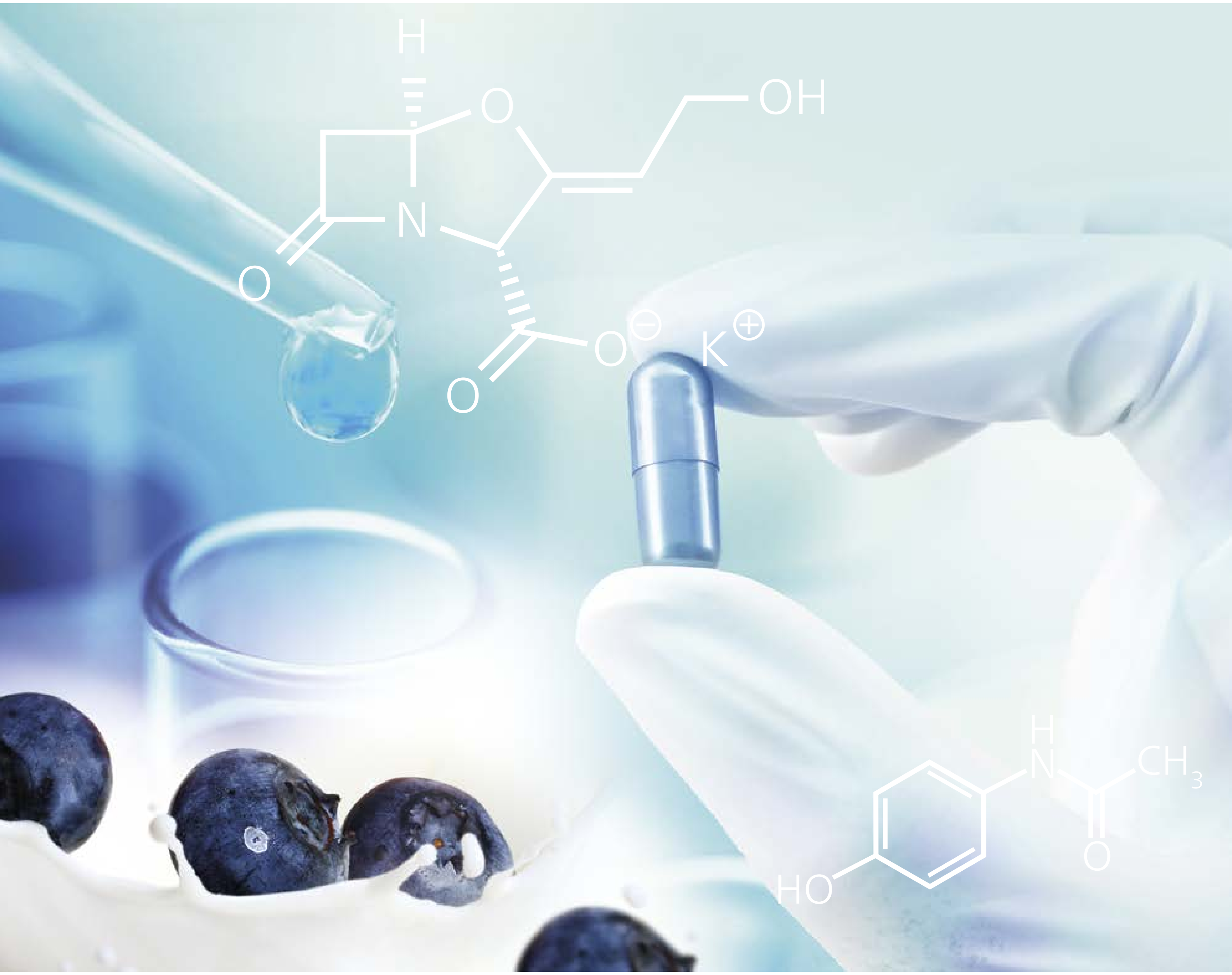
NETZSCH

Proven Excellence.



Investigation of Pharmaceuticals, Foods and Cosmetics with the NETZSCH *Nevio* Instrument Series

with Proteus® Protect

Analyzing & Testing

Nevio
High-end DSC, TGA and STA equipments

THERMAL ANALYSIS

Essential for Every Laboratory ...

Thermal Analysis is a set of techniques which have been used in countless laboratories around the globe to analyze and characterize organic and inorganic substances – whether solid or liquid. Classical Thermal Analysis assesses changes in material properties during heating or cooling with regard to mass loss, dimensional changes or phase transitions. The methods most frequently applied are:

- Differential scanning calorimetry (DSC)
- Thermogravimetric analysis (TGA)
- Simultaneous thermal analysis (STA, which is a combination of DSC and TGA)

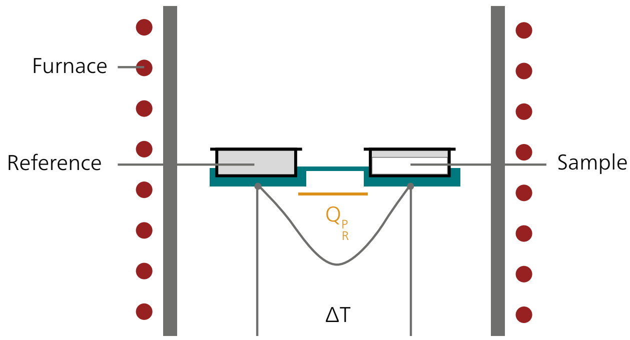
Differential scanning calorimetry (DSC) is by far most commonly employed, followed by thermogravimetric analysis. Both techniques are also included in various pharmacopeias (European – EP, Japanese – JP, American – USP, Chinese – ChP, etc.).

The NETZSCH *Nevio* instrument line is specifically designed to meet the needs of the chemical, pharmaceutical, cosmetics and foods branches. It is therefore optimal for research and development, quality control and contract testing in these areas.

The devices are easy to operate, precise and reliable, and offer a lot of clever solutions, including a handful of ways to automate your day-to-day work.

... in the Chemical, Pharmaceutical, Cosmetics and Foods Industries

Information Obtained from DSC and TGA

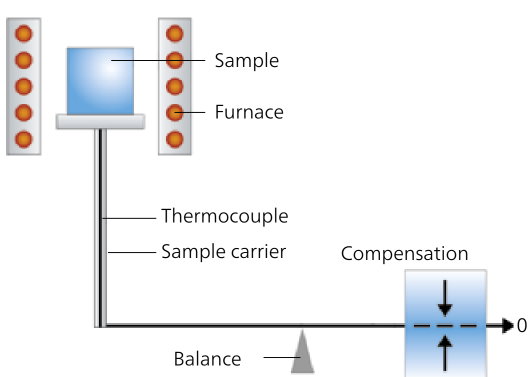


Cell of the DSC 204 ***F1***/214 *Nevio*

DSC measures the change in heat-flow difference into a sample and a reference material while they are subjected to a controlled temperature program. In a heat-flux DSC, the difference in heat flow between sample and reference is derived from the temperature difference between sample and furnace and reference and furnace or between sample and reference.

DSC Results

- Melting temperatures and enthalpies (enthalpies of fusion)
- Polymorphism
- Crystallization temperatures and enthalpies
- Glass transitions (e.g., amorphous content)
- Solid-solid interactions
- Compatibility
- Phase diagrams
- Eutectic purity
- Solid-fat content
- Reaction temperatures and enthalpies
- Cross-linking reactions (curing)
- Specific heat capacity (c_p)
- Oxidation-induction time and temperature (isothermal and dynamic OIT)



Principle of the top-loading TG 209 ***F1/F3*** *Nevio*

Thermogravimetric analysis, or TGA (also known as thermogravimetry, or TG) measures the mass change of a substance while the sample is subjected to a controlled temperature program.
“Top-loading arrangement” simply means that the sample is located above the balance. This ensures safe and easy handling.

TGA Results

- Thermal stability
- Compositional analysis
- Mass changes
- Decomposition behavior
- Pyrolysis
- Water amount
- Identification of solvents (also intercalated ones)
- Oxidation
- Shelf life
- Thermal kinetics (combined with Kinetics Neo)
- Identification of evolved gases (coupled to a gas analyzing system such as FT-IR, MS or GC-MS)

The Complementary Methods DSC and TGA

The strength of DSC lies in its capability of detecting and monitoring a material's phase transitions. However, the reason for a DSC effect is not always obvious; it might be:

- a polymorphic transition,
- a melting effect, or
- an effect caused by a mass loss.

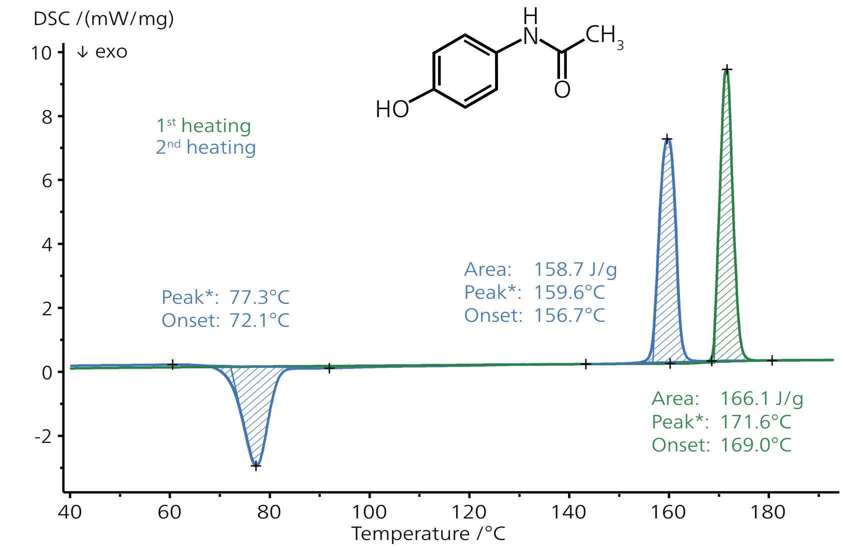
Therefore, DSC and TGA are very often used as complementary techniques. By applying the methods in combination, it is possible to distinguish whether an effect is related to structural changes and to determine in which temperature ranges mass changes occur. This information facilitates interpretation of the effects detected – especially when a sample's composition is unknown.

Improving Interpretation by Coupling Evolved Gas Analyzers to Thermal Analyzers

In order to gain a deeper understanding of what happens during evaporation and decomposition processes, it is possible to couple an evolved gas analyzer (e.g., an FT-infrared spectrometer (FT-IR), mass spectrometer (MS), or gas chromatograph-mass spectrometer (GC-MS)) to the thermal analyzer.

Many laboratories already use FT-IR, and for them, coupling to a thermal analyzer is only logical. However, FT-IR is not capable of recognizing homonuclear diatomic molecules such as N_2 and O_2. In such cases, then, mass spectrometry is usually the method of choice – as it also is under other specific sets of circumstances. GC-MS is often coupled to thermal analyzers such as TGA and STA in situations where complex gas mixtures are present, such as with the decomposition of large organic compounds.

Meaningful Conclusions Drawn from Thermal Analysis Curves

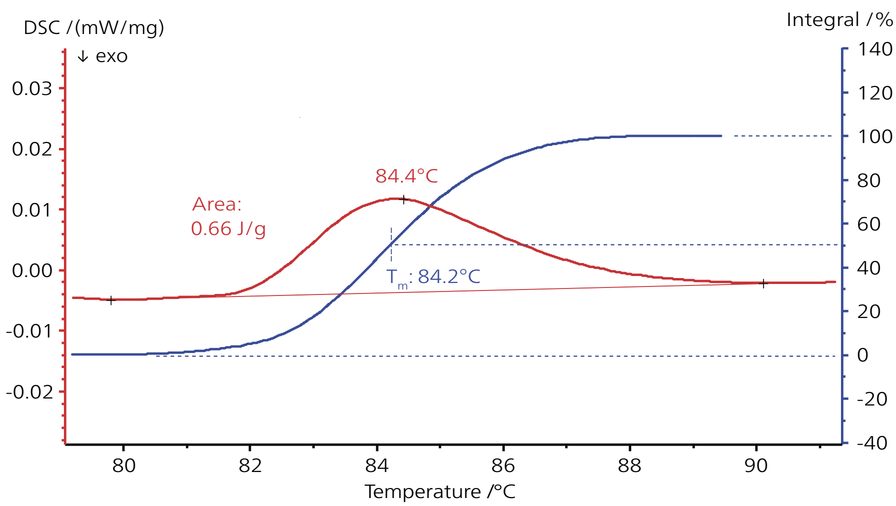


DSC measurement on paracetamol (4-acetaminophenol); sample mass: 2.6 mg, Al crucibles with pierced lid, heating rate: 10 K/min, nitrogen atmosphere

Polymorphism of Paracetamol

Upon application of a heating-cooling cycle, this sample exhibits just one DSC peak within the 1st heating (green). The extrapolated onset temperature at 169°C correlates well to the melting point of the crystalline form I.

No crystallization takes place during the subsequent cooling (not shown here). However, a post-crystallization (exothermal) occurs at 77°C (peak temperature) within the 2nd heating (blue). The resulting modification is not the same as what was present before. The extrapolated onset temperature of less than 157°C is a sign for the presence of form II with a theoretical melting temperature of 156°C.



DSC measurement (red) on an aqueous protein solution; sample masses: 1.38 mg (protein)/4.16 mg (water), stainless steel pressure crucibles, heating rate: 5 K/min, nitrogen atmosphere; integral of the DSC curve (blue).

Denaturation of Double-Stranded DNA

During the thermal treatment of desoxyribonucleic acid (DNA), the helical structure transitions into isolated single strands. This transition can be observed as an endothermal effect in the DSC thermogram (red). By plotting the heat flow versus time during the transition as an integral (blue), the temperature at which 50% of the helical structure has been denatured can be determined. This temperature is a measure of the stability of the helix and is also designated as the melting temperature (T_m) of DNA.

Characterizing Materials ...

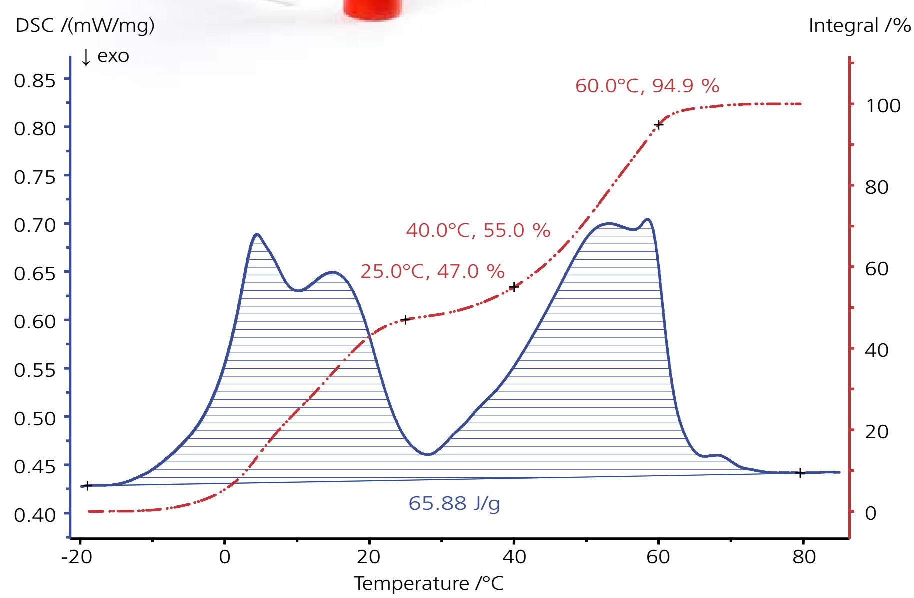
Solid-fat content investigations to ensure smooth application of lip balms

Maintaining the Feel and Spreadability of a Lip Balm over a Broad Temperature Range

Lip balms usually consist of various waxes or fats plus cosmetic additives which care for the lips. Shown here is the melting behavior of a commercial lip balm between -20°C and 85°C, recorded by DSC. Altogether, five superimposed peaks can be seen.

The melting progression is reflected by the integral curve (red). At 25°C, 47% of the mixture is already molten (liquid portion) and 53% (= 100% minus 47%) is still solid. Therefore, the amount of the "solid-fat content" in the present case is 53% at 25°C, 45% at 40°C and just 5.1% at 60°C.

The portion which is already molten at room temperature serves for creaminess and smooth application.

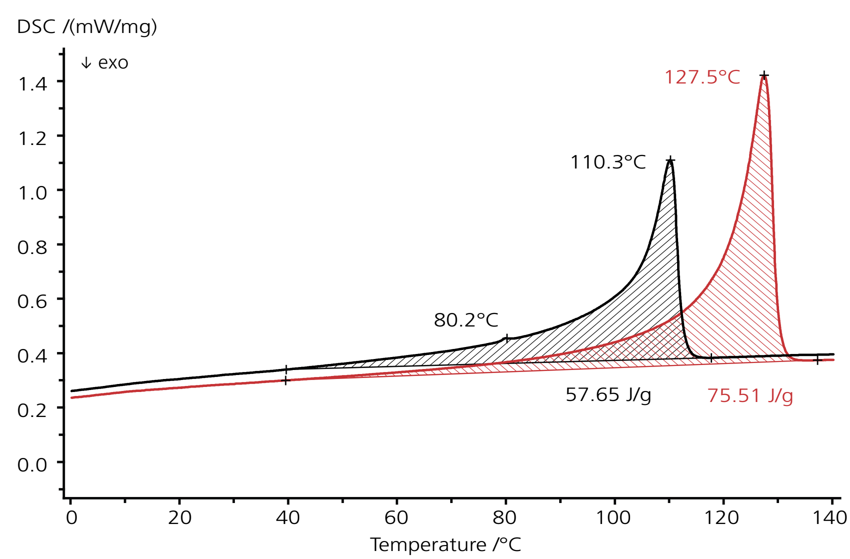


DSC measurement on a lip balm (blue curve); sample mass: 9.68 mg, Al crucibles with pierced lid, heating rate: 10 K/min, nitrogen atmosphere

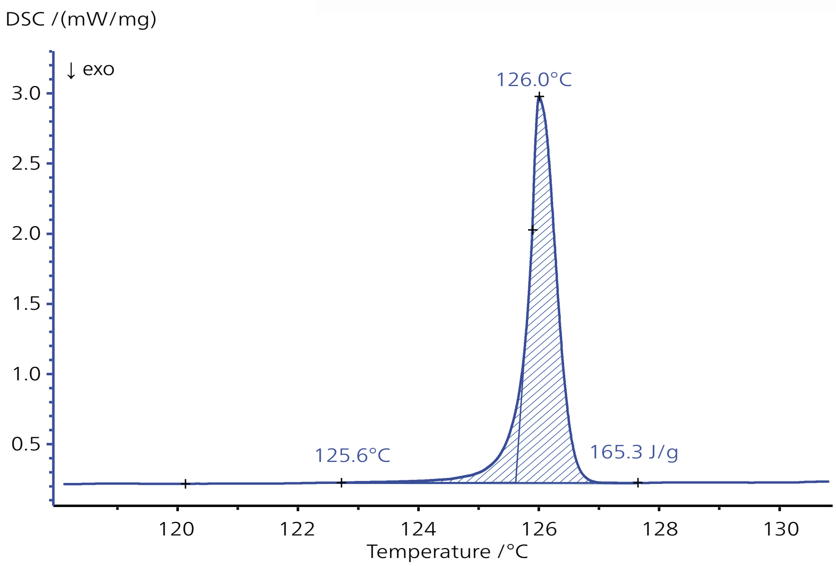
Characterization of Packaging Materials for Quality Control

Here, the DSC profiles of two different compound films based on polyethylene (PE) are depicted. The peak temperatures of the endothermal melting effects indicate that the red curve is correlated to PE-HD (high-density polyethylene), whereas the black curve is most probably related to low-density polyethylene (PE-LD).

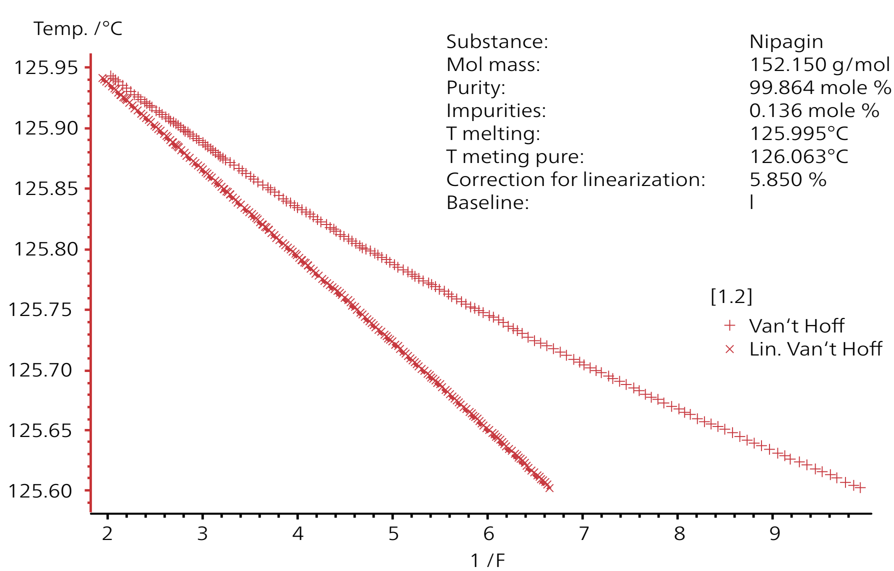
In the case of the black curve, an additional small effect can be seen at approx. 80°C which indicates the presence of further additives.



DSC measurements of two PE-based films, 2nd heating each; sample masses: 5.08 mg and 5.12 mg, Al crucibles with pierced lid, heating rate: 10 K/min, nitrogen atmosphere



DSC measurement on nipagin (chemical name: methyl 4-hydroxybenzoate); sample mass: 2.12 mg, Al crucibles with pierced lid, heating rate: 0.7 K/min, nitrogen atmosphere



Purity evaluation based on the DSC measurement above

Purity of Nipagin

Verification of the Polymorphic Form

Nipagin, or methylparaben, exists in various polymorphic forms. The monoclinic form I, which was measured here, exhibits a melting point at 126°C.

Determination of the Purity

The eutectic purity of a material can be determined from the DSC melting peak using the Van't Hoff equation (procedure described in ASTM E928).

The resulting Van't Hoff plot displays a nonlinear curve (the real behavior of the sample material) along with a linearized one. Plotted is the temperature versus 1/F , the reciprocal value of the part of the peak which corresponds to the already molten material at a certain temperature. The purity can be calculated from the slope of the corrected linear curve. At 1/F = 0, the theoretical melting temperature of 100% pure nipagin has been determined to be 126.063°C. The melting temperature of the nipagin at hand is determined to be 125.995°C. The resulting purity is given as 99.864%. All calculations are carried out automatically by the NETZSCH software.

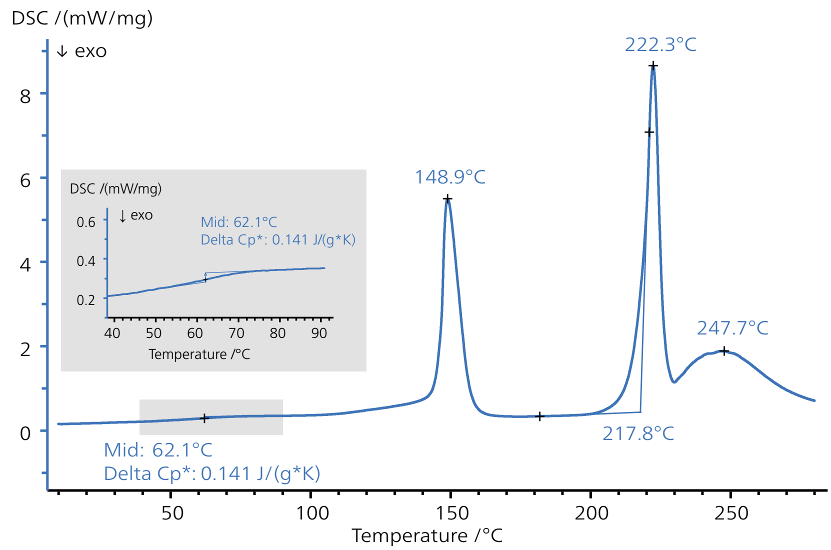
… in Terms of Processing

Glass Transition of Spray-Dried Lactose

Lactose (crystalline disaccharide sugar) is frequently used in food technology or as an excipient in pharmaceutical products. Depending on the production process, amorphous areas may exist. They are recorded as glass transitions in the DSC curve. Here, α-lactose monohydrate (FlowLac 90) was investigated by DSC. The sample is spray-dried and exhibits an amorphous content of 10 to 15%.

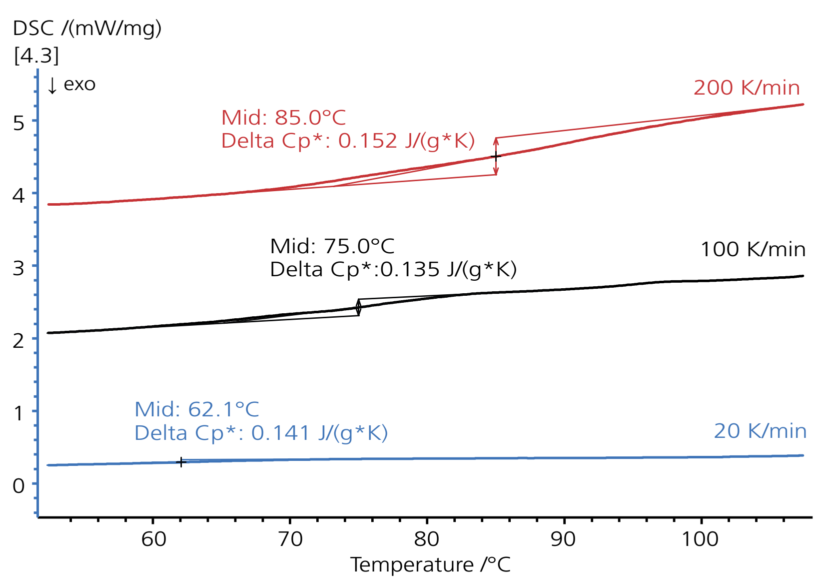
The DSC curve above illustrates the thermal behavior of α-lactose monohydrate including dehydration at around 149°C (peak temperature) and melting of the water-free α-lactose at 222°C (peak). The relatively broad effect at 248°C (peak temperature) is often a superposition of the melting of β-lactose and the initiation of material decomposition. A small glass transition related to the amorphous parts occurs at 64°C (mid point, inset).

When the heating rate is increased, the step height of the glass transition (delta c_p) also increases visibly (lower plot). Thus, it is easier to evaluate. As heating rates rise, however, all effects are shifted to higher temperatures. Here, the T_g is shifted from 62.1°C to 85°C (mid points) by multiplying the heating rate tenfold.

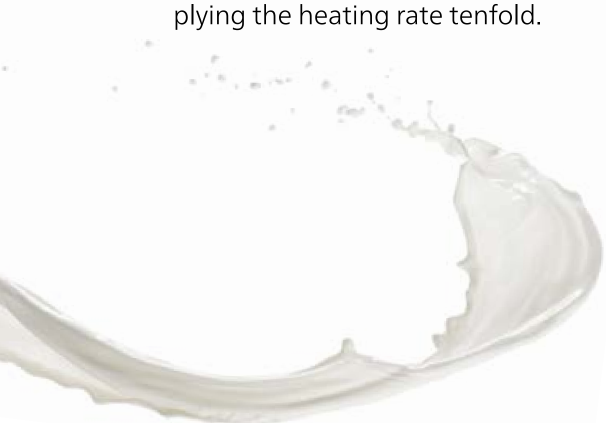


DSC measurement on α-lactose monohydrate; sample mass: 4.5 mg, Al crucibles with pierced lid, heating rate: 20 K/min, nitrogen atmosphere

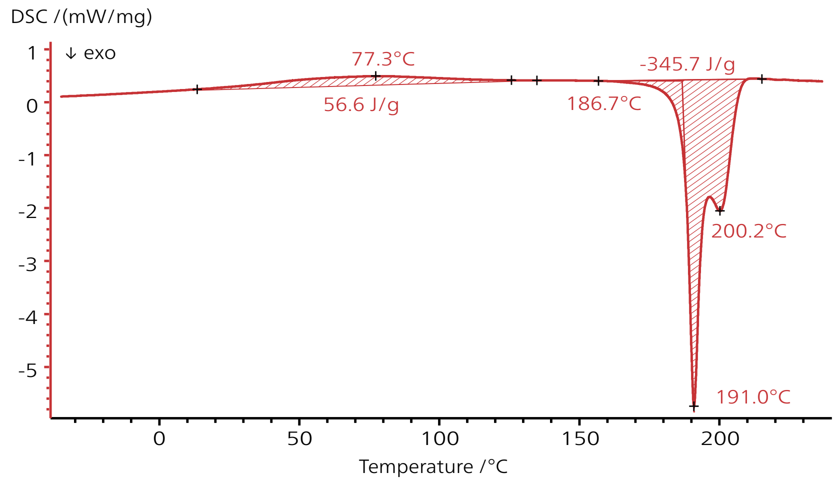
The amorphous content of a substance is directly related to its stickiness and flowability, which influences the processing of milk powder-containing products.



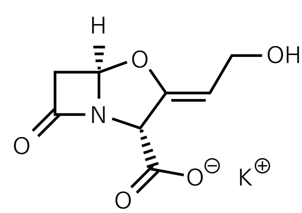
DSC measurements on α-lactose monohydrate; sample masses: 4.2 mg - 4.7 mg, Al crucibles with pierced lid, heating rates: 20 to 200 K/min, nitrogen atmosphere



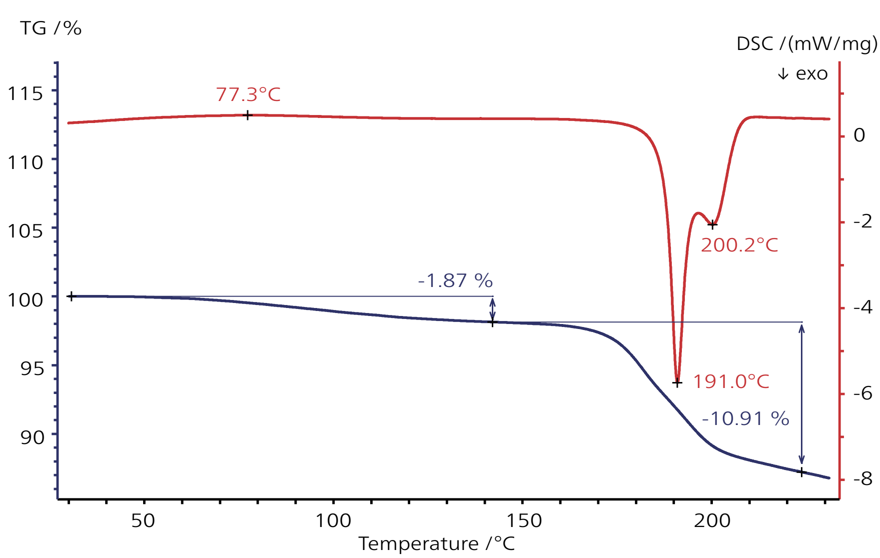
and Storage ...



DSC measurement on potassium clavulanate; sample mass: 2.3 mg, Al crucibles with pierced lid, heating rate: 10 K/min, nitrogen atmosphere



Structure of potassium clavulanate ($C_8H_8KNO_5$)



Joint presentation of DSC (red) and TGA (blue) results on potassium clavulanate; the TGA experiment was conducted under the same conditions as the DSC test.

Thermal Stability of Potassium Clavulanate

Hygroscopicity: A Challenge for Shelf Life

Potassium clavulanate is classified as hygroscopic. Therefore, the condition of the supplied material is crucial to its shelf life. Here, DSC and TGA-FT-IR measurements were carried out to elucidate the condition of this chemical.

DSC Measurement

During heating in nitrogen atmosphere, the DSC curve (upper plot) shows two effects: a stretched endothermal one with a peak temperature at 77°C and a double exothermal peak starting at 187°C (extrapolated onset).

TGA-FT-IR Measurement

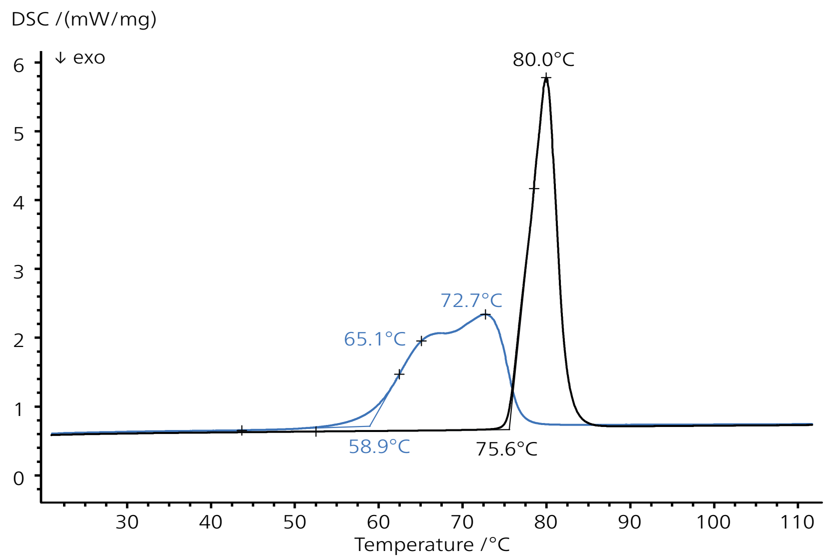
The TGA-FT-IR measurement (lower plot) reveals that the two effects are caused by mass losses with step heights of 1.9% and nearly 11%, respectively. The results of the coupled FT-IR measurement (not shown here) prove that the first mass loss is due to the release of water and the second (related to the double exothermal DSC peak) is due mainly to the release of CO_2. This suggests that decomposition already begins at just above 150°C.

Based on these findings, it can be concluded that the potassium clavulanate supplied has a water content of almost 2% (probably surface water). Since water loss already begins at slightly above room temperature, a change in the material could be induced by warm and dry storage conditions. At higher temperatures, only decomposition but no melting can be detected.

Compatibility of Materials in a Physical Mixture – Ibuprofen

Here, the thermal behavior of pure ibuprofen (black) is compared to that of a 90:10 mixture of ibuprofen with magnesium stearate (blue). Magnesium stearate is often applied as an excipient in the production of tablets.

The pure ibuprofen (black) exhibits one DSC peak with an extrapolated onset temperature of approx. 76°C. The DSC profile for the mixture (blue), however, does not reveal what would be expected if the substances were compatible; i.e., this peak plus an additional separate one. Instead, the DSC curve for the mixture reveals a double peak at 65°C and 73°C (peak temperatures). This indicates that there is an interaction between the two materials.



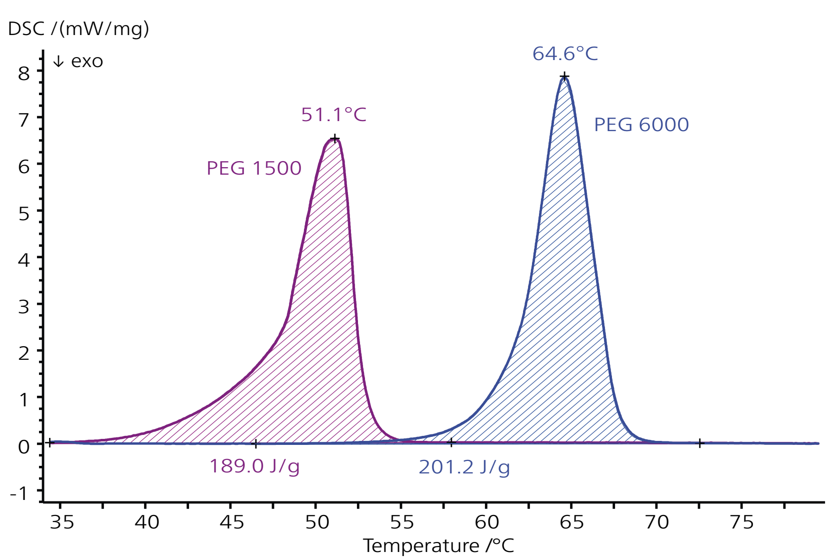
DSC measurement on ibuprofen and a mixture of ibuprofen with magnesium stearate at a ratio of 90:10; sample masses: 5.36 and 5.17 mg, Al crucibles with pierced lid, heating rate: 10 K/min, nitrogen atmosphere; up to 200°C no further effect is visible.

Identification of Substances by Their Melting Regions

Polyethylene glycol, PEG, refers to a group of water-soluble polymers of various chain lengths. They are used in pharmacy or in cosmetics, for example, as emulsifiers in creams and ointments.

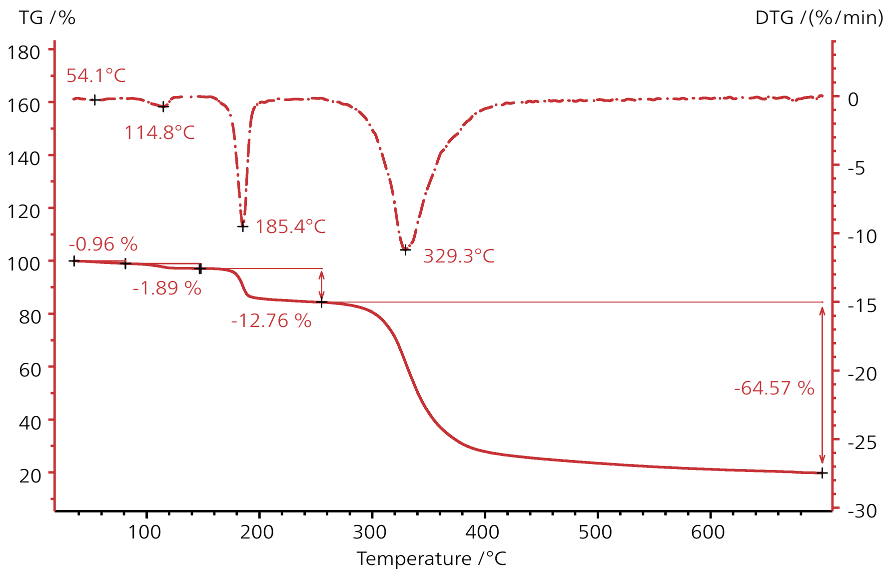
The added characteristic number represents the average molecular mass of the polymer and is related to its melting region. PEGs with average molecular masses of more than 1000 are solids with a wax-like appearance.

By means of DSC, it is easy to study their melting behavior and to distinguish between different PEG types.

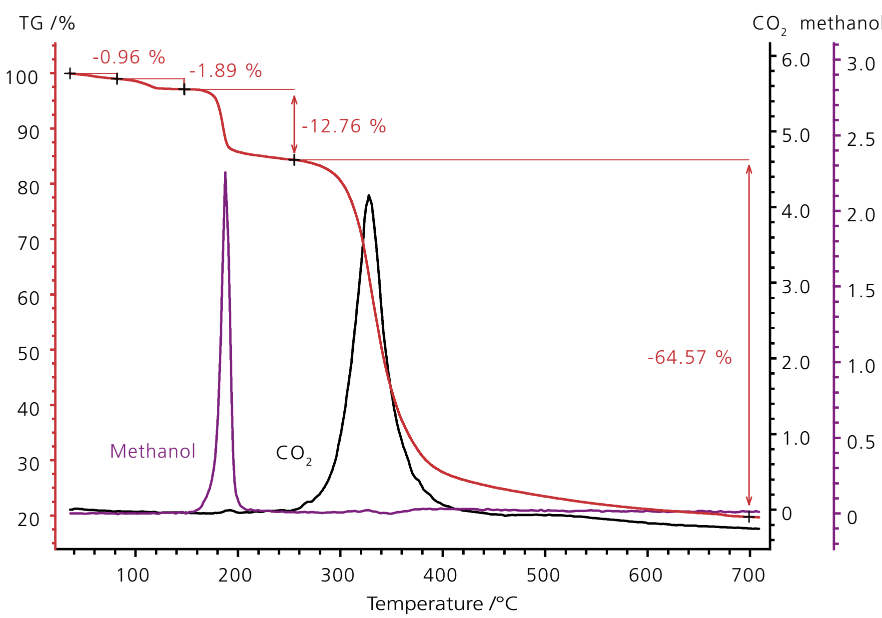


DSC measurements on polyethylene glycol 1500 and 6000; sample masses: 2.13 mg and 1.22 mg, Al crucibles with pierced lid, heating rates: 10 K/min, nitrogen atmosphere

... and More



TGA measurement on aspartame; sample mass: 7.46 mg, Al_2O_3 crucible, heating rate: 10 K/min, nitrogen atmosphere

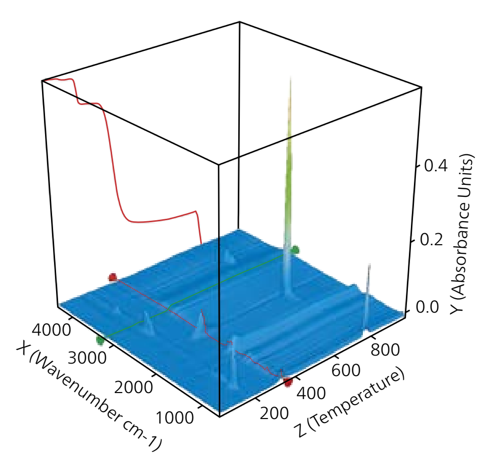


Presentation of the TGA (red) curve of aspartame and the corresponding traces of methanol and carbon dioxide (as examples), derived from the associated FT-IR measurement. A trace represents the course of the absorption intensity of a specific FT-IR band as a function of time or temperature.

Why Does Aspartame Lose Its Sweetening Power During Heating?

Aspartame is not suited for baking and cooking. The reason is that it already starts to decay before it even reaches 250°C.

Derived from the associated TGA-FT-IR experiment, there is a two-step mass change at 54°C and 115°C (DTG peaks), due to the evolvement of surface water (1st step) and dehydration. The mass step of 12.8% at 185°C (DTG peak) is associated with the release of methanol (see lower graph) and is an indicator for the beginning of degradation of the sweetener. In the subsequent step, CO_2 is among the substances which can be found in the gas phase, which suggests further decomposition of aspartame. By comparing the TGA curve with the particular FT-IR traces, you can see at a glance which gas evolves during which mass change.



3D presentation of all measured FT-IR spectra, incl. TGA curve and TGA sample temperature

The NETZSCH *Nevio* Line

A NEW CONCEPT FOR UNPARALLELED EASE OF USE

Carrying out investigations in the fields of pharmacy, cosmetics or foodstuffs?
Your top choice is the new NETZSCH *Nevio* instrument line.

TG 209 ***F3*** *Nevio*

The workhorse for quality assurance and process optimization

- Robust and extremely reliable
- Variety of sample carriers for greatest flexibility
- c-*DTA*® for monitoring caloric effects (optional)
- Large filter system for trapping decomposition products (optional)
- Gas-tight design
- High sample throughput thanks to the automatic sample changer with 20 positions (optional)

DSC 214 *Nevio*

Heat-flux DSC with the fastest heating and cooling rates on the market

- Space-saving design
- Perfectly synchronized sensor/crucible arrangement for excellent reproducibility
- High sample throughput thanks to the automatic sample changer with 20 positions (optional)

Made in Germany

NETZSCH – MORE THAN 60 YEARS OF EXPERIENCE IN MANUFACTURING TOP-CLASS THERMAL ANALYSIS DEVICES.

	TG 209 ***F3** Nevio*	DSC 214 *Nevio*
Temperature range (max.)	RT to 1000°C	-170°C to 600°C
Cooling rate/heating rate (max.)	100 K/min / 200 K/min	500 K/min
Measuring range/ weighing range (max.)	2000 mg*	± 750 mW
Enthalpy accuracy	n/a	± 1%**
TGA resolution	0.1 µg	n/a
Indium Response Ratio	n/a	> 100 mW/K
Exchangeable sensors	Yes	n/a
Cooling options	n/a	▪ Air compressor: RT to 600°C ▪ Compressed air: < 0°C to 600°C ▪ Intracooler: -70°C to 600°C ▪ Liquid nitrogen: -170°C to 600°C
Gas atmospheres	Inert, oxidizing, static and dynamic	Inert, oxidizing, static and dynamic
Mass flow controller for purge/protective gas	Optional, 3 (0 to 250 ml/min)	3, integrated (0 to 250 ml/min)
Gas flow regulation	With MFCs: software-controlled	Software-controlled
Automatic Sample Changer (ASC)	Optional	Optional
Software	min. *Proteus*® 8	min. *Proteus*® 8
Proteus® software extensions included	▪ *SmartMode* ▪ *ExpertMode* ▪ *AutoCalibration* ▪ *c-DTA*®	▪ *SmartMode* ▪ *ExpertMode* ▪ *AutoCalibration* ▪ (Advanced) *BeFlat*® ▪ *AutoEvaluation* ▪ *Identify*
Software extensions (optional)	▪ *AutoEvaluation* ▪ Temperature modulation ▪ *Proteus*® *Protect* ▪ *Identify* ▪ *Peak Separation* ▪ Kinetics Neo ▪ *Thermal Simulations*	▪ Temperature modulation ▪ Specific heat capacity (c_p) ▪ *Proteus*® *Protect* ▪ *Purity Determination* ▪ *Peak Separation* ▪ *Kinetics Neo* ▪ *Thermal Simulations*
Size (W x H x D) – incl. ASC, without physical connections	575 mm x 460 mm x 560 mm	350 mm x 445 mm x 560 mm

* minus weight of crucible
** for indium

Key Technical Specifications

NETZSCH *Nevio* Instruments Offer

DSC 204 ***F1*** *Nevio*

Premium differential scanning calorimeter

- Various exchangeable sensors optimized for different applications
- Extremely efficient – automatic sample changer for up to 192 samples and automatic piercing device (optional)
- Unsurpassable indium response ratio (outstanding sensitivity with simultaneous high resolution)

TG 209 ***F1*** *Nevio*

High-quality ultra-microbalance for research and development

- Vacuum-tight design
- Corrosion-resistant ceramic furnace
- c-*DTA*® for monitoring caloric effects
- Large filter system for direct trapping of decomposition products
- Pre-configured for coupling to gas analyzing systems (FT-IR, MS or GC-MS)
- High sample throughput for measurements over night or during the weekend – automatic sample changer for up to 192 samples and automatic piercing device (optional)

STA 449 ***F3*** *Nevio*

Specialized for demanding tasks

- Modular setup, adjustable to a variety of requirements, e.g., for measurements under relative humidity
- Vacuum-tight
- Pre-configured for coupling to gas analyzing systems (FT-IR, MS or GC-MS)
- Automatic sample changer for up to 20 samples (optional)

Everything You Need in One Package

	TG 209 ***F1** Nevio*	DSC 204 ***F1** Nevio*	STA 449 *F3 Nevio*
Temperature range (max.)	(10°C) … RT to 1100°C	-180°C to 700°C	-120°C to 675°C[3]
Max. cooling rate/ max. heating rate	200 K/min	200 K/min	50 K/min
Measuring range/ weighing range (max.)	2000 mg[1]	± 750 mW	35000 mg[1] /± 250 mW[4]
Enthalpy accuracy	n/a	< 1%[2]	± 1 ... 3%
TGA resolution	0.1 µg	n/a	0.1 µg
Indium Response Ratio	n/a	> 100 mW/K	> 85 mW/K[2) 5)]
Sensors	Interchangeable	Exchangeable	Interchangeable
Cooling options	n/a	▪ Air compressor: RT to 700°C ▪ Compressed air: < 0°C to 700°C ▪ Intracooler: -85°C to 600°C ▪ Liquid nitrogen: -180°C to 700°C	▪ Compressed air: < 0°C to 675°C[3] ▪ Liquid nitrogen: -150°C to 1000°C[3]
Gas atmospheres	Inert, oxidizing, static and dynamic	Inert, oxidizing, static and dynamic	Inert, oxidizing, reducing (forming gas), humid, vacuum, static, dynamic
Gas-tight/vacuum-tight	Vacuum-tight	Gas-tight	Vacuum-tight
Mass flow controller for purge/protective gas	3, integrated (0 to 250 ml/min)	3, integrated (0 to 250 ml/min)	Optional, 3 (0 to 250 ml/min)
Automatic Sample Changer (ASC, optional)	192 positions	192 positions	20 positions
Proteus® software including	*SmartMode, ExpertMode, AutoCalibration, BeFlat*®, *c-DTA*®, *AutoEvaluation, Identify*	*SmartMode, ExpertMode, AutoCalibration, BeFlat*®, specific heat capacity, *AutoEvaluation, Identify*	*AutoEvaluation*
Software extensions, optional	Temperature modulation, *Proteus*® *Protect*, *Peak Separation*, Kinetics Neo, Thermal Simulations, *c-DTA*®, *Identify*, specific heat capacity	Temperature modulation, *Proteus*® *Protect*, *Peak Separation*, Kinetics Neo, Thermal Simulations, *c-DTA*®, *Identify*, specific heat capacity	Temperature modulation, *Proteus*® *Protect*, *Peak Separation*, Kinetics Neo, Thermal Simulations, *c-DTA*®, *Identify*, specific heat capacity

1) minus weight of crucible
2) for indium
3) optimized temperature range for pharmacy, cosmetics and foodstuffs; depending on the selected furnaces: total temperature range: -150°C up to 2400°C
4) for thermocouple type E
5) in Al_2O_3 crucibles

Key Technical Specifications

EVOLVED GAS ANALYSIS

Unveiling the Processes Behind Mass Losses

Coupling a gas analyzing system to the TG 209 ***F1*** *Nevio* or the STA 449 ***F3*** *Nevio* allows for deeper insight into a material's behavior and facilitates identification and quantification of the gases released.

The following coupling possibilities are available:

	PERSEUS FT-IR**	*Aeolos* Quadro MS (via capillary)	FT-IR (via capillary)	GC-MS (via capillary)	*PERSEUS* ** FT-IR + MS	*PERSEUS*** FT-IR + GC-MS	FT-IR (capillary) + MS
TG 209 ***F1*** *Nevio* to 1100°C	✓	✓	✓	✓	✓	✓	✓
STA 449 ***F3*** *Nevio**	✓	✓	✓	✓	✓	✓	✓

* temperature range of the instrument is depending on the selected furnace; total temperature range: -150°C to 2400°C
** *PERSEUS*® corresponds to direct coupling, without transfer line

Any of these instrument combinations can additionally be equipped with an automatic sample changer (ASC). Also in this case, the *Proteus*® software is able to operate and control the thermal analyzer and the gas analyzer simultaneously.

TG 209 ***F1*** *Nevio* simultaneously coupled to an FT-IR (Bruker INVENIO with external gas cell) and MS (QMS 403 *Aëolos Quadro*) via capillary

PERSEUS STA 449 ***F3*** *Nevio* coupled to a GC-MS via capillary

Saving 50% of Benchtop Space with the PERSEUS Coupling

Top-Loading Arrangement of NETZSCH TGAs Ensures Optimum Protection of the Balance

Warm gases have a tendency to rise. This chimney effect causes the purge gas (which comes from below in top-loading balances) to pull the released products away from the sample and transport them to the gas outlet at the top of the furnace. The risk of contaminating the balance (which is located beneath the sample) is thus minimized; this makes top-loading balances ideal for coupling to evolved gas analyzers.

NETZSCH Systems Provide a Pure Inert Gas Atmosphere for Evolved Gas Analysis (EGA)

In order to detect minimal concentrations of evolved products in the gas phase, the background level in a gas analyzing system has to be as low as possible, especially with regard to H_2O and CO_2 coming from the environment. Additionally, mass spectrometers used as GC detectors are very sensitive to greater amounts of residual oxygen. Thus, a prerequisite for the successful investigation of released gases is vacuum tightness or – at least – gas tightness, which is the case for any NETZSCH TGA/STA instrument.

Proteus® Software

A New Expression of Efficiency

The NETZSCH *Proteus*® software package offers far more than conventional software for controlling instruments and evaluating measurement data. It is intuitive and easy to handle (especially when using the *SmartMode* interface), it supports the operator with a variety of clever and useful features (e.g., the unique *AutoEvaluation*), and it contains an expert system called *Identify* (see page 20).

Proteus® Software – All-in-One

The philosophy behind *Proteus*® software is to provide everything necessary for carrying out and evaluating test runs in a single package. The only functionalities which are not part of the base package are specific ones such as c_p determination or *Proteus*® *Protect* (see next page); these are optionally available.

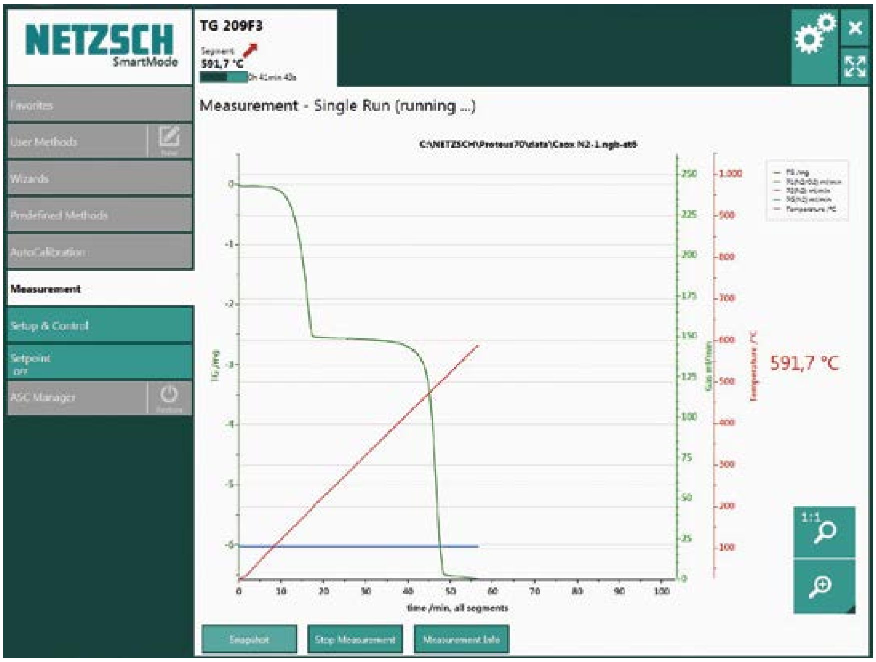
Instrument-Independent Methods

The *Proteus*® software is based on measurement methods which can both handle the desired temperature program and evaluate the resulting curve, if desired. The methods can be used for any device of the same type (for example, DSC 204 ***F1*** *Nevio* and DSC 214 *Nevio*) and of comparable configuration in a lab.

SmartMode and *ExpertMode*

Proteus® offers two user interfaces for DSC and TGA instruments: the simplified *SmartMode* (see next page), which is particularly advantageous if a touch monitor is preferred, and *ExpertMode*, for anyone who favors a more classical interface. The operator can switch between the two presentation formats, even if an automatic sample changer (ASC) is being used.

	DSC 204 ***F1*** *Nevio*	DSC 214 *Nevio*	TG 209 ***F1*** *Nevio*	TG 209 ***F3*** *Nevio*	STA 449 ***F3*** *Nevio*
SmartMode	✓	✓	✓	✓	n/a
ExpertMode	✓	✓	✓	✓	✓
AutoCalibration	✓	✓	✓	✓	n/a
(Advanced) *BeFlat*® (DSC)	✓	✓	✓	n/a	Optional
c-DTA®	n/a	n/a	✓	✓	Optional
AutoEvaluation	✓	✓	✓	✓	✓
Temperature modulation	Optional	Optional	Optional	Optional	Optional
Specific heat capacity (c_p)	✓	Optional	n/a	n/a	Optional
Proteus® *Protect*	Optional	Optional	Optional	Optional	Optional
Purity Determination	Optional	Optional	n/a	n/a	Optional
Identify	✓	✓	✓	Optional	Optional



SmartMode – There's no need to be an expert in TGA to start a measurement!

Proteus® Protect

Meeting the Requirements of 21 CFR Part 11

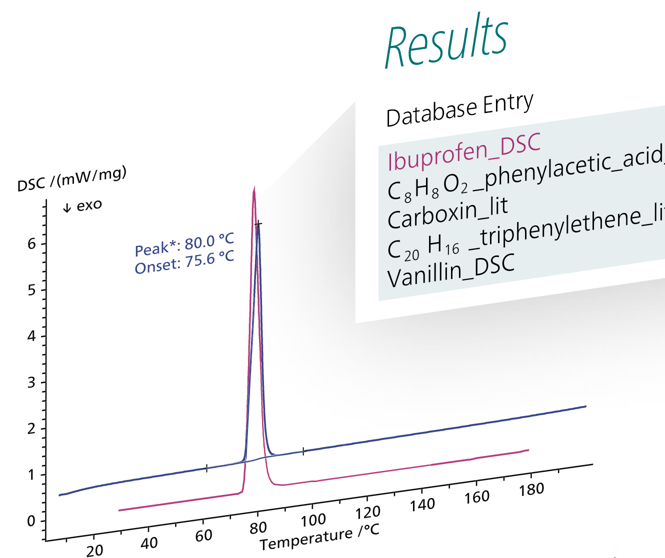
Proteus® Protect – Always on the Safe Side

Proteus® with *Proteus Protect* ensure data integrity at the highest level and meets the requirements of 21 CFR Part 11 or EU Annex 11.

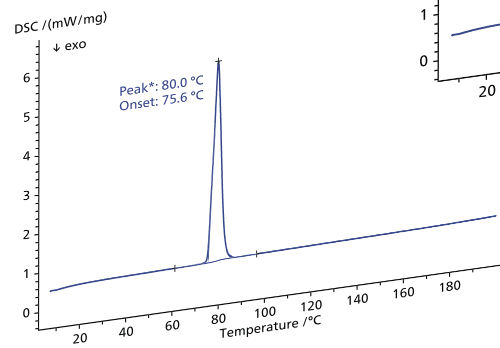
- Measurement data cannot be overwritten.
- Every relevant action is documented within an Audit Trail which can be printed and exported.
- For protection of data privacy, only authorized persons have access to this Audit Trail.
- User management allows for the assignment of permissions to users.
- There is password management for effective access control.
- A watchdog function triggers automatic logout following a defined period of inactivity.
- A signature module ensures that only approved calibrations or methods are used as a basis for new measurements and that only approved evaluations are published.

Proteus®

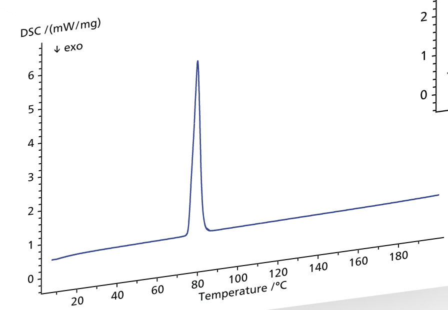
THE ONLY SOFTWARE THAT ACTIVELY SUPPORTS YOU IN YOUR DAILY WORK



Identify of auto-evaluated measurement



AutoEvaluation of measurement



Measurement curve of unknown material

AutoEvaluation – The First Truly Self-Acting Evaluation Routine

The unique *AutoEvaluation* function detects and evaluates thermal effects – i.e., peaks or mass changes – without any user intervention. Intelligent algorithms are capable of handling DSC and TGA curves fully automatically and thus of generating completely objective results.

Experienced users can take these results as a second opinion. The operator has full control at all times, though, and – if desired – can recalculate values or run manual evaluations.

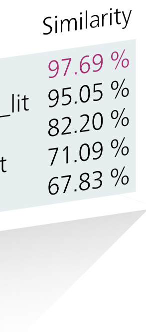
Identify – The Curve Recognition and Database System

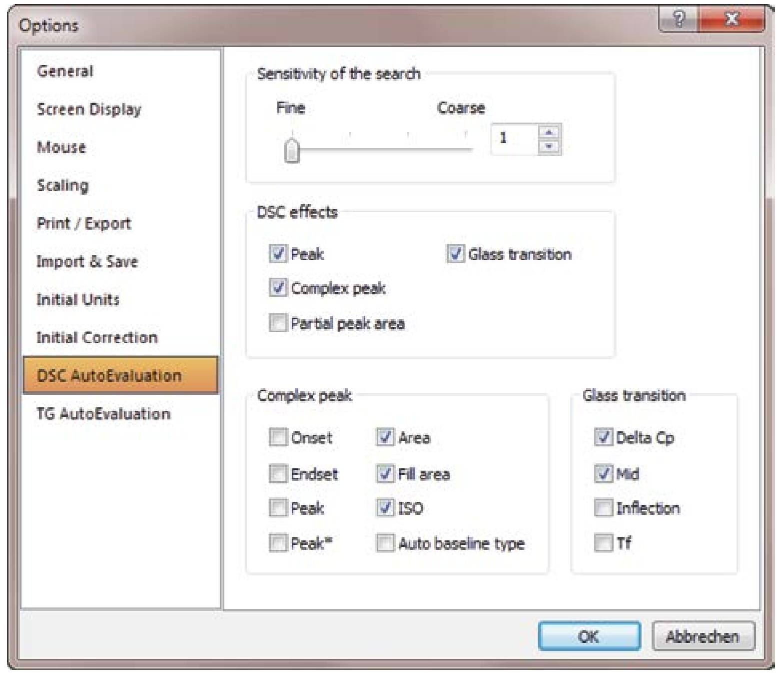
Identify marks a real turning point in the field of thermal analysis. This software package allows for the identification and classification of materials via database comparison with just one click.

In the case of DSC and TGA curves, the comparison is **effect-based**, which ensures fast and efficient evaluation. The result is a similarity hit list as shown above. To refine the database search, DSC and TGA data can also be used in combination.

Besides one-on-one comparisons with individual curves or literature data, it is also possible to check whether a particular curve belongs to a certain class. These classes may consist of sets of data for various types of the same material or of reference curves for Pass/Fail testing within the scope of quality control.

Both the libraries and classes are boundless and users can expand them easily with experiments and knowledge of their own. The libraries provided by NETZSCH contain more than 1,200 entries related to a variety of application areas, including pharmaceuticals and organics.





ADDITIONAL HELPFUL SOFTWARE FEATURES

Customization of Graphs via *AutoEvaluation* Setting

For maximum convenience, each user can individually define which values should be displayed when using *AutoEvaluation*. The resulting graph can be adapted to anybody's needs.

SuperPosition of Curves

This simulation tool gives you an idea of how curves which are composed of several components might appear. The prerequisite is full compatibility (i.e., no interactions) among the various materials involved.

Based on DSC or TGA measurements, this software feature calculates the superposition; the user can define the mass ratio (in %) of each component. The *SuperPosition* function can be applied in quality control or deformulation studies, among others.

Curve Averaging Based on Absolute or Relative Values

The one for absolute values (mW or Δm in mg) takes into consideration the sample masses of the various curves which are the basis for averaging, whereas the one for relative values (mW/mg or Δm in %) just applies the number of measurements as denominator.

All over the world, the name NETZSCH stands for comprehensive support and expert, reliable service, both before and after sale. Our qualified personnel from the technical service and application departments are always available for consultation.

In special training programs tailored for you and your employees, you will learn to tap the full potential of your instrument.

To maintain and protect your investment, you will be accompanied by our experienced service team over the entire life span of your instrument.

IQ/OQ

Installation, Commissioning and Instrument Qualification

Installation and commissioning includes a complete configuration and parameterization of your instrument as well as basic instruction for the operators. Additionally, our service engineers are prepared to carry out the installation qualification (IQ) and operational qualification (OQ) of the instrument on-site in line with USP <1085> or GAMP 5 to ensure proper installation and correct operation. If required, they also assist users in performance qualification (PQ).

Calibration Service

In addition to on-site calibrations following the installation of a new instrument, our well-trained service personnel also perform regular recalibrations, if desired.

... and More

WHEREVER YOU ARE — WE ARE AT YOUR SERVICE

Our Expertise in Applications

The NETZSCH Thermal Analysis applications laboratories are a proficient partner for nearly any Thermal Analysis issue. Our involvement in your projects begins with proper sample preparation and continues through meticulous examination to diligent interpretation of the measurement results. Our diverse methods and state-of-the-art measuring stations will provide solutions for all your thermal needs.

Within the realm of thermal analysis and the measurement of thermophysical properties, we offer you a comprehensive line of the most diverse analysis techniques for materials characterization.

The NETZSCH applications laboratories are located in:

- Germany (Selb — headquarters)
- USA (Burlington, MA)
- China (Shanghai)

Demonstration measurements, however, are also offered at other locations around the globe. Please ask your NETZSCH representative for details.

TECHNICAL SERVICE

- Maintenance and Repair
- Software Updates
- Exchange Service
- Instrument Qualification (IQ/OQ)
- Calibration Service
- Spare Part Assistance
- Moving Service

TRAINING

- Training
- Comprehensive Instrument and Method Training

LABORATORY

- Application Service and Contract Testing

The NETZSCH Group is a mid-sized, family-owned German company engaging in the manufacture of machinery and instrumentation with worldwide production, sales, and service branches.

The three Business Units – Analyzing & Testing, Grinding & Dispersing and Pumps & Systems – provide tailored solutions for highest-level needs. Over 3,500 employees at 210 sales and production centers in 35 countries across the globe guarantee that expert service is never far from our customers.

When it comes to Thermal Analysis, Calorimetry (adiabatic & reaction) and the determination of Thermophysical Properties, NETZSCH has it covered. Our 50 years of applications experience, broad state-of-the-art product line and comprehensive service offerings ensure that our solutions will not only meet your every requirement but also exceed your every expectation.

Proven Excellence.

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