BP805T · B.Pharm Semester VIII · Theory Notes

Sterile Dosage Forms and Novel Drug Delivery System

Unit I — Fundamentals, Polymers & Materials for NDDS

Unit I (12 hours)

Pills & Python Notes

From-zero teaching standard: every technical term is defined before use.

Syllabus coverage: Unit I (12 hours).

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CHAPTER 1: Limitations of Conventional Dosage Forms and Classification of NDDS

Learning objectives

After reading this chapter, you should be able to:

1 Explain what NDDS (novel drug delivery system) means in simple words.

2 List at least six limitations of conventional dosage forms (tablets, capsules, injections).

3 Explain first-pass metabolism with an example.

4 Explain what solubility and permeability mean and why both are needed for a drug to work.

5 Define sustained release, controlled release, and targeted delivery — and state the difference between them.

6 Classify NDDS into major types and give one example of each.

7 Describe the four basic drug release mechanisms — diffusion, dissolution, osmosis, and erosion — with a simple example of each.

Definitions

- **Dosage form:** The final physical form in which a medicine is given to the patient — for example, a tablet, capsule, syrup, or injection. The dosage form decides how the drug enters the body.
- **Conventional dosage form:** The traditional, "old-style" dosage forms used for a very long time — ordinary tablets, capsules, syrups, and simple injections. They release the drug quickly and all at once, and they do not control where or how long the drug acts.
- **Novel drug delivery system (NDDS):** A "new-style" way of delivering a drug to the body. Instead of releasing the drug all at once, an NDDS controls the rate (speed), the site (place), and/or the duration (time period) of drug release, so the drug works better and causes fewer side effects. "Novel" means new or innovative; "delivery system" means the carrier or technology that carries the drug.
- **Sustained release:** A dosage form that releases the drug slowly over a long time (for example, over 12 or 24 hours), so that the patient needs fewer doses.
- **Controlled release:** A dosage form that releases the drug at a predictable, planned rate and pattern, decided by the design of the system (for example, the same amount every hour). Controlled release is the broader term — sustained release is one type of controlled release.
- **Targeted delivery:** Delivery of the drug specifically to the diseased organ or tissue (for example, only to the tumour), while avoiding healthy tissues.
- **Bioavailability:** The fraction (percentage) of the given drug dose that actually reaches the blood circulation in active form. If 100 mg is swallowed and only 10 mg reaches the blood, the bioavailability is 10%.

- **First-pass metabolism:** The breakdown of a drug by the liver before it reaches the general blood circulation. A drug swallowed orally goes from the stomach and intestine to the liver first (through the portal vein); the liver may destroy a large part of it. Because of this, less drug reaches the body than the dose given.

Terminology

- **Rate:** Speed at which the drug is released (for example, 10 mg per hour).
- **Site:** The place in the body where the drug should act (for example, the lungs, the eye, or a tumour).
- **Duration:** How long the drug keeps working (for example, 12 hours).
- **Plasma concentration:** The amount of drug present in the blood plasma at a given time.
- **Therapeutic window:** The range of drug concentration in blood that is effective but not toxic — not too low (no effect) and not too high (side effects).
- **Peak (Cmax):** The highest drug level in blood after a dose.
- **Trough (Cmin):** The lowest drug level in blood just before the next dose.
- **Half-life (t½):** The time taken for the drug concentration in the body to fall to half of its value.
- **Solubility:** How much drug can dissolve in a liquid (for example, in water). Measured in mg per mL.
- **Permeability:** How easily a dissolved drug can cross (pass through) a body membrane, such as the wall of the intestine.
- **Fick's law (simple meaning):** The rule that says drug movement by diffusion depends on the concentration difference — drug moves faster when the difference between high and low concentration is bigger.
- **Burst release:** Unwanted sudden release of a large amount of drug at the beginning, instead of a slow controlled release.
- **Depot:** A store or reservoir of drug placed in the body (for example, under the skin) that releases the drug slowly over weeks or months.
- **Smart / stimuli-responsive system:** An NDDS that releases the drug only when it senses a signal from the body — for example, changes in pH, temperature, or the presence of a specific enzyme.

Explanation

A conventional dosage form, like an ordinary tablet, works in a very simple way: you swallow it, it dissolves in the stomach or intestine, and the whole drug is released quickly. The blood level of the drug goes up fast (a peak), then falls as the body removes the drug, and then you must take the next dose. This "up and down" pattern has many problems.

Limitation 1 — Poor solubility: Many drugs do not dissolve well in water. If the drug does not dissolve, it cannot be absorbed — it simply passes out in the stool. It is like sugar that does not dissolve in cold water; if it stays as solid grains, the body cannot use it.

Limitation 2 — Poor permeability: Even if the drug dissolves, it must cross the wall of the intestine to reach the blood. Some drugs cannot cross this wall easily. Both solubility and permeability are needed: the

drug must first dissolve (solubility) and then cross the membrane (permeability). Scientists describe this with the BCS (Biopharmaceutics Classification System), which simply divides drugs into four classes based on whether their solubility and permeability are high or low. A drug with low solubility and low permeability is the hardest to deliver.

Limitation 3 — First-pass metabolism: When you swallow a tablet, the drug goes from the intestine to the liver through the portal vein before it reaches the rest of the body. The liver is the body's "chemical factory" and it may destroy much of the drug. Example: a patient swallows 100 mg of a drug; the liver destroys 70 mg; only 30 mg reaches the blood — bioavailability is only 30%. To get enough drug into the body, the doctor must give a larger dose, which can cause more side effects. Some drugs are almost fully destroyed by the liver, so they cannot be given orally at all.

Limitation 4 — Toxicity and side effects: A conventional tablet releases the whole drug at once, so the blood level shoots up very high (a peak) and then falls very low (a trough). At the peak, the high level can damage healthy organs — side effects. At the trough, the level may fall below the useful range — the drug stops working. The drug also goes everywhere in the body, not only to the diseased part, so healthy tissues are also affected. Example: a strong painkiller tablet may relieve pain but also irritate the stomach because the drug reaches the stomach in a high concentration.

Limitation 5 — Frequent dosing and poor patient compliance: Many conventional drugs must be taken 3–4 times a day. Patients forget doses ("compliance" means following the doctor's instructions correctly). Missed doses mean the treatment fails.

Limitation 6 — No control over where the drug goes: An ordinary tablet cannot be told "go only to the liver" or "go only to the tumour." It spreads throughout the body.

Limitation 7 — Short duration of action: The drug is removed from the body quickly (short half-life), so its effect does not last long.

NDDS was developed to solve exactly these problems. An NDDS is like a "smart packet" for the drug: it can release the drug slowly over a long time (sustained/controlled release), it can deliver the drug only to the diseased site (targeted delivery), and it can protect the drug from being destroyed before it reaches its target. This gives steadier blood levels (no big peaks and troughs), fewer side effects, fewer doses, and better results.

The three key ideas of NDDS are:

- **Rate:** how fast the drug comes out (slow and steady instead of all at once).
- **Site:** where the drug goes (only the diseased tissue, not everywhere).
- **Duration:** how long it keeps working (hours, days, or even months from one dose).

Classification

NDDS can be classified into the following major types:

1. **Controlled release systems:** Release the drug at a planned, steady rate over a long time. Examples: sustained-release tablets, osmotic pumps (tablets that push drug out using water pressure), matrix tablets.
2. **Targeted drug delivery systems:** Carry the drug directly to the diseased organ or cell. Examples: drug-loaded nanoparticles aimed at tumour cells, antibody–drug conjugates (a drug attached to an antibody that finds the cancer cell).

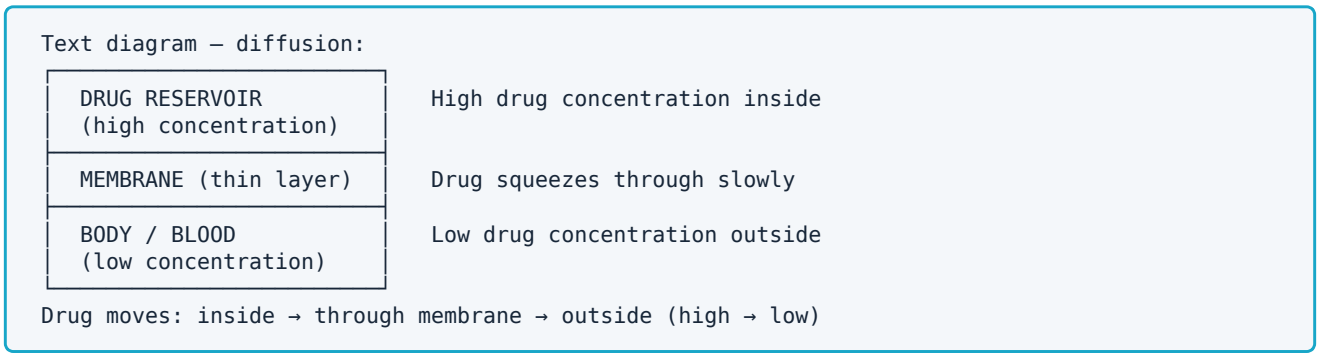
3. **Stimuli-responsive (smart) systems:** Release the drug only when they sense a body signal. Examples: pH-sensitive capsules that open only in the intestine (not the stomach), temperature-sensitive gels, enzyme-triggered release at an inflamed site.
4. **Chronotherapeutic systems:** Release the drug according to the body's daily clock (circadian rhythm). Example: a blood-pressure tablet taken at night that releases the drug in the early morning, when heart attacks are most common.
5. **Transdermal systems (through the skin):** Deliver the drug through the skin into the blood. Example: nicotine patches to stop smoking, pain-relief patches. The drug enters the blood directly and avoids first-pass metabolism by the liver.
6. **Mucosal systems (through mucous membranes):** Deliver the drug through the moist lining of the mouth (buccal/sublingual), nose, or other mucosa. Example: a tablet kept under the tongue for quick action; drugs absorbed here also bypass the liver's first-pass effect.
7. **Implantable and injectable depot systems:** A small device or injection placed in the body that releases drug for weeks or months. Examples: contraceptive implants under the skin (work for years), long-acting injections for mental illness given once a month.
8. **Vesicular systems:** Tiny bubble-like carriers made of membranes that hold the drug inside. Examples: liposomes (bubbles made of phospholipids, like the body's own cell membranes), niosomes.
9. **Polymeric systems:** Drug carriers made from polymers (long-chain molecules), which can be biodegradable. Examples: PLGA nanoparticles, drug-loaded microspheres.
10. **Ocular systems:** Drug delivery to the eye. Examples: eye inserts placed in the lower eyelid that release drug slowly for days, in-situ gelling eye drops that turn into a gel on the eye.
11. **Pulmonary systems (through the lungs):** Drug inhaled into the lungs. Example: asthma inhalers (metered-dose inhalers, dry powder inhalers). The lungs have a huge surface area, so absorption is fast.
12. **Nasal systems (through the nose):** Drug sprayed into the nose. Example: nasal sprays for migraine or allergies. The nose has a rich blood supply for fast absorption and a possible route toward the brain.

Mechanisms

There are four basic mechanisms by which a drug is released from an NDDS. Most real products use one main mechanism, sometimes a combination.

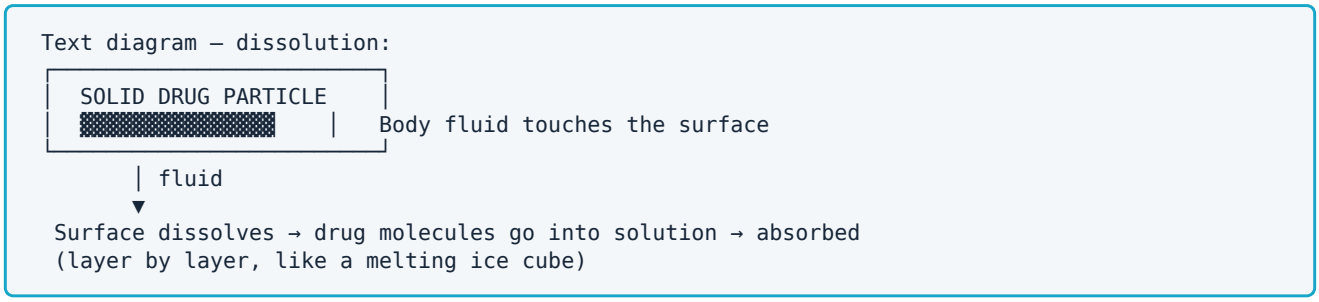
1. Diffusion

Simple meaning: The drug moves by itself from a place of high concentration to a place of low concentration, passing through a membrane or a polymer layer — like the smell of perfume spreading from an open bottle across a room. **How it works:** The drug is stored in a reservoir (a core) surrounded by a membrane. Because the drug concentration is high inside and low outside, drug molecules slowly pass through the membrane into the body. The speed of movement follows Fick's law: bigger concentration difference → faster movement; thicker membrane → slower movement. **Example:** A transdermal patch — the drug slowly diffuses from the patch, through the skin, into the blood, giving a steady supply for 24 hours.



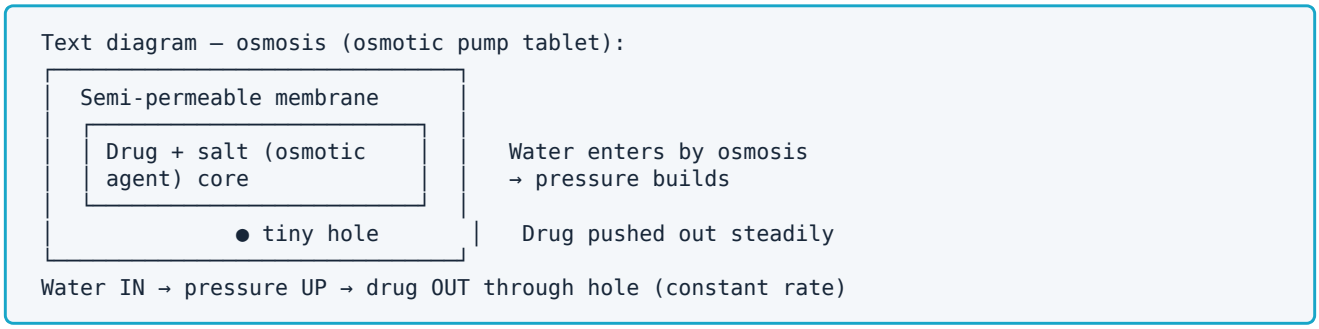
2. Dissolution

Simple meaning: The solid drug slowly dissolves in the body fluid, like a sugar cube dissolving in tea — the drug is released as fast as it dissolves. **How it works:** The drug is present as solid particles inside a tablet or capsule. Body fluid enters, the drug dissolves layer by layer, and the dissolved drug is absorbed. The release rate depends on how fast the drug dissolves (its solubility) and the surface area of the particles (smaller particles dissolve faster). **Example:** A sustained-release tablet made of a slowly dissolving wax matrix — the wax does not dissolve quickly, so the drug inside is freed little by little as the surface dissolves.



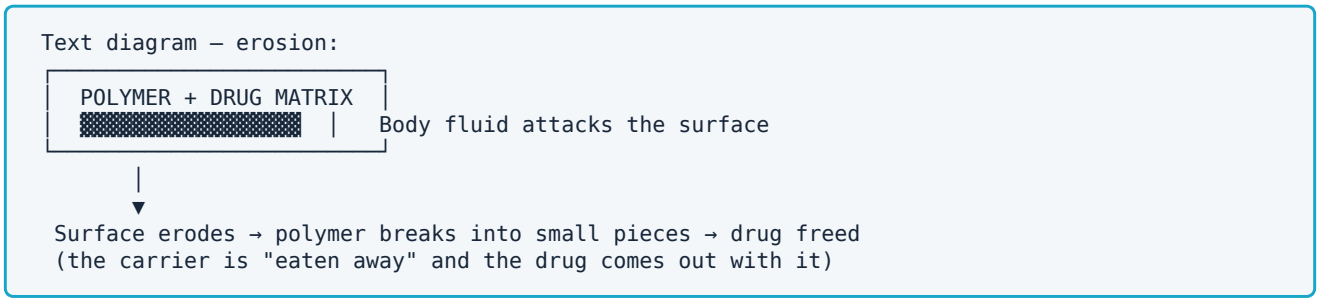
3. Osmosis

Simple meaning: Water is pulled through a special membrane into the tablet; the water pressure inside pushes the drug out through a tiny hole — like filling a balloon with water until the water is forced out through a small opening. **How it works:** The tablet has a core containing the drug plus a salt (the "osmotic agent"), covered by a semi-permeable membrane (lets water in, but not drug out) with one tiny laser-drilled hole. In the intestine, water enters through the membrane by osmosis; pressure builds up inside; this pressure pushes the drug solution out through the tiny hole at a steady rate. **Example:** Osmotic pump tablets for blood pressure or diabetes that give the same amount of drug every hour for 24 hours.



4. Erosion

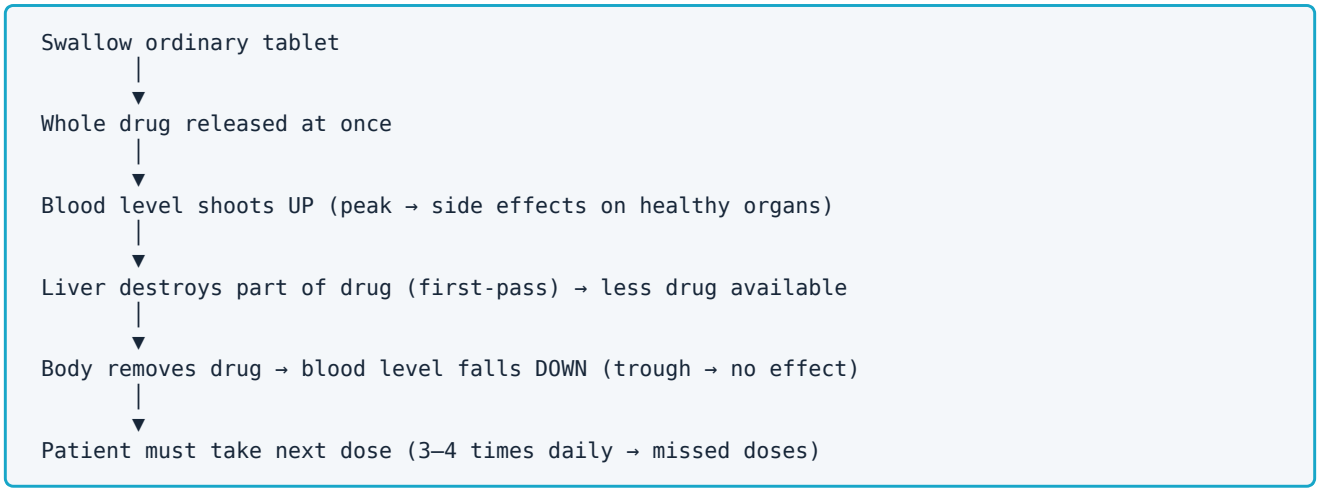
Simple meaning: The carrier material itself slowly wears away (erodes) in the body, freeing the drug as it breaks down — like a bar of soap getting smaller each time you use it, releasing soap with every wash. **How it works:** The drug is mixed inside a biodegradable polymer. Body fluids slowly break the polymer chains (by hydrolysis), the surface erodes layer by layer, and trapped drug is released. The release rate depends on how fast the polymer erodes. **Example:** Biodegradable implants and PLGA microspheres that erode over weeks or months, releasing the drug the whole time, then disappear completely — no need to remove them.



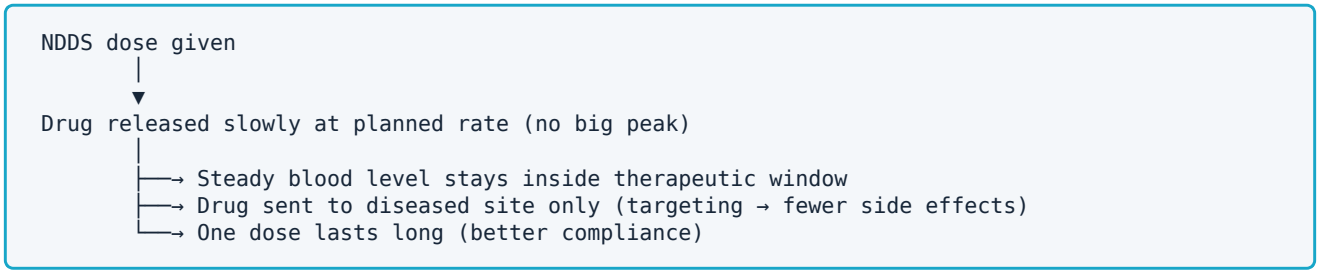
Key takeaway: Diffusion = drug passes through a barrier; dissolution = solid drug melts into fluid; osmosis = water pressure pushes drug out; erosion = the carrier itself breaks down and frees the drug.

Diagrams and flowcharts

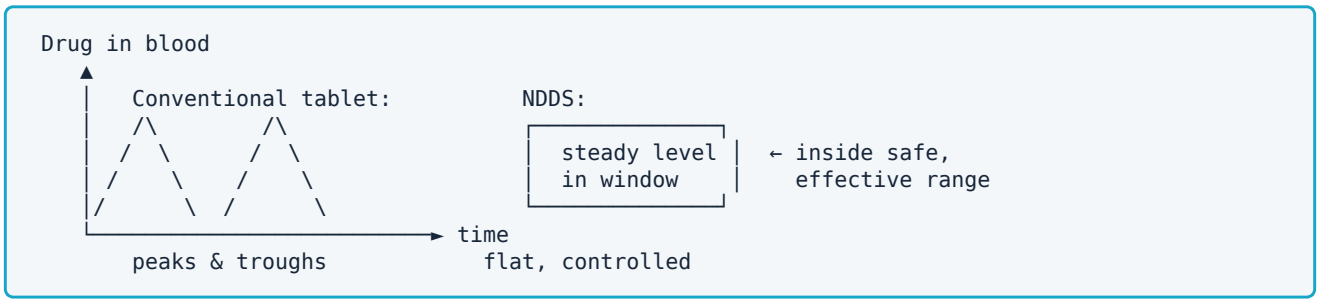
Flowchart 1 — Why conventional dosage forms fail (the problem chain):



Flowchart 2 — How NDDS solves the problems:



Text diagram — Blood level comparison:



Infographic concepts

(Describe these as layout ideas a designer could draw — one idea per box.)

1 **"The leaky bucket vs the drip bottle":** A leaky bucket (conventional tablet) empties all water at once; a drip-irrigation bottle (NDDS) gives water drop by drop for the whole day. Caption: "Same total water — very different delivery."

2 **"The liver toll plaza":** A highway (bloodstream) with a toll plaza (liver) where 70 of 100 drug "cars" are stopped (first-pass metabolism); a bypass flyover (transdermal patch / injection) lets the cars skip the toll. Caption: "Some routes avoid the liver's toll."

3 **"The four release mechanisms":** Four panels — perfume spreading in a room (diffusion), sugar cube in tea (dissolution), water balloon with a pinhole (osmosis), melting soap bar (erosion). Caption: "Four ways an NDDS frees its drug."

4 **"Targeted delivery = addressed letter":** An ordinary tablet is a pamphlet thrown to the whole city; a targeted nanoparticle is a letter with the exact address of the diseased cell. Caption: "Right drug, right place."

5 **"Peaks and troughs roller-coaster vs NDDS flat road":** A roller-coaster track (conventional blood levels) versus a smooth flat highway (NDDS levels) with the therapeutic window marked as a safe green zone. Caption: "Stay in the safe zone."

Tables

Table 1 — Conventional vs novel dosage forms:

Feature	Conventional dosage form	NDDS
Drug release	All at once, fast	Slow, at a planned rate
Blood level pattern	Peaks and troughs (up-down)	Steady, inside therapeutic window
Dosing frequency	2–4 times daily	Once daily, weekly, or monthly
Site of action	Whole body (non-specific)	Can target diseased tissue
Side effects	More (high peaks affect healthy organs)	Fewer (controlled levels)
Patient compliance	Poor (frequent doses)	Better (fewer doses)
Example	Ordinary paracetamol tablet	Transdermal patch, osmotic pump tablet

Table 2 — The four drug release mechanisms at a glance:

Mechanism	Simple meaning	What controls the rate	Example product
Diffusion	Drug moves from high to low concentration through a membrane	Membrane thickness, concentration difference (Fick's law)	Transdermal patch
Dissolution	Solid drug dissolves slowly in body fluid	Drug solubility, particle surface area	Wax-matrix sustained-release tablet
Osmosis	Water enters, pressure pushes drug out of a tiny hole	Membrane water permeability, salt amount	Osmotic pump tablet
Erosion	Carrier breaks down and frees the drug	Polymer breakdown (hydrolysis) rate	Biodegradable implant, PLGA microspheres

Table 3 — BCS classes (simple view):

BCS class	Solubility	Permeability	Delivery difficulty	Simple example idea
Class I	High	High	Easy	Dissolves and crosses well
Class II	Low	High	Moderate — needs solubility help	Needs a solubility-boosting NDDS
Class III	High	Low	Moderate — needs permeability help	Needs a permeability-boosting NDDS
Class IV	Low	Low	Hardest	Needs both solubility and permeability help

Worked examples and calculations

Example 1 — Bioavailability after first-pass metabolism. Question: A patient swallows a 200 mg tablet. The liver destroys 150 mg during first-pass metabolism. What is the bioavailability? Step 1: Drug reaching blood = dose given − drug destroyed = 200 mg − 150 mg = 50 mg. Step 2: Bioavailability (%) = (drug reaching blood ÷ dose given) × 100 = (50 ÷ 200) × 100. Step 3: 50 ÷ 200 = 0.25; 0.25 × 100 = 25%. **Answer: Bioavailability = 25%.** This is why the doctor must give a bigger oral dose than an injection dose.

Example 2 — Comparing peak levels: conventional vs NDDS. Question: A conventional tablet releases 500 mg in 1 hour. An NDDS releases the same 500 mg evenly over 10 hours. What is the release rate per hour of the NDDS? Step 1: Total drug = 500 mg; total time = 10 hours. Step 2: Rate = total drug ÷ total time = 500 ÷ 10 = 50 mg per hour. **Answer: 50 mg/hour steady release** — no sudden 500 mg peak, so fewer side effects.

Example 3 — Dosing frequency and compliance. Question: A conventional drug must be taken 4 times daily for 30 days (120 doses). An NDDS version is taken once daily (30 doses). How many fewer doses must the patient remember? Step 1: Conventional doses = 4 × 30 = 120. Step 2: NDDS doses = 1 × 30 = 30. Step 3: Difference = 120 − 30 = 90. **Answer: 90 fewer doses** — much easier for the patient to follow.

Example 4 — Diffusion rate and Fick's law (conceptual calculation). Question: A patch releases drug through a membrane. If the concentration difference across the membrane doubles, what happens to the diffusion rate (Fick's law)? Step 1: Fick's law (simple form): rate ∝ concentration difference (rate is proportional to the difference). Step 2: Difference becomes 2× → rate becomes 2×. **Answer: The diffusion rate doubles.** (Similarly, doubling the membrane thickness would halve the rate.)

Analogies

1. **Conventional tablet = dumping a bucket of water on a plant; NDDS = drip irrigation.** The bucket floods and most water runs off wasted (side effects); drip irrigation gives the plant exactly what it needs all day.
2. **First-pass metabolism = a toll plaza on the highway.** Drug "vehicles" travelling from the intestine to the body must pass the liver toll plaza, where many are stopped. Patches and injections take the bypass flyover and skip the toll.
3. **Therapeutic window = the comfortable zone of a room's temperature.** Too cold = drug not working; too hot = side effects. NDDS is like an air conditioner that holds the temperature steady in the comfortable zone.
4. **Targeted delivery = a courier with the exact address.** An ordinary tablet is like throwing pamphlets from a helicopter over the whole city; a targeted nanoparticle is a courier who delivers the parcel only to the correct house (the diseased cell).
5. **Erosion = a melting bar of soap.** Each wash wears the soap down a little and releases soap — the same way an eroding implant releases drug as it breaks down.
6. **Osmosis pump = a water balloon with a pinhole.** As water fills the balloon, pressure pushes water out of the pinhole at a steady stream — the same way water entering the tablet pushes the drug out.

Pharmacy relevance

- As a pharmacist, you will dispense NDDS products (patches, sustained-release tablets, inhalers, long-acting injections) and must counsel patients differently: for example, "do not cut, crush, or chew this tablet" — breaking a sustained-release tablet destroys the control mechanism and the whole dose releases at once (dose dumping), which can be dangerous.
- You must recognise which products bypass first-pass metabolism (sublingual tablets, patches) and why their dose is smaller than the oral dose of the same drug.
- Patient counselling on compliance: explaining that a once-daily NDDS works only if taken regularly helps treatment succeed.
- In industry and hospital pharmacy, NDDS knowledge is needed for formulation development, quality control of release testing (dissolution testing), and choosing the right product for patients who cannot swallow or need long-term therapy.

India context

- India is one of the world's largest makers of generic medicines, and Indian companies manufacture many sustained-release and controlled-release products for both Indian patients and export.
- NDDS is especially relevant in India for diseases needing long treatment: tuberculosis (long drug courses where missed doses cause drug resistance), diabetes and hypertension (daily lifelong medicines where once-daily NDDS improves compliance), and contraception (long-acting implants and injections used in family welfare programmes).
- Pharmacies across India commonly dispense sustained-release (SR) tablets and transdermal patches; pharmacists must counsel patients in simple local language not to break or chew SR tablets.

- Government health programmes benefit from depot/long-acting injections (for example, in mental health and family planning) because one dose covers weeks, reducing the need for daily clinic visits in rural areas.

Key points

1 NDDS = novel drug delivery system: controls the rate, site, and duration of drug release.

2 Conventional forms release drug all at once → peaks (side effects) and troughs (no effect), frequent dosing, poor compliance.

3 First-pass metabolism: the liver destroys part of an oral drug before it reaches the blood → lower bioavailability.

4 A drug needs both solubility (dissolve) and permeability (cross membranes) — described simply by the BCS classes.

5 Sustained release = slow release over long time; controlled release = planned, predictable release pattern; targeted delivery = drug sent to the diseased site.

6 Four release mechanisms: diffusion (high → low concentration, Fick's law), dissolution (solid dissolves slowly), osmosis (water pressure pushes drug out), erosion (carrier breaks down).

7 NDDS types: controlled release, targeted, smart/stimuli-responsive, chronotherapeutic, transdermal, mucosal, implantable/injectable depot, vesicular, polymeric, ocular, pulmonary, nasal.

Common confusions

1 **Sustained release vs controlled release:** Sustained release only means "slow and long." Controlled release means the release follows a planned, predictable pattern (which is usually also slow and long). All sustained-release products are a type of controlled release, but "controlled" additionally promises predictability of the pattern.

2 **NDDS vs "new drug":** NDDS is a new *delivery method* for a drug — the drug molecule itself may be very old (for example, an old drug put into a new patch). Do not confuse a novel delivery system with a newly discovered drug.

3 **Bioavailability vs absorption:** Absorption is the drug crossing into the blood; bioavailability is how much of the dose finally reaches the blood in active form after all losses (including first-pass metabolism). A drug can be well absorbed but still have low bioavailability if the liver destroys most of it.

4 **Targeted delivery vs local action:** A skin cream acting on the skin is local action. Targeted delivery usually means a carrier (like a nanoparticle) injected into the blood that finds and accumulates at the diseased site inside the body.

5 **Diffusion vs dissolution:** Diffusion is drug *molecules moving* through a barrier from high to low concentration; dissolution is *solid drug turning into solution*. A tablet first dissolves, then the dissolved drug diffuses — they are two different steps.

Common mistakes

1 Saying "NDDS increases the dose" — NDDS usually allows a *smaller* total dose because the drug is used more efficiently; it does not mean giving more drug.

2 Chewing or crushing a sustained-release tablet — this destroys the release-controlling layer and causes dose dumping (the whole dose released at once), which can be toxic. Always counsel patients: swallow SR tablets whole.

3 Thinking first-pass metabolism happens for injections — injected drugs enter the blood directly and skip the liver's first pass (that is why injection doses are smaller than oral doses of the same drug).

4 Mixing up "rate" and "site" — a sustained-release tablet controls the *rate* (slow release) but still goes everywhere in the body; it is not *targeted* unless designed to go to a specific site.

5 Forgetting units in calculations — always write mg, mg/hour, or % clearly; a bare number in an exam answer loses marks.

Mnemonics

1 **The three keys of NDDS — "RSD": R**ate, **S**ite, **D**uration — "NDDS controls the RSD of drug delivery."

2 **Four release mechanisms — "D-D-O-E" ("Dad Does Odd Errands"): D**iffusion, **D**issolution, **O**smosis, **E**rosion.

3 **Problems of conventional forms — "SPLiT-FTD": S**olubility poor, **P**ermeability poor, **L**iver first-pass loss, **T**oxicity peaks, **F**requent dosing, **T**roughs (no effect), **D**uration short — "Conventional forms SPLiT the treatment."

4 **BCS classes — "1-2-3-4, high-high is easy, low-low is war":** Class I (high/high) is easy; Class IV (low/low) is the hardest battle.

5 **First-pass = "Liver Toll":** Picture the liver as a toll plaza that stops drug vehicles — "No toll for injections and patches."

Exam summary

NDDS (novel drug delivery systems) are new-style carriers that control the rate, site, and duration of drug release, overcoming the limitations of conventional dosage forms: poor solubility, poor permeability, first-pass metabolism by the liver (lowers bioavailability), toxicity from high peaks, loss of effect at troughs, frequent dosing with poor compliance, non-specific distribution, and short duration of action. Key terms: sustained release (slow, long release), controlled release (planned, predictable release pattern), targeted delivery (drug to diseased site only), bioavailability (fraction of dose reaching blood), therapeutic window (safe effective concentration range). The BCS simply classifies drugs by high/low solubility and permeability. NDDS types include controlled release, targeted, stimuli-responsive/smart, chronotherapeutic, transdermal, mucosal, implantable/injectable depot, vesicular, polymeric, ocular, pulmonary, and nasal systems. Four release mechanisms: diffusion (high→low concentration through a membrane, Fick's law), dissolution (slow dissolving of solid drug), osmosis (water entry creates pressure that pushes drug through a tiny hole), and erosion (carrier breaks down, freeing drug).

One-minute revision

- NDDS controls **rate, site, duration** of drug release.

- Conventional problems: poor **solubility**, poor **permeability**, **first-pass** liver loss, **peaks** (toxicity) and **troughs** (no effect), frequent dosing.
- Bioavailability = % of dose reaching blood; first-pass lowers it.
- Sustained = slow/long; Controlled = planned/predictable; Targeted = right place.
- Mechanisms **D-D-O-E**: Diffusion, Dissolution, Osmosis, Erosion.
- Never crush/chew SR tablets → dose dumping.

MCQs

1 NDDS primarily controls which three aspects of drug delivery?

(a) Colour, taste, and smell (b) Rate, site, and duration of drug release (c) Price, packaging, and brand (d) Tablet size, shape, and coating **Answer: (b)**

1 First-pass metabolism mainly occurs in the:

(a) Kidney (b) Liver (c) Lungs (d) Skin **Answer: (b)**

1 A drug swallowed orally reaches the liver first through the:

(a) Portal vein (b) Renal artery (c) Pulmonary vein (d) Coronary artery **Answer: (a)**

1 If 100 mg is given orally and 40 mg reaches the blood, the bioavailability is:

(a) 40% (b) 60% (c) 100% (d) 140% **Answer: (a)**

1 Which statement about sustained release and controlled release is correct?

(a) They mean exactly the same thing (b) Sustained release is one type of controlled release; controlled release promises a planned, predictable pattern (c) Controlled release always acts faster (d) Sustained release targets only tumours **Answer: (b)**

1 In Fick's law of diffusion, doubling the concentration difference across the membrane:

(a) Halves the diffusion rate (b) Doubles the diffusion rate (c) Stops diffusion (d) Has no effect **Answer: (b)**

1 An osmotic pump tablet releases drug because:

(a) The tablet melts in the stomach (b) Water enters by osmosis and pressure pushes drug out through a tiny hole (c) The patient chews the tablet (d) Stomach acid dissolves the coating instantly **Answer: (b)**

1 Erosion-controlled release works because:

(a) The drug evaporates (b) The carrier polymer breaks down and frees the drug as it erodes (c) The drug is destroyed by light (d) The tablet floats on water **Answer: (b)**

1 Which route avoids first-pass metabolism?

(a) Oral tablet swallowed normally (b) Transdermal patch (c) Oral syrup (d) Chewable tablet **Answer: (b)**

1 A BCS Class IV drug has:

(a) High solubility and high permeability (b) Low solubility and low permeability (c) High solubility and low permeability (d) No solubility at all **Answer: (b)**

1 "Dose dumping" can occur when a patient:

(a) Takes the tablet with water (b) Crushes or chews a sustained-release tablet (c) Takes the tablet after food (d) Stores the tablet in a cool place **Answer: (b)**

1 A chronotherapeutic system releases drug according to:

(a) The patient's body weight (b) The body's daily clock (circadian rhythm) (c) The tablet colour (d) The season of the year **Answer: (b)**

Viva and application questions

1 **What is an NDDS in one line?** — A new-style drug carrier that controls the rate, site, and duration of drug release for better effect and fewer side effects.

2 **Why is the oral dose of a drug usually larger than its injection dose?** — Because of first-pass metabolism: the liver destroys part of the oral dose before it reaches the blood, while injections bypass the liver.

3 **What is the therapeutic window?** — The blood concentration range where the drug is effective but not toxic — not too low, not too high.

4 **Name the four drug release mechanisms.** — Diffusion, dissolution, osmosis, and erosion (D-D-O-E).

5 **Why should a sustained-release tablet never be crushed?** — Crushing destroys the release-controlling layer, causing dose dumping — the whole dose releases at once, which can be toxic.

6 **Give one example each of diffusion-controlled and osmosis-controlled delivery.** — Diffusion: transdermal patch; osmosis: osmotic pump tablet.

7 **What is the difference between targeted delivery and sustained release?** — Targeted delivery sends the drug to a specific diseased site; sustained release only slows the release rate but the drug still goes everywhere.

8 **A pharmacist sees "SR" on a tablet strip — what counselling will you give?** — Swallow whole with water, do not chew/crush/split, take at the same time daily, and do not double the dose if one is missed without asking the doctor/pharmacist.

References

- Indian Pharmacopoeia (latest edition — confirm the current edition): general chapters on dosage forms and dissolution testing.
- British Pharmacopoeia / United States Pharmacopeia (latest editions — confirm the current edition): monographs on modified-release dosage forms.
- ICH guidelines (as per the latest guidelines — confirm the current version): quality and stability guidance relevant to novel dosage forms.

- Standard B.Pharm pharmaceutics textbooks covering novel drug delivery systems and controlled release (latest editions).
- Review articles on NDDS classification and drug release mechanisms from standard pharmaceutical science journals (no fabricated citations listed here).

CHAPTER 2: Polymers and Materials for NDDS

Learning objectives

After reading this chapter, you should be able to:

1 Explain what a polymer is and why polymers are the backbone of most NDDS.

2 Define "biodegradable" and "biocompatible" and explain why both properties matter inside the body.

3 Describe five key polymers — PLA, PLGA, PCL, chitosan, gelatin — including how each degrades.

4 Explain how PLGA breaks down by hydrolysis, step by step.

5 Explain what surfactants are, what HLB means simply, and how micelles and liposomes form.

6 Describe solid lipid nanoparticles (SLNs) and the roles of lecithin, phospholipids, Span, and Tween.

7 Describe inorganic NDDS materials — silica, gold, iron oxide nanoparticles, and MOFs — and their special uses.

8 Explain the GRAS concept and the FDA Inactive Ingredient Guide (IIG) database, and state the regulatory caution for NDDS excipients.

Definitions

- **Polymer:** A very large molecule made by joining many small repeating units (called monomers) together in a long chain — like a long train made of many identical bogies. Plastics, starch, and proteins are all polymers.
- **Monomer:** The small single unit that joins with others to form a polymer — one "bogie" of the train.
- **Biodegradable:** A material that the body can break down into small, harmless pieces (usually by water or enzymes) and then remove — like how a banana peel rots away and disappears. A biodegradable implant disappears on its own, so no surgery is needed to remove it.
- **Biocompatible:** A material that does not harm the body — it does not cause poisoning, severe inflammation, or rejection when placed inside the body. "Bio" = life/body, "compatible" = friendly with.
- **Hydrolysis:** Breakdown of a chemical bond by water. "Hydro" = water, "lysis" = breaking. Many biodegradable polymers break down because water slowly cuts their chains.
- **Surfactant:** A substance that sits between oil and water and helps them mix — "surface-active agent." One end of the molecule likes water, the other end likes oil.

- **Amphiphile:** A molecule with two opposite likings — one part water-loving (hydrophilic) and one part oil-loving (hydrophobic/lipophilic). All surfactants are amphiphiles.
- **Micelle:** A tiny ball formed by surfactant molecules in water: the oil-loving ends hide inside the ball and the water-loving ends face outward toward the water. Oily drugs can be hidden inside the centre of the ball.
- **Liposome:** A tiny bubble made of a double layer of phospholipids (like the wall of the body's own cells), with water both inside and outside the bubble. It can carry water-soluble drugs in its watery core and oil-soluble drugs in its wall.
- **Nanoparticle:** A particle extremely small — between about 1 and 1000 nanometres (a nanometre is one-billionth of a metre). Because they are so small, nanoparticles can travel in the blood and enter tissues that bigger particles cannot.
- **GRAS:** "Generally Recognized As Safe" — a status meaning experts generally agree that a substance is safe for its intended use, based on long history of use or scientific evidence. It is a starting point for safety, not a free pass for every new use.
- **Excipient:** Any inactive substance in a medicine other than the drug itself — for example, binders, coatings, colours, and the polymers and lipids used to build an NDDS. "Inactive" means it is not the medicine, but it still must be safe.

Terminology

- **Erosion (of polymers):** The wearing away of the polymer from its surface inward, layer by layer, as its chains are cut.
- **Bulk erosion vs surface erosion:** In surface erosion, the polymer wears away only from the outside (like a melting soap bar); in bulk erosion, water enters the whole piece and it breaks down everywhere at once (like a biscuit going soggy all through).
- **Lactic acid / glycolic acid:** The small, natural breakdown products of PLA and PLGA — both are substances the body already knows how to handle and remove.
- **HLB (Hydrophilic–Lipophilic Balance):** A number scale (roughly 0 to 20) that tells how water-loving or oil-loving a surfactant is. Low HLB (~3–6) = oil-loving (good for water-in-oil mixtures); high HLB (~8–18) = water-loving (good for oil-in-water mixtures and solubilising).
- **Phospholipid:** A natural fat-like molecule with a water-loving head and two oil-loving tails — the main building block of cell membranes and liposomes. Lecithin is a common natural mixture rich in phospholipids.
- **Solid lipid nanoparticle (SLN):** A nanoparticle made of a fat (lipid) that is solid at body temperature, stabilised by surfactants in water — like a tiny solid butter ball carrying drug, floating in water.
- **MOF (metal–organic framework):** A sponge-like material built from metal ions joined by organic linkers, full of tiny pores that can be filled with drug — like a microscopic honeycomb warehouse for drug molecules.
- **IIG (Inactive Ingredient Guide) database:** The US FDA's public list/database of inactive ingredients (excipients) that have already been used in approved medicines, with the route and amount used. Formulators check it to see whether an excipient has been used safely before.

- **Self-assembly:** Molecules arranging themselves automatically into organised structures (like micelles) without outside help, simply because of their water-loving and water-hating parts.
- **Surface functionalisation:** Attaching special molecules (like targeting antibodies) onto the surface of a nanoparticle so it can find the diseased site.

Explanation

Most NDDS are not just "drug powder in a capsule" — they are carefully built structures, and polymers are the main building material. A polymer gives the NDDS its shape (a microsphere, a nanoparticle, an implant, a gel), controls how fast the drug comes out, and then ideally disappears harmlessly from the body. For a polymer to be used inside the body, it must be biocompatible (does not harm the body) and, for implants and depots, biodegradable (breaks down and disappears so it need not be removed).

The five key polymers:

1. PLA (polylactic acid): Made from lactic acid units. It is a stiff, slow-degrading polyester. Water slowly cuts its chains (hydrolysis), producing lactic acid, which the body removes naturally. Because it degrades slowly (over months), PLA is good for long-acting implants and sutures that must stay strong for a long time.

2. PLGA (poly(lactic-co-glycolic acid)): A copolymer — a chain made of two different monomers mixed together: lactic acid and glycolic acid. This is the most famous NDDS polymer. Its big advantage is tunability: by changing the ratio of lactic to glycolic acid, scientists can decide how fast it degrades. More glycolic acid = faster water entry = faster degradation (weeks); more lactic acid = slower degradation (months). It breaks down by hydrolysis into lactic acid and glycolic acid, both removed naturally by the body. Used in long-acting injectable microspheres, nanoparticles, and implants.

3. PCL (polycaprolactone): Another polyester, but it degrades even more slowly than PLA (over many months to years) because water enters it with difficulty. It is soft and flexible. Used where very long action is needed, such as long-term implants and tissue scaffolds.

4. Chitosan: A natural polymer obtained from chitin, which comes from the shells of crabs and prawns. It is positively charged, which is special: body surfaces like mucus are negatively charged, so chitosan sticks to them (mucoadhesion) — useful for nasal, buccal, and eye delivery where the carrier must stay in place. It is broken down by enzymes in the body (like lysozyme) into harmless sugars. Being natural and positively charged, it is also useful for carrying negatively charged drugs and genetic material.

5. Gelatin: A natural protein obtained from collagen (from animal bones and skin). It melts/dissolves in warm water and forms gels on cooling — that is why it is used to make capsule shells. In NDDS it is used for nanoparticles, microspheres, and gels. It is broken down by enzymes (protein-cutting enzymes) in the body. Because it comes from animals, its source and purity must be carefully controlled.

Degradation order (fastest to slowest): PLGA (high glycolic) > PLGA (high lactic) > PLA > PCL. Chitosan and gelatin degrade by enzymes rather than simple water hydrolysis, so their speed depends on the enzyme environment.

Lipids and surfactants: Not all NDDS are polymer-based. Many use fats and soap-like molecules. Lecithin (a natural mixture rich in phospholipids, obtained from soya or egg) and pure phospholipids are the building blocks of liposomes — because they look like the body's own cell membranes, the body accepts them well. Span (oil-loving, low HLB) and Tween (water-loving, high HLB) are common laboratory surfactants used to stabilise emulsions and nanoparticles — Span helps make water-in-oil systems, Tween helps make oil-in-water systems and keeps nanoparticles from clumping. Solid lipid nanoparticles (SLNs)

are made of a lipid that is solid at body temperature (like a tiny solid fat ball), with surfactants coating the outside to keep them suspended in water; they are useful for carrying poorly soluble (oily) drugs and for targeting the lymphatic system.

Inorganic systems: Some NDDS use non-living, mineral/metal materials:

- **Silica nanoparticles:** Tiny particles of silica (like very fine sand/glass) full of pores — the pores can be filled with drug, and the surface can be decorated with targeting molecules. They are stable and easy to modify.
- **Gold nanoparticles:** Tiny gold particles. Gold is chemically stable and the body tolerates it; gold particles can be seen in imaging and can be heated with light for combined therapy (heat + drug). Used in research for targeted cancer delivery and diagnostics.
- **Iron oxide nanoparticles:** Magnetic particles. Because they respond to magnets, they can be guided with an external magnet and they show up in MRI scans — useful for combined imaging and drug delivery (theranostics).
- **MOFs (metal–organic frameworks):** Microscopic sponge-like crystals of metal ions linked by organic molecules, with enormous internal pore space — they can hold a very large amount of drug for their size, and the pores can be designed to release drug in response to signals like pH.

Excipients and regulation: Every polymer, lipid, surfactant, and inorganic material used in an NDDS is an excipient and must be proven safe. Two important concepts: **GRAS** ("Generally Recognized As Safe") — a substance widely accepted as safe for its intended use; and the **FDA IIG (Inactive Ingredient Guide) database** — a public list of excipients already used in approved products, showing the route (oral, injection, etc.) and the maximum amount used. A formulator checks the IIG to see if an excipient has a history of safe use by that route. Caution: being in the IIG or being GRAS does not automatically approve a *new* use — a new route, a much larger amount, or a new patient group still needs safety data, as per the latest guidelines (confirm the current edition).

Classification

A. Polymers by origin:

1. **Natural polymers:** From nature — chitosan (crab/prawn shells), gelatin (animal collagen), albumin (blood protein), alginate (seaweed), starch/cellulose derivatives.
2. **Synthetic polymers:** Man-made — PLA, PLGA, PCL (all polyesters); also non-degradable ones like certain silicones and acrylics used where the device stays permanently.

B. Polymers by degradability:

1. **Biodegradable:** Broken down in the body — PLGA, PLA, PCL (by water hydrolysis); chitosan, gelatin (by enzymes).
2. **Non-biodegradable:** Stay intact and must be removed or stay permanently — used in some implants and transdermal patch backings.

C. Lipids and surfactants:

1. **Natural lipids:** Lecithin, phospholipids (liposome builders).
2. **Synthetic surfactants:** Span series (oil-loving, low HLB), Tween series (water-loving, high HLB).

3 **Solid lipids for SLNs:** Fats solid at body temperature (e.g., stearic acid-type lipids, triglycerides) — chosen to be solid so the particle keeps its shape.

D. Inorganic systems:

1 **Silica-based:** Mesoporous silica nanoparticles (pore-filled drug carriers).

2 **Metal-based:** Gold nanoparticles (stable, imaging + therapy), iron oxide nanoparticles (magnetic, MRI-visible).

3 **Framework materials:** MOFs (metal–organic frameworks — ultra-high drug loading in pores).

E. Excipient safety categories (regulatory view):

1 **GRAS substances:** Generally recognised as safe for the intended use.

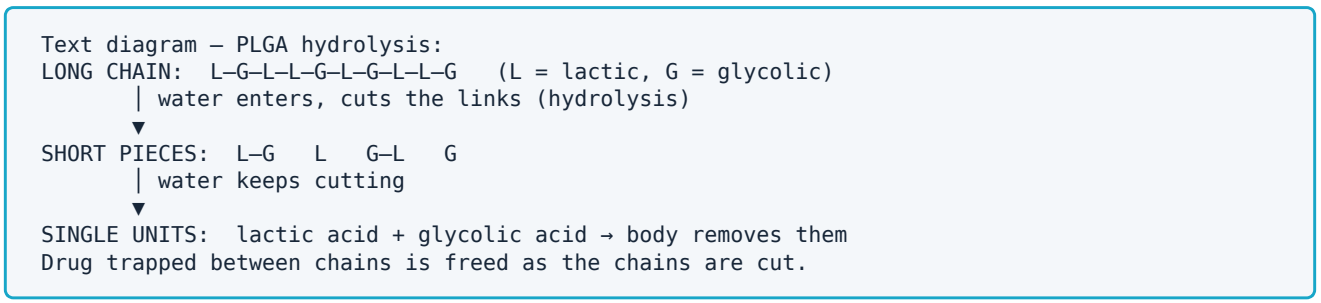
2 **IIG-listed excipients:** Already used in an approved product by a given route and amount — lower regulatory risk.

3 **Novel excipients:** Never used in an approved product — need full safety testing, the longest and costliest path.

Mechanisms

1. Hydrolysis and erosion of polymers (PLGA example)

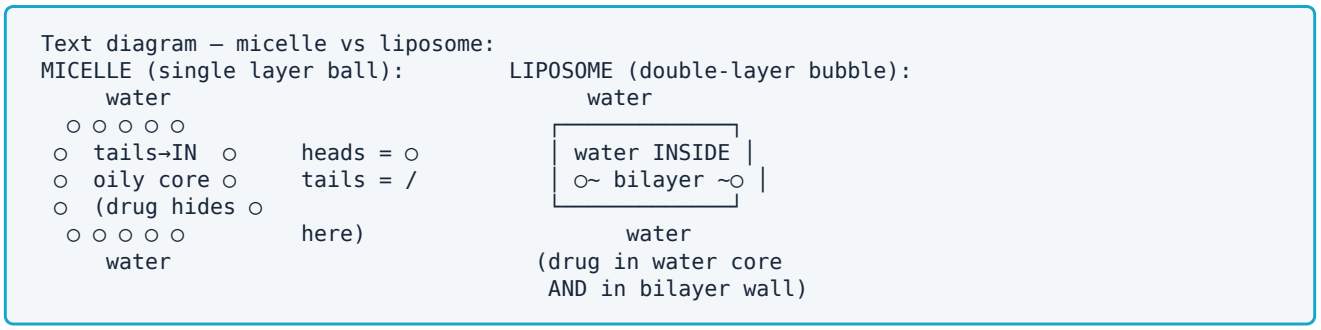
Simple meaning: Water molecules slowly cut the long polymer chains into smaller and smaller pieces, until only tiny natural acids remain — like cutting a long rope into shorter and shorter bits until only threads are left. **Step by step:** (1) Water from body fluid enters the PLGA particle. (2) Water attacks the ester bonds (the links between monomers) and cuts them — this is hydrolysis. (3) The long chains become short chains (oligomers), then single lactic acid and glycolic acid molecules. (4) These small acids dissolve and the body removes them through its normal metabolism. (5) As chains are cut, the particle surface erodes and trapped drug is freed — drug release and polymer disappearance happen together. **Key control:** More glycolic acid in the chain = water enters faster = faster cutting = faster drug release. This is why PLGA's monomer ratio is called "tunable."



2. Self-assembly of amphiphiles (micelle and liposome formation)

Simple meaning: Surfactant molecules arrange themselves automatically in water — oil-loving ends hide together away from water, water-loving ends face the water — like a crowd of people with umbrellas huddling so the umbrellas face outward in the rain. **How micelles form:** In water, above a certain concentration, surfactant molecules gather into balls: hydrophobic (oil-loving) tails point inward forming an oily core, hydrophilic (water-loving) heads point outward. Oily drugs dissolve in the oily core — this is how micelles carry poorly soluble drugs in water. **How liposomes form:** Phospholipids have two tails, so

they form a double layer (bilayer) instead of a ball — the bilayer closes into a bubble (liposome) with water inside and outside. Water-soluble drugs sit in the inner water; oil-soluble drugs sit inside the bilayer wall. **HLB link:** The HLB number predicts behaviour — high-HLB surfactants (like Tween) favour oil-in-water structures such as micelles; low-HLB surfactants (like Span) favour water-in-oil structures.

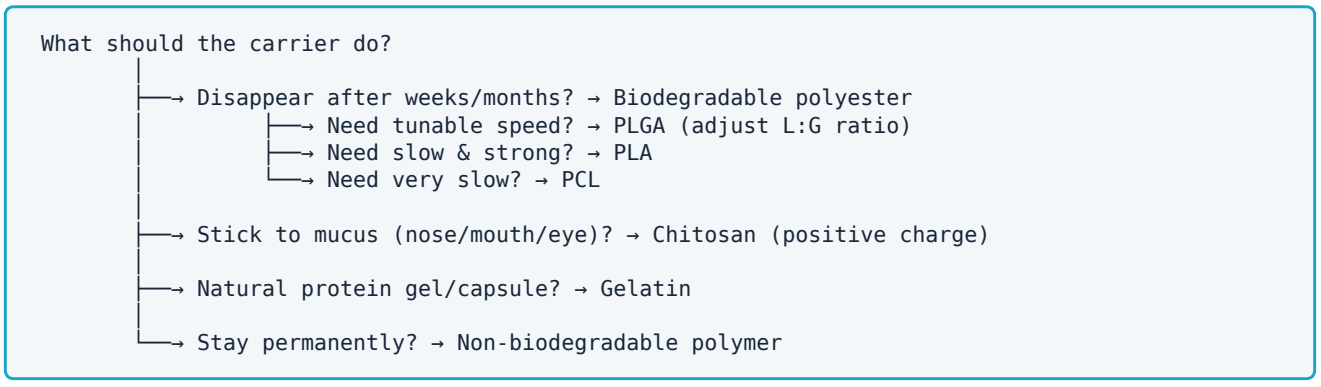


3. Surface chemistry of inorganic particles

Simple meaning: The surface of a silica, gold, or iron oxide particle can be chemically decorated — like sticking address labels and handles onto a delivery box — so the particle goes to the right place and behaves safely in blood. **How it works:** (1) The bare particle surface has reactive groups (e.g., –OH on silica, gold–sulphur bonds on gold). (2) Targeting molecules (antibodies, peptides) are attached to these groups — the particle now recognises diseased cells. (3) A protective coating (often a water-loving polymer layer) is added so blood proteins do not clump the particles and the body's defences ignore them longer. (4) For iron oxide, the magnetic core lets a doctor guide particles with a magnet and see them on MRI; for MOFs, the pore walls can be given pH-sensitive "gates" that open only at the target. **Key takeaway:** With inorganic particles, the *surface* decides where the particle goes and how the body treats it — the core just carries the drug or provides the special property (magnetism, imaging, heat).

Diagrams and flowcharts

Flowchart 1 — Choosing a polymer for an NDDS:



Flowchart 2 — PLGA degradation and drug release together:

```
PLGA particle with drug inside
        │
        ▼
Water enters the particle
        │
        ▼
Hydrolysis: water cuts ester bonds in chains
        │
        ├──→ Chains get shorter → surface erodes
        │          │
        │          ▼
        │    Trapped drug is freed (release)
        │
        └──→ Final pieces: lactic acid + glycolic acid
                   │
                   ▼
             Body removes them naturally (no removal surgery)
```

Text diagram — HLB scale:

```
HLB scale (0 ──────────── 20)
◄── oil-loving ─────┼──── water-loving ──►
     Span            Tween
   (low HLB ~3–6)   (high HLB ~8–18)
   water-in-oil      oil-in-water, micelles,
   systems           solubilising
```

Infographic concepts

1 **"The tunable rope":** A rope (PLGA chain) made of blue beads (lactic) and red beads (glycolic); scissors (water) cut red links faster. Two ropes side by side — more red beads = rope cut in weeks; more blue beads = rope lasts months. Caption: "Change the bead ratio, change the release speed."

2 **"The umbrella huddle" (self-assembly):** People with umbrellas (surfactant molecules) standing in rain (water), huddling so umbrella tops face out and bodies hide inside — forming a micelle ball; a double ring of people forms a liposome bubble. Caption: "Molecules arrange themselves — no hands needed."

3 **"The disappearing implant":** Four frames — a solid implant under skin on day 1, smaller at month 1, tiny at month 3, gone at month 6 with drug fully delivered. Caption: "Works, then vanishes — no second surgery."

4 **"The sponge warehouse" (MOF):** A honeycomb/sponge with drug parcels stored in every pore, with a gate that opens only at the diseased site. Caption: "Huge storage in a tiny crystal."

5 **"Excipient safety ladder":** Three steps — bottom: novel excipient (full safety testing needed); middle: IIG-listed (history of safe use by that route); top: GRAS (widely accepted as safe). Caption: "Check the ladder before choosing an excipient."

Tables

Table 1 — The five key polymers compared:

Polymer	Full name / source	Type	How it degrades	Degradation speed	Why used in NDDS
PLA	Polylactic acid (synthetic)	Polyester	Hydrolysis → lactic acid	Slow (months)	Strong, long-acting implants
PLGA	Poly(lactic-co-glycolic acid) (synthetic)	Copolyester	Hydrolysis → lactic + glycolic acid	Tunable: weeks to months	Most versatile; microspheres, nanoparticles
PCL	Polycaprolactone (synthetic)	Polyester	Hydrolysis (very slow)	Very slow (months–years)	Very long-term implants
Chitosan	From crab/prawn shells (natural)	Polysaccharide	Enzymes → harmless sugars	Depends on enzymes	Mucoadhesive (sticks to mucus); nasal/buccal/eye
Gelatin	From animal collagen (natural)	Protein	Enzymes (protein-cutting)	Depends on enzymes	Capsule shells, gels, nanoparticles

Table 2 — Surfactants and lipids at a glance:

Material	HLB nature	Role in NDDS	Example use
Lecithin / phospholipids	Amphiphilic (natural)	Liposome building blocks	Liposomal drug carriers
Span	Low HLB (oil-loving)	Water-in-oil emulsifier	Stabilising certain emulsions
Tween	High HLB (water-loving)	Oil-in-water emulsifier, solubiliser	Nanoparticle stabiliser, micelles
Solid lipids (SLN matrix)	Fat, solid at body temperature	Solid core of SLN	Carrying poorly soluble drugs

Table 3 — Inorganic NDDS materials:

Material	Special property	Main NDDS use
Silica nanoparticles	Porous, easy-to-modify surface	Drug loading in pores + targeting
Gold nanoparticles	Stable, visible in imaging, heat with light	Targeted cancer delivery, diagnostics
Iron oxide nanoparticles	Magnetic, MRI-visible	Magnetic guidance, imaging + delivery
MOFs	Huge pore volume, designable gates	Very high drug loading, stimuli release

Worked examples and calculations

Example 1 — PLGA ratio and degradation choice (conceptual). Question: Two PLGA batches: Batch A = 50:50 lactic:glycolic; Batch B = 85:15 lactic:glycolic. Which degrades faster, and why? Step 1: Recall: more glycolic acid → water enters faster → faster hydrolysis. Step 2: Batch A has 50% glycolic; Batch B has 15% glycolic. Step 3: 50% > 15%, so Batch A absorbs water faster. **Answer: Batch A (50:50) degrades faster** — used when drug release over weeks is wanted; Batch B suits release over months.

Example 2 — Drug loading in a microsphere batch. Question: 200 mg of PLGA microspheres contain 20 mg of drug. What is the drug loading (% w/w)? Step 1: Drug loading (%) = (weight of drug ÷ weight of microspheres) × 100. Step 2: 20 ÷ 200 = 0.10. Step 3: 0.10 × 100 = 10%. **Answer: 10% w/w drug loading.**

Example 3 — Encapsulation efficiency. Question: 50 mg of drug was used to prepare liposomes, but only 35 mg was found trapped inside the final liposomes. What is the encapsulation efficiency? Step 1: Encapsulation efficiency (%) = (drug trapped ÷ drug used) × 100. Step 2: 35 ÷ 50 = 0.70. Step 3: 0.70 × 100 = 70%. **Answer: 70% encapsulation efficiency** — 30% of the drug was lost during preparation.

Example 4 — Choosing surfactant by HLB. Question: You must prepare an oil-in-water nanoemulsion (oil droplets in water). Should you pick Span (low HLB) or Tween (high HLB)? Step 1: Oil-in-water needs a water-loving (high HLB) surfactant to stabilise oil droplets in water. Step 2: Tween = high HLB; Span = low HLB. **Answer: Tween** — Span would suit the reverse (water-in-oil) system.

Example 5 — SLN solid-lipid check. Question: A lipid melts at 70°C. Body temperature is 37°C. Can it form the solid core of an SLN? Step 1: SLN core must be solid at body temperature. Step 2: Melting point 70°C > 37°C, so the lipid stays solid inside the body. **Answer: Yes** — it remains solid at 37°C and can form an SLN core.

Analogies

1. **Polymer = a long train of bogies; hydrolysis = uncoupling the bogies one by one.** Water is the worker that unhooks each coupling until the train becomes single bogies (acids) that are carried away.
2. **PLGA ratio = a recipe for dissolving sugar:** More glycolic acid is like using powdered sugar (dissolves fast); more lactic acid is like using sugar cubes (dissolves slowly). Change the recipe, change the speed.
3. **Micelle = a huddle of people with umbrellas in the rain.** Umbrella tops (water-loving heads) face the rain; bodies (oil-loving tails) hide inside — and an oily drug hides with them in the middle.
4. **Liposome = a soap bubble with a double skin.** It carries watery cargo in its hollow centre and oily cargo dissolved in its skin — just like the body's own cells.
5. **MOF = a honeycomb warehouse.** Thousands of tiny storage rooms (pores) in one crystal, each holding drug parcels, with gates that open on signal.
6. **Chitosan sticking to mucus = a magnet on a fridge door.** Chitosan is positively charged, mucus is negatively charged — opposite charges attract, so the carrier stays where it is placed instead of being washed away.
7. **GRAS/IIG = a driving licence check.** Before letting a new driver (excipient) on the road (into a medicine), you check whether they already hold a valid licence (IIG history) or are widely known to be safe drivers (GRAS).

Pharmacy relevance

- As a pharmacist, you handle products built on these materials daily: gelatin capsule shells, liposomal injections, and long-acting PLGA microsphere injections — knowing the material tells you how to store and counsel (e.g., liposomes may need cold storage; "do not freeze" on some biologics-style products).
- In formulation and industry roles, polymer choice decides the product's release duration — picking PLGA 50:50 vs 85:15 is a real development decision.
- Understanding HLB helps in dispensing and compounding emulsions and creams: the wrong surfactant choice breaks the emulsion.
- Recognising GRAS and IIG concepts helps you answer "is this excipient safe?" — you know where formulators check safety history, and you can explain to patients that "inactive" does not mean "untested."

India context

- India has a large pharmaceutical industry that manufactures PLGA/PLA-based long-acting injectables and liposomal products, both for Indian patients and for export to regulated markets.
- Chitosan is especially relevant for India: it comes from prawn and crab shell waste from India's large seafood industry — a "waste to wealth" story where shell waste becomes a valuable pharmaceutical polymer.
- Gelatin capsules are made in huge quantities in India; pharmacists should know gelatin's animal origin because some patients (for example, strict vegetarians) ask about it — vegetarian (starch/HPMC-based) capsule alternatives exist for such patients.
- Lecithin from soya is widely available in India and used in both food and pharmaceutical industries; Indian formulators use it in emulsions, liposomes, and nutritional products.
- Iron oxide nanoparticles' MRI visibility connects to India's growing diagnostic imaging network, where combined imaging-plus-therapy ("theranostic") research is active in cancer centres.

Key points

1 Polymers are the main building material of NDDS — they give shape, control release, and (if biodegradable) disappear afterwards.

2 Biocompatible = does not harm the body; biodegradable = the body breaks it down and removes it.

3 PLA: slow polyester → lactic acid. PLGA: tunable copolymer (lactic + glycolic); more glycolic = faster degradation. PCL: very slow polyester.

4 Chitosan: natural, positively charged, mucoadhesive (sticks to mucus), enzyme-degraded. Gelatin: natural protein, enzyme-degraded, used in capsules and gels.

5 PLGA degrades by hydrolysis: water cuts ester bonds → shorter chains → lactic + glycolic acids → body removes them; drug is freed as erosion proceeds.

6 Surfactants are amphiphiles; HLB (0–20) tells water-loving vs oil-loving nature; Tween (high HLB) for oil-in-water, Span (low HLB) for water-in-oil.

7 Micelles: single-layer balls with oily core (carry oily drugs). Liposomes: phospholipid bilayer bubbles carrying both water-soluble (core) and oil-soluble (wall) drugs.

8 SLNs: solid-lipid-core nanoparticles for poorly soluble drugs. Inorganics: silica (porous), gold (stable/imaging), iron oxide (magnetic/MRI), MOFs (huge pore loading).

9 GRAS = generally recognised as safe; IIG = FDA database of excipients already used in approved products — but neither automatically approves a new use; safety must be confirmed as per the latest guidelines.

Common confusions

1 **Biodegradable vs biocompatible:** Biocompatible means "does not harm the body"; biodegradable means "the body breaks it down." A material can be biocompatible but NOT biodegradable (it stays forever but harmlessly). For implants that must vanish, you need both.

2 **PLA vs PLGA:** PLA is made of lactic acid only; PLGA is a copolymer of lactic AND glycolic acids. The "G" in PLGA (glycolic) is what makes the degradation speed tunable.

3 **Micelle vs liposome:** A micelle is a single-layer ball with an oily core (only oily drugs inside); a liposome is a bilayer bubble with water inside and outside (carries water-soluble drugs in the core AND oil-soluble drugs in the wall).

4 **HLB high vs low:** High HLB = water-loving (Tween, oil-in-water); low HLB = oil-loving (Span, water-in-oil). Students often reverse them — remember "High HLB loves water."

5 **GRAS does not mean "approved for everything":** GRAS status and IIG listing are about a specific use, route, and amount. A new route or much larger dose still needs safety data.

Common mistakes

1 Saying PLGA degrades into "plastic waste" — it degrades into lactic acid and glycolic acid, natural substances the body metabolises and removes.

2 Calling every nanoparticle a "liposome" — liposomes are specifically phospholipid bilayer vesicles; polymeric nanoparticles, SLNs, and inorganic particles are different systems.

3 Using a low-HLB surfactant (Span) to stabilise an oil-in-water system — it will fail; match HLB to the emulsion type.

4 Forgetting that chitosan's mucoadhesion comes from its positive charge — in exams, link "positive chitosan ↔ negative mucus" explicitly.

5 Writing "FDA approved the excipient" loosely — the IIG lists excipients used in approved *products*; excipients themselves are not separately "approved." Use careful wording.

Mnemonics

1 **Five polymers — "Please Pass Cold Chai Gently":** **P**LA, **P**LGA, **P**CL, **C**hitosan, **G**elatin.

2 **Degradation speed — "PLGA fast, PLA slow, PCL slowest":** chant "G-L-P, fast to slow" — more **G**lycolic = faster; **L**actic slows; **P**CL slowest.

3 **HLB — "High loves water":** High HLB = water-loving (Tween); Low HLB = oil-loving (Span). "Tween is High like the tide coming in."

4 **Micelle vs liposome — "Ball vs Bubble":** Micelle = single-layer **ball** (oily core); Liposome = double-layer **bubble** (water core).

5 **GRAS — "Generally Regarded As Safe"**: "Grandma Recognises A Safe ingredient" — safe by long, recognised use.

Exam summary

Polymers are the backbone of NDDS: they form the carrier, control drug release, and ideally biodegrade afterwards. Biocompatible = harmless to the body; biodegradable = broken down and removed by the body. Key synthetic polyesters: PLA (slow hydrolysis → lactic acid), PLGA (tunable copolymer of lactic and glycolic acids — more glycolic = faster degradation; hydrolyses to both acids which the body removes), PCL (very slow). Natural polymers: chitosan (from shellfish shells; positively charged → mucoadhesive; enzyme-degraded) and gelatin (animal protein; enzyme-degraded; capsule shells). Surfactants are amphiphiles; HLB (0–20) measures water-loving vs oil-loving nature — high HLB (Tween) suits oil-in-water

systems, low HLB (Span) suits water-in-oil. Above a certain concentration, amphiphiles self-assemble: micelles (single-layer balls, oily core for oily drugs) and liposomes (phospholipid bilayer bubbles carrying water-soluble drugs in the core and oil-soluble drugs in the wall). SLNs are nanoparticles with a lipid core solid at body temperature, stabilised by surfactants. Inorganic systems: porous silica nanoparticles, gold nanoparticles (stable, imaging/heat therapy), iron oxide nanoparticles (magnetic, MRI-visible), and MOFs (metal–organic frameworks with huge pore volume for high drug loading). Excipient safety: GRAS (generally recognised as safe) and the FDA IIG database (excipients already used in approved products by route and amount) guide selection, but neither automatically approves a new use — confirm as per the latest guidelines.

One-minute revision

- Backbone of NDDS = **polymers**; need **biocompatible** (harmless) and often **biodegradable** (body removes it).
- **PLGA**: tunable — more glycolic = faster hydrolysis → lactic + glycolic acids.
- Speed order: PLGA (fast) > PLA > PCL (slowest); chitosan/gelatin degrade by **enzymes**.
- **Chitosan** = positive charge → sticks to mucus (mucoadhesive).
- HLB: **High loves water** (Tween, o/w); Low loves oil (Span, w/o).
- Micelle = ball (oily core); Liposome = bubble (bilayer, water core).
- Inorganics: silica (pores), gold (imaging), iron oxide (magnetic/MRI), MOFs (sponge, huge loading).
- GRAS + IIG guide excipient safety — new uses still need data.

MCQs

1 PLGA is a copolymer of:

(a) Lactic acid and citric acid (b) Lactic acid and glycolic acid (c) Glycolic acid and stearic acid (d) Acetic acid and lactic acid **Answer: (b)**

1 PLGA degrades in the body mainly by:

(a) Oxidation (b) Hydrolysis of ester bonds by water (c) Light exposure (d) Freezing **Answer: (b)**

1 Which PLGA batch degrades faster?

(a) 85:15 lactic:glycolic (b) 50:50 lactic:glycolic (c) Both degrade at the same speed (d) Neither degrades **Answer: (b)**

1 Chitosan is obtained from:

(a) Seaweed (b) Crab/prawn shells (chitin) (c) Petroleum (d) Corn starch **Answer: (b)**

1 Chitosan sticks to mucus (mucoadhesion) because it is:

(a) Negatively charged and mucus is positive (b) Positively charged and mucus is negatively charged (c) Magnetic (d) Radioactive **Answer: (b)**

1 A surfactant with high HLB (e.g., Tween) is best for:

(a) Water-in-oil emulsions (b) Oil-in-water emulsions and micelles (c) Dry powders only (d) Metal polishing **Answer: (b)**

1 A micelle carries oily drugs in its:

(a) Watery outer surface (b) Oily inner core (c) Protein coat (d) Metal centre **Answer: (b)**

1 A liposome can carry:

(a) Only water-soluble drugs (b) Only oil-soluble drugs (c) Water-soluble drugs in its core and oil-soluble drugs in its bilayer wall (d) No drugs at all **Answer: (c)**

1 An SLN has a core that is:

(a) Gas at body temperature (b) Liquid at body temperature (c) Solid lipid at body temperature (d) Made of pure water **Answer: (c)**

1 Iron oxide nanoparticles are special because they are:

(a) Magnetic and visible on MRI (b) The cheapest of all materials (c) Soluble in water like sugar (d) Made of plastic **Answer: (a)**

1 MOFs can hold large amounts of drug because of their:

(a) Huge internal pore volume like a sponge (b) Heavy metal weight (c) Bright colour (d) Sweet taste **Answer: (a)**

1 The FDA IIG database lists:

(a) Approved drug brand names (b) Inactive ingredients already used in approved products, with route and amount (c) Doctor prescriptions (d) Hospital addresses **Answer: (b)**

Viva and application questions

1 **Why is PLGA called a "tunable" polymer?** — Changing its lactic:glycolic ratio changes how fast water enters and hydrolyses it, so the degradation speed (and drug release) can be tuned from weeks to months.

2 **What do PLGA breakdown products become?** — Lactic acid and glycolic acid, which the body metabolises and removes naturally — no surgery needed to remove the implant.

3 **Why is chitosan useful for nasal drug delivery?** — It is positively charged and sticks to negatively charged nasal mucus (mucoadhesion), so the formulation stays in the nose instead of being washed away.

4 **What does HLB tell you, in one line?** — How water-loving or oil-loving a surfactant is: high HLB loves water (Tween, oil-in-water), low HLB loves oil (Span, water-in-oil).

5 **Micelle or liposome for a water-soluble drug?** — Liposome, because it has a watery core; a micelle's core is oily and suits oil-soluble drugs.

6 **Why coat an inorganic nanoparticle's surface?** — To attach targeting molecules and add a protective layer so blood proteins don't clump it and the body tolerates it longer.

7 **A formulator wants a 3-month depot. PLGA 50:50 or PCL?** — PCL (or high-lactic PLGA), because 50:50 PLGA degrades in weeks — too fast for 3 months.

8 **Does GRAS status guarantee an excipient is safe for injection?** — No — GRAS/IIG history is tied to a specific use, route, and amount; a new route or higher amount needs fresh safety data as per the latest guidelines.

References

- Indian Pharmacopoeia (latest edition — confirm the current edition): chapters on excipients and dosage forms.
- United States Pharmacopeia / National Formulary (latest edition — confirm the current edition): excipient monographs.
- FDA Inactive Ingredient Guide (IIG) database (as per the latest update — confirm the current version): public listing of inactive ingredients used in approved products.
- ICH guidelines (as per the latest guidelines — confirm the current version): quality, safety, and stability guidance for pharmaceutical excipients and novel carriers.
- Standard B.Pharm pharmaceutics and NDDS textbooks (latest editions): polymers, liposomes, nanoparticles, and excipient safety.
- Review articles on biodegradable polymers, lipid nanoparticles, and inorganic nanocarriers from standard pharmaceutical science journals (no fabricated citations listed here).

Audience: B.Pharm Semester VIII students in India. Written from absolute zero in very simple English. Every technical term is defined before it is used. Flow: technical concept → simple explanation → example → diagram → key takeaway. No fabricated regulatory numbers, fees, limits, timelines, or statistics.