Strengthening Traditional Medicine Systems in Nepal through Chemical and Pharmacological Research

Hari Prasad Devkota[1], Anjana Adhikari-Devkota[1], Atisammodavardhana Kaundinnyayana[2] ,Dhaka Ram Bhandari[3]

[1]*Graduate School of Pharmaceutical Sciences, Kumamoto University, Kumamoto, Japan*

[2]*School of Health and Allied Sciences, Pokhara University, Pokhara, Nepal*

[3]*Gandaki Province Academy of Science and Technology, Pokhara, Nepal*

CORRESPONDENCE

Dr. Hari Prasad Devkota
Graduate School of Pharmaceutical Sciences, Kumamoto University, Kumamoto, Japan
Email : devkotah@kumamoto-u.ac.jp

ARTICLE INFO
Article History
Submitted: 30 May, 2021
Accepted: 15 July, 2021
Published: 8 August, 2021

Source of support: None
Conflict of Interest: None

ABSTRACT

Medicinal plants are an integral part of traditional medicine systems all over the world. Nepal, rich in biodiversity and ethnic, linguistic, and cultural diversity, possesses different traditional and folk medicinal practices for thousands of years. These systems have been using many locally available medicinal plants as crude drugs, which are not always properly documented. Detailed documentation and research related to the conservation and cultivation of medicinal plants should be carried out. Scientific studies related to chemical analysis, standardization, evaluation of pharmacological activities, and safety should be carried out to strengthen these systems of traditional medicine. Adequately designed clinical studies are necessary to provide evidence for their therapeutic efficacy.

Keywords: Documentation; Healthcare; Nepal; Traditional medicine; Traditional knowledge, Standardization

INTRODUCTION

About 60% of the world's population relies on traditional medicines as primary healthcare, and the percentage is even higher in developing countries.[1] About 85% of the crude drugs used in traditional medicines are derived from plant sources and they have been used from ancient times to prevent and treat diseases. Medicinal plants also serve as an essential source of modern drugs (Figure 1).[2] In addition, various medicinal plants are also used as herbs and spices in food recipes, functional foods and supplements, cosmetics, fragrances and food preservatives. [3,4]

Nepal, a small country in South Asia, covers an area of 147,181 square kilometers.[5] However, the climate ranges from tropical to alpine regions due to the wide range of altitude variations (about 60 m-8848 m). Thus, Nepal is rich in biodiversity and is also suitable for cultivating and conserving wide varieties of biological resources, including medicinal and aromatic plants.[6] Nepal contains more than 7000 plant species, and among them, many species are reported to be of known therapeutic value. In addition, many new plant species are yet to be discovered, which may contribute to the healthcare and biotechnology industry..

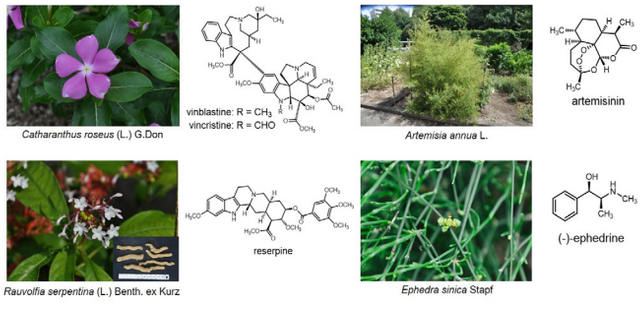

Figure 1: Some examples of plant derived modern drugs

In Nepal, traditional medicine systems including Ayurveda, Tibetan traditional medicine (Amchi) and other folk medicines, which use medicinal plants as their main components, are practiced since the time immemorial .[7] Some examples of common plant-derived crude drugs are represented in Figure 2. The documented evidence of the use of medicinal herbs in Nepal's traditional medical system dates back to at least 500 AD.[8] And the history of formulation production in Nepal goes back at least to the era of King Pratap Malla (1641-1674 AD).[9] Singh Durbar Vidya Khana was the first Ayurveda drug manufacturing company and produced about 160 herbal formulations .[10] At present, many private companies manufacture and sell herbal drug formulations. In addition, central and/or affiliated colleges of Agricultural and Forestry University, Tribhuvan University, Kathmandu University, Pokhara University, Purbanchal University, etc. are involved in the education and research of various aspects of medicinal plants from taxonomy, traditional uses, phytochemistry and evaluation of pharmacological activities. Similarly, Nepal Academy of Science and Technology (NAST), Gandaki Province Academy of Science and Technology (GPAST), Department of Plant Resources (DPR) and other governmental organizations and research oriented private, non-governmental organizations (NGOs) are also involved in the research of medicinal plants and their products.

Figure 2: Some of the representative plant-derived crude drugs commonly used in Nepal.

A*:* fruits of *Terminalia chebula* Retz. (local name: "Harro"), B: fruits of *Terminalia bellirica* (Gaertn.) Roxb. ("Barro"), C: fruits of *Phyllanthus emblica* L. ("Amala"), D: roots of *Glycyrrhiza glabra* L. ("Jethimadhu"), E: stem bark of *Cinnamonum* sp. ("Dalchini"), F: rhizomes of *Neopicrorhiza* sp. ("Kutki"), G: powder of rhizomes of *Curcuma longa* L. ("Besar"), H: rhizomes of *Zingiber officinale* Roscoe ("Aduwa/Sutho"), I: rhizomes of *Rheum sp.* ("Padamchal").

Although not widely documented and studied by modern scientific methods, these medicinal systems have been an integral part of the national health care system and highly revered by society due to their connection to the Vedic, Buddhist, and other traditional philosophies.[10,11] However, many plant species used in these conventional medicine systems have not been scientifically studied for their chemical constituents, pharmacological activity, safety, and quality control. The empirical investigations on these plants are the need of time.[12] Medicinal plants are one of the most widely discussed natural resources as having the potential to make a significant contribution to the economy of Nepal for many years. However, there has not been much notable progress in their utilization in healthcare (as traditional medicines) or the economy through proper product development and commercialization research. This article outlines a few research areas that can help strengthen Nepal's traditional medicine system and overall healthcare.

DOCUMENTATION OF TRADITIONAL MEDICINE KNOWLEDGE, PRACTICES AND MEDICINAL PLANTS

Nepal is rich not only in biodiversity but also in terms of ethnicity, languages, and cultures. According to the census of 2011, about 125 ethnic groups live in Nepal and a total of 123 languages were documented .[5] Many of these ethnic groups have their distinct history, culture, languages, and medicinal practices. However, the number of people of some ethnic groups is decreasing in recent years and it is affecting the knowledge of language and traditional medicinal practices. A recent study by Camara-Leret and Bascompte[13] reported that the language extinction results in the loss of medicinal knowledge; thus proper documentation of traditional medicine knowledge is essential.

In Nepal, more than 700 species are reported to have medicinal value. However, the exact number of these medicinal plants varies among sources. There have been various attempts on the documentation of medicinal plants of Nepal in the form of books such as "Plants and People of Nepal" by Manandhar (2002)[6], which documents more than 700 medicinal plants. Similarly, "A Compendium of Medicinal Plants in Nepal" by Baral and Kurmi (2006) covers a total of 1792 medicinal plants.[14] There are many other books published on ethnobotany and medicinal plants of Nepal in recent years.[7,8,15,16] Hundreds of ethnobotanical surveys have also been conducted to document the local uses of medicinal plants by communities in Nepal in several geographical locations in Nepal.[17–24] Common people refer to medicinal plants by the vernacular names in their local language. In many cases, the same plant may have different local names, or

different plants may also have the same local name. This often creates problems in the identification of plants if the people do not have sufficient taxonomical information and knowledge about local languages. Thus, an easily accessible database about the traditional medicinal practices of Nepal, including details about plant's scientific names, descriptions, local names in different languages, is of immediate need. The digitalization of herbaria, adding photographs of plants, and traditional medicines preparation process will help conserve local knowledge and support future scientific studies. Many medicinal plants in Nepal have high market value, but they are near extinction due to overexploitation through improper collection practices. Thus, the governmental organizations involved in these fields should make a policy to conserve these medicinal plants before their extinction. Governmental and public organizations should be involved in research to properly cultivate these plants in designated areas for continuous supply for future product development and commercialization.

RESEARCH RELATED TO CHEMICAL ANALYSIS, QUALITY CONTROL, PHARMACOLOGY, AND SAFETY

The chemical constituents and pharmacological activities of the crude drugs used in traditional medicines depend upon various factors such as the geographical location of the cultivation area, climatic conditions, vegetation phase, genetic characterizes, etc. These crude drugs may contain whole plants, leaves, stems, flowers, fruits, roots, rhizomes, etc., and there are always differences in chemical constituents in different parts of the same plant. For use as medicines for a specific therapeutic outcome, the active chemical constituents in these crude drugs should be properly identified. If the constituents and quantity (doses) vary among different formulations, their therapeutic outcome will not be the same. In most cases, formulations used traditional medicines are composed of several crude drugs originating from other plants; it is not easy to have consistent quality of their chemical constituents. Because of this reason, the therapeutic outcomes of the traditional medicines may vary and are often questioned. Therefore, one of the main challenges is to identify active constitutes and standardize them.

Many pharmacopeias worldwide have defined the criteria for such identification and quality control procedures from crude drugs. [25,26] Unfortunately, due to the lack of our Pharmacopoeia in Nepal, we do not have any specific criteria for the quality control of these natural medicines available in the Nepalese market. Thus, extensive research is one of the most essential steps in preparing the manographs or pharmacopoeial standards for an individual plant-based natural medication. Some basic steps can be the preparation of thin-layer chromatography (TLC), high-performance liquid chromatography (HPLC), and gas chromatography (GC) profiles/fingerprints for proper identification.[27] The next step should be to identify and quantify active chemical constituents present in these medicines, which requires extensive instrumental analysis involving chromatography, mass spectrometry (MS), and nuclear magnetic resonance spectroscopy (NMR). Due to the lack of such instruments in Nepal, collaboration with research institutes/universities in other countries is essential.

Providing the scientific evidence for the therapeutic efficacy of traditional medicines is another challenge. Possible mechanisms of pharmacological activities of extracts and/or isolated compounds should be explored using the in vitro and animal models. Similarly, safety and possible toxicities should also be studied. The study of the molecular basis of the synergistic effect of multiple active ingredients present in the traditional formulation also needs a high degree of attention.[28] A further step in the pharmacological study would be appropriately designed clinical studies to provide evidence for therapeutic efficacy. Patwardhan (2011) suggested that apart from the randomized controlled clinical trials, various valid alternatives should also be used for the same.[29] The difference between the modern and the traditional formulation methods should also be studied with respect to their effect, inactivity and safety. All these research activities will contribute to the development of evidence-based traditional medicines.

DEVELOPMENT OF INTEGRATIVE MEDICINE APPROACH

In the past few decades, there has been significant progress in the education and practice of modern medicine (sometimes referred to as western medicine) in Nepal.[30] The development of various diagnostic procedures, therapeutic agents, and health education has contributed significantly to improving healthcare in Nepal. However, access to modern medicine is not sufficient in rural areas of Nepal due to various factors such as economic conditions, lack of transportation and infrastructures and healthcare institutions, unavailability of required medicines, etc.[31] In most Nepalese communities, the pluralistic healthcare environment exists where people use modern medicines and many other traditional/folk medicines for socio-cultural and socio-religious reasons.[30,31] Undergraduate and post-graduate education systems in Ayurveda have been established in Nepal and are widely practiced, and various governmental and private institutions provide the Ayurveda and other traditional medicine services to common people.[7] However, the pharmacovigilance of

herbal medicines is not well-practiced, and the current pharmacovigilance system of Nepal does not sufficiently cover traditional medicines.[32] Many people believe that herbal medicines are natural and safe and do not exert side effects. However, there are hundreds of reports of toxicity of herbal medicines, including renal and hepatic toxicities.[33–36] Thus a proper understanding of their chemical constituents, mechanisms of actions, therapeutic efficacy, possible side/adverse effects and drug interactions is necessary.

Countries like Japan and China have been practicing integrative medicine approaches and traditional medicines, i.e., Kampo medicines in Japan and Traditional Chinese Medicines (TCM) in China are scientifically studied, standardized and properly regulated.[37–41] Therefore, they are well incorporated into national healthcare systems. For example, Kampo medicine formulations usually contain the standard mixtures of a few to tens of crude drugs originated from plant, animal, or mineral sources. They are officially approved, and 148 Kampo formulations are covered by the National Health Insurance System of Japan, and many are also sold as over-the-counter (OTC) medicines.[39–41] There is no specific license system for Kampo practitioners, and most of the physicians who have studied modern medicine in universities also practice Kampo medication. Katayama (2013) reported that about 80–90% of physicians prescribe Kampo drugs in daily practice.[42] The total market of Kampo medicines in Japan is reported to be about 2.5% of the total pharmaceutical market.[41] On the other hand, The Japanese Pharmacopoeia covers many crude drugs used in Kampo formulations. [25,26]

Taking examples of Japan and China, traditional medicine systems in Nepal should be properly documented, standardized, and proven scientifically through properly designed clinical studies. Furthermore, for traditional medicines having sufficient evidence, they should be appropriately formulated and marketed.

MULTIDISCIPLINARY COLLABORATION BETWEEN DIFFERENT SECTORS OF SOCIETY

From documentation of traditional practices to research and development of medicinal plants, a multidisciplinary research approach is necessary involving various sectors.[43] Good collaboration between universities, communities, government, and private sectors is essential (Figure 3). Local communities have enormous knowledge about traditional medicines, where they can contribute to providing knowledge. On the other hand, they also serve asthe producers (cultivators/collectors) of medicinal plantsand consumers of final products.

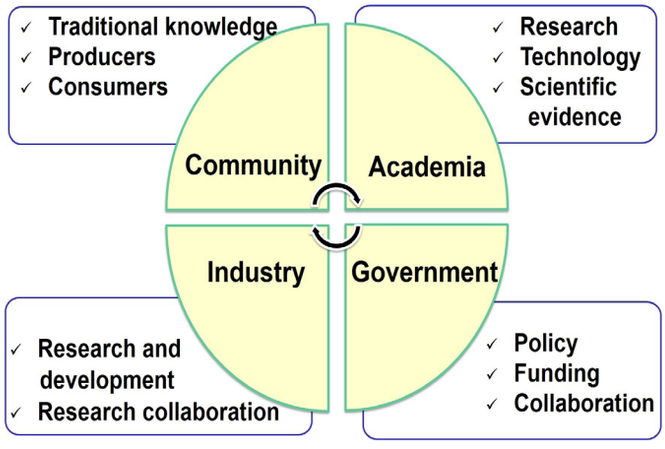

Figure 3: Collaboration between different sectors of society for strengthening traditional medicines research

The academic institutions (universities) and research organizations have the most crucial role in documenting traditional knowledge and its critical analysis, scientific studies related to chemical constituents, pharmacological activities, and safety (Figure 4). The researchers working in these institutions can do bridging activities between many sectors in society. They can support communities through technology transfer, science communication, and providing education and technical support for medicinal plants' cultivation, collection, and processing. Governmental authorities, state governments, and local municipalities can support community research organizations through funding and formulating proper policies. They can also help in bridging the communities to academia or private sectors. The private sectors (pharmaceutical and food companies) should be involved

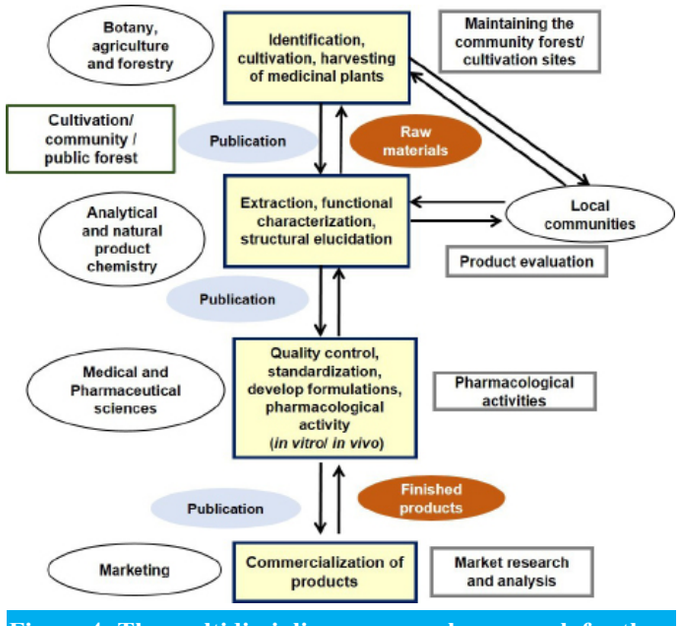

Figure 4: The multidisciplinary research approach for the commercialization of medicinal plant-based products

in researching and developing medicinal plant-based formulations, their quality control, and pharmacological evaluations. Private companies can buy medicinal plants from local communities and sell them as finished products through proper and sustainable commercialization practices. Establishing Medicinal Plant Gardens and Museums of Traditional Medicines in collaboration with different organizations can help research and educate traditional medicines and medicinal plants for researchers/students. These Gardens and Museums will also be a good resource for educating common people about the importance of conserving traditional knowledge and biodiversity. Photograph of the Museum of Traditional Medicines at the School of Health and Allied Sciences, Pokhara University, Pokhara, Nepal, are provided in Figure 5.

Figure 5: Photograph of Museum of Traditional Medicines at School of Health and Allied Sciences, Pokhara University, Pokhara, Nepal

CONCLUSION AND FUTURE PROSPECTS

Nepal is rich in biodiversity and traditional medical knowledge; however, the proper documentation of such resources and scientific studies are insufficient. Multidisciplinary research is essential in strengthening the traditional medicine system in Nepal, involving collaboration between various sectors such as community, academia, government, and private companies. Research on quality control, pharmacological activity and safety, and clinical studies to evaluate therapeutic efficacy are essential to establish evidence-based traditional medicine systems.

REFERENCE

1. Kunwar RM, Bussmann RW. Ethnobotany in the Nepal Himalaya. J Ethnobiol Ethnomed. 2008;4. doi:10.1186/1746-4269-4-24.
2. Atanasov AG, Waltenberger B, Pferschy-Wenzig EM, et al. Discovery and resupply of pharmacologically active plant-derived natural products: A review. Biotechnol Adv. 2015;33(8):1582-1614. doi:10.1016/j.biotechadv.2015.08.001.
3. Devkota HP, Watanabe M. Role of medicinal plant gardens in pharmaceutical science education and research: An overview of medicinal plant garden at Kumamoto University, Japan. J Asian Assoc Sch Pharm. 2020;9:44-52.
4. Khanal A, Devkota HP, Kaundinnyayana S, Gyawali P, Ananda R, Adhikari R. Culinary herbs and spices in Nepal: A review of their traditional uses, chemical constituents, and pharmacological activities. Ethnobot Res Appl. 2021;21:40.
5. Central Bereau of Statistics. Population Monograph of Nepal Volume II (Social Demography).; 2014.
6. Manandhar NP. Plants and People of Nepal. Timber Press, Inc.; 2002.
7. Gewali MB. Aspects of Traditional Medicine in Nepal. Institute of Natural Medicine, University of Toyama, Japan; 2008.
8. Watanabe T, Rajbhandari KR, Malla KJ, Devkota HP, Yahara S. A Handbook of Medicinal Plants of Nepal Supplement I. Ayurseed L.E.I.; 2013.
9. Khanal DP. History of pharmaceutical development in Nepal. J Manmohan Meml Inst Heal Sci. 2017;3(1):86-93.
10. Koirala RR. Country Monographs on Traditional System of Medicine.; 2007.
11. Koirala R., Khaniya BN. Present Status of Traditional Medicines and Medicinal & Aromatic Plants Related Resources & Organizations in Nepal. Nepal Health Research Council; 2009.
12. Astutik S, Pretzsch J, Kimengsi JN. Asian medicinal plants' production and utilization potentials: A review. Sustain. 2019;11(19):5483. doi:10.3390/su11195483
13. Cámara-Leret R, Bascompte J. Language extinction triggers the loss of unique medicinal knowledge. Proc Natl Acad Sci U S A. 2021;118(24):e2103683118. doi:10.1073/pnas.2103683118.
14. Baral SR, Kurmi PP. A Compendium of Medicinal Plants of Nepal. Mrs. Rachan Sharma; 2006.
15. Watanabe T, Rajbhandari KR, Malla KJ, Yahara S. A Handbook of Medicinal Plants of Nepal. Ayurseed L.E.I., Kanagawa; 2005.
16. Kunwar RM, Sher H, Bussmann RW. Ethnobotany of the

Himalayas. Springer; 2021.

17. Adhikari M, Thapa R, Kunwar RM, Devkota HP, Poudel P. Ethnomedicinal Uses of Plant Resources in the Machhapuchchhre Rural Municipality of Kaski District, Nepal. Medicines. 2019;6(2):69. doi:10.3390/medicines6020069.

18. Bhattarai NK. Medical Ethnobotany in the Karnali Zone , Nepal. Econ Bot. 1992;46(3):257-261.

19. Kunwar RM, Fadiman M, Cameron M, et al. Cross-cultural comparison of plant use knowledge in Baitadi and Darchula districts, Nepal Himalaya. J Ethnobiol Ethnomed. 2018;14(1). doi:10.1186/s13002-018-0242-7

20. Manandhar NP. Ethnobotanical note on folk lore remedies of Baglung district Nepal. Contrib Nepalese Stud. 1993;20(2):183-196.

21. Manandhar NP. An inventory of some herbal drugs of Myagdi district, Nepal. Econ Bot. 1995;49(4):371-379. doi:10.1007/BF02863087.

22. Luitel DR, Rokaya MB, Timsina B, Münzbergová Z. Medicinal plants used by the Tamang community in the Makawanpur district of central Nepal. J Ethnobiol Ethnomed. 2014;10(1):1-11. doi:10.1186/1746-4269-10-5.

23. Rokaya MB, Münzbergová Z, Timsina B. Ethnobotanical study of medicinal plants from the Humla district of western Nepal. J Ethnopharmacol. 2010;130(3):485-504. doi:10.1016/j.jep.2010.05.036.

24. Uprety Y, Poudel RC, Asselin H, Boon E. Plant biodiversity and ethnobotany inside the projected impact area of the Upper Seti Hydropower Project, Western Nepal. Environ Dev Sustain. 2011;13(3):463-492. doi:10.1007/s10668-010-9271-7.

25. Kameyama Y, Matsuhama M, Mizumaru C, Saito R, Ando T, Miyazaki S. Comparative Study of Pharmacopoeias in Japan, Europe, and the United States: Toward the Further Convergence of International Pharmacopoeial Standards. Chem Pharm Bull (Tokyo). 2019;67(12):1301-1313. doi:10.1248/cpb.c19-00621.

26. The Ministry of Health Labor and Welfare of Japan. The Japanese Pharmacopoeia, 17th Edition.; 2016.

27. Devkota HP, Adhikari-Devkota A, Takano A, Yahara S, Basnet P. HPLC and TLC Fingerprints of Selected Nepalese Natural Medicines and Medicinal Plants. J Nepal Pharm Assoc. 2017;28:1-11.

28. Li FS, Weng JK. Demystifying traditional herbal medicine with modern approaches. Nat Plants. 2017;3(8):1-7. doi:10.1038/nplants.2017.109

29. Patwardhan B. Ayurveda GCP Guidelines: Need for freedom from RCT ascendancy in favor of whole system approach. J Ayurveda Integr Med. 2011;2(1):1-4. doi:10.4103/0975-9476.78175.

30. Marasini B. Health System Development in Nepal. JNMA J Nepal Med Assoc. 2020;58(221):65. doi:10.31729/JNMA.4839.

31. K.C. B, Heydon S, Norris P. Access to and use of medicines in the Annapurna region of Western Nepal and possible impacting factors. J Pharm Policy Pract 2019 121. 2019;12(1):1-12. doi:10.1186/S40545-019-0172-3.

32. Shrestha S, Danekhu K, Sapkota B, Jha N, KC B. Herbal pharmacovigilance in Nepal: challenges and recommendations. F1000Research 2020 9111. 2020;9:111. doi:10.12688/f1000research.22133.1

33. Oh SJ, Cho JH, Son CG. Systematic review of the incidence of herbal drug-induced liver injury in Korea. J Ethnopharmacol. 2015;159:253-256. doi:10.1016/J.JEP.2014.11.027.

34. Liu C, Fan H, Li Y, Xiao X. Research Advances on Hepatotoxicity of Herbal Medicines in China. Biomed Res Int. 2016;2016. doi:10.1155/2016/7150391.

35. Calitz C, Du Plessis L, Gouws C, et al. Herbal hepatotoxicity: Current status, examples, and challenges. Expert Opin Drug Metab Toxicol. 2015;11(10):1551-1565. doi:10.1517/17425255.2015.1064110.

36. P P, LK W, E E. Adverse effects of herbal medicines: an overview of systematic reviews. Clin Med. 2013;13(1):7-12. doi:10.7861/CLINMEDICINE.13-1-7.

37. Wang J, Guo Y, Li GL. Current Status of Standardization of Traditional Chinese Medicine in China. Evidence-based Complement Altern Med. 2016;2016. doi:10.1155/2016/9123103.

38. Gao H, Wang Z, Li Y, Qian Z. Overview of the quality standard research of traditional Chinese medicine. Front Med China. 2011;5(2):195-202. doi:10.1007/S11684-011-0134-X

39. Motoo Y, Arai I, Hyodo I, Tsutani K. Current status of Kampo (Japanese herbal) medicines in Japanese clinical practice guidelines. Complement Ther Med. 2009;17(3):147-154. doi:10.1016/j.ctim.2008.09.003

40. Maegawa H, Nakamura T, Saito K. Regulation of traditional herbal medicinal products in Japan. J Ethnopharmacol. 2014;158(PART B):511-515. doi:10.1016/j.jep.2014.07.012.

41. Arai I, Kawahara N. Kampo pharmaceutical products in the Japanese healthcare system: Legal status and

quality assurance. Tradit Kampo Med. 2019;6(1):3-11. doi:10.1002/tkm2.1204.

42. Katayama K, Yoshino T, Munakata K, et al. Prescription of Kampo drugs in the Japanese health care insurance program. Evidence-based Complement Altern Med. 2013;2013. doi:10.1155/2013/576973.

43. Devkota HP. Research and development of natural product-based medicines and functional foods in Nepal. In: Fifth National Science Day 2074 Smarika. Ministry of Science and Technology, The Government of Nepal; 2017:53-58.