



 Toyama Prefectural Institute for Pharmaceutical Research

Research Center for Drug Development and Quality Control

Center for Innovation in Pharmaceutical Development and Drug Delivery

Medicinal Plants Center



# Institute for Pharmaceutical Research

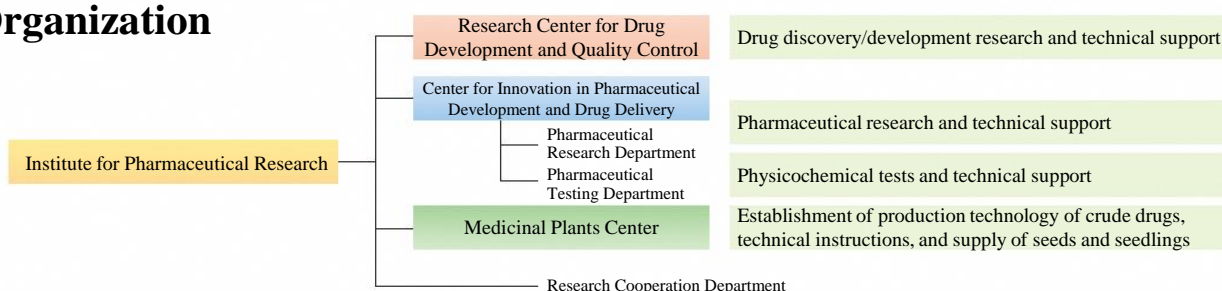
The Institute for Pharmaceutical Research attempts to ensure the quality, efficacy, and safety of drugs and other medical products through research and development, tests, and technology guidance relating to pharmaceutical affairs. And it is contributing to the promotion of pharmaceutical industry in Toyama Prefecture and to the maintenance and improvement of the health of resident .

Toyama Institute for Pharmaceutical Research is the only public research institute specialized for pharmaceutical affairs in Japan and is also a facility unique to Toyama Prefecture where the pharmaceutical industry has been developed as a traditional local industry.

## History

October 1929	Nonprescription Drug Laboratory was established by Toyama Prefecture Nonprescription Drug Trade Association (Sengoku-machi, Toyama City).
April 1932	The laboratory was transferred to the prefectural government, and renamed as Toyama Prefectural Nonprescription Drug Laboratory.
September 1935	The laboratory was moved to within the prefectural office building (1 Shin-Sougawa, Toyama City).
April 1944	Renamed as Toyama Prefectural Institute for Pharmaceutical Industry Service.
November 1947	Renamed as Toyama Prefectural Pharmaceutical Division Laboratory.
August 1952	Renamed as Toyama Institute for Pharmaceutical Research when its new building was constructed (1-4 Chitose-machi, Toyama City).
April 1967	Reorganized into 3 departments of General Affairs Department, Pharmaceutical Research Department, and Pharmaceutical Testing Department.
April 1980	The medicinal plant garden was incorporated as an affiliated institute of the institute (located at Hirono, Kamiichi-machi of Nakaniikawa-gun).
April 1983	The medicinal plant garden was renamed as Medicinal Plants Center.
October 1985	The Institute was relocated at the building newly constructed (Prior location: 17-1 Nakataikoyama, Kosugi-machi, Imizu-gun) Reorganized into 4 departments of General Affairs Department, Pharmacological Research Department, Biotechnology and Japanese/Chinese Medicine Research Department, and Pharmaceutical Testing Department.
March 2015	Opening of Pharmaceutical Development and New Drug Research Support Laboratory.
April 2016	Establishment of Cooperative research base of National Institute of Health Sciences.
April 2018	Renamed as Institute for Pharmaceutical Research and reorganized into 3 centers of Research Center for Drug Development and Quality Control, Center for Innovation in Pharmaceutical Development and Drug Delivery, and Medicinal Plants Center.
May 2018	Opening of Research Center for Drug Development and Quality Control.
April 2019	Establishment of Research Cooperation Department. Opening of new Training facilities in Medicinal Plants Center.

## Organization



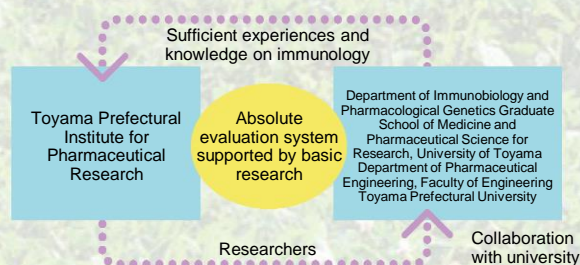


# Research Center for Drug Development and Quality Control

## Overview

Research Center for Drug Development and Quality Control is working on drug discovery/development research and technical support using medical devices and environments available for various research objectives and approaches from in vitro to in vivo conditions.

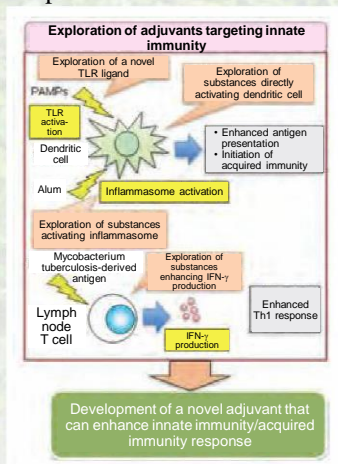
This center has also performed an exploratory research into drug discovery seeds targeting immune cells, in collaboration with Department of Immunobiology and Pharmacological Genetics Graduate School of Medicine and Pharmaceutical Science for Research, University of Toyama (endowed chair at the University in Toyama) from FY 2007 until FY 2018 and with Department of Pharmaceutical Engineering, Faculty of Engineering Toyama Prefectural University since FY 2018.



## Drug discovery/development research

### Research for practical use of intranasal vaccines and prevention of viral infections: development of vaccines effective in elderly people

Intranasal influenza vaccine is attracting attention as a next-generation vaccine in measures against an unpredictable, new type of influenza, as well as for preventing infections with influenza viruses. Since this vaccine requires adjuvants (immunostimulator) that enhance the immune response, basic research for the development of new adjuvants for vaccines has been performed jointly with pharmaceutical companies.



### Research on prevention of lifestyle diseases by the regulation of immune system

Metabolic syndrome occurs due to chronic inflammation and immune abnormality. This center has explored active ingredients that improve dysfunction and cell death in the liver, pancreas, and fat tissue associated with the onset and has aimed for medicinal applications.



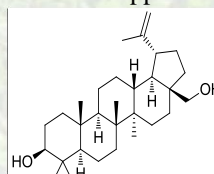
Measurement of antibody concentrations

As a result of the research, glycyrrhiza ingredients were found to inhibit the activation of NLRP3 inflammasome that causes the onset of lifestyle diseases such as type 2 diabetes. Therefore, analysis research on the mechanism of action has been performed.



Glycyrrhiza

A "new drug research based on the restorative effect of white birch constituent, betulin, on cancer immunosuppression" found that a white birch bark constituent, betulin, recovered immune suppression by cancer cells and has investigated the anti-tumor effect of betulin.



Betulin

## Activity Support by Toyama Pharmaceutical Research Association

Toyama Pharmaceutical Research Association was established in 1955 for the purpose of improvement of quality and skills of individual members and contribution to the development of pharmaceutical industry (number of members: 98 individuals in 71 companies [as of June 2018]). This association holds three lectures a year and conducts joint research. The association always recruits new members who support the purpose of this association. Please feel free to contact us for any inquiries.

Contact information » Pharmaceutical Research Association Office within Toyama Prefectural Institute for Pharmaceutical Research  
TEL: 0766-56-6026

### <Implementation of cooperative research by Research Committee>

Cooperative research has been performed for themes decided by each of analysis, drug manufacturing, and biology committees under the instruction of staff of this center. The results of research have been published in the "Home Medicine Development Research Symposium" and other events.



## Research activity/technical support

Research Center for Drug Development and Quality Control has installed high grade analytical equipment and has performed technical support for various needs to promote research and development of high-value added products such as bio-pharmaceutical products.

- Rapid analysis of the cause of disease and proteins as therapeutic target
- Structural characterization of substances as drug discovery seeds and quality attribute analysis of bio-pharmaceutical products
- Development of innovative medications targeting immune/inflammation based on natural/crude drug by using biological technology/mass spectroscopy
- Rapid development of novel pharmaceutical products and improvement of manufacturing/quality control



Mass spectrometer room



Liquid chromatography-time-of-flight mass spectrometry system



Liquid chromatography-tandem quadrupole mass spectrometry system



Multifunctional ultra high performance liquid chromatography



Intermolecular interaction analysis system



Cell sorter

By installing the consulting office and installing conference rooms for training, Research strategy consultation and human resource development for companies and other organizations in Toyama Prefecture have been performed.

- Improvement of technical capacity of companies and training of technicians in the Prefecture in the biology field and formulation technology field.
- Participation and cooperation in 'summer school', in experience learning for high school and junior high school students and in training at university in the Prefecture
- Respective workshops at Toyama Pharmaceutical Association/Pharmaceutical Research Association



Flow cytometer



Inductively coupled plasma mass spectrometer



Consulting office



Large conference room that can accommodate 120 participants

### Analysis committee

**Contents:** A group of mid-level quality control personnel will jointly work on the challenges of the current test method.

**Recent theme:** investigation on the efficiency of the test of a drug and consideration of mass spectrometer

### Drug manufacturing committee

**Contents:** young and middle-level formulation technicians specify themes each year and perform pharmaceutical research on solid dosage form.

**Recent theme:** research on the development of mini-tablets and orally disintegrating tablets

### Biology committee

**Contents:** biological test personnel perform research on the quality assessment of bio-pharmaceutical products.

**Recent theme:** quality assessment of bio-pharmaceutical products (biological assays)



# Pharmaceutical Research Department, Center for Innovation in Pharmaceutical Development and Drug Delivery

## Overview

Pharmaceutical Research Department is working on the development and research of products with a priority on ingestibility, the promotion of product development by pharmaceutical companies through utilization of trial machinery, and human resource development through training for drug manufacturing.

## Research activity

### Development and research of products with a priority on ingestibility

This department has performed pharmaceutical research of “mini-tablet” (a small tablet with around 3 mm in diameter) as infant formulation that is easy to take and the development and research of chewable tablets of Chinese herbal medicine that can be taken without water.



Multi-tip punch and guide

## Instruction activity

### Facility use (fee-based service)

Our drug manufacturing machinery for pilot production has been opened for companies to utilize for their research of formulation.

This department prepares drug manufacturing facilities etc enabling a consistent manufacturing of tablets and granules.

### Facilities enabling pilot production from drug substances to formulations and packaging (mixing → granulation → size reduction → tableting → film coating → packaging)



## Technical consultation

Technical consultation on product development and other matters has been performed by the formulation technology advisor.

## Human resource training activity

### Training of drug manufacturing

Training of drug manufacturing has been performed for researchers and technicians, college students, and high school students. In this training, granules and tablets are experimentally produced using our drug manufacturing machinery for pilot production and physical properties of the granules and tablets are evaluated.

Picture of training of drug manufacturing for students of the Faculty of Pharmacy and Pharmaceutical Sciences, University of Toyama





# Pharmaceutical Testing Department, Center for Innovation in Pharmaceutical Development and Drug Delivery

## Overview

Pharmaceutical Testing Department is working on technical support for tests of a drug.

## Technical support activity

### Facility use (fee-based service)

Our facilities and analytical equipment have been opened for companies to utilize for their tests of drug. Lending service of the Japanese pharmacopoeia standard thermometer, particle counters, and other tools is also available.

### Technical training and consultation

A lecture of analytical techniques for new appointees belonging to the quality control department of companies has been held on regular basis. Technical consultation and instruction on questions concerning tests of drug have also been performed on an as-needed basis.



Lecture of analytical techniques

### Project securing reliability of analysis data

This department has implemented the external investigation of accuracy control concerning tests of drug for drug manufactures in cooperation with Toyama Pharmaceutical Association. The results of investigation are explained in the report meeting and an individualized instruction is provided to improve the testing accuracy when the evaluation results are inadequate.



Dissolution tester

## Participation in project to develop the information on the quality of generic drugs\*

This department has participated in a project that is primarily conducted by National Institute of Health Sciences for the creation of the appropriate environment for promoting the use of generic drugs.

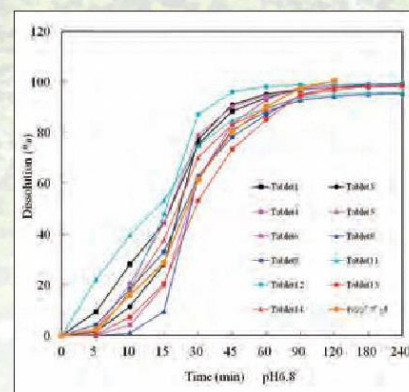
\* Project evaluating the quality equivalence of generic drugs to the original drugs through comparison of dissolution curves (graph on the lower right) with the dissolution tester (picture on the upper right), in order to secure the reliability of generic drugs.

## Tests and studies

Tests of drugs that were collected from drug manufacturers and markets by the Prefecture have been performed. In project to promote the branding of the Toyama peony, a multi-component analysis of the peony has been performed using ultra high performance liquid chromatography.

## Review of the drug marketing approval application form

The specifications and test methods described in the drug marketing approval application form are reviewed.



"Dissolution curves" obtained from the dissolution test

## Cooperative research base of National Institute of Health Sciences

This department has worked on cooperative research/research cooperation on the establishment of test methods concerning the standards for crude drug extracts. With progress of this research, the promotion of research and development of new drugs can be expected.



# Medicinal Plants Center

## Overview

Medicinal Plants Center is working on the establishment of methods for cultivation/formulation and processing of medicinal plants, the supply of seeds and seedlings, and the instruction on spread of cultivation of medicinal plants so that the spread of cultivation can contribute to the development of mountain villages. This center also holds a medicinal plant observation tour and always open the medicinal plant specimen garden so that the citizens in the Prefecture can become more familiar with medicinal plants.

## Research activity

### Project to promote the branding of the Toyama peony

The entire center is committed to branding of the high-quality “Toyama Peony” and building a production system of high-value added crude drug. Cultivation and preparation processing test necessary for expansion of sales channels and cultivation promotion has been performed using excellent varieties that were comprehensively selected based on the evaluation of pharmacological effect, component analysis, and availability from the cultivation aspect.



Bonten



Haru-no Yosooi [Spring Dressing]

### Tests for establishing cultivation methods and improvement tests

In order to be able to produce a higher yield and high quality herbal medicine, tests for establishing cultivation methods have been performed for medicinal plants with the cultivation environment appropriate to the climate in the Prefecture.

Improvement tests of the existing cultivation method have also been performed to take measures for recent climate changes such as global warming and for pests and to save labor for cultivation work.

### Tests for establishing methods of formulation and processing to crude drugs

Components of medicinal plants harvested change in the course of formulation and processing to crude drugs; therefore, studies for establishing the optimal method of formulation and processing have been implemented to ensure the excellent quality as medicinal products.



Examination of the formulation and processing of peony at commercial scale

## Cultivation support

There has been recently heightened momentum to cultivate medicinal plants for effective use of fallow field and as measures for abandoned field. This center recommends cultivation of peony and Japanese angelica of which rush season is different from that of rice cultivation.

### Cultivation instructions

Workshops for growers have been held, and the on-site instructions on cultivation techniques have been performed.

### Supply of seeds and seedlings

Seeds and seedlings of medicinal plants grown at our center are supplied to farmers (fee-based service).



Harvest of peony with digger

## Dissemination of knowledge regarding medicinal plants

A field observation tour has been held for general population in the Prefecture. Consultation on medicinal plants is available as needed.

This center cultivates about 230 varieties of peony. Many residents in the Prefecture have visited the center at the middle and end of May, the timing of flowering of peony.



Peony in full bloom