

Review Article

Whole Medical Systems versus the System of Conventional Biomedicine: A Critical, Narrative Review of Similarities, Differences, and Factors That Promote the Integration Process

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Background. There is an increasing need for a worldwide professional integration of conventional medicine and traditional/complementary whole medical systems (WMSs). However, the integration is perceived by conventional medicine as problematic or unacceptable, because of a supposed lack of evidence for specific effects of WMSs therapies and supposed prescientific or unscientific paradigms of WMSs. **Objectives.** To review the literature on the features of WMSs, similarities and differences between conventional medicine and WMSs, and scientific and clinical practice issues that should be dealt with in order to promote the integration process. **Methods.** A critical, narrative review of the literature on six WMSs. **Results and Conclusions.** Key factors for the integration of WMSs and conventional medicine are as follows: legal frameworks, quality standards, high-quality research on safety and efficacy of WMS interventions, infrastructure, and financial resources. For scientific assessment of WMSs, there are unresolved ontological, epistemological, and methodological issues and issues of diagnostics, therapy delivery, and outcome assessment in clinical practice. Future research not only should be directed at quality assurance and generating the necessary data on safety and efficacy/effectiveness but also should address more fundamental (ontological, epistemological, and methodological) issues, in order to overcome the differences between WMSs and conventional medicine.

1. Introduction

“Medicine is a science and practice of intervention, manipulation, and control concerned with curing sick people, caring for sick people, preventing maladies, and promoting health” [1] (p. IX). Throughout human history, different cultures in all parts of the world have had their own type of medicine. In Western countries and cultures, conventional, biomedical-based medicine has been developed, rooted in the natural sciences that had developed since the Middle Ages, [2]. In many non-Western cultures but also in Western cultures, several types of whole medical systems (WMSs) [3], that is, complete systems of theory and practice that have evolved

independently over time in different cultures and apart from conventional medicine or Western medicine [3], have been developed.

Currently WMSs, often referred to as traditional and complementary medicine (T&CM) or (traditional and) Complementary and Alternative medicine (TCAM/CAM), and conventional medicine are found in almost all countries in the world. WMSs are in increasing demand by patients and are also studied in universities (e.g., the Academic Consortium for Integrative Medicine & Health in the USA). According to the “Traditional Medicine Strategy: 2014–2023” of the World Health Organization (WHO), “the public and consumers of health care worldwide continue to include

T&CM in their health choices. This obliges Member States to support them in making informed decisions about their options” [4] (p. 18). “As the uptake of T&CM increases, there is a need for its closer integration into health systems. Policy makers and consumers should consider how T&CM may improve patient experience and population health” [4] (p. 19). A central argument in favor of integrating T&CM into conventional medicine is that T&CM has additional knowledge and interventions on preventive and curative health promotion [5]. The integration can therefore contribute to current issues in public health and healthcare such as developing strategies of healthy ageing, promoting self-management, and controlling healthcare expenditures [6, 7]. Positive examples demonstrating and supporting the WHO strategy of integrating the best of both of worlds from T&CM and conventional medicine are the integration of the AYUSH (Ayurveda, Yoga, Naturopathy, Unani, Siddha, and Homeopathy (AYUSH)) system in the conventional system in India [8], the increasing use of mindfulness techniques in the treatment of depressive disorders [9], and the use of traditional medicinal systems in reducing the prescription of antibiotics in Thailand as one of the strategies to fight the global antimicrobial resistance problem [10].

This WHO position on integration of T&CM and conventional medicine is in contrast with the developments in many Western countries. Whereas many traditional medical systems were tolerated in clinical practice next to or integrated with conventional medicine in many Western countries until the end of the 20th century, this situation has rapidly changed, as a result of two interrelated developments regarding science-based medicine:

- (i) The first development is the increasing dominance of evidence-based medicine (EBM) in medicine since the 1990s [11]. As a result, ideally, only therapies with high-quality scientific evidence (from systematic reviews and meta-analyses of randomized controlled trials) on safety and (cost) effects are accepted in medicine [12]. And although in practice many conventional medical guidelines for a large part are based on lower quality scientific evidence (including clinical expertise), for opponents of the integration of T&CM and conventional medicine, a lack of high-quality scientific evidence is often used as an argument against integration.
- (ii) The second development has to do with the roots of science in theory development and theory testing [13]. In the last decades, the dominance of the biomedical model in medicine has led to scientific criticism of WMSs due to their theoretical basis that is perceived as not being in agreement with biomedical theories, but based on paradigms deemed as prescientific or unscientific. Furthermore, there is allegedly no evidence for specific effects of CAM medicinal products for conventional indications as tested in clinical studies according to the EBM paradigm [14, 15]. And although in science currently the reductionist model is increasingly challenged and the WMSs theoretical models appear to be content-wise in line with the

systems approaches in science and medicine, opponents of the integration of T&CM and conventional medicine use the assumed prescientific or unscientific theoretical models of WMSs often as an argument against integration.

On the other hand, there are positive examples of integration, like the integrated use of Ayurveda and conventional medicine in treating elephantiasis in India, that resulted in a lifetime achievement award from the International Society of Dermatologists for Oxford professor of Dermatology Terence Ryan; the highly successful integrated treatment of depression with Yoga medicine and conventional medicine in the National Institute of Mental Health and Neuroscience in Bangalore (Bengaluru) in India; and the widely adopted use of Yoga medicine for geriatrics in Japan.

Given the current need for some type of integration of conventional medicine and traditional/complementary medicine in countries all over the world, the large amount of scientific publications and the ongoing scientific debate on this topic among proponents and opponents, we decided to perform a critical review on the literature. Our aim is to provide a transparent overview on similarities and differences between WMSs and the conventional medical system and, based on this overview, identify issues that have to be dealt with in order to overcome the differences. It is expected that this overview will support informed decision-making in the integration process.

2. Material and Methods

2.1. Research Questions. A critical, narrative review of the literature was performed on the following research questions:

- (i) *In order to describe the domain of WMS, what are the historical, clinical practice, ontological, epistemological and methodological aspects of WMSs?*
- (ii) *In order to clarify whether a uniform approach or diverse approaches to their integration are most appropriate, what are the major similarities and differences between the different WMSs?*
- (iii) *In order to clarify the generalizability of experiences from integrating non-WMS CAM therapies with conventional medicine, what are the major differences between WMSs and other “single component” or non-WMS CAM therapies?*
- (iv) *In order to demonstrate the common grounds and issues to overcome in the integration process, what are the similarities and differences between WMSs and conventional medicine?*
- (v) *What are the consequences for the testing of effects of medicinal products (MPs) from WMS (WMPs) and for regulation of WMPs?*
- (vi) *In order to facilitate the integration process, which aspects need attention to promote the integration of conventional medical system and the WMSs?*

2.2. Scope of the Review, Databases, and Search Terms. In order to address the six research questions, we included the following six WMSs: Traditional Chinese Medicine (TCM) [16, 17], Ayurveda [18, 19], Unani Medicine [20], Homeopathy [21], Naturopathy [22], and Anthroposophic Medicine (AM) [23, 24]. A discussion of “all” WMSs around the world was beyond the scope of the paper; the selection includes WMSs established in four large populations/cultures (China, Indian subcontinent, Arabic/Muslim countries, and Western cultures).

Beyond the scope of this article is a comprehensive review of the discussions of the topics of (supposed) lack of evidence on specific effects of WMS treatments and the (supposed) lack of tested WMS theories. Nonetheless, these topics are briefly discussed.

We searched the database PubMed, Google Scholar, and our own literature archives. Combinations of search terms used were as follows: whole medical systems, TCM, Ayurveda, Unani, Homeopathy, Naturopathy, or AM in combination with features, philosophy, methodology, or ontology.

3. Results

3.1. Overview and Historical Development of the Whole Medical Systems. A condensed overview of the WMSs included in this review is presented in Table 1. Of these six WMSs, three (TCM, Ayurveda, and Unani) are based on old traditions (first classical texts in the first millennium BC, predated by oral transmissions from the second millennium BC), each from a specific culture: TCM developed in China in connection with the philosophical traditions of Taoism (Lao Tzu, 605–531 BC) and Confucianism (Confucius: 551–479 BC), with classical TCM texts written in the period 221–207 BC [25, 26]. Ayurveda developed on the Indian subcontinent in connection with Hinduism; classical Ayurveda texts are variously dated c700–200 BC [27, 28]. Unani has roots in Greek medicine (Hippocrates: 460–370 BC; Dioscorides: 40–90 AD; Galen: 130–210 AD); a seminal classical text from mainstream Medieval medicine and still used in Unani is the Canon of Medicine (1025 AD) by Ibn Sina (Avicenna, 980–1037 AD) [29]. These three WMSs have existed in their respective cultures for millennia before the development of natural science-based, conventional medicine [3, 16, 17, 19, 21–23, 30].

Three other WMSs (Homeopathy, Naturopathy, and Anthroposophic Medicine) are comparatively younger (<250 years), although traces of influences by older traditions can be found [31–33]. Seminal publications appeared for Homeopathy in 1796 [34], for Naturopathy in 1848 [35], and for AM in 1925 [36]. These three WMSs were first practiced in Central Europe by medical doctors and were further developed next to conventional medicine within Western cultures.

In the course of globalization, all six WMSs have become disseminated from their original culture into other countries and regions, sometimes with establishment of “second centers” such as for Naturopathy in North America [37] and

Homeopathy in India [38]. Currently, in almost every country in the world, one or more types of WMS are practiced [4].

3.2. Similarities and Differences

3.2.1. Similarities and Differences between the WMSs. Some major *similarities* between the WMSs are as follows:

- (i) Holistic, nonatomistic ontological, epistemological, and practice orientation
- (ii) Aiming at preventive as well as curative health promotion
- (iii) Individualized treatment based on a system approach
- (iv) Medicinal use of a large number of different substances and WMPs, of mostly herbal but also mineral and zoological origin (e.g., 700 herbal species in TCM [39], >1000 substances in homeopathy [40], >4000 herbal species in Ayurveda, and >800 substances in AM [41])
- (v) Nonmedication treatment modalities including massage, physical exercises, hydrotherapy, thermotherapy, and diet (although each modality may be applied differently, cf. Table 1)

Some major *differences* between the WMSs are as follows:

- (i) Use of different languages, including different concepts of levels of wholeness
- (ii) Different diagnostic systems
- (iii) Different specific therapy modalities, for example, acupuncture in WMS and art therapies in AM

Homeopathy has two particular aspects:

- (i) In the development of homeopathy, there have been a strong element of pure empiricism and relatively less emphasis on theory.
- (ii) Homeopathic diagnostics and treatment are usually limited to case taking and the prescription of homeopathic MPs [42]. All homeopathic MPs are manufactured according to specific homeopathic procedures such as potentization, that is, successive dilution, each dilution step involving a rhythmic succession (repeated shaking of liquids) or trituration (grinding of solids into lactose monohydrate). In contrast, treatment in the other five WMSs is to a much larger extent multimodal (Table 1).

A particular aspect of Naturopathy is the widespread use of therapy modalities from other WMSs (e.g., Chinese herbs and homeopathic MPs) or from non-WMS CAM (e.g., food supplements) [43]. In contrast, the other WMSs have a stronger element of uniformity, either in their theory (TCM, Ayurveda, Unani, and AM) or in the use of one specific type of WMPs (Homeopathy).

TCM and Ayurveda have long traditions of mainly oral transmission of WMS knowledge and experience, predating the classical texts [16, 26].

TABLE 1: Overview of six whole medical systems.

	Chinese	Ayurveda	Unani	Homeopathy	Naturopathy	Anthroposophic
Classical texts	221–207 BC	Variously dated c700–200 BC	Avicenna, 1025 AD	Hahnemann, 1796	Gleich, 1848	Steiner & Wegman, 1925
Use (main regions)	East Asia	South Asia	South Asia, Middle East	Europe, India	Europe, English-speaking countries	Europe, South America
Key concepts	2 forces (yin, yang), vital energy (qi), 5 elements, meridians	3 energies or doshas (pitta, vata, kapha), 5 elements	7 naturals (elements, temperaments, humors, organs, forces, actions, spirit)	Like cures like, minimum dose, experiments in healthy persons	Healing power of nature, treat the cause of disease, do no harm, doctor as teacher, treat the whole person, prevention	4 levels of formative forces (physical, life, soul, spirit), 3-fold constitution (nerve-sense, rhythmic, motor-metabolic)
Medicinal products & substances	Herbs, minerals, zoological	Herbs, minerals, zoological	Herbs, oils, perfumes	Homeopathic*	Herbs, homeopathic*, Chinese, food supplements	Homeopathic*, herbs, minerals, zoological, chemically defined
Massage	Tuina, shiatsu	Ayurveda massage	Tadlik massage		Swedish massage	Rhythmic massage
Physical therapy		Hydrotherapy	Hydrotherapy, thermotherapy		Hydrotherapy, thermotherapy, joint manipulation	Hydrotherapy, thermotherapy, external applications
Other nonmedication treatment	Acupuncture, moxibustion	Purgation, lifestyle counselling	Purgation, cupping, leeching	Case taking, lifestyle counselling	Acupuncture, lifestyle counselling	Artistic (music, speech, painting, drawing, clay), biography & lifestyle counselling
Physical exercises	Qigong, Tai-Chi	Breathing	Yes	Yes	Yes	Eurythmy movements
Other self-treatment		Heliotherapy, meditation	Reciting sacred text	Stress reduction	Heliotherapy, relaxation techniques	Meditation
Diet	Yes	Yes	Yes	Yes	Yes	Yes

* Homeopathic medicinal products can be of herbal, mineral, or zoological origin or chemically defined and are defined by specific homeopathic manufacturing procedures (see text).

Particular aspects of AM include the broad spectrum of artistic therapies deployed (painting, clay modeling, drawing, recitation, and music exercises) and the use of AM treatments also in large hospitals offering accident and emergency service within public requirement plans [23]. WMPs used in AM can be manufactured according to specific anthroposophic methods or methods used for herbal, homeopathic, or conventional MPs [41].

3.2.2. WMSs versus Other “Single Component” or Non-WMS CAM Therapies. The major differences between WMSs and single component CAM interventions are as follows:

- (i) Some single component (or fixed combination of) CAM interventions can be conceptualized within the conventional biomedical paradigm: for example, a number of vitamins are used as CAM therapy, while their purported pharmacological effects are conceptualized on the levels of cell biology or biochemistry. In contrast, WMS interventions are not so easily understood on these levels (although the difference is not absolute [5]).
- (ii) Single component CAM interventions can be protocolled for specific conventional and/or CAM indications, whereas this is not the case for WMS interventions.
- (iii) Individualized, multimodal CAM treatment entails the combination of several treatment modalities that are tailored to the needs of the individual patient. When this happens within a WMS, all treatment modalities are understood within and derived from one conceptual framework, leading to a uniform treatment approach. When diverse single component CAM interventions are combined, a uniform conceptual understanding is often not possible, leading to eclecticism.

3.2.3. Similarities and Differences between WMSs and the System of Conventional Biomedicine. The main similarities between WMSs and some developments in conventional medicine are as follows:

- (i) The development of a personalized medicine/individualization approach in addition to the current mainstream protocolled approach [44, 45]
- (ii) The use and role of professional judgment in some domains of clinical practice (e.g., interpretation of radiographs) [45, 46]
- (iii) The increasing use of complex interventions [47–49]
- (iv) System approaches in diagnostics and therapy (e.g., systems biology, epigenetics, emergentism, metabolomics, “network medicine,” “polypharmacology,” and “polytarget treatment”) [5, 50–52]
- (v) Shared decision-making [45, 53]
- (vi) A holistic dynamic health concept [5, 54]
- (vii) The use of pattern recognition methodologies [55, 56]

- (viii) The notion that RCTs are not applicable everywhere [57, 58] with a shift towards more pragmatic trials [45, 48, 58, 59] and other study types [48, 60]
- (ix) The notion that conducting clinical studies for multiple clinical conditions and their respective diverse therapy options has its limitations, due to excessive complexity and prohibitive costs
- (x) The increasing role of patient preferences and patient autonomy
- (xi) The real-world situation that, in many medical fields (e.g., paediatric surgery, emergency medicine, and vaccination), RCT-based practice is only marginal and often critically questioned

The main *differences* between the WMSs and the conventional medicine system are summarized in Table 2 [61].

3.3. Integration of WMSs and the Conventional Medicine System. The integration of WMSs and conventional medicine entails some key, interdependent factors:

- (i) Legislation: therapy providers and WMPs
- (ii) Education: practitioners of the two integrating medical systems that have to work together for a period of years to build up experience and confidence in effective team work
- (iii) Quality standards for WMS treatment: training of providers, delivery of treatment, and pharmaceutical quality of WMPs
- (iv) Scientific research on the safety and efficacy of WMP interventions
- (v) Infrastructure and financial resources

Regarding scientific research and quality benchmarking, there are specific issues pertaining to the inherent properties of WMSs:

- (i) Ontological, epistemological, and methodological issues relevant for the overall understanding and assessment of WMSs
- (ii) Specific issues relevant for diagnostics, therapy delivery, and outcome assessment in clinical practice

These issues are discussed in the following subsections.

3.3.1. Legislation, Quality Standards, Research, Infrastructures, and Resources. Of paramount importance for integration is the recognition of WMSs in *legislation*, in particular

- (i) recognition of WMS therapy providers, their training schools and diplomas;
- (ii) regulatory provisions enabling the registration or marketing authorisation of WMPs.

TABLE 2: Differences between conventional medicine and whole medical systems (WMSs).

	Conventional medicine	WMSs
Worldview/philosophy	Biomedical/humanistic model	Holistic/spiritual/bio-psycho-spiritual-social model
Health	Default situation of the machine	Result of self-regulating inner activity (e.g., of the organism or psychosocial) Restoring wholeness/balance (Re)establishment of the harmony between the functions of body, soul and spirit
Disease	Breakdown of the machine Deviance from biological norms Has no intrinsic meaning	Expression of system imbalance and/or insufficiency of the wholeness creating forces Disequilibrium between biological, psychological, social and spiritual forces Entails a potential for human development
Diagnosis	Group level (often, not always)	Individual level System level
Treatment	Group-oriented guidelines/protocols (often) Fighting disease Requires external resources Use of pharmacotherapy with predominantly specific effects and high use of technology	Complex individualized interventions Health promotion Requires internal resources/body, mind and spirit are interrelated and must all be considered in healing Use of WMS pharmacotherapy and nonmedicinal therapies with system effects

Such recognition is dependent on establishing *quality standards*:

- (i) For therapy providers (e.g., WHO benchmarks for training in TCM [26], Ayurveda [62], Unani Medicine [63], and Naturopathy [33]; CEN [French: Comité Européen de Normalisation] standards for health care provision by medical doctors with additional qualification in Homeopathy [64])
- (ii) For the pharmaceutical quality of WMPs (e.g., the Anthroposophic Pharmaceutical Codex [41]).

Scientific and societal recognition also depends on high-quality evidence for efficacy/effectiveness and safety of WMPs and nonmedication treatment in WMSs; hence, integration also includes the funding, conduct, and publication of *scientific research* studies in order to generate and disseminate such evidence. In order to promote quality standards and scientific research, *infrastructures* and *financial resources* are needed.

In some countries these tasks are given national priority: for example, the Government of India supports research, education, quality standardization, and infrastructure building for seven WMSs (AYUSH: Ayurveda, Yoga, Naturopathy, Unani, Siddha, Homeopathy, and Sowa-Rigpa), since 2004 within the newly established Ministry of AYUSH [65].

One example of infrastructure building is establishing Integrative Medicine centers in academic hospitals, where specific WMS modalities (not necessarily the entire WMS) are developed, applied, and tested. This model has been implemented in the USA and organized in the Academic Consortium for Integrative Medicine & Health, based on four pillars: (1) the horizontal relationship between the

doctor/therapist (coach) and the patient (coproducer); (2) the active role of the patient in prevention (lifestyle), wellbeing, and therapy and healing processes; (3) the use of evidence-based safe and effective conventional and complementary therapies; and (4) the use of healing environments [66].

3.3.2. Fundamental Ontological Aspects. All studied WMSs take a *nonatomistic, holistic ontological* position towards the nature of reality. This means that they all conceptualize, each in a different form, in addition to material elements and forces, the existence of nonmaterial forces working in nature and man, which also play a role in health and disease. For example, a central concept of TCM is Qi, a vital energy or life force that moves in the body through a system of pathways called meridians [16]. Similar concepts are found in Ayurveda (“prana” [67]) and Unani (“arwah” or vital spirit [29]). AM has the concept of four levels of formative forces working in man: formative physical forces and three nonmaterial forces (life, soul, and spirit) [23, 30]. Homeopathy conceptualizes the nonmaterial effects of high potentized substances [21] and also Naturopathy is based on holistic and vitalistic principles [22].

3.3.3. Conceptual and Epistemological Aspects. In line with the nonatomistic, holistic ontological position, central concepts of WMS are holistic. Concepts of the human being emphasize the wholeness and complexity of the human being [68]; its emergent, nonlinear dynamic, and epigenetic properties; and its ability of self-organization and adaptation as a network system [69]. Health is conceptualized as the ability to balance and actively restore the wholeness of

the human being [5]. Within the WMS practice methods, there is an essential role for intuition and expert knowledge in diagnostics and decision-making [45], while treatment also takes into account context factors and the uniqueness, constitution, and complexity of the individual [45, 70]. In conceptualizing causality, WMSs emphasize systems causality [71], effects that involve global and patterned shifts across multiple subsystems of the person as a whole, and the role of context/placebo and intention effects [69].

3.3.4. Methodological Aspects. A review on clinical and epidemiological research in CAM [48] demonstrates that, for research on therapy effects, there is consensus that both efficacy and effectiveness studies have their own place, validity, and importance. Some authors argue that efficacy research should be prioritised over effectiveness research to legitimise the use of CAM and to help to increase acceptance. Other authors state that efficacy research to examine specific effects should not be undertaken until overall effectiveness of the therapy in question is demonstrated, in order to prevent misuse of scarce resources. This discussion also reflects different opinions on the importance and value of specific and nonspecific effects within the whole of clinical practice. An integrative research approach has been described as simultaneous research into mechanisms and overall effectiveness of CAM treatments. Contemporary methodological standards of medical research can be applied to CAM research, but it might be necessary to adapt the research designs in some areas, in order to account for the complexity of CAM interventions [72]. CAM-specific challenges must be addressed, such as the problem of strict standardization of diverse treatments and study participants leading to lack of external validity. RCTs do not answer all research questions and are expensive to conduct. Placebo-controlled RCTs might be inappropriate for some specific CAM modalities. There is a need for additional methods, for example, pragmatic studies [73], observational studies, mix of qualitative and quantitative studies, and $n = 1$ studies.

In treatment studies, there is on the one hand the tendency to operationalize WMS interventions into a “treatment package” that can be used also outside the original WMS context, and on the other hand the critique that some essential aspects (e.g., individualization) or therapy components may become excluded by such operationalization, leading to reduced efficacy and misperceptions of the “true” traditional WMS intervention [74].

Outcomes should be broader than symptom reduction alone, they should contain several levels of the whole human being, including physical, mental, spiritual, and social factors [70]. Health economic evaluation of CAM treatments was seen as particularly relevant in modern healthcare. Research into the mechanisms of placebo, context, or meaning effects were also seen as important to determine appropriate control groups and their respective explanatory power, in order to explain potentially contradictory study results and to maximize these effects in clinical practice. Newer evaluation models such as program theory, the theory on “the mechanisms that mediate between the delivery (and receipt) of

the program and the emergence of the outcomes of interest” [75, 76], encompass a wide range of health-related changes that include process aspects, such as the emergence of new meanings and understanding during or after treatment, as well as longer term changes in health, wellbeing, and health-related competences and behavior [77].

Another proposed model is a “reversed research strategy” for assessing CAM, starting with studies of the context, paradigms, philosophical understanding, and utilization, then subsequently the safety status of the whole system, comparative effectiveness of the whole system, and specific efficacy of components, and finally the underlying biological mechanisms [49, 78]. Other, expressly nonhierarchical models include a circular information synthesis of different evidence forms [45, 60] and an “evidence house” [79].

3.3.5. Clinical Practice Aspects. Main topics with regard to WMS practice methods pertain to the development of whole system diagnostics and interventions; the development and application of quality control systems for individualized diagnostics and treatment and the use of multidisciplinary complex interventions [80]; the role of protocols, guidelines, and expert knowledge in clinical practices of a whole system approach [81]; and the use of double (conventional and WMS) diagnoses.

A WMS diagnosis is a diagnosis on the level of the individual patient and is system-based. In practices where WMS is integrated with conventional medicine, we therefore find double diagnoses. Diagnostics on the individual and system level often includes pattern recognition methods which require interrelated expert knowledge, intuition, and system thinking skills [82].

In WMS therapy the focus is on the sick patient in his or her whole complexity, including physical, mental, spiritual, and social factors. These are interconnected and need to be addressed in total and on multiple levels. The repertoire of CAM treatment is often multimodal and complex, and its application highly individualized. CAM treatments and counselling are provided as integrative systems with interacting components. Accordingly, the effects of complex approaches are often larger than the sum of the components’ effects. WMS therapy aims to support and stimulate autoprotective and salutogenetic potentials (self-healing and self-regulatory abilities), mostly with the active cooperation of the patient or of his/her organism. WMS practices also require a good patient-practitioner interaction (therapeutic relationship) and cocreation of the patient in varying therapeutic contexts [45]. Clinical evaluation includes patient-determined outcomes as well as patient satisfaction [70]; notably, these outcome measures are also becoming increasingly used in evaluation of conventional treatments.

3.3.6. Quality and Clinical Safety of WMPs. Regarding the pharmaceutical quality and clinical safety of WMPs, there is a difference in the historical development of the older and newer WMSs.

In the 20th century, homeopathic and anthroposophic MPs have been marketed in European countries such as Austria, France, Germany, and Switzerland as drugs, manufactured according to Good Manufacturing Practice standards, and subject to modern drug regulation including pharmacovigilance. Toxicologically relevant starting materials (e.g., aconite and cinnabar) are highly diluted according to safety requirements of European regulations [83]. Adverse reactions to these MPs are infrequent and usually of mild to moderate severity; anaphylactic reactions occur but are very rare [40, 84, 85].

In contrast, MPs from Chinese, Ayurveda, and Unani medicine have historically been produced for local use. In modern times, industrial-scale production has developed with less rigorous quality control, and MPs have been regulated as food or food supplements or have been imported for use without regulation. Some WMPs have been associated with repeated, severe adverse reactions, including liver and kidney toxicity (sometimes fatal) [86–88], heavy metal poisoning [89–93], epileptic seizures [94], and adrenal suppression from undeclared addition of corticosteroids to herbal products [90]. There are further concerns regarding environmental contaminations (e.g., air pollution, soil contaminations), cultivation practices (e.g., pesticides, fungicides, microorganisms, endotoxins), manufacturing procedures (e.g., microorganisms, endotoxins), and inappropriate use [95, 96]. In order to overcome these problems, pharmacovigilance systems have been established in the main producing countries of Chinese, Ayurvedic, and Unani MPs [97, 98], and there are considerable efforts to improve the quality standards for these WMPs [99, 100].

3.4. Mismatches and Aspects Needing Attention

3.4.1. Mismatches. Currently, based on the described differences, there are mismatches between the current scientific empirical (EBM) and theoretical (biomedical model) demands and the properties and specificity of WMSs. We describe these mismatches here by means of the example of WMPs, with the demands and their application in drug regulation on the one hand and WMPs and the inherent properties of WMS on the other hand. The main mismatches are as follows:

- (1) WMPs are insufficiently tested because they are not in line with conventional interests and biomedical models.
- (2) WMPs are generally handled as standardized conventional medicinal product (CMP) interventions, whereas they should also be handled as part of a complex intervention.
- (3) WMPs are handled as CMPs, that is, symptom reducing, fighting disease therapy, whereas they should be handled as a curative, health promotion therapy that supports the self-healing abilities of the organism.
- (4) WMPs are tested for conventional indications based on group-oriented taxonomy and diagnostics,

whereas they should be tested for individualized WMP indications.

- (5) WMPs are assumed to have specific biochemical effects like CMPs have, but WMP therapy is directed at higher levels, aiming at the regulation and harmonizing (e.g., Dosha balancing in Ayurveda) of overarching, complex physiological processes, and the transformation of physiological and psychological processes and capacities into more mature and integrated states (Schad, 2008; Simon, 2009).
- (6) WMPs are often judged on efficacy by regulatory authorities as new CMPs, whereas they should also be regarded as part of a traditional WMS with long-standing use, developed following a reverse pathway compared to CMPs (Fønnebo et al., 2007; Kienle et al., 2011).

The main consequences of these mismatches are as follows:

- (1) The dominance of the biomedical model has resulted in an a priori negative image and rejection of WMPs by scientists of conventional biomedicine, whereby, seen from a reductionist, mechanistic position, effects of WMPs are regarded as mere nonspecific, context effects, not worthy of serious scientific scrutiny.
- (2) As a consequence of this attitude of rejection, there is an underrepresentation of WMS scientists in academic institutions and scarce public funding of academic WMP research.
- (3) Many WMPs are not tested in clinical research and can therefore not obtain ordinary marketing authorization.
- (4) WMPs are most often not tested according to their theoretical higher order, system level effects but are tested in conventional RCTs with a single product approach. Therefore the precision of the tested WMP treatment is decreased, with an increased high risk of “false-negative results” (meaning: in reality the treatment has beneficial effects but these are not captured in the research study).
- (5) WMPs often do not appear in guidelines for treatment of specific conventional indications since many WMPs are not in line with mainstream biomedical theories, are not tested in clinical research, and are not part of the expert knowledge of the developers of conventional treatment guidelines.

This development is not restricted to WMPs: there is an increasing call for excluding all WMS modalities from healthcare and for stopping the development of Integrative Medicine, since many WMS interventions are perceived to lack a plausible scientific efficacy model and because relevant results of clinical studies are lacking, for reasons described above.

However, as described previously, there are also positive examples of the integration of WMSs and conventional medicine in practice, examples of high-quality evidence of

specific effects of WMS treatment for conventional indications, and WMSs theoretical models that appear to be content-wise in line with the systems approach in science and medicine (see Introduction).

3.4.2. Aspects That Need Attention to Promote the Integration of the Conventional Medical System and the WMSs. From this overview of the differences between the conventional medical system and the WMSs, a number of issues can be deduced that should be dealt with in science and clinical and regulatory practice, in order to overcome the differences and facilitate the integration processes of the best of both worlds.

(i) Ontological issues

- (a) Future research and scientific discussion should focus on the nature of reality (matter, organism, mind, . . .), the tenability of the nonatomistic holistic position of WMSs within the so-called holism-reductionism debate, and ontological issues to overcome in the integration process.

(ii) Conceptual and epistemological issues

- (a) Future research and scientific discussion should focus on developing and testing theories that are system- and complexity-oriented and that are compatible with both WMS and conventional medicine.
- (b) Specific theories that conceptually may bridge the two approaches should be further studied: theories of health, disease, healing [101]; individualization in diagnostics and treatment; and health promotion.

(iii) Methodological issues

- (a) Future use of research methodologies/designs should focus on
- (1) a “reversed research strategy” for assessing CAM;
 - (2) taking into account the complexity of CAM interventions and the role of expert knowledge, intuition, and individualization of diagnostics and therapies;
 - (3) the health economic evaluation of CAM treatments;
 - (4) the mechanisms of placebo, context, or meaning effects [102].

(iii) Clinical practice issues

- (a) Future development and implementation of integrative treatment approaches should take into account
- (1) alternatives for protocols and guidelines that are in line with the holistic and individualizing treatment approaches;

- (2) the integrated use of dual diagnoses (from both systems);
- (3) the integrated use of analytical and system thinking [18];
- (4) the optimal integration of “fighting disease” and “health promotion” treatment options.

(iv) Regulatory issues

- (a) Regulatory frameworks must be modified in order to match the specific features of WMPs.
- (b) New conceptualizations regarding benefit-risk assessment, research synthesis from different types of evidence (not just RCTs), and the evaluation of WMPs are needed. This in line with the opinion of the EU commission that has acknowledged the need for appropriate regulation also of WMPs [103].

3.4.3. Lack of Evidence of Specific Treatment Effects and Prescientific or Unscientific Theories. Whereas the main argument of many people from conventional medicine is that integration of WMSs and conventional medicine is unacceptable due to an assumed lack of evidence of specific effects from WMS treatment and because of alleged prescientific or unscientific theories, we here discuss these issues in more detail.

Apart from the fact that there are some good quality studies demonstrating specific effects of a single WMS therapy for a conventional indication [104], the described features of WMS approaches demonstrate that WMS therapy most often is aiming at system effects and at restoring balances rather than symptom reduction and often contains different treatments as part of a complex intervention. This situation makes it often difficult to test one single, protocol-based treatment for a conventional indication. If this type of evidence would be mandatory, the precision of the tested treatment would be decreased, with an increased high risk of “false-negative outcomes” (meaning: in reality the treatment has beneficial effects but these are not captured in the research study). In addition, it would lead to a feasibility bias against WMSs. This was the reason for the development of the previously described different “reversed research strategy” for assessing CAM [49] and the model of nonhierarchical, circular information synthesis of different evidence forms [60].

With regard to the theories, WMSs theories are (nonatomistic) holistic and not reductionistic and therefore often regarded as prescientific or unscientific. However, the current situation is that throughout different fields of research, scientists increasingly question the ability of pure reductionist theories to describe and explain the complexity of biological organizations [51]. Therefore, new theories (e.g., systems biology, emergence, and epigenetics) originating from the research fields of the biological complexity in organisms and the genome project demonstrate a shift from reductionist towards more holistic concepts. [21] To our opinion, based on these shifts in science, more openness and acceptance towards (nonatomistic) holistic theories is warranted.

4. Discussion

There is an increasing need for a worldwide professional integration of conventional medicine and traditional/complementary whole medical systems. However, in many Western countries, the integration is perceived by conventional medicine as problematic and not acceptable. We therefore reviewed the literature on the features of WMSs, the similarities and differences between conventional medicine and WMSs, and future scientific and clinical practice issues that should be dealt with in order to promote the integration process.

Key factors for the integration of WMSs and conventional medicine are as follows: legal and regulatory frameworks for therapy providers and WMPs; quality standards for the training of therapy providers, the delivery of treatment, and the pharmaceutical quality of WMPs; high-quality scientific research on the safety and efficacy of WMS interventions; and adequate infrastructure and financial resources in order to carry out these tasks.

For scientific research and quality benchmarking, there are fundamental issues pertaining to the inherent properties of WMSs: ontological, epistemological, and methodological issues relevant to the overall understanding and assessment and issues relevant to diagnostics, therapy delivery, and outcome assessment in clinical practice. Many of these issues are as yet unresolved, with contradictory positions among scientists and stakeholders of conventional biomedicine and WMSs, respectively, and with mismatches for resource allocation and drug regulation.

The main contribution of this article is that it will provide (more) overview and clarity on this topic for both WMSs and conventional medicine. It will give objective input for rational discussions on the integration topic. In addition, it will support organizations in their preparation and decision-making during the integration process.

A limitation of the article is that we did not include all WMSs, for example, Yoga medicine, osteopathy, Campo, or WMSs from Africa or South America. Also we did not employ all possible search terms, for example, Ayurvedic (in addition to Ayurveda). A topic that is beyond the scope of this article is that we did not discuss the (supposed) lack of evidence on specific effects of WMS treatments and the (supposed) lack of tested theories of WMSs [15] in depth. However, we described the fundamental (ontological, epistemological, and methodological) underlying differences between WMSs and conventional medicine that are related to these issues (evidence of specific effects and lack of tested theories) and made clear why both sides have different perceptions on these issues.

Future research activities not only should be directed at the “forefront issues” of quality assurance and generating the necessary data on safety and efficacy/effectiveness of WMS interventions but also should address the more fundamental (ontological, epistemological, and methodological) issues, in order to overcome the differences between WMSs and conventional medicine.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

References

- [1] K. Sadegh-Zadeh, “Handbook of analytic philosophy of medicine,” in *Philosophy and Medicine*, vol. 113, p. 1133, Dordrecht Heidelberg London New York: Springer, 2012.
- [2] W. F. Bynum and R. Porter, *Companion Encyclopedia of The History of Medicine*, Routledge, 2013.
- [3] NCCAM, “Complementary, Alternative, or Integrative Health: What’s In a Name?” 2013; <http://nccam.nih.gov/health/whatisnccam?nav=gsa>.
- [4] World Health Organization, *WHO traditional medicine strategy: 2014–2023*, 2013.
- [5] E. Baars, *Evidence-Based Curative Health Promotion: A Systems Based Biology-Orientated Treatment of Seasonal Allergic Rhinitis with Citrus/Cydonia Comp*, Wageningen University, Wageningen, the Netherlands, 2011.
- [6] E. W. Baars and P. Kooreman, “Correction: A 6-year comparative economic evaluation of healthcare costs and mortality rates of Dutch patients from conventional and CAM GPs (BMJ Open (2014) 4, (e005332)),” *BMJ Open*, vol. 4, no. 9, Article ID e005332, 2014.
- [7] P. Kooreman and E. W. Baars, “Patients whose GP knows complementary medicine tend to have lower costs and live longer,” *European Journal of Health Economics*, vol. 13, no. 6, pp. 769–776, 2012.
- [8] S. R. B. Shrivastava, P. S. Shrivastava, and J. Ramasamy, “Mainstreaming of Ayurveda, Yoga, Naturopathy, Unani, Siddha, and homeopathy with the health care delivery system in India,” *Journal of Traditional and Complementary Medicine*, vol. 5, no. 2, pp. 116–118, 2015.
- [9] S. G. Hofmann, A. T. Sawyer, A. A. Witt, and D. Oh, “The effect of mindfulness-based therapy on anxiety and depression: a meta-analytic review,” *Journal of Consulting and Clinical Psychology*, vol. 78, no. 2, pp. 169–183, 2010.
- [10] N. Sumpradit, T. Fongthong, S. Pumtong, S. Suttajit, and N. Kiatying-Angsulee, “Scaling up evidence-based interventions toward sustainability: A case study of antibiotics smart use program in Thailand,” *Journal of Microbiology, Immunology and Infection*, vol. 48, no. 2, p. S24, 2015.
- [11] D. L. Sackett, W. M. C. Rosenberg, J. A. M. Gray, R. B. Haynes, and W. S. Richardson, “Evidence based medicine: What it is and what it isn’t. It’s about integrating individual clinical expertise and the best external evidence,” *British Medical Journal*, vol. 312, no. 7023, pp. 71–72, 1996.
- [12] BMJ, *What Conclusions Has Clinical Evidence Drawn about What Works, What Doesn’t Based on Randomised Controlled Trial Evidence?* 2013; <http://clinicalevidence.bmj.com/x/set/static/cms/efficacy-categorisations.html>.
- [13] M. Curd and S. Psillos, *The Routledge Companion to Philosophy of Science*, Routledge, 2013.
- [14] C. Lewis, “Trick or treatment? Alternative medicine on trial,” *Acupuncture in Medicine*, vol. 27, no. 1, pp. 39–39, 2009.
- [15] M. Anlauf, L. Hein, H.-W. Hense et al., “Complementary and alternative drug therapy versus science-oriented medicine,” *GMS German Medical Science*, vol. 13, pp. 1–47, 2015.
- [16] G. Li, F. Wang, S. Wang et al., “Whole medical systems in lung health and sleep: focus on traditional chinese medicine,” in *Integrative Therapies in Lung Health and Sleep*, pp. 269–303, Springer, 2012.
- [17] C. N. Lam and L. Soh-Leong, *Traditional Chinese medicine: A healing approach from the past to the future. Multicultural*

- Approaches to Health and Wellness in America*, Praeger Publishers, Westport, CT, 2014.
- [18] C. Kessler and A. Michalsen, "The role of whole medical systems in global medicine," *Forschende Komplementärmedizin*, vol. 19, no. 2, pp. 65–66, 2012.
- [19] C. Kessler, M. Wischnewsky, A. Michalsen, C. Eisenmann, and J. Melzer, "Ayurveda: between religion, spirituality, and medicine," *Evidence-Based Complementary and Alternative Medicine*, vol. 2013, Article ID 952432, 11 pages, 2013.
- [20] Y. Abdelhamid, "Unani Medicine, Part I. Integrative Medicine," *A Clinician's Journal*, vol. 11, no. 2, pp. 24–30, 2012.
- [21] G. Viganò, P. Nannei, and P. Bellavite, "Homeopathy: from tradition to science?" *Journal of Medicine and the Person*, vol. 13, no. 1, pp. 7–17, 2015.
- [22] K. M. Tippens, E. Oberg, and R. Bradley, "A dialogue between naturopathy and critical medical anthropology: toward a broadened conception of holistic health," *Medical Anthropology Quarterly*, vol. 26, no. 2, pp. 257–270, 2012.
- [23] G. S. Kienle, H. Albonico, E. Baars, H. J. Hamre, P. Zimmermann, and H. Kiene, "Anthroposophic medicine: an integrative medical system originating in Europe," *Global Advances in Health and Medicine*, vol. 2, no. 6, pp. 20–31, 2013.
- [24] P. Heusser, *Anthroposophy and Science - an introduction*, Peter Lang, New York, NY, USA, 2016.
- [25] J. L. Tang, B. Y. Liu, and K. W. Ma, "Traditional Chinese medicine," *The Lancet*, vol. 372, no. 9654, pp. 1938–1940, 2008.
- [26] *Benchmarks for Training in Traditional/Complementary And Alternative Medicine: Benchmarks for Training in Traditional Chinese Medicine*, vol. 30, World Health Organization, Geneva, Switzerland, 2010.
- [27] A. Chopra and V. V. Doiphode, "Ayurvedic medicine: core concept, therapeutic principles, and current relevance," *Medical Clinics of North America*, vol. 86, no. 1, pp. 75–89, 2002.
- [28] P. Garodia, H. Ichikawa, N. Malani, G. Sethi, and B. B. Aggarwal, "From ancient medicine to modern medicine: ayurvedic concepts of health and their role in inflammation and cancer," *Journal of the Society for Integrative Oncology*, vol. 5, no. 1, pp. 25–37, 2007.
- [29] "Unani medicine," in *Encyclopædia Britannica*, 2016, The Editors of Encyclopædia Britannica.
- [30] P. Heusser, C. Scheffer, M. Neumann, D. Tauschel, and F. Edelhäuser, "Towards non-reductionistic medical anthropology, medical education and practitioner-patient-interaction: the example of Anthroposophic Medicine," *Patient Education and Counseling*, vol. 89, no. 3, pp. 455–460, 2012.
- [31] v.-D. Melchart, R. Brenke, and G. Dobos, *Naturheilverfahren. Leitfaden für die ärztliche Aus-, Fort und Weiterbildung*, Schattauer Verlag, Stuttgart, Germany, 2002.
- [32] R. Steiner, "Introducing Anthroposophical Medicine. Twenty lectures to doctors," *Dornach*, vol. 21, 1999.
- [33] World Health Organization, *Benchmarks for Training in Traditional/Complementary And Alternative Medicine: Benchmarks for Training in Naturopathy*, vol. 20, World Health Organization, Geneva, 2010.
- [34] S. Hahnemann, "Versuch über ein neues Prinzip zur Auffindung der Heilkräfte der Arzneisubstanzen, nebst einigen Blicken auf die bisherigen," *Journal der praktischen Arzneykunde und Wundarzneykunst*, vol. 2, no. 3, pp. 391–439, 1796.
- [35] L. Gleich, "Ueber die Nothwendigkeit einer gänzlichen Umgestaltung der sogenannten Heilwissenschaft unserer Tage," *Augsburg*, vol. 112, 1848.
- [36] R. Steiner and I. Wegman, *Fundamentals of therapy*, Kessinger Legacy Reprints, Whitefish, MT, USA, 2010.
- [37] World Naturopathic Federation Report, *Findings from the 1st World Naturopathic Federation survey*, World Naturopathic Federation, Toronto, Ontario, Canada, 2015.
- [38] A. K. Ghosh, "A short history of the development of homeopathy in India," *Homeopathy*, vol. 99, no. 2, pp. 130–136, 2010.
- [39] X. Li, Y. Chen, Y. Lai, Q. Yang, H. Hu, and Y. Wang, "Sustainable utilization of traditional chinese medicine resources: systematic evaluation on different production modes," *Evidence-based Complementary and Alternative Medicine*, vol. 2015, Article ID 218901, 10 pages, 2015.
- [40] G. Bornhöft and P. F. Matthiessen, *Homeopathy in Healthcare - Effectiveness, Appropriateness, Safety, Costs*, Springer Berlin Heidelberg, Berlin, Heidelberg, 2011.
- [41] International Association of Anthroposophic Pharmacists, *Anthroposophic Pharmaceutical Codex APC, Third Edition*, International Association of Anthroposophic Pharmacists, Dornach, 2013.
- [42] G. Köhler, *Lehrbuch der Homöopathie 3rd edition*, Hippokrates Verlag, Stuttgart, 1984.
- [43] World Health Organization, *Benchmarks for Training in Traditional /Complementary And Alternative Medicine: Benchmarks for Training in Naturopathy*, vol. 13, WHO Press, Geneva, 2010.
- [44] M. J. Joyner and N. Paneth, "Seven questions for personalized medicine," *The Journal of the American Medical Association*, vol. 314, no. 10, pp. 999–1000, 2015.
- [45] G. S. Kienle, H.-U. Albonico, L. Fischer et al., "Complementary therapy systems and their integrative evaluation," *Explore: The Journal of Science and Healing*, vol. 7, no. 3, pp. 175–187, 2011.
- [46] L. Daston and P. Galison, *Objectivity*, Zone Books, Brooklyn, NY, USA, 2007.
- [47] P. Craig, P. Dieppe, S. Macintyre, S. Mitchie, I. Nazareth, and M. Petticrew, "Developing and evaluating complex interventions: the new Medical Research Council guidance," *British Medical Journal*, vol. 337, Article ID a1655, 2008.
- [48] H. F. Fischer, F. Junne, C. Witt et al., "Key issues in clinical and epidemiological research in complementary and alternative medicine—a systematic literature review," *Forschende Komplementärmedizin/Research in Complementary Medicine*, vol. 19, no. 2, pp. 51–60, 2012.
- [49] V. Fønnebo, S. Grimsgaard, and H. Walach, "Researching complementary and alternative treatments—the gatekeepers are not at home," *BMC Medical Research Methodology*, vol. 7, article 7, 2007.
- [50] X. Wang, H. Sun, A. H. Zhang, W. J. Sun, P. Wang, and Z. G. Wang, "Potential role of metabolomics approaches in the area of traditional Chinese medicine: as pillars of the bridge between Chinese and Western medicine," *Journal of Pharmaceutical and Biomedical Analysis*, vol. 55, no. 5, pp. 859–868, 2011.
- [51] H. Walach and D. Pincus, "Kissing descartes good bye," *Forschende Komplementärmedizin*, vol. 19, no. 1, pp. 1–2, 2012.
- [52] American Association for the Advancement of Science, "The Art and Science of Traditional Medicine Part I: TCM Today—A Case for Integration," *Science*, vol. 346, no. 6216, pp. 1569–1569, 2014.
- [53] M. J. Barry and S. Edgman-Levitan, "Shared decision making—the pinnacle of patient-centered care," *The New England Journal of Medicine*, vol. 366, no. 9, pp. 780–781, 2012.
- [54] M. Huber, J. A. Knottnerus, L. Green et al., "How should we define health?" *British Medical Journal*, vol. 343, no. 7817, Article ID d4163, 2011.

- [55] E. Stolper, M. Van De Wiel, P. Van Royen, M. Van Bokhoven, T. Van Der Weijden, and G. J. Dinant, "Gut feelings as a third track in general practitioners' diagnostic reasoning," *Journal of General Internal Medicine*, vol. 26, no. 2, pp. 197–203, 2011.
- [56] G. van der Bie, *Wholeness in Science A methodology for pattern recognition and clinical intuition*, Bolk's Fundamental Companions, Louis Bolk Instituut, Driebergen, Netherlands, 2012.
- [57] L. Bird, A. Arthur, and K. Cox, "Did the trial kill the intervention? experiences from the development, implementation and evaluation of a complex intervention," *BMC Medical Research Methodology*, vol. 11, article 24, 2011.
- [58] A. M. May and J. Mathijssen, "Alternatieven voor RCT bij de evaluatie van effectiviteit van interventies!?" 2015.
- [59] K. E. Thorpe, M. Zwarenstein, A. D. Oxman et al., "A pragmatic-explanatory continuum indicator summary (PRECIS): a tool to help trial designers," *Journal of Clinical Epidemiology*, vol. 62, no. 5, pp. 464–475, 2009.
- [60] H. Walach, T. Falkenberg, V. Fønnebø, G. Lewith, and W. B. Jonas, "Circular instead of hierarchical: Methodological principles for the evaluation of complex interventions," *BMC Medical Research Methodology*, vol. 6, article no. 29, 2006.
- [61] M. Pérard, N. Mittring, D. Schweiger, C. Kummer, and C. M. Witt, "MERGING conventional and complementary medicine in a clinic department - a theoretical model and practical recommendations," *BMC Complementary and Alternative Medicine*, vol. 15, no. 1, article 172, 2015.
- [62] World Health Organization, *Benchmarks for Training in Traditional/Complementary And Alternative Medicine: Benchmarks for Training in Ayurveda*, vol. 48, World Health Organization, Geneva, Switzerland, 1996.
- [63] World Health Organization, *Benchmarks for Training in Traditional/Complementary And Alternative Medicine: Benchmarks for Training in Unani Medicine*, vol. 20, World Health Organization, Geneva, Switzerland, 2010.
- [64] Board of DIN Standards Committee Services, *Services of Medical Doctors with additional qualification in Homeopathy (MDQH) - Requirements for health care provision by Medical Doctors with additional qualification in Homeopathy*, Beuth Verlag, Berlin, 2015.
- [65] Ministry of AYUSH, 2017, <http://ayush.gov.in>.
- [66] Academy of Integrative Health & Medicine, 2017, <https://www.aihm.org/about/what-is-integrative-medicine/>.
- [67] Y. S. Jaiswal and L. L. Williams, "A glimpse of Ayurveda – The forgotten history and principles of Indian traditional medicine," *Journal of Traditional and Complementary Medicine*, vol. 7, no. 1, pp. 50–53, 2017.
- [68] M. Koithan, I. R. Bell, K. Niemeyer, and D. Pincus, "A complex systems science perspective for whole systems of complementary and alternative medicine research," *Forschende Komplementarmedizin*, vol. 19, no. 1, pp. 7–14, 2012.
- [69] I. R. Bell and M. Koithan, "Models for the study of whole systems," *Integrative Cancer Therapies*, vol. 5, no. 4, pp. 293–307, 2006.
- [70] M. J. Verhoef, L. C. Vanderheyden, T. Dryden, D. Mallory, and M. A. Ware, "Evaluating complementary and alternative medicine interventions: in search of appropriate patient-centered outcome measures," *BMC Complementary and Alternative Medicine*, vol. 6, article 38, 2006.
- [71] S. Galea, M. Riddle, and G. A. Kaplan, "Causal thinking and complex system approaches in epidemiology," *International Journal of Epidemiology*, vol. 39, no. 1, Article ID dyp296, pp. 97–106, 2010.
- [72] H. Boon, H. MacPherson, S. Fleishman et al., "Evaluating complex healthcare systems: a critique of four approaches," *Evidence-based Complementary and Alternative Medicine*, vol. 4, no. 3, pp. 279–285, 2007.
- [73] B. Patwardhan, "Ayurveda GCP guidelines: need for freedom from RCT ascendancy in favor of whole system approach," *Journal of Ayurveda and Integrative Medicine*, vol. 2, no. 1, pp. 1–4, 2011.
- [74] B. Patwardhan, "Integrity of Ayurveda," *Journal of Ayurveda and Integrative Medicine*, vol. 7, no. 4, pp. 189–190, 2016.
- [75] C. H. Weiss, "Theory-based evaluation: Past, present, and future," *New Directions for Evaluation*, vol. 1997, no. 76, pp. 41–55, 1997.
- [76] A. Brousselle and F. Champagne, "Program theory evaluation: Logic analysis," *Evaluation and Program Planning*, vol. 34, no. 1, pp. 69–78, 2011.
- [77] C. Paterson, C. Baarts, L. Launsø, and M. J. Verhoef, "Evaluating complex health interventions: A critical analysis of the 'outcomes' concept," *BMC Complementary and Alternative Medicine*, vol. 9, article no. 18, 2009.
- [78] B. Patwardhan, A. D. B. Vaidya, M. Chorghade, and S. P. Joshi, "Reverse pharmacology and systems approaches for drug discovery and development," *Current Bioactive Compounds*, vol. 4, no. 4, pp. 201–212, 2008.
- [79] W. B. Jonas, "Building an evidence house: Challenges and solutions to research in complementary and alternative medicine," *Forschende Komplementarmedizin und Klassische Naturheilkunde*, vol. 12, no. 3, pp. 159–167, 2005.
- [80] S. E. Dodds, P. M. Herman, L. Sechrest et al., "When a whole practice model is the intervention: developing fidelity evaluation components using program theory-driven science for an integrative medicine primary care clinic," *Evidence-Based Complementary and Alternative Medicine*, vol. 2013, Article ID 652047, 11 pages, 2013.
- [81] S. Savers, "Clinical roundup: selected treatment options for depression," *Alternative and Complementary Therapies*, vol. 20, no. 1, pp. 52–59, 2014.
- [82] T. Adam and D. De Savigny, "Systems thinking for strengthening health systems in LMICs: Need for a paradigm shift," *Health Policy and Planning*, vol. 27, no. 4, p. -iv3, 2012.
- [83] M.-L. Buchholzer, C. Werner, and W. Knoess, "Current concepts on integrative safety assessment of active substances of botanical, mineral or chemical origin in homeopathic medicinal products within the European regulatory framework," *Regulatory Toxicology and Pharmacology*, vol. 68, no. 2, pp. 193–200, 2014.
- [84] G. S. Kienle, A. Glockmann, R. Grugel, H. J. Hamre, and H. Kiene, "Clinical research on anthroposophic medicine - Update of a health technology assessment report and status Quo," *Forschende Komplementarmedizin*, vol. 18, no. 5, pp. 269–282, 2011.
- [85] M. C. Jong, M. U. Jong, and E. W. Baars, "Adverse drug reactions to anthroposophic and homeopathic solutions for injection: A systematic evaluation of German pharmacovigilance databases," *Pharmacoepidemiology and Drug Safety*, vol. 21, no. 12, pp. 1295–1301, 2012.
- [86] R. Teschke, A. Wolff, C. Frenzel, J. Schulze, and A. Eickhoff, "Herbal hepatotoxicity: a tabular compilation of reported cases," *Liver International*, vol. 32, no. 10, pp. 1543–1556, 2012.
- [87] F. Wu and T. Wang, "Risk assessment of upper tract urothelial carcinoma related to aristolochic acid," *Cancer Epidemiology Biomarkers and Prevention*, vol. 22, no. 5, pp. 812–820, 2013.

- [88] P. Zhao, C. Wang, W. Liu, and F. Wang, "Acute liver failure associated with traditional chinese medicine: report of 30 cases from seven tertiary hospitals in china," *Critical Care Medicine*, vol. 42, no. 4, pp. e296–e299, 2014.
- [89] S. K. Karri, R. B. Saper, and S. N. Kales, "Lead encephalopathy due to traditional medicines," *Current Drug Safety*, vol. 3, no. 1, pp. 54–59, 2008.
- [90] S. Prakash, G. T. Hernandez, I. Dujaili, and V. Bhalla, "Lead poisoning from an Ayurvedic herbal medicine in a patient with chronic kidney disease," *Nature Reviews Nephrology*, vol. 5, no. 5, pp. 297–300, 2009.
- [91] L. Creemers, M. Van Den Driessche, M. Moens et al., "Safety of alternative medicines reconsidered: Lead-induced anaemia caused by an Indian ayurvedic formulation," *Acta Clinica Belgica*, vol. 63, no. 1, pp. 42–45, 2008.
- [92] S. J. Genuis, G. Schwalfenberg, A.-K. J. Siy, and I. Rodushkin, "Toxic element contamination of natural health products and pharmaceutical preparations," *PLoS ONE*, vol. 7, no. 11, Article ID e49676, 2012.
- [93] L. Breeher, M. A. Mikulski, T. Czczok, K. Leinenkugel, and L. J. Fuortes, "A cluster of lead poisoning among consumers of ayurvedic medicine," *International Journal of Occupational and Environmental Health*, vol. 21, no. 4, pp. 303–307, 2015.
- [94] M. Wu, M. Fang, Y. Hu, and X. Wang, "Four types of traditional Chinese medicine inducing epileptic seizures," *Seizure*, vol. 21, no. 5, pp. 311–315, 2012.
- [95] J. N. Lai, J. L. Tang, and J. D. Wang, "Observational studies on evaluating the safety and adverse effects of traditional Chinese medicine," *Evidence-Based Complementary and Alternative Medicine*, vol. 2013, Article ID 697893, 9 pages, 2013.
- [96] S.-H. Liu, W.-C. Chuang, W. Lam, Z. Jiang, and Y.-C. Cheng, "Safety surveillance of Traditional Chinese Medicine: current and future," *Drug Safety*, vol. 38, no. 2, pp. 117–128, 2015.
- [97] M. Baghel, "The national pharmacovigilance program for Ayurveda, Siddha and Unani drugs: Current status," *International Journal of Ayurveda Research*, vol. 1, no. 4, p. 197, 2010.
- [98] L. Zhang, J. B. Yan, X. M. Liu et al., "Pharmacovigilance practice and risk control of Traditional Chinese Medicine drugs in China: current status and future perspective," *Journal of Ethnopharmacology*, vol. 140, no. 3, pp. 519–525, 2012.
- [99] H. M. Gao, Z. M. Wang, Y. J. Li, and Z. Z. Qian, "Overview of the quality standard research of traditional Chinese," *Frontiers of Medicine*, vol. 5, no. 2, pp. 195–202, 2011.
- [100] P. Gupta, P. Daswani, and T. Birdi, "Approaches in fostering quality parameters for medicinal botanicals in the Indian context," *Indian Journal of Pharmacology*, vol. 46, no. 4, pp. 363–371, 2014.
- [101] J. Reich and C. Michaels, "Becoming whole: the role of story for healing," *Journal of Holistic Nursing*, vol. 30, no. 1, pp. 16–23, 2012.
- [102] C. M. Greco, R. M. Glick, N. E. Morone, and M. J. Schneider, "Addressing the 'It Is Just Placebo' pitfall in CAM: methodology of a project to develop patient-reported measures of nonspecific factors in healing," *Evidence-Based Complementary and Alternative Medicine*, vol. 2013, Article ID 613797, 9 pages, 2013.
- [103] "Communication from the Commission to the Council and The European Parliament concerning the Report on the experience acquired as a result of the application of the provisions of Chapter 2a of Directive 2001/83/EC, as amended by Directive 2004/24/EC, on specific provisions applicable to traditional herbal medicinal products," in *Document on the Basis of Article 16i of Directive 2001/83/EC*, Commission of the European Communities, Brussels, 2008.
- [104] W. Tröger, D. Galun, M. Reif, A. Schumann, N. Stanković, and M. Miličević, "*Viscum album* [L.] extract therapy in patients with locally advanced or metastatic pancreatic cancer: a randomised clinical trial on overall survival," *European Journal of Cancer*, vol. 49, no. 18, pp. 3788–3797, 2013.