*, which has the effect of nourishing Yin and enriching blood, resolving phlegm and eliminating blood stasis. New prescription 5 is composed of *gardenia jasminoides*, *radix scrophulariae*, *pericarpium citri reticulatae*, processed *epimedium*, *polygala*, which has the effect of clearing heat and cooling blood, dry dampness and resolving phlegm. New prescription 6 is composed of *massa medicata fermentata*, stir-baked malt, *carthamus tinctorius*, stir-baked *semen raphani*, which has the function of invigorating the spleen and stomach, promoting blood circulation and removing blood stasis. New prescription 7 is composed of *curcuma aromatica*, *phellodendron amurense*, *semen raphani*, *rhizoma anemarrhenae*, stir-baked *rhizoma dioscoreae*, which has the function of nourishing Yin and clearing heat, promoting the circulation of qi and reducing phlegm. New prescription 8 is composed of *rhizoma anemarrhenae*, *rhizoma alismatis*, *chrysanthemum*, stir-baked *rhizoma dioscoreae*, which has the effect of nourishing Yin and clearing heat, moistening



lung and relieving cough. These eight new prescriptions can be flexibly applied according to the clinical manifestations and four diagnosis parameters. The analysis of common Chinese medicine, Chinese medicine combinations, Chinese medicine pairs and new prescriptions are all in line with Professor Li Jun's analysis of the pathogenesis. The results can be more clear, more clinical guidance, more convenient for students to learn [13].

The positive role of data mining can not be denied in the research progress of modern Chinese medicine [14,15]. This study uses the auxiliary platform of TCM inheritance to systematically excavate and sort out the clinical experience of professor Li Jun of famous TCM treatment in Shaanxi Province. It concluded the characteristics of his treatment of insomnia, and analyzed and excavated the rules of the prescription. And used cluster analysis to get eight new prescriptions. This move can better inherit and carry forward the academic thought of the famous traditional Chinese medicine, and then promote the development of traditional Chinese medicine cause [16].

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### Data Availability

The datasets used during the current study are available from the corresponding author on reasonable request.

### Conflict of Interest

The author states that this article has no conflict of interest.

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