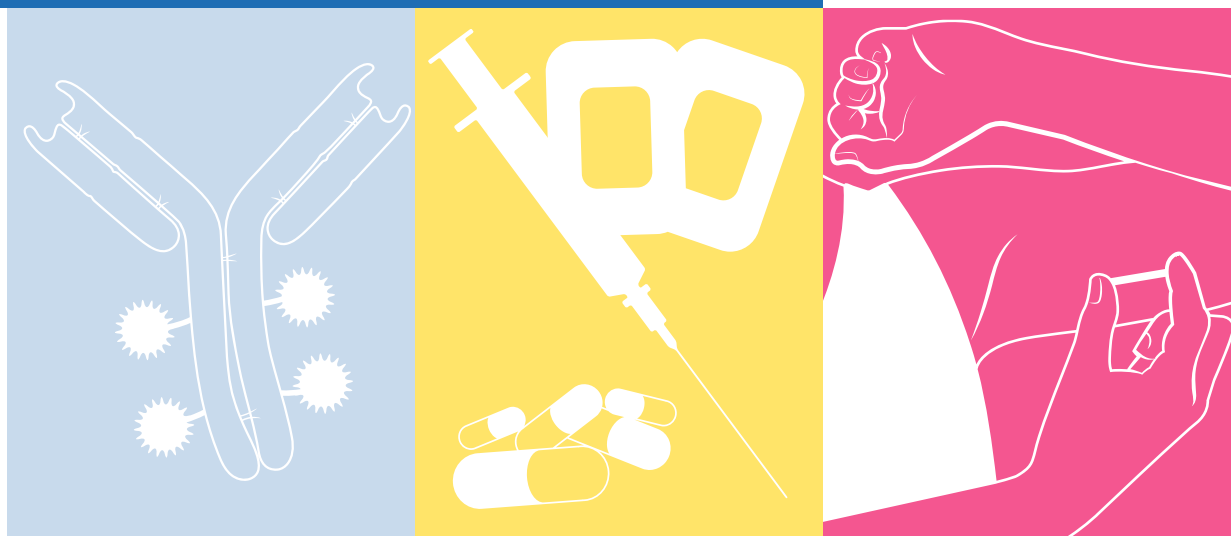
TAG
Treatment Action Group

Illustrated Glossary for Long-Acting Technologies



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Illustrated Glossary for Long-Acting Technologies[1,2]

Active pharmaceutical ingredient (API)

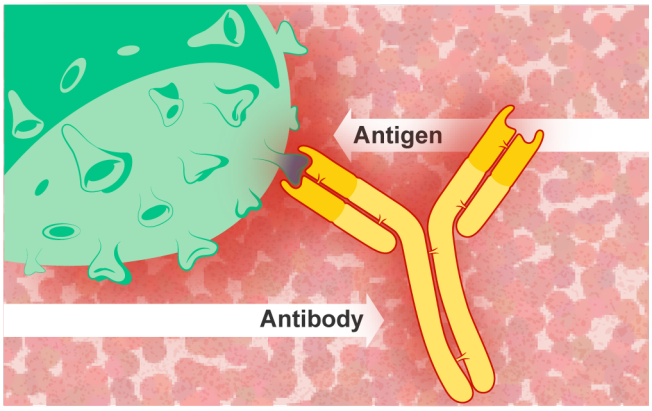
Sometimes known as the drug compound, the raw material or chemical ingredient(s) that makes up the pharmaceutically active substance in a medicine or vaccine. [3]

Adverse reaction (or adverse event

Unwanted side effect or experience, such as weight gain or irritability, caused by using a medicine or vaccine. Adverse reactions can occur immediately or over time.

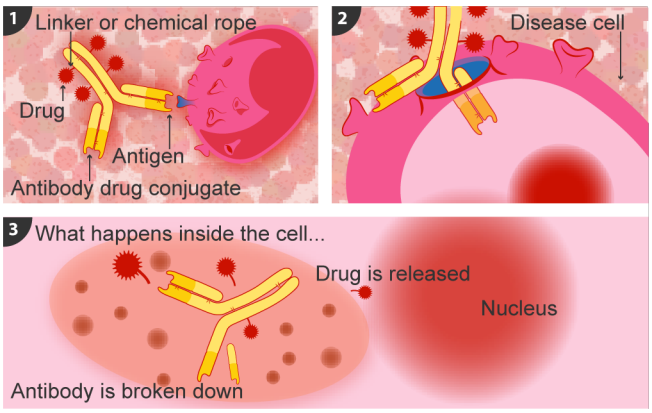
Antibody

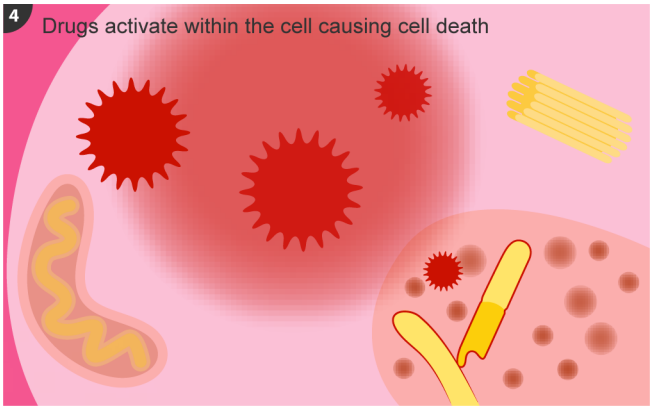
Proteins made by B-cells that attach to viruses, bacteria, or parasites and mark them for destruction. The immune system produces antibodies when it detects disease. Antibodies come in several flavors, including IgA (in the oral mucosa), IgG (in the blood), and IgM. IgG antibodies are Y-shaped.



Antibody drug conjugates

Highly potent biologic medicines designed to kill diseased cells. Antibody drug conjugates link a small drug molecule, or active pharmaceutical ingredient (API), to an antibody. The antibody targets a specific antigen protein found on the surface of targeted disease cells. Once it finds and binds to the specific diseased cell by recognizing the specific antigen, the antibody drug conjugate enters the cell. The medicine is released from within to kill the target cell without harming other healthy cells.[4,5,6]





Aqueous carrier (or aqueous vehicle; water-soluble carrier)

A liquid solution used to dissolve or dilute active pharmaceutical ingredients as part of creating the medicine formulation.

Basic compounds

Any substance that, when dissolved in water, increases the concentration of hydroxide ions. In practical terms, it is any compound that, when combined with an acid, forms water and a salt. This salt is often the active form of the medicine.[7] Some active pharmaceutical ingredients are base compounds.

Bioavailability

The extent to which a medicine or other substance, after being taken orally, topically, or by injection, is used by the body. Many factors affect bioavailability, including how the medicine is metabolized (processed) in the gut and liver and how the medicine is distributed throughout the body to the active site or tissue.

Clinical endpoint

Measures the direct outcome in a clinical trial. This outcome is used to objectively measure the intervention under study, for example, a medicine's effect. Some common endpoints include whether the medicine has severe toxicity, relieves symptoms, or improves a patient's quality of life, such as how a patient feels or their chances of survival. Primary endpoints determine if the outcome matches the objectives of the study. Secondary endpoints relate to the primary endpoint, are aligned with secondary questions, and need to be defined upfront. They may give more nuanced information in the trial, may or may not bring definitive conclusions, and could point the direction for future studies, such as treatment adherence and overall quality of life.

Clinical proof-of-concept

Preliminary evidence from clinical trials (studies in humans) that indicates a given potential agent works in humans as proposed. Generally done in Phase II trials, this helps investigators determine whether to continue with the development of a medicine.

Commercialization partner

Industry partner that helps bring a medicine to market by facilitating clinical trials, manufacturing, scale-up, distribution, exportation, regulatory approval, licensing, and marketing.

Controlled release (in relation to drug loading)

When medicines are produced, many factors influence the amount of active pharmaceutical ingredient, or drug compound, that can be included. Stability, bioavailability, and features that may limit performance all need to be considered. The amount of a drug compound (or API) present relative to other medicinal ingredients is called the drug loading.

Crystalline forms of active pharmaceutical ingredients

Active pharmaceutical ingredients (API), also known as drug compounds, can form crystals that may impact the physical properties of the API. It may be important to control the type and size of crystals to avoid variations, such as different crystal shapes, in the API so medicines are the same each time they are produced. Different crystal types may, for example, affect APIs' temperature stability and bioavailability.

Development partner

An industry partner that establishes manufacturing and scaling-up production of long-acting medicines. Technology transfer is licensed to the industry partner to conduct the manufacturing and bring the long-acting treatments to market.

Direct-acting antivirals (DAAs)

All-oral, often highly effective medications for treating hepatitis C in 12 weeks, though people with liver disease or other health conditions may need to be treated longer to achieve sustained virological response—that is, when the virus is undetectable. DAAs can achieve sustained virological response in over 95% of patients, and the latest regimens treat all genotypes of the virus with similar results.

Drug potency

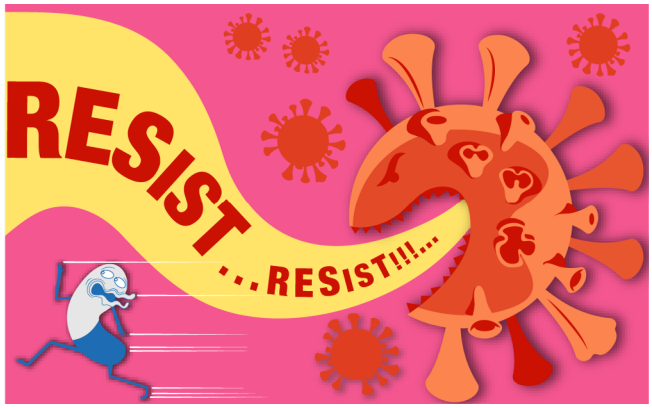
Amount of an active pharmaceutical ingredient needed to produce a specific effect. For example, if 5 mg of Medicine A relieves pain as effectively as 20 mg of Medicine B, then Medicine A is four times as potent as Medicine B.[8]

Drug product

Medicine in its complete dosage form containing the active pharmaceutical ingredient (drug compound) and, generally, inactive ingredients[9] and other ingredients that help the medicine work. These products, ready to be packaged and brought to market, may take the form of pills, sprays, injections, creams, drops, etc.[10]

Drug resistance

When the characteristics of the disease-causing organism prevent the treatment therapy from being effective. Drug resistance can be caused by changes in the genetic structure of a virus, bacterium, or parasite, which allow it to multiply and block the treatment from working for a person. With antibiotics, drug resistance can occur when patients do not take antibiotics as prescribed, when they are prescribed for non-bacterial infections, or when they are prescribed too often. In people living with HIV, drug resistance can occur when people do not adhere to medications as prescribed, for example, by forgetting a dose. When this happens, the medication can kill non-mutated microbes, allowing mutants to multiply.



Drug strength

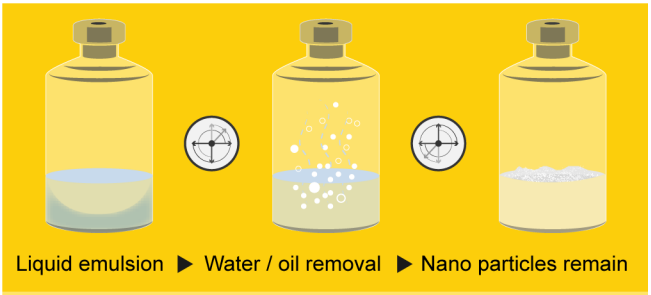
Amount that the drug compound, or active pharmaceutical ingredient, is contained in or delivered from a medicine. Measured in mass (milligrams, grams, micrograms) or units of activity.

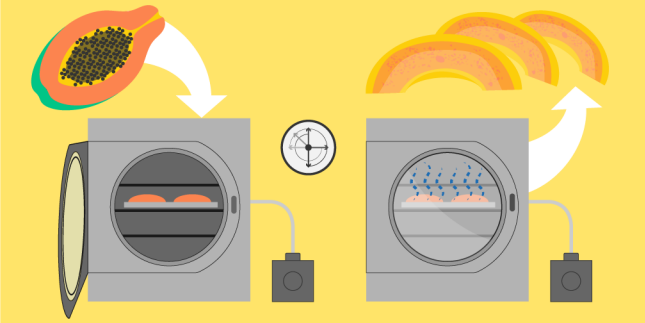
Emulsion

When two liquids do not mix, stirring them together so that one forms droplets within the other is known as an emulsion. In many cases, water is often the liquid used to form the main body of the emulsion, with the droplets being formed from oily or lipid-like materials. Milk is one example of an emulsion. Emulsions are commonly used for topical applications or as part of nutrition therapy administered intravenously.

Emulsion-templated freeze drying

Emulsion-templated freeze drying was invented at the University of Liverpool and is used within the LONGEVITY project to develop long-acting medicines. It allows very poorly water-soluble active pharmaceutical ingredients (drug compounds) to be processed by dissolving them in oily droplets and mixing them with water to form an emulsion. When this is frozen and freeze dried, the water and oily droplets are removed to leave behind very small (nano- or micro-) particles of drug compounds that can be used to form medicines. The method allows for medicines with high drug loadings to be formed and it enables poorly water-soluble drug compounds to be used in long-acting medicines. The particles are also small enough to pass through an injection needle.[11]

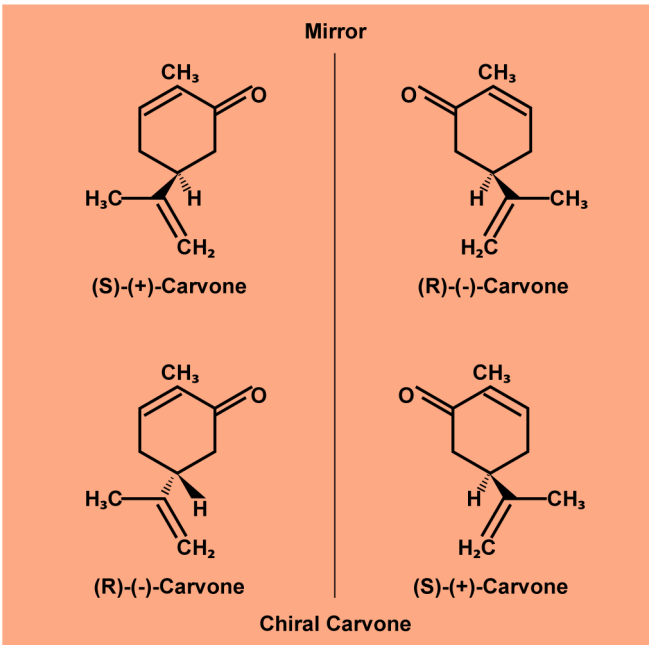


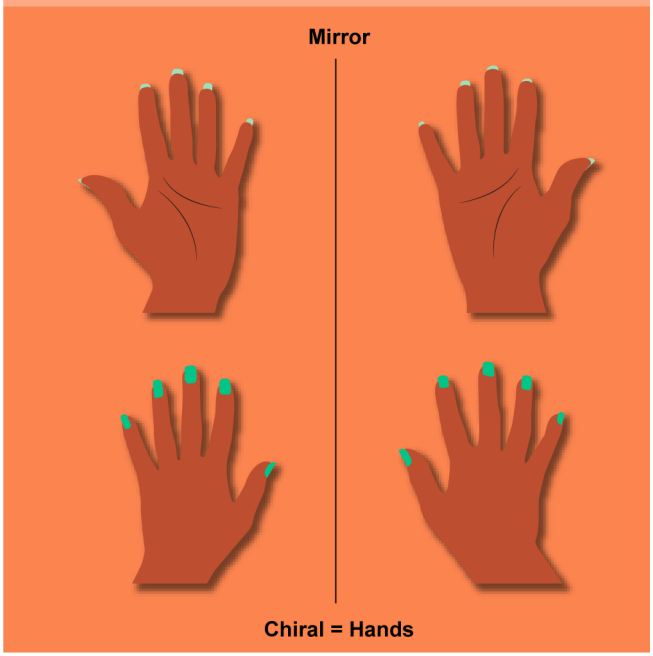


Dehydrated and freeze dried fruit, like papaya, is an analogy – the emulsion-templated freeze drying process removes water from the liquid emulsion, leaving nano particles of a drug compound.

Enantiomers

A pair of molecules that are perfect mirror images of one another. These mirror-image pairs cannot be placed on top of one another (just like our hands, our thumbs and little fingers are on opposite sides).[12] [13]





Ethambutol

First-line anti-tuberculosis medication used in combination with other medications, such as isoniazid and rifampin.

Excipient

Inactive substance(s) in a medicine formulation that are safe and approved. This includes, for example, bulking agents to accurately dispense medications, lubricants to reduce friction, preservatives, and sorbents to remove moisture that helps deliver the medicine in the body.

Fumarate salt

Active pharmaceutical ingredients (drug compounds) may be basic (a base compound) and may form salts with organic acids. Fumaric acid has been used to form salts with many drug compounds to help with their formulation into medicines. The odorless, white powder that dissolves in water can be used to regulate acidity.

Genetic polymorphism

A polymorphism should not be confused with a drug polymorph. A genetic polymorphism is a variation in the genetic code of the host or the pathogen; such variations occur normally in populations and define differences between individuals from the same species. Certain polymorphisms have been associated with medicine pharmacokinetics or pharmacodynamics, and the field of pharmacology that studies this is pharmacogenetics.

Genotype (GT)

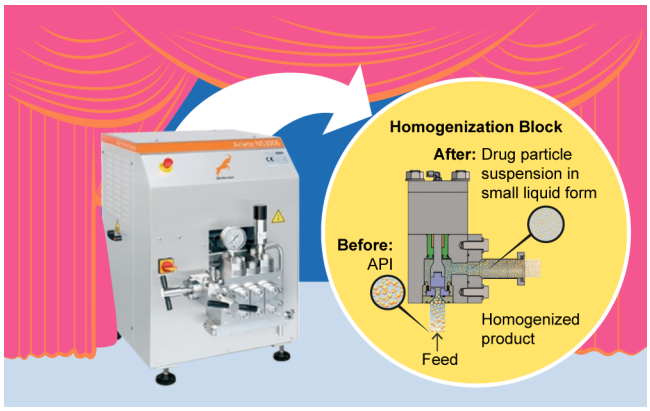
Different genetic subtypes of HCV, or a way to categorize HCV based on similar genes. HCV has seven genotypes, labeled 1 through 7, but six genotypes are the most commonly found. There are also subtypes labeled with letters, for example, genotypes 1a and 1b. Genotypes respond differently to medicines that treat and cure HCV. Notably, pangenotypic (all-genotypes) DAAs have similar curative (or sustained virological response) rates for all genotypes.

Half-life of a drug compound/active pharmaceutical ingredient

The time required for a drug compound or API to be reduced, or metabolized and/or eliminated, by 50% in the body.[14]

High pressure homogenization

A process that uses high pressure to reduce an active pharmaceutical ingredient to extremely small particles and distribute them uniformly throughout a liquid to form a drug particle suspension. As a result, the droplets have higher surface areas and can promote chemical stability for a longer shelf life.[15] [16]



Impurities

Unwanted chemicals that remain with the active pharmaceutical ingredients during the medicine manufacturing process. This can, but does not always, affect the medicine's safety and efficacy.

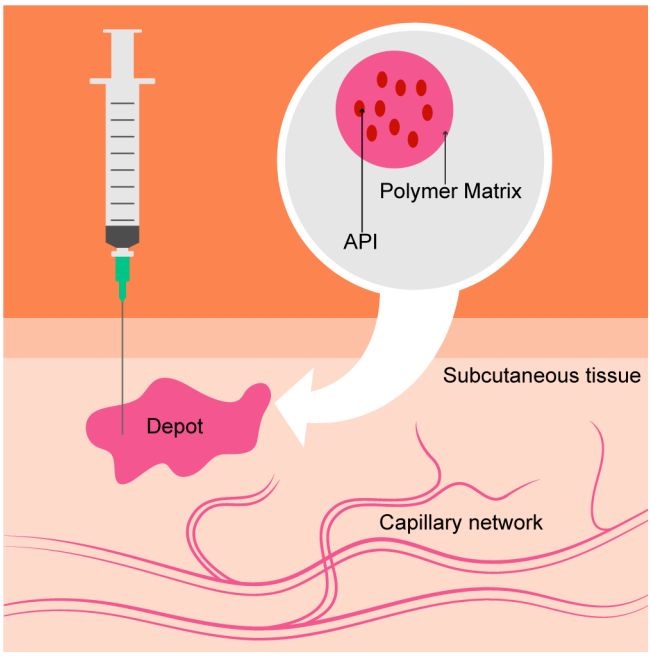
In situ-forming depots/implants

A liquid injection that, after administration, forms a solid or partially solid structure resembling an implanted device. The structure forms a reservoir of active pharmaceutical ingredients, or drug compounds, that are released and broken down in the body over an extended period of time. Some opportunities involve two syringes, which allows multiple drug compounds and excipients to be combined prior to injection into the muscle or under the skin. Issues of locating and monitoring the depot, temperature stability in the body, ease of mixing the medicines, and scalabilty in

the manufacturing process should be taken into account when considering this treatment option.

In situ-forming gel

An injectable medicine formulation that turns into a partially solid structure (gel) after injection to control the release of active pharmaceutical ingredients over a sustained period of time.

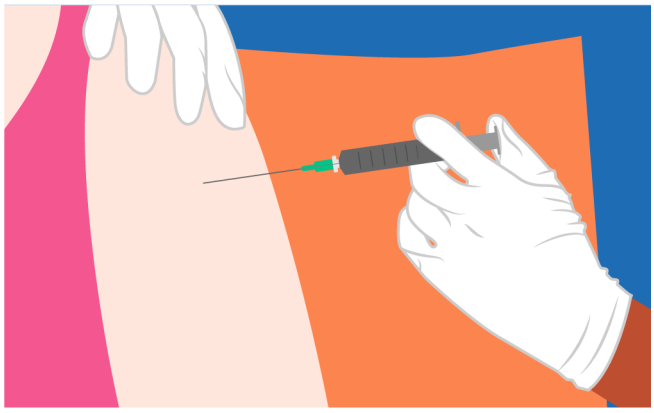


Injectable monoliths

Medication-releasing solid implants that release active pharmaceutical ingredients over extended periods of time. These are most widely used in the birth control field, for example, intrauterine devices and contraceptive implants that release pregnancy-blocking hormones. They require insertion and removal by trained specialists. Biodegradable versions of these technologies that breakdown with natural processes in the body have been explored for other long-acting medicines.

Intramuscular administration

A medicine injected into the muscle tissue. Intramuscular administrations are generally given in the arm, thigh, hip, or buttocks.



Level of purity

The amount of impurities or contamination in chemical compounds, including active pharmaceutical ingredients and excipients. Impurities are not always problematic, but measuring, understanding, and controlling impurities is important. Impurities may also form if the medicine is not stable during storage, so this is monitored carefully during new medicine development.

Lipids

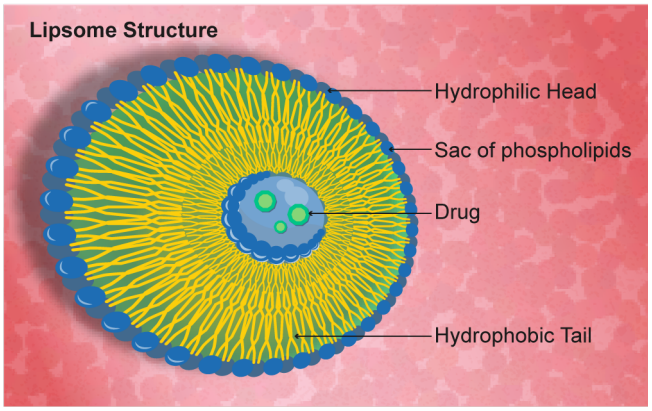
Natural molecules that are found in living cells. They are often used in medicine development and include fats and naturally-derived oils.

Lipophilic

Describes molecules, including active pharmaceutical ingredients, that are able to dissolve in lipids.

Liposomes

A tiny single layer bubble (or sac of phospholipids) surrounding a water droplet that helps carry medicines in the body. Liposomes may be used to help with the formulation of lipophilic or water-soluble active pharmaceutical ingredients and can increase absorption into tissues.



Long-acting injectables (LAI)

Medicine formulation that is injected as a shot in the muscle (intramuscularly) or under the skin (subcutaneously) and delivers medication over an extended period of time, such as over weeks or months.[17] LAIs could address treatment adherence, provide discretion, and allow for fewer clinic visits and prescription refills.

Long-acting parenteral

Similar to long-acting injectables but with a different route of administration. They release over time and can be injected under the skin, in the muscle, through veins, in the abdomen—any route except oral.

Long-acting technologies (LAT or sustained release, controlled release, extended release, protracted drug release, prolonged drug release)

Terms used interchangeably to describe any technology that can prolong a patient's exposure to a medication. These technologies can come in the form of injections, small implants, vaginal rings, and patches, among others.

Low-soluble (or poorly water-soluble) active pharmaceutical ingredient

Drug compounds that do not dissolve well in water and do not disperse well in the body.[18]

Lower potency

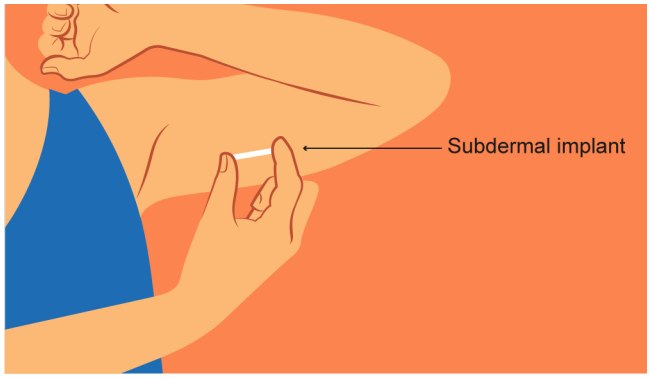
A drug compound that requires higher doses to produce the desired effect.

Macrolide

Class of antibiotics that are formed from large ring-shaped molecules. Macrolides are natural products and can treat a variety of respiratory infections, such as pneumonia; sexually transmitted infections; and certain skin infections, such as cellulitis and leprosy.

Medical implants

Small medicine delivery devices inserted inside or attached to the surface of the body. These include prosthetics, stents, chemotherapy ports, pacemakers, etc. They can be made from metal, plastic, or ceramic. Implants can either be placed permanently (e.g., stents or hip implants) or removed once they are no longer needed (e.g., chemotherapy ports or screws to repair broken bones).[19] Small rods inserted under the skin and vaginal rings are being developed for long-acting HIV treatment.



Medication (treatment) adherence

A patient takes the medication consistently, at the same time, dosage, and frequency, according to the treatment plan, which is based on the medicine's pharmacologic and resistance profile

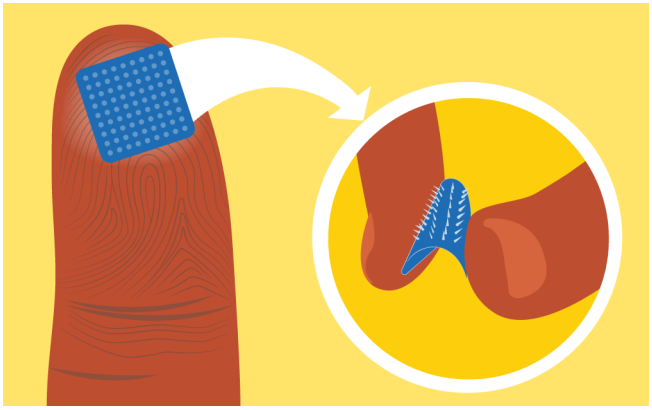
and agreed to by both the patient and doctor. It is important to ask your doctor for instructions to follow when taking the medication so that it works in your body.[20] This is the preferred term in health care today, as it takes a patient-centered approach to health care.

Medicine composition

The list, including quantities, of raw ingredients used to make a medicine. This includes both active and inactive substances.

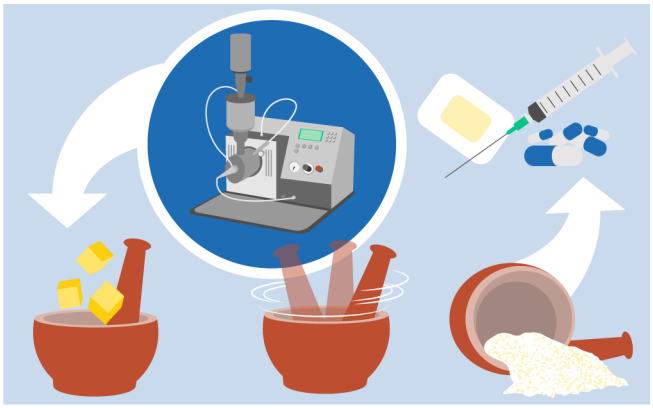
Microneedles

Microneedles are devices that allow active pharmaceutical ingredients to be delivered through the skin. The needles are very small, from 25 to 2000 micrometers (μm), and are too small to generate pain, therefore they may be an alternative for people who are afraid of needles. Microneedle patches have also been created (10–2000 μm high and 10–50 μm wide), allowing arrays of many needles to be applied with a single patch. The needles may be solid, hollow, coated with active pharmaceutical ingredients, or made of the drug compound so they dissolve after application.



Milling (also known as bead milling or nano milling)

Active pharmaceutical ingredients may be "ground" or "milled" to form particles that have dimensions below 1000 nanometers in liquid or water-based form.[21] This process can maximize the bioavailability of poorly water-soluble medicines by increasing the surface area of the active pharmaceutical ingredient. Thus, scientists can condense a larger amount of the medicine into a smaller volume and prepare it for a small medicine delivery system, such as a shot, implant, or patch.[22] The milling process can be understood as grinding down the particles to nano- size.



Nano

Nano is a unit prefix meaning "one billionth." Used primarily with the metric system, it means a factor of 10−9 or 0.000000001. It is frequently encountered in science in front of units of time and length. A human hair is approximately 100,000 nanometers (nm) in diameter (or 100 micrometers).

Nanocrystals

Nanocrystals are crystalline structures that are less than 1 micrometer (μm) in size (1 μm = 1000 nm). When active pharmaceutical ingredient molecules organize themselves into clusters they form crystals, and these may be in the form of nanocrystals. Many active pharmaceutical ingredients are poorly soluble in water.

Nanocrystals can be produced from bead milling or homogenization processes to create fine particles that dissolve more easily.

Nanodispersions

Some active pharmaceutical ingredients are not soluble in water. To help with the formation of liquid medicines, the APIs may be converted into tiny particles by processes such as milling and then dispersed in water. If the particles are nano-sized, they are called nanodispersions (or nanoparticle suspensions).

Nanoemulsions

An emulsion that has one liquid dispersed within another where the droplets of the dispersed liquid are less than 100 nm.[23] This may lead to enhanced performance of a medicine.

Nanoformulations

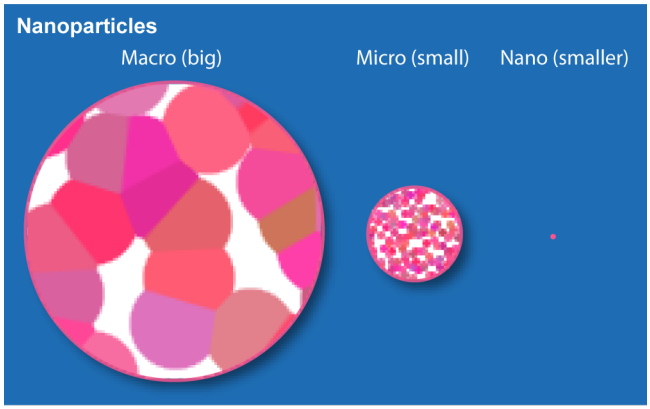
Medicines may need a poorly soluble active pharmaceutical ingredient to be processed into nanoparticles to help with its performance. When this is accomplished, the formulation is termed a nanoformulation. Many medicines, such as antivirals, antipsychotics, antidepressants, and contraception, contain nanoparticles and may use processes such as bead milling and high pressure homogenization.

Nanomedicines

A nanomedicine is any health care treatment or diagnostic device that uses nanoparticles to deliver its benefit or action. Many medicines that benefit from nanomedicine processes and approaches are already in clinical use. The field continues to evolve, and medicines that cannot be developed using older technologies often utilize nanomedicine technologies to bring medicines to patients.

Nanoparticles

A nanoparticle is a particle of material that is smaller than 1 micrometer (1 µm = 1000 nm). Nanoparticles may be formed from different types of material including metals and ceramics. When they are made from active pharmaceutical ingredients, they may contain many thousands of molecules and are bigger than dissolved molecules. Because many active pharmaceutical ingredients do not dissolve well in water or body fluids, reducing the particle size down to the nanometer scale helps medicines deliver benefits to patients.



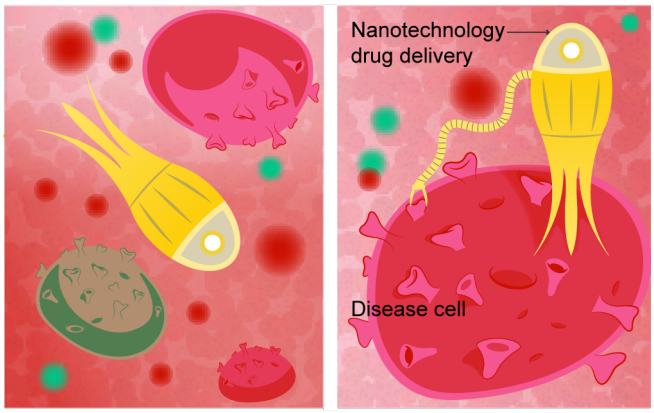
Artistic rendering. Not to scale.

Nanosuspensions (or solid drug nanoparticle suspensions)

Liquid suspension formulations containing tiny particles (less than 1 micrometer [µm]) of a medication that may be poorly water-soluble. These formulations increase solubility in medicines with poor solubility, poor permeability (poor absorption and distribution in the body), or both and may allow for intravenous administration.[24]

Nanotechnology

Science and engineering carried out at the nano level (between 1 and 100 nanometers [nm]). Nanotechnology can create new ways to deliver heat, light, medicines, or other substances into cells.[25]



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Niosomes

A type of liposome that uses non-ionic surfactants rather than naturally-derived phospholipids to form its spherical structure. As with liposomes, a core of water is contained within the niosome and a lipophilic bilayer is formed. Niosomes provide an alternative to liposomes in the formulation of lipophilic or water-soluble active pharmaceutical ingredients.

Nitroimidazole class

Class of medicines used against parasitic and bacterial infections. The anti-tuberculosis medicine delamanid and pretomanid are nitroimidazoles.

Non-responder

A patient who does not respond satisfactorily to a medication.

Non-salt or free form of active pharmaceutical ingredients

Active pharmaceutical ingredients may be either base compounds or weakly acidic compounds. These are called non-salt or free forms of the API. They may require neutralizing to form a salt to improve their performance in a medicine.

Non-polymeric nanoparticles

Nanomedicines use nanoparticles to help deliver benefits for patients. In some cases, the active pharmaceutical ingredient is encapsulated in a polymer coating to form a nanoparticle or embedded in a polymer nanoparticle to help carry it to the site of disease in the body. Options that do not use a polymer are called non-polymeric nanoparticles.

Nucleoside/nucleotide-based NS5B inhibitor

Class of medicines that bind to the active “NS5B” site, or protein, on the hepatitis C virus, which is found across all HCV genotypes. The medicine blocks the NS5B protein and prevents the replication of the virus. Sofosbuvir is a commonly prescribed DAA in this class.

Oil-based injections

Oil-based injections suspend the active pharmaceutical ingredient in an oil, such as castor, coconut, palm, sesame, or soybean oil, to deliver the medicine via intramuscular injections. The relatively easy-to-manufacture oils can help with the slow release of the medicine over the course of weeks or each month; however, they may lead to an undesirable injection volume.

Organic anion transporting polypeptide (OATP)

Human cells have specific proteins on their surface that use energy to transport molecules (including medicines) into or out of the cell. There are over 300 transporter proteins in humans, and OATPs are a specific family of transporters that are involved in the uptake of medicines into the cell. They have an extremely important role in controlling the amount of medicine in the body by influencing their absorption in the intestine or their elimination through the kidneys and liver. Multiple medicines interacting with the same OATP transporter can cause important drug-

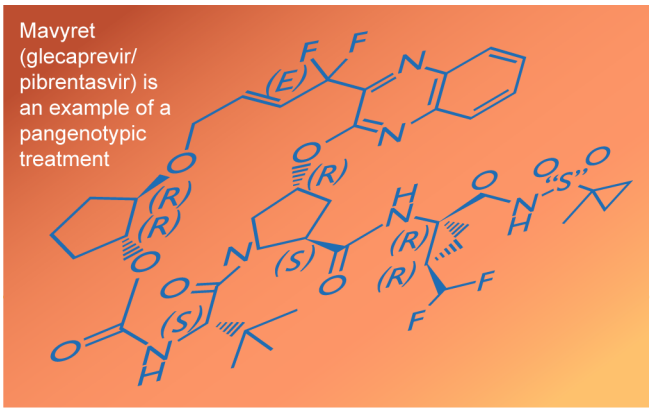
drug interactions, so regulatory agencies and scientists are extremely interested in medicinal affinity for these proteins.

Oral lead-in phase

Taking an oral version of a treatment to establish tolerability and safety before giving a patient a long-acting injectable formulation that takes longer to leave the body. In the prescribed regimen for cabotegravir/rilpivirine (Cabenuva), a patient takes oral cabotegrevir every day for five weeks (lead-in) before being given the long-acting injection—a shot in the buttocks administered either every month or every two months.

Pangenotypic

Direct-acting antiviral treatments that can effectively cure all HCV genotypes at nearly equivalent rates.



Particles

Particles are small fragments of matter of varying size. They may be classified as macroscopic (in the macro scale such as cm or mm), microscopic (in the micro scale such as the micrometer [µm]), or nanoscopic (in the nano scale such as the nanometer [nm]).

Peak plasma concentrations

The highest medicine levels achieved in the plasma, sometimes achieved after taking multiple doses.

Pharmacodynamics (PD)

Loosely defined as the impact of the medicine on the body or the disease. In real terms, pharmacodynamics refers to either the effectiveness or the toxicity of the medicine. Pharmacodynamics is often studied in parallel with the pharmacokinetics of the medicine to understand the relationship between drug compound concentrations and effect (that is, the pharmacokinetic-pharmacodynamic relationship or PK-PD).

Pharmacokinetics (PK)

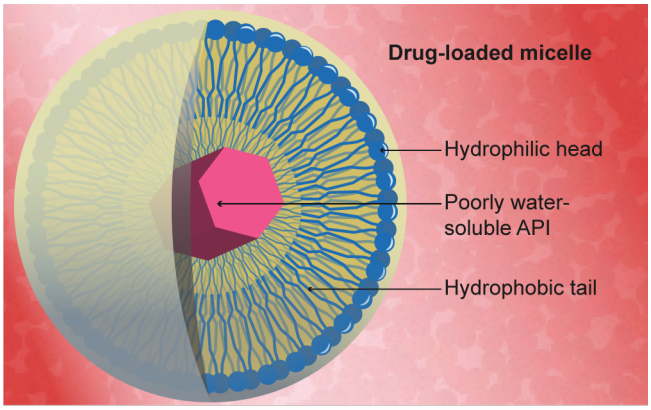
Loosely defined as the impact of the body on the medicine and is the study of drug compound concentrations in the bloodstream or other cells and tissues in relationship to time. After administration, drug compound concentrations gradually increase as the medicine is absorbed, and once fully absorbed, the concentrations fall due to the clearance of the medicine via the liver or kidneys.

Pharmacology

Field in medicine concerned with the uses and effects of medicine and how medicines work.

Pill fatigue (or medication fatigue)

A condition where an individual may be tired of taking or unmotivated to continue taking one or more medications over a prolonged period of time.



Polymeric micelles

A nanoscopic object (10–500 nm) that is formed from the assembly of surfactant molecules in water. It is similar to a liposome but has a lipophilic core surrounded by a hydrophilic (water-liking) outer layer. Polymeric micelles are made from polymers that have hydrophilic and lipophilic blocks connected together that then assemble in water to form the lipophilic core surrounded by the hydrophilic corona. Poorly water-soluble active pharmaceutical ingredients that need help to dissolve may be formulated into medicines using polymeric micelles.

Polymeric nanoparticles

Nanomedicines use nanoparticles to help deliver benefits for patients. In some cases, the active pharmaceutical ingredient is encapsulated in a polymer coating to form a nanoparticle or embedded in a polymer nanoparticle to help carry it to the site of disease in the body. These are called polymeric nanoparticles.

Polymorphs

Active pharmaceutical ingredient molecules pack together to form crystals. They may pack together in several different ways, resulting in different crystal shapes. For example, water packs together to form different snowflake structures. The different crystal shapes are called polymorphs and each polymorph may have different behavior, such as different melting points, different speed to dissolve, and different stability.

Controlling the polymorph of an active pharmaceutical ingredient can be very important.[26]

Preclinical proof-of-concept

Not yet tested in humans. Laboratory or animal models indicate that a treatment candidate works as proposed. This early stage in medicine development establishes evidence that it meets the drug formulation targets and characteristics (target formulation profile) in isolation (e.g., in a petri dish) and inside a living, nonhuman organism (e.g., in mice). This stage provides preliminary data suggesting possible medicine bioavailability, absorption, metabolism, and some potential adverse events.

Prodrug

Precursor in a medicine that is a biologically inactive chemical compound until it is converted into an active pharmaceutical ingredient once it enters the body.

Solubility

All active pharmaceutical ingredients and excipients will dissolve to form solutions in a solvent. Solubility in water is important to understand for medicine development, and the mass of material that can be dissolved into a unit volume of water is defined as the water solubility of the active pharmaceutical ingredient or excipient. This may vary with pH and temperature.

Solution-based injections

Injectable medicines may be formulated by dissolving an active pharmaceutical ingredient into a solvent if a suitable solvent can be identified. Some active pharmaceutical ingredients are not soluble in water and may require the use of oils, such as castor, sesame, soybean, coconut, or palm oils. The resulting solutions may be injected through either intramuscular or subcutaneous routes.

Subcutaneous

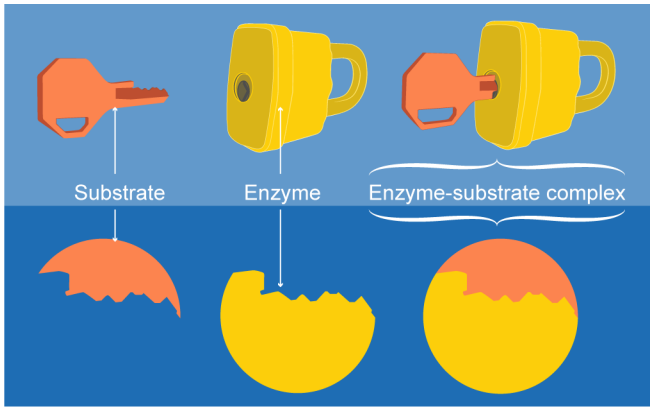
Under the skin.

Submicron particles

Particles that are less than 1 micrometer (μm) in size and are in the nano scale.

Substrates

The function of cells is governed by a huge number of proteins that are expressed and coded within the genome of the organism. Both the host and the pathogen express their own complement of different proteins, and the proteins that are important in pharmacology are either receptors, enzymes, or transporters—central in pharmacokinetics or pharmacodynamics. These proteins have binding pockets into which drug compounds or other molecules in the body can dock. When a molecule has been demonstrated to dock with a particular protein it is said to be a substrate for that protein. In the case of enzymes, the enzyme usually catalyzes a change in the chemical structure of the substrate, which can facilitate elimination of the medicine.



Surfactant (or surface modifier)

Chemical compound that can be used as an excipient for medicine formulation. The molecules have a combination of parts that are hydrophilic (water loving) and lipophilic (fat loving). They can adsorb onto surfaces to change the properties of the surface by making them more hydrophilic, or they may be used in water to form micelles, which are spherical structures with a lipophilic core that can help dissolve active pharmaceutical ingredients in water.

Suspension-based injections

Injectable medicines that use active pharmaceutical ingredients that are not soluble in water rely on forming particle suspensions (also known as dispersions). They may be nanoscale or microscale. The particle suspension may be injected under the skin or in the muscle tissue.[27]

Sustained plasma exposure

In the field of pharmacokinetics, it is often desirable to understand the amount of medicine in the blood over the time between taking the medicine and the point at which the medicine is fully disappeared. In this context, exposure describes the total amount of medicine the individual is exposed to. Long-acting medicine delivery systems prolong the length of time the medicine is within the bloodstream and are therefore described as providing a sustained plasma exposure.[28]

Trough (or minimum plasma concentrations)

Regardless of how a medicine is given (via a pill, injection, implant, or other routes), the concentrations within the blood and other tissues gradually increase in the hours or days after administration. Once the full dose has been depleted, the medicine is then gradually cleared from the body and the next dose must be given. The point immediately before the next dose, when concentrations are at their lowest, is the minimum or trough concentration, which is abbreviated to “Cmin” or “Ctrough.” For antivirals, the risk of treatment failure is sometimes higher at the trough concentration, so regulators and scientists can be very interested in these measurements for some medicines.

Endnotes

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