REVIEW
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History, philosophy and modern research of traditional Mongolian medicine

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Author contributions

Xi-Ye-Le Mu and Ming-Hai Fu conceived and disigned the manuscript. Xi-Ye-Le Mu, Lan Feng, Na Ta, Li Bai and Ru-Re A collected the data. Xi-Ye-Le Mu and Lan Feng worte the original draft. Gen-Na Ba and Ming-Hai Fu reviewed the manuscript.

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

TMM, traditional Mongolian medicine; CHSC, coronary heart Shutong capsule; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoproteins cholesterol; MRP3, multidrug resistance protein 3; MRP4, multidrug resistance protein 4; TNF-α, tumor necrosis factor alpha; FN, fibronectin; COL-IV, collagen type IV; ALB, albumin; Cre, creatinine; BUN, blood urea nitrogen; IL-2, interleukin-2.

Citation

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Abstract

The Mongolian nationality is a legendary ethnic group with a long history. In the long history process, Mongolians have developed broad, profound and gorgeous cultural patterns in many aspects, such as living, diet, clothing, language, writing, dance, art, medicine and health, which has accumulated tremendous achievements and formed its unique tradition. Traditional Mongolian medicine (TMM) is one of the most important ethnic medicines with systematic theories that has been developed over thousands of years among Mongolian people. The study of TMM has the potential to aid in the prevention and treatment of a wide range of diseases, as well as the provision of more effective medical services across the world. This paper reviews the key literature concerned with the origin and history, main theoretical philosophies and the modern research status of TMM. It provides a reference for the study of traditional medicine.

Keywords: traditional Mongolian medicine; developmental history; theoretical system; modernization research

Background

Traditional Mongolian medicine (TMM) is one of the China's four major ethnic medicine. The characteristics of ethnic medicine are ethnic cultural attributes (extensive and profound ethnic cultures), natural science attributes (common characteristics of medicine to cure diseases and save people) and ecological geographical attributes (mainly from and applied in various regions). With the rise of "advocating nature and returning to nature" and the development of "green medicine," ethnic medicine is people-oriented and draws from nature, which is in line with the slogan of human returning to nature, and its research has attracted more and more attention.

Traditional medicine is an inseparable part of the emergence of a culture developing its own theory, diagnostic and treatment methods, and reflects the unique background of each nationality. Therefore, we should consider traditional medicine as a part of the rich cultural heritage of each country of the globe. TMM is one of the world's oldest known medical systems, with a history dating back approximately 5,000 years [1]. Discovery of medicinal materials in ancient times was closely related to the life, activity, and the natural living conditions of the people.

The developmental history of TMM

TMM is a summation of the extensive experience of fighting against diseases for a long time and is one of the most valuable heritages of the Mongolian people [2]. It has originated before the 13th century, formed in the Yuan Dynasty, developed in the Ming and Qing dynasties, flourished in the contemporary era.

Mongolians have lived a nomadic life since ancient times. They lived in the cold, arid or semi-arid grassland, and fed on beef, mutton, and dairy products. Riding, grazing, migrating and fast galloping during the war made them easy to suffer from various injuries like bruises, fractures, and war wound. Under such climatic, geographical, dietary and living conditions, Mongolian ancestors insistently observed the relationship between animals and plants in nature, and initially mastered the nutrition, toxicity of animals and plants and their functions to prevent and cure diseases [2]. Through analyzing and summarizing the experience that has been accumulated to fight diseases during the long period of hunting, nomadism, agricultural production, migration, and fighting, the Mongolian people invented a series of treatments inclusive of regional and ethnic characteristics. For example, fire therapy to resist cold and dampness, osteopathy featured by bone setting and skull setting, as well as diet therapy like kumiss therapy based on the nutrition of the dairy product. This period before the 13th century is the bud and embryonic stage of Mongolian medical science.

In the Yuan Dynasty, TMM had made great progress for two reasons. First, the Chinese medicine and TMM nourished and promoted each other mutually. Second, it received institutional political security in the Yuan Dynasty. Followed the medical system in the Tang and Song dynasties, the government of Yuan Dynasty set up The Imperial Hospital and The Medical Institute of Benevolence to support and promote Mongolian medicine, thus providing a suitable condition for the all-round development of TMM. On the original basis, the TMM medical technologies such as orthopedics and traumatology had gained new progress. At the same time, by absorbing, drawing upon all useful opinions and in-depth research, the Mongolian ancestors had already summed up the understanding that "the origins of disease are no more than cold and fever," thus inventing and enriching "Theory of Cold and Fever" and other TMM medical theory [3], such as human anatomy knowledge, medicine knowledge, first-aid knowledge and infectious disease prevention knowledge. Yuan Imperial doctor Husihui's *Yinshan Zhengyao* (Figure 1A) is the first book of Mongolian medical diet therapy, which laid the foundation for the maturity of TMM after the 16th century [4].

In the Ming and Qing dynasties, with the introduction of Tibetan *Rgyud bzhi* and some ancient Indian medical theories, TMM reasonably absorbed the essence of Tibetan medicine and Indian medicine. Therefore, its basic theoretical research and clinical treatment practice had reached a new level. Taking Tibetan Medicine and ancient Indian Medicine's *"Wuyuan Xueshuo"* in *Four Medical Tantras* (Figure 1B) as references and starting point, on the theoretical basis of *"Three Roots and Seven Elements,"* absorbing the knowledge of Traditional Chinese medicine, and combining the characteristics of Mongolian region and folk therapy, the Mongolian people created an independent Mongolian medical theory system, in which *"Theory of Cold and Fever"* plays the core leading role. In Ixibalazhuer's book *Ganlu Tetralogy* (Figure 1C), he theoretically and practically elaborated the Bone Injury Treatment from many specific perspectives, such as "Trauma Surgery," "Dislocation Reduction," "Bone Injury Therapy," "Town Brain Therapy," etc. The contents were very substantial, in which the special theories of "Six Basic Diseases," "Cold Diseases," "Top Ten Major Symptom" were proposed. At the same time, on the basis of the increasingly rich experience of clinical treatment, a unique medical treatment system with ethnic characteristics came into being. Mongolian Bone Injury Treatment is extremely unique and magical. Mongolian medical expert Chuerjimorgen was famous for the exquisite precision of his treatment in surgery. Thus, he was written into *Draft History of Qing Dynasty*. He is a typical representative of the large number of Mongolian "Miracle Doctors". With the prosperity of Yellow Sect in the Mongolian region, temples in large-scale all were equipped with Mamba Raseng. Mamba Raseng is not only the medical center, but also the base for studYing and researching the theories of Mongolian and Tibetan medicine. It has cultivated a great number of talents in this field. Mongoliajin, located in the Eastern part (now Liaoning Fuxin), is known as "The Birthplace of Mongolian medicine". As early as 1669, RuiYing Temple was built and equipped with Mamba Raseng. Research on Mongolian Medicine Theories was just unfolding. Mongolian doctors also achieved more profound understanding of the nature and flavor of Mongolian drugs. Under such situation, three typical masterpieces of Mongolian Medicine appeared. They are *Baijing Drugs Recognition and Discrimination, Recognition of Drugs* (Figure 1D), *Correct Mongolian medicine authentication* (Figure 1E). Another famous book *Magic Code and Recipe* (Figure 1F) *and Recipe* selected more than 3,000 prescriptions for internal, external, women, children, facial features, fever and infectious diseases. Especially *Ganlu Tetralogy* which made a creative contribution to exploring the basic theories and sorting the traditional therapies laid a solid foundation for the modern Mongolian medicine. In a word, the situation that theory and the practice mutually confirm and promote each other was a major characteristic of the Mongolian Medicine development in this period [5-8].

Figure 1 Famous works. (A) *Yinshan Zhengyao*; (B) *Four Medical Tantras*; (C) *Ganlu Tetralogy*; (D) *Recognition of Drugs*; (E) *Correct Mongolian medicine authentication*; (F) *Magic Code and Recipe*.

The founding of New China ushered in a new era of TMM progress. Under the brilliant care of the Party and State, TMM dramatically developed. Preliminary statistics showed that many new Mongolian medical institutions, research centers as well as TMM schools were established to cultivate Mongolian talents purposefully and designedly. For example, the first TMM school was in Mongoliajin (Fuxin) RuiYing Temple in Liaoning Province by a famous Mongolian doctor Badara. In 1958, Inner Mongolia Medical College, famous as a West Medicine, first set up TMM department. In 1980, Inner Mongolian National Medical College was established in Tongliao and renamed Mongolian Medical College of Inner Mongolia in 1987, and expanded as Inner Mongolia University for Nationalities after merging two other colleges in 2000. In 2016, Tongliao was entitled "Mongolian Medicine Capital of China". A new pattern and a new state for the development of Mongolian medicine came into being. On the basis of inheriting its tradition, ancient Mongolian medicine absorbs the essence of the contemporary era, brimming over with vigor and vitality. It insistently explores and progresses in many aspects such as the connection with global society and modern science and technology, as well as its collaboratization, scientization, scale expansion, informatization and industrialization [5].

Overview on TMM theory

TMM is a unique theoretical system on the basis of ancient philosophy was formed. The theoretical system of TMM mainly includes the theory of Arga-Bilig (Yin and Yang), the theory of five elements (White Astrology and Black Astrology), the theory of three elements (wind, bile, phlegm), the theory of seven constituents and three toxins theory and six basic diseases and theory of cold and heat (see Figure 2) [8].

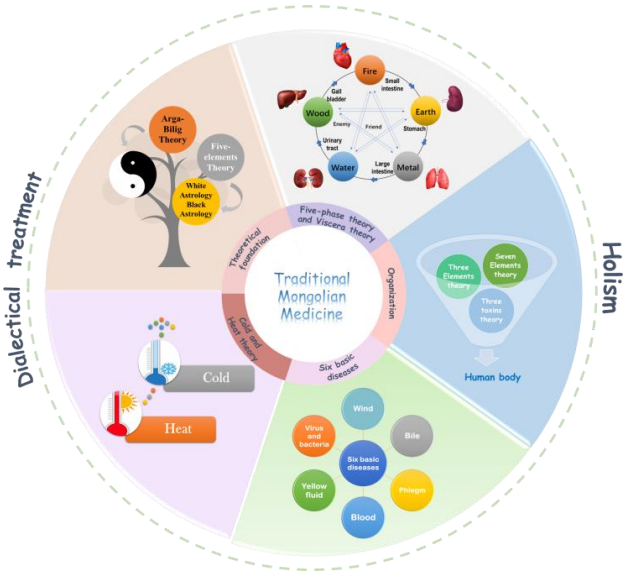

Figure 2 TMM theoretical system

Theory of Arga-Bilig in Medicine

Based on Mongolian ancient philosophy, arga and bilig (Yin-Yang) refer to the balance of nature or the circulation of karma, the good and evil. The arga-bilig is the fundamental principle, which has been applied in Mongolian life and medicine since at least the Stone Age. The original concept of arga and bilig came from the observation of nature and the environment. Arga originally referred to the sunny side while billig referred to the shady side of a slope. Later, this thinking was used to understand other occurrences, which occurred in pairs and had complementary and opposing characteristics in nature. Some examples include: sky and earth, day and night, water and fire, active and passive, male and female. In addition, TMM arga and bilig theory are very similar to that of TCM Yin-Yang. TMM uses the relationship between Yin and Yang to elucidate the tissue structure, physiological function, pathological changes and drug properties of the human body, and is extensively used in the diagnosis and treatment of diseases, as well as in determining the principles of treatment. Of course, owing to the different theoretical systems, the application of Yin-Yang theory in different medical disciplines is also distinct, such as TMM believes that five internal organs (solid organs believed to contain the essence of five elements) belong to Yang and six bowels (organs with hollow accumulated by the essence of five elements) belong to Yin. On the contrary, TCM holds that the five internal organs into Yin and the six bowels into Yang [9, 10].

The human body is also divided into arga and bilig. The upper and right parts of the body, the exterior part of the body, and the back are all arga. The lower and left parts of the body, the interior of the body, and the abdomen are all bilig. The five vital organs are arga; the six hollow organs are bilig. Arga can be viewed as the functional aspect, and bilig can be viewed as the substance aspect. The various functional activities of the body depend on the support of the nutrients. Without nutrients, there would be no sustenance for functional activity. In this way, arga-bilig within the human body are mutually supportive. They act together to protect the organism from invasion by pathogenic factors and to maintain a relative balance within the body.

The theory of arga-bilig is also applied to explain pathological changes. When arga pathogenic factors cause disease, this may lead to an excess of arga, which constrains bilig and gives rise to warm symptoms. When bilig pathogenic factors cause disease, this may lead to a preponderance of bilig, which makes arga deficient and gives rise to cold symptoms. In TMM, the root cause for the occurrence and development of ill health is imbalance between arga and bilig. This is the basic principle for treatment according to TMM. The question is always balance and how to maintain it. In treating a warm syndrome, drugs with a cool quality such as camphor, white sandalwood, solidified cow bile, safron and swertia chirata and accessory therapies such as venesection (bloodletting) and acupuncture should be used in order to decrease the supremacy of arga. Supremacy of bilig leads to hyperfunction of the body as well as coldness. Treatment would necessitate drugs with a warm quality such as zingiber officinalis, black salt, myristica fragrance and accessory therapies such as moxibustion and acupuncture with heat [11, 12].

Theory of five elements

The theory of five elements is a scientific corpus of knowledge that explains the structure and function of all things animate and inanimate, as well as their origin, progress, evolution, extinction and the relationships between them. TMM has two categories of the of five element's theory: five elements of White Astrology and five elements of Black Astrology. Each of these has different principles and application methods.

White Astrology was imported from Indian Ayurvedic medicine (knowledge of life) into TMM through the books, namely: "Ashtanga Hrdayam Samhita" and "Four Medical Tantras" during 16th century. White Astrology embraces the five elements: earth, water, fire, wind and space. These five elements unite the microcosm of the body and the macrocosm of the universe, which become one basic material common to all things.

The five elements' theory of Black Astrology was incorporated from China into TMM around the 14th century [13]. According to Black Astrology, the five elements are wood, fire, earth, metal and water. Unlike white astrology, black astrology focuses on the relationship between these elements: mother, son, friend and enemy. It expresses a comparison and contrast, a structure and activity between the microcosm of the human body and the macrocosm of the universe. It works with the law of the unity of opposites. According to TMM, the five elements of Black Astrology are divided into five parts: categorization, relationship between mother and son, relationship between friend and an enemy, the grouping of the five elements and medical application. The categorization of the five elements of Black Astrology is related to the changing of seasons because seasonal change influences the activities of the human body. For example, in

springtime, snow and ice are melting, the earth is thawing and buds begin to burst. During this period, the wood element becomes dominant and the activities of the liver and gall bladder begin to increase.

In contrast to TCM, TMM has two "five elements," namely the five elements of astronomical calendar and the five elements of destiny. TMM is used to name them "white astrology" and "black astrology". Black astrology is almost the same with the theory of the five elements of TCM, while the white astrology cannot better explain the relationship between viscera and the pulse changes of the five internal organs with the changes of the four seasons. However, the core theory of TMM, the theory of "three elements" and "seven constituents," is mainly based on the white astrology, which leads to the fact that the "black and white" astrology theory in TMM cannot be completely integrated [14-16].

Theory of three elements

Wind (khii), bile (Shar) and phlegm (Badgan) are considered as the main theoretical essences of TMM. Any healthy body naturally contains wind, bile and phlegm; However, the three elements support each other in the body they also contradict each other. Thus, the activities of wind, bile and phlegm are true to the law of the Unity of Opposites, keeping the body in balance, which is very important for health. As long as they are in balance, illness will not occur. Disorder of the body will only occur if any four conditions (diet, behaviour, season or sudden change due to shock, and infectious diseases and so on) affect the body from the exterior. This will disturb the three elements and the body will become sick, i.e., one or other of them will predominate or wind, bile and phlegm balance will be upset. Thus, good health and bad health and cause and effect are two sides of same coin. In a healthy body we consider three elements to be in a state of balance, so this is termed "the three healthy conditions". In contrast, in an unhealthy body, we consider the three elements to be in a state of imbalance, so that this is termed "the three disorders". An imbalance of the elements allows illness to occur (Table 1).

According to arga-bilig theory, there are 3 sorts of pulses in the human body, which are generated by wind, bile and phlegm. The first pulse is of combined arga and bilig. When the embryo is formed in the womb, the combined pulse is separated from the embryo's umbilical cord and aligns itself along the main line of the embryo. The wind comes into existence through this combined pulse and is located in the lower part of the body. The second is an arga pulse. The arga pulse belongs to the fire element. It branches off from the embryo's umbilical cord and stretches itself along the right side and is located in the middle of body. The arga pulse forms bile. The last is a bilig pulse belonging to water and earth elements. It also branches off from the embryo's umbilical cord and establishes itself along the left side and is located in the upper parts of the body. The bilig pulse forms phlegm [6, 12].

In addition, Wind, bile and phlegm have many qualities exist, twenty in all. The wind has six qualities: lightness, mobility, coolness, thinness, hardness and roughness. Bile has 7 qualities: heat, sharpness, oiliness, lightness, pungency, smooth bowel function and moisture. Phlegm has 7 qualities: heaviness, coldness, oiliness, bluntness, smoothness, steadiness and stickiness. These qualities which express normal and pathological functions of the human body.

TMM theories in clinical applications

The seven constituents. According to the TMM clinical philosophy, wind, bile and phlegm represent the theoretical and subjective understanding of the body, whereas the seven constituents represent their objective features. The seven constituents are: nutritional essences, blood, flesh, fat, bone, marrow, and regenerative. The nutritional essences are: digestion in the stomach and intestines produces nutritional essences. Waste is excreted as stools and urine. Blood is produced when nutritional essence reaches the liver. A by-product is bile contained in the gall bladder. Blood feeds flesh and also produces lymph, which is discharged from the "nine holes" which are the eyes, nose, ears, etc. Fat is a by-product of flesh. It is excreted from the body in the form of perspiration and gives an oily quality to the skin. Fat essences feed bone tissue. Its manifestations are bones, teeth, nails, hair and fuzz. Hair and fuzz are also considered as bone tissue in TMM. Marrow: The essence of bone turns into marrow, or the bone produces the marrow. Waste products from marrow are excreted through the large intestine and rectum. Regenerative fluids: Marrow produces regenerative fluid, which is the last constituent and is considered to return to the heart. Its by-product becomes "sperm and semen". These are the basic components of wind, bile and phlegm. If wind, bile and phlegm become imbalanced, they will adversely affect the seven constituents [11, 12].

The seven constitutions. Owing to individual differences, there are seven types of constitutions in TMM. Respectively, wind-dominated, bile-dominated, phlegm-dominated, wind-and-bile-dominated; wind-and-phlegm-dominated, and bile-and-phlegm-dominated and all-three-elements-dominated. The study of human body constitution is an important part of implementing the holistic concept of Mongolian medicine and the principle of syndrome differentiation and treatment [12].

Table 1 Information of three elements

	Wind	Bile	Phlegm
To sustain	Hips and Waist	Liver and Gall bladder diaphragm	Brain
Pulse	Combined of arga and bilig pulse	Arga pulse	Bilig pulse
Body location	Lower body	Middle body	Upper body
Types	Life-sustaining wind; Ascending wind; Pervasive wind; Accompanied by fire wind; Downwards-voiding wind.	Digestive bile; Color-regulating bile; Determining bile; Sight bile; Complexion bile.	Supportive phlegm; Decomposing phlegm; Sensory phlegm; SatisfYing phlegm; Connective phlegm
Qualities	Lightness, mobility, coolness, thinness, hardness, roughness	Heat, sharpness, oiliness, dry, lightness, pungency, smooth bowel function, moisture.	Heaviness, coldness, oiliness, bluntness, smoothness, steadiness, stickiness.
Function	Exhalation and inhalation, permeates nutritional essence, produces stools and urine, the sense organs and sustains the body	Occasions hunger and thirst, digests food, provides body heat clarifies complexion, and intelligence. Promoting courage	Body growth; stabilizes mind; firmly, induces sleep, connects the joints, promotes patience. Tranquillizes the mind

Diagnostic methods. TMM recognizes two causes of sickness, which refer to them as internal and external. The three elements are the internal cause of imbalance. The external cause of imbalance is diet and behavior (regime), season and the influence of unexpected conditions.

TMM physicians must have knowledge of the human body, in both its healthy state and diseased state. Generally speaking, a healthy body is considered a normal state. The body system is analyzed according to the following categories: There are five major body organs (five solid organs): heart, lungs, liver, spleen and kidneys. The digestive and excretory systems consist of six parts (six hollow organs): stomach, small intestine, large intestine, gall bladder, urinary tract, and reproductive or sexual organs "samshi". The three types of excretions are: stool, urine and perspiration [12].

There are three basic methods of diagnosis in TMM: (1) Observation: observation of the symptoms of the external body and observation of the excretions. (2) Palpation: The method of diagnosis is pulse reading. (3) Questioning: The method of diagnosis is by questioning-asking the patient how and when the problem started, its cause, factors, symptoms, location, magnitude of pain and which particular foods harm or help.

Treatments

Generally speaking, the treatment of TMM is divided into two main groups: the principle of treatment and the method of treatment. Both of them are related significantly to the four following methods of treatment: (1) Diet (2) Behavior (3) Medication (4) Physical or accessory therapy.

There remain seven forms of evacuating medicine in TMM: lipid therapy, cathartic therapy, emetic therapy, nasal drug therapy, mild catharsis therapy, fierce catharsis therapy, purging therapy of arteries and veins: (1) lipid therapy refers to the practice of treating disorders with lipid preparations. It is effective at inhibiting excessive wind, tonifYing Yang, moistening the intestines, clearing and brightening the organum sensuum, strengthening the body, and extending life; (2) Cathartic therapy employs a special medication to irritate the digestive tract in order to induce defecation, cleanse the intestines and stomach, and eliminate accumulation. It aids in sickness treatment, stimulates digestion, and cures bile; (3) Emetic treatment is the use of emetic medications to stimulate the digestive tract in order to remove illnesses and toxins. It is also one of the treatments used to remove phlegm. Primarily, it is used to treat gastrosis and thoracopathy, as well as acute alimentary toxicosis and drug poisoning; (4) Nasal treatment heals disorders by absorbing drugs through nasal mucosa. Nasal medication therapy will affect cephalopathy since the nose is the head's entryway. The liquid drugs can be poured into the nose, the plaster filled, and the powder swallowed. This treatment comprises nasal appease and clearing drugs; (5) Mild catharsis therapy treatment cures disorders of the lower body by injecting certain medications into the anus for excretion. The dosage form utilized in this procedure is a high-viscosity, gelatinous liquid combined with water, oil, and milk with a powdered prescription. Its use resembles that of the current medical enema; (6) Fierce catharsis treatment cures disorders of the lower body by injecting certain medications using specialized equipment into the anus. Similar to mild-nourishment therapy, but focused at healing illnesses of the lower body; (7) Purging therapy of arteries and veins refers to the employment of certain medications to stimulate the alimentary canal in order to dredge the pulse and expel diseases from the vascular system and urethra [17].

The final method of treatment is physio-therapy, divided into mild and rough therapy. Rough therapy is made up of venesection, moxibustion and piercing or acupuncture. Mild therapy is composed of hot applications, massage or applying oil and soaking. For example, mild therapy for the wind patient includes massage with year-old butter and hot applications of oil. Rough therapy for the wind patient involves placing moxa on the selected points of wind; these are on the top of the head, the first, fifth and sixth vertebrae of the spinal cord, the sternum, etc. For the bile patient, mild therapy includes soaking and covering therapy and mild purgatives. Rough therapy for the bile patient is venesection and cupping. For the phlegm patient mild therapy would be hot applications, saunas and mild vomiting. Rough therapy for the phlegm patient is hot acupuncture therapy and as much moxibustion as possible.

Modern research on classical TMM formulas

Traditional Mongolian medication has expanded from herbs and plants to include a wider range of raw materials like animals and minerals. There are two kinds of proven recipes. A single recipe using only one medicinal herb for treating diseases and a combined recipe using more than two kinds of medicinal herbs. During the long period of accumulation of experience in composing and formulating the prescriptions, a unique theoretical system on the basis of ancient philosophy was formed [18].

Mongolian medicine formula follows the theory of "Monarch (main medicine), Minister (auxiliary medicine), Assistant, and Guide medicine" and the theory of "taste, effect and digestion," and exert the maximum effect according to the law of syndrome differentiation and treatment, which is the basis of clinical treatment of Mongolian medicine (Figure 3) [12].

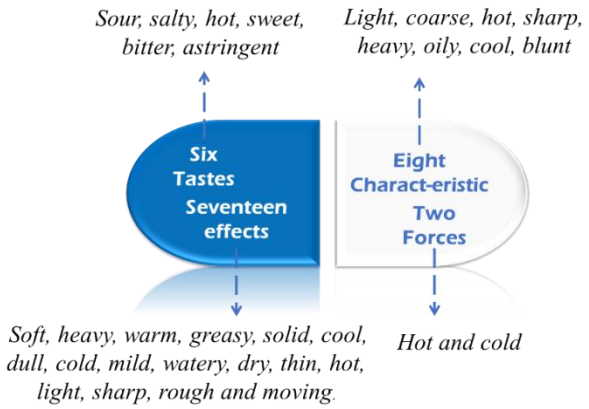

Figure 3 Basic knowledge of Mongolian medicine theory

As the study of pharmacy used in traditional health science is deepening, to the level of body, cell, molecule, membrane, "Antioxidant Preoxidation of Lipids," "Deterioration of Immunization Configuration" the harmonization processes are carried out by integrating different approaches. Furthermore, there are about many formula substances are being introduced into practice such as Tungalag-5 powder, Digda-4, Ruda-6, Senden-4, Baatar-7, Zhenbao pill that relax the central nervous system, intensify harmonization, protect the heart, kidneys, liver and stomach, revive immunity and prevent cancer. In Chinese pharmacopoeia (2020), which includes 12 classical Mongolian medicine (Table 2) formulas and 4 drugs.

Tungalag-5 powder

Tungalag-5 powder, a classical Mongolian medicine formula, has been clinically used to cure digestive disorders for many years. It contains *Punica granatum*, *Carthamus tinctorius, Piper longum, Cinnamomum cassia, Myristica fragrans.* Its properties are to invigorate the stomach's vital functions, remove undigested food, help digestion and absorption, promote bodily heat, and promotes the flow of digestive enzymes and salivary amaltase. It is usually used for treating gastritis due to cold and dampness, stagnation, belching and indigestion. Its main bioactive components are kaempferide, piperine, cinnamaldehyde, hydroxysafflor yellow A, ellagic acid (Figure 4).

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Table 2 Classical TMM formulas

Formula	Action	Indication
Sanzi decoction	Clear heat cool blood detoxification, separation of turbid blood.	Diseases related to heat, dampness, poison and blood stasis
Sema-3 decoction	Antipyretic and diuretic.	Bladder fever, anuresis, edema.
Chagan decoction	Clearing up toxic heat and dispelling wind heat in the treatment of exterior symptom complex.	Epidemic febrile disease chills, fever, headache due to heat in the blood, pains and swelling of the throat, stabbing pain in the region of the chest and ribs.
Tungalag-5 powder	Invigorate the vital functions of the stomach and remove undigested food and to help digestion and absorption.	Gastritis due to cold and damp, stagnation, belching, indigestion.
Shaji-5 powder	Suppresses coughing “vitiated” fever expels pus and blood from lungs.	Chronic inflammation of lungs
Shijed-6 powder	Clearing “phlegm”, new and old dyspeptic function.	Constipation, Irritable bowel syndrome caused by “phlegm” and wind, abdominal distention.
Ruda-6 powder	Remove liver-stagnation and restore the normal function of a depressed liver.	Spasms and convulsions hiccups, vomiting, gastric spasms and indigestion.
Uzem-7 decoction	Stop coughs; Stop asthma.	Colds and influenza, stuffiness sensations in the chest with shortness of breath, distension sensations in the flanks, and symptoms such as flushed cheeks, coughing thick phlegm, and chest pains.
Xusha-7 pill	Restrain heart wind, calm the mind and improve heart function	Angina, heart wind, heart failure, asthma, palpitations.
Zandan-8	Clear heat, cough and relieve pain	Lung fever, Cough, sputum, fever, angina
Rang Agaru-8 powder	Restrain wind, relieve pain, benefit respiration, clear heat.	Cough, sputum, palpitations, shortness of breath, pain in chest and hypochondriac, tracheitis, asthma.
Dali-16	Inhibit phlegm’s wind, relieve cough and asthma, warm stomach and benefit fire, dehumidify, make the essence normal transformation smooth.	Dizziness, thirst, dry throat, lung heat and asthma, heat stroke, spontaneous sweating, stomach fire, headache, toothache.

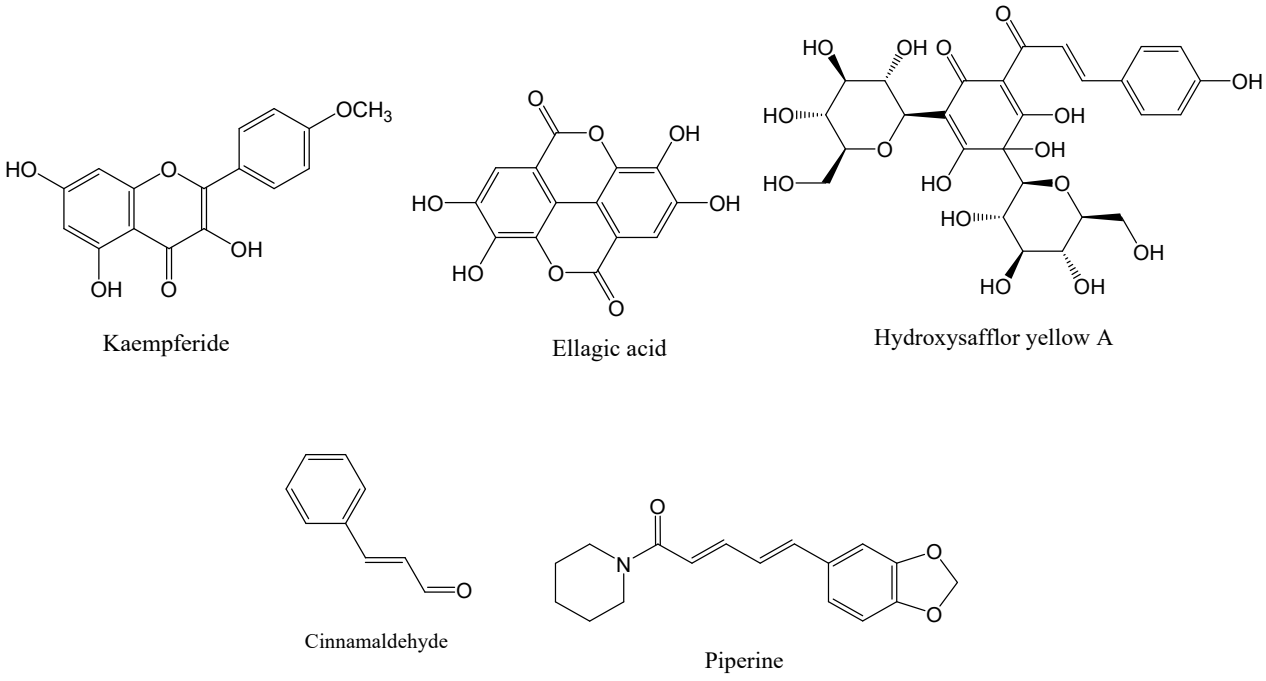


Figure 4 Major active compounds isolated from Tungalag-5 powder

Tungalag-5 powder has a wide range of dyspepsia and other pharmacological effects. Numerous studies have manifest that has a good clinical effect, including irritable bowel syndrome, hyperlipidemia, coronary heart disease, hypertension, diabetes and stroke and other diseases, with definite curative effect [19]. Tungalag-5 powder remarkably decreased the levels of triglycerides (TG), total cholesterol (TC), low-density lipoproteins cholesterol (LDL-C) in serum of experimental hyperlipidemia rats, which showed that it had a benign regulation effect [20-23]. Researchers also discovered that Tungalag-5 powder may be one of the mechanisms of treatment of non-alcoholic fatty liver disease by increasing gene and protein expression of LXRα in 3T3-L1 adipocytes [23]. Modern clinical studies demonstrated that Tungalag-5 powder can improve the clinical manifestations of diarrhea in children [24]. While study on diarrhea model induced by Senna leaf in mice, which can increase the level of serum D-xylose, the phagocytosis of inert carbon particles in the reticuloendothelial system, the production of hemolysin antibody induced by sheep red blood cells and thymus index to further treat diarrhea mice and enhance their immunity [25]. In addition, acetic acid-induced writhing responses in mice that quantitatively determine pain were significantly inhibited by ethanol extract of Tungalag-5 powder [26].

In this prescription, 400 g *Punica granatum* is used as sovereign medicine, 200 g *Carthamus tinctorius* is minister medicine, 50 g *Piper longum,* 50 g *Cinnamomum cassia,* 50 g *Myristica fragrans* are assistant medicine, which dosage is in Chinese pharmacopoeia. However, these studies predominantly focused on pharmacology and lacks modern quality control measures, which cannot fully clarify the effective components and mechanism of Tungalag-5 powder.

Digeda-4 decoction

Digeda-4 decoction is one of the typical formulas of administration of liver diseases. It is named after sovereign medicine- *Lomatogonium carinthiacum* and via combined synergistically action of multiple formula components, including *Picrorhiza scrophulariiflora, Gardenia jasminoides, Dianthus superbus,* with less adverse reactions. Digeda-4, exerts eliminating bile, clearing heat, strengthening stomach, callus, according to the mechanism of TMM. Active compounds in Digeda-4 are a complex combination of Swertiamarin, Geniposide, Picrosid. Research on the chemical constituents of Digeda-4 has been in place since the recent years. Since then, many researchers have focused on content determination from this formula. Nevertheless, few studies on prescription chemical composition.

A study confirms that Digeda-4 might upregulate the nuclear receptor Car and Pxr via expression of multidrug resistance protein 3 (MRP3) and multidrug resistance protein 4 (MRP4) in the acute liver injury of rats induced by pylorus ligation [27]. Another study discovered that Digeda-4 reduce the level of blood lipid, improve the liver function injury and insulin resistance, and has a certain antioxidant, improving oxidative stress and lipid peroxidation reaction [28]. Identification of compounds and blood components in Digeda-4 decoction by UHPLC-Q-TOF-MS/MS, detected those fifty-three compounds, including flavonoids, iridoids, coumarins and isoflavones (Figure 5), with obviously protect liver and promote gallbladder, antibacterial, detumescent analgesia, antiviral [29]. By reviewing clinical studies, it has been found that Digeda-4 decoction have a good application in the treatment of fatty liver, cholecystitis, gallstones, viral hepatitis, liver cirrhosis, as well as pretreatment with Digeda-4 decoction prevents “blood, bile” fever, bad breath, cardiovascular and cerebrovascular diseases, and improve vision, improve immunity and so on [30].

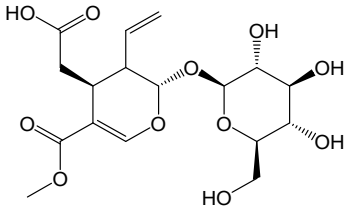
Digeda-4 decoction was also included in the Drug standards for Mongolian Medicines formulated by the Ministry of health of the people’s Republic of China. Considering all of this evidence, it seems that the compound research still lags behind, lack of controllable quality standards, and lack of pharmacology, efficacy and toxicology research.

Saorilao-4 decoction

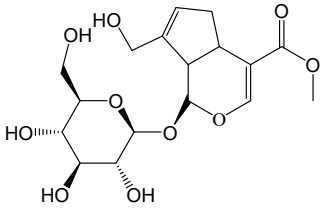
Saorilao-4, a classical prescription, exerted an excellent treatment of lung fever and all kinds of heat cough. According to ancient books, Saorilao-4 is a mixture of 150 g *Radix Glehniae*, 90 g *Glycyrrhiza uralensis*, 90 g *Polygonum bistorta* and 90 g *LacLacc*. There is *Radix Glehniae* plays the major role among Saorilao-4, which has sweet taste, slightly bitter, cool, soft and clear lung heat, cough effect. Its active components of Saorilao-4 have been reported to improve lung heat cough and other diseases in clinical.

Owing to the drug combination superiority in TMMs, the Saorilao-4 is adopted in order to explore the mechanism of their protective action, both in vitro and in vivo. The expression of Smad protein plays a crucial part in the pathogenesis of formation of pulmonary fibrosis in a rat model; against induced idiopathic pulmonary fibrosis has a potential application. This analysis results indicated that Saorilao-4 decoction can significantly ameliorate the pulmonary pathological changes, delay and reverse the progression of pulmonary fibrosis. The mechanism may be related to the inhibition of inflammation, improvement of lipid peroxidation, down-regulation of TGF-β_1 and Smad3 mRNA expression [31]. Then, Saorilao-4 has the potency to anti-tumor effect on the proliferation of human lung cancer NCI-H460 cells in vitro. Through RT-PCR analysis results showed that Saorilao-4 could induce the apoptosis by regulating the expression of GADD45a in human lung cancer cells [32].

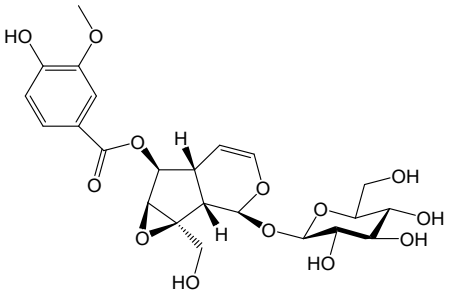
Saorilao-4 decoction has been registered in the drug standards for Mongolian Medicines formulated by the Ministry of health of the people’s Republic of China. However, which chemical composition and pharmacological action of Digeda-4 decoction is involved in the whole formula reports remains defective.



Swertiamarin



Geniposide



Picroside II

Figure 5 Major active compounds isolated from Digeda-4 decoction

Coronary heart Shutong capsule

Cardiovascular diseases cause nearly one-third of all deaths in human beings worldwide. Coronary atherosclerotic heart diseases, also known as coronary heart disease (CHD), is the most common type of cardiovascular disease (CVD) and one of the fatal diseases among humans. Currently, the conventional drugs used to treat CHD are mainly western drugs, which usually aim to act on individual targets, such as beta-blockers, nitrates, statins, calcium channel blockers or angiotensin-converting enzyme inhibitors. Aiming at this phenomenon, researchers have developed the first patented Mongolian medicine in cure coronary heart disease: Coronary heart Shutong capsule (CHSC), which has fewer side effects and unique advantages for treating CHD. CHSC is composed of five herbal medicines: *Fructus Choerospondiatis, Salvia Miltiorrhiza, Flos Caryophylli, Borneolum* and *Concretio Silicea Bambusae.* Previous studies have shown that the formula has four main active ingredients, protocatechuic acid, cryptotanshinone, borneol, and eugenol (Figure 6) [33]. It has multiple functions of promoting blood circulation, removing blood stasis, activating menstruation and collaterals, and purging qi to relieve pain, irritability, difficulty breathing, dizziness, and fatigue.

A large and growing body of literature has investigated Coronary heart Shutong capsule. It markedly alleviated the expression of tumor necrosis factor alpha (TNF-α)and NF-κB in atherosclerotic plaques of mice by high-fat diet induced CHD, probably because it exerts strong inhibit the overactivation of NF-κB signaling pathway and restrain the accumulation of inflammatory cells in the arterial wall [34]. There is evidence that its four main active ingredients have anti-apoptosis and suppress calcium overload in vitro cell experiments, and in rodent studies it exerted their protective effect via their antioxidant and anti-inflammatory activities. In case of a rat model of pressure overload-induced cardiac fibrosis, it was confirmed that mechanism of action might be through TGF-β/Smad3 pathway and so as to achieve notably inhibited differentiation of fibroblasts into myofibroblasts, reduced ventricular remodeling, then finally improved cardiac function [35]. Moreover, a number of multicenter randomized clinical trials have been conducted and provided more evidence for the treatment of cardiovascular diseases by CHSC.

The coronary heart Shutong capsule is guided by Mongolian medicine theory. Much of the current literature on Coronary heart Shutong capsule pays particular attention to its treatment of cardiovascular diseases. Also, according to the investigation, whether combined with western medicine, Coronary heart Shutong capsule have achieved great achievements, and total sales 1 billion yuan.

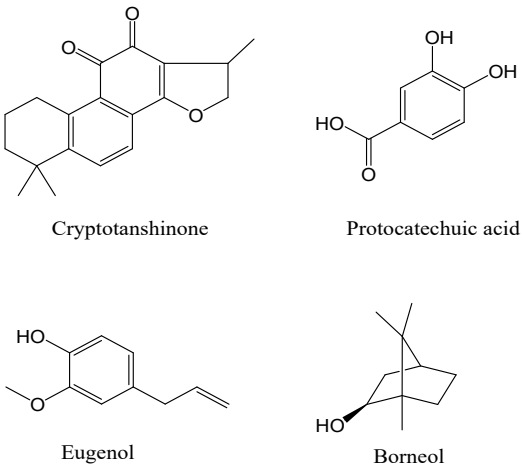


Figure 6 Major active compounds isolated from Coronary heart Shutong capsule

Naran Mandal powder

Naran Mandal powder is a renowned TMM widely used for the treatment of nephropathy in the clinic. It consists of eleven crude herbs: *Punica granatum, Polygonatum odoratum Druce, Cinnamomum cassia Presl, Elettaria cardamomum, Polygonatum kingianum Goll et Hemse, Asparagus cochinchinensis, Piper longum, TribulusL, Carthamus tinctorus L, Malva neglecta Wallr and Mirabilis himalaica (Edgew)*. Naran Mandal powder promote normal flow of urine, tonic for the kidneys and urinary bladder, stop diarrhea both from 'hot' and 'cold' causes, effective against 'cold' disorders such as diarrhea, cold parasites, serumal disorders, and arthritis. Due to lack of digestive heat, proper metabolic functions are impaired and subsequently they bring about disorders such as stomachal tumors and so forth. This drug is especially effective for promoting digestive heat and this, in turn, increases the bodily sustainers and thereby acts as an elixer and tonic.

Naran Mandal powder plays a protective role by inhibiting fibronectin (FN) and collagen type IV (COL-IV) expression, ameliorating the serum levels of albumin (ALB), creatinine (Gre), blood urea nitrogen (BUN), TG, TC, interleukin-2 (IL-2), TNF-α in different degree during Adriamycin-induced renal injury [36]. Recent studies showed that Naran Mandal powder can anti-Fatigue and exercise performance improvement by decreasing the associated antioxidant responses, such as enhancing the activity of antioxidant enzymes, reducing the production of oxygen free radicals, regulating the endocrine system and energy metabolism [37]. A study proved that proliferation of Human gastric cancer MGC803 cells was obviously attenuated and apoptosis was induced after Naran Mandal powder treatment in a dose-dependent manner. Furthermore, the results of many clinical trials have indicated that combination of Naran Mandal powder and western medicine with Type 2 diabetes effectively controlled blood glucose and urinary microalbumin levels, substantial improved clinical symptoms, and no marked changes in liver and kidney functions, and no adverse reactions such as hypoglycemia. Therefore, the combined use of Naran Mandal powder with diformin tablet was more effective than western medicine. These funding suggest that the Naran Mandal powder could be suitable candidates for further development as drugs for diabetes therapy.

Discussion and outlook

Due to unique theoretical system of TMM, it is undoubtedly the source of promoting the development of ethnic medicine [38]. It is necessary to deeply excavate the connotation of its theoretical system and strive to promote the improvement and development of traditional medical system. There remain several aspects about which relatively little is known: identification of inputs in the production of traditional medications, collection of inputs in the proper times, processing and storage. Also, preparation of medications in compliance with technology, putting them into containers in clean environment, labeling the containers and storing them in condition with appropriate moisture, temperature and light exposure are challenges. Additionally, improvement of quality control guidance of medications, increase of the number of medications in the registry, simplification of process of medication licensing and gradual improvement of medication production factories to comply with GMP are needed to be carried out. One of the tough challenges for all researchers in this domain is making better use of modern science and technology, learning from the development experience of other ethnic medicines, further research and development of TMM, better maintaining and giving full play to its characteristics and advantages, adhere to standardization, achieve modernization, and keep forging ahead so as to make greater contributions to the health care and rehabilitation of the people.

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