PRE-CLINICAL RESEARCH ACTIVITY IN THE CHARACTERISTIC FEATURE OF THE CHAIN OF TRADITIONAL MEDICINE RESEARCH

Pham Xuan Phong, Dinh Thanh Ha, Nguyen Van Cuong
Military Institute of Traditional Medicine

Abstract

The Military Institute of Traditional Medicine (MITM) is a leading scientific institution of traditional medicine, developed according to the combined model of 4 organizations: Institute - School - Hospital - Factory. The characteristic feature of the chain of traditional medicine research activities at MITM is the synchronous organization in 03 modules (traditional medical formulation research - pre-clinical research - clinical research). Research results of each module contribute added value and increase the scientific contents of the final output products; in which, pre-clinical research activity plays a very important role. In the coming time, MITM will focus on some of the following breakthroughs: developing the organization, human resources and professional qualifications for the pre-clinical research activity to meet national and international standards.

Keywords: *Pre-clinical research activity, characteristic feature, traditional medicine research activities.*

I. INTRODUCTION

The Military Institute of Traditional Medicine (MITM) is a leading scientific institution of traditional medicine in the Army comprising a first rank hospital.

At present, MITM develops according to the combined model of 4 organizations: *Institute* (generating new scientific and technical knowledge) - *School* (disseminating new scientific knowledge/educating and training high-level manpower) - *Hospital* (applying new scientific and technical knowledge in practice) - *Factory* (transforming new scientific and technical knowledge into commercial products).

In 2024, MITM carries out 38 scientific and technological (S&T) projects at all levels (02 projects at State level, 17 projects at Ministry level and 19 ones at Grassroot level); of which, there is a S&T Program at Ministry of National Defense level including 18 S&T projects, conducted by 5 military S&T units [1].

Scientific fields of S&T projects of MITM vary, such as: research in medicine applying therapy (traditional medicine - TM, modern medicine or combining TM with modern medicine), research in non-medicine therapy (acupuncture, point press, sauna, qigong…),

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research in combining medicine with non-medicine therapies, research in nursing or in management…

This article focuses on research in medicine applying therapy; in which, clarifies the role of pre-clinical research activity on the chain of TM research process generating a new TM product.

II. TRADITIONAL MEDICINE RESEARCH ACTIVITIES OF MITM

2.1. Pre-clinical research activity on the chain of TM research activities at MITM

Through 46 years of construction and development, scientific research activities of MITM have been continuously improved in terms of organization and management. MITM has been granted the Certificate of registration for S&T activities by the Ministry of Science and Technology.

Currently, at the MITM, research on a new traditional medicine is carried out in a sequential chain in 3 modules (stages): *TM formulation research* (performed at the Center for Applied research and Production of TM), *Pre-clinical research* (performed at the Department of Pre-clinical research) and *Clinical research* (performed at the Center for Inheritance and Clinical trials of TM and at other clinical departments).

2.1.1. TM formulation research module

In 2017, the Center for Applied research and Production of TM was established. It is a research and development (R&D) organization of the MITM, performing as a spin-off to do TM formulation research and to produce final TM products.

At this stage, scientists carry out such research activities: building up the formulation of the traditional remedy, analyzing active compounds in the remedy, testing input materials, extracting the remedy, producing semi-products, developing efficient process to construct prototype, making pilot, doing trail production of TM products at laboratory scale, building unit standards for the final new TM products.

After successful completion of the final series, the new TM products will be tested for quality and stability. If met the requirements, the new TM products will be transferred to the next stage of research on animals (pre-clinical research).

2.1.2. Pre-clinical research module

In 1994, the Department of Pre-clinical research was founded. This is the research organization performing the next stage on the chain of R&D activities of MITM,

carrying out research of new TM products on animals.

Presently, the resources to ensure scientific research activities of the Department of Pre-clinical research include both internal and external sources. In addition to utilizing the available human resources and facilities, the Department also mobilize those from outside partner institutions such as: the Military Medical Academy, Hanoi University of Medicine, Hanoi University of Pharmacy, Military Institute of Pharmaceutical Testing and Medical Equipment, Institute of Medicinal Materials...

From this stage, the new TM products will be trialed for safety (acute toxicity, semi-chronic toxicity, chronic toxicity, and other types of toxicity such as local toxicity, cytotoxicity, and genetic toxicity...).

Next, the new TM products will continue to be evaluated for its pharmacological effects on animal models with diseases according to the researcher's purposes. At this research stage, if the research model does not yet exist, scientists must conduct research to create a new pharmacological model to serve the research. This is the analogy method, performed on an equivalent biological model to help investigate the mechanism and effects of the new TM products on the body of animals that replace humans.

And only in animal models, scientists can apply the trial and error method to test new medicines, which means, if the new medicine has acute toxicity, the research will be discontinued; if there is no acute toxicity, the new medicine will be moved to the next study of semi-chronic or chronic toxicity. If the new medicine has chronic toxicity and the risks to the biological body outweigh the benefits, the research of new medicine will also be stopped. If the new medicine has no toxicity (both acute and semi-chronic toxicity) or does exist but is not significant, it will be forwarded to the research phase to evaluate the pharmacological effects on animal models with diseases. And various trial and error activities during this phase will also be conducted, depending on the scientist's research design.

After completing successfully all phases in this pre-clinical research stage, researchers prepare document of the new TM product for the Research Ethics Committee approval before moving on to the clinical trial stage. The Research Ethics Committee of MITM has been granted an operating code by the Ministry of Health.

During 30 years, the pre-clinical research activities of MITM have gradually been improved,

from simple to complex researches on a variety of pharmacological models. Below is an overview of the development process of pre-clinical research activities.

In the early stage, the MITM carried out some of toxicity studies, such as: research on acute toxicity of essential oils on experimental animals, research on the safety of Ky cuc đia hoang pills and Tu vat đao hong pills on experimental animals.

Next stage up to now, MITM has gradually implemented research projects on a variety of pharmacological models on animals such as researches: the anti-inflammatory and pain-relieving effects of Thong phong hoan pills, the effects of Tu than hoan pills on irritable bowel syndrome, the antioxidant effects of Tieu u hoan, the effects of the worms of *Brihaspa astrostigmella Moore* on reproductive function of male rats, the effects of BĐ liquid (extract of *Eucalyptus citriodora* leaves) on soft tissue wounds, the effect of Nhat gan linh capsules on liver fibrosis…

In addition, the MITM is currently conducting many studies to establish experimental models to evaluate effects of new traditional medical products on animals such as: model of chronic kidney failure on white mice, model of liver cirrhosis on white mice, model of cerebral stroke on white rats...

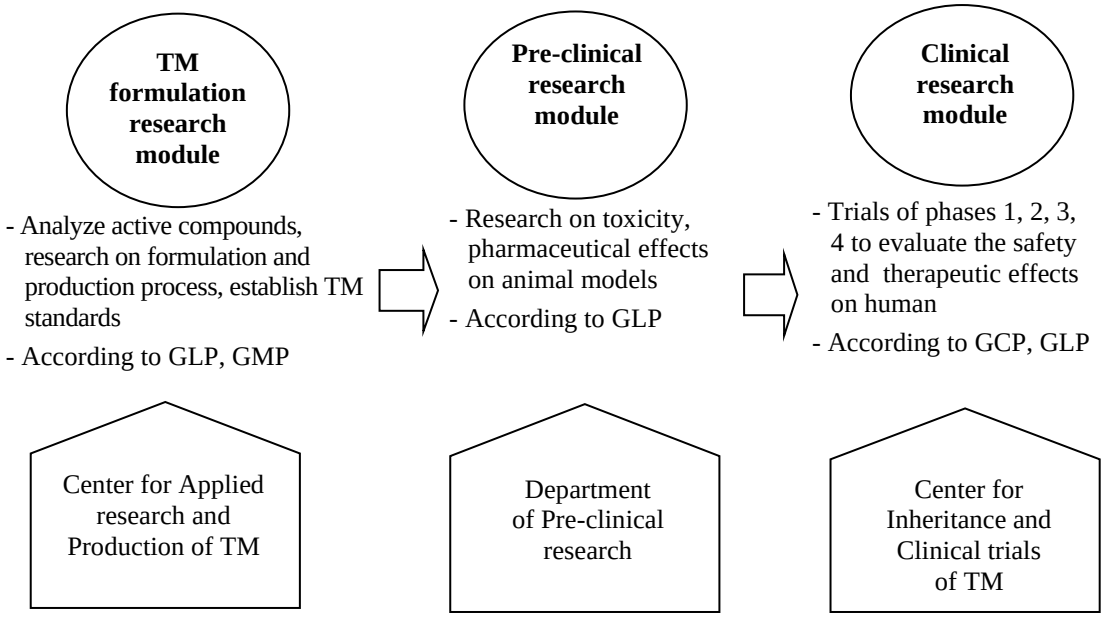
2.1.3. Clinical research module

In 2022, the Center for Inheritance and Clinical trials of TM was established. This is the body in charge of clinical trials - the final stage on the chain of R&D activities of new TM products. The Center is also the coordinator dealing with other clinical departments of MITM to conduct studies on patients in different specialties.

The MITM has been granted a Certificate of Good Clinical Practice (GCP) by the Ministry of Health.

Passing research stages of 3 modules, the quality standards, safety and treatment effectiveness of the new TM product are proven with objective and scientific experimental evidences evaluated by modern medicine equipment and test methods. Besides, the research design also helps retain the specificity and identity of TM according to the system of theory, methodology and clinical practice of TM.

Overview of the chain of 3 modules in doing research at MITM as shown below:



Going on 46 years, the organization of R&D activities in MITM has always been innovated and improved to meet requirements of each development and functional transformation stage, from *Hospital* (treatment, production, R&D, technician training) to *Research Institute* (R&D, postgraduate training, treatment, production). Thereby, the output results of R&D activities in MITM are constantly developed.

Overview of the average number of R&D projects carried out by MITM annually in 3 stages is presented in Figure 1.

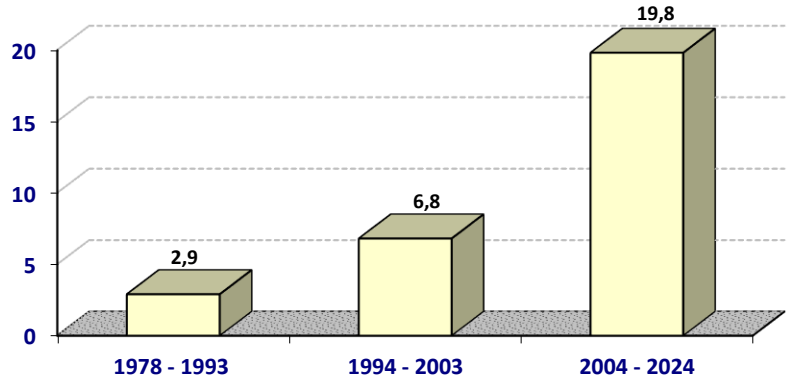


Figure 1. Average number of R&D projects carried out by MITM annually in 3 stages

From these R&D results, the MITM has invented and produced over 60 types of TM products for treatment; of which, currently there are around 30 TM products being paid by the health insurance agency for inpatients and outpatients at MITM.

At present, MITM conducts 38 S&T projects at all levels; in which, there is a S&T Program at Ministry of National Defense level comprising 18 S&T projects at some deferent fields. Regarding the proportion of R&D projects at all levels being carried out by MITM as shown in Figure 2.

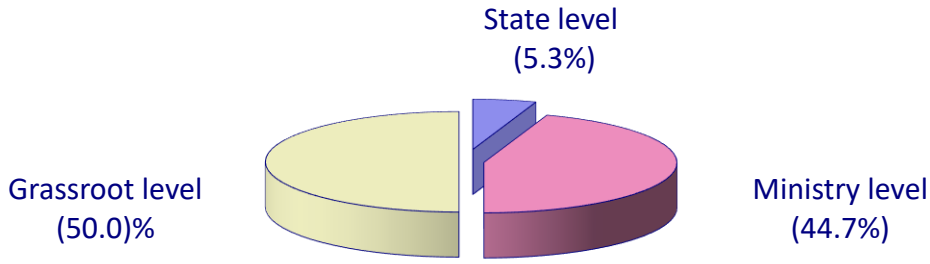


Figure 2. Proportion of R&D projects at all levels being carried out by MITM

2.2. Role of the pre-clinical research organization on the chain connecting activities of R&D - postgraduate training - treatment - production at MITM

With the combined model of 4 organizations: *Institute* - *School* - *Hospital* - *Factory* in MITM, the chain of R&D activities plays a very important role, in which there is the contribution of pre-clinical research module.

If the research project of a new TM product is successful at the TM formulation research module but the pre-clinical research organization does not ensure resources for successful research at the pre-clinical research module, that new TM candidate product will have no practical meaning because it cannot be moved to the clinical research stage to evaluate its treatment effects; and thus a new TM product will not be invented for treatment, as well as for production and commercialization. Therefore the scientific research activities of the organization will also face difficulties.

More over, if it is a doctoral student's graduation project, it will also affect the postgraduate training activity of the organization; in addition, it also affects the publication of the scientific results, negatively impacting the reputation of a leading scientific institution such as the MITM.

Hence, strengthening organization, expanding research cooperation with national and international scientific organizations, investing more resources for pre-clinical research module in order to reach common national and international standards (GLP - good laboratory practice) is

extremely important to improving the R&D capability of all 3 modules at MITM; consequently, contributing to the development of MITM in the current era of S&T revolution boom.

III. DIRECTION FOR PRE - CLINICAL RESEARCH ACTIVITY AT MITM IN THE COMING TIME

3.1. Basis for identifying directions for pre-clinical research activity at MITM in the coming time

3.1.1. Theoretical and policy basis

Identifying some main directions for pre-clinical research activity at MITM in the coming time requires thoroughly grasping the spirits of the guidelines, policies, action programs and instructions of the Central Party, Government, Ministry of National Defense as well as consulting the World Health Organization (WHO) guidelines and must regularly update the new versions of respective documents from these institutions, specifically:

- Party's policy: Directive No. 24-CT/TW dated July 4, 2008 and Conclusion No. 86-KL/TW dated July 10, 2024 of the Party Central Committee Secretariat on the development of Vietnamese TM in new stage [1], [2].

- Government program and guidance from authority agency: Program to develop traditional medicine and pharmacy, combining TM with modern medicine to 2030 issued in Decision No. 1893/QD-TTg dated December 25, 2019 by the Prime Minister [3]; Guidance for pre-clinical and clinical trials of TM and herbal medicine issued in Decision No. 141/QD-K2DT dated October 27, 2015 by the Department of Science, Technology and Training/Ministry of Health [4].

- Direction for developing S&T in the army: Resolution No. 1652-NQ/QUTW dated December 20, 2022 of the Central Military Commission on military science works to 2030 and the following years [5].

- International guidelines: Guideline for Good Laboratory Practice (GLP) for non-clinical research issued by WHO [6]; The WHO TM Development Strategy for the period 2014 - 2023, extended up to 2025 [7].

3.1.2. Practical basis

In addition to the theoretical and policy basis, the direction for the coming time pre-clinical research activity at the MITM also needs to be determined based on the practical basis of R&D results and the S&T development orientation of MITM in particular; as well as the national and international development trend of S&T, the health sector and TM field in general, such as:

- R&D results of MITM in the period 2014 - 2024 [10]; results from organizing and implementing the S&T Program at the Ministry of National Defense level: "Study to develop traditional medicine and pharmacy, combining traditional medicine and pharmacy with modern medicine and pharmacy to improve the quality of health care services for soldiers and people in new stage", code: KCB-CT, period 2023 - 2026, issued in Decision No. 3675/QD-BQP dated October 18, 2021 by the Ministry of National Defense [8]; The MITM's plan on implementing the Resolution No. 1652-NQ/QUTW issued by the Central Military Commission to develop S&T activities to 2030 and the following years [9].

- Today, the rapid development of S&T has profoundly transformed society. S&T has played a huge role, penetrating deeply into all aspects of life, and is a tool to ensure the success of every organization. Science has become the standard measure of all social activities, the striving criterion of all industries and fields. Scientific content is required in every product to meet the increasing demands of consumers, thereby serving as a tool to help compete successfully in the market. The world is in the period of Industrial Revolution 4.0, developing 5G, 6G telecommunication technologies, artificial intelligence (AI), promoting digital transformation, green transformation, and sustainable development. There fore, the field of health science in general and TM in particular cannot be left out of the inevitable development trend of national and international S&T.

TM has a unique advantage that its development is based on green, completely renewable resources (human resource, cultivated herbal resource and natural energy resources). Due to this characteristic, the stronger TM develops, the stronger its regeneration becomes.

3.2. Some directions for pre-clinical research activity at MITM in the coming time

On the basis of the development orientation of the MITM as a leading scientific institution in the new period according to national and international development guidelines, policies and strategies in the field of S&T in general and TM in particular, in the coming time, pre-clinical research activity at MITM need to focus on the following breakthroughs:

- Regarding organization: Develop a plan to mobilize resources, have a specific roadmap to develop in-depth R&D resources for pre-clinical research (Department of Pre-clinical research) meeting GLP standards, connecting synchronously and effectively with TM formulation research and clinical research

modules; closely connect with domestic and foreign research organizations in both TM and modern medicine.

- Regarding human resources: Establish strong research teams, develop leading scientists and talented young scientists in TM pre-clinical research activity.

- Regarding equipment: Invest more facilities and modern pre-clinical research equipment to gradually meet GLP standards.

- Regarding professional: Set aim that all pre-clinical research results meet drug registration requirements; standardize research processes and type II product reports of TM pre-clinical research; meet ethical standards in animal research; set up an international publication roadmap (Scopus, ISI) on TM pre-clinical research results.

- Regarding the scope of research: Expand the scope of herbal research on mainland and island areas, apply the application of digital technological tools such as: Big data, bioinformatics, AI in pre-clinical research models.

IV. CONCLUSION

The characteristic feature of the chain of TM research activities at MITM is the synchronous organization in 03 modules (TM formulation research - pre-clinical research - clinical research). Research output results in each module contribute added value to and increase the scientific content of the new final TM products; in which, pre-clinical research activity plays a very important role. At the end of the R&D stage, the quality standards, safety and treatment effectiveness of the new TM product are proven with experimental evidences of modern medicine as well as the theoretical and practical basis of TM. The TM research activities contribute to improving the treatment effectiveness, postgraduate training and production of MITM.

In the coming time, MITM will focus on breakthroughs in developing organization, human resource, equipment, professional qualifications and expanding the scope of pre-clinical research activity to meet national and international standards.

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