Thermal technique

A thermal technique refers to a method of analysis or characterization in which a physical or chemical property of a substance is measured as a function of temperature or time while the substance is heated or cooled.

Examples of thermal techniques include:

1. Thermogravometric Analysis (TGA) – measures weight change with temperature.
2. Differencial Thermal Analysis (DTA) – measures temperature differences between a sample and a reference.
3. Differencial Scanning Calorimetry (DSC) – measures energy absorbed or released by a sample during heating or cooling.
4. Thermometric Titration – monitors temperature change during a chemical reaction.

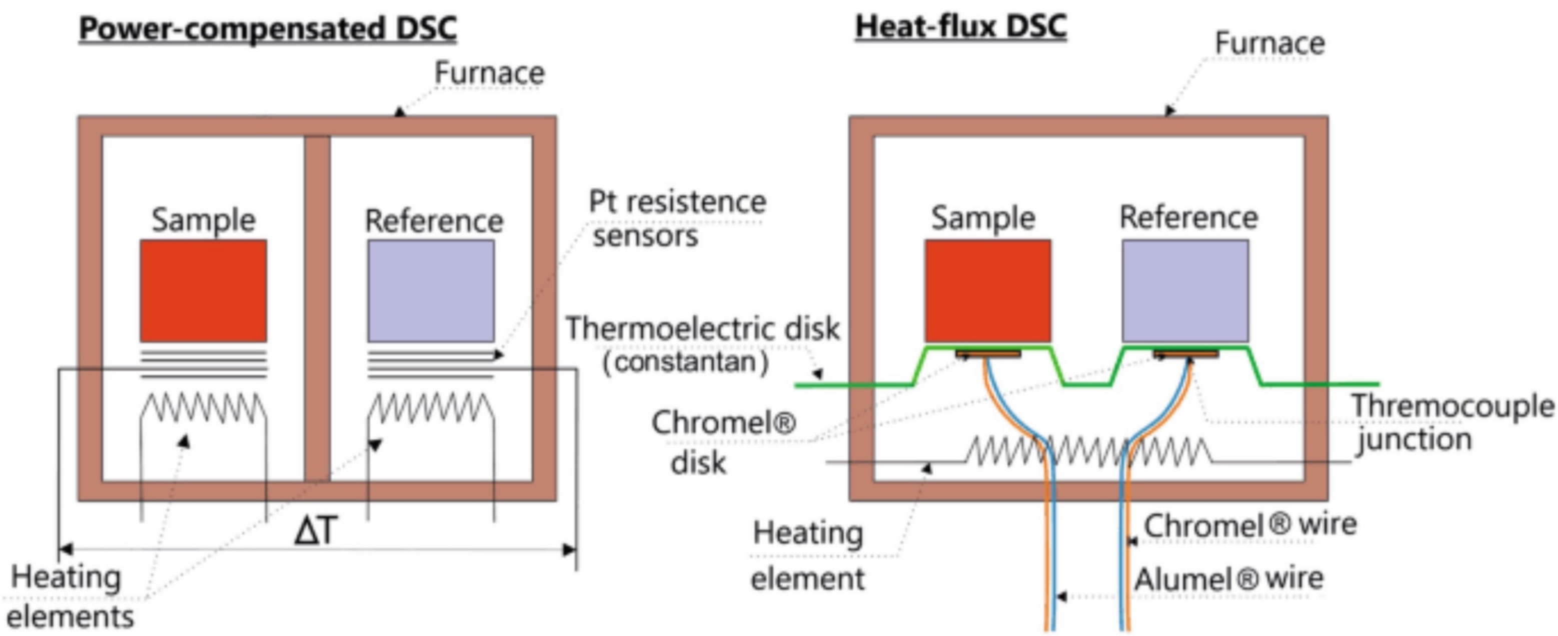
Derivative Thermogravimetry (DTG) – assesses the rate of weight change.

Thermal transition

A thermal transition refers to a change in a material's physical or chemical state when its temperature crosses a certain point.

Examples of Thermal Transitions:

Melting (Melting Point) — solid converts to liquid.
Glass Transition (Tg) — amorphous material transitions from a brittle, glass-like state to a more flexible, rubber-like state.
Crystallization (Tc) — liquid or amorphous material forms a crystalline structure upon cooling.
Vaporization (Boiling Point) — liquid converts to vapor.
Degradation or Decomposition — material starts to break down chemically at higher temperatures.
Curie Transition — in magnetic materials, the point where it drops from ferromagnetism to paramagnetism.



This diagram shows two different types of Differential Scanning Calorimeters (DSC):

1. Power-compensated DSC (Left side)
2. Heat-flux DSC (Right side)

1. Power-compensated DSC -

Let's break down its components:

Furnace: This is a chamber where the temperature is raised or lowered.

Heating elements: These are heaters that produce the heat.

Sample: This is the material you want to study (the red block).

Reference: An inert or non-changing material (the purple block).

Pt resistance sensors: These measure the temperature of both the sample and the reference.
Thermoelectric disk (constantan): This converts the temperature differences into a small voltage (signal).

Working of Power-Compensated DSC

STEP 1 — Initial Setup:

Placement: Put your sample in its holder and a non-reactive or inert material (like alumina) in the other (reference).

Heating: The furnace starts heating both at the same rate.

STEP 2 — Measuring Temperature Difference:

Pt resistance sensors placed underneath each holder constantly measure their temperatures.

STEP 3 — Compensation Principle:

Ideally, the sample and the reference should remain at the SAME temperature.

Whenever the sample absorbs or release heat (say during melting or crystallization), its temperature starts to lag or lead the reference.

STEP 4 — Power Adjustment:

The DSC adjusts its heaters: adding or removing power to keep both at the same temperature.
This additional power is directly related to the energy absorbed or release by the sample.

STEP 5 — Recording:

The difference in power is recorded against temperature.
This forms a curve (DSC curve) which shows thermal transitions — for example, melting, crystallization, or glass transitions — as peaks or drops in power.

2. Heat-flux DSC-

Let's break down its components:

Furnace: This controls the temperature of the entire chamber.

Heating element: This provides the warmth.

Chromel® disk: This helps to transfer the heat evenly.

Chromel-Alumel Thermocouple: This measures the temperature difference between the sample and the reference.

Thermocouple Junction: This is where the two wires connect — this generates a small voltage when there's a temperature difference.

Working of Heat-flux DSC-

Picture two small metal holders placed side by side in a furnace — one holds your sample and the other holds a reference material.

STEP 1 — Initial Setup:

Placement: Put your sample in its holder and a non-reactive or inert material (like alumina) in the other (reference).

Heating: The furnace starts heating both at the same rate.

STEP 2 — Measuring Temperature Difference:

Pt resistance sensors placed underneath each holder constantly measure their temperatures.

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Modulated DSC (MDSC)

What is Modulated DSC?

Modulated DSC is a special form of DSC.
It applies a small sinusoidal (oscillatory) heating or cooling pulse on top of the main linear heating.

This lets you separate complex signals into:

Reversible signals (like glass transitions).
Non-reversible signals (like curing, crystallization, or degradation).

Experimental parameters:-

✅ Sample preparation:

Small, flat, homogenous sample (typically 5–10mg).
Encased in standard DSC pan (aluminum).
Pan is sealed to avoid mass-loss or side reactions.

✅ Heating rate:
Standard: 2°C–5°C per minute (slow).
Superimposable sinusoidal modulation (with an amplititude of ±0.5°C) over this rate.

✅ Cooling rate:
Controlled (typically matching the heating rate).

✅ Modulation frequency:
Often 60 seconds per pulse (but can range from 30–100 seconds).

✅ Resolution:
Higher resolution for weak transitions due to ability to separate signals.

Pharmaceutical Applications:
Distinguish glass transitions from crystallization or relaxation in APIs.
Study compatibility of ingredients in formulations.
Detect polymorphs and purity.
Investigate stability under stress conditions.

Source of Error:

Pan not properly sealed → mass-loss.

Large or uneven samples can cause poor resolution.

Incorrect modulation parameters can produce confusing signals.

Instrument baseline drift.

Advantages:

✅ Allows separation of overlapping events (reversible vs non-reversible).

✅ Higher resolution of weak transitions.

✅ Better glass transition determination (without interference).

✅ Allows for heat capacity (Cp) measurements.

Disadvantages:

Slower and more complex method.

Requires more data processing and expertise.

Higher instrument cost and maintenance.

Hyper DSC (High-Rate DSC)-

Hyper DSC involves heating or cooling at much faster rates (100°C–500°C per minute).

This lets you:

Reduce effects of transformation upon long heating.

Capture fast events.

Improve resolution of weak transitions.

Experimental parameters:

✅ Sample preparation:

Small mass (typically < 5mg).

Thin, flat, well-distributed sample.

✅ Heating rate:

Rapid — typically from 100°C to 500°C per minute.

✅ Cooling rate:

Large and equally fast (100°C–500°C per minute).

✅ Resolution:

Higher for weak or overlapping transitions due to faster scanning.

Source of Error:

-Large temperature gradients in thick samples.

-Heat transfer lag at high heating rates.

-Possible shift in transformation temperatures due to high rate.

Advantages:

✅ Allows you to observe fast transitions.

✅ Better resolution for weak signals.

✅ Saves analysis time — faster scans.

✅ Helps detect metastable phases or forms.

Disadvantages:

Large thermal lag and inaccuracies if rate is too high.

May mask or move transformation signals.

Requires thin, small samples with proper preparation.

Pharmaceutical Applications:

Screening of polymorphs and crystallization under different conditions.

Rapid stability testing for new compounds.

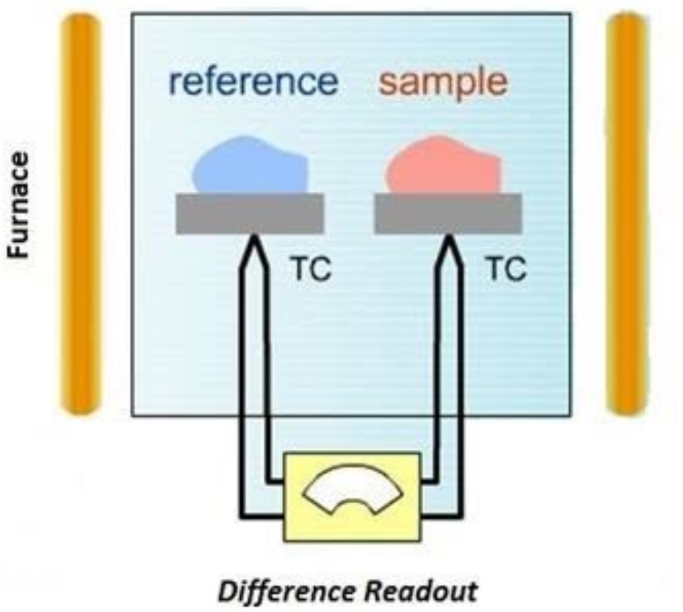
Detect glass transitions and weak signals in complex formulations.

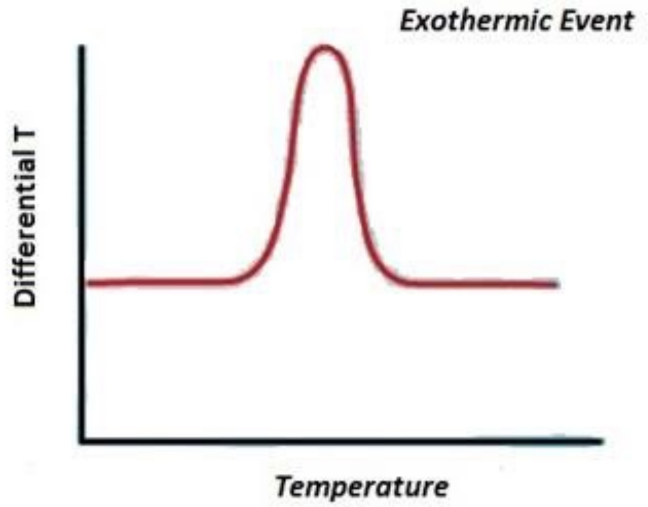
Differencial Thermal Analysis (DTA)

DTA measures the temperature difference between a sample and a reference while both are heated or cooled under identical conditions.

Whenever the sample undergoes a transformation (like melting, crystallization, or degradation), it absorbs or releases heat.

This results in a temperature difference between the sample and the inert reference material. This temperature difference is recorded and displayed as a DTA curve (ΔT vs T).





We have two crucibles or sample holders placed side by side in a furnace:

One with a sample (marked in pink).

One with a reference material (marked in blue).

-Each crucible has its own thermocouple (Tc).

These measure the temperature of each side as we heat them together in the furnace.

-The signals from the two thermocouples are fed into a difference readout.

This means we compute the temperature difference between the sample and the reference.

This forms the DTA signal.

DTA Curve-

✅ The DTA curve shows Differencial T (temperature difference) on the y-axis against Heating temperature on the x-axis.

✅ When a thermal event occurs in the sample (say an exothermic reaction), the sample releases heat.

This release of heat makes its temperature rise faster than the reference.

✅ This results in a positive peak in the DTA curve.
The peak's direction (up or down) shows whether the event is exothermic or endothermic.
This one shows exothermic (goes up).

Instrumentation of DTA

1. Furnace/Heating chamber:
   Provides controlled heating or cooling.

2. Sample holder:
Holds sample and inert reference side by side (typically in metal crucibles).

- Thermocouples:

Measure the temperature of both sample and reference.
Difference (ΔT) is fed into the recorder.

- Amplifier and Recorder:
  Amplifies the small signals and converts them into a DTA curve.

- Control System:
  Maintains linear heating or cooling at a specified rate (say 5°C/minute).

Advantages of DTA:

✅ Allows for direct observation of physical or chemical transitions in a sample.
✅ Applicable to solids, powders, or even melts.
✅ Reliable, simple, cost-effective, and widely used in pharmaceuticals.
✅ Large range of temperatures (typically up to 1600°C).

Disadvantages of DTA:

✅ Less sensitive than DSC for weak transitions.
✅ Quantitative enthalpy determination is less accurate.
✅ Peaks may overlap if many transitions happen close together.
✅ Requires careful calibration.
✅ Large baseline drift can affect signals.

Pharmaceutical Applications of DTA:

✅ Melting point determination of pure drugs.
✅ Detection of polymorphs and pseudopolymorphs.
✅ Drug-excipient compatibility studies — helps identify unwanted interactions.
✅ Measurement of crystallization, glass transitions, and decomposition temperatures.
✅ Quality control during production.

Derivative DTA (DDTA)

Derivative DTA (DDTA) -means we are taking the first derivative of the DTA curve.
The DTA curve normally shows temperature difference (ΔT) between your sample and a reference.
If we compute the derivative, we are looking at the rate of change of this temperature difference as we raise or lower the temperature.
Essentially, Derivative DTA helps us see small or overlapping events much more clearly.

Principle -

Picture DTA as a graph with peaks or drops when your sample melts or transforms.
Derivative DTA converts this into steps or sharper signals, which makes it easier to identify:
✅ The starting point of a transformation.
✅ The peak temperature of a reaction.
✅ If there are two overlapping events, you can separate them more easily.

How it's Done:

We first perform DTA normally — we slowly raise the temperature while recording the temperature difference.

We then apply mathematical differentiation to this data.

This means we calculate $d(\Delta T)/dt$ or $d(\Delta T)/dT$ — which shows how fast the temperature is changing.

Advantages:

✅ Higher resolution: We can separate two overlapping events that are hard to see in DTA.

✅ Enhanced peak identification: We know exactly where a transformation starts or reaches its maximum.

✅ More accurate data: Helps in choosing processing conditions in pharmaceuticals (like choosing proper storage or formulation conditions).

Applications in Pharmaceuticals:

✅ Distinguish polymorphs in a raw material.

✅ Detect glass transitions, crystallization, or melting points more accurately.

✅ Study compatibility of drugs with excipients in formulations.

✅ Monitor thermal stability and purity of a substance.

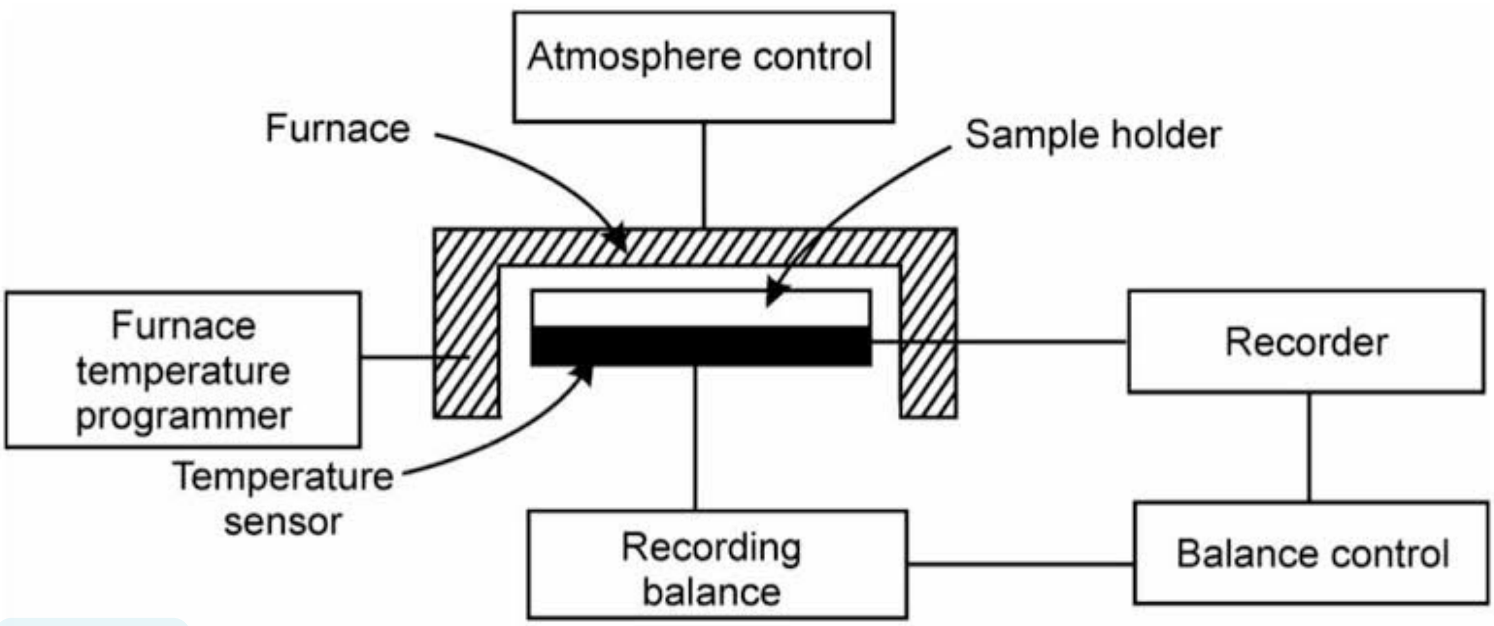
✅ Provide data for choosing proper processing temperatures during formulation.

Thermogravometric Analysis (TGA)

TGA measures the change in weight of a sample as it is heated or cooled in a controlled atmosphere.

-This weight change happens due to:
Degradation,
Dehydration,
Decomposition,
Release of solvent or water, or
Formation of volatile products.

-TGA helps us identify thermal stability and composition of a material.



✅ Furnace:

Provides controlled heating to the sample.
It is typically an electric furnace with a programmable temperature controller.

✅ Sample Holder:

Holds the sample during the heating process.
Usually made of a material that can withstand high temperatures (such as alumina or platinum).

✅ Atmosphere Control:

Controls the atmosphere in which the sample is heated — for example:

Air
Nitrogen
Oxygen

This lets you perform TGA under different conditions (oxidative or inert).

✅ Temperature Sensor:

Monitors the temperature of the furnace and the sample in real time
(typically with a thermocouple).

✅ Recording Balance:

This is a high-precision balance that measures mass during the heating process.

The balance is connected directly to the sample holder.

✅ Balance Control:

Controls and maintains the balance's stability and converts mass signals into electronic signals.

✅ Recorder:

Displays or prints a mass vs. temperature or mass vs. time curve, which shows:

Where mass drops (loss) — related to decomposition, dehydration, or release of gasses.

✅ Furnace Temperature Programmer:

Controls the rate of heating (ramp-up), maintains (isothermal), or cools down the furnace.

This lets you perform custom heating profiles.

HOW IT WORKS

Placement of Sample:
The sample is placed in a crucible or holder and suspended from the balance.

Heating:
The furnace is turned on and its temperature is raised at a controlled rate.

Mass Measurement:
As the temperature increases, the sample may lose mass (for example, by release of water or decomposition products).
This mass change is measured by the balance in real time.

Atmosphere Control:
While heating, a flow of inert or reactive atmosphere can be introduced, depending on the nature of the study.

Data Recording:
Mass is recorded against temperature and displayed or printed by the recorder, yielding a TGA curve.

Factors Affecting TGA Results:

✅ Heating rate:

Too fast or slow can affect when weight drops. Usually slow (10°C/minute) for accurate results.

✅ Atmosphere:

Nitrogen, air, or inert atmosphere can produce different decomposition profiles.

✅ Sample mass and particle size:

Small, evenly dispersed samples produce more accurate results.

✅ Placement of the crucible:

Should be in the center of the furnace for uniform heating.

✅ Moisture or solvent traces:

May cause weight drops at lower temperatures.

Advantages of TGA:

✅ Measures mass directly — highly accurate and sensitive.

✅ Allows us to determine thermal stability, decomposition temperature, and residual mass.

✅ Helps in evaluating moisture, solvent, or volatile content in a sample.

✅ Allows for study under different atmospheric conditions.

✅ Small sample size (typically milligrams).

Disadvantages of TGA:

✅ Measures mass but does not identify what is causing mass drop (need additional methods for complete identification, e.g. mass spectrum of the evolved gasses).

✅ Large or non-uniform samples can produce poor or unreliable results.

✅ Some overlapping events can be difficult to separate.

✅ Requires careful calibration and maintenance of balance.

Pharmaceutical Applications of TGA:

✅ Determining moisture or solvent content in raw materials or formulations.

✅ Assessing thermal stability and storage conditions for drugs.

✅ Studying degradation profiles and decomposition temperatures.

✅ Analyzing excipient compatibility with active ingredients under stress.

✅ Measuring residue after ignition (such as for heavy metal content).

✅ Quality control during formulation process.