Policy Forum

DOI: 10.5582/bst.2016.01105

Traditional, complementary, and alternative medicine: Focusing on research into traditional Tibetan medicine in China

Peipei Song[1], Jufeng Xia[2], Caidan Rezeng[3], Li Tong[3,*], Wei Tang[2]

[1] *Graduate School of Frontier Sciences, The University of Tokyo, Kashiwa-shi, Chiba, Japan;*
[2] *Graduate School of Medicine, The University of Tokyo, Tokyo, Japan;*
[3] *The Research Center of Chinese and Tibetan Medicine, Medicine College, Qinghai University, Xining, Qinghai, China.*

Summary **As a form of traditional, complementary, and alternative medicine (TCAM), traditional Tibetan medicine has developed into a mainstay of medical care in Tibet and has spread from there to China and then to the rest of the world. Thus far, research on traditional Tibetan medicine has focused on the study of the plant and animal sources of traditional medicines, study of the histology of those plants and animals, chemical analysis of traditional medicines, pharmacological study of those medicines, and evaluation of the clinical efficacy of those medicines. A number of papers on traditional Tibetan medicines have been published, providing some evidence of the efficacy of traditional Tibetan medicine. However, many traditional Tibetan medicines have unknown active ingredients, hampering the establishment of drug quality standards, the development of new medicines, commercial production of medicines, and market availability of those medicines. Traditional Tibetan medicine must take several steps to modernize and spread to the rest of the world: the pharmacodynamics of traditional Tibetan medicines need to be determined, the clinical efficacy of those medicines needs to be verified, criteria to evaluate the efficacy of those medicines need to be established in order to guide their clinical use, and efficacious medicines need to be acknowledged by the pharmaceutical market. The components of traditional Tibetan medicine should be studied, traditional Tibetan medicines should be screened for their active ingredients, and techniques should be devised to prepare and manufacture those medicines.**

Keywords: Minority medicine, traditional medicine, evidence-based medicine, components of traditional Tibetan medicines, active ingredient, quality standards

1. Introduction

The increasing prevalence of complex multi-factorial chronic diseases and multi-morbidity has indicated the need for greater therapeutic options. In medical practice, the traditional, complementary, and alternative medicine (TCAM) is an important part of health care along with conventional medicine, and growing numbers of patients are relying on TCAM for preventive or palliative care worldwide. Many studies have indicated that TCAM users were more likely to suffer from one or more chronic conditions, and especially mental, musculoskeletal, and metabolic disorders (*1-3*). The prevalence of TCAM use is reported to be 22.7-66.7% (*4,5*). A meta-analysis indicated an increase in TCAM use for patients with cancer from an estimated 25% in the 1970s and 1980s to more than 32% in the 1990s and to 49% after 2000 (*6*). Data from recent studies have indicated that the rate of TCAM use is 77% or even higher (*7-9*).

Medicines used in TCAM include herbs, herbal materials, herbal preparations, and finished herbal products that contain parts of plants, other plant materials, or combinations thereof, as active ingredients. TCAM practices involving medication and procedure-based health care have been implemented; as an example, acupuncture is now used worldwide. According to reports supplied by 129 countries, 80% (103 countries)

Released online in J-STAGE as advance publication June 13, 2016.

**Address correspondence to:*
Dr. Li Tong, The Research Center of Chinese and Tibetan Medicine, Medicine College, Qinghai University, No.16, Kunlun Road, Xining 810001, Qinghai, China.
E-mail: qhdx2011@126.com

recognized the use of acupuncture as of 2012 (*10*).

The World Health Organization (WHO) stresses that TCAM can play an important role in achieving the goal of "Health for All" and the WHO is dedicated to facilitating the integration of TCAM and modern medicine worldwide (*11*). With the implementation of the "WHO Traditional Medicine Strategy 2002-2005," great efforts were made to advance TCAM by developing national and regional policies and regulations. Furthermore, the "WHO Traditional Medicine Strategy 2014-2023" has also been formulated to promote the safe and effective use of TCAM (*10*). Current data indicate that over 100 million Europeans are currently TCAM users, with one-fifth regularly using TCAM and the same number preferring health care that includes TCAM; there are many more TCAM users in Africa, Asia, Australia, and North America (*10*).

In China, TCAM includes traditional Chinese medicine (TCM) as well as minority medicines such as traditional Tibetan medicine, Mongolian medicine, Uygur medicine, and Dai medicine. Among the minority medicines that originated more than 2,300 years ago, traditional Tibetan medicine has developed into a mainstay of medical care in Tibet and it has spread from there to China and then the rest of the world (*12*). In China today, traditional Tibetan medicine plays an important role in the health care system in the Tibet Autonomous Region and other Tibetan regions including Qinghai Province, Tibet Autonomous Region, Gannan Prefecture of Gansu Province, Ganzi Prefecture and Aba Prefecture of Gansu Province, and Diqing Prefecture of Yunnan Province. However, the development of traditional Tibetan medicine faces several challenges, particularly with regard to evaluation of its safety and efficacy, control of its quality, and standardization. Traditional Tibetan medicine must take several steps to modernize and spread to the rest of the world: the pharmacodynamics of traditional Tibetan medicines need to be determined, the clinical efficacy of those medicines needs to be verified, criteria to evaluate the efficacy of those medicines need to be established in order to guide their clinical use, and efficacious medicines need to be acknowledged by the pharmaceutical market.

2. Traditional Tibetan medicine: Types and characteristics

Traditional Tibetan medicine is a form of medicine guided by a traditional system of practices and theories. Traditional Tibetan medicine is an important part of minority medicines and an integral part of herbal medicine and natural medicine. Plants used to prepare traditional Tibetan medicines are typically cold-resistant, drought-resistant, and perform intensive photosynthesis. Traditional Tibetan medicines include a large number of biologically active substances, trace elements, and amino acids. The efficacy of traditional Tibetan medicines is greater than that of similar traditional medicines from regions at lower altitudes.

There are about 2,000 to 3,000 traditional Tibetan medicines available in China. Based on long-term collection of specimens and statistical data (*13*), plants used in traditional Tibetan medicine come from 191 families, 692 genera, and 2,085 species. Animals used in traditional medicines come from 57 families, 111 genera, and 159 species. Minerals used in traditional Tibetan medicine include 80 types of compounds. The abundant sources of traditional Tibetan medicines suggests that some of these medicines may offer promise as clinical treatments.

In 2012, a study analyzed 439 traditional Tibetan medicines in the Chinese Pharmacopoeia, the Drug Standards of the Ministry of Health of the People's Republic of China (Volume: Traditional Tibetan Medicine), the Tibetan Drug Standards, and the related literatures. It also investigated 711 traditional Tibetan medicines formulations from 40 medical facilities and pharmaceutical companies (*14*). The study found that 502 raw ingredients were used in hospital formulations and formulations described in the literature; 416 of those raw materials had been documented, including 287 herbs, 78 animals, and 51 minerals.

Currently, over 200 traditional Tibetan medicines have been incorporated into the Chinese Pharmacopoeia. Rannasangpei, Shiwuweiheiyao pills, Jiuweiniuhuang pills, and 40 other medicines have been approved, and 78 medicines have been incorporated into the Catalogue of Medicines Covered by National Basic Medical Insurance (*15*).

3. Pharmacological research and its clinical application: Status and challenges

A number of published papers have described studies of traditional Tibetan medicine. In 2003, a study classified and statistically analyzed 14 relevant books and 543 relevant papers published from 1953 to 2002 (*16*). That study suggested that the focus of research into traditional Tibetan medicine has shifted from study of the plant and animal sources of traditional medicines to the study of the histology of those plants and animals, chemical analysis of traditional medicines, pharmacological study of those medicines, and determination of their efficacy in clinical settings.

Research in the 1950s consisted primarily of an introduction to traditional Tibetan medicine and study of the plant and animal sources of traditional medicines. In the early 1970s, research consisted primarily of the study of the plant and animal sources of traditional medicines and surveys of the literature. In the late 1970s, research consisted primarily of the ethnobotanical study of traditional medical texts, chemical analysis of traditional medicines, and pharmacological study of those medicines. Starting in the 1980s, studies on traditional Tibetan medicine diversified, including study of the plant and animal sources of traditional medicines, study of the histology of those plants and animals, chemical analysis of traditional medicines, pharmacological study of those medicines, and clinical evaluation of the efficacy of those medicines. In recent years, pharmacological research and its clinical application have become the focus of research on traditional Tibetan medicine.

3.1. *Pharmacological research on traditional herbal Tibetan medicine*

Basic research on traditional Tibetan medicine started late, but several studies have made great progress. A number of pharmacological studies of the active compounds of traditional herbal Tibetan medicines have been published (Table 1). For instance, studies have suggested that salidroside, an active compound extracted from *Rhodiola eoccinea*, has anti-aging action, it alleviates fatigue, it has antioxidant action, and it improves memory (*17-19*). Studies have indicated that salidroside alleviates hydrogen peroxide-induced endothelial injury by improving mitochondrial activity (*20*) and it improves microcirculation (*21*). Thus, salidroside has been used to treat high-altitude erythrocytosis. *Crocus sativus L.*, which is rich in crocin, crocetin, and safranal, is used as an anti-tumor treatment (*22*). *C. sativus* protects the heart from subchronic diazinon toxicity by decreasing lipid peroxidation and apoptosis (*23*).

3.2. *Pharmacological research on patent medicines of traditional Tibetan medicine*

Following the development of modern pharmacology, many pharmacological studies on patent medicines of traditional Tibetan medicine have been published. For instance, sea buckthorn cream (Shaji Gao) was widely used to "clear heat" (antipyretic action), relieve a cough, promote blood circulation to dispel blood stasis, and treat an ulcer. Flavones, the main ingredients

Table 1. Active ingredients and pharmacological analysis of traditional herbal Tibetan medicines

Raw material (*Ref.*)	Active ingredients	Pharmacological analysis
Rhodiola rosea L. (*17-21*)	Salidroside	anti-aging action, alleviating fatigue, antioxidant action, improving memory; increasing mitochondrial activity to protect from H_2O_2-induced endothelial injury; improving microcirculation.
Crocus sativus L. (*22,23*)	Crocin, crocetin, safranal	anti-tumor activity; protecting the heart from subchronic diazinon toxicity by decreasing lipid peroxidation and apoptosis.
Swertia (*24-27*)	Triterpenes, flavonoids, chimonin, gentiamarin, swertiamarin	inhibiting hepatitis B, cirrhosis, and *E. coli*; anti-tumor activity; scavenging NO_2^-; slightly inhibiting growth of the S180 mouse cancer cell line and moderately inhibiting growth of the RS321 tumor cell line.
Phyllanthus emblica (*28-31*)	ellagic acid, gallic acid, sesquiterpenoids, volatile oils	antioxidant action; anti-tumor activity; antibiosis; anti-inflammatory action; protecting the cardiovascular system.
Hypecoum erectum L. (*32-35*)	Alkaloids (hypecorin), cis-anethole, cardiac glycoside	anti-inflammatory action; antibiosis; anti-viral action; liver protection; analgesic action.
Aconitum carmichaelii Debx. (*36-39*)	Alkaloids (bulleyaconitine A, lappaconitine), flavonoids, steroids	analgesic action; anti-inflammatory action; cardiotonic activity; anti-tumor activity; antiepileptic action; antiparasitic action.
Terminalia chebula Retz. (*40-43*)	Tannins, phenolic acids, triterpenes, flavonoids, volatile oils	antioxidant action; preventing diabetes mellitus; antibiosis; anti-inflammatory action; analgesic action.
Meconopsis (*44-47*)	Flavonoids, alkaloids	treating fractures; increasing blood circulation to dissipate blood stasis; analgesic action.
Herpetospermum pedunculosum (*48-51*)	Herpetone, dehydrodiconiferyl alcohol, Herpetolide C	treating hepatitis, cholecystitis, or indigestion.
Corydalis (*52-55*)	Isoquinoline alkaloid	treating a cold, fever, hepatitis, edema, gastritis, cholecystitis, or hypertension; antibiosis, analgesic action, anti-inflammatory action, anti-arrhythmia, liver protection; pharmacological action on the cardiovascular system, central nervous system, and smooth muscle.
Gentiana macrophylla Pall. (*56-58*)	Iridoid glycoside, secoiridoid glycoside	improving the flow of interstitial fluid and removing algogenic substances, treating arthritis, rheumatism, or muscular constriction.

in sea buckthorn cream, have been found to treat arrhythmia, improve the function of cardiomyocytes, treat a thrombus, counteract hypoglycemia, scavenge oxygen radicals, inhibit tumor growth, and facilitate bacteriostasis (*59-61*). RanNaSangPei (RNSP) decreases blood viscosity, it reduces blood pressure, it alleviates angina pectoris, and it is effective at treating cardiovascular diseases (*62,63*). Ershiwuwei Donkey Blood Pills are used to treat rheumatoid arthritis, ankylosing spondylitis, and rheumatoid arthritis (*62*).

3.3. *Challenges in the pharmacological study of traditional Tibetan medicine*

In recent years, the pharmacological study of traditional Tibetan medicine has made some progress, but the methods used in research are mostly traditional. The lack of in-depth and extensive pharmacological study of traditional Tibetan medicines means that traditional Tibetan medicine is still far from modern. Methods of modern pharmacology, such as chronopharmacology, *in vitro* pharmacology, component analysis, and pharmacokinetics, should be capitalized upon in order to improve the quality of research, determine the mechanisms of action of traditional Tibetan medicines, and obtain international recognition of the efficacy of those medicines.

3.4. *Clinical application: Traditional Tibetan medicine preparations*

Traditional Tibetan medicine has been used clinically to treat common ailments, frequently encountered diseases, altitude sickness, and endemia, and traditional Tibetan medicines have been developed to treat 5 types of diseases including cardiovascular diseases, hepatobiliary diseases, gastrointestinal diseases, rheumatism, and gynecological diseases.

There are more than 20 dosage forms for traditional Tibetan medicine, such as decoctions, powders, pills, ointments, lotions, and medicinal liquors. Although there are many traditional Tibetan medicine dosage forms, the types of preparations, the diversity of dosage forms, and their clinical are expected to be improved. Modern techniques to prepare and manufacture drugs should be used to accelerate the development of novel drugs while retaining the characteristics of traditional Tibetan medicine.

4. Study of the chemical constituents of traditional Tibetan medicines and quantitative analysis of those traditional medicines

4.1. *Promoting a quantitative analysis of traditional Tibetan medicines*

Chemical constituents are the reason for a medicine's effect. From 2003 to 2013, studies of traditional Tibetan medicine focused on extraction, identification, and quantitative determination of the chemical constituents of traditional medicines. Chemical constituents of about 100 traditional Tibetan medicines, such as Tibetan *Artemesia capillaris*, *Lamiophlomis rotata* Kudo, and *Arenaria serpyllifolia* L., were extensively studied.

High performance liquid chromatography (HPLC) was widely used to establish quality control standards by quantitatively analyzing a traditional medicine's chemical constituents. Zhong *et al*. used HPLC to analyze gallic acid in the traditional Tibetan medicine Sanguo Tang Lozenges (*64*). De *et al*. used HPLC to prolife Sanguo Tang San (*65*). Luo *et al*. used HPLC to determine the flavonoid content of Shibawei Dujuan Pills (*66*). Xie *et al*. used HPLC to quantitatively detect shikimic acid and gallic acid in *Geranium pretense* L. and they established quality control standards for quantitative analysis of *Geranium pratense* (*67*).

Besides, Li *et al*. used Fourier transform near-infrared (FT-NIR) spectroscopy to quantitatively analyze salidroside and p-Tyrosol in the traditional Tibetan medicine *R. crenulata*. They found that FT-NIR spectroscopy provided a precise and rapid method for quantitative analysis of the major active ingredients in *R. crenulata* and that it could be used to control the quality of *R. crenulata* (*68*).

4.2. *Examining the active compounds in traditional Tibetan medicines to provide indicators for quality control*

About 500 papers have been published on the chemical constituents of traditional Tibetan medicines, but these papers have only scratched the surface of traditional Tibetan medicine. Unknown active compounds hamper the establishment of drug quality standards and the development of novel drugs. Thus, new techniques such as droplet countercurrent chromatography, supercritical extraction, infrared absorption spectroscopy, thin slice scanning, gas chromatography mass spectrometry, liquid chromatography mass spectrometry, and nuclear magnetic resonance could be used. These techniques could improve studies of the active compounds in traditional Tibetan medicines, examine various indicators to direct production and ensure the consistency, efficacy, stability, and reliability of traditional medicines, promote the modernization of quality standards, and encourage the development and utilization of traditional Tibetan medicines.

5. Evidence-based medicine, quality control, and the modernization and international recognition of traditional Tibetan medicine

Numerous studies have focused on the study of the plant and animal sources of traditional Tibetan medicines, the study of the histology of those plants and animals, analysis of the chemical composition of traditional medicines, pharmacological study of those medicines, and evaluation of the clinical efficacy of those medicines in order to provide evidence for development of traditional Tibetan medicine. However, the traditional Tibetan medicines studied thus far only account for 10% of all traditional Tibetan medicines. Many traditional Tibetan medicines have unknown active ingredients, hampering the establishment of drug quality standards, the development of new medicines, commercial production of medicines, and market availability of those medicines. Traditional Tibetan medicine must take several steps to modernize and spread to the rest of the world: the pharmacodynamics of traditional Tibetan medicines need to be determined, the clinical efficacy of those medicines needs to be verified, criteria to evaluate the efficacy of those medicines need to be established in order to guide their clinical use, and efficacious medicines need to be acknowledged by the pharmaceutical market.

5.1. *Evidence-based medicine and component analysis on traditional Tibetan medicine*

Development of traditional medicines involves many obstacles such as safety, efficacy, and evaluation of quality. Component analysis has been used to meet this challenge and this approach has been used to study the functions and active compounds of traditional medicines (*69-71*). In recent years, component analysis of traditional Tibetan medicines has developed rapidly and has been used to standardize traditional Tibetan medicines (*72,73*). The crux of research into traditional Tibetan medicine is the study of active ingredients based on their mechanism of action. Several studies have examined the compatibility of active ingredients, they have determined the quality of the active ingredients in traditional Tibetan medicines, they have studied the relationship between efficacious ingredients and active ingredients, and they have examined the aspects and targets of the efficacious ingredients of traditional Tibetan medicines.

Studies have suggested that traditional Tibetan medicines developed using modern pharmaceutical manufacturing techniques and animal models of pharmacodynamics could contain components that offer the clinical benefits of traditional Tibetan medicines (*74,75*). Thus, suitable quality standards for traditional Tibetan medicines need to be established to ensure preparations have a specific chemical composition, an identified mechanism of action, and controlled quality. In addition, component analysis of traditional Tibetan medicines can be used to rule out ingredients that are inactive or deleterious, leaving only efficacious ingredients. Thus, component analysis of traditional Tibetan medicine can lead to better symptomatic treatment, it can clarify an ingredient's mechanisms of action, and it can facilitate international acceptance (*72,73*). Component analysis of traditional Tibetan medicines should be performed further in order to provide evidence for the development of traditional Tibetan medicine.

5.2. *Compound screening and new drug development*

Compound screening and new drug development are being used to develop traditional Tibetan medicines. In 2015, a study examined 100 traditional Tibetan medicines in order to discover new anticancer drugs (*76*). The study obtained cyclohexane extracts, acetic ether extracts, and methanol extracts of traditional Tibetan medicines through rapid solvent extraction. The same study used an MTT assay to detect the anti-tumor activity of those medicines in 2 human liver cancer cell lines (HepG2 and SMMC-7721) and it evaluated toxicity in the L02 human liver cell line. Results suggested that 15 traditional Tibetan medicines had anti-tumor activity, with an IC_{50} of less than 150 μg/mL. The identified substances included acetic ether extracts of *Chenopodium album* L., *Carpesium abrotanoides*, and *Aster ageratoides* Turcz. Those extracts had significant anti-tumor activity, with an IC_{50} less than 50 μg/mL, and none were toxic to L02 cells. Those findings offered a glimpse at the development of new anti-tumor drugs from traditional Tibetan medicines.

5.3. *Using modern scientific techniques and modern preparation and manufacturing techniques to promote the research and development of traditional Tibetan medicine*

Research and development of traditional Tibetan medicine should be promoted in order to yield different preparations and to facilitate the clinical use of traditional medicines. However, the characteristics of traditional Tibetan medicine need to be retained while using modern scientific techniques and preparation and manufacturing techniques: *i*) increasing the use of traditional Tibetan medicines by developing new techniques based on the medicine's characteristics; a medicine in powder form, for example, could be improved by superfine grinding and other preparations could be improved by supercritical fluid extraction and separation and purification using macroporous adsorbent resin; *ii*) compounds of raw materials could be improved through screening with pharmacological indicators; *iii*) an appropriate preparation could be chosen based on treatment goals; an injection, for example, is the preparation of choice for acute conditions such as angina pectoris and asthma while slow-release preparations are suitable for chronic diseases; *iv*) selecting a preparation based on a medicine's properties; an oral preparation, for example, is suitable for a drug that is poorly soluble and this preparation could be used to improve drug absorption; *v*) development goals: efficiency, quick results, controlled release, a low dose, a low level of toxicity, and few adverse reactions, consistent timing and site of action, and a fixed rate of action.

6. Conclusion

Traditional Tibetan medicine is gradually becoming more scientifically based and the clinical efficacy of traditional medicines is gradually being determined. Nevertheless, traditional Tibetan medicine still faces several challenges. The consistent quality of traditional Tibetan medicines is directly related to their safety, efficacy, and control of their quality. A number of steps need to be taken in that direction. The sources of traditional medicines need to be explored, basic research needs to be conducted on those medicines, their active ingredients and their mechanisms of action need to be determined, quality standards need to be studied and implemented, traditional preparations need to be screened and more types of preparations need to be developed, and the efficacy of traditional medicines needs to be ensured while limiting their toxicity. These steps will modernize traditional Tibetan medicine and make those medicines more consistent, significantly facilitating the international recognition of traditional Tibetan medicine. Ingredients in traditional Tibetan medicines should be studied, those medicines should be screened for their active ingredients, and techniques should be devised to prepare and manufacture those medicines.

References

1. Bishop FL, Lewith GT. Who uses CAM? A narrative review of demographic characteristics and health factors associated with CAM use. Evid Based Complement Alternat Med. 2010; 7:11-28.
2. Toupin April K, Stinson J, Boon H, Duffy CM, Huber AM, Gibbon M, Descarreaux M, Spiegel L, Vohra S, Tugwell P. Development and preliminary face and content validation of the "Which health approaches and treatments are you using?" (WHAT) Questionnaires assessing complementary and alternative medicine use in pediatric rheumatology. PLoS One. 2016; 11:e0149809.
3. Arjuna Rao AS, Phaneendra D, Pavani ChD, Soundararajan P, Rani NV, Thennarasu P, Kannan G. Usage of complementary and alternative medicine among patients with chronic kidney disease on maintenance hemodialysis. J Pharm Bioallied Sci. 2016; 8:52-57.
4. Peltzer K. Utilization and practice of traditional/complementary/alternative medicine (TM/CAM) in South Africa. Afr J Tradit Complement Altern Med. 2009; 6:175-185.
5. Peltzer K, Pengpid S, Puckpinyo A, Yi S, Vu Anh L. The utilization of traditional, complementary and alternative medicine for non-communicable diseases and mental disorders in health care patients in Cambodia, Thailand and Vietnam. BMC Complement Altern Med. 2016; 16:92.
6. Horneber M, Bueschel G, Dennert G, Less D, Ritter E, Zwahlen M. How many cancer patients use complementary and alternative medicine: A systematic review and metaanalysis. Integr Cancer Ther. 2012; 11:187-203.
7. Naing A, Stephen SK, Frenkel M, Chandhasin C, Hong DS, Lei X, Falchook G, Wheler JJ, Fu S, Kurzrock R. Prevalence of complementary medicine use in a phase 1 clinical trials program: The MD Anderson Cancer Center Experience. Cancer. 2011; 117:5142-5150.
8. Huebner J, Prott FJ, Micke O, Muecke R, Senf B, Dennert G, Muenstedt K, PRIO (Working Group Prevention and Integrative Oncology - German Cancer Society). Online survey of cancer patients on complementary and alternative medicine. Oncol Res Treat. 2014; 37:304-308.
9. Muecke R, Paul M, Conrad C, Stoll C, Muenstedt K, Micke O, Prott FJ, Buentzel J, Huebner J, PRIO (Working Group Prevention and Integrative Oncology - German Cancer Society). Complementary and alternative medicine in palliative care: A comparison of data from surveys among patients and professionals. Integr Cancer Ther. 2016; 15:10-16.
10. The World Health Organization. WHO Traditional Medicine Strategy 2014-2023. *http://www.who.int/medicines/publications/traditional/trm_strategy14_23/en/* (accessed November 05, 2015)
11. The World Health Organization. WHO Traditional Medicine Strategy 2002-2005. *http://apps.who.int/iris/handle/10665/67163* (accessed October 10, 2015)
12. Janes CR. The transformations of Tibetan medicine. Med Anthropol Q. 1995; 9:6-39.
13. Luo SD. Tibetan medcine resource survey and exploitation. China Tibetology. 1997; 4:49-58. (in Chinese).
14. Zhong G, Zhou F, Shi S, Zhou H, Yu J, Ping A, Liu H, Dawa Z. Actuality investigation on general crude drugs and its quality standard of Tibetan medicine. Zhongguo Zhong Yao Za Zhi. 2012; 37:2349-2355. (in Chinese).
15. Cao M, Kong X, Wang L, Zhang J, Wang X, Qin Z, Meng J, Li J, Wang X. The general status of research on traditional Tibetan medicine. Progress in Veterinary Medicine. 2015; 36:105-109. (in Chinese).
16. Meng Z, Wang Y, Yang Y, Xu J. Analysis on literatures of Tibetan medicine. Acta Botanica Yunnanica. 2003; Suppl. XIV:134-140. (in Chinese).
17. Mao GX, Wang Y, Qiu Q, Deng HB, Yuan LG, Li RG, Song DQ, Li YY, Li DD, Wang Z. Salidroside protects human fibroblast cells from premature senescence induced by H(2)O(2) partly through modulating oxidative status. Mech Ageing Dev. 2010; 131:723-731.
18. Ma C, Hu L, Tao G, Lv W, Wang H. An UPLC-MS-based metabolomics investigation on the anti-fatigue effect of salidroside in mice. J Pharm Biomed Anal. 2015; 105:84-90.
19. Si PP, Zhen JL, Cai YL, Wang WJ, Wang WP. Salidroside protects against kainic acid-induced status epilepticus via suppressing oxidative stress. Neurosci Lett. 2016; 618:19-24.
20. Xing S, Yang X, Li W, Bian F, Wu D, Chi J, Xu G, Zhang Y, Jin S. Salidroside stimulates mitochondrial biogenesis and protects against H(2)O(2)-induced endothelial dysfunction. Oxid Med Cell Longev. 2014; 2014:904834.
21. Si YC, Li Q, Xie CE, Niu X, Xia XH, Yu CY. Chinese

herbs and their active ingredients for activating xue (blood) promote the proliferation and differentiation of neural stem cells and mesenchymal stem cells. Chin Med. 2014; 9:13.
22. Bolhassani A, Khavari A, Bathaie SZ. Saffron and natural carotenoids: Biochemical activities and anti-tumor effects. Biochim Biophys Acta. 2014; 1845:20-30.
23. Razavi BM, Hosseinzadeh H, Movassaghi AR, Imenshahidi M, Abnous K. Protective effect of crocin on diazinon induced cardiotoxicity in rats in subchronic exposure. Chem Biol Interact. 2013; 203:547-555.
24. Cao TW, Geng CA, Ma YB, Zhang XM, Zhou J, Tao YD, Chen JJ. Chemical constituents of Swertia mussotii and their anti-hepatitis B virus activity. Fitoterapia. 2015; 102:15-22.
25. Zhou NJ, Geng CA, Huang XY, Ma YB, Zhang XM, Wang JL, Chen JJ. Anti-hepatitis B virus active constituents from Swertia chirayita. Fitoterapia. 2015; 100:27-34.
26. Uvarani C, Arumugasamy K, Chandraprakash K, Sankaran M, Ata A, Mohan PS. A new DNA-intercalative cytotoxic allylic xanthone from Swertia corymbosa. Chem Biodivers. 2015; 12:358-370.
27. Saha P, Das S. Highlighting the anti-carcinogenic potential of an ayurvedic medicinal plant, Swertia Chirata. Asian Pac J Cancer Prev. 2010; 11:1445-1449.
28. Sripanidkulchai B, Junlatat J. Bioactivities of alcohol based extracts of Phyllanthus emblica branches: Antioxidation, antimelanogenesis and anti-inflammation. J Nat Med. 2014; 68:615-622.
29. Yang B, Liu P. Composition and biological activities of hydrolyzable tannins of fruits of Phyllanthus emblica. J Agric Food Chem. 2014; 62:529-541.
30. Golechha M, Bhatia J, Ojha S, Arya DS. Hydroalcoholic extract of Emblica officinalis protects against kainic acid-induced status epilepticus in rats: Evidence for an antioxidant, anti-inflammatory, and neuroprotective intervention. Pharm Biol. 2011; 49:1128-1136.
31. Dang GK, Parekar RR, Kamat SK, Scindia AM, Rege NN. Antiinflammatory activity of Phyllanthus emblica, Plumbago zeylanica and Cyperus rotundus in acute models of inflammation. Phytother Res. 2011; 25:904-908.
32. Tao Y, Zhang YM. Leaf and soil stoichiometry of four herbs in the Gurbantunggut Desert, China. Ying Yong Sheng Tai Xue Bao. 2015; 26:659-665. (in Chinese)
33. Toropova AA, Nikolaev SM, Razuvaeva YG, Fedorov AV, Sambueva ZG, Ubeeva IP. Effect of Hypecoum erectum extract on morphofunctional state of the liver in rats with tetracycline-associated hepatitis. Antibiot Khimioter. 2014; 59:25-28. (in Russian)
34. Nikolaev SM, Fedorov AV, Toropova AA, Razuvaeva Ia G, Sambueva ZG, Lubsandorzhieva PB. Hepatoprotective effect of Hypecoum erectum extract on experimental D-galactosamine-induced damage of rat liver. Eksp Klin Farmakol. 2014; 77:18-22. (in Russian)
35. Nikolaev SM, Fedorov AV, Razuvaeva Ia G, Sambueva ZG, Toropova AA. The choleretic and hepatoprotective effect of Hypecoum erectum extract. Eksp Klin Gastroenterol. 2014; 10:59-63. (in Russian)
36. Wang DP, Lou HY, Huang L, Hao XJ, Liang GY, Yang ZC, Pan WD.A novel franchetine type norditerpenoid isolated from the roots of Aconitum carmichaeli Debx. with potential analgesic activity and less toxicity. Bioorg Med Chem Lett. 2012; 22:4444-4446.
37. Tong P, Wu C, Wang X, Hu H, Jin H, Li C, Zhu Y, Shan L, Xiao L. Development and assessment of a complete-detoxication strategy for Fuzi (lateral root of Aconitum carmichaeli) and its application in rheumatoid arthritis therapy. J Ethnopharmacol. 2013; 146:562-571.
38. Tan Y, Liu X, Lu C, He X, Li J, Xiao C, Jiang M, Yang J, Zhou K, Zhang Z, Zhang W, Lu A. Metabolic profiling reveals therapeutic biomarkers of processed Aconitum carmichaeli Debx in treating hydrocortisone induced kidney-yang deficiency syndrome rats. J Ethnopharmacol. 2014; 152:585-593.
39. Xu W, Zhang J, Zhu D, Huang J, Huang Z, Bai J, Qiu X. Rapid separation and characterization of diterpenoid alkaloids in processed roots of Aconitum carmichaeli using ultra high performance liquid chromatography coupled with hybrid linear ion trap-Orbitrap tandem mass spectrometry. J Sep Sci. 2014; 37:2864-2873.
40. Lee HS, Cho HY, Park KW, Kim IH, Kim JT, Nam MH, Lee KW. Inhibitory effects of Terminalia chebula extract on glycation and endothelial cell adhesion. Planta Med. 2011; 77:1060-1067.
41. Hazra B, Sarkar R, Biswas S, Mandal N. Comparative study of the antioxidant and reactive oxygen species scavenging properties in the extracts of the fruits of Terminalia chebula, Terminalia belerica and Emblica officinalis. BMC Complement Altern Med. 2010; 10:20.
42. Nayak SS, Ankola AV, Metgud SC, Bolmal U. Effectiveness of mouthrinse formulated from ethanol extract of Terminalia chebula fruit on salivary Streptococcus mutans among 12 to 15 year old school children of Belgaum city: A randomized field trial. J Indian Soc Pedod Prev Dent. 2012; 30:231-236.
43. Gautam MK, Goel S, Ghatule RR, Singh A, Nath G, Goel RK. Curative effect of Terminalia chebula extract on acetic acid-induced experimental colitis: Role of antioxidants, free radicals and acute inflammatory marker. Inflammopharmacology. 2013; 21:377-383.
44. Fan J, Wang Y, Wang X, Wang P, Tang W, Yuan W, Kong L, Liu Q. The antitumor activity of Meconopsis horridula Hook, a traditional Tibetan medical plant, in murine leukemia L1210 cells. Cell Physiol Biochem. 2015; 37:1055-1065.
45. Fan J, Wang P, Wang X, Tang W, Liu C, Wang Y, Yuan W, Kong L, Liu Q. Induction of mitochondrial dependent apoptosis in human leukemia K562 cells by meconopsis integrifolia: A species from traditional Tibetan medicine. Molecules. 2015; 20:11981-11993.
46. Shang X, Wang D, Miao X, Wang Y, Zhang J, Wang X, Zhang Y, Pan H. Antinociceptive and anti-tussive activities of the ethanol extract of the flowers of Meconopsis punicea Maxim. BMC Complement Altern Med. 2015; 15:154.
47. Wangchuk P, Keller PA, Pyne SG, Lie W, Willis AC, Rattanajak R, Kamchonwongpaisan S. A new protoberberine alkaloid from Meconopsis simplicifolia (D. Don) Walpers with potent antimalarial activity against a multidrug resistant Plasmodium falciparum strain. J Ethnopharmacol. 2013; 150:953-959.
48. Pan HJ, Mao H, Peng WF, Fan SY, Fang QM, Liu XF. Planting area estimation of Chinese Tibetan medicine Herpetospermum pedunculosum based on RS&GIS-by case study of Lengqi and Xinglong town in Luding county. Zhongguo Zhong Yao Za Zhi. 2014; 39:3018-3022. (in Chinese)
49. Li LY, Deji LM, Wei YF, Zhong GY. Literature

data investigation in semem of Herpetospermum pedunculosum. Zhongguo Zhong Yao Za Zhi. 2005; 30:893-895. (in Chinese)
50. Zhang M, Deng Y, Zhang HB, Su XL, Chen HL, Yu T, Guo P. Two new coumarins from Herpetospermum caudigerum. Chem Pharm Bull (Tokyo). 2008; 56:192-193.
51. Lee J, Choi J, Lee W, Ko K, Kim S. Dehydrodiconiferyl alcohol (DHCA) modulates the differentiation of Th17 and Th1 cells and suppresses experimental autoimmune encephalomyelitis. Mol Immunol. 2015; 68:434-444.
52. Kim JH, Ryu YB, Lee WS, Kim YH. Neuraminidase inhibitory activities of quaternary isoquinoline alkaloids from Corydalis turtschaninovii rhizome. Bioorg Med Chem. 2014; 22:6047-6052.
53. Lei Y, Tan J, Wink M, Ma Y, Li N, Su G. An isoquinoline alkaloid from the Chinese herbal plant Corydalis yanhusuo W.T. Wang inhibits P-glycoprotein and multidrug resistance-associate protein 1. Food Chem. 2013; 136:1117-1121.
54. Huang QQ, Bi JL, Sun QY, Yang FM, Wang YH, Tang GH, Zhao FW, Wang H, Xu JJ, Kennelly EJ, Long CL, Yin GF. Bioactive isoquinoline alkaloids from Corydalis saxicola. Planta Med. 2012; 78:65-70.
55. Lee TH, Kim KH, Lee SO, Lee KR, Son M, Jin M. Tetrahydroberberine, an isoquinoline alkaloid isolated from corydalis tuber, enhances gastrointestinal motor function. J Pharmacol Exp Ther. 2011; 338:917-924.
56. Huang CY, Hsu TC, Kuo WW, Liou YF, Lee SD, Ju DT, Kuo CH, Tzang BS. The root extract of Gentiana macrophylla Pall. Alleviates cardiac apoptosis in lupus prone mice. PLoS One. 2015; 10:e0127440.
57. Jia N, Li Y, Wu Y, Xi M, Hur G, Zhang X, Cui J, Sun W, Wen A.Comparison of the anti-inflammatory and analgesic effects of Gentiana macrophylla Pall. and Gentiana straminea Maxim., and identification of their active constituents. J Ethnopharmacol. 2012; 144:638-645.
58. Chen LY, Chen QL, Xu D, Hao JG, Schläppi M, Xu ZQ.Changes of gentiopicroside synthesis during somatic embryogenesis in Gentiana macrophylla. Planta Med. 2009; 75:1618-1624.
59. Pandurangan N, Bose C, Banerji A. Synthesis and antioxygenic activities of seabuckthorn flavone-3-ols and analogs. Bioorg Med Chem Lett. 2011; 21:5328-5330.
60. Geetha S, Ram MS, Sharma SK, Ilavazhagan G, Banerjee PK, Sawhney RC. Cytoprotective and antioxidant activity of seabuckthorn (Hippophae rhamnoides L.) flavones against tert-butyl hydroperoxide-induced cytotoxicity in lymphocytes. J Med Food. 2009; 12:151-158.
61. Mishra KP, Chanda S, Karan D, Ganju L, Sawhney RC. Effect of Seabuckthorn (Hippophae rhamnoides) flavone on immune system: An in-vitro approach. Phytother Res. 2008; 22:1490-1495.
62. Shi JM, He X, Lian HJ, Yuan DY, Hu QY, Sun ZQ, Li YS, Zeng YW. Tibetan medicine "RNSP" in treatment of Alzheimer disease. Int J Clin Exp Med. 2015; 8:19874-19880.
63. Du W,Huang F, Shao J, Luo Y, Zhen L, Liu Y, Shang Y. Progress in pharmacological and clinical research of Qishiwei Zhenzhu Wan. Chinese Journal of Experimental Traditional Medical Formulae. 2013; 6:377-381. (in Chinese).
64. Zhong Y, Zhang Q, Wu H. An HPLC technique to analyze gallic acid in the traditional Tibetan medicine Sanguo Tang Lozenges. Journal of Medicine & Pharmacy of Chinese Minorities. 2010; 12:46-47. (in Chinese)
65. De L, Yang Z, Ji J, Yang J, Luo S, Lan S, Tang C, Zhang Y. Preliminary study for antioxidant components of Tibetan medicine Sanguo Tang San by TLC-bioautograhpy and HPLC fingerprinting. Chinese Journal of Experimental Traditional Medical Formulae. 2012; 18:98-102. (in Chinese).
66. Luo X, Chen Z, Yang L. Determination of flavonoids in Tibetan medicine Shibawei Dujuan Pills by HPLC. Chinese Journal of Ethnomedicine and Ethnopharmacy. 2014; 22:17-20. (in Chinese).
67. Xie S, Song L, Wan J, Tong Z, Tan R, Liu X. Determination of shikimic acid and gallic acid in Geranium pretense L. by HPLC. Chinese Traditional Patent Medicine. 2014; 36:2526-2531. (in Chinese).
68. Li T, He X. Quantitative analysis of salidroside and p-tyrosol in the traditional Tibetan medicine Rhodiola crenulata by Fourier Transform Near-Infrared Spectroscopy. Chem Pharm Bull (Tokyo). 2016; 64:289-296.
69. Wang CC, Feng L, Liu D, Cui L, Tan XB, Jia XB. Research thoughts on structural components of Chinese medicine combined with bioinformatics. Zhongguo Zhong Yao Za Zhi. 2015; 40:4514-4519. (in Chinese)
70. Zhang D, Duan X, Deng S, Nie L, Zang H. Fingerprint analysis, multi-component quantitation, and antioxidant activity for the quality evaluation of Salvia miltiorrhiza var. alba by high-performance liquid chromatography and chemometrics. J Sep Sci. 2015; 38:3337-3344.
71. Zeng L, Wang M, Yuan Y, Guo B, Zhou J, Tan Z, Ye M, Ding L, Chen B. Simultaneous multi-component quantitation of Chinese herbal injection Yin-zhi-huang in rat plasma by using a single-tube extraction procedure for mass spectrometry-based pharmacokinetic measurement. J Chromatogr B Analyt Technol Biomed Life Sci. 2014; 967:245-254.
72. Gao F, Wang Z, Ji Y. Component theory of the efficacy of the components of Tibetan medicine. China Journal of Traditional Chinese Medicine and Pharmacy. 2014; 29:2747-2749. (in Chinese)
73. Wang Z, Gao F. Construction and research technique of component Tibetan medicine. World Science and Technology/ Modernization of Traditional Chinese Medicine and Materia Medica. 2011; 13:1009-1012. (in Chinese)
74. Qu Y, Li JH, Zhang C, Li CX, Dong HJ, Wang CS, Zeng R, Chen XH. Content determination of twelve major components in Tibetan medicine Zuozhu Daxi by UPLC. Zhongguo Zhong Yao Za Zhi. 2015; 40:1825-1830. (in Chinese)
75. Wang M, YanY, Zou H, Zhu G, Zhao T, Wu H. Correlation between active components alignment and medicinal function of Peony and Licorice decoction. Journal of International Pharmaceutical Research. 2015; 42:101-106. (in Chinese)
76. Song P, Xu C, Ma Y, Lv J, Yang J, Wang C, Yang X. *In vitro* anti-hepatoma screening of 100 commonly used Tibetan medicines. Journal of South-Central University for Nationalities (Nat. Sci. Edition). 2015; 34:64-67. (in Chinese).

(Received May 2, 2016; Revised June 6, 2016; Accepted June 8, 2016)