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Research Article

Traditional Medicine, Drug and Clinical Developments

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ABSTRACT

It is recognized that natural plants and their phytochemicals often show unexpected therapeutic responses, relatively lower toxicities in disease managements and longer therapeutic outcomes in chronic diseases. Many medicinal practices based on tradition in east are not familiar with doctors educated with west society. Many traditional treatments are lack of systematic evaluation and education. Long history of natural plants utility for managing numerous chronic diseases was still popular, especially in China and India. Attentions should be made to translate and boost drug discovery and development from traditional medicine (TM). Seeking wisdom from TM is a modern therapeutic challenge to different diseases that are shortage of curability and broad-ranges by modern medicine (MM) globally. Methods and clinical routine for TM are introduced.

To speed up TM investigations in broad-areas, introducing herbal applications and drug development help us to translate medical insights into new pharmaceutical achievements—including theory, practice and updating of new experimental models (animal or disciplinary), plant chemical entity (extracting, structural and evaluation), pharmacological mechanisms (pathophysiology and drug responses) and clinical applications (diagnosis, convention, quintessence and prescriptions) that is still popular in Asians. The therapeutic convention between east and west is different in many ways (diagnosis and treatment logical). However, they are gradually merged under the circumstances of modern era. With the assistance of modern medical educations and artificial intelligence, these progress and merge of therapeutics will be continued. Knowledge progress from ancient wisdoms can provide boundless insights and strategies in managing different clinical diseases and drug discovery worldwide.

KEYWORDS

Medicinal plant, Traditional medicine, Medicinal chemistry, Infectious disease, General practice, Respiratory diseases.

Introduction

Medical practice worldwide

Human beings are vulnerable in nature. He/she is easy to catch diseases or loss of life without public health or medical care. Drug treatment is the commonest options for disease prevention and treatments. Drug licensing and development is an important area for biomedical progress and studies. Generally, drug treatment is easy to handle and relative cost-effective.

Drug category and studies

Different chemical structures and features of drugs show different availability and utility in the clinic. They vary in costs, availability, patents and therapeutic efficacy and actions. The vast characteristics of different types of drugs ask for systematic study of different drug structures and clinical utility.

Natural drug and benefits

Many modern drug treatments for major diseases, especially chronic diseases from the angles of modern medicine (MM) came from natural resources (medicinal herbs or plants) worldwide [1-8]. Today, medicinal plants or chemicals (phytochemicals) still consist noticeable share in drug licensing and disease treatments worldwide. Without natural plant and early medical tradition, systematic drug evaluation and treatment is unimaginable. To introduce with early medical traditions and drug development, contribution and co-work between different aspects of medical disciplines with herbs or plants should be associated and boosted.

Natural Drugs, History and Benefits

Drug development associate with TM

Different from modern therapeutic drugs (synthetic, bio-agents or phytochemical drugs), natural-borne plants or herbs (traditional medicine, TM) have rich history (over two thousand years) and unique therapeutic utility modality [8,9].

An aspect of higher therapeutic index (general herbal medicine oriented, response versus toxicity) may more likely overcome drug-resistance and raw material capacity of therapeutic curability increased unexpectedly. For example, in the initial stage of drug discovery, the most effective antibiotics (penicillin, streptomycin or cephalosporin) are natural chemical products. They are much better than many of synthetic agents like (sulphonamide) in managing serious human microbial infection [9]. Also, honey that is derived from plants can effectively treat bacteria and other infections for skin infection and human immunity [10,11]. Many drug development chain and clinical paradigm discovery should be based on high-efficiency drug evaluation and licensing from resources of plants worldwide.

Pharmacological and therapeutic differences

Overall, the MM was transformed from TM via industrial revolution. Due to the short period of industrial development (100-200 years), many traditions and knowledge of old medicine was not kept worldwide. Many ancient wisdoms have not been completely utilized in drug discovered and development in modern era. Education, tradition and knowledge of TM to ordinary drug developers will benefit and be usefulness in long courses of medical progresses. This Article discusses this relations and common knowledge for TM in pathways of drug development.

Pharmacological and therapeutic differences between TM and MM show property of multilateralism and dramatically systemic changes. Several approaches will fill the gaps in knowledge and technology respectively;

Modern techniques for TM and medical and pharmaceutical studies

- Small quantity of effective elements in natural plants. It makes drug evaluation expensive, false-negative and labor-intensity. Miniature drug sensitivity techniques are recently developed for evaluating drug responses from a plenty of trace and similar phytochemicals in multiple herbs and plants
- Similarity among chemical structures in different plants or microbial. It makes compound evaluation difficulty to compare in suitable ways; Different herbs or plants have similar compounds. Single-cell multi-omics techniques may help such comparisons.
- Computational evaluation for different and novel compounds may speed up such large-scale compound evaluation in plant derivatives
- Modern medicine welcomes drug combination. Ancient wisdom should be borrowed
- Seeking therapeutic philosophy and combination from TM tradition and practice
- Genome-wide study of disease pathology, phenotypes and therapeutics for herbs and phytochemicals

Table 1: Medical philosophy and convention between east and west.

Modern	Traditional (Chinese)
Small quantity of elements in natural plants	Herbs needs to be correctly used
Similarity of chemicals in different herbs	Many herbs are used to different diseases
Drugs to treat in pathogen or diseases	Herbs to treat symptoms (own systems)
Computational for diagnosis & treatment	Herbs are formulized by famous doctors
Treating diseases by single agents	Treating diseases by multiple agents

Features of herbal or plant characters

- Focus on major types of plants for different diseases treatments
- Similarity in chemical structures in different plants and microbial. It makes new compound discovery difficult and costly
- Knowing diagnosis of TM in general
- Why many phytochemicals are more effective than synthetic compounds for deadly diseases, like cancer and HIV infections

Unique features of TM in China

Herbal medicine (HM) has a lot to understand for medical doctors and pharmacologists (medicinal chemistry, pharmacotherapy and medical philosophy, similarity and differences) [6]. Two domains (TM verses MM) support with each other and separate them apart. TM in China is separated and precedent than MM. Understanding, relationship and integration between them may push forward the frontiers for medical science and provide rich pharmaceutical insights and improvements. Different health problems and treatment between TM and MM will produce and predict the therapeutic differences between responses, toxicity and outcome.

Bridging the gap of knowledge and convention between east and west should be promoted. This article tries to introduce areas and disciplines of this scientific progress. Utility of TM knowledge and convention needs no extra-costs to pay patents. It is world intelligence heritage that can provide boundless and high-quality of disease treatment facing continuing challenge in modern era.

Technical barriers

Technical advance is indispensable part of factors to overcome the limitation of current phytochemical discovery, preclinical evaluation and treatment study. Despite technique advances in the past decade, pharmacological efforts to drug discovery is still like a drop in the oceans and high economic burden according to current drug development convention [12-15]. As a result, new initiatives must be carried out to overcome these kinds of drawbacks and challenge—including inventions and campaigns of new evaluative models, low-damage extracting system from microbial and plants (high extracting efficiency and structure identification) [16-30].

Revisit drug utilities resources (past reference records, wide-distributed books and experience from ancient medical wisdoms) can reach some unexpected outcomes for researchers and patients [25]. To implement this campaign, technical innovation and miniature takes leading-role to testify them [31-34]. This mini-review addresses the sources and systems of chemical analyzes on this matter and highlights it with modern points of view, especially from traditional Chinese philosophy.

Different Medical Relations

Relation of Chemistry and Techniques

Drug development is initially a topic of chemistry, including chemical extracts, structure analysis and efficacy responses. Efficacy evaluation by different pharmacological modalities determine and quality and costs of drug development. From the status of current drug development, general chemical structure and characters can be guessed for which types of diseases or targets will be possibly effective. With an advanced technique, a lot of new compounds are separated and purification from vast number of plants or microbial. Economic burden will be reduced for growing compound isolations and cost-effective therapeutics.

Since a lot of newly purified compounds from plants are trace elements, efficacy and responses will be evaluated by miniature techniques. Technical and theory advances (miniature and high-throughput) are only driving-forces for new drug discoveries and updating [35-37]. Knowing this principle can save a lot of money and workload in drug evaluation and development. To update these principle and systems, different kinds of medical knowledge is indispensable for innovation and clinical applications. In addition, different countries have different medical levels and backgrounds. These different medical knowledge is the focus of this article.

Relation between chemistry and drug targets

From the status or pathways of current drug development, general chemical structure and characters can be guessed for which types of diseases will be possibly targeted. and knowledge of compound dosages in the clinic. Knowing some data or principle, we can save a lot of money and workload in preclinical studies and clinical applications based on high-throughput techniques and different pharmacological systems of drug evaluation and development.

To update these principle and systems, different kinds of medical knowledge and philosophy should be associated. In addition, since different countries have different medical levels and pharmaceutical backgrounds, their association and principle will be discovered from one disease to multiple diseases [20].

Relation of TM and drug discoveries

TM has much of knowledge and customs to do for boosting the basis of modern healthcare and drug development. Due to the limitation of today's medical background and knowledge for clinicians and pharmacologists, we introduce different ways of drug develop and medical knowledge of TM in this article.

Many Asian countries, especial China, Japan and South Korea have modern customs and history of treating a wide variety of diseases from natural materials (herbs, plants and acupuncture). These medical practices came back approximately 2000 year ages. A lot of manufactured products from herbs have been widely sold in these countries. These products are very useful for current clinical therapies and drug development in the future.

Relation of ancient books and current traditions

Several medical books of this kind mark the long and complicate tradition and practice in history. For example, cold symptoms among large human population in ancient times (similar as epidemics for viral infections like seasonal flu, avian flu and microbial infections) were treated by TM more than two thousand years [9], which probably makes China and India the most populated countries worldwide. Table 2 shows early books of TM in China. (Table 2). In TM in China, human infections can be regarded as different pathogen of (heat, cold or wind among human bodies). Treatments or drugs will be different for different types of diseases.

Table 2: Earliest books for Chinese medicine in different areas.

Areas	Publications	Authors
Health maintaining	Huang-di-nei-jing	Lost
Acupuncture	Huang-di-nei-jing	Lost
Different herbal property	Shen-nong-beng-cao-jing	Lost
Basis for herb applications	Shang-han-zha-bing-leng	Zhong-Jin Zhang
Emergency	Zhou-hou-bei-ji-fang	Hong Ge
Pulse diagnosis	Mei-jing	Shu-He Wang

Different from therapeutic modalities of TM, MM treatment of a variety of diseases, like leukemia vary greatly in techniques (spontaneous, transgenic approaches, adaptive transfer models, genomic editing, xenograft and others) [35-37]. They are ever-improving and renewable. These similarities and variation of therapeutic areas should be noted for following trends.

Therapeutic Models of TM in China

Explanation for TM for infectious diseases

Repeated utilities of herbal medicine for viral epidemic control and managements had been reported since the era of Zhong-Jin Zhang (AD150-219) in China [18]. According to norm or theory of TM in China, virus-induced fever can be caused by different mechanisms, patient's deficiency in "Yang"—inner energy or outside/inside illness invade (environmental risk factors). TCM doctors can combat these virus-induced patterns of symptoms (like fever, cough and respiratory tract stress) by strengthening, modulating and offsetting these damaged activities in human organs by different medicines [17-22]. The formulated herbal medicines contain large component chemical admixtures like drug combinations in western ways of medical practice (Table 3). Several examples are outlined in Table 3.

Table 3: System comparison for infectious disease between TM and MM.

Diagnosis (partly)	
Western	**China**
Microbial or neoplasia (types or drug sensitivity) Virus (types, strains or sequence) Blood (cell counts and biomarkers)	Pulse (sites, Qi and condition) Tongue color or thickness (heat or cold) Face color (infected organs)
Pathogen	
Modern	**Tradition**
Infectious (viral, bacteria, fungi or others)	**Fever or others** (wind, cold, heat, integrity)
Treatment (partly)	
Western	**Examples in China**
Pathogen inhibitor or immunity(anti-inflammatory, antiviral, antibiotics & vaccine	**Herbal medicine** (Ma-Huang san, Gui-Zhi soups, Double Huang-Lian, Huang-bai

Clinical practice for Chinese tradition

Common practice for different disease management had been systematically initiated since the era of Zhong-Jin Zhang (AD159-210) in China. In his book (Shang-han-zha-bing-leng), he listed a lot of different combination and formulas of plants for various diseases. In Chinese, common doctors treat various patients from these fixed formulas with minus changing according to special targeting on symptoms and organ defect in patients. No genetic abnormality or molecular profiles needs to determine.

These human organs are divided as; heart, liver, spleen, lung and kidney (not similar as western anatomy) and seven pathogens (wind, wet, dry, cold, inner or outside heat and hot). Since these physiological organs are divided as heart, liver, spleen, lung and kidney, new knowledge should be learnt in west pharmacologists or drug developer. Treatment of same symptoms may utilize different drugs (herbs or plants and combination). Correspondingly, one plant formulas may treat different diseases.

Apart from different modalities in disease formation, different therapies and outcomes may occur in diagnosis and medicine between tradition and modern. It can be exemplified as many evidence and theory. Several years' knowledge in TM can help drug evaluation and development in general.

Detailed information will be exemplified in the following

Several formulated soups for cold symptoms (headache, cough, low fever for mild cases) and critical stage (high-fever, bleeding and respiratory tract stress—deadly virus infection (similarity to avian flu or season flu) were applied by Master Zhang, including "Gui-Zhi Soup", "Ma-Huang Soup", "Da-Qing-Long Soup" and "White-Tiger Soup" [9]. These cheap medicinal herbs can be available all the times without any specific preparations (viral detection) and restrictive manufactures (patent coverage or pharmaceutical knowhow).

Historically, this custom has been successively managing a great numbers of virus-infected endemics and save the life of millions over the long history of China (over the past 2,000 years). It suggests that this type of treatment should also be further studied and used in Ebola, HIV, avian flu, Zika epidemic control and eliminations [18-24].

Marketing and popularization in new era

In the future, integration custom of east and west may be emerged in many areas of earth. To suit with medical practice in modern era, TM is transformed from one patient one prescription to formed drugs targeting or formulas in a great patient population. Several formulated soups or balls are given to different patients. This formed TM popularity began at the beginning of last century in China and Japan. This process helps the popularity of HM and TM in China, Japan and south Korea.

Model comparison and integration of disease diagnosis

In the future, integrative therapies of both east and west may be promising and more effective in the clinic. TM knowledge and treatments are based on abnormal symptoms, patient's physiological conditions and functionality of different human organs [16]. Many pathogenic symptoms of serious diseases

such as pulmonary obstructions, fever and mental health can be remedied by TM of herbal medicines [27-30]. Although very few chemical compounds have been systematically identified for Ebola, avian flu, Zika therapeutics in ancient TCM books in China, some phytochemical drugs from microbial or plants in western countries have been available to exhibit higher therapeutic index than synthetic chemical agents [9]. In the earliest, ingredients from microbial or plants, like penicillin were very expensive. Now, these drugs are much cheaper due to technical advancements [6]. From reviewing ancient medical or pharmaceutical books in eastern, we can more easily find effective agents or clinical evidence for many diseases.

Interaction of Evaluative Methodology

Situation analysis

Currently, human diseases are wide-range and diversity for pathology and drug targets [38-59]. Updating drug development architecture, especially natural chemical drug is quite necessary. How to enhance efficacy of evaluative systems for different compounds and disease types (high-throughput evaluative systems and low quantity of chemicals) is a paramount tasks and modern challenge [35,36].

Due to greatly similarity and diversity of phytochemical composition and different diseases, most plants are wide reported with same biological or pharmacological activities, like anticancer, antimetastatic, anti-hyperglycemia, antibiotic, anti-viral, anti-hypertension, free-radical, immune-regulation. Many herbs show such pharmacological activities of many similar diseases. Approximately half pharmacological treatment study for herbs is crud extracts. However, these kinds of pharmacological reports commonly have no special interests for preclinical and clinical therapeutic studies.

Table 4: Collective outlines for new compound evaluation.

Chemical studies	Genetic or molecular systems	Different diseases
Plant selection Plant features Plant category Compound separating Compound purity Structural identification Physicochemical Synthesis Cost consideration Patent Structural category Derivatives Conjugates Drug delivery Nano-agents Safety ADME Side-effective	Reactive oxidative reaction Signal transduction Anti-proliferative efficacy Multi-omics Cerebral edema Genetic regulation RAS, AKT/mTOR, AMPK & others DNA chelating or break Glucose imbalance COX-1, COX-2 & others Gut macrobiotics Inorganic elements Glycolipids Insulin Cerebral volume Different cell viability Enzyme activity Phosphatase/kinase Cell receptors Body immunity Nuclei factors Transmembrane pulp Cell apoptosis Different biomarkers Brain structural and damage Hyperglycemia Sex hormone Prostate function Lipodystrophy Cholesterol Neurotransmitters Growth factors Cytokine or chemokines Cancer plasticity Anti-viral Microbial (viral, bacteria, fungi & protozoan) Blood coagulation Hematological cells (count & types) Lymphatic cell (count & types)	Infectious diseases Cardiovascular Oncology Leukemia Immune-regulation Diabetes Childhood diseases Hematology Dermatology Bronchial Thyroid Gastrointestinal Orthopedics Psychiatric disorders Senile Urinary Nutritional abnormal Sports Kidney Gynecology Andrology Pulmonary Hepatic conditions Heart condition Neoplasm metastasis Rehabilitation Vasculature Goat Multiple sclerosis Pancreatic diseases Epilepsy Psoriasis Vitiligo Arthritics Central Nerve system Neurodegenerative

High-efficacy of phytochemical drug discoveries

With the huge number of evaluative models and disease categories in initial screening, high-efficacy drug development is one of the ultimate goals for pharmaceutical industry. For a newly separated compound, you may wonder what is the disease of this compound targeting? You may be at lost for this problem. If you have a new compound, how do you begin your studies? Its efforts must like a drop in the ocean. To counteract with this limitation, more specific evaluative models and technology should be used in pharmacological logic and studies (Table 4).

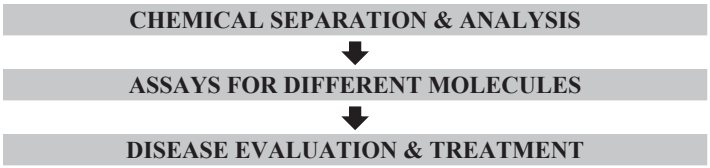

Figure 1: Favorable evaluation of new compounds.

Technical advances

Technical advances, especially in molecular or genomic targets can be more useful in overall pathogenic conditions. Among these new methods, high-throughput, like miniature devise or single-cell multi-omics techniques can bridge the gap between lab endeavors and clinical outcomes of systematic studies [35-37].

By these new techniques, trace amount of pure phytochemical composition can be isolated and compared. For different pathogenesis as many as possible. Following sections like cancer will address it into practical ones (Table 5). A great leap for herb treatment application may be achieved by utility of these modern biotechnology and methodology in general evaluations [37]. Different diseases have different features of pathogenesis and drug targets [38-67].

Table 5: Miniature or new models for cancer activity evaluation.

Evaluative systems	New technology
Chemical isolation	Extracting method perfection and identification
Tumor culture	3-D-culture, organoids & sphenoid
Drug sensitivity testing	Tunable microfluidics & high-throughput
Biomarkers profiling	Single-cell multi-omics
In vivo models	Xenografts & metastatic models in animals

Cost for drug developments

Drug manufactory is highly competitive and risk-taking. Nevertheless, drug discovery, development and manufacture cost much more than ever before [33]. As a consequence, it therefore results in relieving economic burden for medical insurance and patients. Government funding and supports play unique role that will boost country ability in drug development.

Despite drug development that made to alleviating symptoms and deaths improve, high-cost of disease therapies for chronic or deadly diseases changes slightly, especially for the costs of general drugs. Thus herbal therapies may stand out because there is in-exhaustive source of plant compounds in nature and commercial markets in China and India. In addition, numerous drug targets are present. Thus, herbal drug discoveries and developments has great potential and bright future.

Evaluative streamlines

The first step for drug evaluation is random and waste of funds. You may not know how to choose first disease types. We should try to streamline evaluative protocols according to pathways and network (Table 6).

Table 6: Drug evaluative system workflow.

Major techniques	Aims and outcomes for evaluation
High-throughput techniques	Whether it has therapeutic potential or outcomes
Bioassay *in vitro*	Receive 3-8 matched illness for animals
Animal tests *(in vivo)*	Preclinical study of drug responses or toxicity
Clinical validation	High-rate of compound licensing & success

Medical tradition and challenge

Overall, the translation from herbal medicine into modern drug discoveries needs in depth knowledge and cutting-edge technology. In the past, a great amount of work for phytochemical drugs has been carried out long period of times. Generally, almost half chemical drugs are coming from natural microbial, plant and animals. The benefit of HM is drug combination [68-70] and personalized medicine [71-79]. Despite these successes, many obstacles still need to overcome by computational network, [80] and animal models [81-85]. Yet, currently no specific drug developmental system has been widely followed. In this regard, special attention should be focused on natural drug development and evaluative system promotion and cost-reduction.

Chemical and analytical methodology

Drug evaluation and development needs enough compounds to continue. Its contents need ever-growing quantity and purity. Chemical features (structural, quantity, purity and toxicity) should be perfected one by one. Chemical extractive technology determines the structures and quantity of new compounds to be isolated from plants. Currently, the quality of compound isolation is based on different extractive solvents, temperature, pressure, and immobile phase of chromatography, parts of plants and others. However, many articles and experiments in this field were similar in above conditions and no novelty has been created. Some new technology that can help to isolate trace phytochemical composites, especially in low temperature should be used for expanding new agent discoveries. This kind of medicinal chemistry study is indispensable for continuing progresses.

- Ø Provides extractive technology of phytochemicals, like supercritical fluid technology
- Ø Capability of technology of large-scale plant cell cultures for rare and precious plants worldwide

Ø Changing the extractive solvents and methods (different solvents, a variety of temperature and suitable forms of chromatography

Diagnostic and Therapeutic Development

Herbal medicine in new era

Herbal medicine (HM) never lost its territory in China no matter how strong the western medicine influences are spread well in almost all medical circles globally. The hidden foundation for HM presence is due to its simplicity and medical uniqueness that we do not fully understand yet. The aims and focuses on this matter are more popular from our personal visions. We do wish that TM or HM can be influential in many science disciplines, especially in phytochemical drug development and licensing promotions in more countries. Certainly, TM is not always omnipotence. Their disadvantages are also multiples from MM points of views. The most important issue for TM needs to improve itself in knowledge and clinical capability. This is a modern challenge and new trends in pharmacotherapies.

Tradition renew?

Without knowledge regeneration and refreshment, no big breakthroughs will be made in the field of herbal treatment. As a result, a big momentum for the promotion and studies of TM against deadly virus, such as avian flu, HIV/AIDS, or malaria in China is important and useful [17-22].

Accordingly, overwhelming paradigms of HM in long-history (>2000 years) can be kept up was a miracle. Many TM books and theories published in ancient China should be carefully compared with MM knowledge, promote drug evaluation in preclinical or clinical investigation and suggested to traditional renew.

Learning from past

Discovery of artemisinin is exemplified as a new direction. The discovery of this drugs had a survey from ancient records and modern glory (curing life more than million in patients with malaria) worldwide. The major difference for artemisinin discovery with others (like penicillin or digoxin) is from random to ancient records. Qing-Hao-Su (artemisinin) was isolated from herb in native China countryside (sweet wormwood; Artemisia apiacea). This may be not a coincidence. Potential relationships and breakthroughs may be hidden behind ancient books. We may continue these searches for natural drug development in the future.

Pharmacological property of different drugs

Facing the situations of high risks, growing costs and low productivity in modern drug developments [13-16], scientific or technologic efforts should be specified, mainly ranging from cardiovascular, gastrointestinal, infectious, metabolism, central nerve system, and malignant diseases. The advantages of phytochemical drugs are relatively less undesired side-effects and drug cocktail features (mixture ingredients) suitable for deadly viral infectious control and incurable disease managements. Of course, the drug combinations of TM play unique roles for a variety of deadly virus infections and advanced-stage cancer treatments [49-52].

Good clinical therapeutic paradigms and strategies should be continually and sustainably built worldwide. Natural chemical compound treatment commonly benefits to many chronic diseases (taking medicine lifelong in MM). Many of them are currently incurable by MM such as hypertension, type 2 diabetes and others [53-56]. By TM paradigms, some curable therapeutic effects and outcomes may be achieved.

Presently, many first-line drugs against highly mortality diseases, such as microbial-infections, malaria and cancer are more popular and welcomed by phytochemical compounds. Marked advantages of disease managements have been achieved after the discoveries and developments of natural chemical agents, such as penicillin, artemisinin, doxorubicin, camptothecin and so on.

Relation and balancing between risks and responses

The key for disease chemotherapies is the balance between therapeutic responses and toxicities, displaying as therapeutic index gain for new drugs. However, it is difficult to evaluate them in experiments and clinics. To begin with them, it needs to produce enough nature-borne compounds at the beginning of pharmacological evaluation and studies.

The purity of phytochemicals should be high. No or low toxic organic solvents will be kept for therapeutic evaluation. Some healthy separation methods, like supercritical fluids (liquid CO_2) or others should be more frequently utilized. Natural chemotherapeutic agent is expensive for drug purifications and resource limitations from normal environments. To begin with compound evaluation, it needs to produce enough nature-born compounds of therapeutic studies and unique toxic information from other routes like plant cell cultures and healthy extractive reagents.

Many currently incurable diseases, such as HIV-infections or neoplasm metastasis in human bodies [50,51,68-70] might come from insufficient of phytochemical drugs in early stage of experimental and clinical evaluation. In previous studies, phytochemicals can kill pathogens in relatively lower concentrations. This kind of chemical experience should guide us into new horizon.

However, modern technologies are available to reduce the cost of natural chemical production and drug price in the long run. Owing to technical advances, growing number of phytochemical drugs can be introduced into drug markets, clinical applications and produced regularly.

Educational promotion

HM or medical plants in China is different from global medicinal disciplines and regularly western ideology. In addition, many first-line and second-line pure therapeutic chemical drugs such as campthothecine, harringtonine and others were discovered by

western scientists from plant resources. However, some physiology and therapeutic association for many plants were long reported in eastern countries, like India, Pakistan and China [86-88]. To keep up this tradition, existing knowledge should be well educated and distributed and passed down because this will provide great medical opportunity and challenge for all mankind.

Medicinal chemists and pharmacologists worldwide are paying rising attentions on new agent discovery from reviewing volumes of past medical books for various diseases, symptoms and episodes, especially in infectious disease, metabolic, cardiovascular, psychiatric illness and cancer. They will be expanded in new drug licensing and productions.

Although these types of information are very valuable for MM and drug development, these TM books are unpopular in normal medical circles, even in China. These types of information educational course will be promoted in medical schools or continuing education. As a result, regenerating these types of medical practice and drug develop education should be new topics of medical or pharmacology progress in China or other countries. We hope that scientists or medical doctors in western countries can also join in and push forward the boundary of new hypotheses and paradigms proposing, updating, and validating in TM and new drug development systems.

Integration and mutual support between TM and MM

Human disease treatment by TM is still one of hotspots in modern China and growing popularity and benefit worldwide. To bridge the gap between TM and MM, many comprehensive hospitals in China have the special branches or department for many deadly diseases, like cancer therapeutics or other chronic diseases.

Disease treatments by HM is a favorable topic and hotspot in India, Pakistan, and China [86-88]. According to the principles and rules of TM, human bodies are affected and circulated by Qi or bloods (inner upright strength, nutritional supply, pathogenesis and external risk factors). Seeking general medications by changing the medical courses of both TM and MM is proved to be higher quality and outcomes of therapeutic response improvements. Its contains the efficacy of disease prevention, risk factor inhibition and body-functionality strengthen. Utility of both types of therapeutics can improve disease control and survival benefits.

Adjuvant therapeutics

According to current therapies, most herbal, plants, or phytochemicals are used as adjuvant therapeutic agents to treat high-risk or chronic diseases—induction of immune regulation and body functional recovery [89]. These sides of disease therapies show great medical potential or therapeutic response promotion for emerging diseases (outbreak of new diseases). In developed countries, adjuvant therapies can provide indispensable nutrient, cardiovascular complication alleviation and antioxidants for changed organs or tissues, like neoplasm metastasis and others [41,42].

Despite promising in future, adjuvant therapies are not mainstreams of clinical health care in developing or developed countries. At this stage of medical advancements, HM are mostly combined with modern medicine and effective with therapeutic outcomes. Generally, drug combinations can be a good therapeutic models for HIV or advanced cancer patients.

New Drug Developed Modalities

Drug development comparison

Drug development alteration and approaches from earliest to latest have different ideology, knowledge, modality, technique, and pipeline supporting (Figures 2 and 3). How to combine these pathways and information is important avenues and reports for improving disease treatments. Chemical, biological and computational integration to earliest knowledge will be helpful to promote drug development in notable way and new modality establishment.

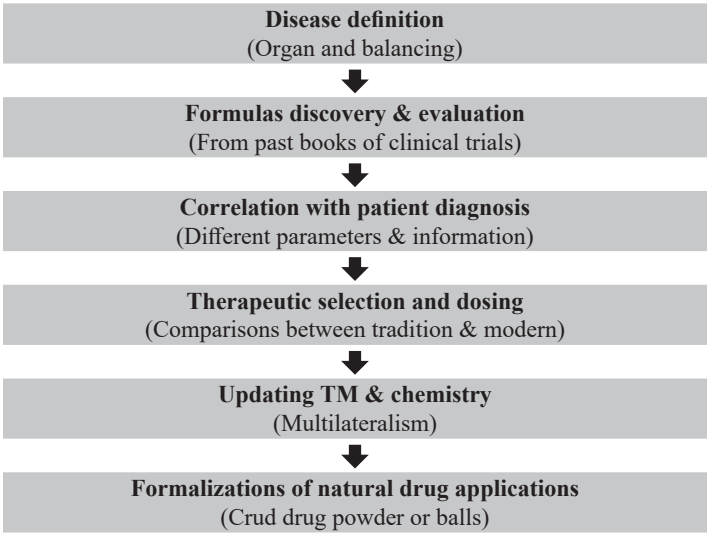

Figure 2: Chinese versions of drug developments in formulas.

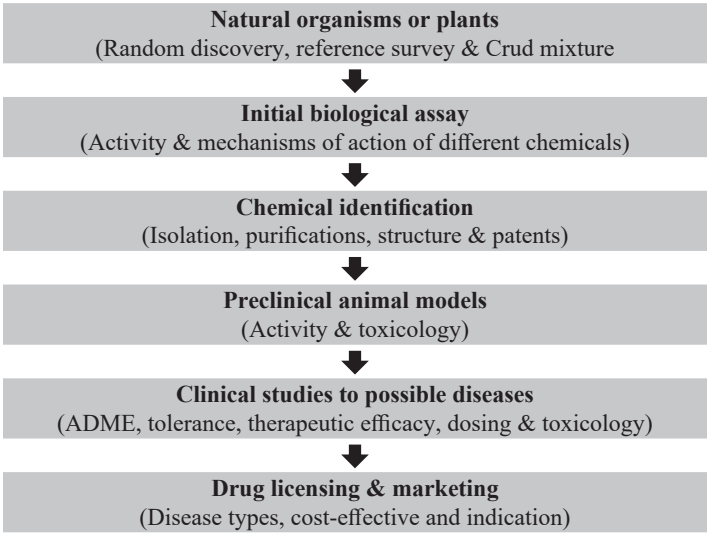

Figure 3: Current models of drug discoveries in chemistry.

Heritage broadening and advances

The qualities of phytochemical agent developments might be improved by deeper understanding TM theories, knowledge, treatment routines, and new modalities. Yet a great difference between western and eastern medical systems exists and mutual impacts. The different ways of discovering phytochemical agents may come from understanding, thinking, and philosophy of ancient wisdoms.

The slow progress of TM is caused by the shortage of knowledge regeneration, heritage passage, and technical advancements, like drug combination and dosing against HIV/AIDS or cancer metastasis [68-70]. Without massive knowledge upholding and distribution worldwide, this side of medical or pharmaceutical heritages and insights will be gradually faded away. TM advancement will boost drug development in modern era.

- Ø Body functional balancing in every types of five entities
- Ø Drug combination in a normal practice
- Ø Drug doses (king, court, assists and soldiers)—Chinese ways of different plant doses

Toxicity evaluation and undesired side-effects

Compound toxicity plays unique role for disease treatment, curability and outcomes of patient's survival. The size and tolerance of compound toxicities and side-effects (maximum efficacy and treatment failure) determines the efficacy and quality of drug treatment to patients. Current experiments and clinical information for herbal evaluation and clinical practice (drug doses and efficacy) is largely devoid in modern ways. More toxic study for plants or phytochemical composition is urgently required. Totally, the toxicity and efficacy of phytochemicals can be improved by structural modification or derivatives. These pharmaceutical work can be commonly used in different stages of drug development.

Currently, many ordinary people believe that natural-borne herbs have less toxicity than normal. This is a misleading point of view. But many natural-borne chemotherapeutic agents generally show much less toxicities than those of synthetic chemical agents at same therapeutic ranges and levels. Natural chemical drugs are somewhat like gifts from the god and we shall cherish them in future generations. Since many plants have general side-effective and efficacy in TM books, we may know many aspects of plants in future studies.

Herbs for emerging viruses or bacteria

There are tremendous different types of viruses in this planet. Many virus emergency and epidemics, like COVID-19, Ebola and Zika viruses infect people all of sudden. Many infectious viruses emerge without specific treatment recommendations or preparedness. To these patients, herbal medicine legendary formulas across the history may be better choice than none. These traditions are very helpful. We herein suggest that TM or phytochemical compositions might be workable avenues for future scientific investigations on different virus-induced pathogenesis and targeted therapeutics by proved plant formulas.

Joint-efforts between pharmaceuticals and medicine

Drug development is medically and pharmacologically progressing year on year, especially in evaluative and diagnostic techniques. More risk factors and drug targets are covered for drug studies and new knowledge. More recently, personalized medicine is similar option from TM in China. Many specificities and knowledge can be borrowed each other (existing formulas in traditional medical books). Figure 4 shows some features of common knowledge in drug evaluation and development. We wish new topics can be created in this field and help patients more with improved therapies (Figure 4).

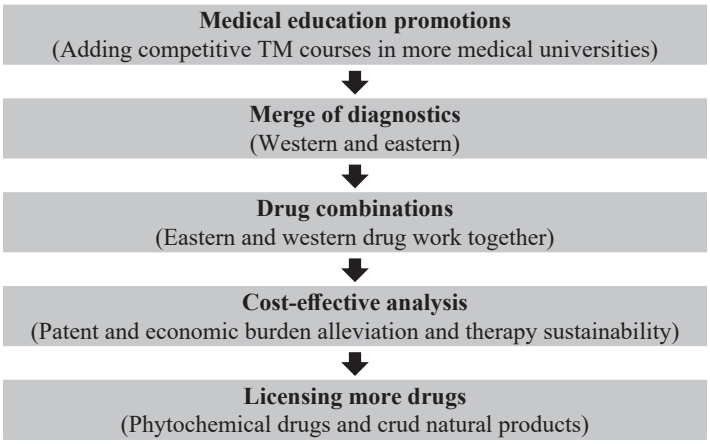

Figure 4: Roadmap for phytochemical drug promotion.

Conclusion

Phytochemical agents or herbal drugs are important options for chronic diseases and against new viral spread. New compound discovery pipelines must be established for favorable phytochemical drug developments and wider clinical applications in uncharted territories. Old tradition can enlighten drug development in unexpected successes. In the future, we must focus on the discovery of natural chemotherapeutic agents and developments of more effective therapeutic drugs on this basis. In order to do this, integration of western and eastern medical practices is a top priority. We shall adhere this dogma forever.

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