

Pharmaceutical Excipients

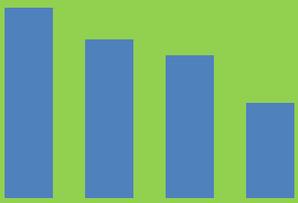
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Prepared For:

Pharmaceutical Technology-I

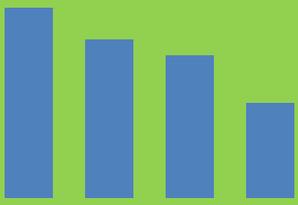


Definition:

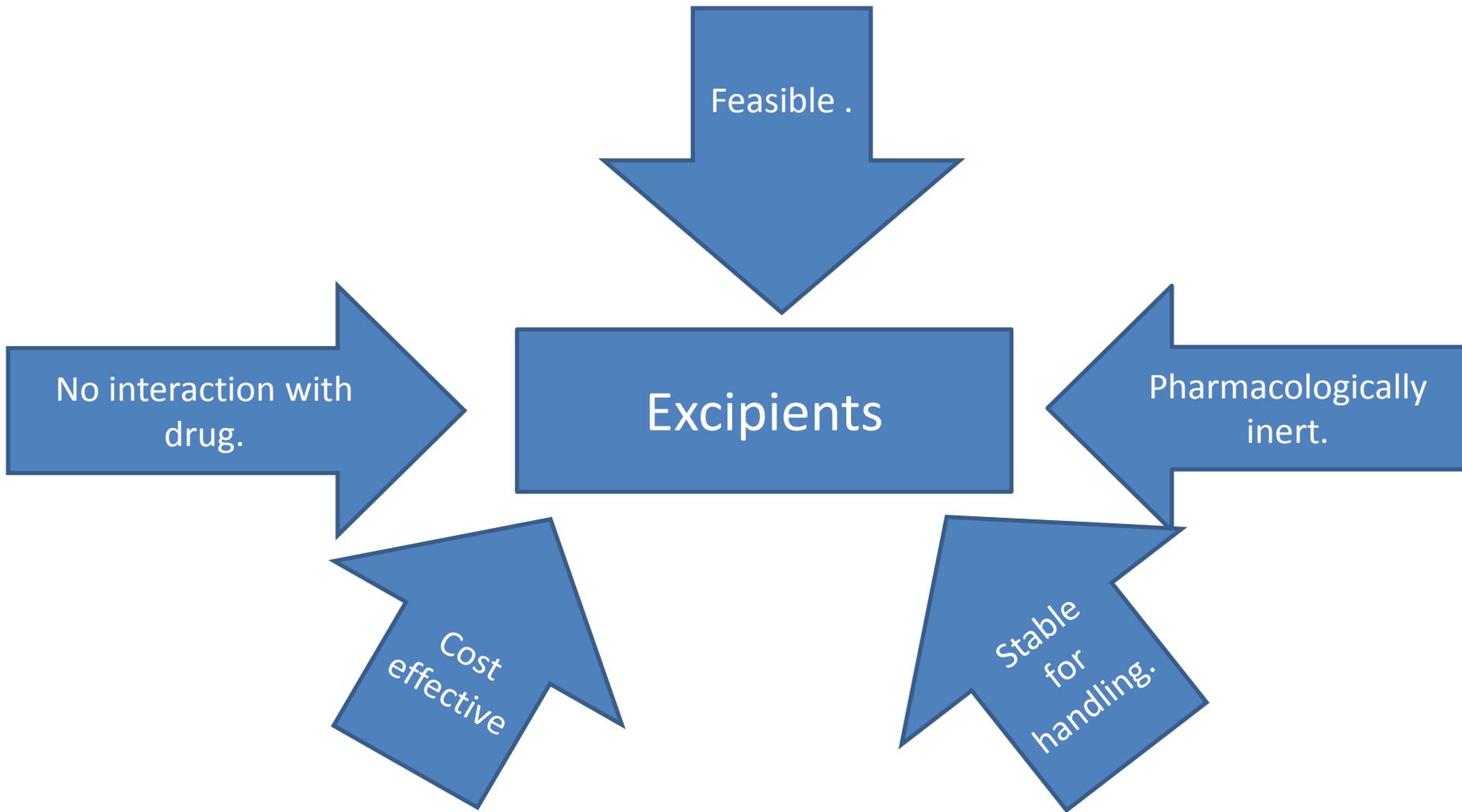
An excipient is a pharmacologically inactive substance formulated alongside the active pharmaceutical ingredient of a medication.

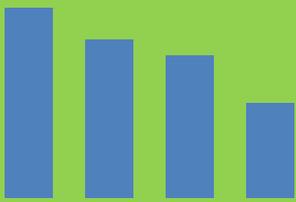
Purposes served by excipients:

- Provide bulk to the formulation.
- Facilitate drug absorption or solubility and other pharmacokinetic considerations.
- Aid in handling of “API” during manufacturing .
- Provide stability and prevent from denaturation . etc.



Ideal properties of Excipients:





A list of Pharmaceutical Excipients used in pharmaceutical preparations usually:

Fillers.

Binders.

Disintegrants.

Coatings.

Sorbents.

Antiadherent.

Lubricants.

Glidants.

Preservatives.

Antioxidants.

Flavoring Agents.

Sweetening Agents.

Coloring Agents.

Solvent & Co-solvent.

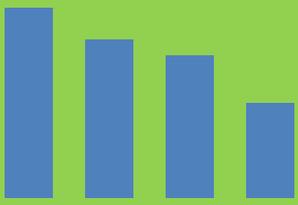
Buffering Agents.

Chelating Agents.

Viscosity imparting Agents.

Surface Active Agents.

Humectants .



Fillers:

Fillers typically also fill out the size of a tablet or capsule, making it practical to produce and convenient for the consumer to use.

Function of fillers:

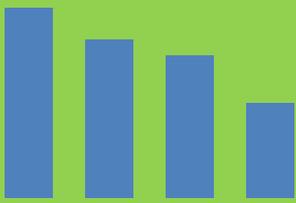
Fillers add volume and/or mass to a drug substance, thereby facilitating precise metering and handling thereof in the preparation of dosage forms . Used in tablets and capsules.

Typical features of fillers:

A good filler should typically be inert, compatible with the other components of the formulation, non-hygroscopic, relatively cheap, compactible, and preferably tasteless or pleasant tasting.

Examples:

Plant cellulose and dibasic calcium phosphate are used popularly as fillers . A range of vegetable fats and oils can be used in soft gelatin capsules. Other examples of fillers include: lactose, sucrose, glucose, mannitol, sorbitol, calcium carbonate, and magnesium stearate.



Binders:

Binders hold the ingredients in a tablet together . Binders ensure that tablets and granules can be formed with required mechanical strength, and give volume to low active dose tablets .

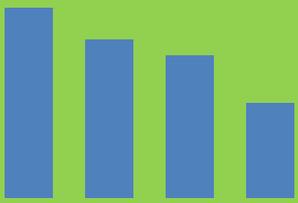
Typical features of binders:

A binder should be compatible with other products of formulation and add sufficient cohesion to the powders .

Classification and examples:

Binders are classified according to their application,

- Solution binders are dissolved in a solvent (for example water or alcohol can be used in wet granulation processes). Examples include gelatin, cellulose, cellulose derivatives, polyvinylpyrrolidone, starch, sucrose and polyethylene glycol.
- Dry binders are added to the powder blend, either after a wet granulation step, or as part of a direct powder compression (DC) formula. Examples include cellulose, methyl cellulose, polyvinylpyrrolidone and polyethylene glycol.



Disintegrants:

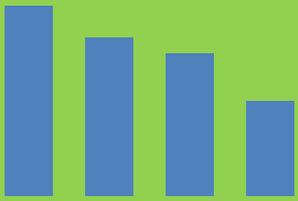
Disintegrants are substances or mixture of substances added to the drug formulations, which facilitate dispersion or breakup of tablets and contents of capsules into smaller particles for quick dissolution when it comes in contact with water in the GIT.

Ideal properties of disintegrants:

Good hydration capacity , poor solubility , poor gel formation capacity .

Examples:

polyvinylpyrrolidone , carboxymethyl cellulose, sodium starch glycolate etc.



Coating Agent:

Coating is a process by which an essentially dry, outer layer of coating material is applied to the surface of a dosage form and agents which are used in this coating process is called coating agents.

Types:

Three types of coating agents are used pharmaceutically,

Film coating.

Sugar coating.

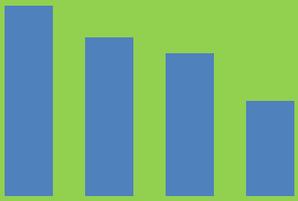
Compression coating.

Function of coating agents:

Protection, masking, elegance, ease of swallowing, identification etc..

Examples:

HPMC, MC, HPC etc..



Sorbents:

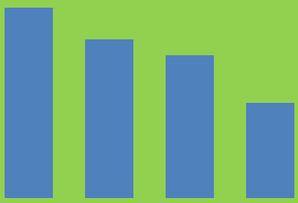
Sorbents are materials that soak up oil from the water.

Types and examples of sorbents:

- Natural sorbents- peat moss, sawdust, feathers, and anything else natural that contains carbon.
- Synthetic sorbents- polyethylene and nylon etc..

Functions of sorbents:

Sorbent are used for tablet/capsule moisture-proofing by limited fluid sorbing (taking up of a liquid or a gas either by adsorption or by adsorption) in a dry state.



Antiadherents:

Antiadherents or anti-sticking agents prevent adhesion of the tablet surface to the die walls and the punches and as a consequence counter the picking or sticking of tablet.

Examples:

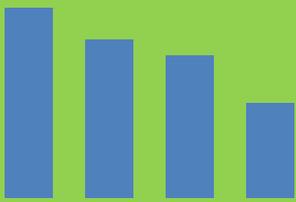
Water insoluble lubricants such as magnesium stearate can be used as antiadherents , as can talc and starch.

Lubricants:

Lubricants prevent ingredients from clumping together and from sticking to the tablet punches or capsule filling machine. Lubricants also ensure that tablet formation and ejection can occur with low friction between the solid and die wall.

Types:

- Hydrophilic- Generally poor lubricants, no glidant or anti-adherent properties.



- Hydrophobic-Most widely used lubricants in use today are of the hydrophobic category. Hydrophobic lubricants are generally good lubricants and are usually effective at relatively low concentrations. Many also have both anti-adherent and glidant properties. For these reasons, hydrophobic lubricants are used much more frequently than hydrophilic compounds. Examples include magnesium stearate.

Roles of lubricants:

1. True Lubricant Role:

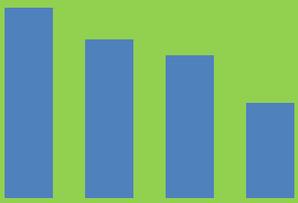
- To decrease friction at the interface between a tablet's surface and the die wall during ejection and reduce wear on punches & dies.

2. Anti-adherent Role:

- Prevent sticking to punch faces or in the case of encapsulation, lubricants
- Prevent sticking to machine dosators, tamping pins, etc.

3. Glidant Role:

- Enhance product flow by reducing interparticulate friction



Examples of lubricants:

Polyethylene glycol, Magnesium stearate, Stearic acid and its derivatives.

Glidants:

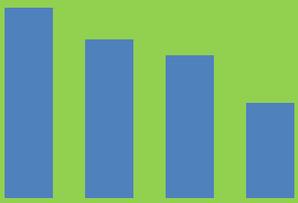
A substance (as colloidal silica) that enhances the flow of a granular mixture by reducing inter-particle friction and that is used in the pharmaceutical production of tablets and capsules.

Functions of glidants:

Glidants are used to promote powder flow by reducing interparticle friction and cohesion. These are used in combination with lubricants as they have no ability to reduce die wall friction.

Examples:

Fumed silica, talc, and magnesium carbonate.



Preservatives:

Preservatives are substances that commonly added to various foods and pharmaceutical products in order to prolong their shelf life.

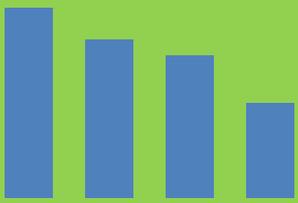
Ideal_properties_of_preservatives:

In concept, the preservative system protects the product against microbial proliferation but does not compromise product performance. In practice, this means that it must:

- Exert a wide spectrum of antimicrobial activity at low inclusion levels.
- Maintain activity throughout product manufacture, shelf life and usage.
- Not compromise the quality or performance of product, pack or delivery system.
- Not adversely affect patient safety or tolerance of the product.

Examples:

Methyl & Ethyl parabens, Propyl paraben, Benzoic acid and its salts, Sorbic acid and its salts.



Antioxidant:

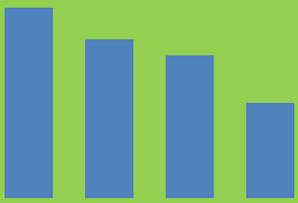
An antioxidant is a molecule that inhibits the oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons or hydrogen from a substance to an oxidizing agent.

Ideal Properties of Antioxidants:

- Effective at a low, nontoxic concentration
- Stable and effective under normal conditions of use, over a wide pH and temperature range
- Soluble at the required concentration
- Compatible with a wide variety of drugs and pharmaceutical excipients
- Free from objectionable odor, objectionable taste
- Colorless in both the original and oxidized form
- Nontoxic both internally and externally at the required concentration
- Reasonable cost
- Unreactive (does not adsorb, penetrate, or interact) with containers or closures

Examples:

BHT(Butylated Hydroxy Toluene), BHA(Butylated Hydroxy Anisol), Sodium sulfite, Ascorbic acid etc..



Sweetening agents:

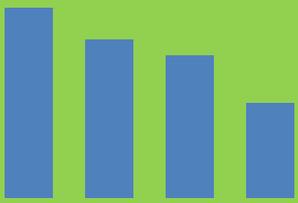
Sweetening agents are employed in liquid formulations designed for oral administration specifically to increase the palatability of the therapeutic agent.

Example:

Sucrose, Saccharine, Aspartame, Sorbitol etc.

Uses of sweetening agent:

The main sweetening agents employed in oral preparations are sucrose, liquid glucose, glycerol, sorbitol, saccharin sodium and aspartame. Aspartame is an artificial sweetening agent. The use of artificial sweetening agents in formulations is increasing. The use of sugars in oral formulations for children and patients with diabetes mellitus is to be avoided.



Flavoring agents:

Flavouring agents are added to increase patient acceptance. The four basic taste sensations are salty, sweet, bitter and sour. It has been proposed that certain flavours should be used to mask these specific taste sensations.

Example:

Clove oil, citric and syrup, glycerin, rose oil, orange oil, menthol etc..

Coloring agents:

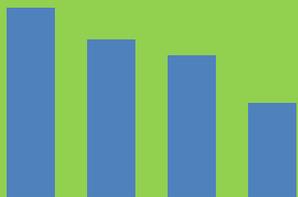
Coloring agents are pharmaceutical ingredients that impart the preferred color to the formulation.

There are two types of coloring agents

- 1.Natural and
- 2.synthetic

Example:

- 1.White: Titanium dioxide
2. Blue :Brilliant blue ,Indigo carmine
3. Red :Amaranth Carmine
- 4.Yellow: saffron
- 5.Green
- 6.Brown: caramel



Solvent

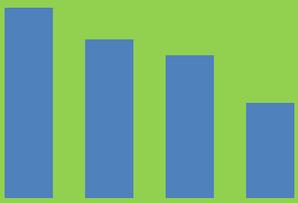
A solvent is a substance that can dissolve a solute (a chemically different liquid, solid or gas) resulting in solution. A solvent is usually a liquid but it can also be solid or a gas. A solvent never changes its state forming a solution.

Solvent classification

Solvents can be broadly classified into two groups ; They are

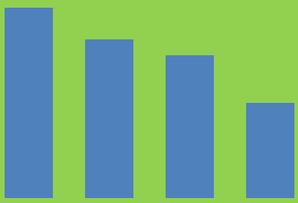
- Polar
- Non polar

Normally solvation of a solvent depends upon its classification. Generally polar solvent dissolves polar compound best and non polar solvent dissolves non polar compound best.



Example and uses of solvent

- The first choice for a solvent is water in which a drug is freely soluble.
- Water –miscible solvent such as Chlordiazepoxide hydrochloride can be used to improve solubility and stability.
- Oils are used as emulsion, intramuscular injections and liquid fill oral preparation.
- Aqueous methanol is widely used in HPLC and is the standard solvent in sample extraction.
- Other acceptable non-aqueous solvents are glycerol ,propylene glycol, ethanol and are used generally for a lipophilic drug.

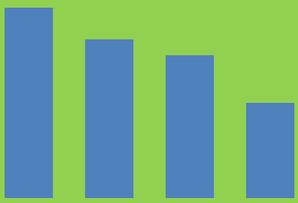


Co-solvent

Co-solvents are defined as water-miscible organic solvents that are used in liquid drug formulations to increase the solubility of poorly water soluble substances or to enhance the chemical stability of a drug.

Properties of co-solvent

- Co-solvent increases the solubility of a drug.
- An ideal co-solvent should possess values of dielectric constant between 25 and 80.
- The most widely used system that will cover this range is a water/ethanol blend.
- It should not cause toxicity or irritancy when administered for oral or parental use
- Other co-solvents are sorbitol, glycerol, propylene glycol and syrup..



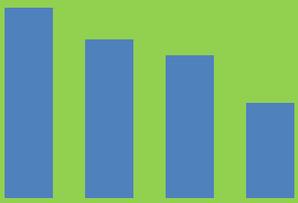
Chelating agent

Chelating agents are molecules that are capable of forming complexes with the drug involving more than one bond it's a complex compound contains one or more ring in its structure .

For example; ethylene diamine is bidentate and ethylene diamine tetraacetic acid is hexadentate.

Example and uses of chelating agent

- EDTA: ethylene diamine tetraacetate is used for the estimation of metals ions .
- EDTAH₄: ethylene diamin tetraacetic acid is used for softening water.
- Calcium Disodium Edetate: it is used in the treatment of heavy metal poisoning mostly caused by lead.
- Disodium Edetate: it is used in hypercalcemic states. It is also useful ion the treatment of cardiac arrhythmias.



Buffering agent

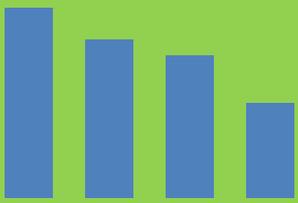
These are materials which, when dissolved in solvent will enable the solution to resist any change in pH should an acid or an alkali be added. The choice of suitable buffer depends on the pH and buffering capacity required.

Features of buffering agent

It should have a low toxicity, it should be buffered at the range of 7.4 as the pH of the body is 7.4, it should be non-irritant.

Examples of buffering agent

Most of the buffering system are based on carbonate, citrates, gluconates, lactates, phosphates, or tartrates etc.



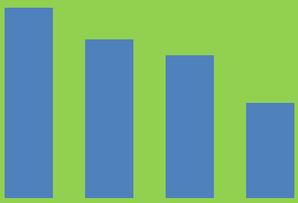
Viscosity imparting agents : These agents are used when it is desirable to increase or decrease the viscosity of a liquid either to serve as adjacent for palatability or to improve pour ability. They are also called thickening agents.

Viscosity imparting agents are of two types:

- a) Viscosity modifier-Viscosity modifiers decrease the viscosity of a liquid to improve pour ability and make it more palatable.
- b) Viscosity enhancer- Viscosity enhancers increase the viscosity of a liquid to improve pour ability and make it more palatable.

Most commonly used viscosity imparting agents are :

- Hydroxyethylcellulose
- Hydroxypropylmethylcellulose
- Methylcellulose
- Polyvinyl alcohol
- Polyvinylpyrrolidone

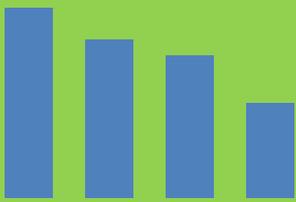


Humectant : A humectant attracts and retains the moisture in the nearby air via absorption, drawing the water vapor into and/or beneath the organism/object's surface. Humectants absorb water vapors from atmosphere till a certain degree of dilution is attained. Aqueous solutions of humectants can reduce the rate of loss of moisture.

Ideal properties of humectants :

- It must absorb moisture from atmosphere and retain the same under the normal conditions of atmospheric humidity.
- It should be colorless or not of too intense color.
- It should have good odor and taste.
- It should be nontoxic and nonirritant.
- It should be noncorrosive to packaging materials
- It should not solidify under normal conditions.
- It should not be too costly.

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Classification of humectants with examples :

There are **three** types of humectants such as inorganic humectants, metal organic humectants and organic humectants.

Inorganic humectants:

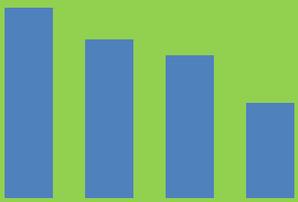
These are limited used in cosmetics. Calcium chloride is an example. It has compatibility problems and corrosive in nature. Hence it is not frequently used in cosmetics.

Metal organic humectants:

These are limited used in cosmetics because of compatibility problems, corrosive nature and pronounced taste. The example of this class is sodium lactate.

Organic humectants:

These are widely used in cosmetics. They include polyhydric alcohols, their esters and ethers. The most commonly used organic humectants are glycerol, ethylene glycol, polyethylene glycol (PEG), diethylene glycol, tri ethylene glycol, propylene glycol, dipropylene glycol, glycerin, sorbitol, mannitol, glucose.



Surfactants : Surfactants are compounds that lower the surface tension (or interfacial tension) between two liquids or between a liquid and a solid and increase the solubility. They are also known as surface active agents.

Properties of surfactants : A surfactant must fulfill two structural requirements:

- a) A surfactant must contain a lipophilic region.
- b) A surfactant must contain a hydrophilic region.

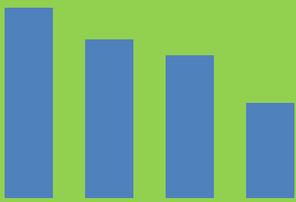
In a surfactant both hydrophilic and lipophilic region must be balanced because then both the regions will be concentrated at an interface and therefore surface tension will be lowered.

Types of surfactants :

There are of **four** types of surfactants based on the charge of the hydrophilic region :

1. **Anionic surfactant** (here the hydrophilic region is negatively charged i.e. an anion)

Sodium lauryl sulphate - It is used as an excipient on some dissolvable aspirins and other fiber therapy caplets.



2. **Cationic surfactant** (here hydrophilic region is positively charged i.e. a cation)

Cetyl trimethyl ammonium bromide (cetrimide) - is an effective antiseptic agent against bacteria and fungi.

3. **Non-ionic surfactants :**

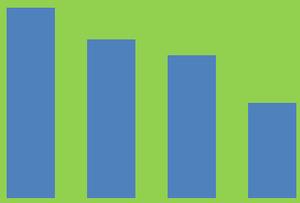
Tween 80 (polyoxyethylene sorbitol monooleate)- Polysorbate 80 is an excipient that is used to stabilize aqueous formulations of medications for parenteral administration

Span (sorbitan ester of lauric acid)

4. **Amphoteric surfactant :**

Lecithin- it acts as a wetting, stabilizing agent and a choline enrichment carrier, helps in emulsifications and encapsulation, and is a good dispersing agent.

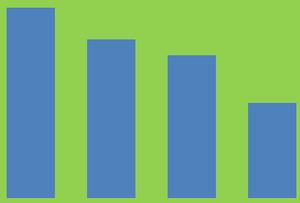
N-dodecyl alanine.



CONCLUSION

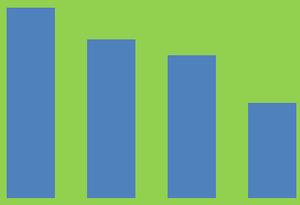


The real importance of ensuring an excipient's quality and performance is often underestimated. In reality, the functionality of the excipient can help determine whether or not a drug succeeds or fails. The possible consequences of not carefully choosing the best excipient for formulation include manufacturing complications, compromised stability, poor bioavailability of the API, unintended side-effects, and even serious adverse reaction or death of the patient. So to avoid these undesirable outcomes it is very important to select the right excipient for the formulation and guarantee its quality.



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THANK YOU

