Sugemule-10: Source of prescription and modern clinical application

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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.

Keywords:
clinical application
prescription interpretation
prescription source
Sugemule-10

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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 Oxyphylla 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 Oxyphylla 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.
medicines 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 dispensary (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 dispensary, 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 GaoShi 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 measure 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).

| Source of prescription | Amount of individual drug |
|------------------------|--------------------------|
|                        | A | B | C | D | E | F | G | H | I | J |
| Four Medical Classics  | 1 L 8 q 5 q 5 q 2 f 1 q 4 q 3 q 3 q 3 q 3 q |
| Qin • Que Ji Za La Shen San Zhu | 2 q 1 q 1 q 1 q 1 q 1 q 1 q 1 q 1 q 1 q 1 q |
| Si Bu Gan Lu            | 2 L 2 L 1 L 1 L 1 L 1 L 1 L 1 L 1 L 1 L 1 L |
| Gao Shí Ge Mei Lin Prescription | 3 q 5 q 5 q 1 q 5 f 2 L 5 q 1 q 1 q 1 q 1 q 1 q |
| A Er Shan Xi Ma         | 5 q 3 q 3 q 2 q 8 f 1 q 3 q 2 q 5 f 1 q 8 f 1 q 8 f 1 q 8 f |
| Tong Wa Ga Ji De        | 5 q 2 q 2 q 2 q 8 f 5 f 8 q 2 q 5 q 5 q 5 q 5 q 5 q 5 q 5 q |
| Secret Prescriptions of Mongolian Medicine | 5 q 3 q 3 q 2 q 3 f 3 q 2 q 2 q 2 q 2 q 2 q |
| Sea of Medical Law      | 1 L 8 q 5 q 5 q 2 f 1 q 4 q 3 q 3 q 3 q 3 q |
| Standards for Mongolian medicine in Inner Mongolia | 150 g 60 g 60 g 60 g 0.1 g 150 g 60 g 60 g 60 g 60 g 60 g |
| Mongolian Medicine Prescriptions | 15 g 9 g 9 g 6 g 9 g 12 g 10 g 7 g 7 g 7 g 7 g |
| Chinese Medical Encyclopedia • Mongolian Medicine | 25 g 10 g 10 g 10 g 2.5 g 40 g 10 g 10 g 10 g 5 g 5 g |
| Medicines Standards of the Ministry of Health of People’s Republic of China (Mongolian Medicine Sub-volume1998) | 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. A &Cervi Cornu Pantorchicum. A: 5g/ml Mongolian doctors are used to referring to Amomi Rotundus Fructus, when they say 5g/ml; B: Zingiberis Rhizoma; C: Bibo Piperis Longi Fructus; D: Bright Salt; E: Moschus; F: Crab; G: Malvae Fructus; H: Caesalpiniae Cristae Semen; I: Syzygium cumini (L.); J: Mangiferica indica (L.); Sgml-10 in Tong Wa Ga Ji De has additional Myristicea 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 dispensary.

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2.3. Pharmacognosy origin

In the classics of past dynasties, Sugemule-10 has two main formulas; the original formula in Four Medical Classics is composed of Anmom Rotundus Fructus, Zingiberis Rhizoma, Bright Salt (Halite), Piperis Longi Fructus, Moschus, Crab, Malvae Fructus, Caesalpiniae Crista Semen, S. cumini, and M. indica, while the other prescription contains Myristicae Semen, Anser Meat and donkey meat in addition to the 10 drugs, which is recorded in Tong Wa Ga ji de (Ji, 2014), and belongs to the dialectical prescription. The prescription compatibility, usage, and dosage form in other ancient books are consistent with those in Four Medical Classics. We found that Sugemule-10 included in the ancient Mongolian medical books is mainly recorded in the 16th, 17th, 18th, and 19th centuries. The formula is more recorded in the annotation collections of Four Medical Classics (Table 2).

It can be seen from Table 2 that A, B and D have the same prescriptions. Although BaoRiGa, Ginger (Zingiberis Rhizoma) and Ga (Zingiberis Rhizoma) are named differently in each prescription, they are actually different names of the same drug. In C, Zingiberis Rhizoma was replaced by Kaempferiae Rhizomae. There is no change in the formula of the remaining group. Zingiberis Rhizoma is hot, and Kaempferiae Rhizoma is warm, and the effects are basically the same. The effect of Kaempferiae Rhizoma to drive cold is weaker than that of Zingiberis Rhizoma. By 1988, when it was included in the Inner Mongolia Mongolia Patent Medicine Standard, all the five drugs except for Sugemule, Zingiberis Rhizoma, Piperis Longi Fructus, Moschus, Crab were used as substitutes. Althaea rosa (L.) Cavan, could replace Malvae Fructus, and all of them had diuretic and detumescent functions, and compared with Malvae Fructus, A. rosea had the effect of treating spermatorrhea. The drugs with diuretic and renal cold removal functions were basically unchanged when the Drug Standard of Ministry of Public Health of the Peoples Republic of China were included, while the drugs with renal beneficial effects were replaced.

2.3.1. Origin of monarch medicine in Sugemule-10

The monarch drug Sugemule has multiple botanical origins in the classic medical books of Mongolian medicine (Luo, 1998) as follows: 1. ripe fruits of Amomum kravanh Pierre ex Cagnep or Amomum compactum Soland ex Moton (A. cardamomum auct. non L.) (حسبَحْ)cha gansuge mu le); 2. ripe fruits of A. oxyphylla (حسبَحْ)boorisuge mu le); 3. ripe fruits of Elettaria cardamomum (L.) Maton (حسبَحْ)ten tegesuge mu le), Zingiberaceae; 4. ripe fruits of Amomum villosum Lour or A. villosum Lour. var. xanthoides L. Wu et Senjen or A. longiligulare T. L. Wu. All of the above are perennial herbs of Zingiberaceae, and have similar functions and indications. In the past generations of Mongolian medicine, Sugemule usually refers to Amomum Rotundus Fructus. At present, Alpiniae Oxyphyllae Fructus with the same nature, flavor and efficacy is commonly used as the alternative medicine. According to the Ministry-Promulgated Drug Standards, the monarch drug of Sugemule-10 should be the mature fruits of A. oxyphylla.

2.3.2. Origin of minister medicine in Sugemule-10

Caesalpiniae Cristae Semen [also known as Zhou leng wu re, Wu yu wen du ge, and Zhan Balai], S. cumini and M. indica are collectively referred to as the three seeds in the classic medical books of Mongolian medicine. Caesalpiniae Cristae Semen is pungent in flavor, warm in nature; it can dispel the cold of stomach and kidney, and invigorate the kidney. S. cumini, also known as QiHerge-wureor Temuerhao Muha in Mongolia, is the ripe fruits of S. cumini; it is sweet, astringent in flavor, warm and light in nature, and can nourish and strengthen kidneys. It is used to treat cold and cold lower body, waist and hip pain, frequent urination, spermatorrhea, muscle pain, kidney heat, shock injury, ischuria, bladder stones, etc. M. indica, also known as Mango Jimusi in Mongolia, Abalaiand Sabalai in Tibet, is the fruits of M. indica; it is sour, sweet in flavor, warm, heavy, greasy in nature, and has the effects of invigorating the kidney, eliminating kidney cold. It is used to treat kidney shock and low back pain, kidney heat, with the effect of eliminating cold and reinforcing the kidney. In Inner Mongolia, the Mongolian medicine doctors often use the dry fruits of N. nuclifera, which is similar to M. indica in nature, flavor and effi cacy. It is also called white lotus, lotus seed, lotus rice, lotus flesh and alternative Nelumbinis Semen (Jianlanzi in Chinese). Seeds of White flower Calacila are the ripe fruits of C. minax of Fabaceae family. It has a bitter flavor, cold nature and can dispel blood stasis, relieve pain, clear heat and dehumidify. Torreyae Semen is the fruits of Torrey grandis *Merrillii* (Taxaceae family). The above three are alternatively used, replacing the three seeds (Luo, 2006). Nelumbinis Semen, also known as sweet lotus seed, is the ripe fruits of *N. nucifera*. Mongolian medicine doctors use mature dried fruits as medicine.

2.3.3. Origin of assistant medicine in Sugemule-10

Bright Salt (processed) is known as Zhu Mu Sa Wu, Mao Lu Er Da Bu Si in TMM. Its main ingredient is sodium chloride, the flavor is salty, sweet, the nature is warm and it is heavy, soft and sharp. It is Mongolian medicine that can regulate stomach fire and eliminate Badagan. Badagan refers to a mucus-like substance in the body that has the characteristics of coldness. In addition to the general cold symptoms, the dysfunction of Badagan can easily lead to the stagnation of water and the increase of various secretions. Bright Salt can inhibit Heyi and improve eyesight. *NaoSha* is the crystal of *Sal ammoniac*, a kind of ammonium chlorodode; it is known as *He Le Chao Ri Ge Qi Da Bu Su*, Zha Za in TMM, and has salty, bitter, pungent flavor. It is warm, astringent, sharp, heavy, slightly toxic (processed) and can diuresis, detumescence, detoxify and dry yellow water. It is used for ischuria, edema, renal fever, bladder fever, hematuria, stones, etc. According to the theory of Mongolian medicine (Chinese Medical Encyclopedia Mongolian Medicine Editorial Committee, 1992), the treatment of edema is to regulate stomach fire, suppress Heyi, dry dampness and diuresis; therefore, in TMM *Sal ammoniacas* used as a substitute of Bright Salt. In TMM, *Zhan Ba* includes three types. *Malvae Fructus*, known as *E Bu Le Zhu* *ErQiQeGe*, MaNing Zhan Ba in TMM, is the dry and mature fruit of *Malva verticillata* L., Malvacese. It is sweet, astringent, cool in nature, and is sharp, heavy, dry; it can open the veins, induce diuresis and disperse swelling, dry pus, relieve diarrhea, quench thirst and is used to treat ischuria and bladder stones. *Zhao Sun QiQiGe* (*Mao Zhan Ba*) is the dried ripe fruits of *Malva mauritian* L.; its nature, flavor, function and indications are the same as *Malvae Fructus*. Flower of Hollyhock is the dried flower of *Althaea rosea* L.; in TMM, it is known as *Ha Lu QiQiGe*. The Mongolian name is *E Ri Zhan Ba*. It is salty, sweet in flavor, cold in nature, and can induce diuresis, disperse swelling, clear kidney/bladder heat, stop nocturnal emission and hematuria. It is used as the substitute of *Malvae Fructus*. Among the above three, *Malvae Fructus* is the best (Yi, 2015), and the currently used *Zhan Ba* is *Malvae Fructus*.

2.3.4. Origin of guide medicine in Sugemule-10

The botanical origin of Ga, Zingiberis Rhizoma, BaoRiGa (Zingiberis Rhizoma), processed Ginger and Ga Zha is the rhizome of *Z. officinal*, the perennial herb of Zingiberaceae. *ManGa*, ZaGa and GaZha are rhizomes of *Kaempferia galanga* L., Zingiberaceae. These are basically similar in nature, flavor and efficacy; they can dispel cold, Badagan, Heyi, and regulate stomach fire. According to the Ministry-Promulgated Drug Standards, Zingiberis Rhizoma in Sugemule-10 should be the dry rhizome of *Z. officinal*.

According to the above analysis, Sugemule-10 is a prescription recorded in Four Medical Classics, and the above-mentioned...
Table 2
Evolution of Sugemule-10 (Sgml-10) composition.

| No. | Literary works                                   | Names       | Composition                                                                 | Efficacy                                                                                                     | Publication years |
|-----|-------------------------------------------------|-------------|----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|-------------------|
| 1   | Four Medical Classics                           | Sgml-10 A   |                                                                           | A1: Eliminate kidney cold, diuresis, stone disease                                                          | 8th century       |
| 2   | Hundred Experience Treasure Pearl               | Sgml-10 Ditto A |                                                                         | Ditto A                                                                                                     | 1511–1577         |
| 3   | Medical Know-how Secrets                        | Sgml-10 Ditto A |                                                                         | Ditto A                                                                                                     | 1682              |
| 4   | Blue Liu li                                     | Sgml-10 Ditto A |                                                                         | Ditto A                                                                                                     | 1689              |
| 5   | Qin • Quejüa la shen san zhu                   | Sgml-10 B   |                                                                           | Ditto A                                                                                                     | 1690              |
| 6   | Lan Ta Bu                                       | Sgml-10 Ditto A |                                                                         | Ditto A                                                                                                     | 1691              |
| 7   | Gaoshige Meilin Prescription                   |             |                                                                           | Eliminate kidney cold, kidney Heyi disease, spermatorrhrea                                                  | 1751–1785         |
| 8   | Kai jing yaAo qi er                             | Sgml-10 Ditto A |                                                                         | Eliminate kidney cold                                                                                       | 17th century      |
| 9   | Puji Prescriptions                              | Sgml-10 Ditto A |                                                                         | Ditto A                                                                                                     | 1813              |
| 10  | Sea of Medical Law                              | Sgml-10 Ditto B |                                                                         | Kidney stone, urinary obstruction, kidney Heyi disease                                                       | 1829              |
| 11  | TongwaGaji de                                   | Sgml-10 Ditto B Myristica Semen, donkey Flesh, Anser Meat Ditto A |                                 | Ditto A + kidney Heyi disease, kidney Awada disease                                                         | 1888              |
| 12  | The Dual Key to Diagnosis and Medicine          | Sgml-10 Ditto A |                                                                         | Eliminate kidney cold                                                                                       | 18th century      |
| 13  | Zhe Dui Ning Nuuer                              | Sgml-10 Ditto A |                                                                         | Eliminate kidney cold, kidney Heyi disease, urinary tract infection + Ditto A                                | 19th century      |
| 14  | Gaoshige Meilin Prescription                   | Sgml-10 C   |                                                                           | Ditto A                                                                                                     | 19th century      |
| 15  | A Collection of Secret Recipes of Mongolian Medicine | Sgml-10 Ditto C |                                                                         | Ditto A + treatment of all cold syndromes in the waist                                                     | 1964              |
| 16  | Mongolian Medicine Prescriptions                | Sgml-10 Sgml, Crab, Processed Ginger, Piperis Longi Fructus, Bright Salt, Malvae Fructus, Cervi Cornu Panthorichum, White Nelumbinis Semen, Nelumbinis Semen, Lotus Seed |                                 | Insufficient essence, cold kidney, cold waist, turbid stone leaching, poor urination                       | 1986              |
| 17  | Standards for Mongolian Medicines in Inner Mongolia | Sgml-10 Sgml, Ga, sal-ammoniac, Piperis Longi Fructus, Moschus, Crab, Torreya Semen, Nelumbo nucifera Gaertn., Hollyhock Flower |                                 | Ditto A + kidney deficiency, low back pain, ischemia                                                       | 1988              |
| 18  | Chinese Medical Encyclopedia • Mongolian Medicine | Sgml-10 Shi Wei Dou Kou Powder |                             | Bladder stone, kidney cold and low back pain, ischemia                                                      | 1992              |
| 19  | Medicine Standards of the Ministry of Health of the People's Republic of China | Sgml-10/Yi zhi Wenshen Shiwei Pill | Alpiniae Oxyphyllae Fructus, Zingiberis Rhizoma, sal-ammoniac, Piperis Longi Fructus, Torreya Semen, Nelumbinis Semen, C. minax, Crab, Malvae Fructus, Moschus | Kidney cold, deficiency, low back pain, ischemia                                                                | 1998              |
| 20  | He Li Le Jing Zhu Jie Yi Nan Jing               | Sgml-10 Ditto A |                                                                         | Ditto A                                                                                                     | 1999              |
| 21  | A Er Shan Xi Ma                                | Sgml-10 Ditto C |                                                                         | Ditto A                                                                                                     | 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 disperses 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. Caesalpinia Crisatae 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 pimplies 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 combination 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; Chi 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 Decotion 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 Can 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-DHGZ of Zingiberis Rhizom has the anti-inflammatory activity and reduced the renal fibrosis (Elseweidy, Zaghloul, & Younis, 2016). The ash content of
The clinical application of Sugemule-10.

Lotus seed (Mani, Subramanian, Pillai, & Muthusamy, 2010) usually affects and hinders its clinical rational use. 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.

| 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 + Xiriga-4 Decoction; Noon: Xirimaoou-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/ Gurgunu-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, BugregnAudu – 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 level + 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 | | (Yi & Chen, 2014) |
| AGN              | 63  | Conventional treatment (diuresis, antihypertensive) | conventional treatment + sgml-10 (Xiriga – 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. Xirimaoou-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; Saligarudi and Sa Li Chong are different names for the same formula, which is composed of Terminalia chebula Retz., eclecampane, aconitum and cardamom, calamus and Silver verminion, Moschus, Hollyhock Flower and Canovale Semen, 175 g each, Chinensis Cassie 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; Gurgunu-13 is composed of saffron 10 g clove, bezoar, Moschus, hornbill horn, silver verminion, red sandalwood, T. chebula, Melia chinensis, Gardenia jasminoides and Osmanthus sylvestris 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.
the pulse, diuresis, deswelling of Malvae Fructus, Crab, sal ammoniac for adjuvant; Zingiberis Rhizoma and Bibo Piperis Longi Fructus are envoy drugs.

The efficacy of Sugemule-10 has been mainly in the treatment of kidney cold, urodisalysis 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, Torreyae 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, pillled 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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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, C. (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.