

الصيدلة	الكلية
الصيدلانيات	القسم
Pharmaceutical Technology	المادة باللغة الانجليزية
تقانة الصيدلة	المادة باللغة العربية
الثالثة	المرحلة الدراسية
م.م. عمار عبدالمجيد أحمد	اسم التدريسي
Derjaguin-Landau and Verwey-Overbeek theories	عنوان المحاضرة باللغة الانجليزية
DLVO نظريات	عنوان المحاضرة باللغة العربية
6	رقم المحاضرة
Pharmaceutical Dosage forms and Drug Delivery Systems By Haward A. Ansel; latest edition.	المصادر والمراجع
Sprowel's American Pharmacy.	

محتوى المحاضرة

Introduction to DLVO Theory

The DLVO Theory combines the Derjaguin–Landau and Verwey–Overbeek theories.

It explains the stability of colloidal systems by analyzing the balance between attractive and repulsive forces.

Understanding this theory is crucial for various applications in fields like material science and biotechnology.

Historical Background

The DLVO Theory was developed in the 1940s by Derjaguin and Landau, and later expanded by Verwey and Overbeek.

It emerged from the need to understand colloidal stability and interactions, laying the groundwork for modern colloid science.

Pharmaceutical Relevance

Pharmaceutical suspensions are composed not of a single particle of drug suspended in a liquid medium but rather of multiple particles.

This leads to multiple particulate interactions.

These interactions can be thought of as the interactions of the diffuse layers around individual particles, and hence the electrical double layer provides the basis for understanding interparticulate interactions.

The DLVO theory describes these interactions.

Key Concepts of DLVO Theory

At the heart of DLVO Theory are two primary forces:

- van der Waals attraction
- Electrostatic repulsion

The interplay of these forces determines the stability of colloids.

The DLVO theory is concerned with predicting the stability of lyophobic (“solvent-hating”) colloids.

It calculates the energies of attraction and repulsion between similar particles and predicts the overall energy of interaction.

From this, deductions can be drawn about whether particles will merge and settle or stay uniformly distributed in the medium.

This is crucial in pharmaceutical suspension formulation, since dose reproducibility is best achieved with a system that remains consistently well dispersed.

Importance of DLVO Theory

- Van der Waals Forces
 - Weak attractive forces that act between molecules.
 - In colloidal systems, they play a significant role in promoting aggregation.
 - Understanding them helps predict when colloidal stability will be compromised.

- Electrostatic Repulsion
 - Arises from charged surfaces of colloidal particles.
 - When particles are similarly charged, they repel each other, contributing to stability.
 - Prevents coagulation and maintains stable colloidal dispersions.
-

Total Energy of Interaction

To calculate the total energy of interaction (VT) between two particles:

$$V_T = V_R + V_A$$

- V_R = energy of electrical repulsion (positive sign).
- V_A = energy of van der Waals attraction (negative sign).

The V_T curve changes with the distance between particles.

DLVO Diagram – Zones of Interaction

There are three important zones on the DLVO curve:

1. Primary minimum
2. Primary maximum
3. Secondary minimum

Particle behavior depends on which zone they are in.

Remember: all particles have some thermal energy and show movement (Brownian motion, gravity, agitation).

Primary Minimum

- Defined as a minimum because V_T is below zero (overall attractive).
- Defined as primary because it is the largest negative deviation from zero.

- Attraction $>$ Repulsion \rightarrow particles move closer together.
 - Kinetic energy (kT) is insufficient to overcome V_T (attractive).
 - Leads to irreversible aggregation:
 - First loose flocculation, then hard coagulation.
 - Undesirable in pharmaceutical suspensions \rightarrow poor reproducibility of dosing.
-

Primary Maximum

- Defined as a maximum because V_T is above zero (overall repulsive).
- Defined as primary because it is the largest positive deviation from zero.
- Repulsion $>$ Attraction \rightarrow particles remain separate (deflocculated).

At first, this seems ideal: reproducible dosing.

- If particle kinetic energy $<$ V_T \rightarrow repulsion dominates \rightarrow particles stay apart.
- If kinetic energy $>$ V_T (e.g., at higher temperature) \rightarrow barrier is overcome \rightarrow particles fall into the primary minimum \rightarrow aggregation.

Thus, designing suspensions in the primary maximum zone is risky.

Secondary Minimum

- A shallow well in V_T , overall weakly attractive.
- Particles form floccules = loose, reversible aggregates.
- Two cases:
 - If kinetic energy $<$ V_T \rightarrow particles weakly attracted, remain in flocculated state.
 - If kinetic energy $>$ V_T \rightarrow particles move apart, behave independently.

In both cases → minimal irreversible coagulation.

👉 This is the desired zone for pharmaceutical suspensions.

General Suspension Formulation Considerations

1. Solubility

- Decision: solution vs suspension depends on aqueous solubility.
- Dosing volume fixed (oral = 5 mL, eye drop = 10 μ L).
- If solubility too low → design suspension.

Ways to suppress solubility:

- Antisolvent addition (reduce solubility).
 - pH adjustment:
 - Weak acid = less soluble at low pH.
 - Weak base = less soluble at high pH.
 - Prodrug formation: e.g., esters often less soluble.
-

2. Formulation Excipients

Flavours, sweeteners, colours

- Needed for children (palatability).
- Colours have minimal physical effect (low conc.).
- Sucrose traditionally used, but restricted (dental caries, diabetes).
- Modern sweeteners: saccharin (Na salt), acesulfame (K salt), aspartame (avoid in PKU).

Antimicrobial preservatives

- Required whenever water is present.
- Examples:
 - Sucrose \geq 67% w/v (rare now).

- Benzalkonium chloride (~0.01%): cationic surfactant, affects zeta potential.
- Sorbic acid, Benzoic acid (~0.2%): effective un-ionized, partial ionization affects diffuse layer.
- Parabens (~0.2%): stable, do not ionize at product pH.

Buffers

- Maintain narrow pH range.
- May suppress solubility.
- Add charges to the system → influence flocculation.
- Also affect preservative ionization and efficacy.

Chemical stabilizers

- Antioxidants: ascorbic acid (~0.2%), sodium metabisulfite (~0.1%).
- Chelators: EDTA.

