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Review

Sugemule-10: Source of prescription and modern clinical application

Xiangmei Chen^{d,e}, Liangliang^{a,b,*}, Hadanbaoligao Zhang^a, Buriebao^{b,c}, Xiulan Wang^e, Wurihan Tai^b^a Affiliated Hospital of Inner Mongolia Minzu University, Tongliao 028005, China^b NMPA Key Laboratory for Quality Control of Traditional Chinese Medicine (Mongolian Medicine), Tongliao 028000, China^c National and Local Joint Engineering Research Center for Mongolian Medicine Research and Development (Development and Reform Commission), Tongliao 028000, China^d Key Laboratory of Mongolian Medicine R&D Engineering, Ministry of Education, Tongliao 028000, China^e Mongolian Medicine Research and Health Science Center of Inner Mongolia Minzu University, Tongliao 028000, China

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ABSTRACT

Sugemule-10, one of the traditional Mongolian medicine (TMM) formulae, is derived from *Four Medical Classics* (Vol. 4) and composed of 10 Mongolian medicines. It is used to treat kidney cold, low back pain, urinary obstruction, kidney/bladder stones, and is the main prescription for kidney cold. The current research on Sugemule-10 is mostly focused on its clinical efficacy, and few papers are available upon its historical changes. Therefore, we systematically reviewed Sugemule-10 from the aspects of prescription source, prescription interpretation, efficacy evolution, and modern clinical applications.

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* Corresponding author.

E-mail address: llmy.03@163.com (Liangliang).

1. Introduction

Sugemule-10, also known as Yizhi Wenshen Shiwei Pill, is a classic prescription for the treatment of kidney disease in traditional Mongolian medicine (TMM). It is the main formula for treating kidney cold, described in *Four Medical Classics*, the famous ancient authoritative medical works in Mongolia and Tibetan areas integrating Mongolian medical practice and theory and consisting of four volumes. General Principles (Vol. 1) consists of 26 chapters, elaborating programmatic exposition of human physiology, pathology, diagnosis and treatment; The treatise book (Vol. 2) consists of 31 chapters, elaborating human physiology and anatomy, pathology, etiology, pathogenesis, health care knowledge, drug properties, diagnostic methods and treatment principles; Secret formula (Vol. 3) consists of a total of 92 chapters, discussing the diagnosis and treatment of various diseases. Supplement (Vol. 4) consists of a total of 28 chapters, discussing the pulse diagnosis, urine diagnosis, prescription drug compatibility, drug processing, function and route of administration and external treatment (bloodletting, moxibustion, fire moxibustion, external application, and cupping) (Yu, 1991). Sugemule-10 is composed of 10 Mongolian drugs, such as *Amomi Rotunds Fructus*, *Zingiberis Rhizoma*, Bright Salt (Halite), *Piperis Longi Fructus*, *Caesalpiniae Cristae Semen* (dry mature seeds of Leguminous plant *Caesalpinia crista* L.), *Malvae Fructus*, the ripe fruits of *Syzygium cumini* (L.) Skeels, the fruits of *Mangifera indica* L., Crab (the dry whole of *Eriocheir sinensis* H. Milne-Edwards), and *Moschus* (the dry secretion from the sachet of mature male musk deer *Moschus berezovskii* Flerov, horse musk deer *Moschus sifanicus* Przewalski or protomusk deer *Moschus moschiferus* Linnaeus).

Sugemule-10 has been used up to now. With the different living practice, geography and climate environment of Mongolian grassland people, the dosage and proportion of prescriptions have changed. The Monarch drug *Amomi Rotunds Fructus* was replaced with *Alpiniae Oxyphyllae Fructus* with the same nature, taste and effect. The diuretic effect of sugemule-10 was improved by using *Sal-Ammoniac* instead of Bright Salt. *Torreyae Semen*, *Nelumbinis Semen*, *Caesalpinia minax* Hance were replaced by “three seeds” in Sugemule-10: *Nelumbinis Semen* are sweet, astringent, mild-natured, rich in protein, calcium, phosphorus, etc., with spleen, antidiarrheal, invigorating the kidney and astringent essence,

nourishing the heart and calming the nerves, its effect is same as *Caesalpiniae Cristae Semen* in the “three seeds”; *C. minax* has a very bitter taste and has the effect of treating hiccups, dysentery, stranguria, hematuria, etc. It is slightly different from the effects of nourishing the kidney, stopping diarrhea, and drying yellow water of *Syzygium jambos* (L.) Alston. *Torreyae Semen* is sweet and mild-natured, mainly in the treatment of hookworm, ascariasis, taeniasis, and abdominal pain due to parasites. Compared with tonifying kidney and removing kidney cold function of mango kernel, there is a big difference in efficacy. It can be seen that the efficacy of *Torreyae Semen* is different from that of mango kernel. The reasons for this may be related to factors such as climate change, different geographical locations, lack of drug sources or changes in disease spectrum in the process of Mongolian medicine in the past dynasties. According to the change of the prescription, the effect of Sugemule-10 in nourishing the kidney and dispelling cold in the kidney may be weaker than before.

Sugemule-10 is widely used in clinical urinary system diseases such as urinary tract infections, urinary stones, nephritis, nephrotic syndrome, and others. It also has a certain effect in the treatment of cold diseases and secondary nephropathy. At present, Sugemule-10 is mostly studied in the clinical efficacy, and the review article reflecting its historical evolution is rare. Its material basis, quality evaluation, and pharmacology, etc. have not been reported. Therefore, this paper systematically combs and analyzes the classical formula from the aspects of origin research, formula solution, efficacy evolution, modern application and so on, in order to provide reference for the subsequent research and development of this classic formula. The ten individual drugs of Sugemule-10 currently are shown in Fig. 1.

2. Textual research on source of Sugemule-10

2.1. Name

Four Medical Classics (Vol. 4) records that Sugemule-10 was named after its monarch drug Sugemule (*Amomi Rotunds Fructus*) and the number of compatible individual drugs. Sugemule-10 is also recorded in classic works *Qin • Que Ji Za La Shen San Zhu*, an annotated collection of Vol. 4 of the *Four Medical Classics* (Da, 1988), *Gan Lu Si Bu* that is the earliest monograph series of ethnic

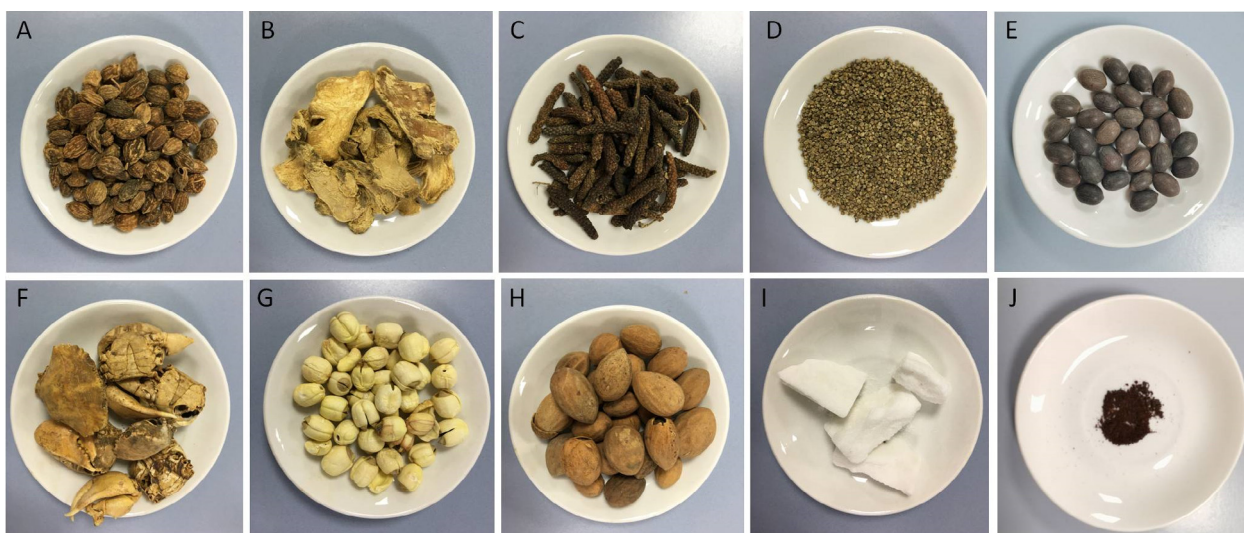


Fig. 1. Ten drugs of sugemule-10 include six ripe fruits and two volatile ingredients in single herb, crab and Sal-Ammoniac as follows. A: *Alpiniae Oxyphyllae Fructus*; B: *Zingiberis Rhizoma*; C: *Piperis Longi Fructus*; D: *Malvae Fructus*; E: *Caesalpinia minax* Hance; F: Crab; G: *Nelumbinis Semen*; H: *Torreyae Semen*; I: *Sal-Ammoniac*; J: *Moschus*.

medicine with Mongolian medicine characteristics discovered so far (Song, 2015); Collection of traditional prescriptions of Mongolian medicine (Gao, 2015; Luo, 2009; Ji, 2014), and *Mongolian Medicine Prescriptions* is Mongolian medicine dispensatory (Yu, 1986). Hundreds of Mongolian medicine prescriptions, various pills, powder and paste preparation, as well as detailed prescription functions, indications, usage and dosage specifications, and prescription sources were collected in *Standards for Mongolian Medicines in Inner Mongolia* compiled by the *Inner Mongolia Mongolian Patent Medicine Standards* (Ancient Health Department of Inner Mongolia Autonomous Region, 1988). In *Chinese Medical Encyclopedia • Mongolian Medicine*, a professional reference book that gives a complete, systematic and in-depth description of the theoretical system and clinical treatment methods of Mongolian medicine (Chinese Medical Encyclopedia Mongolian Medicine Editorial Committee, 1992), it is recorded as Shiwei Doukou Powder. It consists of *Amomi Rotundus Fructus*, *Zingiberis Rhizoma*, *Bibo Piperis Longi Fructus*, *Sal-Ammoniac*, *Malvae Fructus*, *S. cumini*, *Caesalpiniae Cristae Semen*, *Moschus*, crab, *M. indica*, and the dosage form is powder. In the *Medicine Standards of the Ministry of Health of People's Republic of China* (Committee of the Ministry of Health of the People's Republic of China, 1998), it is named Yizhi Wenshen Shiwei Pill. It consists of *Alpiniae Oxyphyllae Fructus*, *Zingiberis Rhizoma*, *Bibo Piperis Longi Fructus*, *Sal-Ammoniac*, *Malvae Fructus*, *C. aminax*, *Nelumbinis Semen*, *Moschus*, crab, *Torreyae Semen*, and the dosage form is water pill. It can be seen that the classic medical books of Mongolian medicine over the past dynasties usually record the name of Sugemule-10 uniformly, and the preparation methods include powder and pill, i.e., 10 medicines are crushed and sieved to be made into powder or water pill. Presently, it is formulated in accordance with the *Ministry-Promulgated Drug Standards* (Committee of the Ministry of Health of the People's Republic of China, 1998), and named Sugemule-10 (also known as Yizhi Wenshen Shiwei Pill); the dosage form is water pill.

2.2. Dosage

The usage of Sugemule-10, recorded in the books of past dynasties, is relatively same with the oral dosage of 3–5 g/time and 1–2

times/day. When the *Inner Mongolia Mongolian Patent Medicine Standards* was published before 1986, the units of weight were liang and qian which are the traditional Chinese units. 1 qian is 3.125 g, and 1 liang is 31.25 g.

The proportion and dosage of single drug in Sugemule-10 were recorded in the annotation collection of *Four Medical Classics*, e.g., *He Li Le Jing Zhu Jie Yi Nan Jing*, an annotated collection of *Four Medical Classics*, *Secret Prescriptions of Mongolian Medicine* that is Mongolian medicine dispensatory, *Pu Ji Prescriptions*, *Blue Liu Li* that are an annotated collection of *Four Medical Classics*, *Kai Jing Ya Aqier* that is an annotated collection of subsequent books of the *Four Medical Classics*, *Qin • Que Ji Za La Shen San Zhu* that is an annotated collection of subsequent books of the *Four Medical Classics*, etc., which are the same as those in *Four Medical Classics*. Sugemule-10 recorded in *Medical Know-how Secrets* that is an annotated edition of the secret formula of *Four Medical Classics* and *Hundred Experience Treasure Pearl* including Mongolian internal medicine, surgery, gynecology, and pediatrics comprehensive medical works was quoted from *Four Medical Classics*, and there was no dose related record. Sugemule-10 recorded in therapeutic works such as *Gao Shi Ge Mei Lin Prescription*. *Tong Wa Ga Ji De*, a comprehensive work on Mongolian medicine written in the 19th century, and *Zhe Dui Ning Nuo Er*, a comprehensive work on Mongolian medicine written in the 19th century, etc. are all quoted from the *Four Medical Classics*, and the single drug dose is not explained. Therefore, the doses of each component of Sugemule-10 are based on the records of *Four Medical Classics*, and the prescriptions follow the principle of TMM formula, i.e., the monarch, minister, assistant and guide drugs are used in different dosages. It can also be seen that according to the change of the disease, the main symptom and the secondary symptom, the amounts of monarch, minister, assistant and guide drugs are dialectically adjusted, especially the proportion of monarch medicine. Since the *Inner Mongolia Mongolian Patent Medicine Standards*, the international unit of measurement gram is used as the unit of measurement for individual drug in the formula, and the amount of individual drug in the formula has been fixed. At present, Sugemule-10 is prepared according to the *Ministry-Promulgated Drug Standards* (Table 1) (Committee of the Ministry of Health of the People's Republic of China, 1998).

Table 1
Comparing amount of individual drug of Sugemule-10 recorded in various books.

Source of prescription	Amount of individual drug									
	A	B	C	D	E	F	G	H	I	J
<i>Four Medical Classics</i>	1 L	8 q	5 q	5 q	2f	1 q	4 q	3 q	3 q	3 q
<i>Qin • QuejiZa La Shen San Zhu</i>	2 q	1 q	1 q	1 q	1 q	1 q	1 q	1 q	1 q	1 q
<i>Si Bu Gan Lu</i>	2 L	2 L	1 L	1 L	1 L	1 L	1 L	1 L	1 L	1 L
<i>Gao Shi Ge Mei Lin Prescription</i>	3 q	5 q	5 q	1 q	5f	2 L	5 q	1 q	1 q	1 q
<i>A Er Shan Xi Ma</i>	5 q	3 q	3 q	2 q	8 f	1 q	3 q	2 q	5f	1 q
<i>TongWaGajiDe</i>	5 q	2 q	2 q	2 q	8 f	5f	8 q	2 q	2 q	2 q
<i>Secret Prescriptions of Mongolian Medicine</i>	5 q	3 q	3 q	2 q	3f	3 q	2 q	2 q	2 q	2 q
<i>Sea of Medical Law</i>	1 L	8 q	5 q	5 q	2f	1 q	4 q	3 q	3 q	3 q
<i>Standards for Mongolian Medicines in Inner Mongolia</i>	150 g	60 g	60 g	60 g	0.1 g	150 g	60 g	60 g	60 g	60 g
<i>Mongolian Medicine Prescriptions</i>	15 g	9 g	9 g	6 g	9 g ^A	12 g	10 g	7 g	7 g	7 g
<i>Chinese Medical Encyclopedia • Mongolian Medicine</i>	25 g	10 g	10 g	10 g	2.5 g	40 g	10 g	10 g	10 g	5 g
<i>Medicine Standards of the Ministry of Health of People's Republic of China (Mongolian Medicine Sub-volume1998)</i>	150 g	60 g	60 g	60 g	0.1 g	150 g	60 g	60 g	60 g	60 g

Note: liang (L), qian (q), fen (f) was an ancient unit of weight, 1 qian = 5 g; 1 liang (tael) = 50 g.; 1 fen = 0.3 g; Five books *He Li Le Jing Zhu Jie Yi Nan Jing*, *Hundred Experience Treasure Pearl*, *Medical Know-how Secrets*, *Blue Liu Li*, and *Zhe Dui Ning Nuo Er* all quoted *Four Medical Classics* (Vol. 4), without indicating the dose of Sugemule-10. Δ*Cervi Cornu Pantotrichum*. A: Sgml Mongolian doctors are used to referring to *Amomi Rotundus Fructus*, when they say Sgml; B: *Zingiberis Rhizoma*; C: *Piperis Longi Fructus*; D: *Bright Salt*; E: *Moschus*; F: Crab; G: *Malvae Fructus*; H: *Caesalpiniae Cristae Semen*; I: *Syzygium cumini* (L.); J: *Mangifera indica* (L.); Sgml-10 in *Tong Wa Ga Ji De* has additional *Myristicace Semen*, *donkey Flesh*, and *Anser Meat*, 2 q respectively. *A Er Shan Xi Ma*: Mongolian Medicine clinical treatment works; *Sea of Medical Law*: Mongolian medicine dispensatory.

Table 2
Evolution of Sugemule-10 (Sgml-10) composition.

No.	Literary works	Names	Composition	Efficacy	Publication years
1	<i>Four Medical Classics</i>	Sgml-10	A	A1: Eliminate kidney cold, diuresis, stone disease	8th century
2	<i>Hundred Experience Treasure Pearl</i>	Sgml-10	Ditto A	Ditto A1	1511–1577
3	<i>Medical Know-how Secrets</i>	Sgml-10	Ditto A	Ditto A1	1682
4	<i>Blue Liu li</i>	Sgml-10	Ditto A	Ditto A1	1689
5	<i>Qin • QuejiZa la shen san zhu</i>	Sgml-10	B	Ditto A1	1690
6	<i>Lan Ta Bu</i>	Sgml-10	Ditto A	Ditto A1	1691
7	<i>Gan Lu Si Bu</i>	Sgml-10	Ditto B	Eliminate kidney cold, kidney Heyi disease spermatorrhoea	1751–1785
8	<i>Kai •Jing yaAo qi er</i>	Sgml-10	Ditto A	Eliminate kidney cold	17th century
9	<i>Puji Prescriptions</i>	Sgml-10	Ditto A	Ditto A1	1813
10	<i>Sea of Medical Law</i>	Sgml-10	Ditto B	Kidney stone, urinary obstruction, kidney Heyi disease	1829
11	<i>TongwaGaji de</i>	Sgml-10	DittoB + <i>Myristica Semen, donkey Flesh, Anser Meat</i>	DittoA1 + kidney Heyi disease, kidney Awada disease	1888
12	<i>The Dual Key to Diagnosis and Medicine</i>	Sgml-10	Ditto A	Eliminate kidney cold	18th century
13	<i>Zhe Dui Ning Nuoe</i>	Sgml-10	D	Eliminate kidney cold, kidney Heyi disease, bladder stone, urinary tract infection + DittoA1	19th century
14	<i>Gaoshige Meilin Prescription</i>	Sgml-10	C	Ditto A1	19th century
15	<i>A Collection of Secret Recipes of Mongolian Medicine</i>	Sgml-10	DittoC	Ditto A1 + treatment of all cold syndromes in the waist	1964
16	<i>Mongolian Medicine Prescriptions</i>	Sgml-10	Sgml, Crab, Processed Ginger, <i>Piperis Longi Fructus, Bright Salt, Malvae Fructus, Cervi Cornu Pantotrichum, White Nelumbinis Semen, Nelumbinis Semen, Lotus Seed</i>	Insufficient essence, cold kidney, cold waist, turbid stone leaching, poor urination	1986
17	<i>Standards for Mongolian Medicines in Inner Mongolia</i>	Sgml-10	Sgml, Ga, <i>sal-ammoniac, Piperis Longi Fructus, Moschus, Crab, Torreya Semen, Nelumbinis Semen, Nelumbo nucifera Gaertn., Hollyhock Flower</i>	Ditto A1 + kidney deficiency, low back pain, ischuria	1988
18	<i>Chinese Medical Encyclopedia • Mongolian Medicine</i>	Shi Wei Dou Kou Powder	Ditto B	Bladder stone, kidney cold and low back pain, ischuria	1992
19	<i>Medicine Standards of the Ministry of Health of the People's Republic of China</i>	Sgml-10/Yi zhi Wenshen Shiwei Pill	<i>Alpiniae Oxyphyllae Fructus, Zingiberis Rhizoma, sal-ammoniac, Piperis Longi Fructus, Torreya Semen, Nelumbinis Semen, C. minax, Crab, Malvae Fructus, Moschus</i>	Kidney cold, deficiency, low back pain, ischuria	1998
20	<i>He Li Le Jing Zhu Jie Yi Nan Jing</i>	Sgml-10	Ditto A	Ditto A1	1999
21	<i>A Er Shan Xi Ma</i>	Sgml-10	Ditto C	Ditto A1	2009

Note: Puji Prescriptions: Mongolian medicine formulae; Awada: The main symptom of spinal Heyi disease is hunchback; Heyi: Heyi explained from the perspective of yin-yang theory that it has two sides, but from the perspective of five-element theory, it belongs to *qi*. In the normal physiological activities of the human body, Heyi has the function of maintaining life activities, promoting blood operation, managing breathing, decomposition of food, conveying essence and dregs, enhancing physical strength, making the function of facial features normal and clear consciousness, vaccinating and passing generations, and controlling the function of reflex of limb activities. It is also the regulator of Xila and Badagan who can maintain relative balance and guide the body to maintain health and prolong life; Heyi disease: The gas element of Heyi belongs to the five elements, which itself has the characteristics of lightness and astringency, as well as the function of inducing heat and cold evil, so it shows these characteristics in the pathological process. Heyi has the characteristics of aggravating and complicating both heat syndrome and cold syndrome. It is, therefore, the cause of all diseases, the precursor and the end of all diseases, pervading the body, and serving to spread them. Heyi disease is more common in the elderly, Heyi physique and physical weakness. A: Sgml, BaoRiGa (*Zingiberis Rhizoma*), Bright Salt, *Piperis Longi Fructus, Moschus, Crab, Malvae Fructus*, three seeds (*Caesalpiniae Cristae Semen*, seeds of *S. cumini*, seeds of *M. indica*); B: Sgml, Ga (Mongolian collectively refers to ginger as A), Bright Salt, *Piperis Longi Fructus, Moschus, Crab, Malvae Fructus*, three seeds; C: Sgml, *Kaempferiae Rhizoma* (dried rhizome of *K. galanga* in Ginger family), Bright Salt, *Bibo Piperis Longi Fructus, Moschus, Crab, Malvae Fructus*, three seeds. D: Sgml, Ginger, Bright Salt, *Piperis Longi Fructus, Moschus, Crab, Malvae Fructus*, three seeds.

medicinal materials have a precise composition and are compatible with the current Mongolian medicine clinical use and the *Medicine Standards of the Ministry of Health of People's Republic of China (MMD)*. There is no doubt that it is an empirically based TMM formula. During the process of long-term use, due to the changes in Mongolian medical medicine experience, usage, medicine growth area, output, market circulation, etc., the alternative medicine has appeared. The origins of *Piperis Longi Fructus*, *Moschus* and Crab are unambiguous.

3. Textual research and changing of efficacy

Sugemule-10, with a warm nature, is the main Mongolian medicine prescription for treating kidney cold; it can dispel kidney cold and induce diuresis. *Four Medical Classics* records that it is warm in nature, dispels Heyi and Badagan, removes stomach and kidney cold; it invigorates stomach fire, induces diuresis and disperse swelling, removes yellow water, and relieves pain. It is especially effective in treating kidney cold and ischuria. Sugemule as the monarch medicine, has a bitter and spicy taste, warm in nature, light, dry, greasy, sharp, have the effects of eliminating kidney cold, suppressing He yi, regulating stomach fire, etc. *Caesalpiniae Cristae Semen*, *S. cumini* and *M. indica* as the minister medicine, eliminate kidney cold, nourish and strengthen the kidney. *Malvae Fructus*, Crab and Bright Salt, as the adjuvant medicine, open the veins, induce diuresis and disperse swelling. *Zingiberis Rhizoma* and *Piperis Longi Fructus*, as the medicine guides, eliminate “Badagan” and “Heyi”. The combination of these drugs constitutes a prescription with the functions of treating ischuria and dispelling kidney cold, and has a significant effect on damp-cold nephropathy.

Later classics all use this as a guideline, which have an excerpt from the original text or excerpt part of the content of *Four Medical Classics*. There are three main aspects of the pathogenesis of nephropathy: 1. The stone is formed by the evil accumulation of Badagan and yellow water, blocking the urethra, or the kidneys are damaged due to “San Gen” (Three Roots: Badagan, Heyi, and Xila) disorders, resulting in the kidney deficiency and failure to pass water; the ischuria follows, with dripping urine, dysuria, and even complete urethra obstruction, etc. 2. The Heyi predominating nephropathy can be caused by brute force, weight-bearing fatigue, chronic illness and weakness, overwork, while the cold predominating nephropathy can be caused by cold and humid, having cold and indigestible food for a long time; the symptoms are cold lower limbs, tinnitus, dizziness, difficult or dripping urine, nocturnal emission, pain in the waist and kidneys and radiating to the surroundings, no fixed point in the pain, insomnia, weak pulse, clear and foamy urine, etc. 3. The insufficient decomposition of essence and dross can be due to the imbalance between Three Roots and Seven Elements (Due to various adverse factors inside and outside the body, the seven elements are in abnormal states such as partial prosperity and partial decline, which damage the body and are called seven elements disease. The seven elements are the material tea bases on which the three roots depend to exist and form the body and promote its continuous life activities. The generation and development of the seven elements and the three energies of digestion (referring to digestion of Xila, decomposed Badagan and Heyi) are especially directly related to the normality of digestion of Xila and its distribution of heat energy throughout the body.), increasing malignant blood and yellow water, which stagnate in the gallbladder, kidney, bladder and affect the normal function of organs; the evil blood and yellow water are silted up and become lumps. There is no sensation in the initial stage of kidney stone, but when it matures, the waist cannot be pitched, the body is heavy, and there is falling pain; there may be dripping

urine, or obliteration or blood in the urine. If the stone pimples descend into the bladder, the pain will be relieved immediately.

Sugemule-10 is a good remedy for diseases caused by these three key pathogenesis (Chinese Medical Encyclopedia Mongolian Medicine Editorial Committee, 1992). When later generations of physicians use Sugemule-10, most of who emphasize the use of a function of the original prescription, with certain development. For example, in *Zhao Ri Ge Tu Ha Mu Bu Clinical Essence* (A collection of famous Mongolian medical cases) (Jin, 2012), it is used to treat difficult or dripping urination, spermatorrhea, and pain in the waist and kidneys; in *Bao Yin Zha Bu Medical Records* (A collection of famous Mongolian medical cases) (Zhou, 2013), Sugemule-10 is used to treat facial edema, low back pain, hematuria, oliguria, poor appetite, cold lower limbs; Chai Da lai (Chai, 2007) used it as the adjuvant treatment of lower limb pain caused by lumbar disc protrusion; Wu Ren hua used Xieriga-4 Decoction combined with Sugemule-10 to treat benign prostatic hyperplasia and the effect was obvious (Yan & Zhang, 2020). Sugemule-10 is also effective in treating acute nephritis (Wu & Shi, 2010).

4. Application and development in clinical therapy

4.1. Clinical application of Sugemule-10

Mongolian medicine Sugemule-10 is widely used to treat urinary system diseases, such as cold nephropathy, stone, puffiness, urinary obstruction, and with remarkable curative effects. There are numerous related experiences for reference (Song, 2015; Ga & Ma, 1999; Gao, 2013; Fu, 2006; Se et al., 2017; Qing & Bao, 2012; Ha, 2014; La & La, 2014; Na, et al., 2014; Zhan, 2014; Liu, 2006), such as those recorded in the classic medical books *Yue Guang Medical Classics* (Clinical medical-oriented works), *Si Bu Gan Lu* (Monographs on ethnic medicine and pharmacology with Mongolian medicine characteristics.), *Guan Bu Medical Case* and *Jin Yu Medical Case* (All are collections of Mongolian medical cases), etc. Using CNKI as the source database, we searched for “Yizhi Wenshen Shiwei Pill”, “Sugemule-10”, “Shiwei Doukou Powder”, “Mongolian Medicine for Urinary System Diseases”, and “Mongolian Medicine for Nephropathy”, and 24 related documents were retrieved. According to the literature, Sugemule-10 has shown a good effect against urinary system diseases, especially for cold-type ones, such as urinary tract infection, urinary tract stone, lumbar and hip pain, ischuria, kidney/bladder stone, etc.; it also has certain adjuvant treatment effects on nephritis, hematuria, and proteinuria (Table 3).

4.2. Research value

At present, the quality research of Sugemule-10 only pays attention to the content determination of individual compounds. Zhang et al. used thin layer chromatography (TLC) and high-performance liquid chromatography (HPLC) to determine the main components of *Alpiniae Oxyphyllae Fructus* and *Bibo Piperis Longi Fructus*, nootkatone and piperine respectively (Zhang et al., 2013; Xu et al., 2008). The physical and chemical methods are used to distinguish white *sal-ammoniac* and Crab (Zhang et al., 2013). There are many studies on pharmacology of component drugs of Sugemule-10, e.g., the monarch drug *Alpiniae Oxyphyllae Fructus* has the function of anti-oxidant stress and improves the renal pathological function, it also showed the diuretic and anti-diuretic effects (Du et al., 2017; Lee et al., 2019; Li, Tan, Wei, & Zhang, 2016; Ni, 2019; Xie et al., 2018). The 10-DHGD of *Zingiberis Rhizom* has the anti-inflammatory activity and reduced the renal fibrosis (Elseweidy, Zaghoul, & Younis, 2016). The ash content of

Table 3
Clinical application of Sugemule-10.

Disease syndrome	No.	Control group	Sgml-10 treatment group	Clinical efficacy	Course of treatment	References
Renal calculi	30	–	Sgml-10 + Sema-3 Decoction	Cure rate 90 %; improvement rate 6.66 %; inefficiency 3.33 %	12 days/course	(Bao & Han, 2000)
Urolithiasis	22	–	Sgml-10 + Sema-3 Decoction	Cure rate 86.4 %; improvement rate 9.1 %; inefficiency 4.5 %	1–20 days	(Ming & Da, 2009)
UTI	100	–	Morning: Sgml-10 + Xiriiga-4 Decoction; Noon: Xirimaodu-8; at night: Saligaridi + Xiriga-4 Decoction	Cure rate 93 %; were markedly effective; two were ineffective; total effective rate 98 %	7 days/course; general treatment is 4–6 courses	(Kong & Kong, 2000)
UTI	50	–	Yizhi Wenshen Shi wei Pill Sa Li Chong	Cure rate was 82 %; significant rate 10 %; improvement rate 8 %; total effective rate 100 %	Average treatment 1.5 months	(Li, 2012)
DMUTI	–	–	Sgml-10 Tonglaga-mu5/ Gurigumu-13	Significantly improve clinical symptoms	–	(Wu, 2014)
NS	38	–	Morning: Bai Kou-13; Noon: Sgml-10/Jili-3; Evening: Sa Li Chong	Cure rate 65.8 %; improvement rate 23.7 %; inefficiency 10.7 %; total effective rate 89.5 %	3 months/course	(Si, Li, & Qi, 1996)
CRF	62	–	Sgml-10, Narenmandula-11, Saligarudi, BugrenArula –10, Sema-3, Xiriga-4	Effective rate 8 %; improvement rate 90.3 %; invalid rate 1.6 %; total effective rate 98.3 %	Symptoms and biochemical indexes improved significantly after 1 month	(Bao et al., 2003)
DN	80	control the blood glucose leve + ACEI/ARB, statins/fibrates, Aspirin/Jinshuibao Capsules	Basic treatment + Zhenbao Pill/ Sarigaridi, /Sgml-10	Total effective rate: 95 % Sgml-10 group vs control group, $P < 0.05$	1 month/course	(Hu et al., 2018)
HSPN	1	–	Sgml-10, Buren Aru –10,	Reduced edema, normal urinary volume, improved biochemical indicators	44 days	(Yi & Chen, 2014)
AGN	63	Conventional treatment (diuresis, antihypertensive)	conventional treatment + sgml-10 \Xieriga –4 Decoction	Total effective rate 91.89 %; treatment group is better than control group ($P < 0.05$)	4 weeks	(Wu & Shi, 2010)
CGN	40	Benazepril, Hydrochlorothiazide, Aspirin	Control treatment + sgml-10/ Narenmandula, with Sema-3	Total effective rate is higher than control group ($P < 0.05$)	4 months	(Wu, 2015)

Note: Sema-3 Decoction: It is composed of tribulus, *Malvae Fructus* and crab. Xirimaodu-8: It is composed of 100 g phellodendron, 40 g liquorice, piper, *Moschus*, 25 g gardenia and safflower, 75 g Chinese ink and bear bile; Saligaridi and Sa Li Chong are different names for the same formular, which is composed of *Terminalia chebula* Retz., elecampane, aconitum and cardamom, calamus and *Silver vermilion*, *Moschus*, *Hollyhock Flower* and *Canavalee Semen*, 175 g each, *Chinensis Cassia* and black cloud loquat leaves 12 g each, Violetgrass 22 g each madder ink, bear bile and red flower 5 g each. Tonglaga-5: By pomegranate 35 g cinnamon, cardamom, each 5 g red flower 20 g with; Gurigumu-13 is composed of saffron 10 g clove, bezoar, *Moschus*, hornbill horn, silver vermilion, red sandalwood, *T. chebula*, *Melia chinensis*, *Gardenia jasminoides* and *Osmanthus xylanthus* 5 g each; CRF: Chronic renal failure; CGN: Chronic glomerulonephritis; AGN: Acute glomerulonephritis; NS: Nephrotic syndrome; UTI: Urinary tract infection; DMUTI: Diabetes with urinary tract infection; HSPN: DN: Diabetic Nephropathy.

lotus seed (Mani, Subramanian, Pillai, & Muthusamy, 2010) reduced the blood sugar in streptozotocin-induced diabetic rats. However, there are few modern pharmacological studies on Sugemule-10, the studies of pharmacological material basis, compatibility/identification, quality standard and quality control are rare, and its mechanism of action is not investigated, which seriously affect and hinder its clinical rational use.

5. Discussion and conclusion

Sugemule-10 formula follows the principle of Mongolian medicine formula formulation, that is, the dosage of monarch, minister,

assistant and agent is made in different doses. It can also be seen that the dosage of monarch, minister, assistant and agent is dialectically adjusted according to the changes of symptoms, main syndrome and secondary syndrome, and the king medicine accounts for a large proportion.

Sugemule-10 formula monarch medicine is Sugemule; suppression of “Badagan Heyi”, tonifying the kidney, diuresis, kidney cold, nourishing strong kidney effect of the three seeds for the minister medicine, the current replacement of the three seeds including kidney lotus seeds; At present, substitutes for the three seeds include lotus seeds which benefit the kidney; Kill insects to eliminate accumulation, moistening lung to arrest cough *Caesalpinia minax*, Its efficacy is different from that of the *Four Medical Classics*; open

the pulse, diuresis, deswelling of *Malvae Fructus*, Crab, sal ammoniac for adjuvant; *Zingiberis Rhizom* and *Bibo Piperis Longi Fructus* are envoy drugs.

The efficacy of Sugemule-10 has been mainly in the treatment of kidney cold, urodialysis and calculi. With the change of Mongolian living environment and climate, different regions of drug growth, production, market circulation and other differences, the current used assistant drugs have changed, drug efficacy has changed, The dosage form from powder to pill should be convenient to carry, pill metabolism in the body is slow, the action time is longer and so on.

So far, there is very little basic research and experimental research on Sugemule-10. In the future studies, the preparation process should be investigated, quality standards be established, the chemical composition, content and metabolic processes be clarified, and the systematic pharmacodynamic evaluation be carried out with regard to its main clinical indications. The choice of multi-origin medicinal materials is a universal problem in the study of classic prescriptions. For example, in Sugemule-10, the mature fruit of *C. minax*, i.e. Seed of White flower *Cacalia*, is used as the substitute of *Syzygium cumini* according to the *Ministry-Promulgated Drug Standards (Committee of the Ministry of Health of the People's Republic of China, 1998)*.

The historical records of the administration method are relatively uniform, but with the development of the times, the source of medicines changes, and the dosage should be adjusted according to the efficacy of the medicine. The *Ministry-Promulgated Drug Standards (Committee of the Ministry of Health of the People's Republic of China, 1998)* should be adopted to prepare Sugemule-10, which is composed of *Alpiniae Oxyphyllae Fructus* and *Crab150g* respectively, *Zingiberis Rhizoma*, white *sal-ammoniac*, *Piperis Longi Fructus*, *Malvae Fructus*, *Torreya Semen*, *Nelumbinis Semen* and *C. minax* 60 g respectively, *moschus* 0.1 g; nine medicines are crushed into fine powder and the *moschus* is finely ground, then they are mixed well, pill with water, polished, and dried immediately. Since most of individual drug in Sugemule-10 contain fatty oils and volatile oils, the pulverization, preparation process and technology should be re-examined according to national standards to ensure maximum efficacy. Meanwhile, the quality control indicators for classic famous prescriptions should first be screened based on the monarch, minister, adjuvant and guide principles of the prescription itself. The selected indicators should represent the efficacy of the individual drug in the prescription. Secondly, based on the characteristic spots of TLC and characteristic peaks of the chromatograph, the qualitative and quantitative analyses of high abundance compounds should be conducted. Our group used TLC and HPLC to qualitatively analyze the monarch, minister, adjuvant and guide drugs of Sugemule-10 and quantitatively analyze nootkatone and poplarflavin of the monarch drug and gingerol of the adjuvant *Zingiberis Rhizoma*.

The safety and effectiveness of classic Mongolian medicine prescriptions have been tested in long-term applications. Sugemule-10 has important clinical value in the treatment of urinary system diseases and has great development prospects. Our comprehensive analyses provide useful ideas and references for the modern clinical application of Sugemule-10 and the development of compound preparations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

- Yu, T. Y. D. (1991). *Four Medical Classics* (2nd ed. p. 1039). Chifeng: Inner Mongolia Science and Technology Press.
- Ancient Health Department of Inner Mongolia Autonomous Region (1988). *Inner Mongolia Mongolian Patent Medicine Standards* (Supplementary Edition p. 173). Chifeng: Inner Mongolia Science and Technology Press.
- Bao, Y., & Han, G. M. (2000). Mongolian medicine Sugemule-10 in the treatment of M 30 cases of kidney stones. *Chinese Journal of Ethnic Medicine (supplment)*, 6, 12.
- Bao, Y. H., Li, Q. M., & Han, W. L. J. (2003). Mongolian medicine in the treatment of 62 cases of chronic renal insufficiency. *Chinese Journal of Ethnic Medicine*, 9(1), 15.
- Chai, D. L. (2007). 300 cases of lumbar disc herniation were treated by combining Chinese and Mongolian medicine with Western medicine. *Forward Forum (Healthy China)*, 2, 34–35.
- Chinese Medical Encyclopedia Mongolian Medicine Editorial Committee (1992). *Chinese Medical Encyclopedia • Mongolian Medicine (Chinese Edition)*. Shanghai: Shanghai Science and Technology Press. 271, 66–69, 79, 88.
- Da, R. M. M. R. B. L. B. S. Z. R. G (1988). *Qin • QUE JI ZHA LA SHEN SAN ZHU*. Hohhot: Inner Mongolia People's Press. 267.
- Du, G., Xiao, M., Zhang, X., Wen, M., Pang, C., Jiang, S., ... Xie, Y. (2017). *Alpinia oxyphylla* Miq. Extract changes miRNA expression profiles in d b/d b - mouse kidney. *Biological Research*, 50(1), 9.
- Elseweidy, M. M., Zaghoul, M. S., & Younis, N. N. (2016). 10-DHGD ameliorates cisplatin-induced nephrotoxicity in rats. *Biomedicine & Pharmacotherapy*, 83, 241–246.
- Fu, S. (2006). *Holy spring* (p. 103). Hohhot: Inner Mongolia People's Press.
- Ga, R. L., & Ma, E. L. G. (1999). *YUE GUANG Medical Classics. Inner Mongolia Institute of Traditional Chinese and Mongolian Medicine* (p. 271). Hohhot: Inner Mongolia People's Press.
- Gao, S. G. (2015). *GAO SHI GE MEI LIN Prescription* (p. 122). Hohhot: Inner Mongolia People's Press.
- Gao, T. Y. (2013). *GAO EN BU Medical Case* (p. 69). Chifeng: Inner Mongolia Science and Technology Press.
- Ha, D. J. D. (2014). *WEI RI BU Medical Case* (pp. 216–218). Chifeng: Inner Mongolia Science and Technology Press.
- Hu, S. L., Si, Q. G. R. L., & Tang, Y. H. (2018). The clinical efficacy analysis of Mongolian medicine in the treatment of early type 2 diabetic nephropathy. *Chinese Journal of National Medicine*, 24(2), 12–13.
- Ji, G. M. D. D. Z. Z. M. S. (2014). *TONG WA GA JI De*. Hohhot: Inner Mongolia People's Press. 73. 169.
- Jin, M. D. S. (2012). *ZHAO RI GE TU HAN BU Clinical Essence* (p. 108). Chifeng: Inner Mongolia Science and Technology Press.
- Kong, J. Y., & Kong, C. Y. (2000). Mongolian medicine treats 100 cases of urinary tract infection. *Chinese Journal of National Medicine*, 6(4), 30.
- La, X. D. R. B., & La, S. H. (2014). *Medical Case of LA XI DONG REI BU* (pp. 24–25). Chifeng: Inner Mongolia Science and Technology Press.
- Lee, Y. S., Sung, Y. Y., Yuk, H. J., Son, E., Lee, S., Kim, J. S., & Kim, D. S. (2019). Anti-hyperuricemic effect of *Alpinia oxyphylla* seed extract by enhancing uric acid excretion in the kidney. *Phytomedicine: International Journal of Phytotherapy and Phytopharmacology*, 62.
- Li, Y. H., Tan, Y. F., Wei, N., & Zhang, J. Q. (2016). Diuretic and anti-diuretic bioactivity differences of the seed and shell extracts of *Alpinia oxyphylla* fruit. *African Journal of Traditional, Complementary and Alternative Medicines*, 13(5), 25–32.
- Li, Y. T. (2012). Mongolian medicine treats 50 cases of urinary system infection. *Chinese Journal of Ethnic Medicine*, 18(6), 64.
- Liu, B. Y. L. (2006). *Mongolian Medicine Canon* (p. 76). Hohhot: Inner Mongolia People's Press.
- Luo, B. S. Z. (2009). *A E SHAN XI MA* (p. 128). Hohhot: Inner Mongolia People's Press.
- Luo, B. S. (1998). *Recognizing Pharmacy* (1st Edition, pp. 179–183). Beijing: National Publishing Press.
- Luo, B. S., & (Mongolian) (2006). *Mongolian Pharmacy (1st edition)* (pp. 295–296). Hohhot: Inner Mongolia People's Press.
- Mani, S. S., Subramanian, I. P., Pillai, S. S., & Muthusamy, K. (2010). Evaluation of hypoglycemic activity of inorganic constituents in *Nelum bonucifera* seeds on streptozotocin-induced diabetes in rats. *Biological Trace Element Research*, 138 (1–3), 226–237.
- Ming, Y., & Da, G. D. (2009). 22 cases of urolithiasis treated by Mongolian medicine Sugemule-10. *Chinese Journal of Ethnic Medicine*, 15(4), 9.
- Na, M. J. L., Han, B. G. N., & Bao, Y. T. (2014). *Secret Prescriptions of Mongolian Medicine* (p. 140). Chifeng: Inner Mongolia Science and Technology Press.
- Ni, Y. L. (2019). *Analysis of the mechanism of action of Alpiniae Oxyphyllae Fructus in the treatment of diabetic nephropathy based on intestinal flora and metabolomics*. Hainan Medical College). Master's Thesis.
- Pharmacopoeia Committee of the Ministry of Health of the People's Republic of China. (1998). *Medicine Standards of the Ministry of Health of People's Republic of China* (p. 155). Hohhot: Inner Mongolia People's Press.
- Qing, B. T., & Bao, H. J. (2012). *JIN YU Medical Record* (pp. 35–42). Chifeng: Inner Mongolia Science and Technology Press.

- Se, R. N., Wu, L. J. T., & Ha, S. Q. (2017). *DUO GE RI ZHA BU MEDICAL CASE* (p. 104). Hohhot: Inner Mongolia People's Press.
- Si, Q. Q., Li, G. H., & Qi, G. Q. T. (1996). Mongolian medicine treats 38 cases of refractory Nephrotic syndrome. *Chinese Journal of Ethnic Medicine*, 62(4), 4–17.
- Song, B. G. (2015). *Si Bu GAN LU* (p. 104). Hohhot: Inner Mongolia People's Press.
- Wu, J. M. (2015). Clinical observation of 20 cases of chronic glomerulonephritis treated with integrated Mongolian and western medicine. *Chinese Journal of Ethnic Medicine*, 21(8), 37–38.
- Wu, R. H., & Shi, T. Y. (2010). Clinical observation on the treatment of acute glomerulonephritis with combination of Mongolian Medicine and Western Medicine. *Chinese Journal of National Medicine*, 16(4), 17–18.
- Wu, R. T. Y. (2014). The clinical experience of Mongolian medicine in the treatment of diabetes with urinary tract infection. *Chinese Journal of Minority Medicine*, 20(6), 27–28.
- Xie, Y., Xiao, M., Ni, Y., Jiang, S., Feng, G., Sang, S., & Du, G. (2018). *Alpinia oxyphylla* Miq. extract prevents diabetes in mice by modulating gut microbiota. *Journal of Diabetes Research*, 4230590.
- Xu, J., Tian, Y., & Kang, T. G. (2008). Determination of the content of piperine in *Alpiniae Oxyphyllae Fructus* Wenshen Shi Wei Pills by HPLC. *Chinese Folk Medicine*, 2, 21–22.
- Yan, W. H., & Zhang, P. L. (2020). Ultrasonic observation and efficacy evaluation of Mongolian medicine Sug mul-10 combined with Mongolian medicine Xiriga-4 Decoction in the treatment of benign prostatic hyperplasia. *Chinese Journal of Minority Medicine*, 26(11), 5–6.
- Yi, R. G., & Chen, S. N. (2014). Mongolian medicine treats 1 case of allergic purpura Nephritis with Nephrotic syndrome. *Chinese Folk Medicine*, 23(7), 2–3.
- Yi, X. B. (2015). *BAI JING JIAN (1st Edition)* (pp. 145–146). Mongolian. Chifeng: Inner Mongolia Science and Technology Press.
- Yu, Q. X. (1986). *Mongolian Medicine Prescriptions* (pp. 344–345). Hohhot: Inner Mongolia People's Press.
- Zhan, B. L. (2014). *Sea of Medical Law* (pp. 637–711). Chifeng: Inner Mongolia Science and Technology Press.
- Zhang, P., Zhao, D. L., & Ha, S. Q. M. G. (2013). Quality standard of Mongolian medicine *Alpiniae Oxyphyllae Fructus* Wenshen Shi Wei Pills. *Chinese Journal of Experimental Formulas*, 19(13), 75–78.
- Zhou, T. B. (2013). *BAO YIN ZHA BU Medical Record (Mongolian)* (pp. 59–62). Chifeng: Inner Mongolia Science and Technology Press.