

# Autism Spectrum Disorder Related TCM Symptoms and TCM Herbs Prescriptions: A Systematic Review and Meta-Analysis

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The purpose of this research is aimed at finding effective classical herbs prescriptions and providing references for further research on the autism treatment by consulting modern literature, ancient books and monographs. We took full advantage of CiteSeer, CNKI, PubMed, VIP and other literature databases as the major methods in this study to review the modern literature of autism during 1989-2014 and summarized them. We have also sorted out many prescriptions which used to treat autism in modern literature. In the traditional Chinese medicine (TCM) terms, the highest frequency of symptoms used to diagnose autism are "dullness", "mutistic", "soliloquy", "five kinds of retardation", "five weaknesses", "fetal toxicity" and "infantile metopism". By consulting ancient books and monographs, we found TCM associated with treatment of the aforementioned autism descriptors used by TCM. The results of this research is as following: Collecting over 4,706 research articles about autism spanning approximately 26 years, we reviewed the research of autism with respect to TCM and western medicine regarding its etiology, symptoms and treatment. We found the highest frequency TCM terms used to describe diagnostic symptoms of autism are "dullness", "mutistic", "soliloquy", "five kinds of retardation", "five weaknesses", "fetal toxicity" and "infantile metopism". Those descriptors were used as keywords to search related prescriptions from ancient books and monographs. More than 300 prescriptions were obtained. Finally, we verified clinical applications of these prescriptions, noting the frequency of use as a single medicine. We also collated pharmacological effects of the prescriptions, and the frequency of usage in the treatment of autism symptoms. The conclusion has been reached that TCM emphasizes a holistic treatment strategy with comprehensive aftercare. In addition, ancient physicians recorded many prescriptions about treatment of autism related symptoms in the ancient books and monographs, and some prescriptions are still applied in clinical autism treatment in current practices. In conclusion, seeking effective prescriptions and medicine from the perspective of TCM is of great importance.

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**Key Words:** Autism, prescriptions, herbs, TCM

## INTRODUCTION

Autism spectrum disorder (ASD) is a developmental disability which occurs before the age of three and is usually diagnosed after one year old. The main symptoms are language development disorders of different levels interpersonal communication barriers, narrow interests and inflexible behavior patterns. Even to the extent that some children suffer from epilepsy, gastrointestinal diseases and

sleep disorders. This is a lifelong disorder of increasing prevalence and community concern.<sup>1</sup>

Based on the community Report on Autism (March 2014) from the Center of Disease Control (CDC) in the USA, about 1 in 68 children were identified by the data from 11 Autism and Developmental Disabilities Monitoring (ADDM) sites and the data covering 2012.<sup>2</sup> According to other data published in 2014 from USA, the total number of global autism patients had reached 67 million.<sup>3</sup> At present, the incidence of autism is rising, but the effect of treatment and prognosis are still not satisfactory.

The ancient time mentioned in this review refers to the period before 1911 which was the end of year of last Chinese

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dynasty of Qing. in that period, the TCM did not have a disease called autism, however, it had the records of the symptoms associated with autism, such as "dullness", "mutistic", "soliloquy", "five kinds of retardation", "five weaknesses", "fetal toxicity" and "infantile metopism". Dullness, also known as dementia, is a result of abnormal digestive function of the spleen and stomach by TCM theory. Spleen and stomach damages lead to inner sputum and dampness, blinding the heart, and then impacting on intelligence. From model medicine perspectives, mutistic is mainly caused by genetic predisposition. Symptoms of mutistic are unwillingness to speak and reply. Soliloquy means absence of mind and muttering and its cause is deficiency of "heart qi" which meant the "state of mind" here and lack of physical recuperation. Five kinds of retardation include slowness in standing, walking, hair growth, tooth eruption and speech. These five kinds of retardation are caused by the parents' unhealthy body which led to the congenital deficiency of infants. The Five weaknesses refer to flaccid head, flaccid nape, flaccid hands and feet, infantile flaccidity of muscle and flaccid mouth. Their causes are insufficiency of essence and blood. Fetal toxicity that refers

to environmental factors including exposure to certain toxic substances during pregnancy.<sup>4</sup> Infantile metopism is a congenital disfigurement of the forehead in which the frontal suture unclosed.

TCM treats autism according to different pathological lesions, time of the disease and place of morbidity. Chinese medicine prescriptions for treating autism stress the principle of "monarch, minister, assistant and guide"<sup>5,130</sup> that are the well-known principles for the composition of prescriptions. "Monarch drug" is the key ingredient in the prescription, "minister drug" promotes the "monarch drug" to exert curative effect, and "assistant drug" strengthens the effect of the prescription or restrict toxin, and "guide drug" directs other ingredients to work on the affected part. This principle could not only make reasonable use of each herb, but also make the prescription by appropriately adding and subtracting in specific circumstances, which has important instructive significance for rational clinical use of medicines. Therefore, this article aims to find effective prescriptions and provide reference for better treatment of autism through collecting modern literature and ancient medical books.

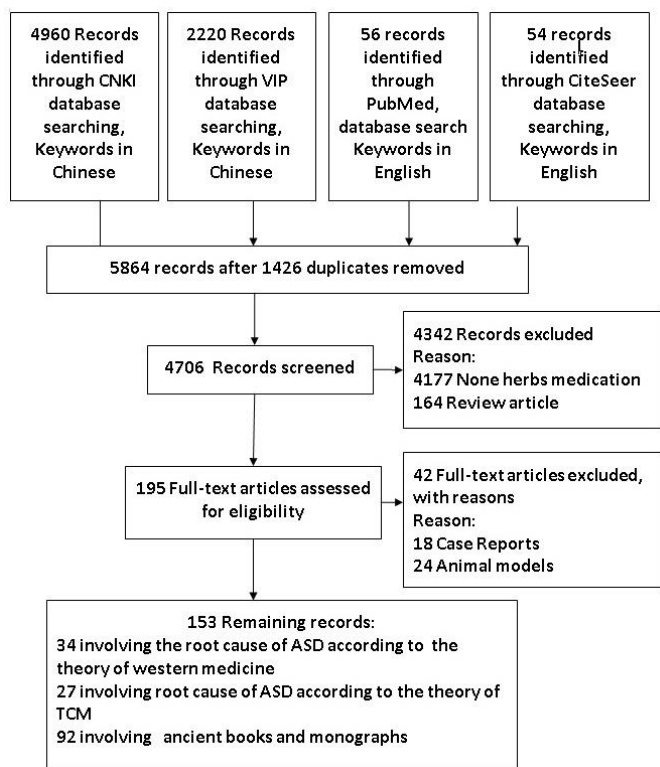


Figure 1. PRISMA flow chart for the literature search and collection process.

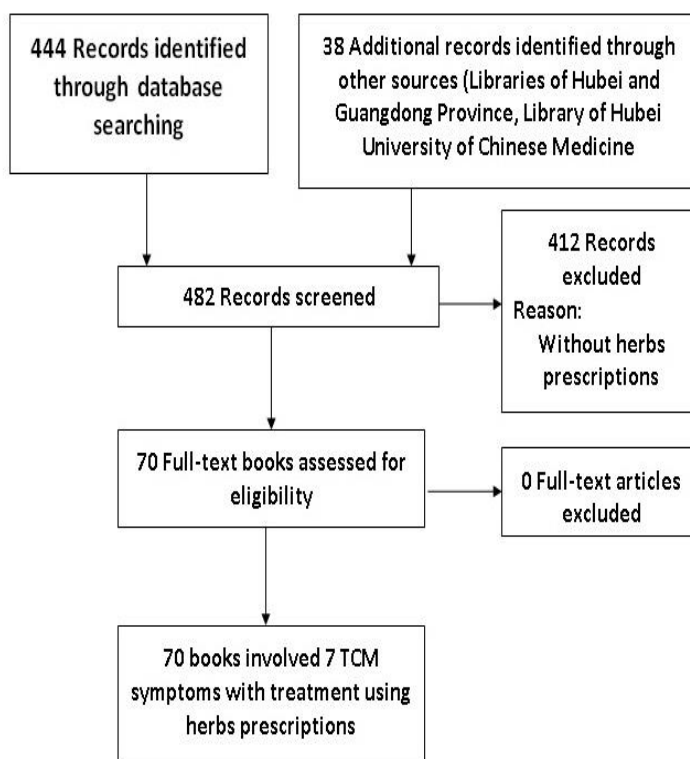


Figure 2. PRISMA flow chart for the ancient books search and collection process.

## METHODS

### Search Strategy and the Goals

To overcome the challenges on searching the effective TCM herbs prescription for treating autism from ancient Chinese medical books, the first step is to setup a rational of search strategy as autism has not been defined in TCM. This search starts with modern medical literature with "Autism" as a keyword in Chinese against two major medical literature

databases including the China Knowledge Resource Integrated Database (CNKI) and Chinese Scientific Journals Database (VIP).

Also, using "Autism" and "Chinese medicine" as keywords in English against two major data based used in the worldwide, PubMed and CiteSeer. The results describing autism related TCM symptoms will be used for a further

search against the ancient Chinese medical books database to collect the ancient herbal prescriptions that treat those symptoms.

The goals of this search are:

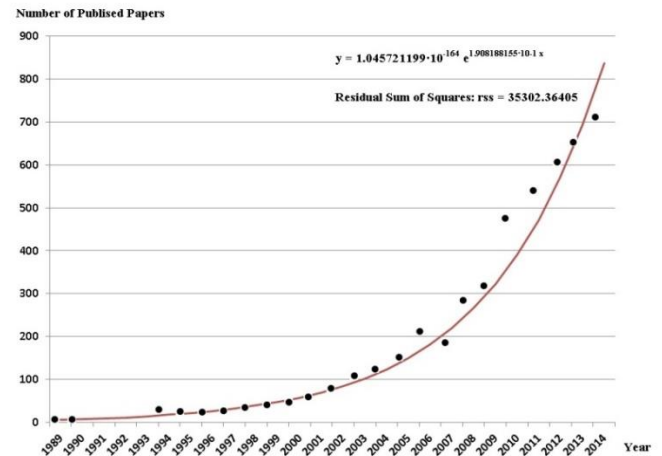
1. To find the records that has herbs prescriptions, then to identify the effective herb medicine to treat the autism.
2. To find the TCM symptoms that been used currently to diagnose Autism. Those will be the key to use in the further search against the ancient Chinese medical books to collect the ancient herb prescriptions that used to treat autism related TCM symptoms.
3. To review the updated information on the etiology of autism. That will be used to identify the valuable herbs that provide effective treatment regarding the cause of autism.
4. To review the updated information on biomarkers for autism diagnosis. This will be very useful information to help development of the next generation of herbal prescriptions as a tool for measuring effectiveness and accuracy of the herb medicine.

### Selection Criteria and Work Flow

We systematically reviewed and observed the studies and related ancient books of TCM. The selection processes were divided into three groups:

1. The selection of autism treatment by using herbs prescription.  
For the autism treatment by using herbs prescription, the search time range was 25 years, from 1989 to 2014. The PRISMA work flow has been used in our review process for the literatures search, see **Figure 1**.
2. Ancient Chinese medicine literature search  
For the ancient Chinese medicine literature search, the keywords of the TCM symptoms have been used to search and select the ancient herbs prescriptions against the ancient Chinese medicine literature database<sup>6</sup> and other library books resources. That part actually is an original data mining research work that has added into this review. The following PRISMA flow chart indicates this process, **Figure 2**.
3. Update information on etiology and biomarkers of autism  
Even many records in the first group can be used, but this review exclusion process filtered out many valuable literatures that specific on the etiology and biomarkers of autism. This search process will collect more specific subjects on etiology and biomarkers of autism for last 5 years data range using PubMed database. Using "autism or ASD" as keywords, 14,876 records have been found and narrow down to the time rang for 2014 only, 4,224 have been found including 380 reviews. Around additional 40 papers have been selected with etiology and biomarkers of autism related contents.

All of the research works in this review will be summarized into three sections, current etiology and treatment, the usage of herbs prescriptions and the pharmacological effects of Chinese medicine in prescriptions.



**Figure 3.** Number of published literature of autism by year.

## RESULTS

### Etiology and Treatment of Autism

We made full use of CiteSeer, CNKI, PubMed, VIP and other literature databases to review modern literature on autism subject to over 4,706 articles during 1989-2014, and the number of published papers increased every year exponentially. As it shows in **Figure 3**, through the literature we found out research of autism on TCM and western medicine on the aspects of etiology, symptoms, and treatment.

#### 1. Autism etiology

Nowadays, many scholars think it is probably a complex combination of genetic and environmental factors which causes autism. Moreover, there are toxic exposure, immunocompromised nerve function disorder and other factors.

##### 1.1. Genetic factors

At present, TCM believed it is the deficiency of the congenital and kidney-essence that leads to minds blocked, spirits nonnutritive, and failure of the liver-qi's free coursing and ascending,<sup>7</sup> which contribute to the causes of autism. Furthermore, Liu Wuli<sup>8</sup> and Liu Gang<sup>9</sup> argued that autism is relevant to brain lesions, such as injury, and genetic factors. Western Medicine insists that the etiology of autism is complex, and the key pathogenic factor is genetic factor.<sup>10</sup> Recently, Mitchell et al<sup>11</sup> reported that the bioactivefolate is deficient in some cases of autism, and may possibly be influenced by B vitamin-related genes in select neurodevelopmental syndromes. Nardone et al<sup>12</sup> reported that the locus encompassing C11orf21/TSPAN32 has multiple hypomethylated CpGs in the autistic, which suggest a possible role for epigenetic processes in the etiology of ASD. Wittkowski et al<sup>13</sup> reported a novel study-specific criterion for 'genome-wide significance' and found axonal guidance and calcium signaling are involved in autism.

However, research on genetic factors of autism are mainly centralized on family and twin studies etc. and those were mostly in molecular genetics level.

### 1.2. Environmental factors

Family environment and the condition in which child is raised are also the risk factors of autism.<sup>14</sup> Exposure to valproate,<sup>15</sup> an antiepileptic drugs<sup>16</sup> can increase the risk of disease. Especially valproate, which will seriously influence the development of the cognitive function,<sup>17</sup> bringing neurological problem, finally causing autism. Environmental factors were also the cause of "mutistic" and "soliloquy" in TCM, which caused psychological and physiological changes of children by receiving certain stimuli, and then symptoms of autism occur.

### 1.3. Toxic exposure in the pregnancy and perinatal period

Medical history and vaginal bleeding during pregnancy, premature delivery, expired produces, cesarean section, low birth weight, neonatal asphyxia and jaundice may be associated with autism.<sup>18</sup> These etiologies are closely related with "fetal faint" and "fetal toxicity" in TCM, and they have the same pathological characteristics. Recent review<sup>[19]</sup>, arranged the related literature into three categories as following:

(a) studies examining estimated toxicant exposures in the environment during the preconceptional, gestational and early childhood periods; (b) studies investigating biomarkers of toxicants; and (c) studies examining potential genetic susceptibilities to toxicants. They found 92% of the fall into the toxicant exposures in the environment. Toxicants implicated in ASD included pesticides, phthalates, polychlorinated biphenyls (PCBs), solvents, toxic waste sites, air pollutants and heavy metals, with the strongest evidence found for air pollutants and pesticides. They concluded that the etiology of ASD may involve, at least in a subset of children, complex interactions between genetic factors and certain environmental toxicants that may act synergistically or in parallel during critical periods of neurodevelopment, in a manner that increases the likelihood of developing ASD.

### 1.4. Immune dysfunction

Research on immunology about autism mainly refer to nerve immunology, immunogenetics, autoimmune, immune cells, cytokines, gastrointestinal factors and immunodeficiency.<sup>20</sup> The different cell types in CNS that have both roles, the brain function and the CNS immune response. Abnormal immune responses in the brain cells in ASD patient may influence neural function and development.

### 1.5. Nerve functional disturbance

TCM thinks that autism occurs in the brain, and western medicine also demonstrates that the abnormal growth and density change of neurons in the brain may be main causes of autism. Coordination among brain regions decreased or correlation between brain nerve insufficient may cause autism.<sup>21</sup> The role of the P50 component of the auditory event-related potential in early sensory processing has been examined in relation to the gating of irrelevant or repetitive stimulus information ('sensory gating').<sup>22,23</sup> Lv et al<sup>4</sup> reported that that P50 sensory gating is deficient in children with ASD. The function of sensory gating in children with ASD didn't change with the age, but only with the speed of processing conditioned stimulus (S1) increased with the age.

### 1.6. Metabolic disorder

Some studies have found that autism may be associated with metabolic disorders of some metal elements. Tetrahydrobiopterin is an essential cofactor for critical metabolic pathways, including those involved in the production of monoamine neurotransmitters and nitric oxide. A recent report indicated that a series of ASD who were found to have CNS tetrahydrobiopterin deficiency.<sup>25</sup> The lack and impaired absorption of trace elements such as calcium, iron in the brain lead to abnormal neural cells in the process of proliferation and differentiation. Excretion disorder of lead and mercury may cause brain damage.<sup>26</sup> The causes of autism are also related to folate metabolism.<sup>27</sup> Some research indicate that the effects of secretin, neurotoxin in the gastrointestinal tract and central nervous system may be associated with autism.<sup>28,29</sup> These symptoms are related with "five kinds of retardation" and "five weaknesses" in TCM. Both of them have the same pathological symptoms like hypoplasia and retardation due to psychological and physiological disease caused by metabolic disorders.

### 1.7. Oxidative stress

Oxidative stress may affect mitochondrial function, and impaired mitochondria in turn increases oxidative stress. It was oxidative stress product which stimulate autoimmune process of organism and attack nerve cells in the brain that make contribution to the development of autism spectrum disorders (ASD).<sup>30</sup>

## 2. Research progress on the biomarker

The underlying mechanism of ADS development is still unknown. Many recently research efforts could be concluded into the exploring the biomarkers category to markedly improving classification, detailed measurement or predication accuracy of degree of ASD.

### 2.1. Neuroimaging

ADS patient MRI data analysis found significant differences in groups by age of the interaction in sulcal-based morphometric analysis at the sub-lobar scale and also observed sulcal abnormalities were localized in regions where cortical thickness was increased.<sup>31</sup> This strongly suggests that sulcal shape differences could be the signature of disrupted maturational process that affects this pathology. Another team using MRI looked for differences between Autism Spectrum Condition (ASC) participants, controls and unaffected siblings of ASC participants, the results showed differences in the cerebellum, parietal lobule, left occipital, left angular gyrus and, to a lesser extent in other regions.<sup>32</sup> Zhou et al.<sup>33</sup> using the small-world network analysis based on the cortical thickness revealed reduced total and global efficiency in ASD, they concluded that caudate volume, caudate-cortical fMRI and IFG pars opercularis as well as triangularis fMRI to be highly predictive of phenotypic features in ASD.

### 2.2. Cortical function

Corradi-Dell'Acqua et al<sup>34</sup> using fMRI compared the control participants with ASD and found that spared low-spatial frequency(LSF) face processing in ASD while cortical

analysis of high-spatial frequency(HSF) expression cues appears affected, then suggesting that ASD might be characterized by a difficulty in integrating multiple local information and cause global processing troubles unexplained by losses in low spatial frequency input. Kim et al.<sup>35</sup> reviewed recent findings regarding differentiation of cortical neurons from human pluripotent stems cells and efforts to establish in vitro model systems to study ASD using personalized neurons. Using induced pluripotent stem (iPSC) technology, it is possible to generate limitless supplies of human ASD-special cortical neurons, which can revolutionize experimental analysis of ASD.

### 2.3. Brain connectivity

Bos et al 2014<sup>36</sup> reported that using fMRI technique, subtle changes in network connectivity in patients with ASD, the global architecture of resting-state networks appears to be intact. This argues against recent suggestions that changes in connectivity in ASD may be most prominent during development. Kana et al.<sup>37</sup> 2014, summarized the past 10 years including 2014's literature on brain connectivity in autism. Neuroimaging and postmortem studies have provided evidence for disruptions in functional and structural connectivity in the brains of individual with ASD, but still struggle with methodological and conceptual issues inherent to discover relationships between brain and behavior. Functional connectivity magnetic resonance imaging (fcMRI) studies suggest that differential findings are not only region- or network-specific, but also state-specific, then suggesting that research on brain connectivity in autism should be placed in a developmental framework in order to more precisely pin-point the sources of age-related group differences in functional connectivity. Mcgrath and colleagues found that altered white matter microstructure is related to disruptions in functional connectivity during visuospatial processing, especially in connections between left occipital lobe and five paired regions in the left hemisphere.

### 2.4. EEG for the automatic identification and MEG for the auditory response

Elderidge et al.<sup>38</sup> 2014 reported that based on the children with ASD exhibit hype-reactivity or hypo-reactivity to sensory stimuli, however, they found that with an objectively superior method of comprehensive artifact rejection that applies to every electroencephalography (EEG) study likely does not exist, therefore, their research reported that a streamlined approach to artifact rejection combined with robust feature leads to highest classification accuracy for ADS patients. Edgar et al.<sup>39</sup> 2014, reported that using magnetoencephalography(MEG) recording whole cortex activities by auditory stimulation, the result showed that M50 responses were delayed in ASD compared to typical development (TD) group bilaterally. They also found that for an 11 years old patient, if a long inter-trial interval is used, lack of a left and especially right M100 offers neurobiological insight into abnormal sensory processing that may underlie language or cognitive impairment in ASD.

## 3. Treatments for autism

### 3.1. TCM therapy

Chinese medicine treatments usually used Chinese medicine, acupuncture, acupoint massage and comprehensive therapy and other treatments for autism.

For instance, Li Aiwu<sup>40</sup> used the compound of Si Ni Bei as the basic prescription, adding and subtracting prescription at the right time, with an appropriate amount to treat autism. Children's understanding and language ability significantly improved after treatment. Lan Sheng rong<sup>41</sup> treated autism children with sleep disorders by Tian Ma Gou Teng yin with foot massage method, which enhanced the children's independence and sleep quality. Acupuncture treatments, for example, Luo Guang Feng<sup>42</sup> and Wu Zhifeng<sup>43</sup> applied "Jin's Three-needle" therapy to autism children, and the curative effect was obvious. Zhang Quanming,<sup>44</sup> Li Huimin,<sup>45</sup> treated children with autism through acupuncture, and after treatment, the IQ of children, behavior quotient of the social adaptation and the language ability were markedly improved. Li Congming<sup>46</sup> combined TCM with acupoint massage to treat autism, which obtained a certain curative effect. Moreover, as the children were initially out of the autistic state, other accompanied symptoms also got better. In the treatment of 30 cases, Li Nuo<sup>47</sup> adopted TCM five lines of music with acupuncture and massage therapy, communication ability and intelligence of children improved significantly after treatment.

### 3.2. Western medicine therapy

Western medicine mainly includes western medicines, stem cell transplantation, hyperbaric oxygen combined with rehabilitation training, sensory integration training, psychological intervention for the treatment of autism.<sup>48</sup>

At present, western medicine in the treatment of autism include antipsychotic, anticonvulsant, and 5-selective serotonin reuptake inhibitors, oxytocin.<sup>49</sup> But their effects are not obvious, producing some side effects; some even have serious drug dependence At present, the early treatments of autism are mainly about intervention therapy, sensory integration training and behavior modification; in addition, medication is needed as well.

## The Herbs Prescriptions for the Treatment of Autism

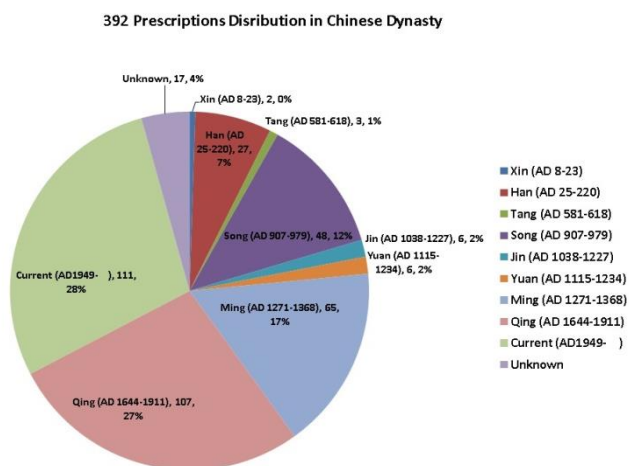
### Prescriptions collecting

By consulting ancient books and monographs based on the seven kinds of symptoms that related to autism which mentioned above, 392 prescriptions for the treatment of those symptoms were found from 70 ancient books and monographs. The **Figure 4** showed the distribution of 392 herbs prescriptions in the different Chinese Dynasties.

### The ancient books and monographs

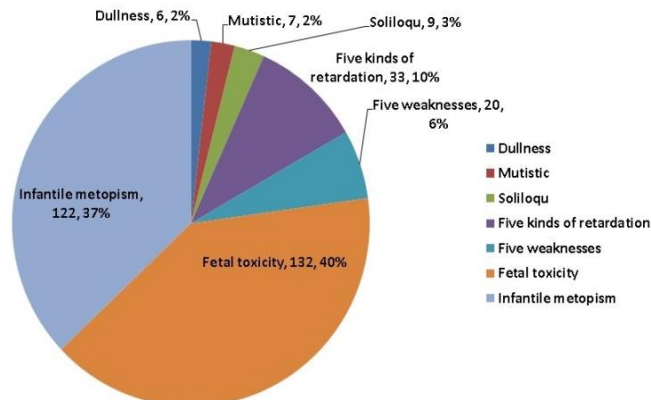
The summary data, in **Figure 5**, showed that the autism symptoms have been treated in China more than 2000 years ago. The total number of books that have the prescriptions for treating the autism symptoms increased from Song to

Qing dynasty for the ancient books and monographs category. The total numbers of prescriptions showed higher since Ming dynasty.



**Figure 4.** The summary data for the books that have the prescriptions to treat the 7 symptoms of autism by Chinese dynasty.

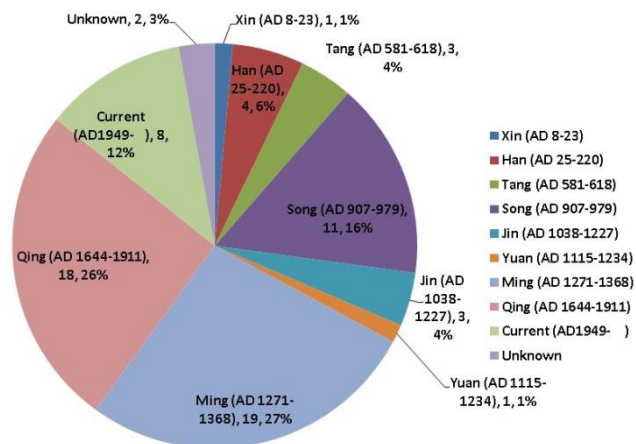
**Number of Herbs Prescriptions for 7 TCM Symptoms**



**Figure 6.** The summary data of 392 classic ancient herbs prescriptions that used to treat the 7 symptoms of autism.

Some prescriptions, such as Hu Gu pill, Bu Zhong Yi Qi decoction, Chang Pu pill, Zuo Gui pill and so on were still used in modern clinic to treat autism and its associated traits.

**The distribution of 70 Chinese Medical Books in Chinese Dynasty**



**Figure 5.** The distribution of 70 selected ancient Chinese Medical Books in Chinese Dynasties.

### The herbs prescriptions

There are 392 classic ancient herbs prescriptions that used to treat the 7 symptoms of autism. See **Figure 6**.

### Modern clinical application of the prescriptions

The modern clinical applications of the collected prescriptions have been reviewed in the study. We have found that there are 23 prescriptions still used to treat autism from 28 papers. The most of them reported that using the prescriptions had positive improvement for treating the patients' symptoms. We have also found that those 23 prescriptions have been collected in the Chinese Pharmacopoeia or People's Republic of China Ministry of Health pharmaceutical standards of Chinese medicine prescription preparations 2010 Edition.<sup>50,51</sup>

Ye Jianfei<sup>52</sup> created "Anti-Autism Number 1" on the basis of Di Huang Yin Zi, Kai Xin powder and Tong Qiao Huo Xue decoction, and reported the prescription showed certain curative effect in the treatment of children with autism. Yong<sup>53</sup> employed Chai Hu Gui Zhi Long Gu Mu Li decoction in treatment of autism, there was some gratifying progress after treatment, for instance, problems of sensory integration, hyperactivity, enuresis, and sleep had a certain improvement. Yan Yufen<sup>54</sup> linked Jia Wei Wen Dan decoction with teaching and training programs to correct 25 cases of children with autism. After treatment, symptoms took a turn for the better. The hyperactivity reduced, the span of concentration increased. In addition, self-injury, shocking head, screaming, smirking, rotation and other abnormal behaviors diminished. Its total effective rate was 84%. Li Dexing<sup>55</sup> used Hu Gu pill to treat a patient who had an inflexible tongue and unclear pronunciation and other similar symptoms. After three months of medication, the patient spoke more clearly than before, and half a year later, the patients speak fluently and could join into normal social interaction. Zhou Zhongying<sup>56</sup> adopted Bu Zhong Yi Qi decoction to treat a patient who had stiff tongue and couldn't speak clearly. After taking the medicine for a week, patient could speak clearly without recurrence during the next six months. Gu Mingming<sup>57</sup> combined Liu Wei Di Huang pill with Chang Pu pill to cure a 6 year old child. After a month of medication, the patient could speak more fluently and recovered after another three months of medication. Through the observation of curative effect of Liu Wei Di Huang pill on 50 cases of patient with dementia, Qing Zhaoqian<sup>[58]</sup> found that it had some positive effect in improving the patient's intelligence, life skills and memory, etc. Yang Shizhen<sup>[59]</sup> applied Zuo Gui pill to treat a patient who was sluggish in eyes and slow in response. It worked well after taking this medicine for two months and basically recovered with the following 3 months of medication. Zhang Yu<sup>60</sup>

treated a variety of psychiatric disorders based on Zhi Zi Chi decoction, the efficacy was satisfactory. Zhou Ronggen<sup>61</sup> treated 23 cases of patients with dementia by Bai Hu decoction. Through this process of treatment, the symptoms like memory loss, aphasia agnosia, abnormal behavior and

reading difficulties were improved obviously. Chen Jianhong<sup>62</sup> utilized Si Jun Zi decoction and Huang Lian Jie Du decoction to treat 30 cases of patients with dementia. The curative effect was good and the total effective rate was 80.3%.

**Table 1.** Frequency of use of Chinese medicine.

Disease	Medicine	Frequency (%)	Disease	Medicine	Frequency (%)
five weakness	<i>Poria cocos</i>	36.7	five kinds of retardation	<i>Angelicae sinensis radix</i>	36.2
	<i>Rehmanniae radix praeparata</i>	33.3		<i>Acorus tatarinowii</i>	34.0
	<i>Panax ginseng</i>	30.0		<i>Poria cocos</i>	34.0
	<i>Glycyrrhiza uralensis</i>	30.0		<i>Paoniae radix rubra</i>	31.9
	<i>Rhizoma dioscoreae</i>	26.7		<i>Rehmanniae radix praeparata</i>	29.8
	<i>Rhizoma atractylodes macrocephala</i>	23.3		<i>Ophiopogon japonicus</i>	25.5
	<i>Rhizoma chuanxiong</i>	20.0		<i>Panax ginseng</i>	25.5
soliloquy	<i>Radix astragali</i>	20.0	dullness	<i>Glycyrrhiza uralensis</i>	25.5
	<i>Glycyrrhiza uralensis</i>	55.6		<i>Acorus tatarinowii</i>	80.0
	<i>Panax ginseng</i>	44.4		<i>Poria cocos</i>	60.0
	<i>Cinnamomi ramulus</i>	44.4		<i>Panax ginseng</i>	50.0
	<i>Rheum officinale</i>	22.2		<i>Angelicae sinensis radix</i>	45.0
	<i>Ophiopogon japonicus</i>	22.2		<i>Rehmanniae radix praeparata</i>	45.0
	<i>Mangnolia officinalis</i>	22.2		<i>polygala tenuifolia</i>	40.0
mutistic	<i>Rehmanniae radix praeparata</i>	22.2	fetal toxicosis	<i>Alpiniae oxyphyllae semen</i>	35.0
	<i>Poria cocos</i>	22.2		<i>Rhizoma dioscoreae</i>	30.0
	<i>Panax ginseng</i>	85.7		<i>Artemisiae scopariae herba</i>	56.4
	<i>semen zizyphi spinosae</i>	57.1		<i>Glycyrrhiza uralensis</i>	45.3
	<i>Coptis chinensis</i>	57.1		<i>Poria cocos</i>	29.9
	<i>Cinnamomi ramulus</i>	42.9		<i>Gardeniae fructus</i>	29.1
	<i>Acorus tatarinowii</i>	42.9		<i>Saposhnikovia radix</i>	26.5
infantile metopism	<i>polygala tenuifolia</i>	28.6	infantile metopism	<i>Paoniae radix rubra</i>	23.1
	<i>Platycladi semen</i>	28.6		<i>Rheum officinale</i>	20.5
	<i>Prunus semen</i>	28.6		<i>Rhizoma atractylodes macrocephala</i>	19.7
	<i>Poria cocos</i>	52.3		<i>Rehmanniae radix praeparata</i>	30.8
	<i>Rhizoma dioscoreae</i>	31.8		<i>Achyranthis bidentatae radix</i>	23.4
	<i>Rehmanniae radix</i>	30.8		<i>Moutan Cortex</i>	23.4
	<i>Alismatis rhizoma</i>	30.8		<i>Zingiberis rhizoma recens</i>	22.4

## Use Frequency and Pharmacological Effects of Chinese Medicine in Prescriptions

### Frequency of use of Chinese medicine

Filtering Chinese medicine of high frequency of use from more than 300 prescriptions, we received 32 kinds of Chinese medicines with high frequency of use, such as *Acorus gramineus Soland*, *Poria*, *Angelica*, *ginseng*, etc. The results are shown in **Table 1**.

### Pharmacological effects of Chinese medicine

We verified pharmacological effects of these 32 kinds of Chinese medicines with high frequency of use through literature review, which were mainly improving the immune system, calming the nerves, improving gastrointestinal tract, enhancing memory, and so on. These pharmacological effects were closely associated with the treating the cause of autism. The results were shown in **Table 2**.

## DISCUSSION AND CONCLUSION

We summarized symptoms and their targeted prescriptions related to autism in the ancient books, and have found some of the prescriptions were still being used to treat autism in modern times, such as *Hu Gu pill*, *Bu Zhong Yi Qi decoction*, *Chang Pu pill*, *Zuo Gui pill* and so on. In addition, we also consulted the Chinese medicines which have high frequency of use in the prescriptions and mapping with modern

pharmacological research results and showed that the pharmacological action of these Chinese medicines might improve the treatment of autism and its associated symptoms based on the etiology that we have known so far. We thought that the prescriptions and Chinese medicines of TCM could be as a breakthrough point to further research of autism for effective drug in treatment of autism, and we believed that it would be the most valuable work.

TCM has made it clear that autism occurs in the brain, and closely related with heart, spleen, liver and kidney. In TCM therapy of autism, Chinese medicine follows the overall thoughts of Chinese medicine to treat autism by invigorating the spleen, eliminating phlegm, opening mind, tonifying the kidney, nourishing the heart, building the brain. Treating autism is mainly tonifying spleen, eliminating phlegm, inducing resuscitation, tonifying kidney, nourishing heart, and invigorating brain.

Chinese herbal medicine compound takes effect with multi components, multi target, multi mechanism and multi-tache synthetically. It could adjust organism function and change its usage when faced with different diseases, and its side effects are slight. Hence, compound Chinese medicine in the treatment of autism has irreplaceable advantages compared with Western medicine. Therefore, it is feasible

from the perspective of Chinese medicine to search prescriptions and Chinese medicines to cure autism. Studies have shown that Chinese medicines we collated chiefly have

the functions of improving immunity, protecting the brain and nervous tissue, adjusting gastrointestinal, in a word, they can improve related symptoms of autism.

**Table 2.** Use frequency and pharmacological effects of Chinese medicine in prescriptions.

Chinese medicine name	Pharmacological effects									Literature sources
	A	B	C	D	E	F	G	H	I	
<i>Poria cocos</i>	+				+				+	[63-68]
<i>Rehmanniae radix praeparata</i>	+				+			+		[69-71]
<i>Panax ginseng</i>	+							+		[72-73]
<i>Glycyrrhiza uralensis</i>	+						+			[74-76]
<i>Rhizoma dioscoreae</i>	+	+					+			[77-78]
<i>Rhizoma atractylodes macrocephala</i>	+		+			+				[79]
<i>Rhizoma chuanxiong</i>		+						+	+	[80-84]
<i>Radix astragali</i>	+								+	[85]
<i>Paeoniae radix alba</i>	+	+			+				+	[86-90]
<i>Cinnamomi ramulus</i>			+	+						[91]
<i>Rheum officinale</i>	+		+							[92-93]
<i>Ophiopogon japonicus</i>	+									[94]
<i>Magnolia officinalis</i>		+	+							[95-96]
<i>Radix scutellariae</i>	+	+	+	+						[97]
<i>semen zizyphi spinosae</i>	+	+	+		+					[98-100]
<i>Coptis chinensis</i>	+	+	+			+				[101-103]
<i>Acorus tatarinowii</i>		+			+	+				[104-105]
<i>polygala tenuifolia</i>		+			+			+		[106]
<i>Platycladi semen</i>	+				+	+		+		[107-108]
<i>Prunus semen</i>						+	+			[109]
<i>Angelicae sinensis radix</i>	+	+								[110-112]
<i>Alpiniae oxyphyllae semen</i>		+		+	+					[113-115]
<i>Corni fructus</i>	+									[116]
<i>Cuscutae semen</i>	+									[117-118]
<i>Artemisiae scopariae herba</i>			+						+	[119-120]
<i>Gardeniae fructus</i>			+						+	[121-122]
<i>Saposhnikovia radix</i>	+									[123]
<i>Schizonopetae herba</i>	+		+		+					[124-125]
<i>Alismatis rhizoma</i>	+			+						[126]
<i>Achyranthis bidentatae radix</i>	+	+						+		[127]
<i>Moutan Cortex</i>	+	+	+							[128]
<i>Zingiberis rhizoma recens</i>		+	+							[129]

**Note:** A: Improve immune, B: Protect the nerve, C: anti-inflammatory, D: Antiallergic, E: Calm down nerves, F: Improve the gastrointestinal, G: Eliminating phlegm, H: Enhance memory, I: Protect liver

As we have learned from this review, recently biomarkers for the autism measurements have been extensively investigated in different perspectives. That is not only for helping on more precisely diagnoses the autism, but also can be used to measure the effectiveness of herbs medicinal treatment

However, the traditional prescriptions have disadvantages of large dose, perishable, inconvenient carrying. Also the outcome of effects of using compound the Chinese herbal medicine still needs to be determined. Therefore, in the absence of effective drugs and treatments, it is of far-reaching significance to create new forms of Chinese medicines which are convenient of carrying and taking on the foundation of the prescriptions and medicines to extract active ingredients.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

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