A. Spheroids and Vectorized Shapes

Spheroids and vectorized shapes are two concepts related to drug formulation. Spheroids are three-dimensional structures that mimic human tissues, used in research to test drug efficacy and for targeted drug delivery. Vectorized shapes (or vectorization) are drug delivery systems designed to transport active ingredients to specific targets in the body, improving tissue distribution and protecting the active molecule.

Spheroids

• What are they? They are spheres formed from cells that can be used as 3D cell culture models.
Objective:
o Drug testing: They allow the simulation of physiological conditions (such as solid tumors) for drug testing that is more relevant than 2D cell cultures.
o Drug delivery: Their size and structure can improve the delivery of active ingredients.

• Advantage:
o They mimic the architecture and metabolism of tissues in vivo.
o They are useful for studying drug resistance and treatment infiltration.

o They are more reproducible, less expensive, and faster than animal models.

Vector Forms

• What are they? They are systems that transport an active ingredient to a specific target in the body.

• Objective:
o Tissue distribution: To modify how a drug is distributed in the body, making it less dependent on its own physicochemical properties.
Specificity: Ensuring that the drug acts at the intended site by selecting a vector with a positive tropism for the target tissue.

Qualities required for a vector:

Non-toxic and biodegradable.

Appropriate size and shape for incorporation of the active ingredient and for internalization into the target cell.

Stable but reversible binding to the active ingredient.

Protection of the active ingredient during transport.
Relationship between the two:
Spheroids are used as a model for developing and testing drug delivery systems, particularly in cancer research.

A delivery system can be designed to deliver the active ingredient within a spheroid, thus simulating the distribution and efficacy of a treatment in vivo.

01. Microparticle Drugs:

Microparticle drugs are drug delivery systems where the active ingredient is encapsulated in tiny particles, typically between 1 and 1000 µm. This technology aims to protect the drug, improve its presentation, or control its release in the body, for example, for extended-release applications, targeting specific areas, or for patients with swallowing difficulties. The drug "MICROPAKINE" is an example of a drug packaged in microparticles (granules).

Main Uses and Benefits

• Easier Administration: Microparticles, especially micro-tablets, are easier to swallow, which is particularly helpful for children or the elderly.

• Extended Release: Microencapsulation allows for controlled drug release over a longer period, thus reducing the frequency of dosing.

Protection of the active ingredient: Encapsulation protects the active ingredient from premature degradation, ensuring that it arrives intact at its destination.

• Targeted delivery: Microparticles can be designed to target specific areas of the body, thus improving efficacy and reducing side effects.

2. Nanoparticles:

Nanoparticle-based drugs, or nanomedicines, are treatments that use particles of nanometer size (between a few tens and a few hundred nanometers) to encapsulate and deliver active ingredients. This technology allows for better protection of the therapeutic molecule, more targeted delivery to diseased cells through surface modifications, and potentially fewer side effects.

Principles of Operation

• Encapsulation and Protection: The active ingredient is encapsulated within the nanoparticle, protecting it from degradation by the body. This also allows it to cross certain barriers, such as the blood-brain barrier.

• Targeting: The surface of the nanoparticles can be modified to bind specifically to diseased cells, much like a "key" in a "lock," optimizing treatment efficacy while minimizing interactions with healthy cells.

• Administration: These drugs can be administered orally or intravenously and are designed to accumulate in specific organs, such as tumors.

Examples of Applications

Cancer Treatment:

o Iron oxide nanoparticles are used to treat brain tumors via magnetic hyperthermia therapy (NanoTherm®).

o Alpha-hfnium nanoparticles are being studied to increase the effectiveness of radiotherapy by injecting the particles directly into the tumor.

o Anticancer drugs encapsulated in liposomes (PEGylated liposomes) are used to treat cancers such as ovarian or pancreatic cancer (Onivyde®).

Advantages and Challenges

• Advantages: Targeted delivery, improved efficacy, reduced side effects.

• Challenges: The complexity of synthesis and scaling up to industrial production can be significant limitations for the development of these therapies.

A liposomal drug is a preparation in which the active ingredient is encapsulated in micro-vesicles of lipids called liposomes. This technology improves treatment efficacy by allowing for better absorption, precise targeting (e.g., to tumors), sustained release, and a potential reduction in side effects. Liposomes are used in various medications, including anticancer drugs, antifungals, and dietary supplements.

Advantages of Liposomal Drugs

• Improved Absorption and Bioavailability: Liposomes protect the drug from degradation and facilitate its passage through cell membranes.

Targeted delivery: They can be designed to target specific areas of the body, such as a tumor, thus increasing the effectiveness of treatment in the affected area.

• Reduced side effects: By delivering the drug in a more targeted manner, the amount of active substance in other parts of the body can be reduced, thereby decreasing unwanted side effects.

• Controlled delivery: They can allow for a slower and more prolonged release of the active ingredient.

Composition and function

• A liposome is a biodegradable vesicle made of a phospholipid bilayer, a type of fat.

• It contains an aqueous compartment.

• The active ingredient is encapsulated either in the aqueous compartment (if it is water-soluble) or in the lipid bilayer (if it is fat-soluble).

Liposomes can be engineered in the lab to carry other substances, such as genes in gene therapy.

Examples of Use

• Oncology: Treatment of pancreatic cancer (ONIVYDE pegylated liposomal) and breast cancer (Myocet liposomal).

• Antifungals: Treatment of invasive fungal infections (AMBISOME liposomal).

• Dietary Supplements: Improved absorption of vitamins (such as vitamin C) or other nutrients.

• Hygiene Products: Moisturizing gel for intimate shingles based on liposomal hyaluronic acid (Mucogyne gel).

B. Pharmaceutical Forms in Development

1. Bioencapsulated Drug:

"Bioencapsulation" is not a standard term for a drug, but refers to techniques related to the encapsulation of active ingredients to improve their delivery or stability.

This can involve the microencapsulation of drugs (active ingredient in a polymeric or lipid coating) or bioequivalence (comparison of the bioavailability of a generic drug with its brand-name counterpart).

Microencapsulation

• Definition: A technique consisting of encapsulating an active material (such as a pharmaceutical active ingredient) inside microparticles.

• Objective: To protect the active ingredient, control its release over time, or improve its performance.

• Examples:
o Microcapsules: A liquid or solid core surrounded by a membrane.

o Microspheres: The active ingredient is dispersed in a matrix (polymeric or lipid).
Application: Very varied, from medications (including cancer treatments) to cosmetics and food products.

Bioequivalence
• Definition: A study demonstrating that a generic drug behaves similarly to a reference (brand-name) drug after administration.

• Objective: To prove that the generic drug is "bioequivalent" so that it can be dispensed.

• Method: Comparison of the concentrations of the active ingredient in the blood or urine over time after administration of the two drugs.

In summary
• The term bioencapsulation can refer to microencapsulation (a manufacturing process) or bioequivalence (a study for generic drugs).

• Microencapsulation allows for the encapsulation of small molecules, cells, or other active substances to control their release.
Bioequivalence is a crucial regulatory step for the marketing of generic drugs, requiring proof of their equivalence to the original drug.

2. Implants:

A "medicated implant" can refer to a contraceptive implant that releases hormones to prevent pregnancy, or to other types of implants that release medication over a long period, such as for the treatment of opioid addiction. Implants are placed under the skin and slowly release the active ingredient for sustained action, eliminating the need for daily doses.

Contraceptive Implant
• How it works: A small rod inserted under the skin of the upper arm that continuously releases a progestin to block ovulation.

• Duration: Effective for up to 3 years.
Advantages: Does not require daily administration, convenient, and does not contain estrogen.

• Risks: It is essential to check its position by palpation and consult a healthcare professional if you have any concerns, as very rare cases of migration are possible.

• Possible side effects: Irregular periods (bleeding or absence of periods), acne, weight gain (if appetite is increased).

Other drug implants
• How they work: Devices designed to slowly release medication over several months.

• Example: Naltrexone implants are used to help treat opioid addiction by reducing cravings and blocking the effects of the drug, according to Istanbul Med Assist.
Advantages: Useful for people who have difficulty adhering to a daily treatment regimen, as they ensure a consistent drug delivery.

03. Mesoporous Materials of Pharmaceutical Interest

Mesoporous materials are of great pharmaceutical interest because they serve as controlled-release systems for drugs, storing the active ingredient and releasing it gradually. Their porous structure, with pores ranging from 2 to 50 nm, provides a large specific surface area, ideal for applications such as drug delivery. They are also used in related fields such as medical imaging.
Vectorization and Targeting: Their surface can be chemically functionalized to specifically target diseased cells or tissues.

• Medical Imaging: Research is underway to use mesoporous nanomaterials in imaging to improve the visualization of certain biological structures or processes.

Types of Mesoporous Materials
• Silica and Alumina: These are common examples of mesoporous materials, often used for their chemical properties and stability.

• Carbon-Based Materials: Mesoporous activated carbon is an example of a carbon-based material used for its adsorption properties.

• Other Oxides: Niobium, titanium, zirconium, and cerium oxides can also be used to create mesoporous materials.
Advantages of Mesoporous Materials
• Large Specific Surface Area: The large surface area allows for the loading of a significant amount of active ingredient.

• Adjustable Pores: The pore size can be adjusted to control the drug release rate.

• Surface Modification: The pore surface can be modified to give the material specific properties.

4. Bioadhesive Forms:

Bioadhesives can be in various forms, such as gels, films, particles, or liquids that transform into gels, and are designed to adhere to biological surfaces. These forms are used in medical applications for drug delivery or tissue sealing, ensuring controlled and prolonged release, or sealing on wet surfaces.
Common Forms
• Gels: Often used in dermatology, they form a transparent film on the skin after application and dry quickly.

• Films: Designed to adhere to mucous membranes for a specific duration, improving local drug absorption.

• Particles: Administered orally, buccally, or transdermally, these particles break down upon contact with bodily fluids and enzymes.

• Liquid-to-Solids: Some liquid adhesives are designed to react with tissues and form a gel or polymer network that adheres to the surface.

Applications
• Drug Delivery: Bioadhesive forms allow for prolonged and localized drug release, reducing dosing frequency and side effects.
Tissue Closure: Internal bioadhesives are used to seal leaks in internal organs (heart, brain) or for skin grafts.

• Specific Applications:
o Internal Use: To seal leaks in blood vessels or organs.
o External Use: For wound closure or epidermal grafts.

5. Iontophoresis:

Iontophoresis does not use medication itself, but an electric current to deliver ionized substances (such as analgesics or anti-inflammatories) into the skin. It is used to treat various conditions such as hyperhidrosis (excessive sweating), muscle and joint inflammation, and cellulite, by locally administering the medication via the electric current.
Principle of Operation
• Application of the substance: A substance in aqueous solution is applied to the skin, for example, an analgesic or anti-inflammatory gel.
• Use of an electric current: A direct electric current is applied to promote the local and superficial penetration of the substance into the skin.

Therapeutic Applications
• Hyperhidrosis: Helps reduce excessive sweating of the hands, feet, or armpits.

• Musculoskeletal Inflammation and Pain: Used to relieve pain associated with muscle and bone injuries, as well as joint disorders.

• Cellulite: May be indicated for the treatment of cellulite.

• Warts: May be used to treat warts on the feet and hands.
Key Points
• Iontophoresis is a transdermal (through the skin) administration method.
• The procedure is generally only slightly painful.
• The duration and frequency of sessions should be determined in consultation with a healthcare professional (such as a podiatrist).

06. Cyclodextrin Colloidal Systems

Colloidal cyclodextrin drug systems are formulations that utilize the "cage" structure of cyclodextrins to encapsulate active ingredients, particularly poorly soluble drugs. This improves their solubility, bioavailability, and stability, reduces their toxicity, and facilitates their administration. These inclusion complexes can be incorporated into various formulations, including "pickling"-type emulsions stabilized with cyclodextrin nanoparticles, for topical or systemic pharmaceutical applications.
Mechanisms and Advantages

• Encapsulation and Solubilization: The hydrophobic cavity of cyclodextrins can accommodate hydrophobic molecules (poorly soluble drugs), making them soluble in water.

• Improved Stability: Encapsulation protects drugs from degradation due to heat, light, acidity, or oxidation.

• Modified Pharmacokinetic Properties: Cyclodextrins can influence drug release, thus improving its bioavailability and efficacy.

• Reduced Side Effects: By encapsulating the active ingredient, cyclodextrins can limit undesirable interactions with other tissues and molecules, thereby reducing side effects.

Examples of applications

• Oral formulations: Improved bioavailability of poorly soluble drugs.

• Topical formulations: Improved skin penetration or stability of cosmetic formulas.

• Innovative delivery systems: Inclusion complexes can be used to form emulsions or other dispersible colloidal systems for various applications.