Internal Ex-Post Evaluation for Technical Cooperation Project (SATREPS[1])

conducted by Ghana Office: April 2020

Country Name	Studies of Anti-viral and Anti-parasitic Compounds from Selected Ghanaian Medicinal Plants (SATREPS)
Republic of Ghana	

I. Project Outline

Background	In rural areas in Ghana, despite of the number of people suffering from HIV/AIDS, access to modern medical facilities are geographically and economically limited, and anti-retroviral therapy (ART) against HIV/AIDS was not progressing. In addition, effective medicines for persistent and latent infections were inadequate, and development of more effective medicines was therefore needed. Besides HIV/AIDS, regarding trypanosomiasis[2] (considered as a neglected tropical disease (NTDs)[3]), control and therapies against the diseases were not developed. Due to the limited access to modern medical facilities, people in rural areas have been taking traditional medical treatment which utilizes Ghana-original herbs. In Ghana, more than 3,000 kinds of herbs grow naturally, of which 1,000 active ingredients have been identified, but verification of their efficacy and safety or functional analysis were not sufficiently conducted. Herbal medicine and plants-derived compounds having a very strong pharmacological effect had been found, and strong political concern was given to providing scientific evidence for traditional medicine. There were needs for research on the safety of novel compounds extracted from Ghana-original herbs and anti-HIV/anti-parasitic active compounds.		
Objectives of the Project	Through collaborative research activities with Japanese research institutes, the project aimed at improving research and development capacity of Ghanaian research institutes for Ghanaian medicinal plants-derived anti-viral and anti-parasitic compounds, thereby contributing to continuous studies for pre-clinical and clinical trial of the potential compounds with a certain level of activity and safety in in-vitro experiments conducted in the project. 1. Expected Overall Goal: N.A. [Refer to "Special Perspectives Considered in the Ex-post evaluation"] 2. Project Purpose: Research and development capacity of Ghanaian research institutes for Ghanaian medicinal plants-derived anti-viral and anti-parasitic compounds are improved through collaborative research activities with Japanese research institutes.		
Activities of the Project	Project site: Accra (Greater Accra Region) and Mampong (Eastern Region). 1. Main activities: i) Establishment of the safety of crude extract and isolated compounds with anti-HIV and anti-trypanosomal activity, ii) establishment of bio-assay[4] systems of crude plant extracts, separation and purification of novel compounds, iii) analysis of active compounds with their structure-activity relationship, preparation of the Standard Operating Procedure (SOP), etc. 2. Inputs (to carry out above activities) Japanese Side 1) Experts from Japan: 5 2) Training in Japan: 19 persons 3) Equipment: Cooled centrifuge, high-performance liquid chromatography, fluorescence microscopes, etc. 4) Local cost for research activities, etc. Ghanaian Side 1) Staff allocated: 30 persons 2) Land and facilities: office and research space at the Noguchi Memorial Institute for Medical Research (NMIMR), research space at the Centre for Scientific Research into Plant Medicine (CSRPM), etc. 3) Local cost for research activities, electrical construction for the storehouse of reagents and consumables, etc.		
Project Period	April 2010 to March 2015	Project Cost	(ex-ante) 430 million yen, (actual) 481 million yen
Implementing Agency	Noguchi Memorial Institute for Medical Research (NMIMR), Centre for Scientific Research into Plant Medicine (CSRPM)		
Cooperation Agency in Japan	Tokyo Medical and Dental University, Nagasaki International University		

II. Result of the Evaluation

[Special Perspectives Considered in the Ex-post evaluation]

- Though the Overall Goal was not set at the ex-ante evaluation, the terminal evaluation tells that the Expected Overall Goal would be continuous research for drug development (pre-clinical and clinical trials) on the compounds which had activity and safety in in-vitro experiment during the project period. At the ex-post evaluation, continuation status of this research was verified as the Expected Overall Goal.

1 Relevance

<Consistency with the Development Policy of Ghana at the time of ex-ante evaluation and project completion>

HIV/AIDS control was considered as an important issue following malaria in the "Ghana Poverty Reduction Strategy II" (2006-2009) and also in the "National Strategic Framework II" (2006-2010). At the time of the project completion, the Ministry of Health (MOH) put a priority on development of medicinal plants-derived pharmaceuticals as well as evidence-based traditional herbal medicine.

<Consistency with the Development Needs of Ghana at the time of ex-ante evaluation and project completion>

[1] SATREPS: Science and Technology Research Partnership for Sustainable Development.

[2] Trypanosomiasis is a zoonotic disease transmitted by tsetse flies.

[3] NTDs are communicable diseases that prevail in tropical and subtropical conditions in 149 countries. As of February 2020, eighteen diseases are specified as NTD by WHO, including Dengue, Rabies, and Trachoma.

[4] Bio-assay is a method for examining effects of chemical substances using microorganism and experimental animals.

HIV prevalence rate was 1.9% (2007), and the rate among the youth increased from 1.9% (2003) to 2.6% (2007). Some existing drugs for trypanosoma brought serious side effects, and development of safe and effective drugs were needed. Also, MOH had needs for acquisition of patent on the science and technology research outcomes from the viewpoint of the intellectual property protection and biodiversity conservation.

<Consistency with Japan's ODA Policy at the time of ex-ante evaluation>

In the "Country Assistance Program for Ghana" (2006), one of the Strategic Objectives was improvement of basic social services in deprived areas. Related to this objective, infectious disease control focusing on HIV/AIDS and parasitic diseases including malaria is one of the priority areas.

<Evaluation Result>

In light of the above, the relevance of the project is high.

2 Effectiveness/Impact

<Status of Achievement for the Project Purpose at the time of Project Completion>

The Project Purpose was partially achieved by the project completion. Research and development capacity of NMIMR and CSRPM were partially improved through collaborative research activities with Japanese research institutes, as the indicators show. As anti-HIV compounds, procyanidin trimer (procyanidin C1) demonstrated the strongest activity amongst isolated multimers, but it was not determined as a final candidate compound. (Indicator 1). Regarding anti-trypanosomal compounds, three novel compounds were determined, one of which demonstrated an acceptable level of efficacy in animal testing was considered as a candidate anti-trypanosomal compound (Indicator 2).

<Continuation Status of Project Effects at the time of Ex-post Evaluation>

The project effects have partially continued. Attempts have been made to identify other compounds from cacao shell, although no candidate for an anti-HIV so far has shown the required effect due to lack of collaboration between the two institutes such as further joint research and technical support.

Both NMIMR and CSRPM have continued research on medical plant-derived compounds based on the project outputs. NMIMR has screened 113 medicinal plant extracts. Also, NMIMR has got a cell line panel for cancer and normal cell. In addition, it has tested the toxicity of compounds utilizing the experience obtained from research. CSRPM, in collaboration with NMIMR, has conducted structural modification of determined compounds, research on further detailed mechanism of action analysis in vitro, verification of in-vivo efficacy and safety, pharmacokinetic and pharmacodynamic analysis, and so on.

Most pieces of research equipment provided by the project have been utilized and majority are still functional and in use except the automated analyzer for screening cells.

<Status of Achievement for the Expected Overall Goal at the time of Ex-post Evaluation>

The Expected Overall Goal was not achieved. As of the time of ex-post evaluation, no trials have been conducted on candidate compounds for both anti-HIV and anti-trypanosomal. For anti-HIV therapeutic products, although a compound that activates latently infected HIV provirus was identified, there was no evidence to show the therapeutic effect and hence no need to go ahead to perform clinical trials. As for anti-trypanosomal compound, some level of activity was confirmed in the in-vivo analysis. However, the effects of the identified compounds were not concluded, so there has not been motivation for NMIMR to proceed to pre-clinical and clinical trials. Both institutes would proceed to do pre-clinical and clinical trials if they identify any compound with the required effects in-vivo.

<Other Impacts at the time of Ex-post Evaluation>

Firstly, based on the project experience, approximately 20 articles have been generated by the Clinical Pathology Department of the University of Ghana, and three international articles have been published by researchers in NMIMR in collaboration with TMDU and Nagasaki International University (NIU). Also, researchers from NMIMR together with TMDU and NIU made 15 poster presentations at conferences of the Biomedical Society in Japan and four oral presentations at international conferences such as the Annual Biomedical Convention in Japan organized by the Biomedical Society. Secondly, US and international patents on the identified compounds that had been applied during the project period was approved in 2016. However, US patent renewal has been suspended since 2017. This is because required studies for renewal have not been conducted. However, a domestic patent on the already identified compounds through the project, was obtained in 2017 and the renewal has been continued by NMIMR. No biohazards from research on anti-HIV and trypanosomal compounds have been confirmed at CSRPM or NMIMR.

<Evaluation Result>

Therefore, the effectiveness/impact of the project is fair.

Achievement of the Project Purpose and Overall Goal

Aim	Indicators	Results
(Project Purpose) Research and development capacity of Ghanaian research institutes for Ghanaian medicinal plants-derived anti-viral and anti-parasitic compounds are improved through collaborative research activities with Japanese research institutes.	1. At least one candidate anti-HIV compound is determined for pre-clinical trial.	Status of achievement: Partially achieved (Not continued.). - Procyanidin trimer (procyanidin C1) was purified from Theobroma cacao and identified as a compound that activates latently infected HIV provirus. However, it was unclear whether a therapeutic product with such a mechanism of action would be clinically effective for HIV latent infection. (Ex-post evaluation) - No new compound has been found.
	2. At least one candidate anti-trypanosomal compound is determined for pre-clinical trial.	Status of achievement: Achieved (Continued). - Three novel compounds (one with a novel basic structure and two with its derivatives) with anti-trypanosomal activity from the Ghana-native plant were determined, demonstrating efficacy and safety in vitro experiments. (Ex-post evaluation) - Studies were conducted on some compounds on anti-trypanosome effect to get a point where further analysis (isolation) was performed.

Source: Terminal Evaluation Report, JST Completion Report, interview with CPMR and NMIMRIHH.

3 Efficiency

Although the project cost exceeded the plan due to inflation, the project period was as planned (ratios against the plan: 112% and 100%, respectively). Outputs were produced as planned. Therefore, the project efficiency is fair.

4 Sustainability

<Policy Aspect>

Development of anti-HIV drugs has been prioritized in the "National HIV/Aids Strategic plan" (2016-2020). In addition, prevention of NTDs has been prioritized in programs of the Ministry of Health and other Ministries like the Ministry Gender and Social Welfare.

<Institutional Aspect>

There has been no institutional arrangement for utilization of research outcomes for collaboration among the two institutions, pharmaceutical companies, and government agencies, because of unstable outcomes from clinical tests.

On the other hand, CSRPM has sustained an appropriate organizational structure for research activities such as the Board of Directors where key stakeholders can make high-level management decisions for the center. The center is also equipped with a laboratory and instrumentation room sufficient for research activities. After the embargo on public sector employment was lifted, CSRPM has been in the process of recruiting approximately 65 research and support staff. NMIMR has departments and laboratories dedicated to specific activities, and it has established a center for proof of concept for diagnosis and treatment, which gives technical advice to NMIMR on research activities. NMIMR has utilized research outputs for the training of students and conduct of related research works for drug development. For operation and maintenance of the research facility and equipment installed by the project, CSRPM has had in-house technicians who manage instrumentation rooms and laboratory. Major repairs are outsourced. NMIMR has the Laboratory Manager and facility coordinators. It has also prepared protocols for those without proficiency in using the equipment as part of preventive maintenance practices.

<Technical Aspect>

At CSRPM, two Research Assistants who were hired for the project got employed permanently. CSRPM has annual conferences such as the Annual Biomedical Convention where scientists discuss and share information on new innovations and findings, in order to sustain research capacity. Also, at NMIMR, young researchers who worked with the project have continued their studies. Research assistants have completed or been about to complete a Ph.D. in virology, drug development, and parasitology. In addition, two of the temporal Research Assistants hired by the project have been employed at NMIMR.

<Financial Aspect>

CSRPM has signed the minutes of understanding with the Morehouse School of Medicine of the University of Georgia of the United States to secure necessary research funds on plant medicine for sickle cell, HIV and other areas. It has conducted analysis for the private sectors on commercial terms and also has generated income from sales of the center's own plant medicines. These funds have used also for maintenance of the facility. In addition, CSRPM has received a grant from the West African Health Organization to refurbish laboratories. NMIMR has received financial support from the Research Development and Innovation Division of the University of Ghana to conduct research activities including those based on the project outputs.

<Evaluation Result>

Therefore, the sustainability of the effects is high.

5 Summary of the Evaluation

The Project Purpose was partially achieved by the project completion. Although any final candidate compound was not determined as anti-HIV compounds, a candidate anti-trypanosomal compound was identified. Even since the project completion, both NMIMR and CSRPM have strove for research activities in order to reach pre-clinical or clinical trials for anti-HIV and anti-trypanosomal compounds. . As for the efficiency, the project cost exceeded the plan, but the project period was as planned.

Considering all of the above points, this project is evaluated to be satisfactory.

III. Recommendations & Lessons Learned

Recommendations for Implementing agency:

- It is recommended to both NMIMR and CSRPM to collaborate with each other to identify a candidate compound for anti-HIV through joint research and knowledge sharing.

Lessons learned for JICA:

- No candidate of anti-HIV compound has not been identified until the time of ex-post evaluation. In a project for drug development, it takes quite a lot of time from Basic research to pre-clinical and clinical trials, if some outputs are difficult to be produced during the project period, it should be necessary to start to develop a collaboration system with the private sector or universities in terms of conducting joint research or getting financial support before the project completion, so that the research could be sustained for producing the planned outputs.

Microplate reader (Infinite 200 pro)

Automated analyzer for screening cells (EasyCyte 5HT)