Modern Research of Tibetan Medicine

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Abstract

Tibetan medicine is one of the important components of our national medicine. In recent years, research on Tibetan medicine has gradually deepened from quality control, formulation research, chemical composition, and pharmacological effects. In addition, clinical application and experimental research have made great progress. This paper summarizes the latest developments in Tibetan medicine theory and experimental research, in order to provide reference for the development and clinical application of Tibetan medicine in the future.

Keywords: Modern theory, Tibetan medicine, Traditional theory

Tibetan Medicine

Tibetan medicine is a medical system with national characteristics formed by the Tibetan people through long-term practice under the guidance of the Tibetan medicine theory, constantly absorbing and integrating traditional Chinese medicine, Indian medicine, Arab medicine, and other traditional medical theories. Tibetan medicine, known as "the miraculous flower on the grassland," is a natural medicine used by the Tibetan people for prevention, treatment, and health care. It is a valuable culture inherited by the Tibetan people to this day and is also a treasure in the treasure house of Chinese medicine. With a long history, Tibetan people have been migrating and living in remote areas for a long time due to the long-term war. As a result, they have unique national and regional features, which make Tibetan medicine more mysterious. In recent years, with the national attention, it has gradually embarked on the development path. Tibetan medicine has attracted more and more attention because of its various kinds and remarkable curative effects, especially in the treatment of digestive system diseases, gynecological diseases, arthritis, and cardiovascular and cerebrovascular diseases. With the strong support of the state, the Tibetan medicine industry has developed rapidly and has been listed as the second largest support industry in Tibet, which has laid the foundation for Tibetan medicine to go to the world and let more people know and apply it. This article will elaborate on the following aspects.

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Traditional Theory Research of Tibetan Medicine

After thousands of years of cultural accumulation, oral transmission from generation to generation, and attentive research by Tibetan medical workers, Tibetan medical theory has become a mature and perfect independent subject. Tibetan medicine takes the theory of three causes as its theoretical core. The "three causes" are not "internal causes, external causes, and not internal and external causes" as mentioned in traditional Chinese medicine but "Long, Chi Ba, and Bacon" in Tibetan medicine. These three elements are inherent substances in the human body, namely "three causes." They restrict each other and make the organism in a relatively stable state. When one of the elements appears abnormal state such as excessive decay or dysfunction, the organism will lose its balance and cause disease. Therefore, in Tibetan medicine, diseases are usually divided into three categories: Long disease, Chi Ba disease, and Bacon's disease. In pharmacy, Tibetan medicine is guided by the five-source theory, which holds

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that all living things originate from the five sources (Tu, Shui, Feng, Huo, and Kong). The growth of drugs also originates from the five-source theory. Based on the five-source theory, Tibetan medicine theories such as six flavors (sweet, sour, bitter, pungent, salty, astringent), 8 natures (cold, hot, light, heavy, blunt, sharp, moist, and dry), and 17 effects (soft, raw, warm, moist, stable, cold, blunt, cool, soft, thin, dry, arid, hot, light, sharp, rough, and moving) are derived, forming Tibetan medicine theory with national characteristics. The specific principle of its medication system is contrary treatment (i.e., the treatment of cold diseases with hot drugs), similar to the "contrary treatment" in traditional Chinese medicine.

The theory of Tibetan medicinal property emphasizes the relationship among 5 sources, six flavors, 8 natures, and 17 effects and considers the heaven and earth, medicine, the process of medicine *in vivo*, and the therapeutic effect of medicine as a unified whole.[1] Based on the principles of Tibetan medicine such as "five sources," "six tastes," and "three tastes after digestion," Dang-Zhi[2] established a basic data framework for the pharmacological mechanism of Tibetan medicine and made a textual research on the efficacy of the Tibetan medicine prescription. It was found that the "Suo Luo Xi decoction" has resistance to the effect of "Chi Ba" and "Long" in the aspects of "5 sources," "6 tastes," "3 tastes after digestion," and "17 effects," which provides a theoretical basis for the clinical treatment of lung fever, cough, and other diseases caused by "Chi Ba" and "Long." This data mining method can guide the development of new Tibetan medicine, pharmacological analysis, clinical medication, diagnosis and treatment of diseases, and many other fields.

Research on Modern Theory of Tibetan Medicine

Tibetan medicine is guided by the Tibetan medicine theory. Applying the research methods of modern pharmacy, the therapeutic substance of Tibetan medicine is actually chemical substance in the effective. Therefore, we need to take advantage of modern science and technology to conduct in-depth research on the treatment process, pharmacodynamic substance basis, and chemical components of Tibetan medicine, and expound the treatment process, mechanism, and effect relationship of drugs from the structure, nature, pharmacological effects, toxic reactions, and other aspects of pharmacodynamic substances. In the process of developing Tibetan medicine, we should take the theory of Tibetan medicine as the foundation. Many botanicals are used by both Chinese medicine and Tibetan medicine, but they are different in usage and dosage. As a result, in the process of studying Tibetan medicine, we should pay more attention to take the Tibetan medicine theory as a guide and study the difference in the use of Tibetan medicine and traditional Chinese medicine based on their respective medical theories. This study will discuss the quality control, drug dosage form, chemical composition, and pharmacological effects of Tibetan medicine.

Resource

According to the Tibetan medical books, such as Crystal Beads Materia Medica (the famous Tibetan medical scientist Dumar Danzeng Pengcuo in 1840 collected the great achievements of Tibetan medicine and collected a comprehensive collection of Tibetan medicine books, which laid the foundation for the formation and development of Tibetan medicine), there are >2000 kinds of Tibetan medicines, of which plant medicines are the most, and the total amount is about 1500 kinds. In addition, there are >160 kinds of animal medicine and a small amount of mineral medicine.

The Qinghai–Tibet Plateau is a vast region, covering four climatic zones: subtropical, temperate, cold temperate, and frigid zones, with complex climatic conditions, great difference between north and south climates, and wide vertical difference. Therefore, the plant composition is complex, and the species are numerous. Dashang Luo has carried out field investigations in most areas of the plateau in the past 20 years, collecting data and a large number of specimens and samples. After identification and collation, there are 2085 species of Tibetan medicinal plants belonging to 692 genera and 191 families. Among them, there are 50 species of fungi belonging to 35 genera and 14 families; 6 species of lichens belonging to 4 families and 4 genera; 5 genera and 5 species of bryophytes belonging to 5 families; 118 species of ferns belonging to 55 genera of 30 families; 47 species and 3 varieties of tree plants belonging to 5 genera and 12 genera; and 141 varieties of 1 895 species belonging to 581 genera of 131 families of angiosperms, of which Compositae occupies the first place. In addition, there are 159 species of animal medicine belonging to 57 families, 111 genera, and 80 kinds of mineral medicine. At present, there are >3000 kinds of Tibetan medicines collected, including 2272 kinds of botanicals, 214 kinds of animal medicines, and >50 kinds of mineral medicines. Among them, 86 kinds of Tibetan medicines are specially produced at high altitude, and 360 kinds are most commonly used in Tibetan clinic. Such as the commonly used varieties are *Terminalia chebula*, *Terminalia billerica*, and *Phyllanthus emblica* (often referred to as "three major fruits"), *Saussurea involucrata*, and *Caesalpinia crista*.[3-6]

Study on quality control of Tibetan medicine

The research on Tibetan medicine has gradually entered the modern research from the initial research on traits, origins, ecology, medicinal properties, and pharmacology. The study of Tibetan medicine has been developed rapidly using modern new technology and methods, such as quantitative analysis, fingerprint, molecular structure, and molecular biology. Take the Chinese Pharmacopoeia as an example. According to the statistics, the 2015 edition of the Chinese Pharmacopoeia contains 8 Tibetan medicines and 19 Tibetan prescriptions. Although the varieties are small, the standard level is significantly higher. The comparison results of the revised Tibetan quality standards are shown in Table 1. It shows that with the advancement of science and technology, the quality control standards for Tibetan medicine contained in the Chinese Pharmacopoeia have also been improved.

Table 1: The comparison of quality standards of the partial Tibetan medicines recorded by the last three versions Chinese Pharmacopoeia

Tibetan medicines	2005 version	2010 version	2015 version
F. hippophae	Content determination of HPLC: Using hydrolyzed flavonoid aglycone luteolin as an indicator	Established specificity and active ingredient detection: Content determination of HPLC with behenyl methyl ester and 8-O-acetylanthanidin methyl ester as indicators	Same as 2010 version
T. billerica	TLC identification project: Using gallic acid as a control index, increased determination of water, impurities, and extractives	TLC identification project indicators changed from gallic acid to *T. billerica* (enucleation) reference medicinal materials	Same as 2010 version
P. emblica	TLC identification project: Using gallic acid as a control index	TLC identification project indicators changed from gallic acid to *P. emblica* reference medicinal materials Increased contents detection: Using gallic acid as an indicator	Increased medicine Powder identification
Xiaotong Tiegao	Not included	Not included	Content determination of HPLC with behenyl methyl ester and 8-O-acetylanthanidin methyl ester as indicators

F. hippophae: Fructus hippophae, T. billerica: Terminalia billerica, P. emblica: *Phyllanthus emblica*, HPLC: High-performance liquid chromatography, TLC: Thin-layer chromatography

Wan[7] carried out thin-layer chromatography and high-performance liquid chromatography (HPLC) analysis on Pangna, which is one of the commonly used Tibetan folk medicines. They took aconitine as the index component and compared it with *Aconitum gymnandrum* Maxim. and *Aconitum kongboense* Lauener. which were easy to be confused. As a result, they improved the original quality standards of the Pangna and established a characteristic spectrum, which contributed to the quality control of Pangna. Du *et al*.[8] established a high-specific polymerase chain reaction method for the identification of alpine salamander and its counterfeit products *Pachytriton labiatus* and *Gehyra mutilata* using DNA barcode identification technology. This method provides an effective way to identify many unknown sources of Tibetan medicine.

With the deepening of modern research on Tibetan medicine, the quality standard of Tibetan medicine has developed from single-index content determination to multi-index determination and from single medicine to compound prescription. For example, Li *et al*.[9] used ultrafast liquid chromatography–photodiode array detector to establish a rapid method for simultaneous determination of five chemical constituents in the Tibetan medicine *Pterocephalus hookeri* and to achieve simultaneous determination of multicomponent indicators, so as to provide a scientific basis for the study of chemical composition and quality control of *P. hookeri*. In the evaluation of multi-indicator quality, it is necessary to ensure that there are enough and high-purity chemical reference substances. However, it is difficult to separate the chemical reference substances from some medicines or the monomer is unstable, which leads to the lack of reference substances or difficult to obtain. To solve this problem, Zhimin Wang conducted a "quantitative analysis on multi-components by single marker" (QAMS) study, that is, using the relative correction factor between chemical components and using one component to synchronously monitor multiple components (when the reference substances are not available or difficult to obtain).[10,11] Wan[12] used QAMS method using penduletin as an internal reference substance, which can simultaneously determine the contents of chrysosplenoside D, pendulin, and chrysosplenoside B in the *Chrysosplenium nudicaule* Bunge. Compared with the external standard method, it can save the cost of multicomponent assay and control the quality of medicinal materials, which can provide technical reference for the multicomponent quantitative determination of other ethnic medicines. Similarly, for the quality control of Tibetan medicine compound prescriptions, the method of QAMS can also be used.[13-15] These new methods have laid a good foundation for the establishment of a quality control model for Tibetan medicine that reflects the overall view and reflects the safety and effectiveness and has played a positive role in improving the quality control of Tibetan medicine.

Study on dosage forms of Tibetan medicine

There are >20 kinds of Tibetan medicines in traditional dosage forms, such as water pills, powders, butter pills, decoctions, medicinal liquors, pastes, ashes, plaster, anointing, jewels, and herbs. Among them, powders and pills are the most commonly used models in clinical practice, followed by decoctions. In recent years, new dosage forms such as tablets, granules, capsules, oral liquids, and suppositories have been gradually applied to improve the quality of medicines and meet the requirements of convenient transportation, carrying, and use. New research and development of Tibetan medicine forms have been carried out. For example, Nuodikang capsule, which has been put on the market now, has the effect of benefiting qi for activating blood circulation and dredging pulse to relieve

pain and has an obvious effect on various cardiovascular and cerebrovascular diseases and cardiovascular neurasthenia. There is also the application of Qizhengxiaotong Plaster and Rhodiola capsules in the market. The application prospects are very broad. As shown in Table 2, the following is the classification of formulations of Tibetan medicines included in the 2015 edition of the Chinese pharmacopoeia.

To give full play to the pharmacodynamics and establish a scientific and reasonable quality standard of *Fructus hippophae* compound that follows the characteristics of Tibetan medicine, Yang[16] optimized the extraction technology of *F. hippophae* compound by single-factor experiment and orthogonal test. In addition, new technology and excipients were used to develop new dosage forms for *Lamiophlomis rotata* (Benth.), and the main dosage forms are self-microemulsifying soft capsules, pellets, lyophilized powder injection, dispersant, and cataplasma.[17] Lu[18] combined *Gentianopsis paludosa* and *Sophora alopecuroides L* and prepared a colon-targeting capsule for the clinical treatment of ulcerative colitis by optimizing the extraction process and screening the molding process of the prescription. However, the development of these new dosage forms is still in the early stage of research, and there are few clinical applications. Therefore, the research and development of new dosage forms of Tibetan medicine should focus on the clinical application, which will be conducive to the development of Tibetan medicine and new drug research.

Studies on chemical constituents of Tibetan medicinal materials

In recent years, with the people's understanding of Tibetan medicine and the state's attention to ethnic medicine, the research on the chemical composition and pharmacological effects of Tibetan medicine has been greatly developed.

Alkaloids

Most plants in Tibetan medicine contain alkaloids. For example, the main characteristic component of the Regunba, which represents Corydalis Tibetan medicine, is isoquinoline alkaloid. Modern pharmacological studies have proved that a great number of alkaloids in this genus have analgesic, anti-inflammatory, anti-arrhythmia, and liver-protecting activities and have pharmacological effects on the central nervous system, cardiovascular system, smooth muscle, etc., but the research foundation of the related chemical components, pharmacological effects, and pharmacognosy is very weak. According to the literature, among the >300 chemical components isolated from aconite Tibetan medicine plants, 244 chemical components belong to alkaloids. Among them, the diterpene alkaloids are recognized as active

Table 2: A classification of partial Tibetan medicines recorded preparations collected in the 2015 edition of the Chinese Pharmacopoeia

Tibetan medicine classification	Name	Efficacy	Dosage form	Property
Cardiovascular system	Bawei Chenxiang Powder	Clearing heart fire, nourishing heart, tranquillization, opening the orifices	Powder	Rx
	Nuodikang Capsule	Benefiting qi for activating blood circulation, promoting Coronary for relieving pain	Capsule	OTC
Nervous system	Twenty-five Pearl Pill	Tranquillization and opening the orifices	Watered pill	Rx
	RNSP	Tranquillization, calming down, clearing and activating the channels and collaterals, harmonizing qi and blood, consciousness-restoring resuscitation	Watered pill	Rx
	Ershiwuwei Shanhu Pills	Opening the orifices, removing obstruction in collaterals, relieving pain	Watered pill	Rx
Hepatobiliary system	Ershiwuwei Songshi Pills	Clearing heat toxicity, dispersing stagnated liver qi for promoting bile flow, resolving macula	Watered pill	Rx
	Shisanwei Pangna Powder	Clearing heat toxicity, cooling liver heat for promoting bile flow	Powder	Rx
Respiratory system	Jiuwei Shihuihua Powder	Clearing heat toxicity, arresting cough, tranquillization	Powder	Rx
Digestive system	Renqing Mangjue	Clearing heat toxicity, nourishing liver and stomach, improving eyesight, inducing resuscitation, curing sore, nourishing for bodybuilding	Watered pill	Rx
	Jie Bai Pills	Strengthening spleen and harmonizing stomach, relieving pain and arresting vomiting, separating clear and excreting turbid	Water-honeyed pill	OTC
Motor system	Duyiwei Tablets	Promoting blood circulation for relieving pain, removing stasis for stopping pain	Tablet	Rx
	Duyiwei Capsules	Promoting blood circulation for relieving pain, removing stasis for stopping pain	Hard capsule	Rx
	Xiaotong Plaster	Promoting blood circulation and removing stasis, relieving swelling and pain	Plaster	OTC

RNSP: Ranasampel, Rx: Prescription drug, OTC: Over the counte

ingredients of aconite Tibetan medicine plants and have various pharmacological activities[19-23] such as antitumor, anti-arrhythmia, antiplatelet aggregation, and immune regulation.

Flavonoids

Lu and Xu[24] investigated the flavonoid aglycons in the Tibetan medicine *Oxytropis falcata*. For the first time, eight flavonoids were isolated and identified, respectively, 2',4'-dihydroxy-4-methoxychalcone (1), 2',4'-dihydroxychalcone (2), 5,7-dihydroxy-4'-methoxyflavone (3), 7-hydroxy-4'-methoxy dihydroflavone (4), 3',7-dihydroxy-2',4'-dimethoxyisoflavan (5), 2'-hydroxy-4'-methoxychalcone (6), 2'-methoxy-4'-hydroxychalcone (7), and 2',4'-dihydroxydihydrochalcone (8). Wang *et al*.[25] studied the anti-inflammatory and antioxidant activities of compounds 1, 3, and 7-hydroxy dihydroflavone. It was found that compound 1 and 7-hydroxy dihydroflavone had a good inhibition effect of lipopolysaccharide-induced nitric oxide (NO) production in RAW264.7 cells. Compound 3 showed the strongest free radical scavenging activity *in vitro*, which was closely related to the clinically useful effects of *Oxytropis falcata*, and could be used as the main activity and index component of the plant. The main component of the traditional Tibetan medicine *Meconopsis quintuplinervia* Regel is alkaloids, followed by flavonoids. Studies have shown that[26] the total alkaloids and total flavonoids in the same original medicines of *M. quintuplinervia* Regel have anti-inflammatory and analgesic effects, and there is no significant difference between them, but the analgesic effect of total alkaloids is significantly better than total flavonoids. However, the specific components and mechanism of action of anti-inflammatory and analgesic effects of total alkaloids and total flavonoids of *M. quintuplinervia* Reg. have yet to be further studied. It has been reported in the literature that the extraction rate and chemical composition of the volatile parts of *M. quintuplinervia* Reg. are different by different extract methods. The supercritical CO_2 extraction technology has the advantages of less steps, shorter time consumption, lower extraction temperature, and higher extraction rate, but its cost is relatively expensive. Compared with the supercritical CO_2 extraction method, the traditional steam distillation method has low extraction cost, but some compounds are decomposed and destroyed due to high temperature in the process of extracting volatile oil, and the original natural compound cannot be obtained. Although the ultrasonic extraction method is simple and easy to operate, the solvent is usually too toxic.[27] Therefore, we should consider all aspects of factors when choosing the best method.

Volatile oils

Yang *et al*.[28] separated 76 components from the essential oil of *Gentiana nubigena*. Then the chemical constituents of essential oils were identified and analyzed by Gas Chromatograph-Mass Spectrometer-computer (GC-MS) and NIST mass spectrometry library. The relative content of each component was calculated by the normalization method of chromatographic peak area. Moreover, 71 components including furan aldehyde (11.078%), 5-methyl-2-furanal aldehyde (7.259%), benzoic acid (6.495%), and 4-vinyl-2-methoxyphenol (2.120%) were isolated and identified for the first time in plants. The volatile oil of Sibiraea angustata mainly contains linalool, ocimenone, and 3-bis (1,1-dimethylethyl)- phenol. Wu and Liu[29] intervened the acute myocardial ischemia injury model of mice using *S. angustata* volatile oil and found that *S. angustata* volatile oil had protective effect on myocardial ischemic injury in mice and could reduce the expression of caspase-3 mRNA. Modern experimental results show that[30] the Tibetan medicine *Myricaria germanica* volatile oil can significantly inhibit xylene-induced ear swelling in mice and has certain inhibitory effects on peritoneal capillary permeability induced by acetic acid and mouse granulation proliferation induced by cotton ball implantation, indicating that it has anti-acute inflammation effects. The high-dose group of ombow volatile oil can significantly reduce the number of writhing in mice and has a good analgesic effect.

Glycosides

Hai-Feng *et al*.[31] isolated four phenylethanoid glycosides from 95% ethanol extract of the roots of *Incarvillea compacta* and, respectively, identified as Z-3'''-O-methylisocrenatoside, 3'''-O-methylcrenatoside, crenatoside, and isomartynoside. Compound 1 is a new compound, and compounds 2–4 are isolated from the genus *Artemisia* for the first time.

Other chemical components

In addition, Tibetan medicine also contains a large number of mineral medicines and fecal medicines. These medicinal materials contain a large amount of trace elements. For example, Heibingpian contains various inorganic elements such as iron (Fe), calcium (Ca) and zinc (Zn), potassium (K), copper (Cu), manganese (Mn), cobalt (Co), and titanium (Ti). Chemical components such as organic acids and polysaccharides have also been found in Tibetan medicines.

At present, studies on the chemical constituents of Tibetan medicine mainly focus on alkaloids and flavonoids. Compared with the rich Tibetan medicine resources, these studies are far from enough. Therefore, it is necessary to use HPLC fingerprint technology to systematically analyze the constituents on the premise of determining the basic elements of medicinal materials. Then, according to the analysis results of fingerprints, the corresponding chemical methods and means are used to systematically separate and purify the large groups of ingredients, then the screening of *in vitro* and *in vivo* activities is carried out, and finally, the material basis for the different pharmacological effects of the medicinal materials is screened out.

Study on chemical composition of Tibetan medicine compound

Tibetan medicine has special curative effects in the treatment of cardiovascular system, digestive system diseases, joint diseases, etc. Tibetan medicine mostly uses compound

prescription to treat diseases, and the compound prescription of each Tibetan medicine is an independent small system. Through the combination of different prescription groups, it shows a unique treatment that is not available with a single drug. The prescription principle of the Tibetan medicine is different from the Prescription Principles of Monarch, Minister, Assistant, and Guide in traditional Chinese medicine. The same type of drugs is classified according to the strength of the drug and is divided into kings, ministers, lords, and scorpion medicines. The flavors, natures, and effects of the drugs used are determined according to the nature of the disease.[32]

It is also an important process for the modern research of Tibetan medicine to analyze the chemical composition and pharmacological effects of Tibetan medicine compound and clarify the changes and effects of active ingredients in the prescription, the principal–subordinate relationship and synergy, and the mechanism of pharmacological action.

Wang[33] carried out a fingerprint study on the microporous resin with the best anti-hypoxia effect of Tibetan medicine compound Que Yang Kang. The main chromatographic peaks in the chromatogram have been assigned by retention time and ultraviolet spectrum, mainly from *Rhodiola* phenolic compounds such as salidroside, tyrosol, *Scutellaria*, and Gentiopicroside and flavonoids in Tibetan medicine Gentianae Radix et Rhizoma secoiridoids, and flavonoids in Glycyrrhiza and Rhododendron anthopogonoide. The anti-oxidation effect of salidroside has been confirmed by research, and the chemical constituents of other herbs and their pharmacological effects in the compound need further study.

Nie *et al*.[34] used the TCMSP database to screen out the active component groups in the compound of Sanguo decoction. For the HAPC mechanism, the target analysis was performed by PharmMapper server. The obtained potential targets were introduced into the MAS3.0 database for target annotation and analysis, and finally, the pathway analysis was performed in conjunction with the KEGG database. As a result, a total of 193 potential targets and 70 signaling pathways were predicted, of which 24 targets and 25 pathways were associated with HAPC. The experimental results showed that the components of polyphenols, flavonoids, and terpenoids in Sanguo decoction might enhance the immune function and hypoxic stress ability of the body by participating in cell proliferation, oxidation reaction, endocrine metabolism and inflammatory reaction and so on, so that multitarget and multichannel synergistic anti-HAPC effect could be exerted.

Compared with the research of Tibetan medicinal materials by various scholars, the research on Tibetan medicine compound is very few. At the same time, the author finds that the chemical composition of some Tibetan medicines that have been put into clinical use, such as the Tibetan medicine Ranasampel,[35] is still unstable in chemical composition, and it also hinders the improvement of the research on medicinal materials and quality control level because of the confidentiality of prescriptions. According to the pharmacological theory of Tibetan medicine, Tibetan medicine is similar to traditional Chinese medicine and pays attention to the overall concept. Therefore, research on a single medicinal material often has greater limitations. We must regard the compound as a whole, using the method of extracting and separating the chemical components of the single medicine, as well as the method of content determination and structure identification to analyze the changes of chemical composition before and after compatibility. In addition, the effective ingredients and metabolites cannot be neglected in the study of Tibetan medicine compound. Only when the medicine is absorbed by the human body can it play its therapeutic role. Therefore, the influencing factors in the body cannot be ignored. There are many chemical components in the Tibetan medicine compound, and various active ingredients in each medicine as well as the new ingredients and their metabolites produced in the process of drug extraction and preparation are combined to produce pharmacological effects. Therefore, the study of Tibetan medicine compound is also an important step in the basic research of Tibetan medicine.

Pharmacological effects of Tibetan medicine

In recent years, the research on the role of Tibetan medicine has increased year by year, mainly focusing on the research of analgesic, anti-inflammatory, anti-oxidation, antiviral, antitumor, and antiliver injury.

Antiliver injury effect

The study found that[36] total lignans from Tibetan medicinal *Herpetospermum pedunculosum* seeds can significantly prevent the elevation of alanine aminotransferase and aspartate transaminase in hepatocytes in rats with chronic alcoholic liver injury and increase the content of glutathione (GSH) and catalase in liver tissue and the activity of superoxide dismutase (SOD) and GSH peroxidase (GSH-Px). It enhances the liver's antioxidant capacity and fat metabolism, thereby achieving protection against the liver. In addition, Nie *et al*.'s[37] experimental studies found that Tibetan medicine compound Qishiwei Zhenzhu pill has a protective effect on CCL4-induced acute liver injury in mice, and its protective mechanism is related to downregulation of DNA damage genes Gadd45 and Gadd153 and inflammatory-related factors macrophage inflammatory protein-2 and interleukin-6.

Antioxidant effect

Gao *et al*.[38] found that the hemodynamic parameters of isolated hearts in the salidroside group were improved compared with the control group, indicating that it can protect ischemia-reperfusion injury in isolation. Biochemical indicators show that salidroside can decrease the activity of creatine kinase (CK) and malondialdehyde, increase the activity of SOD and NO synthase, and protect the heart by inhibiting oxidative stress. Wu[39] confirmed that the volatile oil of *S. angustata* has antioxidant capacity using DPPH(1, 1-dipheny1-2-picry1hydrazy1) method.

Antiviral effect

Wang *et al*.[40] tested the anti-tobacco mosaic virus activity of naphthaldehyde compounds in Tibetan medicine *Comastoma*

pulmonarium by half-leaf method and found that it has good anti-tobacco mosaic virus activity. Gao[41] conducted an anti-HIV-1 virus activity study on eight Tibetan drug extracts by *in vitro* pharmacodynamics experiments and found that *Fallopia aubertii*, *Anemone vitifolia* Buch, *Saxifraga melanocentra* Franch, *Comarum salesovianum,* and *Chamaenerion angustifolium* extracts had good antiviral activity. This study will provide experimental basis and foundation for the research of Tibetan medicine and the development of new antiviral drugs.

Analgesic and anti-inflammatory effects

Ruyi Zhenbao pills have a better analgesic effect and partial anti-inflammatory effect,[42] which can significantly reduce the number of writhing in mice with peritoneal inflammation caused by glacial acetic acid and prolong the time of fever-induced lameness in mice ($P < 0.05$). The weight of xylene-induced ear swelling in mice was significantly reduced ($P < 0.05$). In addition, modern pharmacological studies have shown that[43] *Corydalis* species which have been applied in traditional Tibetan medicinal have obvious analgesic and anti-inflammatory effects.

Antitumor effect

Li[44] used *in vivo* antitumor experiments with alkaline alcohol extract (AlF) and acid alcohol extract (AcF) which extracted from the *O. falcata*. Tumor weight, tumorinhibition, thymus index, and spleen index of the mice were measured to compare the antitumor effect of acid alcohol extract (AcF) and alkaline alcohol extract (AlF). The results indicate that both AcF and AlF fractions of *O. falcata* have an obvious antitumor effect in Lewis lung cancer-bearing mice, and further study is needed to explore the antitumor mechanism. Sun[45] conducted an *in vitro* antitumor experiment on water-soluble polysaccharides of different doses of Tibetan medicine *Scindapsus*. The results showed that different doses of water-soluble polysaccharides of *Scindapsus* had the effect of inducing apoptosis of S180-V cells. In addition, studies have shown that[46] the total polysaccharides of *Scindapsus* can enhance the proliferation rate of lymphocytes, increase the intensity of delayed-type hypersensitivity, increase the number of antibody cells, and improve the activity of natural killer (NK) cells and have a good effect in immune regulation such as humoral immunity, cellular immunity, and NK cell activity.

Summary

Tibetan medicine has a long history of development, rich cultural connotations, and distinctive national characteristics and is the crystallization of the collective wisdom of the Chinese people. Tibetan medicine, as a national medicine, is the second only to traditional Chinese medicine. Its unique theoretical system and drug characteristics are the important basis for guiding the clinical use of Tibetan medicine for thousands of years, making it quite effective in the treatment of certain diseases, such as altitude reaction, gastric ulcer, arthritis, epilepsy, and angina pectoris. In addition, since most of the Tibetan medicinal materials are produced in the Qinghai–Tibet plateau and have a special ecological environment, it is considered to have the potential to screen lead compounds from medicinal materials. The researchers used a variety of chromatographic techniques, extracted a new 7H-dibenzo[c, e] oxepin-5-one from *Herpetospermum caudigerum*, named as herpetolide C. Is this newly discovered compound related to the liver and anti-inflammatory effects of the *Herpetospermum*, still to be further studied.[47]

At present, the modernization of Tibetan medicine research, including the reform of dosage forms, extraction of effective components and content determination, the efficacy of Tibetan medicine, pharmacology, and toxicology research are far from Chinese medicine. To better develop and utilize Tibetan medicine, researchers should digitize Tibetan medicine herbs on the basis of ancient Tibetan medicine books and literature and study Tibetan medicinal herbs in depth from production practice and medication practice. To fully embody the national characteristics of Tibetan medicine and realize the correct development of Tibetan medicine, the research of Tibetan medicine must be guided by the theory of Tibetan medicine and the experience of clinical medication. On this basis, modern scientific and technological methods such as high-throughput drug-screening technology, biotechnology, fingerprint analysis technology, and serum pharmacology research methods should be used. By means of multifactor analysis and orthogonal design, the effective components of Tibetan medicines were studied, and the mechanism of pharmacological action was further explained. It also provided a scientific basis for the formulation of quality standards of Tibetan medicines and laid a foundation for the development of new Tibetan medicines.

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Conflicts of interest

There are no conflicts of interest.

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