



Thermo Scientific
Pharmaceutical Extrusion and
Analytical Solutions

Streamline Drug Development and Production
Characterize. Materialize. Analyze.

MCIK
SINCE 1982

엠·씨·아이·케이 주식회사
MATERIAL CHARACTERIZATION
INSTRUMENTS, KOREA

Thermo
SCIENTIFIC

Streamline Drug Process Development

Characterize. Materialize. Analyze.

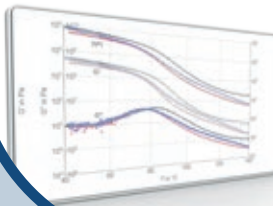
Overcome drug formulation challenges with a scientific approach

When developing new drugs, shortening time-to-market, reducing waste of expensive APIs and minimizing overall development costs provide a distinct competitive advantage for pharmaceutical manufacturers. Let our pharmaceutical process and scale-up expertise help you switch from a batch to a continuous process using twin-screw extrusion technology and analytical solutions, so you can achieve your product development goals.

We can help you **Characterize** drug formulations, **Materialize** the formulation process of poorly soluble APIs and novel Drug Delivery Systems (e.g. implants) and **Analyze** the end product of your development efforts. Reach your drug development goals in less time when you switch from a batch process to a continuous process. We can show you how.

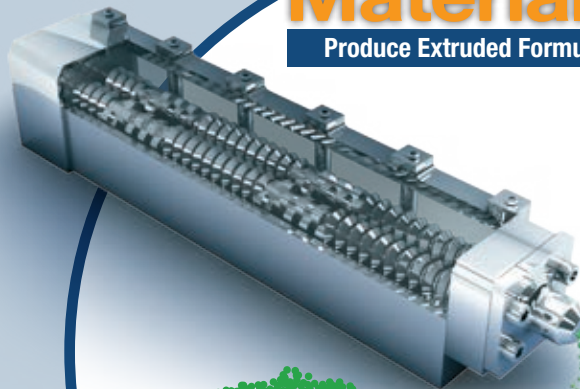
1 Characterize

Understand Formulation Properties



2 Materialize

Produce Extruded Formulations



Phase 0
Preclinical
Research

Pharma mini HME
3–100 g/h

Phase 1
Lab
Scale

Pharma 11
20 g–2.5 kg/h

Phase 2
Process
Development

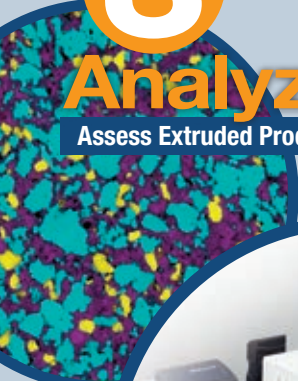
Pharma 16
200 g–5 kg/h

Phase 3
Commercial
Manufacturing

Pharma 24
500 g–20 kg/h

3 Analyze

Assess Extruded Product



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Characterize

Drug Formulation Assessment

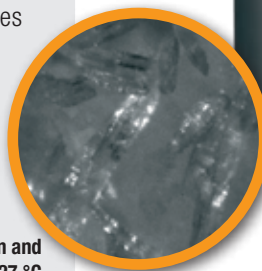
Developing a novel API that exhibits poor solubility and bioavailability into a solid dosage form is crucial for expanding new treatment options. Quickly evaluate new API/excipient formulations with small feasibility studies using instrument solutions that identify the most promising drug candidates that can benefit from a continuous manufacturing process.

Thermo Scientific™ RheoScope Module for the Thermo Scientific™ HAAKE™ MARS™ Rheometer

The HAAKE MARS Rheometer with the RheoScope module is an ideal platform for the simultaneous acquisition of rheological data and microscopic images up to 300 °C with well-defined heating and cooling rates, temperature profiles and shear rates as well as oscillatory testing. Understand sample crystallinity, softening, melting and degradation to streamline formulation development and optimize process variables.

- Integrated optical microscope, digital video camera and temperature control unit
- Image analysis software determines particle size, distribution and structural changes
- State-of-the-art rheometer platform can couple to FT-IR with smart module

Powder mix with 20% Ibuprofen and 80% Soluplus® at 27 °C



MARS Rheometer platform with RheoScope module

Thermo Scientific™ Pharma mini HME Micro-Compounder and Accessories

This GMP compliant, conical micro-compounder for Hot Melt Extrusion (HME) makes it easy to test small formulation batches to determine if your API/excipient is a candidate for HME.

- Requires only 3 g (4 ml) of material for compounding while easy cleaning reduces downtime and hours of labor
- Small footprint reduces clean room volumes, ingredient handling and operator exposure
- Can fit in a laminar flow hood for hazardous API/excipient formulations

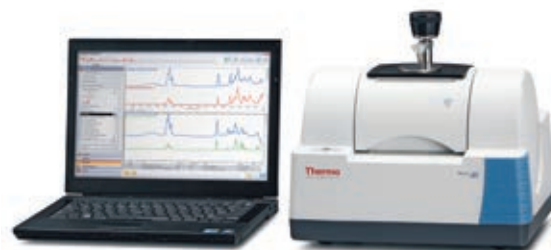


Pharma mini HME

Thermo Scientific™ Nicolet™ iS™5 FTIR Spectrometer

Quickly and easily identify chemical contaminants and mixtures without having to be a spectroscopy expert. Powerful Thermo Scientific™ OMNIC™ software helps identify chemical components and provides quantitative data without cumbersome setup.

- Simple to operate with enhanced algorithms for fast chemical identification
- Diamond ATR accessory ideal for testing solid dosage samples from feasibility studies



Nicolet iS5 spectrometer with diamond ATR accessory

Materialize

Continuous Process Options

Change is good: Switch from batch to a continuous process

The demand on pharmaceutical manufacturers to switch from batch to continuous manufacturing cannot be ignored anymore. Too many competitive advantages come with a shift towards continuous processing to:

- Reduce facility space and capital costs with smaller, efficient equipment footprints
- Minimize loss of raw material and precious API
- Continuously monitor drug quality and ensure 100% inspection
- Increase process flexibility and ability to react to changing market needs

Being a continuous process instrument by nature, the range of Thermo Scientific™ Pharma Twin-Screw Extruders supports the modern formulation scientist with two technologies for creating new solid drug dosage forms; HME or TSG operation. All Thermo Scientific parallel twin-screw extruders are interchangeable between these two processes.

Hot Melt Extrusion (HME) for challenging formulations

Hot melt extrusion (HME) has been used in the plastics and food industries since the 1930s. In the 1980s HME was recognized as a promising technology for enhancing the solubility and bioavailability of poorly soluble APIs. These challenging APIs are often enhanced when they are molecularly dispersed in a polymeric carrier using twin-screw extruders, making HME a valuable technology for the pharmaceutical industry. Promising new actives that cannot otherwise be solubilized, will benefit from HME. The resulting polymer melt is suitable for direct shaping into pellets, spheres, implant, powders, films or patches.

Due to the highly viscous nature of the extrudate, various solid drug delivery forms have been established over the last 25 years using HME such as:

- Controlled release medications
- Patches to deliver transdermal APIs
- Co-extrudates and implants
- Taste-masking formulations
- Fixed dose combinations
- Abuse deterrent formulations



Twin-Screw Granulation (TSG) – Convert to Continuous

Agglomeration of powder mixtures is an important step in the manufacturing process of tablets, which represent over 50% of the most widely used oral dosage forms in use today. Twin-screw extruders can apply shear forces to the powder mixture and disperse the binder liquid to form suitable agglomerates for tableting. With its adaptable screw designs, TSG can be used to form granules with a wide range of desired particle sizes and properties.

Being a time-based rather than a volume-based process, a single modular extruder can produce the required amount of material using only one instrument compared to a batch process requiring multiple sized reaction vessels.

Use the extensive TSG and HME expertise that we can offer to help you seamlessly integrate equipment upstream (e.g., feeders) and downstream (e.g., dryer, coating, forming) for a complete continuous production process from powder to tablet.

Materialize

Pharmaceutical Twin-Screw Extruders

Minimize effort and time when scaling up

Achieve reliable scale-up, reduced time to market, and controlled continuous processing using our Pharma twin-screw extruders for HME and TSG. Successful scale-up starts with precisely engineered extruders that assure geometric similarity throughout the entire product line.

We take a quality-by-design approach to make sure you have a comprehensive understanding of your new process, so you minimize time, number of steps, and materials in achieving your scale-up goals.

Less effort to develop and scale up

Screw elements and barrel design scale geometrically across all Thermo Scientific Pharma twin-screw extruders, allowing easy process scale up.

Fast, easy cleaning between runs

Segmented screw and barrel design quickly disassembles to easily remove residue and support your cleaning validation.

Quickly convert from HME to TSG

Modularity of extruder software and hardware systems allows you to switch continuous processes to fit your formulation challenges.

Waste less material

Twin-screw geometries maximize throughput, efficiently using expensive APIs for formulation development.



Pharma Twin-Screw Extruders	Pharma <i>mini</i> HME	Pharma 11	Pharma 16	Pharma 24
Recommended for	Feasibility	Research Phase 1	Pilot Phase 2	Manufacturing Phase 3
Typical Throughput HME**	3 g batch or 100 g/h	20 g/h–2.5 kg/h	500 g/h–5 kg/h	500 g/h–20 kg/h
Typical Throughput TSG**	*	up to 3 kg/h	up to 15 kg/h	up to 60 kg/h
Dimensions (L × W × H)	650 × 470 × 590 mm	820 × 480 × 410 mm	1750 × 610 × 1220 mm	1900 × 800 × 1300 mm
Downstream Options	<ul style="list-style-type: none"> Take Off Belt 	<ul style="list-style-type: none"> Conveyor Belt Pelletizer 	<ul style="list-style-type: none"> Conveyor Belt Pelletizer Chill Roll 	<ul style="list-style-type: none"> Conveyor Belt Pelletizer Chill Roll
Suitable for	<ul style="list-style-type: none"> Co-Extrusion Implant Production 	<ul style="list-style-type: none"> Co-Extrusion Sheet Extrusion Implant Production 	<ul style="list-style-type: none"> Co-Extrusion Sheet Extrusion Implant Production 	<ul style="list-style-type: none"> Sheet Extrusion High-Volume HME Production
Screw Design	Conical, Co-/Counter-rotating	Parallel, Co-Rotating	Parallel, Co-Rotating	Parallel, Co-Rotating
Max. Torque	5 Nm/shaft	6 Nm/shaft	18 Nm/shaft	52.5 Nm/shaft

* No TSG option ** Depending on formulation

All instruments are made of pharma-grade steel and allow you to meet GMP compliance with access to full validation (e.g., FAT, SAT, IQ/OQ).

Materialize

Smart Process Accessories

The flexibility of the HME process offers you a choice of dosage forms that can be achieved by using Thermo Scientific Pharma extruders. These forms include:

- Powders for tablet pressing
- Extruded sheets for transdermal patches or buccal therapies
- Implants for subcutaneous or intravaginal applications
- Small pellets for capsule filling or direct shaping with injection molding

Did you know that you can design a custom formulation process using a broad array of upstream and downstream accessories for the extruder regardless if you run an HME or TSG process?

See our recommendations below.

	Extrusion Process	Accessory
Upstream: Pre-extrusion Dry raw materials for HME and TSG processes come in a variety of appearances and flow behaviors. It is crucial for the process to precisely and reproducibly meter these powders, granules and pellets into the extruder. These critical upstream accessories become a PAT (Process Analytical Technology) tool that influences overall process performance.	Pre-extruder	Dry Material Feeders Choose from a wide range of volumetric and gravimetric solid feeders with feed screws that adapt to material properties.
	Pre-extruder	Liquid Feeder Devices Select feeders based on temperature-dependent, low and high viscous materials that can be tailored to your specific process needs.
Extrusion Select die designs to create the desired forms needed for producing your solid dosage form downstream.	On-extruder	Sheet Die Designs Form films to produce transdermal patches and mouth dissolvable therapies.
	On-extruder	Co-Extrusion Die Designs Form co-extrudates for contraceptive implants and subcutaneous controlled release forms.
Downstream: Post-extrusion The handling of the still hot and formable extruded material is a crucial part of the manufacturing process. The die design can produce a wide variety of final shapes e.g. films and co-extrudates. Samples can also be shaped for further analysis.	Post-extruder	Chill Roll Precisely control cooling rates to influence the amorphous nature of the drug or control recrystallization.
	Post-extruder	Conveyor belts and strand pelletizers Effectively cool and cut the extrudate strand into pellets of different sizes for direct use or further processing (e.g. milling).
	Post-extruder Sampling	Direct Shaping of Polymer melt Use the Thermo Scientific™ HAAKE™ Minijet Pro Piston Injection Molding System to prepare proof-of-concept samples for analysis.



Analyze

In-Process and Post-Process Assessment

Evaluate your extruded formulation using a variety of techniques to help you optimize your API/excipient mix and extruder parameters. Thermo Scientific analytical solutions include:

- Fourier transform infrared spectroscopy (FTIR) for chemical component identification
- Near Infrared (NIR) for on-extruder monitoring of ingredients
- Raman spectral imaging for studying spatial distribution of chemical ingredients

Thermo Scientific™ HAAKE™ MiniJet Pro Piston Injection Molding System

Quickly prepare small tablet forms of your extrudate using the HAAKE MiniJet Pro system for formulation analysis. You can now reduce costs by efficiently preparing samples from as little as 2 – 12.5 ml of material and avoid wasting expensive ingredients.

- Produce test samples from powders, pellets or melts with minimal material
- Multiple sample geometries are available; standard tablet or custom molds
- Simple design makes it easy to exchange molds with no tools required
- Obtain consistent, reproducible solid forms from the heated cylinder



Thermo Scientific™ Antaris™ II Near-Infrared Analyzers

Monitor chemical composition of your process using analytical methods development platform and sampling system. Near-infrared (NIR) spectroscopy is ideal for quick, reliable material identification and a powerful tool used for multi-component quantitative analysis. Fiber optics makes it an ideal option for in-process monitoring at the extruder die.

- Spectroscopic analysis of active ingredients in formulations
- Made for process analytical technology (PAT) and quality by design (QbD) procedures
- Monitor levels of API and excipients simultaneously
- Multiplexing technology and communication for real-time feedback



Antaris II FT-NIR Method Development System



Antaris MX FT-NIR Process Analyzer with Fiber Optic Probe

Thermo Scientific™ DXR™2xi Raman Imaging Microscope

Identify chemical and structural changes of your extrudate using Raman spectroscopy. Chemical imaging provides visually-driven information for sample evaluation and quality control of solid dosage forms (e.g., extrudates, tablets, films, etc).

- Locate and quantify key components in samples with high-spatial resolution
- Record chemical, structural and morphological changes
- Rapidly image tablets to determine API, excipient and contaminant distribution
- Measure and compare thickness of co-extrusion layers under test conditions



DXR2xi Raman Imaging Microscope

Thermo Scientific™ Nicolet™ iS™ 50 FTIR Spectrometer

Analyze drug formulations and polymorphs using FTIR spectroscopy. The Nicolet iS50 spectrometer provides expanded capabilities to become a flexible analytical workstation. Optional automated beamsplitter exchanger goes from near- to far-infrared spectral analysis with one-touch ease.

- Raman module identifies polymorph and NIR module allows QC methods development
- Built-in diamond ATR provides a second sampling station for quick tablet assessment
- Powerful Thermo Scientific™ OMINC™ software identifies components in minutes



Nicolet iS50 spectrometer with ATR and beamsplitter exchanger

Services

Process Development Services and Consultation



Knowledge and experience working for you

Stay confident knowing that our worldwide instrument training and services are here to enhance your workflow and protect your investment. Your success in developing new therapies is our biggest reward. Start with an in-depth consultation with one of our technical sales experts to find the right solution for your pharma process and budget.

We are able to consult with you:

- Preferred equipment suppliers upstream and downstream of your process to make our instrument integration seamless
- Contract research or manufacturing organization (CRO/CMO) to meet regulatory and scale-up needs

Feasibility made easy

Many of our analytical instruments are available for demonstrations in your own laboratory or process facilities. For twin-screw extruders and compounders, our consultants may advise an Application Feasibility Testing service of your API and polymers/excipients at one of our state-of-the-art facilities in the US and Germany. For special requests we have labs that can handle high-potency, potentially hazardous APIs for unique feasibility studies.

Exceptional post-sale support

Equipment installation supported by certified engineers and IQ/OQ procedures is just the beginning. We offer an array of fee-based optional services after installation that can help you:

- Provide comprehensive training programs for your scientists and technicians
- Extend the warranty coverage with all parts and labor included
- Gain better cost control over inspection and repair equipment with pre-set fees
- Minimize downtime with routine maintenance and calibration as well as emergency response services

Available services may vary between analytical and scale-up equipment, so please review options with your technical sales engineer.

www.thermofisher.com/extruders

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