Textual Research on Name, Variety and Property of the Multi-origin Tibetan Herb "Azhong"

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Abstract By consulting ancient Tibetan medical literature such as books of materia medica, medical works, and prescription books, as well as modern and contemporary literature and materials, and in combination with the interview and investigation of clinical use and expert consultation, we collated and verified the name, variety classification, plant origin, application and other recorded information of Tibetan herb "Azhong", and summarized and analyzed the phenomenon of mixed use or substitution of medicinal plants. According to textual research, it first appeared in the *Four Medical Tantras*. The Tibetan herb "Azhong" is simply recorded in the ancient books and Materia Medica, which are collectively called "Azhong". Since the 15th century, there have been varieties such as Za Azhong, Kan Azhong, Xing Azhong, Pumou Azhong, Zha Azhong, Bang Azhong, and the top grade is called Azhong Nabu and Nacang Azhong, and the bottom grade is Azhong Gabu. According to modern literature, the origin of "Azhong" involves 12 species of plants belonging to 8 genera, 5 families. At present, *Arenaria kansuensis* Maxim, *Ajania purpurea* Shih. and *Thalictrum squamiferum* Lecoy are the mainstream medicinal materials of "Azhong". There is a certain basis for clinical application and theoretical records in the literature in terms of the mutual alternative use of Tibetan medicinal materials such as "Azhong" and traditional medicinal materials in different regions. Therefore, it is necessary to use modern chemical technology and pharmacological experiments to conduct a comparative study on the material basis and biological activity of different varieties of medicinal materials, and carry out a survey on resources and use status, so as to standardize the use of their varieties and origins and improve the safety of clinical medication.

Key words Tibetan medicine; Azhong; Origin; Drug property

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The "Azhong" (ཨ་སྐོང་) family is a generic name, as well as one of the most representative medicinal herbs in the class of "one name corresponding to multiple herbs". It is included in classic works such as *Dumu Materia Medica*[1], *Four Medical Tantras*[2], *Lanliuli*[3] and *Jingzhu Materia Medica*[4]. In modern literature such as the 95 edition of *Ministerial Standard · Tibetan Medicine Volume and Prescription Medicinal Materials for Traditional Chinese Medicine Formulations*, *Arenaria kansuensis* Maxim and *Areneria kensuensis* var. *ovatipetala* Tsui are used as original plants, referred to as "Azhong Gabu", and they are used in 88 classic prescriptions and application prescriptions such as Wuwei Zaozhui Powder, Ershiwuwei Feibing Pills, Ershiliuwei Dida Pills and Ershiwuwei Shihuihua Pills as the main or secondary herb. According to the literature, "Azhong" has the efficacy of treating pneumonia, cough, heat toxin, lung pus, *etc.* It is mainly used in clinical treatment of Tibetan medicine for lung pus, pulmonary fever, tuberculosis, pleural effusion, and sputum that is difficult to cough up. In ancient literature, the name "Azhong" is commonly used for formulas, effects and plant morphology. However, in later literature, due to inconsistent identification criteria such as literature and factions, regional resources, and plant habitats, there are six varieties of Azhong, including Za Azhong, Kan Azhong, Bang Azhong, Zha Azhong, Xing Azhong, and Pumou Azhong, forming a situation of "homonym" and "one name corresponding to multiple herbs". Furthermore, the Chinese names and origins identified in modern and contemporary literature include 12 species such as *A. kansuensis* Maxim, *Ajania purpura* C. Shih., *Androsace tapete* Maxim., *T. squamiferum* Lecoy., *Buddleja crispa* Benth., and *Micromeria Barosma* (W. W. Smith) Hand-Mazz, involving 5 different families: Ranunculaceae, Asteraceae, Caryophyllaceae, Primulaceae, and Loganiaceae. Currently, the variety of Tibetan herb "Azhong" used in Tibetan hospitals and pharmaceutical factories is not uniform, resulting in the use of medicinal materials of the "Azhong" class being considered misuse or abuse. Therefore, in the trend of modern standardization of Tibetan medicine, explaining the historical evolution and literature records on the classification of medicinal materials of the Tibetan herb "Azhong" class can provide more choices or priority choices for preventing and treating diseases or researching drug ingredients in the context of "one name corresponding to multiple herbs". This paper sorted out and verified the naming, variety classification, morphology, efficacy and medication of Tibetan herb "Azhong" by consulting medical records, herbal literature, and famous old experts. This paper provides a literature basis for tracing the origins of Azhong medicinal materials and clarifying the rationality of their use.

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Textual Research on Name and Classification

In the work "*Four Medical Tantras*", "Azhong" is recorded as the correct name in the contents of medicinal formulas and their effects, but the plant morphological characteristics of the Tibetan herb "Azhong" are not recorded, and there are no other aliases or definitions or classifications. In later Tibetan medical works,

multiple varieties are gradually divided. "Azhong" is divided into three categories: "Za Azhong", "Kan Azhong", and "Xing Azhong" in *Annotations to Difficult Problems in Four Medical Tantras* of the 14th century[8]. In this classification, Pumou Azhong appears in *Annotations to Four Medical Tantras of Jinba* of the 14th century[9], and there are two more classifications: Za Azhong and Bang (Russian) Azhong in *Annotations to Four Medical Tantras of Linmanba*. As recorded in *Lanliuli* and *Jingzhu Materia Medica*, "Azhong" is the general name, under which a variety of top- and low-grade of varieties are recorded. The naming method is relatively simple, adding an additional word to the name "Azhong" and classifying the object based on the characteristics of the medicinal material[10]. Some are named after a plant source, such as Kan Azhong (མགན་ཨ་ཀུང་།) and Pumou Azhong (ཕུ་མོད་ཨ་ཀུང་།); some are named after the growing environment, such as Za Azhong (རྫ་ཨ་ཀུང་།), Bang Azhong (ཐང་ཨ་ཀུང་།); there are also varieties named after plant morphology, such as Za Azhong (རྩྭ་ཨ་ཀུང་།), Xing Azhong (ཤིང་ཨ་ཀུང་།); and some names indicate the classification of top- and low-grade products, such as Azhong Gabu (ཨ་ཀུང་དཀར་པོ།)", Azhong Nabu (ཨ་ཀུང་ནག་པོ།), and Nacang Azhong (ནག་ཚང་ཨ་ཀུང་།). Due to different pronunciations and translations of Tibetan nouns, "Zha" and "Za" were mixed in later Chinese translated literature[11], and "Kan Azhong" was referred to as "Zangaiju"[12] and "Yinchenhao"[12].

Textual Research on Ancient Books and Documents of Previous Dynasties

The plant morphology of Tibetan herb "Azhong" is first seen in *Dumu Materia Medica* and *Miaoyin Materia Medica* of the 7th century AD[13], recording that "The monarch drug for lung disease, Azhong, grows on northern slopes. Its leaves are green and the edges of the leaves are split and feather-like. The stems and plants are like German tamarisk, and the flowers look like golden ribbons, with a powdery and oily texture". In *Yutuo Materia Medica* of the 8th century[14], it is recorded that "Azhong grows on shady slopes, and has black and powdery petioles and yellow flowers with a strong odor, a length of one foot or one elbow." The above-mentioned ancient texts such as *Dumu Materia Medica*, *Miaoyin Materia Medica* and *Yutuo Materia Medica* simply record the plant morphology and growth environment of "Azhong". All depict pink powder and similar colors of the flowers and stems, but the records of odor and plant height are incomplete and could not be compared. It is uncertain whether they are the same plant, which may be one of the reasons for the identification of different medicinal herbs in the later stage.

The identification and records of Traditional Tibetan medicine "Azhong" by Tibetan medical practitioners in previous dynasties show that there are different varieties of plants, and they are also summarized into multiple varieties in the literature.

In *Ancestors' Oral Statement* of the 15th century[15], it is recorded that "the Azhong used for the treatment of pneumonia is Kan Azhong, whose leaves are like wormwood leaves, and those from the upper part are authentic products, and those from Namtso is the best". In *Micebuyi · Yaoshi*[16] and *Sixuzhushi · Kezimeichuan*[17], Kan Azhong growing near Namtso is called "Nacang Azhong". In *Annotations to Four Medical Tantras of Jinba* of the 16th century[8], it is recorded that "the plants of Za Azhong are short and sharp, like grass (thin), and the flowers are white, and the roots are claw-like". In *Lanliuli and Complete Collection of Series Wall Charts of The Four Medical Tantras* of the 17th century[17], "Azhong" is divided into four types, among which "Za Azhong" is divided into two types: Azhong Nabu and Azhong Gabu, which are annotated referring to the original text of *Tujian* (*Dumu Materia Medica*): "The black roots are thin, and there are many leaves growing in stack. Those with small stems are of top grade, while white ones are inconsistent with *Tujian*, with thick roots, large leaves and yellow flowers, and they are of the low grade. Xing Azhong has thin roots and leaves that grow like small copper plates in stack, and it can eliminate pneumonia", as shown in Fig. 1. In *Jingzhu Materia Medica* of the 17th century[4], Azhong is divided into three types: "Za Azhong is like grass, and the plants are short and have short and sharp leaves, white and small flowers, hard and claw-like roots, and a woody stem. Kan Azhong is Kanqiongsaiguo (མགན་ཁྱུང་ཚེར་མགོ།)". In the book *Treatise on Medicinal Properties* (Yaoxinglun), it is recorded: "Azhong treats tuberculosis, and the same applies to Kanqiongsaiguo; and Xing Azhong is flower-free Pumou Gabu, which has white leaves like mugwort leaves". The records of "Kan Azhong" in *Lanliuli* and *Jingzhu Materia Medica* are consistent, both classifying it to "Kanba", and it is annotated referring to the original text of *Tujian* (*Yutuo Materia Medica*)[12]: "Kan Azhong grows at the lower part of mountains. The leaves are clustered and stack to the ground. The color is gray, and the length is one elbow and one finger. The flowers are yellow and fragrant, and can subside swelling, and treat sores and gastrointestinal diseases". The leaves are small and fractured like feather, and the stem is hard, and the flowers are yellow. Kan Azhong is commonly known as "Azhong Gabu" in the folk. And in *Yutuo Materia Medica*, it is called "Kanba Gabu (མགན་པ་དཀར་པོ།)". As shown in the book, Kan Azhong, also known as Kanba Gabu and Kanqiongsaiguo, has added functions such as subsiding swelling, reducing carbuncle, astringing sores, purging the lungs and promoting kidney function. *Gamadanpei Yizhu*[18] and *Degelaman Yizhu*[19] of the 18th century record that "Za Azhong" has a plant shape looking like *Thalictrum aquilegiifolium* var. *sibiricum* Linnaeus (ཞྭགས་ཀྱུ), and grows in gravel piles on high mountains. It can be seen from above *Lanliuli* and *Jingzhu Materia Medica*, as typical representative works of Northern and Southern Tibetan medicine, that there are differences in the recognition of Tibetan herb Azhong. The plants recorded in "Za Azhong" and "Xing Azhong" are different, and the plant origins of the two kinds of Za Azhong recorded in the current

Lanliuli have not been determined. *Lanliuli* quotes the plant morphology described in *Dumu Materia Medica* and classifies it to the top grade. It can be seen that the original variety records of Tibetan herb "Azhong" are relatively chaotic, but the names of varieties of top and low grades are relatively unified.

Furthermore, modern literature and Tibetan medicine scholars have different perspectives on the identification of "Azhong". However, through organization, it was found that most of the medicinal herb varieties described in modern literature are clarified and analyzed based on previous literature records. In *Zangyao Jingjing Materia Medica*, "Zha Azhong" is identified as "Azhong Nabu" recorded in *Lanliuli*, and the identified origin is *T. squamiferum* Lecoy., which is classified as the top grade of Tibetan herb "Azhong", while "Za Azhong" recorded in *Jingzhu Materia Medica* is called "Azhong Gabu", and it is identified as *A. kansuensis* Maxim. var. *ovatipetata* Tsui. and *A. kansuensis* Maxim. In *Lanliuli*, "Azhong Gabu" is also identified as a low-grade product of Tibetan herb Azhong, indicating that the current use of *T. squamiferum* Lecoy. and *A. kansuensis* Maxim. may be in a relation of top- and low-grade varieties. The plant morphology of "Kan Azhong" recorded in *Jingzhu Materia Medica* and *Lanliuli* is consistent, but the identification basis has become more complex in modern literature. In specific, Kan Azhong, also known as "Kanba Gabu" and "Kanqiongsaiguo", was subjected to origin identification as *Ajania tenuifolia* (Jacq.) Tzvel. and *Ajania khartensis* (Dunn) Shih.[20-21]. "Kan Azhong" and the origin of "Nacang Azhong" were identified as *Ajania purpurea* C. Shih.[22], and Nacang Azhong was referred to as a genuine product in literature[15-16]. Although there is no record of plant morphology, we believe that "Nacang Azhong" should possess the plant morphological characteristics of "Kan Azhong" because it is classified into Kan Azhong. "Nacang Azhong" may be a genuine medicinal herb of "Kan Azhong", and "Nacang" refers to Shenzha County in the border area between Naqu and Ali[11]. It can be seen that the records of Tibetan herb "Azhong" in ancient materia medica books and herbs are relatively brief. In addition, due to the different factions of Tibetan medicine, literature, and environmental resources used in later literature to identify this medicinal material, there are multiple varieties identified and classified, thus forming the characteristic of "one name corresponding to multiple herbs".

a. Top-grade product of Za Azhong Nabu; b. low-grade product of Za Azhong Nabu; c. Xing Azhong; d. Kan Azhong.

Fig. 1 Illustrations of "Azhong" in the *Complete Collection of Four Medical Classics Series Wall Charts*

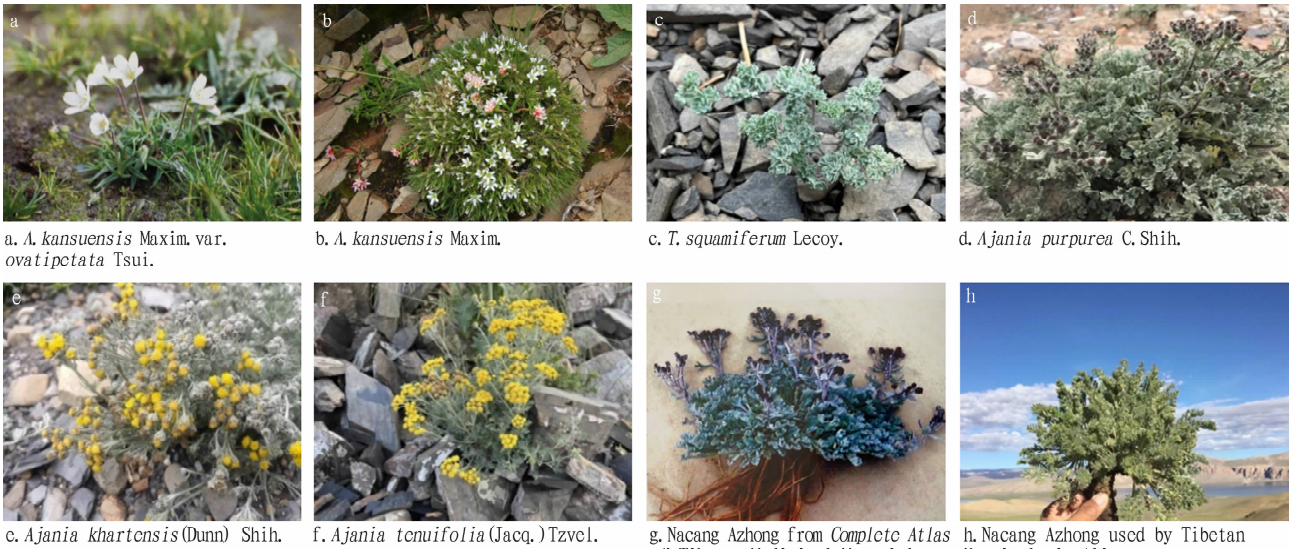
Textual research on modern and contemporary literature

The origins of "Azhong" medicinal herbs recorded in modern literature are relatively complex, and there is no classification of "species, genus and family" for medicinal herbs in historical Tibetan medicine books. The classification and illustrations of Tibetan herb "Azhong" in literature such as *Jingzhu Materia Medica* and *Lanliuli* are relatively simple. Modern literature generally uses these two books as the basis for origin identification, resulting in the appearance of multiple plant origins of the same genus and family in three kinds of Tibetan medicine monographs, including Tibetan, Chinese, and Chinese translations, as well as multiple literal and Chinese names (mostly the names of plant origins). In *Tibetan Medicine Jingjing Materia Medica*, *Diqing Tibetan Medicine*, *Chinese Tibetan Materia Medica*[23], and *Flora of China*[24], it is recorded that the original plant of "Zha Azhong" is *T. squamiferum* Lecoy. According to records such as *Tibetan Medicine Jingjing Materia Medica*, *Chinese Tibetan Medicine*[25], and *Chinese Tibetan Materia Medica*, the origin of "Azhong Gabu" is *A. kansuensis* Maxim. In *Ganlu Materia Medica Mingjing*[26] and *Tibetan Medicine Specimen Illustrated Book · Mingjing*[27], it is recorded that "Za Azhong" is *A. kansuensis* Maxim. var. *ovatipetata* Tsui. In Interpretation of *Tibetan Medicine Jinsui Materia Medica*, *Complete Atlas of Tibetan Medicinal Materials*[28] and *Tibetan Medicine Jingjing Materia Medica*, it is recorded that the origin of "Kan Azhong" was *Ajania purpurea* C. Shih. However, there is still controversy over the origins of Pumou Azhong and Xing Azhong, and Bang Azhong is not used as a medicine. In modern literature, a total of 12 plant species of Tibetan herb "Azhong" have been summarized, including plants in five different families. It indicates that the emergence of plant origins in different families is related to the reference of different Tibetan medicine ancient books by modern literature.

Drug Property Analysis

Summary of medicinal parts, properties and flavors

According to *Dumu Materia Medica*[1], it is recorded that "the abscesses accumulate in the chest cavity can be dried by Azhong, and Bawei Azhong is used to treat pulmonary tuberculosis. *Yutuo Materia Medica*[11] records that "Azhong" treats lung diseases, while *The Four Medical Tantras*[2] records that "Azhong treats lung fever". In *Tips of The Four Medical Tantras*[2], it is recorded that "pulmonary tuberculosis is caused by the accumulation of phlegm in the lungs, and can be treated by bathing with Azhong or its medicinal solution". In *Shiwanquan and Mijue Heice*[29], it is recorded that soaking in Kan Azhong or adding some Jianhua can be necessary for treating tuberculosis, and medicinal baths can also be adopted to treat lung diseases. In Tibetan medical books such as *Jingzhu Materia Medica*[4] and *Lanliuli*[3], it is used to treat pulmonary fever, syndrome of heat toxin, pulmonary abscess, pulmonary carbuncle, and tuberculosis. The herbs are all sweet, astringent, and spicy in flavor, and cool in nature. However, there are slight changes in the medicinal parts and efficacy of the herbs.



a. *A. kansuensis* Maxim. var. *ovatipetata* Tsui. b. *A. kansuensis* Maxim. c. *T. squamiferum* Lecoy. d. *Ajania purpurea* C. Shih.

e. *Ajania khartensis* (Dunn) Shih. f. *Ajania tenuifolia* (Jacq.) Tzvel. g. Nacang Azhong from *Complete Atlas of Tibetan Medicinal Materials* h. Nacang Azhong used by Tibetan Hospitals in Ali

a. *Tibetan Medicine Specimen Illustrated Book · Mingjing*; b. shot in Nyima County, Naqu; c. shot in Ngamring County, Shigatse; d. shot in Xinghai County, Qinghai Province; e. shot in Lhozhag County, Shannan; f. shot in Mila Mountain, Nyingchi.

Fig. 2 Mainstream varieties of "Azhong"

Records of prescriptions including Tibetan herb Azhong

In *Complete Collection of Tibetan Medicine Prescriptions*[29], a total of 88 prescriptions containing Tibetan herbs such as "Azhong", "Azhong Gabu", and "Nacang Azhong" were collected. There are a total of 6 prescriptions included in *Drug Standard of Ministry of Public Health of the Peoples Republic of China: Tibetan Medicine Volume*[30]. We analyzed the treatment of diseases and drug compatibility of the 88 prescriptions containing Tibetan herb "Azhong" and found that the main efficacy of the prescriptions is concentrated in treating lung heat disease, abscess and effusion in the chest cavity, cough and phlegm, throat swelling and pain, *etc.* (Fig. 3). The drug compatibility is based on the efficacy recorded in *the Four Medical Tantras*, and it was mostly used in combination with 160 different medicinal herbs, including herbs used to treat lung heat such as *Pegaeophyton scapiflorum*, *Vitis vinifera* L., *Bergenia purpurascens* and *Crocus sativus*, herbs for treating blood heat disorders such as *Santalum album* L., *Pterocarpus indicus* Willd., *Lagotis glauca* Gaertn. and Radix Arnebiae/Radix Lithospermi, herbs for treating lung diseases such as *Bambusa textilis* McClure and *Glycyrrhiza uralensis*, herbs for treating phlegm and pus such as *Hippophae rhamnoides*, *Dolomiaea souliei*, and *Lancea tibetica*, herbs for treating uroschesis such as *Myristica fragrans* Houtt. and *Eugenia caryophyllata* Thunb., and harmonizing herbs such as *Terminalia chebula* Retz. (Fig. 4). According to statistics and analysis of the flavor changes of various herbs (≥4), the herbs are mainly bitter (37.1%) and sweet (30.4%) in flavor among six flavors; and in the three transformed flavors, bitter (57.7%) and sweet (34.9%) are the main ones. From the seventeen effects of Tibetan herbs, it can be seen that the herbs are mainly cool, blunt, heavy, and thin, and can treat disease properties such as heat, sharp, and light, as shown in Fig. 5.

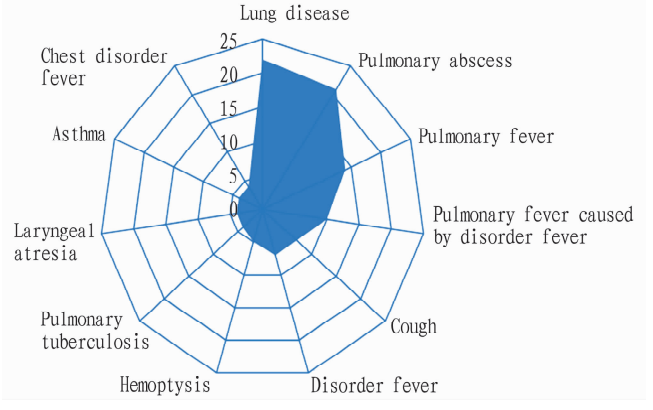


Fig. 3 Map of indications of prescriptions (≥4)

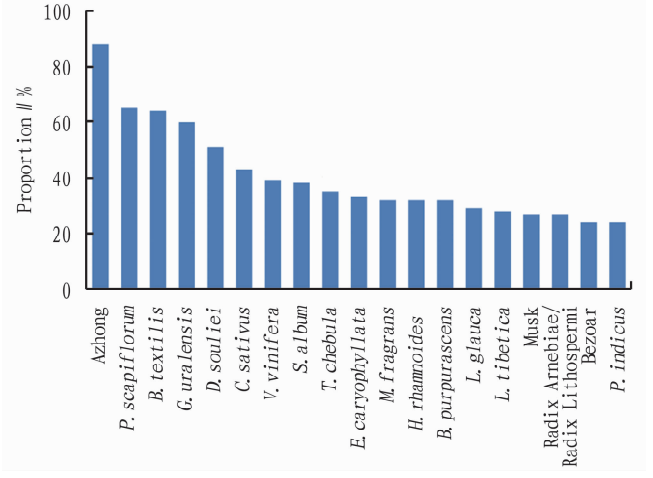


Fig. 4 Statistical chart of medicinal material compatibility of prescriptions (≥24)

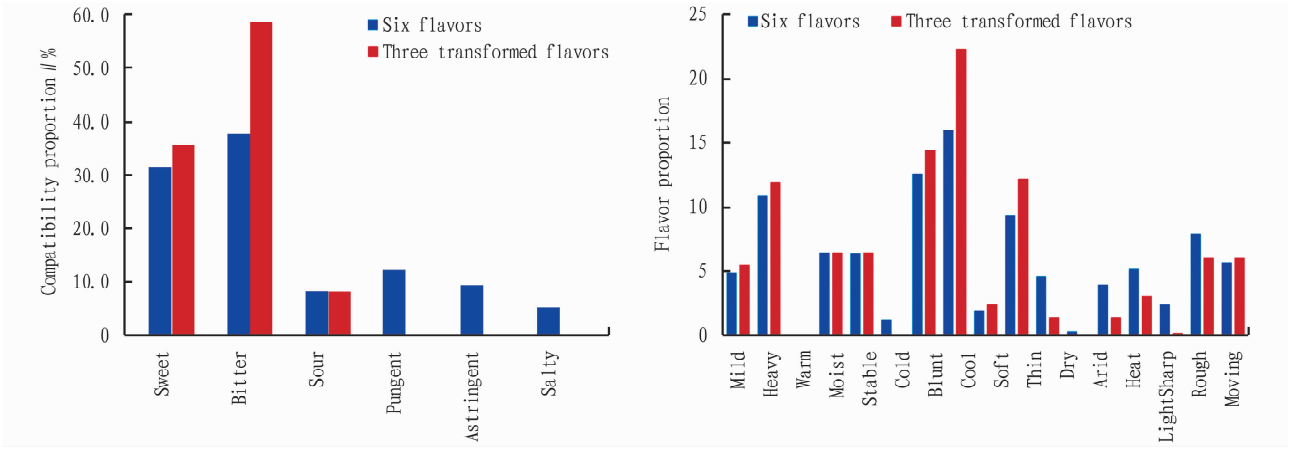


Fig. 5 Analysis chart of flavors, properties and transformed flavors of herbs

Conclusions

In summary, from the perspective of exploring classic prescriptions, we took the development time of Tibetan medicine as the axis and conducted research on the records of "Azhong" in different periods. The results showed that the ancient Tibetan herb Azhong has the same efficacy, prescriptions, flavors and transformed flavors as today, but there are certain changes in its origin, classification, and quality differences. The name "Azhong" is used in Tibetan medical literature and prescriptions before the 14th century, and there is no classification of varieties. Subsequently, six traditional varieties of medicinal herbs are classified under the general name "Azhong" in the literature, resulting in 12 varieties of plants in different families involved in the source of this class of medicinal herbs in modern Chinese translation monographs. At present, the herbs used in the actual clinical prescriptions of Tibetan medicine include *A. kansuensis* Maxim., *Ajania purpurea* C. Shih. and *T. squamiferum* Lecoy. We believe that the later literature is based on the *Four Medical Tantras*, *Dumu Materia Medica*, and *Yutuo Materia Medica*, combined with regional resource conditions, plant habitats, and different habits in medication by different factions of Tibetan medicine. Ancient doctors used medicinal materials with the same property and flavor and efficacy as substitutes and classified them into one category, resulting in the identification and use of different medicinal materials and the situation of "one name corresponding to multiple herbs". It provides more options for the development of Tibetan medicine prescriptions and medicinal materials, and also poses challenges to the quality standards and clinical medication norms of Tibetan medicinal materials.

At present, the most commonly used and widely circulated "Azhong" in clinical practice is *A. kansuensis* Maxim., known as Azhong Gabu. It has been regarded as a low-grade product of Tibetan herb "Azhong" in historical literature, and there have been many studies on its chemical composition and pharmacological effects[49-51]. The use and research of Za Azhong and Kan Azhong are less studied, which may be due to the complex growth environment, limited resources and high altitude issues, which lead to a shortage of supply. However, there is a long record of medication in Tibetan medical literature, which shows that they have therapeutic effects on pneumonia, tuberculosis, pulmonary abscess, cough and phlegm, and they are worthy of further in-depth research. In addition, Zha Azhong, also known as Azhong Nabu, is a top-grade medicinal herb of the "Azhong" class. It belongs to the genus *Thalictrum* L. in the Ranunculaceae family. Studies at home and abroad have shown that this genus of plants contains alkaloids, flavonoids, triterpenes, glycosides and other chemical components[52-53], and has high research value. Similarly, Kan Azhong is a plant of *Ajania* in the Compositae family, which is the origin of traditional Chinese medicine and ethnic medicine. It mainly contains chemical components such as sesquiterpenes, flavonoids, and their volatile oils[54-56]. In the future, it is necessary to use technologies such as GC-MS and UPLC-Q-TOF/MS, combined with modern chemical composition for qualitative and quantitative analysis, and conduct pharmacological activity experiments based on traditional efficacy to compare the differences in chemical composition of different varieties of medicinal materials, evaluate the efficacy differences between medicinal materials of the Tibetan herb "Azhong" class, scientifically explain the characteristics of traditional classification methods for the Tibetan herb "Azhong" class, and further carry out drug quality evaluation.

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