Introducing Pharmacology (Part II)

1. Composition of drugs

In pharmacology, a "drug" is almost never just the active molecule by itself. If you looked at a 500mg tablet of Paracetamol, the tablet actually weighs much more than 500mg. The composition of a drug product (also called a **dosage form**) is a mixture of two main parts: the **API** and the **Excipients**.

1.1. The Active Pharmaceutical Ingredient (API)

The **API** is the "hero" of the medicine. It is the specific chemical or biological molecule that produces the biological effect.

- **Small Molecule API:** Usually a powder created by chemical synthesis (e.g., Aspirin).
- **Biological API:** A protein, antibody, or hormone produced by living cells (e.g., Insulin).

1.2. The Excipients (The "Helper" Ingredients)

Excipients are the inactive substances formulated alongside the API. Even though they don't treat the disease, they are essential for the **Liberation** and **Absorption** phases (we will discuss later).

Key Roles of Excipients:

- **Fillers (Diluents):** APIs are often tiny (a few milligrams). Fillers like **Lactose** or **Starch** add "bulk" so the pill is big enough for a human hand to hold.
- **Binders:** These act like "glue" to keep the powder together in a solid tablet shape.
- **Disintegrants:** These help the pill break apart (**Disintegration**) when it hits the water in your stomach.
- **Lubricants:** These prevent the powder from sticking to the machines in the factory during manufacturing.
- **Preservatives:** These prevent bacteria or fungi from growing in liquid medicines (like syrups or eye drops).
- **Flavoring & Coloring:** To make the medicine easier to swallow (especially for children) and easy to identify.

Feature	Active Pharmaceutical Ingredient (API)	Excipients
Activity	Pharmacologically active (treats the disease).	Pharmacologically inactive (inert).
Quantity	Precisely measured (e.g., 10mg, 500mg).	Usually makes up the majority of the weight.
Purpose	To heal or prevent illness.	To protect, support, and deliver the API.
Safety	Must be studied for toxicity.	Must be "GRAS" (Generally Recognized As Safe).

Why this matters for Biotechnology?

For you as Biotechnology students, the "Excipients" part is very difficult.

Small molecules (like Aspirin) are stable and can be mixed with simple powders.

Biologicals (like vaccines or antibodies) are very "fragile." Their excipients must include stabilizers and buffers to keep the protein from "unfolding" or "denaturing." If the protein unfolds, the drug is ruined.

2. The Three Names of a Drug

When discussing drug composition, it is easy to get confused by names. Every drug has three:

2.1. **Chemical Name:** Describes the molecular structure (e.g., *N-acetyl-p-aminophenol*). This is mostly for chemists.

2.2. **International Non-proprietary Name (INN):** The official, non-proprietary name (e.g., *Paracetamol* or *Acetaminophen*). This is what scientists and doctors use.

2.3. **Brand (Trade) Name:** The name given by the company (e.g., *Panadol* or *Tylenol*).

Type of Name	Example	Context
Chemical Name	*Acetylsalicylic acid*	Chemistry Lab
Generic (INN)	**Aspirin**	Medical School / Exams
Brand Name	**Aspirine UPSA®** or **Bayer®**	Pharmacy Shop

Special Note for Biotechnology Students

*Nomenclature for **Biologicals** (Biologics) is even more specific. Because biological drugs (like antibodies) are so complex, the INN usually includes:*

1. ***A Prefix:** Unique to the product.*
2. ***An Infix:** Tells you the target (e.g., **-li-** for immune system, **-tu-** for tumor).*
3. ***A Suffix:** Always **-mab** for monoclonal antibodies.*

***Example: Adalimumab** (Humira®)*

- ***-mab**: Monoclonal Antibody*
- ***-u-**: Human-derived*
- **-lim-**: Immunomodulator

3. Dosage Form

In pharmacology, a **Dosage Form** (or Galenic form) is the physical state of a drug. Think of the **API** (the medicine) as a letter, and the **Dosage Form** as the envelope. The envelope protects the letter and ensures it gets to the right address.

As Biotechnology students, you must know that the dosage form determines how fast or slow the **Liberation (L)** and **Absorption (A)** phases happen.

3.1. Classification by Physical State

We generally group dosage forms into four physical categories:

A. Solid Dosage Forms

These are the most common because they are stable and easy to carry.

- **Tablets:** Compressed powders. Some are **Enteric-coated** (protected from stomach acid) or **Sustained-release** (releasing medicine slowly over 12–24 hours).
- **Capsules:** The API is inside a gelatin shell. The shell dissolves in the stomach to "liberate" the drug.
- **Suppositories:** Solid at room temperature but melt at body temperature when inserted (rectal or vaginal).

B. Liquid Dosage Forms

These act faster than solids because the drug is already "liberated" (dissolved).

- **Solutions:** The API is completely dissolved in a liquid (like sugar in water). It is clear.
- **Suspensions:** The API is not dissolved; it is small solid particles floating in a liquid. **You must shake these before use!**
- **Syrups:** Thick, sweet liquids used to hide the bad taste of an API.

C. Semi-Solid Dosage Forms

Mainly used for **Topical** (local) application.

- **Ointments:** Mostly oil-based. They stay on the skin for a long time (greasy).
- **Creams:** A mix of oil and water. They are absorbed into the skin faster and are easier to wash off.
- **Gels:** Transparent, water-based "jellies" that feel cool on the skin.

D. Gaseous Dosage Forms

- **Aerosols/Inhalers:** The API is turned into a very fine mist or spray to be inhaled into the lungs (common for asthma).

3.2. Dosage Forms in Biotechnology

This is a critical point for your specialty. Most **Biologicals** (like vaccines or monoclonal antibodies) are proteins.

- **Why can't we make an "Insulin Tablet"?** Because your stomach would digest the insulin protein just like it digests a piece of meat. The drug would be destroyed before absorption.
- **The Biotech Solution:** Most biologicals are formulated as **Injectable Liquids** (in vials or pre-filled syringes). They are injected into the muscle (IM) or under the skin (SC) to bypass the stomach.

Form	Examples	Best For...
Solid	Tablet, Capsule	Convenience and precise dosing.
Liquid	Syrup, Injection	Fast action or patients who can't swallow.
Semi-Solid	Cream, Ointment	Skin infections or rashes (Topical).
Gaseous	Inhaler, Spray	Lung diseases (Asthma/COPD).

4. Categories of Pharmaceutical Preparations

In pharmacology, we also classify drugs based on **where** and **how** they are prepared. we call these **"Categories of Pharmaceutical Preparations."**

4.1. Specialty Drugs (*Médicament de spécialité*)

This is the most common type of drug today. These are medicines prepared in advance by **industrial pharmaceutical companies**.

- **Definition:** A drug that is manufactured in a factory, packaged in a specific box, and sold under a **Brand Name** (e.g., Lipitor) or a **Generic Name** (e.g., Atorvastatin).
- **Key Feature:** It requires a **Marketing Authorization** (called **AMM** in French, or **MA** in English) from government health agencies (like the FDA or EMA) before it can be sold.
- **For whom?** It is standardized for the general population.

4.2. Magistral Preparations (Médicament magistral)

Often called **"Extemporaneous Compounding."**

- **Definition:** A medicine prepared in a local pharmacy by a pharmacist specifically for **one particular patient**.
- **The Scenario:** If a doctor writes a prescription for a unique dose that is not made by a factory (for example, a very small dose for a newborn baby or a cream with a specific mix of three ingredients), the pharmacist makes it "by hand."
- **Key Feature:** It is prepared **after** the pharmacist receives the prescription. It is "custom-made."

4.3. Officinal Preparations (Médicament officinal)

These are often called **"Official Preparations"** or **"Pharmacopoeial Preparations."**

- **Definition:** These are drugs prepared in a pharmacy according to the instructions (the "recipe") found in the **Pharmacopoeia**.
- **What is a Pharmacopoeia?** It is an official book (a "Bible" of pharmacy) that lists the exact ingredients and methods for making common preparations.
- **Key Feature:** Unlike the magistral preparation, the pharmacist can make these in advance and keep them on the shelf to sell to any patient who needs them.
- **Example:** Simple preparations like 70% alcohol, hydrogen peroxide, or certain basic skin pastes.

French Term	English Term	Where is it made?	Recipe Source	For whom?
Spécialité	**Specialty / Proprietary**	Industrial Factory	Company Research	General Public
Magistral	**Magistral / Compounded**	Local Pharmacy	Doctor's Prescription	One specific patient
Officinal	**Officinal / Official**	Local Pharmacy	**Pharmacopoeia**	Any patient

Why this matters for Biotechnology?

As a Biotechnology student, you will mostly work in the Specialty sector. Developing a "Biological Specialty" (like a monoclonal antibody) costs billions of dollars and years of research to get the Marketing Authorization.

However, Magistral preparations are still very important in hospitals for personalized medicine, especially in Pediatrics (for children) and Oncology (cancer treatments).

5. Branded vs. Generic Drugs: The Life Cycle

Every drug starts as an **"Innovator Drug"** or **Branded Drug**.

- **Branded Drug (The "Princeps"):** This is the original drug developed by a pharmaceutical company. Because the company spent billions on research, they receive a **Patent** (legal protection). For about 20 years, no one else is allowed to make that drug.
- **Generic Drug:** Once the patent expires, other companies can make "copies." As we discussed, these must be **Bioequivalent**. They are much cheaper because the second company did not have to pay for the initial 10–15 years of research.

6. Drug Research and Development (R&D)

The journey from a "molecule in a lab" to a "pill in a pharmacy" is long (usually 10–12 years) and divided into two main stages:

A. Pre-clinical Stage (The Lab)

- **Targets:** Scientists find a biological target (like a protein or enzyme).
- **Testing:** The drug is tested on **cells** (in vitro) and **animals** (in vivo).
- **Goal:** To see if the drug is toxic and if it actually works biologically.

B. Clinical Stage (The Humans)

If the pre-clinical stage is successful, the drug enters **Clinical Trials**, divided into three phases:

- **Phase I:** Tested on a small group (20–80) of **healthy volunteers**. (Goal: Safety and dosage).
- **Phase II:** Tested on a larger group (100–300) of **patients** with the disease. (Goal: Does it work?).
- **Phase III:** Tested on thousands of patients (1,000+). (Goal: Confirm effectiveness and monitor side effects).

6. Marketing Authorization: MA (or AMM)

Once Phase III is finished, the company cannot just start selling the drug. They must ask for permission from the government.

- **AMM (French):** *Autorisation de Mise sur le Marché*.
- **MA (English):** *Marketing Authorization*.

What is it? It is a "scientific passport" or "green light" issued by a regulatory agency (like the **FDA** in the USA, the **EMA** in Europe, or the **National Agency** in Algeria).

The Agency evaluates three things:

1. **Quality:** Is the chemistry/biotechnology of the drug consistent?
2. **Safety:** Are the side effects acceptable compared to the benefit?
3. **Efficacy:** Does the drug actually treat the disease?

Note: If a drug has an AMM/MA, it means the benefit to the patient is higher than the risk of side effects.

Summary

Stage	Name	Key Activity
R&D	Discovery & Trials	Lab work followed by human testing (Phases I, II, III).
Regulation	**MA / AMM**	Government review of Safety, Quality, and Efficacy.
Market	**Branded**	Sold under a patent (expensive).
Market	**Generic**	Sold after the patent expires (cheaper, bioequivalent).

7. What are Biosimilars?

A **Biosimilar** is a biological product that is "highly similar" to a branded biological drug (called the **Reference Product**) that is already on the market.

7.1. Why don't we call them "Generics"?

In your biology labs, you know that living cells (bacteria, yeast, or mammalian cells) are not machines. They are "noisy" and variable.

- **Generics:** Because they are made by chemical synthesis, they are **identical** copies. It is like making the same plastic spoon 1,000 times.

- **Biosimilars:** Because they are made by living cells, they are **similar**, but not identical. There are tiny differences in the "post-translational modifications" (like the sugar chains or glycosylation). It is like trying to grow two identical apples from two different trees.

7.2. Comparison: Generics vs. Biosimilars

Feature	Generic (Small Molecule)	Biosimilar (Biologic)
Size	Small and simple (e.g., Aspirin).	Large and complex (e.g., Monoclonal Antibodies).
Production	Chemical reaction in a lab.	Produced by **living cells** in bioreactors.
Structure	Easy to define and copy.	Impossible to copy perfectly.
Clinical Trials	Small studies (Bioequivalence).	Large clinical trials (to prove "Similarity").

7.3. The Regulatory Path for Biosimilars

For a normal **Generic**, the company only has to prove that the drug reaches the blood at the same speed (**Bioequivalence**). They do not usually need to repeat clinical trials.

For a **Biosimilar**, the regulatory agencies (MA / AMM) are much stricter. The company must provide:

1. **Analytical Studies:** Prove the protein structure is almost identical.
2. **Animal Studies:** Prove it is safe in living systems.
3. **Clinical Studies:** Perform "head-to-head" trials in human patients to prove the biosimilar works exactly like the original branded biologic.

Why this matters for Biotechnology?

As future biotechnologists, you might be the ones designing the bioprocess for a biosimilar. You need to understand that:

- ***Quality is everything: A small change in the temperature of the bioreactor or the type of "food" given to the cells can change the final drug.***
- ***Cost Reduction: Biosimilars are cheaper than branded biologics (like those used for cancer or autoimmune diseases), making life-saving medicine available to more people in countries like Algeria.***

Summary

In conclusion, remember: ***Generics*** *are for simple chemicals;* ***Biosimilars*** *are for complex biological proteins. Both enter the market after the* ***Patent*** *expires, but Biosimilars require much more biological testing before they receive their* ***Marketing Authorization (AMM)***.