

Traditional Medicine Based Drug Development

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Abstract

Currently few of traditional medicines have been developed by blending basic sciences and technologies up to the clinical usage. In future standard traditional medicine based botanical therapeutics will be important in biomedicine developments due to economic background in most parts of the world. Today there are many basic experimental research have being doing for plant based materials. But very limited data can be founded for evidence based use of those experimented plant materials in clinical setup. Therefore this is the high time for develop effective evidence based traditional medicine system in the world. This can be done by evaluating traditional medicine remedies for their pharmacodynamics, pharmacokinetics, stability, shelf life and toxicity par with current standards. Challenge of reproducibility and consistency of herbal remedies can be achieved by developing standard assay markers and chemi-informatic approaches. Further conventional concepts of clinical research design methods may not be adequate when evaluating and conducting clinical trials for traditional medicine. Therefore needs to identifying traditional medicine concepts and develop research strategies for achieve full benefits of these medicine systems. Further there is need to develop and validate a range of parameters applicable to modern and traditional medicines in the light of basic sciences like biochemistry and molecular biology.

Keywords: Traditional medicine; Bio medicine; Modern medicine

Introduction

Currently traditional medicine (TM) is used in primary health care systems in most countries parallel to conventional medicine. Therefore TM should be subjected to rigorous research for their efficacy and safety for better health care. At present there is a high necessity for evidence based clinical drug development with changing of global economic scene. When developing novel drugs using TM candidates it is essential to consider novel standard parameters whenever possible. Quality control of TM is also prerequisite of standard clinical trials. When following evidence based clinical herbal product development cycle it is necessary to follow current standard quality controlling methods viz Good Laboratory Practice (GLP); Good Manufacturing Practice (GMP); Good Clinical Practice (GCP); Chemistry, Manufacturing and Controls (CMC) or Pharmaceutical Quality (Figure 1) [1]. World Health Organization (WHO), 2004 has published guidelines for safety issues in herbal product development (Table 1). According to this categorization it is required to be addressed safety and toxicity before clinical usage of TM.

Clinical Trials for TM

Unique characteristics of TM products are that they are multi component mixtures and they have used in humans in sometimes thousands of years [2]. These two exclusive features sometimes lead to biased decisions in clinical practice in TM. Therefore even it is undergone in excessive clinical practice it is utmost important to validate those TM for better development of health care systems. Some international organizations and national authorities have published statements for supporting clinical trials of TM for develop those drugs in ethical manner [3]. The International Conference on Harmonization (ICH) [4] document makes recommendations on information that should be included in a core clinical study report of an individual study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects. The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is unique in bringing together the regulatory authorities and pharmaceutical industry of Europe, Japan and the USA to discuss scientific and technical aspects of drug registration.

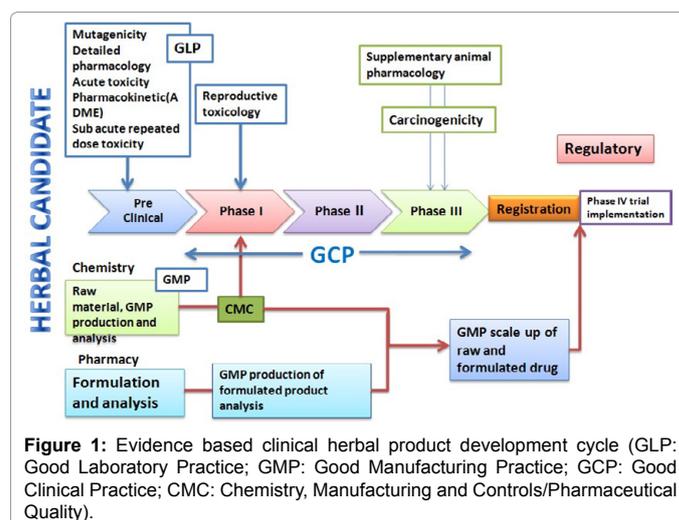


Figure 1: Evidence based clinical herbal product development cycle (GLP: Good Laboratory Practice; GMP: Good Manufacturing Practice; GCP: Good Clinical Practice; CMC: Chemistry, Manufacturing and Controls/Pharmaceutical Quality).

ICH's mission is to achieve greater harmonization to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner [4]. Still most of countries are far behind with guidelines and standardization of TM products for affiliated of ICH. It is much important to achieve global standards in harmonization organizations for remarkable expanded import market for traditional medical products. To achieve these international standards should be assisted by the organizations like World Health

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<p>Category 1: Indigenous herbal medicines</p> <p>These can be used freely by the local community or region, and no safety data would be required. However, if the medicines in this category are introduced into the market or moved beyond the local community or region, their safety has to be reviewed by the established national drug control agency. If the medicines belong to safety category 1, safety data are not needed. If the medicines belong to safety category 2, they have to meet the usual requirements for safety of herbal medicines. Medicines belonging to safety category 3, i.e. 'herbal medicines of uncertain safety', will be identical to that of any new substance.</p>
<p>Category 2: Herbal medicines in systems</p> <p>The medicines in this category have been used for a long time and have been officially documented. Review of the safety category is necessary. If the medicines are in safety categories 1 or 2, safety data would not be needed. If the medicines belong to safety category 3, they have to meet the requirements for safety of 'herbal medicines of uncertain safety'.</p>
<p>Category 3: Modified herbal medicines</p> <p>The medicines in this category can be modified in any way including dose, dosage form, mode of administration, herbal medicinal ingredients, methods of preparation, or medical indications based on categories 1 and 2. The medicines have to meet the requirements of safety of herbal medicines or requirements for the safety of 'herbal medicines of uncertain safety', depending on the modification.</p>
<p>Category 4: Imported/exported products with a herbal medicine base</p> <p>Exported products shall require safety data, which have to meet the requirements for safety of herbal medicines or requirements for safety of 'herbal medicines of uncertain safety', depending on the safety requirement of the importing/recipient countries.</p>
<p>Source: Guidelines for the Regulation of Herbal Medicines in the South-East Asia Region, Based on Developed at the Regional Workshop on the Regulation of Herbal Medicines, Bangkok, 24-26 June 2003, World Health Organization (WHO), 2004</p>

Table 1: Guidelines for the regulation of herbal medicines.

Ethical requirement	Definition
Collaborative partnership	Research leadership must include bilateral representation based on mutual respect between equal partners with community advice. It includes a responsibility to invest in the scientific training and capacity-building for ongoing research in a host country where such resources are not well developed.
Social value	Knowledge gained from the research should have the potential to lead to new generalizable knowledge or improvements in health. Partners should specify in advance to whom benefits will accrue and in what way.
Scientific validity	Research should be designed to produce beneficial and generalizable knowledge. This includes designing research so that it can be feasibly implemented in the settings where it will be conducted.
Fair subject selection	Subjects should be selected on the basis of scientific importance, not based on convenience, vulnerability or bias.
Favorable risk–benefit ratio	The potential benefits of individual participation should outweigh the risks of participation. Benefits to the community or population being studied should also be optimized. Compelling societal benefit can justify risks to individuals in certain circumstances.
Independent review	To maintain the integrity of the research, bodies not tied to the investigators must agree that the risks and potential benefits of the research are justified.
Informed consent	Investigators must obtain valid permission for study participation from subjects in a manner that is sensitive to the cultural context in which the study is conducted.
Respect for subjects	Researchers should have a plan for how the research results will be disseminated; ensuring participants know their right to withdraw, and monitoring the research for relevant adverse events.

Table 2: A comprehensive framework for research ethics.

S. No	Operational guidance: information needed to support clinical trials of herbal products (OG – CTHP)
1.	Conventional modern allopathic medicinal drugs containing a chemically-defined pharmaceutical ingredient, herbal products are, almost always, mixtures of partially or wholly uncharacterized constituents; and that being a mixture provides putative therapeutic advantages of one constituent enhancing the efficacy of one or more others in an additive or synergistic fashion, or of one constituent minimizing the side-effects of others.
2.	OG – CTHP has asserted that assessing their efficacy does not require attempts to purify herbal medicines down to single constituents or chemical entities.
3.	Phase 1 studies in healthy volunteers are generally unnecessary for most herbal medicines if their substantial prior human use conveys reasonable confidence that these regimens can safely be administered to small numbers of carefully monitored clinical participants in phase 2 trials.
4.	Crucial stipulation of the CTHP is that, notwithstanding historical evidence of safety, in both phase 2 clinical trials with small numbers of participants and large phase 3 trials (which include several hundred to several thousand), safety of participants should be assured by a comprehensive literature review as well as by specified protocol provisions.

Table 3: Operational guidance: Information needed to support clinical trials of herbal products (OG – CTHP).

Organization for developing countries and governments also should implement these tasks in their strategic planning.

Ethical Framework for TM

In general research on TM should be followed by the same ethical requirements as all research related to human participants. An ethical framework previously outlined by Emanuel et al. and revised for international research offers a useful starting point for thinking about the ethics of TM research. This framework includes eight ethical requirements for clinical research (Table 2) [5,6]. These ethical requirements are universal and comprehensive but must be adapted to the particular social context in which the research is implemented.

Most of time when conducting TM clinical research has to adapt some methodologies according to relevancy of the context. According to WHO Operational Guidance, Information Needed to Support Clinical Trials of Herbal Products (OG-CTHP) (Table 3) [3], Phase 1 studies in healthy volunteers are generally unnecessary for most herbal medicines if their substantial prior human use conveys reasonable confidence that these regimens can safely be administered to small numbers of carefully monitored clinical participants in phase 2 trials. Crucial stipulation of the OG-CTHP is that, notwithstanding historical evidence of safety, in both phase 2 clinical trials with small numbers of participants and large phase 3 trials, safety of participants should be assured by a comprehensive literature review as well as by specified protocol provisions.

Conclusion

To develop safe and quality drug based on TM is a current needed. For that purposes integrated of basic sciences, modern medicine and TM is essential and it is the golden triangle for novel evidence based drug development n future.

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