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Tibetan Medical informatics: An emerging field in Sowa Rigpa pharmacological & clinical research

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1. Introduction

Tibetan medicine, or Sowa Rigpa (*gso ba rig pa*), the "Science of Healing" as it is known in Tibetan, is one of Asia's great scholarly medical systems alongside Ayurveda and traditional Chinese medicine (TCM). It originated in Central Tibet, formalized between the seventh and twelfth century CE by integrating its own indigenous medical knowledge with that of Indian, Chinese, Persian and Central Asian traditions (Ga, 2010, 2014), and transmitted widely to Mongolia, Bhutan, Nepal, the Indian Himalayas, and even culturally-related areas of Russia (Wangdü, 2016; Bold, 2009; Wangchuk, 2008; Pordié and Kloos). Sowa Rigpa provides a comprehensive knowledge-praxis approach for life course health, disease prevention, and healing methodologies as the main medical system and health resource for Tibetan and Himalayan populations across the Tibetan Plateau, wider trans-Himalayas and surrounding areas. It is based on a specific type of empiricism that developed largely in the 18th century CE and has persisted through contemporary times (Gyatso, 2016). Tibetan medicine focuses on the theory of overall well-being, coordinating diseases of the human body with mental health, and as documented by a growing body of research (Reuter et al., 2013; Luo et al., 2015). It is sought out for a wide range of conditions including chronic metabolic disorders, autoimmune conditions, inflammatory issues and many other acute and chronic diseases of the contemporary era. Today Sowa Rigpa physicians and institutions have extended their reach globally. Through concentrated growth and development regionally from the early 1990s–2000s, Sowa Rigpa has produced a significant industry valued at over half a billion USD as of 2017 (Kloos et al., 2019). Such growth and development have also occurred in the area of information science. This paper seeks to introduce these major informatics developments for Sowa Rigpa, highlighting particularly productive areas for research, and proposing an approach for furthering its development.

Analyses show that policy contexts in China, Nepal, India, Bhutan, Mongolia and other national venues highly influence the form of Sowa Rigpa development in education, practice and research (Kloos et al., 2019). The big data era of "Internet Plus" in China, ushered in by Li Keqiang in 2015, has provided a major influence for the development and policy context of traditional medicines throughout China, including their local regional practices and institutions. Similar trends, though at smaller scales, have developed in other southeast Asian countries such as Japan, Korea and Thailand. National policies focused on the data-driven model are forging a specific type of development for these traditional medical traditions, not just traditional Chinese medicine (TCM) and its regional variations. This context has been particularly influential for Tibetan medicine in China since Tibetan regions of China are not only the principal centers of Tibetan medical education and practice, but Tibetan regions of China significantly lead the Sowa Rigpa pharmaceutical industry (Kloos et al., 2019).

With the development of mass networks linking information technologies, platforms, and forums with artificial intelligence throughout mainland China, Tibetan medical researchers, academic institutions, and government and private hospitals have produced a dramatic output of information types and integrated them into practice for research, clinical and pharmacological purposes. Such practices are providing unprecedented opportunities and challenges for the development of Tibetan medicine (Gongbao et al., 2018).

Likewise, due to Sowa Rigpa's wide-ranging materia medica and vast compendium of complex pharmaceuticals, an increasing number of researchers have begun to investigate its pharmacological constituents, medicine compounding techniques, and nuanced treatment approaches (Jiang et al., 2009; Wangchuk et al., 2011; Li et al., 2016; 2018; Tidwell and Nettles, 2019) to treat disease, alleviate pain and restore health.

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Likewise, researchers in Tibetan medical institutions have recognized the need for presenting the vast body of Tibetan medical knowledge in a form more accessible to disciplines interested in its pharmacological and clinical data by using various discipline-specific methodological proclivities for large data set access and analysis. Data set development allows for detailed quantitative assessments of Tibetan medical clinical and pharmacological practice (e.g., Wangchuk et al., 2012, 2013; Wencheng, 2016; Dhongzhu, 2017, 2018; Zhao et al., 2018; Wencheng et al., 2019) to stand alongside rich, qualitative approaches (e.g., Millard, 2007; Jacobson, 2007; Adams et al., 2010; Craig, 2012; Blaikie, 2013; Blaikie et al., 2015; Gerke forthcoming) the latter of which has hitherto dominated research on Tibetan medicine.

The national policies and discourse around information science in China have even led Tibetan physicians and researchers to formally designate a term for the emerging field of Tibetan medical informatics, using the Tibetan neologism, *Bömen chatrin rikpa* (*bod sman cha 'phrin rig pa*), or the "Science of Communicating Tibetan Medicine" (Geng et al., 2017). Sowa Rigpa educators have even characterized Tibetan medical informatics as promising to shape transmission and innovation of Sowa Rigpa in the contemporary era with emerging basic databases of its medical classics and bibliographies; frameworks for its theoretical architecture; repositories of its materia medica classifications; and digitalization of records for patient cases, prescriptions, and treatments (Zhuoma and Zhaba, 2015) in tandem with practice implementations in data privacy, de-identified records and so forth. Sowa Rigpa researchers, including the current authors, are looking at how artificial intelligence, big data, semantic networks, neural network technology, and bioinformatics can be converted into integrated visualized data forms and processed into useful information. Such data forms can also inform clinical practices and insights (Cairang and Renzeng, 2015). The synthesis of these data sources can, moreover, powerfully influence academic ideas and theories by viewing Tibetan medicine through quantitative and qualitative means (Wencheng,[2] 2016). For example, chemical analysis of compounds associated with taste classifications in Tibetan medicine is developing insights into how Sowa Rigpa understands biopathways of its pharmaceuticals by looking at how they act on complex taste receptor pathways in the body (Rangdrol, 2015; Zhao et al., 2018). This informatization process can facilitate analytical descriptions of how tacit knowledge is procured through traditional training modalities (e.g., Tidwell, 2017), how Tibetan medical theory illuminates critical factors influencing health (e.g., Husted and Dhondup, 2009), and in which ways empirical modes of health inquiry can synergize with quantitative methods (e.g., Wangchuk et al., 2016).

This study constitutes the first analysis of the databases, developments and methodologies of Tibetan medical informatics, and presents the first quantitative assessments from these data sources regarding Tibetan medical works, disease categories, prescription data and pharmacological characterizations. The authors aim to introduce these data sources to a wider research community and propose an analytical structure to inform pharmacological, clinical, textual and cultural research analyses using Tibetan medicine informatics. For example, using informatics methods to explore the last several centuries of complex pharmacological methods and compounding procedures, known as *menjor* (*sman sbyor*),[3] is possible now. These data sets can help analyze historical trends and more recent innovations, and illuminate the novel uses of materia medica in Sowa Rigpa,[4] distinct from and conversant with pharmacology of other medical traditions. Other researchers investigating methods and theory related to ethnopharmacology and major Asian scholarly medical traditions will find these data developments and initial quantitative results particularly useful.

[2] In Chinese publications, Wüntrang Dhondrup is written as Wencheng Dangzhi.

[3] A classical part of Sowa Rigpa, yet emerging as a 'new' discipline of Sowa Rigpa. See, for instance, Tidwell and Nettles (2019).

[4] See, for instance, Gerke (forthcoming).

2. Foundations of Tibetan Medicine

Due to a unique geography, environment and ecological landscape, the Tibetan plateau has provided a context requiring its inhabitants to develop a particular means of subsistence that has driven specific biological and behavioral adaptations aiding survival (Huerta-Sánchez et al., 2014; Li et al., 2016; Meyer et al., 2017). In this context, Tibetan medicine also developed significant understanding of both long-term living practices and the accumulation and transmission of empirical medical knowledge. Engaging, exchanging and integrating related practices and texts from surrounding regions as early as seventh century CE (Martin, 2007; Yoeli-Tlalim, 2012; Liu et al., 2018), early medical scholars fused these translations with that of their own textual corpus, creating a syncretic medical knowledge (Ga, 2014). By the 11th to 13th centuries CE, a systematic approach to Tibetan medical education, theory and clinical practice had been established and canonized (Ga, 2010; McGrath, 2017), including the composition of the Tibetan medical classic called the *Four Treatises* (*Rgyud bzhi*). This classic is still memorized, studied and implemented in practice by all Tibetan physicians. Over the last couple decades, Tibetan medicine has gradually reached an impressive size in Asia with clinical resource development and pharmaceutical industry extending across mainland China and building growth further globally (Rucinska, 2009; Kloos et al., 2019).

Based on Sowa Rigpa's engagement with the "five elements" (*'byung ba lnga*), or "five dynamic properties," inherited from or co-derived with similar theoretical roots as Ayurveda (Zysk, 1991, 1993), systemic properties of material and immaterial forms provided the core theoretical structure informing concepts applying both to its esoteric and exoteric medical and ritual contexts (Wencheng et al., 2017). Correspondent to its counterpart of the three *doṣa* in Ayurveda, elemental theory informed the theoretical framework of the "three *nyépa*" (*nyes pa gsum*)—default functional energetic systems of pathways or activities that, in their default mode, link body constituent, organ, fluid, and energetic signaling dynamics to provide specific systemic functions in the body (Tidwell, 2019). The conceptual framework of the three *nyépa* diverged from that of the *doṣa* in Ayurveda, and facilitated the formation of a medical system that is now articulated in terms of unique views on consciousness, life, death and rebirth (Namdul, 2019); nuanced understandings on mind-body interactions, and remarkably effective treatments for a wide spectrum of diseases.[5]

Imbalance of the three *nyépa* are understood to lead to disease development, and the degree of imbalance directs particular therapeutic regimens for the patient. The three *nyépa* are comprised of *rLung*, *mKhris-pa* and *Bad-kan*, pronounced "*lōōng,*" "*tripa,*" and "*béken,*" respectively (Fig. 1). We retain the phonetic spellings of the individual *nyépa* for reading ease, except for "*rlung*" to distinguish it as a term. The functional activities of the three *nyépa* work in conjunction with and maintain homeostasis throughout the life course starting from the moment of fertilization (Gongbao et al., 2018). As with Tibetan embryology, the theory of digestion and metabolism derive from the five elements and how the "six tastes" (*ro drug*), "eight potencies" (*nus pa brgyad*), and "three post-digestive tastes" (*zhu rjes gsum*) relate to the three *nyépa*. Likewise, evaluation of digestive and metabolic capacity depends on urinalysis, pulse diagnosis, dietary and behavioral influences, psychological factors and so on. It is important to note that all these aspects of Tibetan medical theory and practice have important academic and clinical value.

[5] For recent investigations on Tibetan medical treatment assessments see Vennos et al. (2013); Bauer-Wu et al. (2014); Geng et al. (2017).

Fig. 1. The three mental afflictions and three *nyépa,* interrelated psychophysiologic pathways of health and disease, as depicted in one of the medical allegory trees originating from the classical Tibetan medical thangka scroll paintings first commissioned in the seventeenth century, and re-developed in the early 20th century. Images are adapted from Jampa Trinlé's *Explanation of the Four Medical Tantras through the Eighty Medical Thangkas: Light of the Blue Gaze* (2006), Thangka Two and Thangka Twenty-One, showing detail from physiology and pathology, and the causes and manifestations of disease, respectively, in the unpaginated front matter. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

3. Database sources for Tibetan Medical informatics

In this section, we introduce eight major databases (*gzhi grangs mdzod*) that the current authors identify as forming the initial foundation for Tibetan medical informatics. Researchers in academic institutions and clinicians in hospital settings have developed these databases for both practical and research use, digitally entering the content of classical Tibetan medical works; core Tibetan medical theory; disease classifications; diagnostic indications; treatment approaches; prescription data; electronic de-identified medical records; and related material. These resources form the first of their kind in informaticization of Tibetan medical knowledge. The authors introduce and characterize these databases so that other researchers can make use of them and further build Tibetan medical informatics with an integrated analytical approach. In the following, we provide a brief description of each database, its developer and its accessibility.

1) **Tibetan Medical Historic Classics Database** (*Bod sman gna' dpe gzhi grangs mdzod*) (Fig. 2) was produced by researchers of the Qinghai Provincial Tibetan Medical Research Center. From 1987, various collaborators from Tibetan regions of China, U.S., U.K., Italy, Mongolia, India, and Bhutan assembled the collection of Tibetan medical texts. Currently, the Tibetan Medical Historic Classics Database has compiled 638 types of texts with over 2000 individual works, of 60 million words. Although it has only been accessible for internal use by those affiliated with the Qinghai Provincial Tibetan Medical Research Center, developers aim to launch an open access platform (*mnyam rol gyi 'phrin stegs*) by 2020.
2) **Tibetan Medical Analytical Systems Database** (*Bod sman 'tshol zhib ma lag*) is a database and data mining system developed by Tsering Namjial, a professor of Qinghai Nationalities University, when he founded the Tibetan Medical Data Mining Research Department in 2015. Namjial deposited a majority of the standard historical classics and contemporary texts into this database. Likewise, he entered materia medica specimen identifications, common and botanical name enumerations and translations, source locations, distributions, and images, along with any related identified medicinal compounds available in the published literature. He has also augmented the database with recent additions of formula contents, benefits and functional activities. This has become a critically valuable resource used by Tibetan physicians across Tibet, India, Nepal and abroad. This database system has over 16,000 users, and has logged more than 1400 keywords searched on average monthly. The Tibetan Medical Analytical Systems Database has already significantly supported and facilitated research related to Tibetan medicine.
3) **Northwest Minority Medical Database** (*Byang nub grangs nyung mi rigs gso rig gzhi grangs mdzod*) (Figs. 3 and 4) was developed by the Ethnic Medicine Academic Heritage Innovation Research Center, a new research center of the Ethnic Medicine College of Chengdu University of Traditional Chinese Medicine founded in 2017 by Zhang Yi, a senior professor in the college. The Center conducts research on and gathers literature related to Tibetan medicine and nine other medical traditions such as Yi and Mao in China. The department particularly focuses studies on medicine compounding processes specific to Tibetan medicine, such as *düljong* ('*dul sbyong*),[6] as well as particular treatment approaches. The database is a comprehensive storehouse of medicinal compound and pharmacological data from the various research projects conducted by faculty, students and researchers of the department, and is extending its databases to research conducted externally. Currently, the database contains 410 ancient Tibetan medical texts, more than 1500 compounded formulas and more than 3000 medicinal compounds. It also has stored data from specific *düljong* and treatment approaches. The analyses and graphics presented in the following sections of this paper will draw largely from this database. The completion of the database is planned for 2021, and will simultaneously be launched as an open access platform.
4) Tibetan Medical Journal Database (*Bod sman dus deb gzhi grangs mdzod*) was developed by the Qinghai Provincial Tibetan Medicine Research Center as a database of published peer-reviewed journal articles with subject-specific subsidiary databases. Subsidiary databases compile subsets of articles. For example, in 2016, the Center began developing the database called China's Tibetan Medicine and Behavioral Health Research Database (*Zhong guo zang yi yao dian zi shu ju ku jian she yu ying yong ping tai* (2016-ZJ-Y106)). This database has a collection of over 32,000 articles from publications in English, Tibetan and Chinese. See Drukmokyi ('Brug mo skyid), 2017 regarding further details on the development of and research related to this database. The research center plans to launch an open access form of the database in 2020.
5) Tibetan Pharmacological Activity Prospector (*Bod sman sman nus zhib bsher ma lag*) is a searchable database of the pharmacological activities of Tibetan medicine compounds studied to date. It was developed in 2018 by the Research Center of the Ethnic Medicine College of Chengdu University of Traditional Chinese Medicine. Thus far, the team has categorized, entered and published the tastes,

[6] For descriptions of *düljong,* see Tidwell and Nettles (2019).

potencies, and post-digestive tastes for over 3000 medicinal compounds, primarily sourced from the *Four Treatises* (Gönpo, 1982), in a searchable online database system. This database is not open access yet, but researchers are developing the permissions to do so.

6) Tibetan Medical Disease Library (*Gso rig bang mdzod*) database was developed by Qinghai University Tibetan Medical College, under the direction of Professor Rinchen Dhondup and launched in summer 2019. It catalogues diseases primarily from the *Four Treatises* (Gönpo, 1982) and *Yutok's Embellishment of Realization* (*G.yu thog dgongs rgyan*) (Wangdü, 1982), detailing disease identities, etiologies, and symptoms for the full scope of Tibetan medical disease classification. It also describes degrees of severity for each condition according to the Health Management Bureau of China. This database is open access via the WeChat platform.
7) Great Tibetan Medical Dictionary Database (*Bod lugs gso rig tshig mdzod chen mo gzhi grang mdzod*) is a database that was developed by Lhasa Men-Tsee-Khang for physicians, medical students and researchers. It integrates a searchable medical dictionary expanding upon their published textual copy of the Great Tibetan Medical Dictionary (*Bod lugs gso rig tshig mdzod chen mo*) (Trinlé, 2006a, 2006b). The database is comprised of an extensive number of medical terms and related words, with an accessible database cataloguing illnesses, their etiologic descriptions, prevention indications, diagnostic indicators, and treatment protocols as standards of care in the hospital setting. It also contains formula details, materia medica descriptions, and interrelated pharmacological references. One drawback of this database is that it does not detail the textual sources for its contents. However, the database itself could be the object of analysis in assessing origins for current standards of care. The database was launched in spring 2019. This database is open access via the WeChat platform.[7]
8) Medicine & Astrology Publication Database (*Sman rtsis gnyis kyi rtsom yig grangs mdzod*) was developed by Lhasa Men-Tsee-Khang under the direction of Dr. Yumba. It includes astrological and calendrical data for eight different astrological calculation systems related to Tibetan medicine. Likewise, it intersects with another related database dedicated to astrology alone called the Tibetan Astrology Computational Systems Database (*Bod kyi gnam rig skar rtsis rig pa'i brtsi byed ma lag*). The Tibetan Astrology Computational Systems Database provides calculations for sun, moon, planet, constellation and zodiac positioning relative to period, date, astronomical corrections, search criteria conditions, illness and so forth. It contains data from the various interpretations of the Kalachakra astrological calculations, as well as other distinct astrological systems related to Tibetan medicine. The database also has analytics for comparing and contrasting systems of calculations; correlations of historical origins and relationships; and almanac traditions such as that of Sakya, Tsurpu, Phukpa, Nartang, Mindroling, and Men-Tsee-Khang.

These databases provide a strong foundation for a developing Tibetan medical informatics, akin to its counterparts in traditional Chinese medicine and Ayurveda. For example, in 2008, the basic framework for Traditional Chinese medicine informatics was proposed, along with an outline for its subfields and most promising initial research directions. This proposal laid out the model for the construction of the Digital Virtual Academy of Traditional Chinese Medicine Informatics (Cui et al., 2016). Over the last couple decades, researchers in both TCM and Ayurveda have developed informatics approaches for various applications, such as database development and analytical software to assess clinical data, chemoinformatics, bioinformatics, clinical decision management, image processing, and even integrating some aspects of artificial intelligence. Comparatively, Tibetan medical informatics is just beginning to develop its intersections with information science and related data-driven technologies. The areas of informatics development among TCM, Ayurveda and Tibetan medicine are detailed in Table 1 below.

The coauthors have contributed to several of these informatics developments specific to Tibetan medicine such as data mining, GIS for materia medica distributions, and structural equation modeling for formulas expressing digestion and medicine compounding theory (Wencheng, 2016, Dong et al., 2017; Wencheng et al., 2019). Geng et al. (2017) and Chen and Gesang (2017) have also made contributions toward initiating development of the bio- and chemoinformatics dimensions of Tibetan medical informatics applications as well. Researchers in Tibetan medicine can use a best practices approach derived from the models of TCM and Ayurveda in working toward developments for these other informatics applications. Throughout development and analysis of datasets, it is critical that core concepts of Sowa Rigpa are reflected sufficiently and analytic structures designed appropriately to interrelate theoretical relationships.[8] Artificial intelligence, large data and other systems analysis methods can leverage algorithms to solve macro-complex problems, an approach that is garnering focus in the development of precision medicine (Williams et al., 2018). For Tibetan medical informatics, we are recommending this approach, not to create a Tibetan medical form of precision medicine, but to enrich the capacity for a wider scope of researchers and disciplines to understand and engage Tibetan medical theory, clinical praxis knowledge and pharmacology, and use such tools to develop clinical and pharmacological collaborations across intellectual traditions of medicine and scientific inquiry to understand disease etiologies, patient care and therapeutic/pharmacological synergies with greater insight.

4. Applications of Tibetan Medical informatics

In this section, we present several quantitative assessments from the database sources mentioned above as simple examples of Tibetan medical informatics analysis as well as data visualization techniques. Here, we pick several areas that elucidate key features of Tibetan medical knowledge vis-à-vis an informatics approach, namely: (1) classical works and major schools of thought; (2) disease classification; (3) materia medica and formula types; (4) pharmacology; and (5) clinical case study sources.

4.1. Intellectual history and classical works: digitalization and visualization

In order to appreciate the challenge in digitalizing the numerous works related to Tibetan medicine, we will start with an overview of some recent efforts to create published compilations of the classic works extant to date. According to preliminary statistics, more than 2000 historical Tibetan medical works dating from 8th to 20th century CE have been excavated and preserved in China. More than 800 of those works have been collated, digitalized and published in book form, and

[7] With regard to digital textual collections that have relevance to Tibetan medicine, several other electronic repositories are noteworthy. The Buddhist Digital Resource Center (www.tbrc.org) lists entries for at least 300 historical figures and over 1000 digital works related to Tibetan medicine. A vast project called 84,000 (http://84000.co) is translating the collected scriptures and treatises of the Buddhist canon. As such, it will also undoubtedly provide rich textual data related to Tibetan medical theory and praxis. Thus far, medically related translation entries total 900 instances. Timeless Treasures (http://dharmacloud.tsadra.org/library), a free, public repository of Tibetan Buddhist literature maintained by the Tsadra Foundation, provides an additional textual database resource, including texts with cosmological, ritual and theoretical relations to Tibetan medical theory and practice such as those from the Abhidharma, Kālacakra and *Chöd* (*gcod*) collections.

[8] For example, methodological improvements related to pharmacological analysis are address in Tidwell and Nettles (2019).

Fig. 2. Tibetan Medical Historic Classics Database entry portal.

Fig. 3. Northwest Minority Medical Database entry portal.

Fig. 4. Region-specific search interface of Northwest Minority Medical Database.

more than one hundred have been reprinted as a collection of Tibetan medical classics titled *ĀḤ Classics Collection* (*Āḥ dpe tshogs*) (100 volumes) (Tsokchen, 2005). Works foundational to the Sowa Rigpa canon have been placed in a multi-volume set called *Compendium of Tibetan Medicine's Canonical Texts* (*Bod kyi gso rig kun 'dus*) (60 volumes) (Tsokchen, 2011). A recently completed eighteen volume set, *Expanded Commentary of the 80 Tibetan Medical Thangkas* (*Sman thang rgyas 'grel*) (Tsokchen, 2012) provides detailed explanations on anatomy, physiology, pathology, diagnostics, pharmacology, and therapeutics related to the Tibetan medical classic the *Four Treatises* (*Rgyud bzhi*) (Gönpo, 1982). Numerous works are still being collected and arranged for publication. University of Tibetan Medicine in Lhasa has compiled more than 100 handwritten texts of invaluable historic Tibetan medical, astronomical, and calendrical works and published them in a thirty-volume set entitled *China's Traditional Tibetan Medical Texts (Krung go'i bod lugs gso rig rtsa che'i dpe rnying kun btus)* (Tibetan Medical College, 2013). In addition, the university has collected 410 historic Tibetan medical works, which are in the early stage of a bibliographic project called "Rescue Mining and Database Development of Ancient Tibetan Medical Literature of the Southern Tibetan Medical Tradition in Sichuan" (*Sichuan nan pai zang yiyao guji wenxian de qiangjiu xing wajue zhengli ji shujuku yanjiu*) (Nie et al., 2015, in Chinese).

The Tibetan Medical Historic Classics Database has systematically digitalized and stored many of the compilations that have been collected and published to date, along with historiographic details of the works archived dating back to sources from 7th century CE. The database digital content records at least 3000 distinct Tibetan medical works—both historic and contemporary in origin—with 638 types of documents, totaling more than 60 million words (Zhuoma and Zhaba, 2015). In the following schematics of Fig. 5 and Table 2, the coauthors have used this data to present a historiographical approach blended with historical sources to identify and quantify the prominent figures, schools and classical works in the periods in which they are described to originate from a specific set of medical history texts. The figure and table provide a perspective of how Tibetan physicians integrate historiographic perspectives with historical evidence for their tradition. Such hybrid data figures are helpful to demonstrate the multiplicity of paradigms engaged by contemporary Tibetan physicians in locating schools of thought, historic influences, and even hagiographies. Such a presentation can also help map out non-extant works and assist in building modes to synthesize textual sources with archaeological evidence as has been done for the Pashupati project of Licchavi inscriptions in Nepal, combining extant textual inscriptions, geospatial data and archaeological remains (Coningham et al., 2016).

The set of digitalized texts used for the data depicted in Fig. 5 and Table 2 are four seminal Tibetan medical history works (three early treatises and one contemporary work): Zurkhar Lodröe Gyalpo's

Table 1
Comparison of informatics area applications in Tibetan Medicine, TCM and Ayurveda.

Informatics applications	TCM	Ayurveda	Tibetan Medicine
Clinical Data Warehouse	Zhou et al. (2010)	Patwardhan (2012)	–
Computational Intelligence	Wu et al. (2012); Gu and Chen (2014)	Joshi (2005)	–
Bioinformatics	Wang et al. (2015)	Rath (2006)	Geng et al. (2017)
Chemoinformatics	Ehrman et al. (2007)	Fazlin et al. (2013)	Chen and Gesang (2017)
Informatics Standards	Rastogi (2012)	–	–
Clinical Decision Support System	Zhang and Chen (2009)	Patwardhan (2013); Stranieri et al. (2016)	–
Data Mining	Zhou et al. (2018)	Raja et al. (2015)	Wencheng (2016); Dang-Zhi (2016)
Pharmaco-informatics	Chen (2009)	Somashekhar et al. (2009)	–
Electronic Health Records	Bjering et al. (2011)	Stranieri et al. (2016)	–
Artificial Intelligence	Liang et al. (2018)	–	–
Geographic Information System	Gu et al. (2014)	Deshpande et al. (2004)	Dong et al. (2017)
Image Processing	Zhang et al. (2005)	Miryala et al. (2014)	–
Structural Equation Modeling	Zhao (2012)	–	Wencheng et al. (2019)

Zurkharwa's Intellectual History (*Zur mkhar ba'i shes bya khog 'bubs*) (2006), Desi Sanggyé Gyatso's *The Regent's Medical History* (*Sde srid sman gyi khog 'bubs*) (2006), Deumar Tenzin Püntsok's *Medical History and Hagiographies: Ocean of Blessings and Garland of Delighted Sages* (*Gso ba rig pa'i chos 'byung rnam thar rgya mtsho rba rlbas drang srong dgyes pa'i 'dzum phreng*) (2004) and Jampa Trinlé's edited volume *Sowa Rigpa History* (*Gso ba rig pa lo rgyus*) (2004).[9] These classical works provide a historiographic perspective, as well as integrate some accounts from historical records and even archaeological evidence in the contemporary source. However, these texts primarily provide a historiographic lens in depicting the 26 major Tibetan medical schools and physician-scholar founders that contemporary Tibetan physicians engage in recounting the development of Tibetan medicine, its specific disciplines, and schools of thought over time.

Though the earliest extant medical texts, dated using paleographical dating methods[10] (van Schaik, 2013), originate from the Tibetan imperial period during 8th to 10th century CE (Karmay 2013: 21; Tso, 2016: 221; Samdrup, 2019), depicting non-extant sources prior to this period, such as the earliest period shown in 19th century BCE, frame the historiographic lens informing concepts of tradition, lineage and heritage, as well as relationships with medical traditions in neighboring regions. Likewise, many texts described to exist even after the period of our earliest extant texts, have yet to be located, went missing, or were destroyed during significant historical events. The graphical presentation of the data visualize modes of inheritance and practices recognized by physicians within the tradition.

One particularly important figure is that of Yutok Yönten Gönpo, who appears in Fig. 5 as the founder of Tibetan medicine, indicated by a (1) next to his name. However, he only appears in texts dated after the 12th century CE, and as such, the historical accuracy of his existence has been questioned by recent scholarship[11] (Ga, 2010, 2014). However, a historical figure, or several figures, preceding the recognized author or compiler of the *Four Treatises*, Yutok Sarma Yönten Gönpo, is acknowledged to have existed. Thus, we see both a historiographic depiction as well as historic elements portrayed in considering the founding of the tradition.

Through this visual representation of descriptions of key figures from texts as early as the 8th century to mid-20th century and the periods prior, one can visualize the other figures with which Yutok Yönten Gönpo could be associated and see potential antecedents to his portrayal. Tibetan medical historian-scholar Yang Ga has explored the potential historical figures from whom Yutok Yönten Gönpo may most likely descended, highlighting individuals in the Dré lineage of the imperial period as most likely candidates (2019). The visual representation also demonstrates a relative dearth of works and figures from what Yang Ga describes as the Middle Period of Tibetan medical works: 11 to 12th centuries CE after Rinchen Zangpo translated the Indian medical classic *Aṣṭāṅgahṛdayasaṃhitā* into Tibetan. Analytical works on many newly found classical texts from the Middle Period have received much attention recently by researchers in Tibet (Ga, 2019) and will likely start building a richer picture of this time period. The Later Period, 12th century CE to present, is characterized by the canonization of the *Four Treatises* by Yutok (Sarma) Yönten Gönpo, drawing significantly from the *Aṣṭāṅgahṛdayasaṃhitā* (Ga, 2014), and a fluorescence of works and schools of thought that emerge thereafter. Figures such as Drangti Gyelwa Sangpo, Jangpa Namgyel Drazang Zurkhar Nyamnyi Dorjé and Lhunding Namgyel Dorjé form hubs for specific schools of thought to emerge in Tibetan medicine, such as the Jang and Zur schools, also known as the North and South schools, respectively, the two most influential transmissions before the rise and transformation of Tibetan medical education by Desi Sangyé Gyatso and the Fifth Dalai Lama (Van Vleet, 2015). By examining the enumeration of texts depicted in Table 2 we gain an account of the centuries in which most of the classical Tibetan medical works are described to originate: namely, the 8th, 12th and 17th through 19th centuries CE. These productive periods also correspond to developments in modes of empirical thought and expansions in materia medica catalogue and implemented for formulations. Here a Tibetan medical informatics approach provides data processing power to inform such questions of inquiry.

4.2. Disease classification analytics

Graphically representing data can facilitate scholars in assessing distinctions across enumerations between various Tibetan medical texts and within sections of the *Four Treatises*, for example. The illnesses described in the Oral Instructions Treatise, the third section of the *Four Treatises*, have been digitally recorded in the Tibetan Medical Disease Library, Northwest Minority Medical Database and a database newly developed by the coauthors via their hierarchy and respective classifications within that section of the text. For example, location- and type-classifications for each major illness category are distinguished such that in the *rLung* illness chapter, seven main location classifications are described: head *rlung*, heart *rlung*, lung *rlung*, liver *rlung*, stomach *rlung*, colon *rlung*, and kidney *rlung*. Enumerating the illnesses described and visually representing the data, have allowed researchers to identify patterns and distinctions within and across classifications. These databases have simplified methods to quantify the number of diseases detailed in the *Four Treatises*. The text itself quotes a total of 1616

[9] These four sources are also summarized in the *Tibetan Medical Compendium* (*Krung go'i bod kyi gso rig kun btus*) (Tsokchen, 2011) and catalogued (Ling, 2015).

[10] Van Schaik's paleographic dating method (2013) delineates writing styles according to the historic periods, particularly in Tibetan imperial history, in which they were prevalent.

[11] Since his name or reference does not appear in texts written prior to the 12th century (Ga, 2010, 2014).

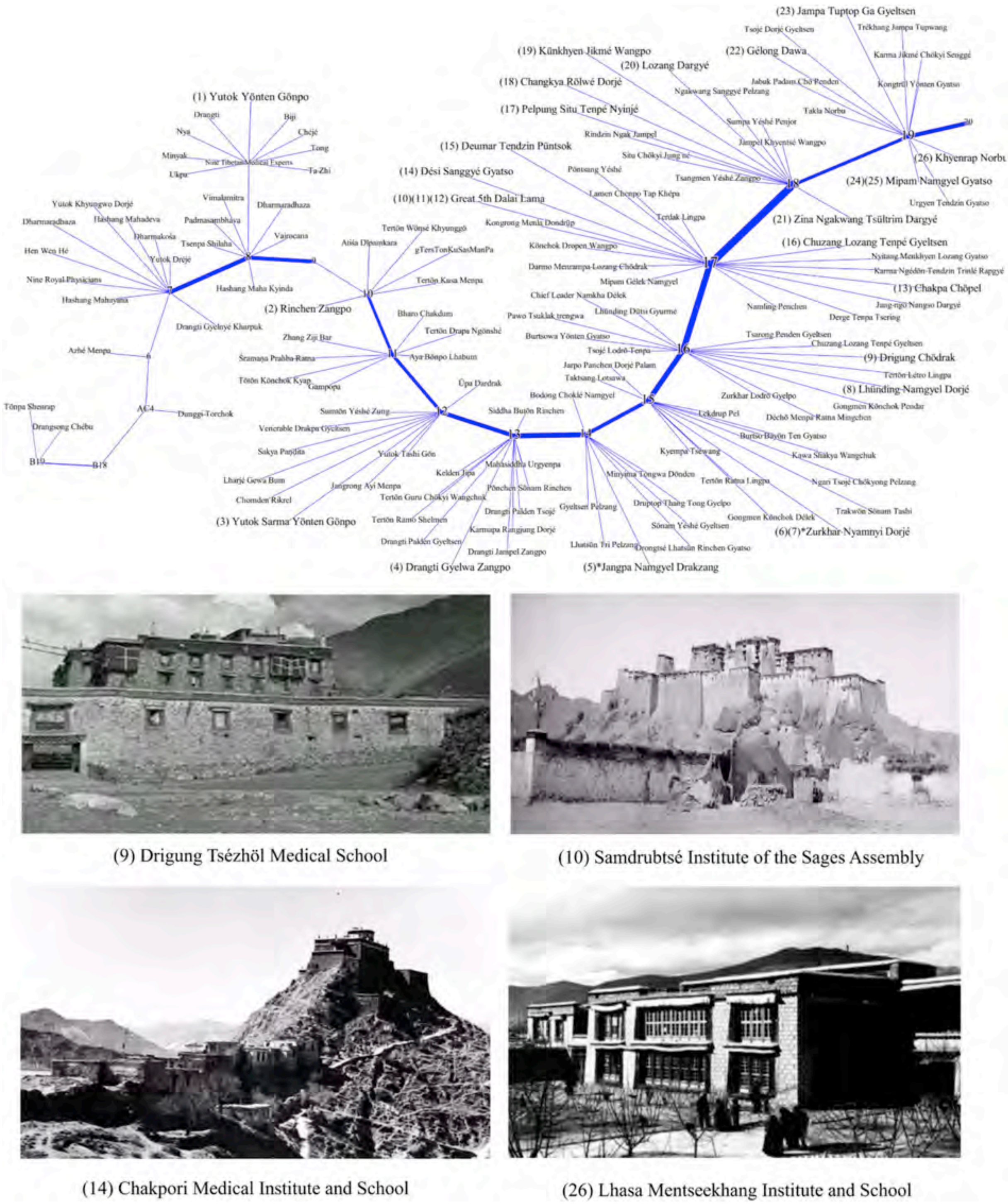

Fig. 5. Schools, key figures and enumerated classical works in Tibetan medicine as depicted from a historiographic perspective in seminal works on Tibetan medical history by Zurkhar Lodrö Gyalpo (2006), Desi Sanggyé Gyatso (2006), Deumar Tenzin Püntsok (2004), and Jampa Trinlé (2004), and further compiled by Feng Ling (2015). Names are given in Tibetan phonetics. Numbers at the nodes of the central blue line provide the era accompanied by the key Tibetan physicians with significant contributions to the development of Tibetan medicine in that era. Major schools developed are indicated chronologically by sequential numbers in parentheses next to their founder. The thickness of the blue line indicates the number of medical texts published during the time period as described by these sources. Data source: Tibetan Medical Historic Classics Database. Figure developer: Wüntrang Dhondrup. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 2
Integrated historiographic and historic perspective on the number of texts ascribed to each period cited in Tibetan medical history texts (Tsokchen, 2011; Ling, 2015)[12] Grey fill indicates eras where texts are enumerated yet not extant. Light grey indicates hybrid extant and non-extant sources.

Century	Texts
19 BCE	6
1 CE	7
8	143
9	3
10	27
11	21
12	123
13	43
14	47
15	90
16	64
17	267
18	135
19	145
20	61
21	1
Total number of works	1183

diseases, yet how precisely these diseases are enumerated has been less clear. These databases allow for researchers to analyze modes of classification to explicate the quoted 1616 disease enumeration, and clarify which categories are nestled within one another but not explicitly quantified. This analysis also allows for greater data manipulation power in, for example, collapsing disease category by location and looking at specific etiologic characteristics that might have similar relationships. For example, the class of diseases related to the biomedical concept of cancer all stem from etiologic relationships to interstitial fluid and poor blood quality (Lhamo, 2016; Tidwell, 2017; Tidwell, 2019).

Fig. 6 depicts the nested hierarchy of each of the fifteen major categories of illnesses catalogued by the *Four Treatises*. The *Tripa* illness category is expanded in the figure to demonstrate further detail. Blue lines delineate subdivisions from particular (*bye brag*) *tripa* functional subtype disorders; red lines delineate subdivisions from general (*spyi*) *tripa* illnesses categorized by location and imbalance form. Clinical diagnostic data can now map onto the theoretical categories to determine what illness types are implemented in diagnostic practice and to what frequency. Visual representation of the data through network analysis facilitate assessments of theory-praxis relationships.

[12] Fig. 5 and Table 2 depict the historical period in which the texts are described to have originated as given by Zurkhar Lodröe Gyalpo (2006), Desi Sanggyé Gyatso (2006), Deumar Tenzin Püntsok (2004), and Jampa Trinlé (2004) and summarized in Tsokchen (2011). The figure and table do not differentiate the earliest extant medical texts available, which only date to 8th to10th centuries (Karmay 2013: 21; Tso, 2016: 221; Samdrup, 2019). Grey fill of historical time periods denotes lack of extant texts mentioned in these sources.

4.3. Materia medica and formula assessments

Using the Northwest Minority Medical Database, the coauthors have analyzed the materia medica presented in the *Four Treatises* text specifically, calculating 1002 materia medica substances (*sman rdzas*) identified. They have begun synchronizing individual materia medica data with GIS spatial location distribution and chemical compound constituents of each specimen. For example, research conducted by Dang-Zhi (2017) used GIS and Maxent to model ecological niches[13] integrated with the materia medica data in an investigation of the growth region distribution of *Rhodiola crenulata* (*sro lo dmar po*), as well as relative regional abundance of a select set of its phytochemicals—-specifically, gallic acid, salidroside, tyrosol, ethyl gallate, p-coumaric acid. The research group aims to build this database gradually with these integrated spatial, compositional, and functional data source studies of materia medica. Other examples include a study on *Rhodiola kirilowii* (*ga dur dman pa*), examining the distribution abundance and phytochemical composition of the plant using 1H-NMR (Daoxin, 2018), as well as a study assessing *Codonopsis pilosula* (Franch.) and *Codonopsis nervosa* (*klu bdud rdo rje*) (Jinsong, 2018) using HPLC and TLC analytics.

The database also looks at groupings of materia medica into formulas. The *Four Treatises* categorizes materia medica constituents into formulas indicated for specific conditions, functional benefits and treatment courses. Fig. 7 visually depicts the formulas in the Oral Instructions Treatise grouped by the fifteen illness categories (colored circle dots) surrounded by formulas common across multiple categories (black dots). Fig. 8 shows formulas from both the Oral Instructions Treatise and the Subsequent Treatise. The current authors calculated and subgrouped the

[13] See Warren and Seifert (2011) for methodological nuances.

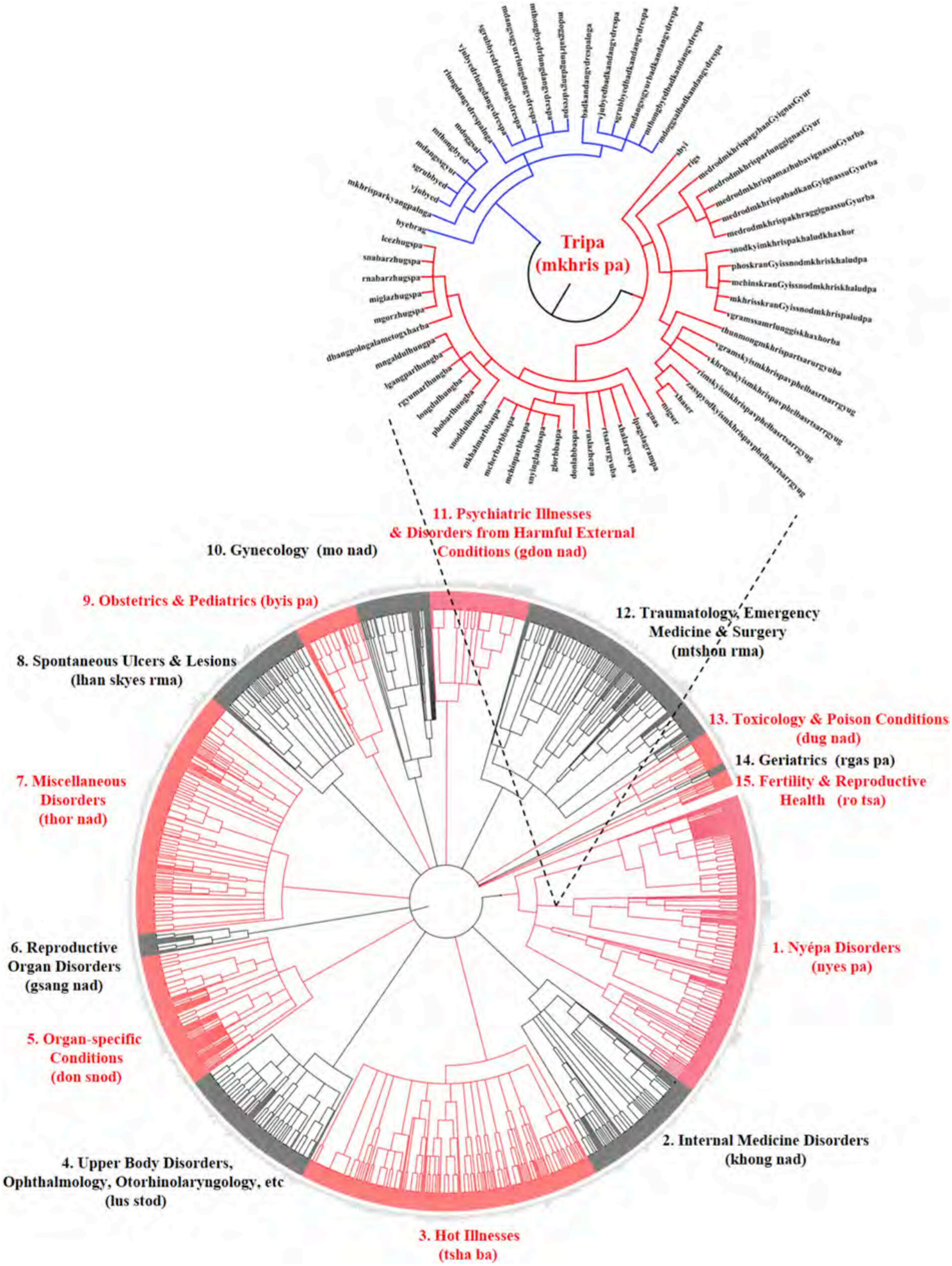

Fig. 6. Detailed diseases categories in the Tibetan medical classic, the *Four Treatises.* This figure depicts the hierarchy of major illnesses and their respective classifications presented in the *Four Treatises*. Initially, the location- and type-classifications for each major illness category was entered into Excel. For example, in the *rLung* illness categories, there are seven main location classifications: head *rlung*, heart *rlung*, lung *rlung*, liver *rlung*, stomach *rlung*, colon *rlung*, and kidney *rlung*. These classifications were entered into an excel spreadsheet in their respective hierarchies, then exported to a txt file. The txt file was uploaded to the data visualization platform *Interactive Tree of Life* (itol.embl.de) to create this graphical depiction of the existing illnesses and their respective hierarchies as detailed in the *Four Treatises*. Note that categories in the hierarchy, such as "location" and "type," are drawn with separate lines in the graphical depiction but are not counted as separate illnesses. Only the final subcategories are enumerated as separate illnesses. This graphical method facilitates analysis of illness classification in the *Four Treatises*. Data source: Database developed by coauthors from *Four Treatises* using Excel, then analyzed and re-compiled for visualization (Research Innovation #: Ky-2018010). Figure developer: Wüntrang Dhondrup.

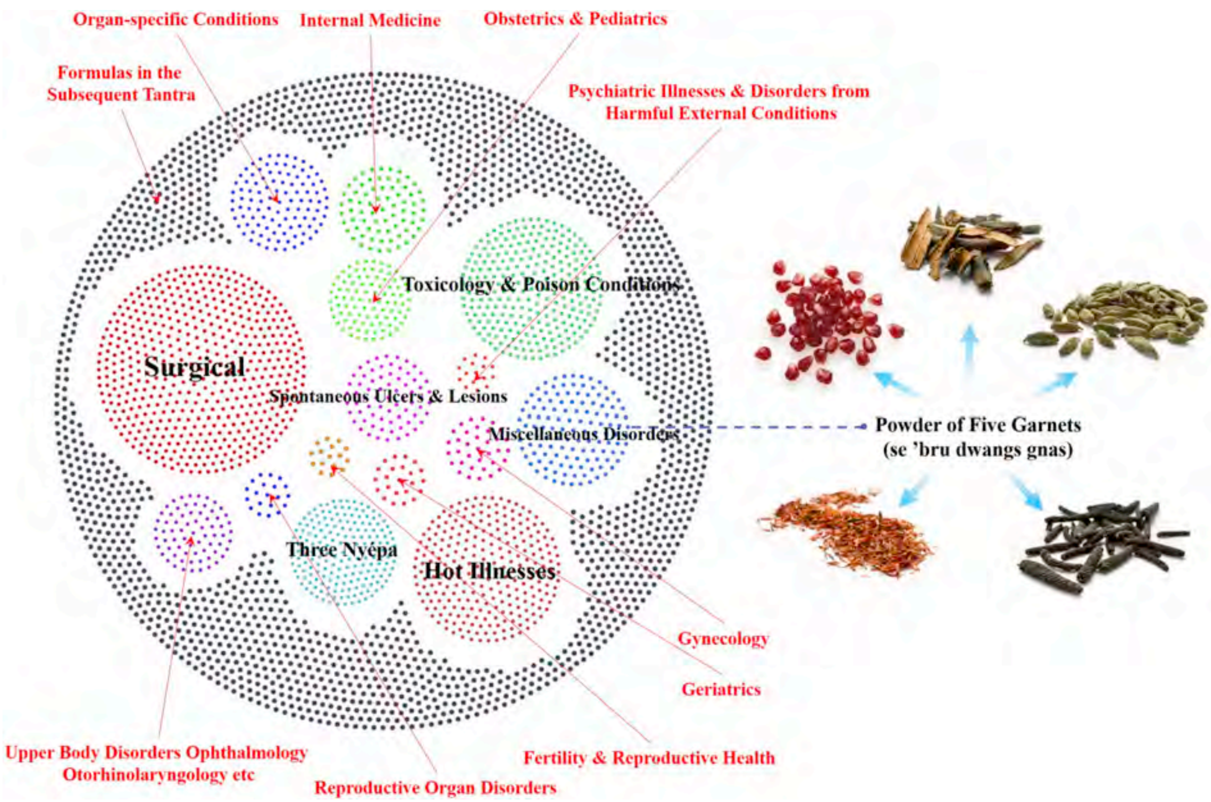

Fig. 7. This figure provides a comprehensive illustration of formulas in the Oral Instructions Treatise (colored circle dots) and those that cross several illness categories (surrounding black dots). To create this visualized presentation, all formulas from the *Four Treatises* were entered into an Excel spreadsheet (see Table 3 below). In the figure above, formulas are grouped according to the fifteen illness categories under which they are presented in the Oral Instructions Treatise. Each dot represents a particular formula. Formulas specific to illness categories are color coded, grouped and several are labeled. Data source: Northwest Minority Medical Database from *Four Treatises* with re-compilation using Excel. Figure developer: Wüntrang Dhondrup. Right side image (Powder of Five Garnets) courtesy of Padma AG. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

2694 formulas detailed in the *Four Treatises* from this database source (see Figs. 7 and 8). The China National Technology Research Center has researched 863 of these formulas identifying major active compounds. *The Great Formulary of the Four Treatises* (*Dpal ldan rgyud bzhi'i sman gyis sgyor sde chen mo*), edited by Khangsar Sonam Chimé (2010), details the 2694 formulas and has begun adding in descriptions of the major active compounds for an upcoming edition. Chimé had a previously published count of 2258 formulas but had not added formulas of lesser ingredients such as single, dual and triple ingredient decoctions in his initial count. The addition of simple formulas provides the current number of 2694 formulas that coincides with the count given herein. Visualized depictions of data help characterize cluster features of data (Fruchterman and Reingold, 1991). For example, the Traumatology section of the Oral Instructions Treatise has been the section of the *Four Treatises* least implemented in practice yet contains the greatest number of formulas as seen in the figure. Fig. 8 depicts a different visualization whereby the Oral Instructions Treatise formulas are in blue clustered by section, and those from Subsequent Treatise are in red and clustered by formula vehicle mode and functional class such as pill, powder, decoction, and purgatives, emetics and cleansings. In the dynamic force mapping of Fig. 8, the more substantial categories of formulas of the Subsequent Treatise are clarified. Powders, decoctions and purgatives dominate the formula repertoire. Table 3 provides a standard tabular depiction of the data that provides the enumerated details per section. In the figures and table above, formulas are grouped according to the fifteen illness categories and fifteen therapeutic approaches under which they are presented in the Oral Instructions and Subsequent Treatises.

Such graphical and visualized depictions can help highlight categorical distinctions of formula richness in the text as well as structure analytic priorities for further investigation. For example, Hu et al. (2018) assessed disease targets and pathways for compounds in three main medicines used for treating interstitial and serum fluid disorders (*chu ser*): amber (*spos dkar*), *Cassia tora* (*thal ka rdo rje*), and *Psoralea corylifolia* (*so ma rA dza*). Since the materia medica are also used in traditional Chinese medicine, the major databases of identified phytochemicals for materia medica were drawn from the Systems Pharmacology Lab online database[14] at Northwest University in Xi'an and the Encyclopedia of Traditional Chinese Medicine.[15] From the identified compounds, two-dimensional shapes of the chemical structures were downloaded from the U.S. National Library of Medicine's National Center for Biotechnology Information.[16] Finally, disease targets for each of the interstitial and serum fluid disorders were identified and compounds linked to the targets. Such data access also allows researchers to begin investigating interrelationships between formulas of different illness categories and activity classes as well. Researchers have begun some of this initial work in compound classes and structures for specific taste profiles (Rangdrol, 2015).

Beyond the *Four Treatises*, researchers can now look at the commentarial literature, some of which provide the main sources for a significant number of the formulas used in contemporary Tibetan practice, to assess commonalities and distinctions across the Tibetan medical literary corpus. Until now, it has been difficult to even enumerate formulas from the root and commentarial texts. Here, the coauthors provide the first enumeration of materia medica substances and their related

[14] Access at: http://lsp.nwu.edu.cn/tcmspsearch.php?qr=Bovis%20Calculus&qsr=herb_en_name&token=f0c9b409b993d7ba9cf2774bc11951fb&tdsourcetag=s_pcqq_aiomsg.

[15] Access at: http://www.nrc.ac.cn:9090/ETCM/index.php/Home/Index/.

[16] Accessed at: https://pubchem.ncbi.nlm.nih.gov/.

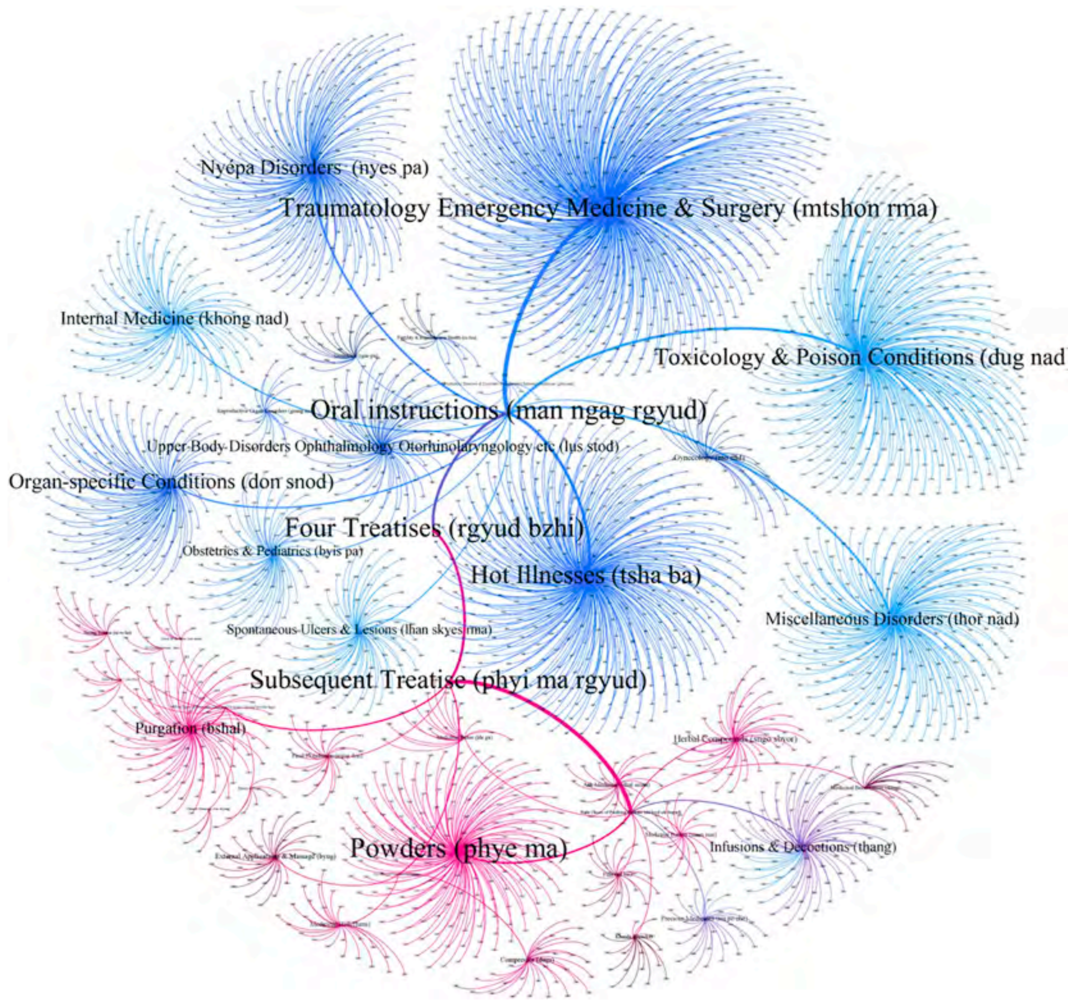

Fig. 8. This figure graphically maps the 2694 distinct multi-compound formulas recorded in the Oral Instructions and Subsequent Treatises of the *Four Treatises*. In the figure above, formulas are grouped according to the fifteen illness categories and fifteen therapeutic approaches under which they are presented in the Oral Instructions and Subsequent Treatises. Formulas are mapped vis-à-vis force-directed graph as final dots, linked by line extensions to their respective textual topical origin in the *Four Treatises*. The dynamic force mapping system Gephi 0.9.2 was employed for the data visualization. Data source: Northwest Minority Medical Database from *Four Treatises* with re-compilation using Excel. Figure developer: Wüntrang Dhondrup.

formulas in the most commonly used materia medica and formulary texts from the 12th to 21st century. The *Manjugosha Materia Medica* (*'Jam dbyangs sngo 'bum*) by Vairocana (2005) lists 170 materia medica substances, *A Treatment Compendium of Precious Materia Medica* (*Gso dpyad rin po che 'khrungs dpe*) (Cairang, 2017)[17] lists 217 substances, *Ocean of Materia Medica* (*Sman Ming rgya mtsho*) by the 3rd Karmapa Karma Rangjung Dorjé (2005) from the 13th century lists 844 substances, *Crystal Orb and Rosary* (*Shel gong shel phreng*) (Deumar Tenzin Püntsok, 2007) from the 17th century lists 2294 substances,[18] and Gawé Dorjé's comprehensive contemporary publication *Stainless Crystal Mirror of Materia Medica* (*'Khrung dpe dri med shel gyi me long* (Dorjé, 1995), now the authority for materia medica identification in Tibetan medicine, lists 3861 substances (Cairang, 2017).[19] After calculating the contributions of 53 classical works contributing to Tibetan pharmacology, including those listed above, the coauthors have calculated there are more than 10,000 distinct materia medica substances among all the materia media handbooks and formularies, including the *Four Treatises* and *Precious Relics of Countless Oral Instructions* (*Man ngag bye ba ring bsel*) (Zurkhar Nyamnyi Dorjé, 2014) (Cairang and Renzeng, 2015). Without entry of these large datasets of information from these texts, and relating it to present research on functional activities of these formulas, it would be extremely difficult to conduct pharmacological analyses across these texts and formulas. Thus, we propose that Tibetan medical informatics provides an unprecedented opportunity for both pharmacological and literature analysis in these sources. Furthermore, there are numerous types of Tibetan materia medica, many of which are regionally specific (Boesi, 2006), particularly implemented in local applications and obtained from local geo-ecologies. Using the Tibetan medical informatics approach described herein, further rigorous analysis of commonalities, innovations, and inconsistencies among compounded formulas from these various sources can be conducted.

[17] This corrects an earlier version of this compilation (Shantigarbha, 2007).

[18] See Luobu (2012) for further analysis on Deumar Tenzin Püntsok's pharmacological contributions.

[19] Jia and Zhang attempted to create a transregional enumeration of the materia medica substances used in Tibetan medicine in their *Dictionary of Chinese Ethnic Medicine* (2016). In their publication, 3105 kinds of medicinal substances used in Tibetan medicines are recorded, including 2644 kinds of plant-derived substances, 321 animal-derived products and 140 mineral-based substances. However, since their publication, Gawé Dorjé released his updated compendium in 2018.

4.4. Tibetan pharmacokinetics and pharmacological modeling of medicine compounding principles

Using the Northwest Minority Medical Database, the coauthors have coded the various principles for which formulas are compounded

Table 3
Number of multi-compound formulas by topical section in the *Four Treatises*.

	Four Treatises' Section (listed in sequential order from Oral Instructions and Subsequent Treatises)	No. of Formulas
Oral Instructions Treatise (*Man ngag rgyud*)		
1	*Nyépa* Disorders (*nyes pa*)	197
2	Internal Medicine (*khong nad*)	101
3	Hot Illnesses (*tsha ba*)	323
4	Upper Body Disorders, Ophthalmology, Otorhinolaryngology, etc (*lus stod*)	85
5	Organ-specific Conditions (*don snod*)	119
6	Reproductive Organ Disorders (*gsang nad*)	20
7	Miscellaneous Disorders (*thor nad*)	197
8	Spontaneous Ulcers & Lesions (*lhan skyes rma*)	71
9	Obstetrics & Pediatrics (*byis pa*)	71
10	Gynecology (*mo nad*)	34
11	Psychiatric Illnesses & Disorders from Harmful External Conditions (*gdon nad*)	8
12	Traumatology Emergency Medicine & Surgery (*mtshon rma*)	495
13	Toxicology & Poison Conditions (*dug nad*)	277
14	Geriatrics (*rgas pa*)	19
15	Fertility & Reproductive Health (*ro tsa*)	15
	Oral Instructions Treatise Subtotal 2032	
Subsequent Treatise (*Phyi ma'i rgyud*)		
1	Infusions & Decoctions (*thang*)	77
2	Powders (*phye ma*)	162
3	Pills (*ril bu*)	22
4	Medicinal Pastes (*lde gu*)	18
5	Medicinal Butters (*sman mar*)	21
6	Ash Medicines (*thal sman*)	22
7	Concentrated syrup decoctions (*khaNDa*)	17
8	Medicinal Beers (*sman chang*)	19
9	Precious Medicines (*rin po che*)	27
10	Herbal Compounds (*sngo sbyor*)	43
11	Oil Therapy (*snum 'chos*)	4
12	Purgation (*bshal*)	84
13	Emesis (*skyugs*)	7
14	Nasal Medication (*sna sman*)	6
15	Mild Enema (*'jam rtsi*)	9
16	Strong Enema (*ni ru ha*)	15
17	Channel Cleansing (*rtsa sbyong*)	4
18	Compresses (*dugs*)	28
19	Medicinal Bath (*lums*)	25
20	External Applications & Massage (*byug*)	30
	Subsequent Treatise Subtotal 640	
Final Conclusion Addendum (*Mjug don yongs gtad*)		
1	Final Conclusion (*mjug don*)	22
	SUM TOTAL	2694

according to Tibetan pharmacology (*menjor*). For example, Table 1 lists a recent Structural Equation Modeling study for the Tibetan medical field (Wencheng et al., 2019). Developing a pharmacokinetics approach from Tibetan medicine's own theory to understand how a compound and its metabolites change through transformations in the gut, this study evaluates a vector structure model called "Ro Nü Zhujé," for the Tibetan terms of "Taste" (*ro*) "Potency" (*nus pa*) and "Post-digestive Taste" (*zhu rjes*). This model was developed from a structural equation in which three vectors describe the pharmacokinetic effects on Tibetan medicinal compounds. These three vectors comprise: (1) a vector describing the contents and activities of the formulation (*sbyor sde*) (B); (2) a vector describing the amount of each constituent (*sbyor tshad*) (T); and (3) a vector describing the compounding method for formula characterizing a compatibility structure (*sbyar thabs*) (D). The formula is $R_m = \sum_{n=1}^{n} (B_1T_1D_1 + B_2T_2D_2 + \ldots\ldots + B_nT_nD_n)$. The formula provides the initial taste profile (R), that is then used as a vector array to assess transformations according to post-digestive taste and potency as the substance moves through digestive and metabolic processes.

Fig. 9 below provides the Tibetan medical conceptual framework used to develop the model. This framework depicts the intermediary relationships between medicinal compound and its metabolic transformation vis-à-vis the three gastropyretic phases (*me drod gsum*), also known as the "three functional digestive phases" to show how compounds differentially engage the three *nyépa* psychophysiological systems to treat illness, specifically the twenty definitional characteristics of illness (*nad kyi mtshan nyid nyi shu*)[20] from *nyépa* imbalance that are treated through the seventeen qualities (*yon tan bcu bdun*)[21] of the antidote (Desi Sanggyé Gyatso, 1994: 317). Each medicinal compound is comprised of properties exhibiting differential aspects of the five elemental dynamics (*'byung ba lnga*)—'earth,' 'water,' 'fire,' 'wind' and 'space' (*sa chu me rlung mkha'*)— defined by their properties of solidity/stability, cohesion/fluidity, maturation/heat, motility/movement, and interactive space, respectively. These elemental dynamics can be condensed into overall 'cooling' (*bsil*) or 'heating' (*drod*) activities that treat hot (*tsha*) or cold (*grang*) illnesses, accordingly.

From a 'material potency' (*rdzas kyi nus pa*) perspective, the medicinal compound's constituent elemental dynamic properties exhibit eight functional activities (*nus pa brgyad*)[22] determined by the identity of the materia medica specimen (*ngo bo'i nus pa*). These functional activities work directly on the twenty definitional characteristics through relationships of affinity, neutrality and opposition (for further details, see Tidwell and Nettles, 2019). The five elemental dynamics of the medicinal compound can also be understood to enact functional activities toward the treatment of illness vis-à-vis another pathway: the potency of taste (*ro gyi nus pa*). The profile of elemental dynamics in a medicinal compound form its taste profile—a varied combination of the six tastes (*ro drug*),[23] which transform sequentially in the three gastropyretic phases (*me drod gsum*), that become three post-digestive taste profiles (*zhu rjes gsum*). The post-digestive tastes are chemical profiles of sweet (*zhu rjes mngar*), sour (*zhu rjes skyur*) and bitter (*zhu rjes kha*) constituents of the medicinal compound that has gone through the digestive processes. This profile determines the medicinal compound's activity as classified by the eight potency characteristics mentioned above. It also determines the medicinal compound's seventeen qualities, which also act directly on the twenty definitional characteristics of the *nyépa*. Compounds can exhibit properties that rely more on their taste, post-digestive taste, and/or potency to act upon the three *nyépa* to gain balance, and can target specific organs, physiological systems, body regions, tissues and/or fluids. The ultimate quality of the medicinal compound (*mthar thug gi yon tan*), and its overall activity in treating illness pathways, is expressed as a sum of its overall activity due to these various aspects of properties of the medicinal compound.

The model illustrated in Fig. 9 is used to analyze the pharmacokinetics of Tibetan prescriptions vis-à-vis the functional effects stemming from the six tastes, three digestive tastes, eight properties and seventeen qualities of the medicine compound as it is transformed by the patient's digestive and metabolic processes. This model was used by Dang-Zhi et al. (2019) in a study assessing the relationship of Tibetan medical theory on the "gastropyretic triad" (*pho ba'i me drod rnam gsum*), post-digestive tastes (a.k.a., chemical profiles), and metabolism of the three nutrients (*zhu rjes gsum dang bcud rigs gsum*) to contemporary biomedical understandings of intestinal flora (*deng rabs pho rgyu'i srin rig*) in treating metabolic syndromes, such as diabetes (*gcin snyi za khu*).

Analytical methods from informatics allow Tibetan medical research to develop quantitative and qualitative modes of describing the

[20] The twenty definitional characteristics of illness (i.e., imbalance in one or more *nyépa*) comprise: rough, light, cold, subtle, hard, mobile, unctuous, sharp, hot, light, odorous, purgative, moist/shearing, pinguid, cool, heavy, dull, smooth, stable, sticky (Gonpo, 1999:60).

[21] The seventeen qualities of the antidote comprise: smooth, heavy, warm, pinguid, stable, unctuous, sharp, hot, light, odorous, purgative, moist/shearing, parched, hot, light, rough, motile/shearing (Gönpo, 1999: 132).

[22] The eight potencies comprise: heavy, oily, cool, blunt, light, rough, hot, sharp (Gönpo, 1999: 132).

[23] The six taste profiles comprise: sweet, sour, salty, bitter, spicy, astringent (Gönpo, 1999: 126).

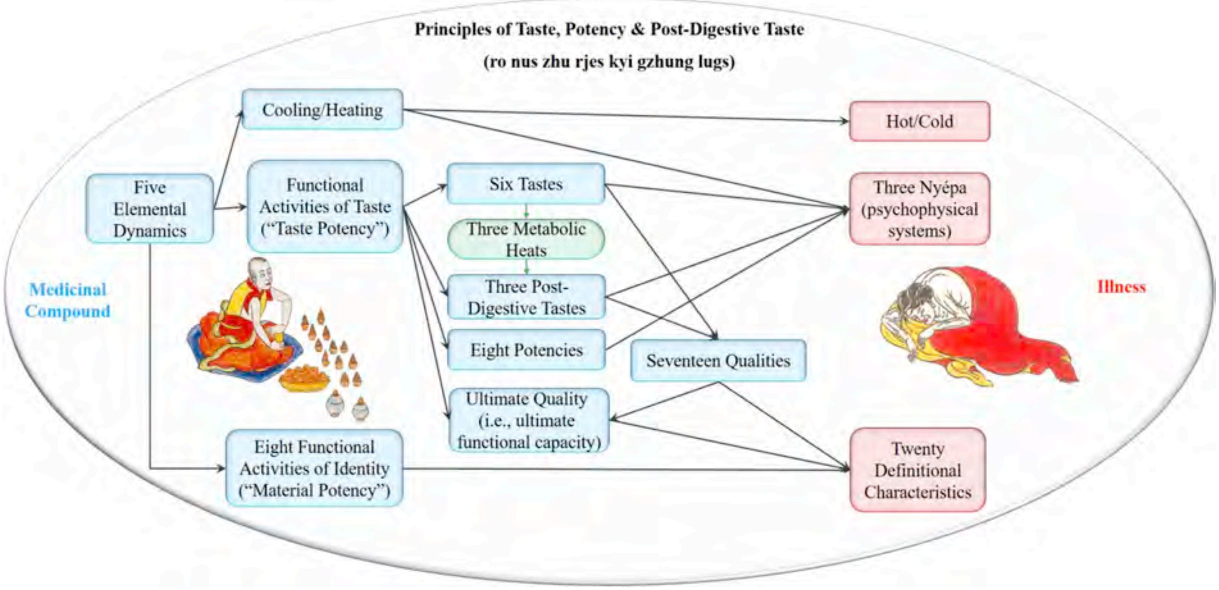

Fig. 9. Diagram of the Tibetan medical conceptual framework on the principles of taste, potency and post-digestive taste (*ro nus zhu rjes kyi gzhung lugs*) used in a recent structural equation modeling study (Wencheng et al., 2019). This framework depicts the intermediary relationships between medicinal compound and its metabolic transformation to differentially engage the twenty definitional characteristics of the three *nyépa* to treat illness. See text above for further description of details. Images from same medical thangka set described in Fig. 1. Images show detail from the ninth thangka featuring sphygmology and first featuring images for urinalysis (Thangka 64), as well as third thangka featuring urinalysis (Thankga 66).

network influences and conditioned systems driving observed phenomenon. This can be instrumental in facilitating network pharmacological approaches to formula analysis in vivo, such as in a recent study by Zhao et al. (2018) with the Tibetan medicinal formula Drépu 3 Tang (*'bras bu gsum thang*). Since most Tibetan pharmaceuticals are complex medicinal substances with up to 140 different ingredients and tens of thousands of chemical constituents, standard chemical analytical techniques are limited (Tidwell and Nettles, 2019). Zhao et al. (2018) used chemical activity data from natural product screening across multiple biological assays to design their study. From the chemical structure data, the team could predict biological targets to aid selection of best assays to test the whole formula for activity. This study highlights how an approach like Tibetan medical informatics allows researchers to integrate systems biology and chemical informatics informed by Tibetan medical theory of formula design and surmount the limitations of single compound analysis by using more integrative methods for multi-compound formula analysis grounded in Tibetan medical theory. Such techniques are being explored for pharmaceuticals of other traditional medical traditions as well (Yuan et al., 2017).

With structural equation modeling and operationalizing Tibetan medicine compounding principles according to how specific functional activities are developed, the rich data of materia medica and formulas can be analyzed through modeling techniques, and synthesized with pharmacological assessments of compound activities. Looking at how Tibetan medicine conjoins substances by elemental dynamic and taste composition, and how the substances are transformed through metabolic processes into distinct chemical profiles allows for greater insights into the functional benefits of individual substances on one hand, to the network pharmacological effects of complex substances on multiple biological targets, on the other hand. Such methods can provide insights into the complexities of Tibetan medicinal compounding and the synergistic activities mobilized by its multi-compound formulas. Informatics approaches allow for these large datasets to ratchet powerful analytics vis-à-vis Tibetan principles of medicine compounding to that of network pharmacology, systems biology and metabolomics to look at how compounds act on multiple pathways, micro-environments and targets. It illuminates both Tibetan medical understandings of pharmacokinetics and pharmacodynamics, but also how complex substances engage and coordinate complex physiologies generally. Such understandings can link with clinical data for informing clinical applications as well as medical theory.

4.5. Clinical case study sources for Tibetan medical informatics and related research productivity

Hospitals, clinics and healthcare institutions in Sowa Rigpa are

Table 4
Journals of Tibetan medicine (*peer-reviewed journals marked with asterisk).

Journal	ISSN	Language	Publisher
Journal of Tibetan Medicine & Astro-science*	2096–210X	Tibetan	Lhasa Men-Tsee-Khang (*Bod rang skyong ljongs sman rtsis khang*)
sMan-rTsis Journal	977-23-20670-5	English	Men-Tsee-Khang (Tibetan Medical & Astro-science Institute)
Tibetan Medicine in China* (*Krung go'i bod kyi gso rig*)	1673–9337	Tibetan	Qinghai Tibetan Medical Research Institute (*Mtsho sngon bod sman zhib 'jug gling*)
Traditional Tibetan Medicine Studies* (*Bod sman slob gso dang zhib 'jug*)	1674–0572	Tibetan	Tibet Medicine University of Tibet (*Bod ljongs gso rig slob grwa chen mo*)
Sorig Journal (*Gso rig ched rtsom phyogs bsdus*)	978-93-87974-59-3	Tibetan	Central Council of Tibetan Medicine
The Journal of Traditional Tibetan Medicine	B01EX0A4H6	English	International Academy for Traditional Tibetan Medicine
China Tibetology Digest* (*Krung go'i bod rig pa'i dpyad rtsom nying btus*)	1002–557X	Tibetan/Chinese/English	China Tibetology Research Center
Tibetan Studies* (*Bod ljongs zhib 'jug*)	1000–0003	Tibetan/Chinese	Tibetan Academy of Social Science

gradually integrating increasingly sophisticated methods of information technology and analytics for both administrative management and clinical practice, as well as to some extent research applications. Today in Tibetan regions of China, as well as some mainland cities, there are 68 public Tibetan hospitals, including 2 provincial and 16 prefectural hospitals, 20 Tibetan medicine research institutes and 70 Tibetan medicine factories. Most of these hospitals, clinics and organizations have instituted electronic record keeping of all related data, such as electronic patient records in the clinical setting, project data in the research setting, and production analytics in the pharmaceutical setting. Deidentifying clinical data from such sources and general data confidentiality has become increasingly important for the growing research applications.

In recent years, there have been increasing numbers of professional and academic conferences presenting pharmacological and clinical research on Sowa Rigpa domestically and internationally. Developments in Tibetan medical research has led to the production of more than five peer-reviewed journals specific to research in the Tibetan medical field, as listed in Table 4. Journal editors have prioritized articles detailing clinical results. One recently published clinical case study example is exemplified by Dhondup et al. (2018) in assessing over 300 chronic atrophic gastritis (*pho rub*) de-identified patient records of pulse, urine, tongue and symptom records as well as gastrointestional endoscopic images that were programmed and analyzed via artificial intelligence for *rlung*, *tripa* and *béken* characteristics. This approach creates a method for differential diagnosis into the traditional schema of the three *nyépa* by looking at endoscopic images based on data analysis of modern and traditional diagnostics. This analysis used a different methodology to affirm previous data (Dhongzhu et al., 2017) with regard to compatibility principles of Tibetan medicinal formulas for treating such patients. Another example of clinical case research recently published is a paper by Dhongzhu et al. (2018) characterizing drugs prescribed for treating chronic atrophic gastritis (CAG), frequency of prescriptions, patient outcomes, association rules, and core and potential new formulae. This combines both a clinical and pharmacological assessment through integration with existing deidentified patient records, and separate follow-up formula analytics. This analysis drew on previous assessments (Dhongzhu et al., 2016) of clinical records and outcomes that has helped standardize treatments of CAG patients with particular characteristics.

Some institutional websites are also providing a preliminary basis for sharing data related to Tibetan medicine and the construction of Tibetan medical informatics. See Table 5 for a brief sample. With greater emphasis on open access and open science practices, such websites may provide an increasingly important role in facilitating access to database resources and informatics analytic instruments. Links to informatics and data systems in Tibetan medicine can facilitate open data sharing; activate experiential knowledge development; open up development spaces for multi-component, multi-target and multi-disciplinary research; and promote rigorous research standards.

The ability for researchers across the world to not only access published research on Tibetan medicine but collected digitalized texts, pharmacological data and deidentified clinical cases provides an invaluable resource to develop Tibetan medical research aimed at analyzing such large and complex data. Before the development of these Tibetan-language Tibetan medical journals, research on Tibetan medicine was restricted to those who could publish in Chinese or English. Likewise, until the development of the Tibetan Medical Journal Database by the Qinghai Provincial Tibetan Medicine Research Center, studies published in these journals were only known by those with a hard copy of the journal. With the digitalization of these journal publications and synchronization with larger repositories of research, systematic reviews of current existing research in Tibetan medicine have become possible (see, for instance, Reuter et al., 2013; Luo et al., 2015).

Table 5
Chief sources pertaining to Tibetan medicine globally.

http://zyxy.qhu.edu.cn/	http://www.tibetmdc.com/
http://www.arurahp.com/	http://www.mentsee.org/
http://www.xzzzqzyy.com/	http://www.tibetanmedicine-edu.org
http://www.isttm.org/	https://padma.ch/de/
http://www.zhzyxw.com/	http://www.aruratibetanmedicine.com/
http://globaltibetmed.org/	http://www.shangshung.org/TMedu/
http://tibetanhealingcenter.info/	http://americantibetanmedicalassociation.org/

5. A research strategy for Tibetan Medical informatics

Since Tibetan medical informatics as a field has only recently emerged, it still lacks a systematic approach to how contemporary standards in the field of informatics can appropriately link with the unique aspects of Tibetan medical theory and clinical and pharmacological experience. In this section, the authors propose an analytic approach.

5.1. Conceptual framework and implications

Tibetan medical informatics is emerging at the intersections of Tibetan medical theory, clinical praxis, and medicine compounding knowledge (*menjor*); systems biology and network pharmacological research of *menjor*; informatics; and management science. We propose that this integrated context allows for the theories and methods of information science to interpret and express Tibetan medical theory and practice through rich data analytics. Applying informatics, through the mode of information acquisition, processing, transmission and utilization, as applied to the complex diagnostic and therapeutic processes of Tibetan medicine can facilitate the process of information transmission and transformation, as well as process and analyze information by means of computers and their programming, uncovering the underlying logic from complex data. Such an approach provides a powerful approach to systems analysis and complex inquiries.

Tibetan medicine has the potential to use its existing links and further develop collaborations with data mining, knowledge discovery, network pharmacology, big data, artificial intelligence, metabolomics, proteomics, and bioinformatics systems to build its repertoire of research methods. Traditional Chinese Medicine Inheritance Support System (TCMISS) (Gongbao et al., 2018) was developed for TCM with this model in mind. Bioinformatic research methods can deeply inform Tibetan medical research by contributing innovative methods to assess large physiological datasets in clinical settings that can reveal key insights for health as facilitated by Tibetan medical treatments. It can also excavate the underlying logic of synergy and functional activities in the extensive number of formulas in Tibetan *menjor*. Though any attempt to digitalize aspects of rich practical experience collapses phenomena into narrow data points, constructing a Tibetan medical informatics can facilitate investigations of the practical experience of Tibetan medicine under the guidance of systems information logic and construct related technical methods to analyze data from multiple levels and angles. As Tibetan medicine grows nationally and globally, this can help facilitate various standards of care that may be unfeasible otherwise.

5.2. Design framework

Many theories of Sowa Rigpa are macro-systematic and micro-complex. They are interlinked and intricately entwined, and at the same time isolatable and singular in their capacity for analysis. They are also multivalent with numerous distinct understandings at a variety of levels. To construct a framework for Tibetan medical informatics, firstly, one should have an in-depth understanding of Tibetan medicine. In order to sort out basic concepts, clarify logic relationships and define content categories, one needs macroscopic inductive thinking, and at the same time, microscopic analytical ability. Of course, Tibetan medical informatics is not only engaging the theoretical framework of Sowa Rigpa, but also analyzing clinical medical records, Tibetan medical

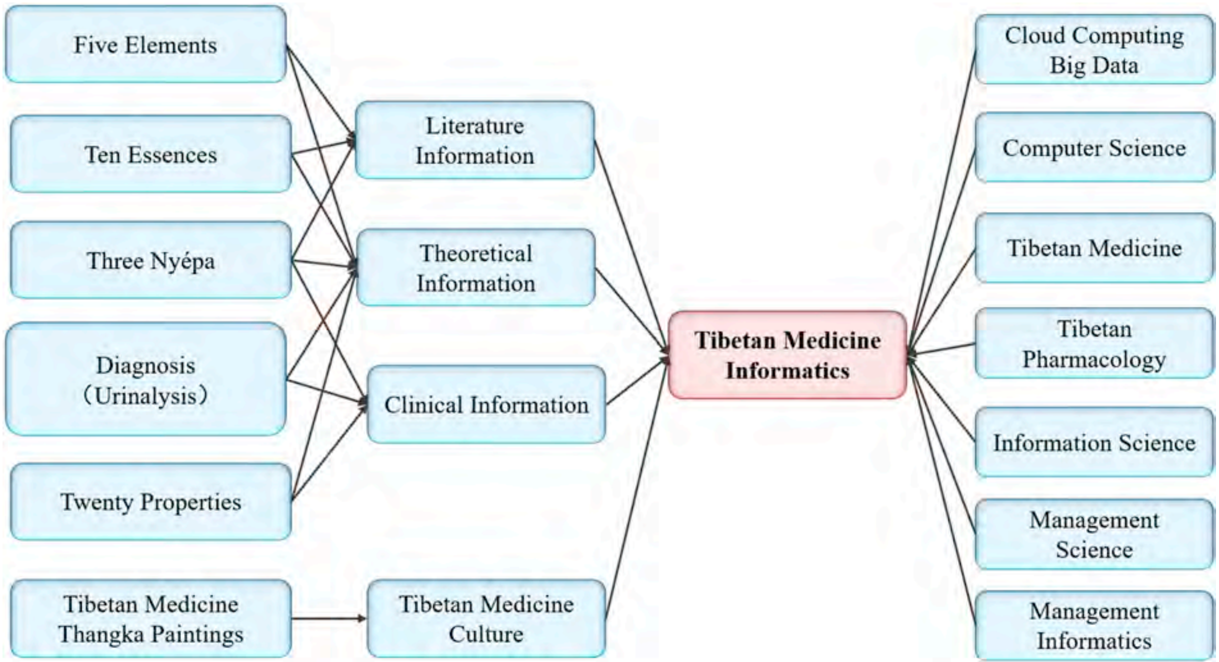

Fig. 10. Framework of Tibetan medical informatics.

culture, and numerous other areas of the field. How do we combine Tibetan medicine with informatics? The framework we propose for Tibetan medical informatics is shown below in Fig. 10.

5.3. Epitaxy

Tibetan medical informatics, through the natural integration of Tibetan medicine and informatics, is the "interface" between Tibetan medical literature, its rich theoretical framework, scientific research methodologies, electronic medical records and computer information systems. Based on the idea of transmission and innovation in Tibetan medicine, and widespread benefits for treating major and tenacious diseases, the current authors have established this data model of Tibetan medicine, proposing the application of artificial intelligence, informatics and data mining approaches, geographic information systems and other methods to provide systematic methods and integrity to such research in Tibetan medicine. To explore the modern development of and increasing demand for Sowa Rigpa, while continuing the transmission that has stemmed from over a thousand years of Tibetan medical theory, we can integrate a mode of research that draws extensively from informatization of its available data. The informatization of Tibetan medicine can be carried out in a variety of fields and in a multi-dimensional manner, but it is based on basic research applied to integrated clinical and pharmacological contexts.

6. Conclusions

Tibetan medical informatics is emerging as a burgeoning field developing expediently through informatization of pharmacological, clinical and textual data and largescale database development. Introducing the current developments of data sources and database networks along with proposing an analytical structure rooted in a Tibetan medical approach allows for the field to take a distinct shape in serving interests both in the Tibetan medical field as well as numerous related research disciplines. Beyond providing computational power of mass data set analysis to pharmacological, clinical and theoretical inquiries; it can provide greater therapeutic benefit by integrating theoretical foundations through textual preservation, intertextual analysis of formulas, materia medica pharmacological assessments, compound analytics, treatment approaches, etiologies, theoretical structures, and physiological data; and clinical case recording with de-identified patient data. It can also simplify practices by etiological analysis of related conditions, nuancing differential diagnostics, and assessing treatment outcomes. Using methods that encode formula data and relate it to biological activity of illness contexts, can help visualize treatment pathways and outcomes. The aim of a comprehensive approach to Tibetan medical informatics is to support greater rigor in research and clinical practice for demonstrating Tibetan medicine's capacity for treatment, illness prevention and, patient care.

The coauthors also recognize an important need for care around data protection practices. Institutional database developers and data procurement systems should be vigilant to protect data for patient anonymity in clinical settings, compound composition in pharmacological settings, and text access rights for particular protected classical works. Such measures protect the tradition from both exploitation and intellectual property rights violations. Systematizing information that has been largely passed down orally over generations and much of which is maintained in secrecy must also be carefully considered as to the aims and outcomes of such actions. Database owners and managers have initiated these data protections, but continued vigilance is critical to both patient anonymity protection, pharmacological knowledge safeguarding, and maintaining intellectual property security. Upholding the rich practical tradition of Tibetan medicine can help safeguard data from being misused by forming gatekeepers of what information gets digitalized and in what form. Gatekeepers are the data producers and administrators – the clinical, education and research institutions housing the database repositories mentioned above.

Challenges to developing Tibetan medical informatics are also significant. The inaccessibility, loss and/or destruction of many classical works that document clinical cases, pharmacopoeias, and regional therapeutic literature limit available resources. Likewise, digitalizing classical works takes time and resources still limit what works have been developed in electronic form. Tibetan medical informatics requires the development of new analytical methods and skills unfamiliar to many Tibetan physicians and researchers. Younger generations may play a role in institutional partnerships for high quality research and practice implementation. In order to facilitate a robust Tibetan medical informatics field, the authors encourage the research and physician-scholar community to focus resources toward filling the gaps laid out in Table 1 and exploring further challenges in the field of limited innovation, a paucity of systematic and applied research, and fragmentation of prominent research published (Nie et al., 2015). The strengths of information science can contribute to developing these areas for the field of Tibetan medical practitioners and researchers. Currently, research and clinical practice tend to operate independently instead of mutually informing one another. Tibetan medical informatics can infuse both sides with insights and further clinical outcomes as well as research understandings.

Due to the nuances of Tibetan medical theory for pharmacological design of multi-compound formulas and its insights into unique physiologies of mind-body pathways in both diagnostics and treatment, Tibetan medicine is well-suited to synergize with the methods of information science. Likewise, by studying Tibet's unique medical theory-praxis characteristics through these methods, we have an opportunity to gain insights about medical traditions and histories from neighboring regions, thereby constructing a unique lens into traditional medicine cultures and ethnopharmacologies from this region of the world and their insights for global human health and well-being. The vast number of classical Tibetan medical works also provides a strong basis for intertextual historical analysis, cross-disease pharmacological pattern assessments, and understanding these intersections across medical traditions. The increasing number of Tibetan medicine hospitals, schools and other institutions across the Tibetan plateau and globally provide a significant data basis. With existing links between traditional medicine and informatics in traditional Chinese medicine and Ayurveda, this study contributes a methodological reference for the construction of Tibetan medical informatics, with a Sowa Rigpa-specific proposal for the analytic approach. It also provides a state of the field as Tibetan medical informatics is just emerging onto the research stage.

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Author contributions

Wüntrang Dhondrup, Dungkar Tso, Gönpo Dhondrup, and Qingfang Luo collected and collated data. Tsering Kyi, Choknyi Wangmo and Xianli Meng analyzed and interpreted the data. Wüntrang Dhondrup, Xiaobo Wang, and Tawni Tidwell revised the manuscript. Yi Zhang and Yongguo Liu conceived and designed the study. Yi Zhang supervised the research group. The final version of the manuscript was read and approved by all authors.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jep.2019.112481.

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