

States of Matter in Pharmaceutical Formulation II

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Lecture agenda:

- **Why States of Matter important in Pharmacy**
- **Gaseous State: Applications & Laws**
 - Ideal and real gas laws
- **Liquefied Gas State: Propellants in MDIs**
- **Solid State: Tablets, Capsules, Powders**
- **Summary: Linking States to Formulation**

Why States of Matter Important in Pharmaceutical formulation

- We manipulate physical states to deliver drugs **safely** and **effectively**.
- **Gas:** Medical gases and inhaled therapies for direct lung delivery.
- **Liquefied Gas:** Propellants in MDIs that create pressurized mists or foams.
- **Solid:** Tablets, capsules, and powders provide stability and precise dosing.
- **Key Variables:** Temperature ($0^{\circ}\text{C} = 273.15\text{ K}$; Kelvin), Pressure (dynes/cm², atmosphere, or mmHg), and Volume (L or cm³) dictate formulation behavior.

Gaseous State: Applications & Laws

Fundamental Gas Laws

• Boyle's Law

$$P_1 V_1 = P_2 V_2$$

- The **Pressure** is **inversely proportional** to **Volume** at constant **Temperature**.
- Critical for understanding compression.

(**pressure** ↑ **volume** ↓)

• Charles's Law

$$\frac{V_1}{T_1} = \frac{V_2}{T_2}$$

- **Volume** is **directly proportional** to **Temperature**.
- Impacts storage and stability.

(**temperature** ↑ **volume** ↑)

• Gay-Lussac's Law

$$\frac{P_1}{T_1} = \frac{P_2}{T_2}$$

- The **pressure** of a given mass of gas is **directly proportional** to its absolute **temperature**, provided the **volume** remains constant.

(**temperature** ↑ **pressure** ↑)

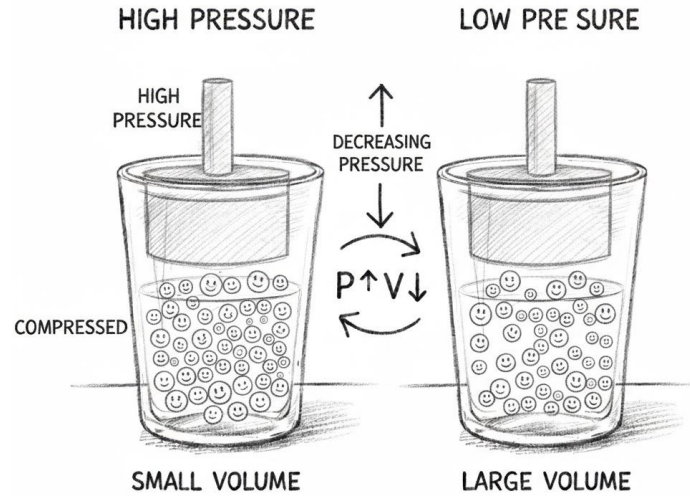
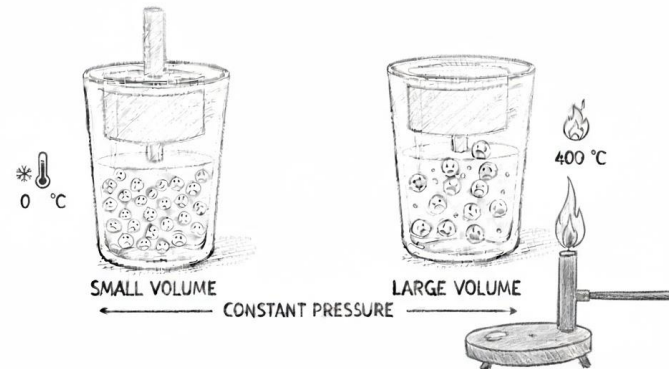
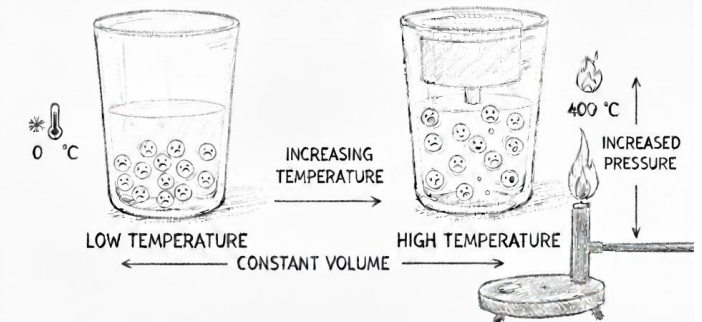
BOYLE'S LAW: $P \uparrow V \downarrow$ **CHARLE'S LAW: $T \uparrow V \uparrow$
(CONSTANT PRESSURE)****GAY-LUSSACS LAW: $T \uparrow P \uparrow$
(CONSTANT VOLUME)**

Figure 1: Visual explanations of common gas laws

Law	Relationship	Constant	Formula
Boyle's Law	Pressure ↑, Volume ↓	Temperature (T)	$P_1 V_1 = P_2 V_2$
Charles's Law	Temperature ↑, Volume ↑	Pressure (P)	$\frac{V_1}{T_1} = \frac{V_2}{T_2}$
Gay-Lussac's Law	Temperature ↑, Pressure ↑	Volume (V)	$\frac{P_1}{T_1} = \frac{P_2}{T_2}$

Ideal Gas Law

- The **Ideal Gas Law** combines several individual gas laws (Boyle's, Charles's, and Avogadro's) into one single equation that describes the relationship between pressure, volume, temperature, and the amount of gas present

$$PV = nRT$$

- No intermolecular interaction
- Collisions are perfectly elastic
- Derived from Boyle's and Charles's
- Relates Pressure, Volume, Temperature, and Moles. The foundation for calculating dose and container pressure.

Variable	Represents	Common Units
P	Pressure	Atmospheres (atm), Pascals (Pa), or mmHg
V	Volume	Liters (L) or Cubic meters (m ³)
n	Amount of Substance	Moles (mol)
R	Ideal Gas Constant	0.0821 L.atom/mole.K (varies by units)
T	Temperature	Must be in Kelvin (K)

Real Gas

- Real gas **do not** obey ideal gas laws as the particles exchange energy when interact with each other.
- Real gases are composed of molecules of a finite volume that tend to attract each other
- The significant molecular volume and intermolecular attractions between gas molecules affect both the volume and the pressure of a real gas respectively.
- The **Van der Waals equation** is a modified ideal gas equation that considers the factors that affect the volume and pressure of real gas

Van der Waals equation

- To measure the intermolecular forces
- When there is **a compression forces** on real gases, we used this equations

- For 1 mole of gas: $\left(P + \frac{a}{V^2}\right)(V - b) = RT$

- For n mole of gas: $\left(P + \frac{an^2}{V^2}\right)(V - nb) = nRT$

- $\left(\frac{a}{V^2}\right)$ indicates the internal pressure per mole resulting from the intermolecular forces of attraction between the molecules.

b indicates the excluded volume., which is about 4X the molecular volume

- When the real gases are **not under any compression forces**, they exhibit as ideal gas and therefore ideal gas equations can be used.

Gaseous Pharmaceutical Formulation

- **Inhalation Delivery:** MDIs (Metered Dose Inhalers), DPIs (Dry Powder Inhalers), and nebulizers rely on gas principles.
- **Mechanism:** Propellant flashes from liquid to gas upon release → rapid expansion breaks liquid into droplets.
- **Target Size:** Lung delivery requires **1–5 μm** . Nasal/topical sprays use larger sizes (10–100 μm).

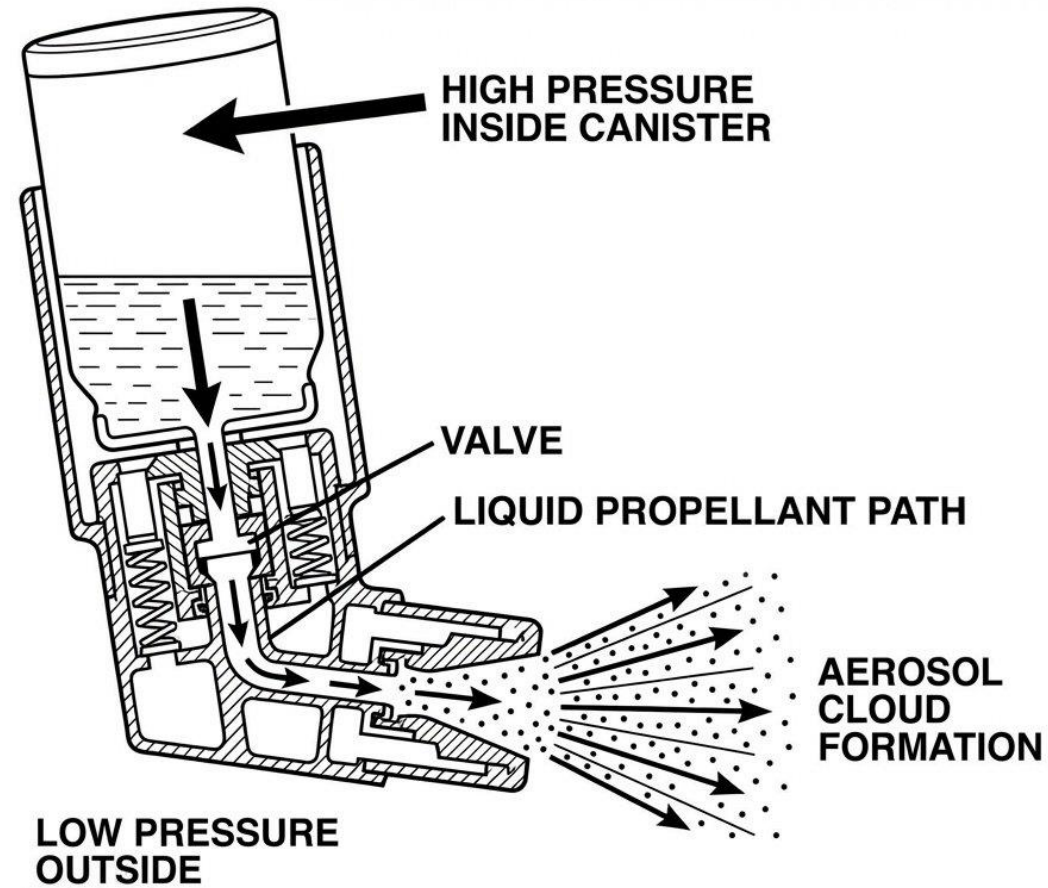


Figure 2: a physical motion of particles inside of aerosol tool

Liquefied Gas State: Propellants in MDIs

- **Concept:** Gas stored as liquid under pressure. Main propellant in metered-dose inhalers (MDIs).
- **Equilibrium Mechanism:** Liquid and vapor phases coexist. As liquid is sprayed, more liquid boils to vapor, maintaining **constant pressure**.
- **Formulation Types:** Can be solutions (drug dissolved) or suspensions (drug dispersed) or emulsions (foams).
- **Formulation Choices:** Must balance vapor pressure (spray force), density (stability), and solvent properties.
- **Note:** Compressed gases (N_2 , CO_2) are different—their pressure drops during use.

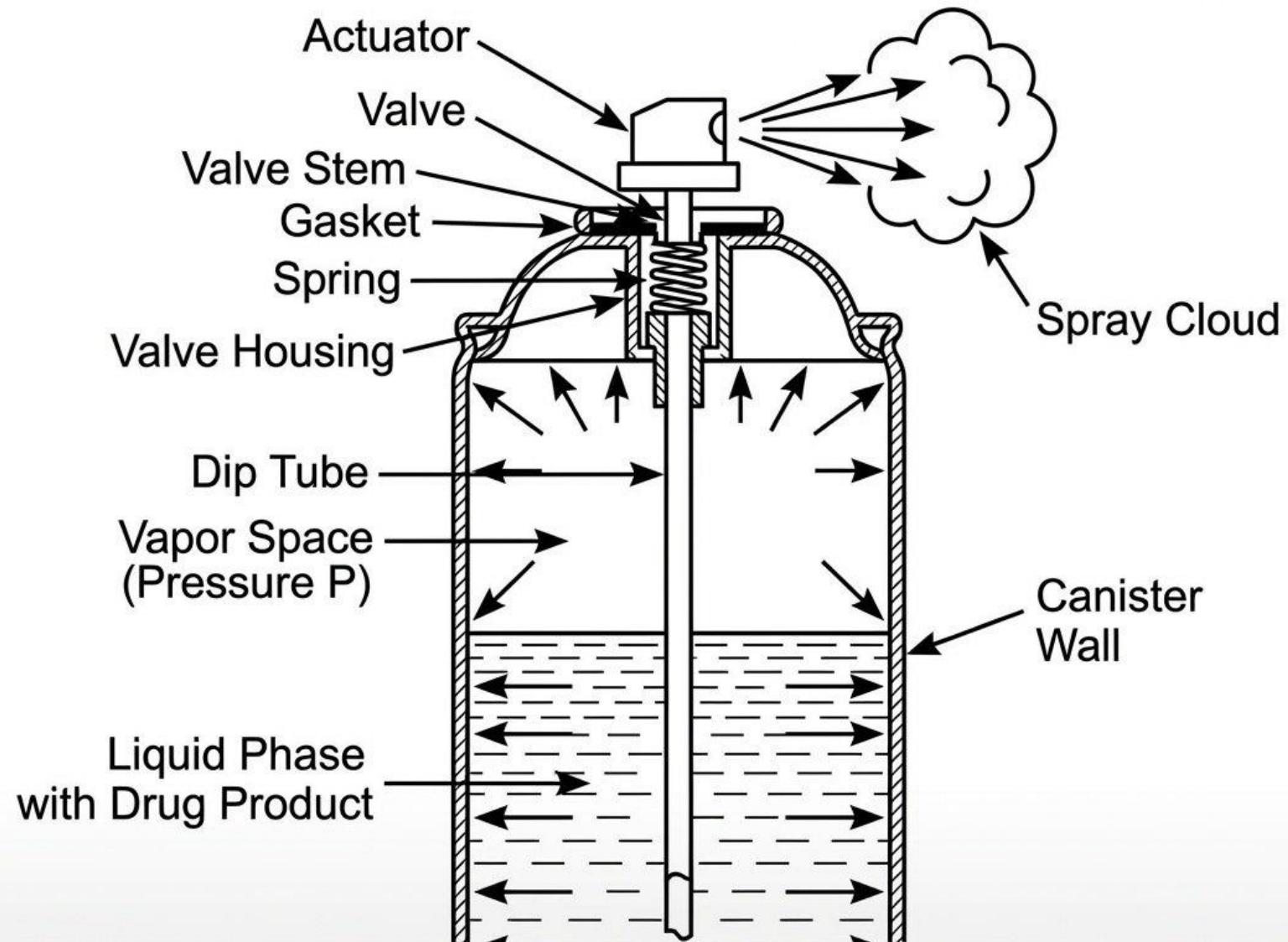


Figure 3: Internal Mechanics of a Liquefied Gas Aerosol

Solid State: Tablets, Capsules, Powders

- **Oral Dosage Forms:** Tablets and capsules are the most common forms due to stability and ease of use.
- **Critical Attributes:** Particle size, shape, flowability, and compressibility dictate quality.
- **Key Excipients:** Diluents (fillers), Binders (glue), Disintegrants (break-up), Lubricants (flow).
- **Process Flow:** Blending → Granulation → Compression → Coating.
- **Quality Tests:** Hardness, friability, disintegration, and dissolution.

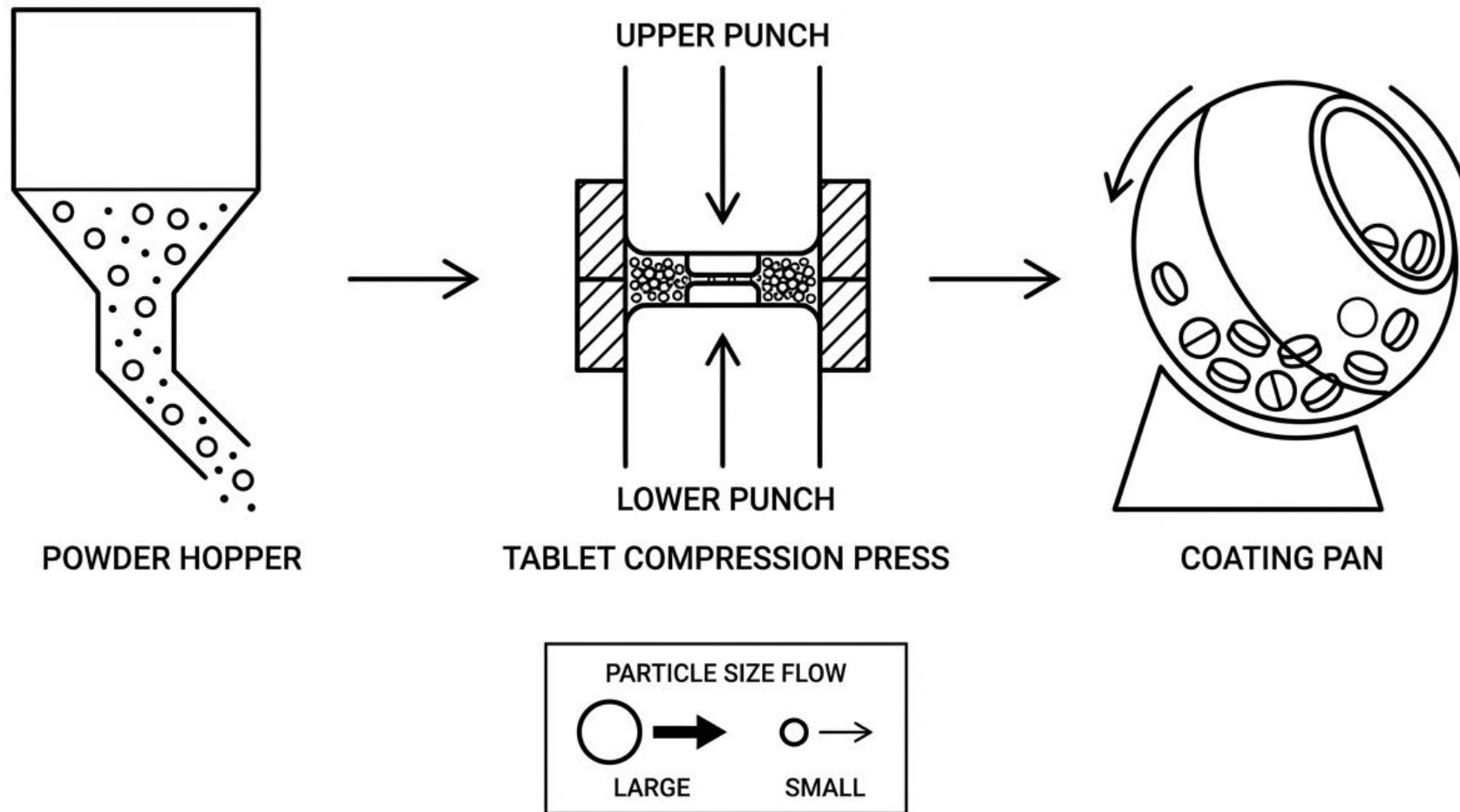


Figure 4: Tablet manufacturing process flow

Linking States to Formulation

Connecting physical laws to patient care decisions

Gaseous State

Delivery depends on P-V-T relationships (Boyle's, Charles's, Ideal Gas laws).

Focus: Cloud formation & accurate dosing via pressure.

Liquefied Gas

Equilibrium between liquid and vapor maintains constant spray pressure.

Focus: Propellant choice, stability, & environment.

Solid State

Ordered structure requires control of particle size, flow, and compression.

Focus: Excipients, disintegration, & shelf-life.

Understanding the physical state allows pharmacists to ensure dose accuracy, stability, and ease of use for the patient.