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Herbert Schwabl
PADMA AG, h.schwabl@padma.ch

Jan M. A. van der Valk
University of Vienna, jan.vandervalk@univie.ac.at

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Herbert Schwabl
Jan M. A. van der Valk

Sowa Rigpa (Tibetan medicine) has been practiced across vast regions of Central and South Asia for centuries. In this medical tradition, it is common practice to dynamically adapt the mainly herbal formulas according to the regional flora and local conditions, and to use local variants of ingredients. Consequently, one Tibetan ingredient name within a specific formula can signify a variety of therapeutically fitting botanical items, which appear quite different from the perspective of modern taxonomy. This has led many researchers to understand the botanical plasticity of Tibetan medical formulas as misidentifications. We develop an alternative approach, exploring the advantages of this plasticity as a necessary practice to fulfill economic and therapeutic needs. This perspective piece questions the biomedical paradigm of single 'active substances,' since botanically unrelated plants with different chemical compositions can be similarly therapeutically effective. From a systems biology perspective, network pharmacology lets us understand the correspondence of illness and medicine as a semiotic process in which herbal formulations act via their 'pleiotropic signatures': complex webs of signal pathways that connect and act on multiple levels of organization in the body.

Keywords: Sowa Rigpa, Tibetan herbal formulas, network pharmacology, active substance, substitution.

Introduction

Herbal medicines have historically been of central importance for human health. Although the global pharmaceutical industry has reduced its overall funding for natural products research over the last decade (Laird 2013), the current market for phytomedicinal products—especially in and from countries such as India (Booker et al. 2016) and China (Dang et al. 2016)—is booming. New trends in poly-pharmacology, systems biology (van der Greef 2011), personalized medicine, and evidence-based phytotherapy aim to capture their complex effects as we enter a post-antibiotic area in the face of alarming antibiotic resistance (Kahrstrom 2013), and to grapple with aging populations, diseases of affluence, and multimorbidity. The Swiss company PADMA Inc., which produces Tibetan herbal formulas according to Good Manufacturing Practices (GMP), is at the forefront of these cutting-edge developments with regard to Sowa Rigpa (Schwabl et al. 2013; Zick et al. 2009). Yet this company has also experienced the many limitations, struggles, and frustrations of getting Tibetan medicines in European markets (Schwabl and Vennos 2015; van der Valk 2017: 253-286). The far-reaching influence of Big Pharma on politicians and regulators has led to well-known commercial, scientific, and regulatory biases on their behalf (see for instance Davis and Abraham 2013). These 'Big Regulations' also presume and enforce universal applicability of a biomedical pharmacology geared towards the development of chemical medicines made up of one or a few highly purified and concentrated 'active pharmaceutical ingredients.'

In this perspective piece, we challenge this notion of 'active substance' by foregrounding the botanical plasticity of Tibetan medical formulas in local practice and across space and time. Sowa Rigpa—the emerging umbrella term for 'Tibetan medicine'—dates back at least to the twelfth century, when the codification of the foundational medical text the *Four Treatises* was initiated (Yang Ga 2014). It has been practiced for centuries in highly diverse settings, from rural master-disciple lineages to monasteries and modern medical hospitals. Today, Sowa Rigpa's regional distribution extends across the Qinghai-Tibet Plateau, the Himalayan region (including Ladakh, India, Nepal, and Bhutan), and north up to Mongolia and Buryatia. Covering these varied contexts, a solid body of ethnographic and historical studies (e.g., Adams et al. 2011; Craig et al. 2010; Hofer 2014; Pordié 2008; Samuel 2013; Schrempf 2007) indicates that Tibetan medical formulas—largely of herbal and mineral composition—are part of a time-tested and socially validated ethnomedical tradition. More specifically, anthropologist Calum Blaikie (2015) has demonstrated the inherent multiplicity of so-called 'classical formulas,' resulting in innumerable variants or avatars in actualized practice. In doing so, Blaikie convincingly argues against the view that these multiple versions of 'the same' drug "represent the corruption of classical purity or inauthentic approximations of a static ideal" (Blaikie 2015: 12). Gerke's (2018) analysis of the authorship and intertextuality of the genre of Tibetan formulas also confirms that knowledge transmission is typically fluid and dynamic in the sense that it relies on re-interpretation, reformulation, and the addition of 'personal signatures.'

Nonetheless, a number of institutional and scholarly discussions have focused on the plasticity of Tibetan formulas in a derogatory way, relying on terms such as the 'misidentification' of ingredients, deviations from an 'original' formula, focusing on the inferiority of 'substitutes,' and the need for standardization and a unified pharmacopoeia (Dawa 1999, 2009; Kletter and Kriechbaum 2001; Ministry of Health (PRC) 1998; PRU 2009).[1] See, for instance, Fernand Meyer (1988: 37, translated from French) for an early example:

> Collections of 'Tibetan' medical material are made by teams of unequal competence, in different epochs and conditions, in regions often far apart from each other. They cannot provide homogeneous material suitable for inclusion in such a work [multi-language dictionaries of medicinal plants]. This explains why under the same Tibetan name we found plants sometimes closely related, but often very different. [...] According to what criteria would we be inclined to prefer one determination to another?

This quote reveals an unjustified prejudice: that one Tibetan ingredient name must correspond to a modern Linnaean concept and be identified as one particular plant, and that only this plant should be the basis of future research (see also Molvray 1988; Kletter and Kriechbaum 2001). However, why should Sowa Rigpa pharmacology follow the path of systematic botany? The preoccupation with weeding out 'geographical bias' and 'sources of confusion' (and diversity!) has its roots in the emergence of modern pharmacy and pharmacognosy. It mirrors the establishment of national pharmacopoeias, based on earlier herbals, within Europe and beyond (see for instance Griffin 2004 for the UK). This approach neglects the inherent advantages of the dynamics of variability. The pharmaceutically trained community is indeed puzzled by this fact of plasticity. As a prerogative for any scientific work the exact definition of each constituent of a formula is demanded, which then leads to the quest of modern pharmacology for the single chemical molecule, the 'active substance,' responsible for therapeutic activity.

The flexible use of a variety of plants in a functionally similar manner, as seen in Sowa Rigpa practice, is a challenge to accept from the perspective of modern pharmacology. Our aim here is to explore the *botanical plasticity* of Sowa Rigpa formulas—the botanically flexible but functionally stable use of plants—in order to provide a bridge between Tibetan medical principles and conventional chemistry, pharmacology, and biomedicine. From a systems perspective[2], the complex yet stable physiological action profile of these variable mixtures defies attempts at extreme standardization. Botanically and chemically entirely different plant species may exhibit similar signatures of action, especially when combined into multi-target 'network medicines' which mirror the complexity of chronic diseases. We thus invite scholars and scientists alike to approach potent substances semiotically in future research; that is, from a functional rather than a strictly material substance-based perspective. The authors recognize that Sowa Rigpa's 'pharmaceutical assemblage' (Kloos 2017) is part of "emergent cosmopolitical technoscientific worlds" (Fischer 2007: 573) that go beyond the purview of Euro-American histories of ideas, even though "[t]he history of almost all modern science [...] must be understood as 'science in a colonial context'" (Seth 2009: 374). By validating and thinking through the botanical plasticity of Tibetan medical formulas, we aim to decenter or provincialize the dominant place of the biomedical concept of 'active substances' in discussions on herbal medicines (cf. Schwabl et al. 2016), both in general and specifically in relation to the potency of multi-compound Asian medical preparations. As such, we contribute to alternative theoretical models generated from within Asian Science and Technology Studies (STS, cf. Fischer 2018), by working *with* Sowa Rigpa (following Lin and Law's work with Chinese medicine, 2014, 2015). That is, we are carving out "a culturally Tibetan way of doing science" (Adams et al. 2011: 23).

Elements, Tastes, Potencies and the Composition of Medicines

Roughly speaking, Sowa Rigpa divides diseases into hot and cold disorders which are defined as a shift in the individual equilibrium of the three bodily dynamics, or *nyépa* (*nyes pa*): *lung*, *tripa* and *béken* (*rlung*, *mkhris pa*, and *bad kan*; often translated as 'wind,' 'bile,' and 'phlegm') (Donden 1986; Tsultrim and Dakpa 2009). According to the theory of the five elements (*'byung ba lnga*), medicinal ingredients can then be selected with characteristics that compensate a disturbance in the patient's elemental balance. Six tastes define the activity of medicines: the elements of earth and water generate the sweet taste, fire and earth produce sour, water and fire produce salty, fire and wind produce pungent, water and wind produce bitter, and the earth and wind elements together produce an astringent taste. Used in a therapeutic setting, the sweet, sour, salty, and hot tastes are seen to counteract *lung* disorders; bitter, sweet, and astringent tastes treat *tripa* disorders; and hot, sour, and salty tastes alleviate *béken* ailments. The potency of medicines is elaborated further in the context of the 'eight powers' (*nus pa brgyad*, which are heavy, oily, cooling, blunt, light, rough, pungent, and sharp) as well as 'seventeen qualities' (*yon tan bcu bdun*) such as smoothness, heaviness, warmth, oiliness, stability, and so forth.

The body of knowledge in Sowa Rigpa dealing with raw materials and 'medicine compounding' or *menjor* (*sman sbyor*), here simply denoted 'Tibetan pharmacology,' lists numerous formulas composed of a variety of components (Cardi 2005; Hofer 2014). Tibetan formulas characteristically contain more than three ingredients, often fifteen to twenty, or even more. The components are mostly herbal (e.g., roots, bark, leaves, flowers, fruits, and resins), which are the focus of this piece. To a lesser extent, minerals are used and, in rare cases, animal- or metal-based substances. These raw materials are classified based on the observed effects and their sensory properties such as taste, texture, and color, which then relate back to the elemental qualities and activities of the ingredients. In Tibetan pharmacology, a substance is classified mainly according to sensory qualities that contribute—as seen from a systems perspective—to a specific functional profile of action. Different components are then combined in a formula to compensate for the disturbance of the individual equilibrium. The components are selected based on their characterization according to three different aspects (Nikolaev 1998): 1) hot or cold, 2) effect on the *nyépa*, and 3) their organotropic properties (i.e., the directed activity of the components towards a specific organ). From a modern perspective, we translate this as a multi-dimensional assignment of qualities to each ingredient and formula.

A Dynamic Tradition

The vast geographical domain where Sowa Rigpa is practiced today covers a wide range of different ecological environments and habitats, with a high diversity of plants as well as vegetation types (Boesi 2005, 2007; Lama et al. 2001; Salick et al. 2006, 2009). Moreover, many raw materials are acquired via different trade routes passing through these regions (Akasoy et al. 2011; Blaikie 2014; Saxer 2009). Across the Himalayan range, ethnobotanical and ethnoecological studies have shattered the illusion of one classic literary body implying a uniform practice, especially when considering the interfaces with popular

and folk knowing practices (Ghimire et al. 2004; Salick et al. 2006). It is common practice to adapt formulas according to a specific environment and patient, and to use local variants of ingredients (Blaikie 2014: 281-293; Czaja 2017; Sabernig 2011). This traditional method has allowed medical practitioners to respond to bottlenecks related to availability, as well as to account for geographical and climatic differences. The formulas, therefore, adapt to different regional, economic, and social demands while maintaining their therapeutic effectiveness. Due to this variability, one specific Tibetan formula with identically denominated ingredients may—from the modern botanical point of view—contain one or more different species or even genera, often without any direct taxonomic connection. This implies that these formulas have a certain botanical plasticity, which characterizes Sowa Rigpa as a dynamic tradition, across time and large geographies. Reasons for these variations may include (1) the availability of raw materials, leading to different species denominated with the same Tibetan name, (2) the wish to improve a formula, or—one should not fully exclude—(3) wrongly interpreting a textual formula (see Czaja 2013). From the perspective of the individual Sowa Rigpa practitioner, the time-tested effectiveness of the used formulas remains more or less undoubted. The therapeutic use and range of indications may therefore be considered robust. As Tibetan pharmacology assigns specific qualities to every ingredient, it is possible and even likely that different plants or substances present themselves with a similar set of qualities; these ingredients are isomorph with respect to their qualities.[3] Consequently, it is possible within one specific formula that one Tibetan ingredient name signifies a variety of therapeutically fitting botanical items. According to modern botanical nomenclature, these items may appear quite different, sometimes even from different species, genera or families (see again Blaikie 2014; Czaja 2017; Sabernig 2011 for examples).

One example is the *agaru* (*a gar ru*) recipe family. The eponymous component *agaru* is most commonly identified as the wood of *Aquilaria* species (e.g., Arya 1998; Meyer 1988). Contemporary *materia medica* literature identifies the red type *agaru armar* (*a ga ru ar dmar*) also as the woods from *Cinnamomum* or *Syringa* spp. (Gawé Dorjé 1995). Moreover, plants such as *Caryopteris mongholica* Bunge or *Carum carvi* L. (seeds) are also used.[4] All variants carry different explanations for why they can be used in a certain formula. In several instances, two or three types of *agaru* (black, white, and red) are used together as a group, sometimes noted as distinct ingredients and sometimes used in combined form.[5] The red type is particularly good for wind-heat conflict disorders (*rlung tshad*), even though its action profile overlaps with the other types of *agaru*. All clearly differ chemically and analytically from each other, but according to the different local traditions have enough similar qualities to act effectively in multicomponent formulas such as Agar 8 or Agar 35.

It remains an open task for fieldwork to investigate the dynamic use of formulas in Sowa Rigpa, specifically the use of different variants of a formula which have been in use in different regions during specific time periods (but see Blaikie 2015; Gerke 2018; Nianggajia 2015; van der Valk 2019). As emphasized earlier, this research should not be directed towards finding the 'real' or 'original' formula. Rather, important topics to consider are which formulas and variants are used, what their specific medical usages are, patient and practitioner experiences and narratives, and the impact of specific regional lineages. Additional important questions are: Where is the border of activity? When is the variability overstretched (i.e., when is the formula not suitably active anymore)?

The Advantages of Plasticity

Botanical plasticity has specific advantages, especially as part of multicomponent preparations. It allows for historical continuity of practice and addresses some of the following challenges of the Anthropocene:

1. Environmental challenges, changes of natural habitats in response to climate change;

2. Challenges of species extinction and protection of endangered species; and

3. Regulatory demands, where modern policies respond to toxicological issues, restrict the use of potentially hallucinogenic plants (e.g., cannabis, opium, betel nut), or apply stricter rules in the interface of medicinal drugs, food supplements, and traditional use of formulas.

Because of the time-tested functional assignment of *materia medica*, the botanical plasticity is linked to a consistent action profile. It is the network of the functional interactions which remains therapeutically stable and robust despite the variable botanical composition. However, how do we understand this when chemical analyses would show significantly different chemical profiles for the different variants? From the perspective of modern pharmacology, one plant on its own is already a multi-substance chemical mixture subject to a

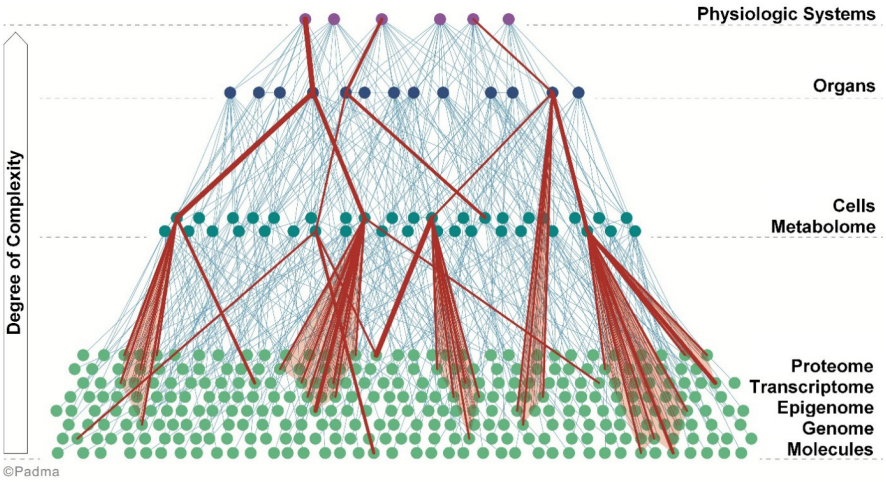

Figure 1. Schematic representation of the network hierarchy in the human organism. Numerous signal pathways make connections between the hierarchies. A hypothetical pleiotropic signature of a Tibetan multi-compound formula is indicated in red, which includes all the involved signal pathways in the body. As the pathways approach the more basic levels (lower complexity), they appear broader, indicating the nonspecific binding capacity of complex herbal mixtures towards a variety of targets. Figure slightly adapted.

(Schwabl et al., 2013)

certain natural variability according to environmental factors (such as harvesting time, climatic conditions, soil contents, and collection practices). Because of the variety of the many chemical molecules present in one plant, its activity can be approached as a typical multi-target drug, addressing a whole range of receptors in the body. Tibetan formulas, usually composed from a minimum of three to many more ingredients, are thus extreme examples of such multi-target drugs. The natural components of such a formula can be described as having the following properties (Efferth and Koch 2011):

1. multiple modes of action on different system levels;

2. presence of single chemical components in low concentrations;

3. lack of total blockage, stimulation, or saturation of bodily receptors due to the low concentration of each single component;

4. a pleiotropic mode of action (i.e., the simultaneous activation of multiple network points); and

5. weak chemical bonds and non-specific actions of components, addressing a broad range of receptors with relatively few side effects.

With this pleiotropic characteristic, the activity profile of a formula expresses itself on the different levels of the organism: from the systemic level down to organs, tissues, cells, and subcellular components such as genes and networks of metabolic pathways. In the case of the multicomponent mixtures of Tibetan medicine, a very broad pattern based on weak interactions in the lower system levels is to be expected. The links and nodes of such a network represent the *pleiotropic signature* of the formula (cf. Schwabl et al. 2013; Figure 1).

Due to the multifunctionality of the pharmacologically active agents in a medicinal plant, the action profile usually results in an overlap of three levels of action (Saller et al. 2011):

1. Specific: orientation to symptoms/symptom complexes or specific diseases, usually effected via defined ligand-receptor interactions;[6]

2. Adaptogenic: orientation to the entire organism and its modes of reaction, which is a non-specific, usually tonifying activity that increases the viability and resilience of the organism; and

3. Systemic: orientation to basic disorders (e.g., inflammatory processes) where the action is exerted on non-localized, systemic processes on lower cellular or metabolic levels.

To understand the activity of herbal drugs, the adaptogenic and systemic parts are most relevant. They act due to their multifocal, multi-target properties and are mostly non-selective and with broad biological activity. This profile offers significant benefits since many diseases are based on complex interactions of numerous targets. Such multi-target and pleiotropic properties may be beneficial for cases of multi-morbidity (i.e., complex combinations of often chronic diseases). The weakly active compounds attack various cellular targets, which differs from the strong selectivity of classical chemical pharmaceuticals with highly concentrated active compounds. If necessary, non-selective multi-target drugs can be combined with selective mono-target drugs. Herbal preparations have 'group effects' (e.g., anti-inflammatory, as a 'system property') and adaptogenic effects in addition to the directly indication-related effects (Saller and Rostock 2012). In Tibetan *menjor* theory, this higher-order activity is for instance reflected in the 'warming' (*drod skyed pa*)

or 'cooling' (*bsil ba*) nature of Tibetan formulas or in humoral terminology such as 'dispels [excess] wind' (*rlung sel*). Further aspects in the composition of a Sowa Rigpa formulation are the expected additive, synergistic, and partially antagonistic effects (cf. Gerke 2018; van der Valk 2019; Tidwell and Nettles 2019). Substances are used that support the main effect, while others neutralize any potentially irritating effects of other ingredients.

If one integrates these characteristics and the three levels of action into a network, it becomes apparent that each plant has a characteristic signature. This is why they are also referred to as 'network remedies' (Gertsch 2011). Due to their pleiotropic character, this pattern is wider and has many weak connections. Chemical mono-substances act much more specifically, with a narrow range of strong chemical connections (Butler 2019). Complex multi-component formulations such as those found in Sowa Rigpa have a pronounced multi-target modality and associated pleiotropy. This is not only because of the higher diversity of components involved, but also due to empirical testing over generations combined with intricate systematic theories and compounding methods. These combination preparations may be particularly suitable as a systemic base therapy, for instance combined with highly selective drugs and/or in multi-morbid patients. Since Sowa Rigpa formulas—in all their variants—were used to treat specific diseases and *nyépa* imbalances over a long period of history, this consistent use provides us with a basis for a time-tested evidence of efficacy (as passed on through different lineages). Each variant of a formula is related to a network of functional interactions which act on the numerous targets of the organism, and it is the network of functional interactions that remains robust despite different botanical species and chemical structures. The different variants of a formula can thus be said to have a similar pleiotropic signature.

The Correspondence of Illness and Medicine

Living systems, including the human organism, can be described as networks of interacting parts that comprise different information and control various circuits. The ultimate goal of such autonomous systems is homeostasis, or the maintenance of the integrity of the system under various external and internal influences (Varela 1979; see also Theise 2005).[7] The elements in the human organism consist of independent sub-networks, which in their totality can be identified as a hierarchy of networks (Auger 1988). The system levels differ according to the internal bond strength, the characteristic reaction time, and the type and number of signals that can be processed. The semiotic interaction potential,[8] the repertoire of processable or answerable signals, defines the possible interactions with the system. The more complex a system, the greater its repertoire. In choosing a therapeutic intervention and planning a treatment protocol, the nature of the therapeutic signals (manual, invasive, pharmacological, narrative) and their sequence must correspond to the semiotic capacity of the system. From the perspective of systems theory, any disease can be interpreted as a typical signature of the complex system or 'organism,' which is connected to its basic structure and dynamics (e.g., genetic, epigenetic, environment, way of life, age, gender). Most diseases do not develop according to a simple, linear path, but instead affect the entire network. This is especially valid considering new findings in systems biology and the 'omics-sciences' (see for instance Buriani et al. 2012 for its application to Chinese medicine). These new scientific branches have begun to decipher the human genome (genomics), extending into epigenomics (considering cellular feedback on the genome), and metabolomics (i.e., the study of the metabolic pathways).

The formation and progression of atherosclerosis, for instance, is influenced by network elements and exogenous risk factors. These include the basic genomic setup, the metabolome with different cell types and organ systems (Ghazalpour et al. 2004), and the epigenome. Accordingly, biomedical diagnostic and therapeutic approaches are highly diversified. On the one hand, they include physiological systems and organs such as the cardiovascular system, the regulation of blood pressure, coagulation, glucose-insulin levels, and plasma lipids. At the cellular level, they also include issues such as chronic inflammation, hormonal balances and imbalances, endothelial functions, and the role of adipose (i.e., fat) tissues. These exogenous and endogenous aspects of a disease signature are to be matched with the reactive capacity of the network organism, which are then included in an individualized therapy profile. By applying this systemic view to the empirical use of a Tibetan formula, we can speculate on the correspondence between the signature 'illness' and the signature 'medicine.' In the case of atherosclerosis, the biomedical signature of such a formula is found in its anti-inflammatory, anti-oxidative, and circulation-promoting properties. The Sowa Rigpa practitioner, on the other hand, also includes lifestyle factors, such as nutritional status, climatic conditions, and patterns of activity, as well as the results of subtle diagnostic methods such as pulse reading or urine analysis. In the Sowa Rigpa framework, a patient with (from a modern biomedical view) atherosclerotic symptoms shows a profile of increased heat (*tripa*) in the blood system and at the same time

reduced mobility (*lung*). From a therapeutic perspective, this requires a drug that has 'cooling' and 'stimulating' effects on the blood circulation (Schwabl and Vennos 2015; Vennos et al. 2013). This demonstrates a preliminary correspondence of the signature of the Tibetan formula with the disease pattern within the coordinates of Sowa Rigpa.

The line of argument presented here allows us, at least in principle, to investigate the functional profile of a formula in both reference frames: biomedical science and Sowa Rigpa. Therapeutic intervention must fit to the semiotic capacity of the system, with each disease state offering a complex set of possible interventions. Tibetan medical practitioners attend to this therapeutic complexity with their individualized repertoire of different medicines and interventions, relying on a systemic analysis of the body-mind through the *nyépa* framework. Since actual variants of a textual formula can have the same semiotic signature, the chemical materiality of a formula is secondary—it is fluid. The functional description of the activity of a medicine in either reference frame prevails over the material, substance-based definition of a formula. The plasticity of the herbal components is characterized by their non-specific mode of action, which dissolves the boundaries of their individual functional profiles. That is, multi-compound herbal mixtures have a pleiotropic mode of action. The more the specificity (connected to its specific chemical materiality) is dissolved, the more the semiotic capacity of the component prevails, and the more important are the systemic and adaptogenic activities of the mixture. Other factors further enrich the semiotic signature, including the sensory characteristics of the formula, the mode of application, and the patient-doctor interaction. Still, the *pharmakon*—the formula in its entirety—remains the centerpiece of the semiotic interaction.

Conclusion

In multi-compound Sowa Rigpa formulas, one ingredient can be represented by a variety of materials without changing the signature of the formula. This botanical plasticity, while retaining the same profile of action, allows the Tibetan medical physician to respond to difficulties in raw material supply as well as to the regional flora and local conditions without altering the essence of the formula. The practice in Tibetan pharmacology to choose among a variety of species while composing a specific formula consequently leads to a different notion of the principle of 'active substance.' The variants of the formula possess a similar action profile and pleiotropic signature, which cannot be traced back to an identical chemical molecular pattern. Due to the cross-linking of the interactions of the many constituents, Tibetan formulas act as network drugs. Looking at the semiotics of a chronic diseased state, network drugs are particularly suitable for multi-morbid patients, either by treating specific symptom complexes or as a systemic therapy in combination with selective drugs.

The practices of Asian medical traditions are still poorly understood in the current biomedical, pharmaceutical and regulatory environment, and are not adequately depicted in official pharmacopoeias. The fixation on rigid ingredient identifications and recipes espoused by the global apparatus of modern biomedical science increasingly restricts the available repertoire of medicinal plants. Sowa Rigpa is designed to react with great flexibility to various challenges. Unfortunately, however, the quest for standardization continues to be followed, even in publications from the Tibetan medical community and by regulatory authorities. The current pharmaceutical regulatory environment is inadequately informed and even hostile towards the idea of plasticity. The main regulation on traditional herbal medicines in Europe (EC 2004), for instance, explicitly demands a documented continuous use of an unchanged composition over a period of at least thirty years to enable market registration (Schwabl 2009). This reductionist approach, based on the quest for molecular 'active substances,' does not do sufficient justice to the inherently functional approach of Tibetan pharmacology.

A renewed focus on the botanical plasticity and pleiotropic signatures of Sowa Rigpa formulas raises interesting questions for further research. Can the limits of functional variation be defined? How can we better understand the dynamic spectrum of activity of Tibetan medical formulas? The herbal network pharmacology perspective laid out here can perhaps serve as a rough translation tool, an imperfect conceptual bridge between sciences that inspires innovative interdisciplinary work between the medical humanities and sciences. This systemic framework can and should be expanded to include psychological, social, historical and geographical semiotic layers. While remaining attentive to the limitations of and the political-economic stakes involved in the emerging 'Asian Medicine/Systems Biology interface' (Scheid 2016), we recognize the need for open-ended theoretical models and regulations that allow Asian medical traditions to flourish more on their own terms, as well as in contexts usually dominated by biomedicine. To this end, nuanced engagements with Tibetan pharmacology and Asian science and technology in general have much to offer.

Herbert Schwabl (PhD, Physics, Technical University Vienna, 1994) has published in the fields of self-organization, quantum physics, and Complementary and Alternative Medicine (CAM), and has (co-)authored interdisciplinary studies on Tibetan medicine. He is chairman of PADMA Inc., which produces Tibetan herbal formulas according to GMP standards in Switzerland (www.padma.ch). Schwabl is also board member of IASTAM (The International Association for the Study of Traditional Asian Medicine). He is involved in political work for CAM as president of the Swiss Association of Manufacturers of Complementary Medicines (SVKH; www.svkh.ch) and a board member of DAKOMED (the Swiss umbrella organization of CAM; www.dakomed.ch).

Jan M. A. van der Valk (PhD, Anthropology, University of Kent, 2017) is an anthropologist and ethnobotanist. He is currently a postdoctoral researcher in the multidisciplinary project 'Potent Substances in Sowa Rigpa and Buddhist Ritual' (2018-2021) at University of Vienna's Department of South Asian, Tibetan and Buddhist Studies. Van der Valk's doctoral thesis traces the techno-scientific transformations of Tibetan medicines from plant to pill, forging links between two key manufacturers, in India and Switzerland respectively. He has been a student of Dr. Pasang Yonten Arya since 2012, and opened the first Tibetan medical (herbal) practice in Belgium (<www.deblauwepapaver.be>).

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Endnotes

1. Historically and up to today, there has been a strong emphasis on identifying the proper substances and their superior and inferior (*mchog dang dman pa*) forms. Within Tibet (and later in exile), Lhasa's identification system—together with several key lineage centers in Kham and Amdo—has been adopted as the ideal standard for understanding substances and their activities (Tawni Tidwell, Personal Communication, March 9, 2019). Even if local variants are accepted, they are often considered inferior substitutes.

2. The study of systems as interacting group of units forming an integrated whole (Klir 1991). As such, systems theory is understood as a general theory underpinning the modern sciences (Laszlo 1973).

3. When and where specimens are harvested further allows practitioners to accentuate certain qualities for therapeutic effect. An Amdo-based variant (which might also be a botanically different species, sub-species, or variety) could be gathered later than a Lhasa-based reference specimen, for instance, to maintain isomorphic qualities. Thanks to Tawni Tidwell for pointing this out.

4. Interview with Dr. Lobsang Dhondup Dripatsang at Padma AG, Switzerland, January 2018.

5. See for example the formula for Agar 35 provided by Dash (1994: 215-217), who mentions all three types of *agaru*.

6. Interactions between a molecule and a protein on or within a target cell. In the classical view of drug action this is called the 'lock-and-key' model. Specific drugs are 'keys' that ideally only fit a single biological target or 'lock.'

7. Francisco Varela and Humberto Maturana introduced the system-theoretic concept of *autopoiesis* to model living beings. Varela then further refined this approach by introducing the concept of autonomy: living systems reproduce and create their own system components (autopoiesis) while maintaining their identity (autonomy). The concept of autonomy allows one to define the signals which can be interpreted by the system in a meaningful manner, and the repertoire of possible responses to these external stimuli.

8. In analogy to Eco (1992). In abstract terms, living structures (as autonomous systems) have a certain repertoire of communication with the environment in terms of signals and responses. This process as well as the classification of signs is the field of semiosis, which can also be applied to the repertoire of therapeutic interventions

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