LIFE SCIENCE

NEWSLETTER OF THE UNIVERSITY RESEARCH FACILITY IN LIFE SCIENCES, THE HONG KONG POLYTECHNIC UNIVERSITY / IS03 / SPRING 2020

Drug Formulation

The journey from ingredients to tablets

MEET OUR NEW DIRECTOR

The University Research Facility in Life Sciences (ULS) has been providing state-of-the-art research equipment to the PolyU research community since its establishment. Many new instruments in the market are indeed essential tools for life science research. In the past 5 years, the ULS has grown together with our users to its present stage. We will continue to make more high-end equipment available so that users can perform high-quality research right on the PolyU campus.

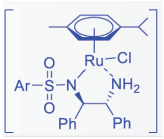
Prof. Thomas Leung, Director of the University Research Facility in Life Sciences (ULS).

> “Our aims are to increase PolyU’s competitiveness in life science research and facilitate interdisciplinary collaborations.”

Our aims are to increase PolyU’s competitiveness in life science research and facilitate interdisciplinary collaborations. To date, the ULS has become a fully functional and well-established life science core research facility, offering access to different types of research equipment as well as research support to our users and PIs.

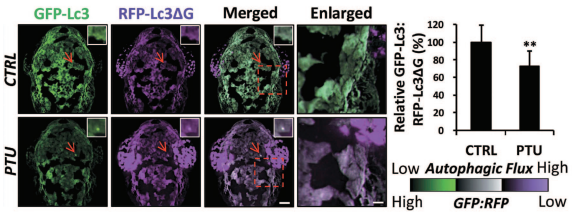
In addition, the ULS is acting as a platform to liaise with researchers from different departments or even other universities. We hope that more researchers can be attracted to set up collaborations and make better use of our equipment. Please do not hesitate to contact us to discuss your research and get advice on how our equipment may assist with your research.

POLYU RESEARCH



Above: Chiral ruthenium(II) *p*-cymene complex of (*R,R*)-diphenyl-1,2-ethylenediamine. *JACS* **141**, 3849 (2020).
Below: PTU treatment activates autophagy in skin cells of zebrafish embryo. *Autophagy* (2020).

1. Prof. W.Y. Yu’s group (ABCT) have successfully demonstrated the enantioselective annulation of 1,4,2-dioxazol-5-ones to γ-lactams by chiral ruthenium(II) *p*-cymene complexes of (*R,R*)-diphenyl-1,2-ethylenediamine in the yield of 97% with excellent enantiomeric excess of 98%. *JACS* **141**, 3849 (2020).



2. Using the Zeiss Lightsheet Z.1 system at the ULS, Dr A. Ma’s group (HTI) reported that 1-phenyl 2-thiourea (PTU) induces autophagy in zebrafish embryos. With PTU being widely used to enhance transparency of zebrafish embryos, their results raise concerns for its use in autophagy-related research. *Autophagy* (2020). Advance online publication.

3. Dr T. Lee’s group (ABCT) investigated the possible role of SHP2 in the development of sorafenib resistance in hepatocellular carcinoma cell lines and patient-derived xenografts, and subsequently examined the potential use of the SHP2 inhibitor SHP099 in combination with sorafenib in treating this deadly disease. *Hepatology* (2020). Advance online publication.

DRUG FORMULATION

The journey from ingredients to tablets

The drug formulation laboratory at the ULS provides a collection of advanced equipment for a complete lab-scale manufacturing process of solid unit dosage form, from hot melt extrusion, spray drying, to dissolution testing, for pharmaceutical research studies.

Compressed tablet is currently the most popular dosage form for pharmaceutical use. It comprises a mixture of active pharmaceutical ingredients (APIs) and excipients. However, the poor bioavailability of potential APIs, which is largely due to the low aqueous solubility and dissolution rate, has imposed a formidable challenge to formulation scientists when such compounds need to be developed into orally bioavailable and therapeutically effective drugs. "Amorphous solid dispersions" is one of the promising strategies to overcome the poor bioavailability of these drug candidates, and hot melt extrusion and spray drying are processes to obtain such amorphous materials.

In the hot melt extrusion process, APIs are mixed with the excipients and fed onto the rotating screw. All materials are then sheared, heated, plastified, mixed and dispersed, and finally pressed into a desired shape **(Fig. 1)**. This improves the bioavailability of drug substances, especially for those having poor water solubility. Besides, specialised drug forms, such as granules, pellets, capsules and films, can be adopted for better drug delivery. The ThermoFisher Hot Melt Extruder Pharma 11 at the ULS is a twin-screw extruder that offers easy material feeding, high kneading and dispersing capacities, and importantly, less tendency to overheat and shorter transit time to prevent degradation of APIs.

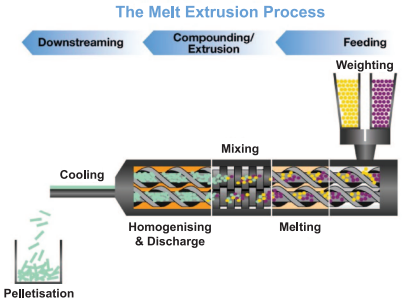


Figure 1. Schematic illustration of a twin-screw extruder and the process of hot melt extrusion. Image courtesy of ThermoFisher Scientific.

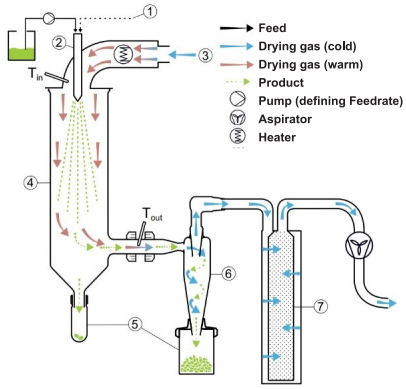


Figure 2. Schematic illustration of the spray drying process. The numerical representation on the figure shows the parts of a spray drier: (1) Feeder for API solution; (2) Atomiser; (3) Drying gas; (4) Spray cylinder; (5) Collection vessel; (6) Cyclone; (7) Outlet filter. Image courtesy of Büchi Labortechnik.

Contrary to hot melt extrusion, spray drying converts a liquid feed of APIs into fine powders. In such process, a solution, a suspension or an emulsion, is atomised into tiny droplets, and subsequently converted to solid particles under a stream of hot drying gas **(Fig. 2)**. The resulting fine powders of APIs will be mixed with excipients in a defined ratio, and further processed with fluidised bed granulation to obtain aggregated granules. During the process, a binder solution is sprayed onto fluidising powder particles to form larger permanent granules **(Fig. 3)** that are in turn dried rapidly under hot air in the fluid bed granulator. The dried granules or powders are then pressed into a desired shape by a tablet presser. At the ULS, the Büchi Mini Spray Dryer B-290, Mini Glatt Fluidized Bed Granulator, and Erweka Tablet Press EP-1 are available to streamline these processes.

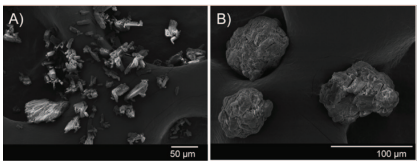


Figure 3. Scanning electron microscopy images of ethenzamide **(A)** powder and **(B)** granules. Adapted from Iwao *et al.*, 2015; *Chem. Pharm. Bull.* **63**, 107.

Before a formulated tablet is tested in an *in vivo* pharmacokinetic study, an *in vitro* dissolution study is performed to examine the release profile and effectiveness of the tablet when dissolving in the fluid of the gastrointestinal tract. This is a critical step in the early stage of drug development and can be performed using the Copley DIS8000 dissolution tester available at the ULS.

COMING SOON

The ULS has recently installed a SCIEX Triple Quad LC-MS/MS System, and upgraded the Leica SP8 and Nikon Super-resolution microscopes with new objectives and software. Please contact our staff for details.

GET IN TOUCH

Y401, Core Y, PolyU
https://uls.polyu.edu.hk
uls.notice@polyu.edu.hk

ULS EQUIPMENT AT A GLANCE

Mass Spectrometry

- Bruker AmaZon Speed ESI-ion Trap-ETD MS
- Bruker UltrafleXtreme MALDI-TOF-TOF MS
- Agilent 6460 Triple Quadrupole LC/MS
- Agilent 6540 Quadrupole-TOF LC/MS
- SCIEX Triple Quad 6500⁺ LC-MS/MS System
- Waters ACQUITY H-Class UPLC with QDa Mass Detector

Fluorescence Microscopy

- Nikon N-SIM/N-STORM/A1 Super-resolution/ Confocal Microscope
- Nikon Eclipse T*i*2-E Live-cell Imaging System
- Nikon SMZ1270i Fluorescence Stereo Microscope
- Nikon NIS-Elements Image Analysis Software
- Leica TCS SPE Confocal Microscope
- Leica TCS SP8 MP Multiphoton/Confocal Microscope
- Zeiss Lightsheet Z.1 Microscope
- Aviris Vision4D Image Analysis Software
- Imaris 3/4D Visualisation/Analysis Software
- MetaMorph Image Analysis Software

Cellular Analysis

- BD FACSAria III Cell Sorter
- BD Accuri C6/FACSVia Flow Cytometers
- Agilent Seahorse XF^{e}24 Extracellular Flux Analyser
- FlowJo Single-cell Flow Cytometry Analysis Software
- Invitrogen Countess II FL Automatic Cell Counter

Biochemical Analysis

- JASCO J-1500 Circular Dichroism Spectrometer
- JASCO CPL-300 Circularly Polarised Luminescence Spectrometer
- Bio-Rad Bio-Plex 200 Suspension Array System
- Malvern MicroCal PEAQ-ITC Automated Isothermal Titration Calorimeter

Genomics and Molecular Biology

- Agena Bioscience MassARRAY Analyser 4 System
- Applied Biosystems QuantStudio 7 Flex Real-time PCR System
- Roche LightCycler 480 Instrument II Real-time PCR System

Small-animal Research

- Perkin-Elmer IVIS Lumina Series III Pre-clinical *In Vivo* Animal Imaging System
- FUJIFILM VisualSonics Vevo LAZR Multi-modality Imaging Platform
- FUJIFILM Vevo LAB Image Analysis Software
- Promethion Metabolic Cage System

General Research

- Drug Formulation Facility
- Bertin Technologies Precellys Evolution Homogeniser
- Labconco Refrigerated Vacuum Concentrator
- Thermo Scientific Cytospin 4 Cytocentrifuge
- Logos Biosystems X-CLARITY Tissue Clearing System

- New or upgraded in 2020