BIO & PHARMA ANALYTICAL TECHNIQUES

Chapter 7 Thermal Analysis

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Chapter Description

- Aims
  - Discuss theory, principles and application of analytical techniques used in material characterization, pre-formulation development, manufacturing process and storage stability.

- Expected Outcomes
  - Explain general facts of thermal analysis including application in other field
  - Illustrate theory and principle of both instruments: DSC and TGA
  - Discuss on the application of both instruments in pharmaceutical

- References

  - Gunzler H. & Williams A. (2002). Handbook of Analytical Techniques. Wiley-VCH, Weinheim, Germany.
  - Mullertz, A., Perrie, Y. and Rades, T. (2016) Analytical Techniques in the Pharmaceutical Sciences (Advances in Delivery Science and Technology). Springer, United States.

MATTER

- **Definition**: Anything that has mass and occupies some place in the space.

- The matter posses properties that are divided in chemical and physical:

    i. **Chemical properties** – characteristics observed after chemical **reaction** (combustion, flammability, oxidation etc)

    ii. **Physical Properties** – characteristics that can be **measured directly** from the matter (Density, Color, form; Solid, liquid or gas, **Boiling point, Melting point)**

THERMAL ANALYSIS (TA)

- It is a branch of materials science → the **properties** of materials are studied as they **change with temperature**

- **DEFINITION:**
- "Precisely determined thermodynamic events such as change of state, can indicate the identity and purity of drugs".
- "Is the measurement of physical-chemical properties of materials as a function of temperature".

- When a material is heated its **structural** and **chemical** composition can **undergo changes** such as fusion, melting, crystallization, oxidation, decomposition, transition, expansion and sintering.

- Using Thermal Analysis such changes **can be monitored** in every atmosphere of interest.

- The obtained information is very **useful in quality control.**

USP 891: TA Obtained Information

- Crystal perfection
- **Polymorphism**
- **Melting temperature**
- Sublimation
- Glass transitions
- Dehydration
- Evaporation
- Pyrolysis
- Solid-Solid Interactions
- **Purity**

TA: INSTRUMENTAL METHODS

Thermal Gravimetric Analysis (TGA)

- **mass change** of a substance measured as **function of temperature** whilst the substance temperature is subjected to a controlled temperature

Differential Scanning Calorimetry (DSC)

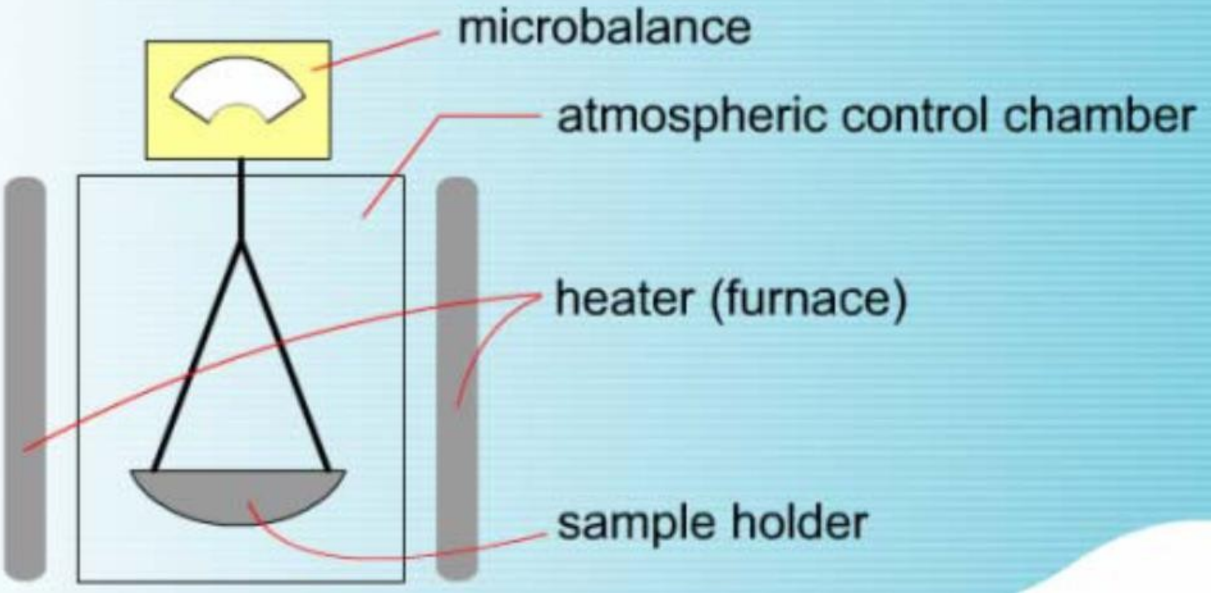
- provides information about thermal changes that **do not involve a change in sample mass**
- more commonly used technique than TGA

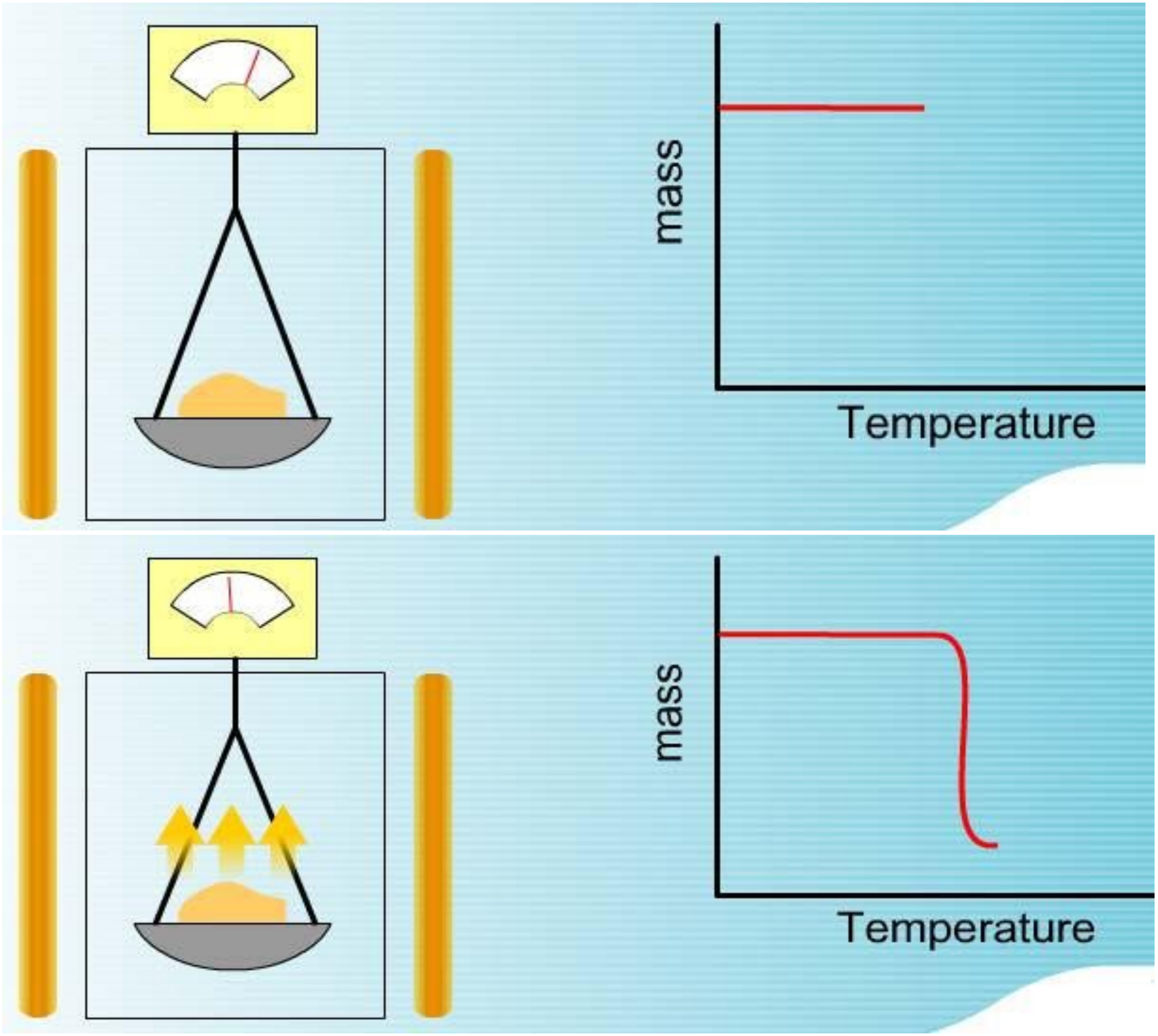
THERMAL GRAVIMETRIC ANALYSIS (TGA)

- It is a type of testing that is performed on samples
- Function: to determine changes in **weight/mass** in relation to **change in temperature.**
- Data recorded in form of curve → "**Thermogram**".
- The **measured weight loss curve** gives information on:
  - changes in sample composition
  - thermal stability
  - derivative weight loss
  - material purity

TGA: basic principles

- Monitor change in **mass** of sample
  - as function of temperature
  - as function of time (at constant temperature)

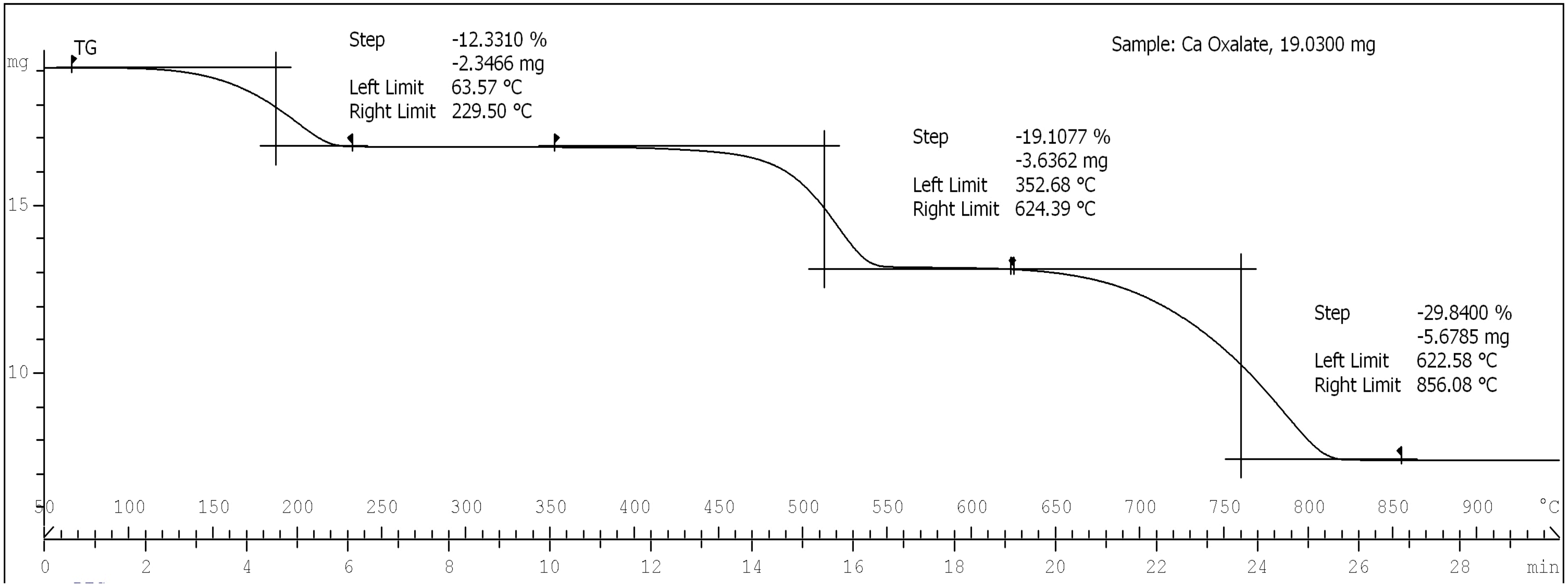



mass
Temperature
mass
Temperature

TGA: parts & components

- **Crucible** – ceramic container to melt the metal/ substance
- The **furnace** (device for high temperature heating) can raise the temperature as high as 1000°C which is made of quartz.
- **Microbalance** – weight/mass measurement.
- **Purge gas system**: Provide safer gas, clear out the system, avoid fire due to high temp., cool down the system

TGA THERMOGRAM



TGA

- The furnace can raise the temperature as high as 1000°C which is made of quartz.
- The auto sampler helps to load the samples on to the microbalance.
- The thermocouple sits right above the sample.
- Care should be taken at all times that the thermocouple is not in touch with the sample which is in a platinum pan.

TGA

TGA: A technique that permits the **continuous weighing of a sample** as a function of temperature and/or as a function of time at a desired temperature

VARIANTS OF TGA

Types:

- DSC-TGA
- DSC-XRD – DSC coupled with X-ray diffraction
- TGA-MS – TG system coupled with a mass spectrometer
- TGA-FTIR – TG system coupled with a Fourier Transform infrared spectrometer
- TGA -MS or -FTIR - evolved gas analysis (EGA)

Applications of TGA

There is a wide range of applications of TGA;

- ✧ Composition of multi-component system
- ✧ Thermal stability of materials
- ✧ Oxidative stability of materials
- ✧ Estimated lifetime of a product
- ✧ Decomposition Kinetics of materials
- ✧ The effect of reactive or corrosive atmosphere on materials
- ✧ Moisture and volatiles contents on materials.

DIFFERENTIAL SCANNING CALORIMETER (DSC)

- It is a thermo-analytical technique in which the difference in the **amount of heat** required to **increase the temperature of a sample** and reference are measured as a function of temperature.

- DSC, is a thermal analysis technique to determine **material's heat capacity (Cp) is changed by temperature.**

- A sample of known mass is heated or cooled.

- The changes in its **heat capacity are tracked** as changes in the heat flow.

- This allows the **detection of transitions (e.g.** melting point, glass transitions, phase changes, and curing)

DIAGRAM OF A DSC APPARATUS

- A DSC apparatus is built around

  - a differential detector
  - a signal amplifier
  - a furnace
  - a temperature controller
  - a gas control device
  - a data acquisition device

DSC : MEASURING TECHNIQUE

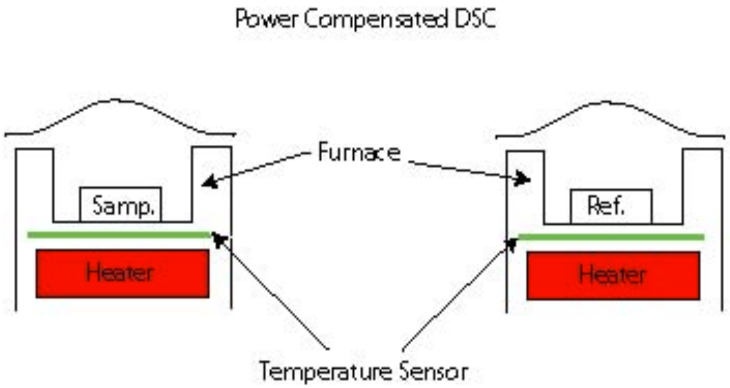
Two types of DSC instruments have been widely used:

HEAT FLOW/POWER COMPENSATED

- Double-furnace DSC in order to measure heat flow, the movement of heat in and out of a sample, directly.
- This allows for very precise control of temperature, very accurate enthalpy and heat capacity measurements, and true isothermal performance.
- Because of its direct measurement of heat flow, it is often called heat flow DSC.

Heat Flow/Power Compensated DSC

- **Sample holder**: Aluminium, platinum, stainless steel pans
- **Sensors**: Pt resistance thermocouples, separate heaters and sensors for sample and references.
- **Furnace**: separate blocks for sample and reference cells.
- **Temperature controller**: differential thermal power is supplied to the heaters to maintain the T of the sample and reference.



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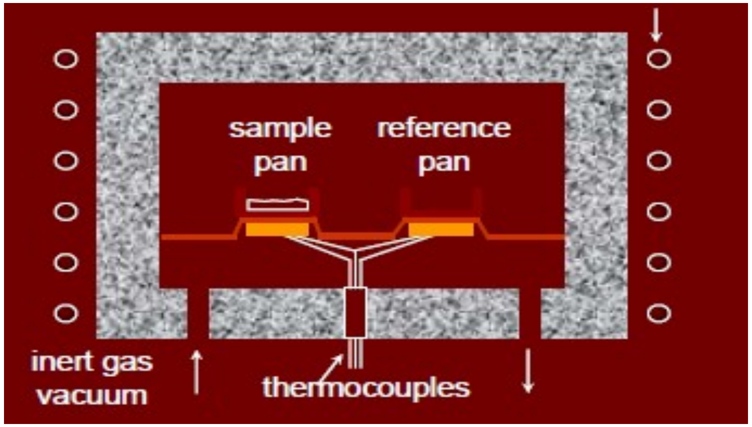
HEAT FLUX

- A large single furnace which acts as an infinite heat sink to provide or absorb heat from the sample.
- The heat flux DSC is based on the Change in Temperature (ΔT) between the sample and reference.
- Heat flux DSCs are less sensitive to small transitions due to single furnace.
- Heat and cool at slower rates than heat flow DSC
- Less accurate values for Cp and enthalpy.

Heat Flux Components

- **Sample holder**: sample and reference are connected by a low-resistance heat flow path
- **Sensors**: Pt resistance thermocouples
- **Furnace**: One block for sample and reference cells.
- **Temperature controller**: T difference between the sample and reference is measured.



HEAT FLOW VS. HEAT FLUX

- both designs have strengths and weaknesses, and if you are doing more than just looking at simple glass transitions and melts, you may need one or the other.

	Heat Flow	Heat Flux
Fast Heating (250 °C/min plus)	Yes	No
Modulated Techniques	Yes	Yes
Accuracy of Cp Values	High	Moderate
Delta H Accuracy	High	Moderate
Ease of cleaning	Very	Moderate
OIT Testing	Moderate	Easy
Isotherm Performance	Excellent	Affected by sample

DSC: APPLICATIONS

- Purity
- Compatibility of API-Excipients
- Characterization: **Comparison between suppliers and processes**
- **Pharmaceutical**: In liquid crystals, metals, pharmaceuticals, and pure organics, you can see phase changes or **polymorphs** and study the degree of **purity in materials**

DSC: ADVANTAGES

- **Fast** and **reliable** research tool.

- DSC allows fast evaluation of possible incompatibilities, because it shows change in the appearance, shift or disappearance of melting, endosperms and exotherms or variations in the corresponding enthalpies of reaction (thermograms).

- Rapid analysis, easy handling, high significance for research, development and quality control.

VARIANTS OF DSC

- **Conventional** – linear temperature (cooling,heating) programme
- **Fast scan DSC** – very fast scan rates (also linear)
- **MTDSC (modulated temperature DSC)** – more complex temperature programmes, particularly useful in the investigation of glass transitions (amorphous materials)
- **HPDSC (high pressure DSC)** – stability of materials, oxidation processes

CONCLUSION OF THE CHAPTER

- Thermal analysis gives information about **changes in material properties as function of temperature**

- Characteristic **thermo-gravimetric curves** are given for specific materials and chemical compounds due to unique sequence from physicochemical reactions occurring over specific temperature ranges and heating rates.

- These unique characteristics are related to the molecular structure of the sample.

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Any Question?

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