Review on Pharmaceutical Excipients Used in Different Dosage Forms

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Abstract- *Excipients are non-API substances that have been adequately evaluated for safety and that are intentionally included in the manufacturing process or in a dosage form of finished pharmaceutical products to alter function. The real importance of ensuring quality and performance is often underestimated. In fact, the functionality of the excipient can help determine whether a drug is successful or not. They can cause unwanted side effects and even serious side effects or patient death. To avoid these undesirable results, it is therefore very important to choose the right excipient for the formulation and to ensure its quality. Therefore, excipient selection should focus on biopharmaceutical, pharmaceutical, and processing and stabilization perspectives. The various interactions of excipients such as drug-excipient interactions, excipient-excipient interactions, and container-excipient interactions can render the excipient deleterious for use in the formulation. To avoid using incompatible excipients and ensure excipients are safe and stable for use in formulation design the excipient study is important.The excipient included in a formulation must be highly stable, safe and effective, and most importantly, perform as expected role in the formulation.*

Keywords- Effectiveness, Excipients, Formulation, design, Interactions

I. INTRODUCTION

The International Pharmaceutical Excipients Council (IPEC) defines excipients as "Non-API substances that have been appropriately evaluated for safety and intentionally incorporated into a drug delivery system.

For example, excipients may assist in the

1. Processing of the drug delivery system during its manufacture,
2. Protect, support or improve stability, bioavailability or patient acceptance,
3. Help in product identification, or
4. Improve any other attribute of the drug's overall safety, efficacy, or manageability during storage or use.[1]

Most medicines contain excipients. They are added for a number of reasons and can improve product performance, for example by enabling formulations, patient acceptability and compliance such as modified release formulations or flavored masked syrups for children, or by providing a more effective and safer drug. The latter can be achieved, for example, by ensuring that peak plasma concentrations are kept below harmful or even toxic levels. Historically, excipients are considered pharmacologically inactive materials and come from a variety of sources, e.g. biological, mineral or chemical syntheses. based etc. Excipients often contain (manufacturing-related) by-products, processing aids and impurities also. Excipients generally have more quantity than the API. Guidelines are available to determine appropriate level of excipients in different formulations. Because excipients are an important part of all pharmaceutical formulations, it is vital for the pharmaceutical scientist to understand the different types/grades of excipients that are available.[2]

Solvents that are used to manufacture a dosage form but are not included in the final product are considered excipients, i.e., granulation liquids that can be dried later must comply with the relevant pharmacopeial requirements unless duly justified. Excipients no longer retain the original concept of "inactive support" due to their impact on both biopharmaceutical aspects and technological factors. The desired effect, the excipient substances correspond to the effectiveness of the active ingredient, is called functionality. The inherent property of an excipient is its functionality. Excipients are generally manufactured by a batch process; Therefore, there is a possibility of variation from batch to batch from the same manufacturer. Excipients that come from different sources may not have identical properties in relation to use in a given formulation. In order to ensure interchangeability under such circumstances, users may wish to determine final performance equivalence or determine such characteristics prior to use. These tests relate to the functionality that the excipient imparts to a particular formulation.[3]

There are approximately 8,000 non-active ingredients used in foods, cosmetics and pharmaceuticals. Excipient manufacturers often deliver their material to different end users. , i.e., Pharmaceutical, food, cosmetics, etc.As a result, excipient suppliers do not necessarily know the end use of their products. An excipient for pharmaceutical use may require additional quality, functionality and safety requirements. The focus on variety and provider is important for the end consumer.[2]

Excipients often have multiple uses within a formulation and for example microcrystalline cellulose can be a filler/diluent, binder or disintegrant in a solid dosage form. Excipients can be added to a formulation to improve flow or compression of the powder and thus improve manufacturability. In addition, excipients are used to improve drug stability, e.g., low moisture content of common fillers (in case of hydrolytic instability) or antioxidants (in case of oxidative instability); to enhance disintegration and thus dissolution, e.g., Disintegrants. The appearance of the final dosage form can be enhanced with additives such as aqueous film coating components. Finally, excipients can also be used to improve oral bioavailability by affecting the solubility or permeability of the drug.[2]

The choice of excipients depends on the form of the dosage form, its functionality and is mainly based on its well-tolerated atmosphere in relation to the active/inactive material and preparation technique. Its function is the vital and formative backbone of dosing form consisting of a solid, semi-solid and liquid dosage form for topical and conventional use. In most cases, the bioavailability of formulations also depends on the choice of excipients and their concentration level in combinations.[5]

Many dosage forms formulated today are complex systems that contain many other components in addition to the active pharmaceutical ingredient (API); these compounds are generally added together with the pharmaceutically active substances to protect, support or improve the stability of the pharmaceutically active substances. It is often observed that the active pharmaceutical ingredient in its pure form does not retain its stability for long, leading to its denaturation or adherence. The wall of the container, making it unsuitable. To stabilize the active ingredient, excipients are added to maintain product stability and ensure the active ingredient retains its stability over a significant period of time, thereby improving the shelf life of the dosage formulation. Adjuvants improve patient acceptance. Excipients often help to improve the bioavailability of the active substance, e.g., with an excipient that can act as a solvent or support the absorption of the drug by the human body. Improve the overall safety and effectiveness of the formulation during storage and use. The US Pharmacopeia National Formulary (USP-NF) classifies excipients based on their function informulations. Binders, disintegrants, etc. Excipients can be classified according to their origin, dosage form and function.[6]

Excipients depending on origin[7]

- Animal source:- Lactose, gelatin, stearic acid, beeswax, honey, musk, lanolin, etc.
- Vegetable source:- Starch, mint, turmeric, guar gum, alginate, acacia, etc.
- Mineral source:-Calcium phosphate, silica, talc, calamine, asbestos, kaolin, paraffin, etc.
- Synthetic:- Boric acid, saccharin, lactic acid, polyethylene glycols, polysorbates, povidone, etc.

The **ideal properties of an excipient** are given below

An excipient should be:-

- Chemically stable
- Non-reactive
- Low sensitivity to devices and processes
- Inert to the human body
- Non-toxic
- Acceptable in terms of organoleptic properties
- Economical
- Efficient in terms of the intended use.[8]

Role of excipients :

Any substance other than the active ingredient that has been appropriately safety evaluated and is included in a drug delivery system to:

- Aid in system processing during manufacture,
- Protect, assist, or enhance drug stability,
- Increase bioavailability, or patient acceptance.
- Help with product identification.
- Improving all other attributes of the drug's overall safety and efficacy during storage or use.
- Help maintain product integrity,
- Improve stability,
- Release modifications/changes.[4]

Excipients Selection Considerations

Excipients can be seen as an essential part of pharmaceutical products and are present in most formulations in a larger proportion relative to the active pharmaceutical ingredient as they make up the majority of the formulation. It is always necessary to select an excipient that meets these requirements the ideal properties for a particular excipient.

The selection of excipients for a formulation should consider the API characteristics, the process, the target formulation, and the potential impact on the formulation.

Some of these API characteristic

- DOSAGE: Choose excipients that improve the consistency and stability of your chemistry active substance.
- PARTICLE SIZE: Choose lubricants with a narrow and controlled particle size distribution that improve tableting properties and prevent segregation (mainly micronized).
- FLOW PROPERTIES: Choose sliders that do not reduce resolution and compression. Controlled particle size should be considered.
- MOISTURE CONTENT: Choose hydrophilic lubricants or lubricants with the ability to absorb excess moisture without diffusing to the surface.
- HYGROSCOPY: Choose excipients with drying properties (highly hygroscopic) and functionality to improve the stability of your active ingredient at any relative humidity and avoid degradation. The best excipient considering the API and other excipients used.
- COMPACTABILITY: Selection may require granulation techniques or the use of co-processed/blended excipients.[9-10]

Formulators must also consider physicochemical properties, stability and compatibility issues, pharmacokinetic properties, permeation properties, segmental absorption behavior, drug delivery platform, intellectual property issues, etc. When choosing an adjuvant for formulation development, this can help determine absorption issues and the desired drug delivery platform. The Quality by Design (QbD) concept helps to understand the normal variability of excipients and their potential impact on formulation development processes.[6]

Different dosage forms containing excipients:

Table 1: Solid dosage form containing different excipients[11]

Excipient	Function	Examples
Solubilizers	Dissolve the drug as only soluble drugs have an effect.	glycerol, propylene glycol
Disintegrants	Decreases the disintegration time for faster release	polyvinylpyrrolidone, CMC
Fillers/diluent	Produce bulk of tablet to match with required strength	lactose, sucrose
Glidants	Promote powder flow by reducing interparticle friction	silica, talc
Antiadherents	Reduces the adhesion between powder (granules)	talc and starch
Binders	Glues tablet ingredients together to avoid separation	gelatin, cellulose
Coating agents	Protect drug from chemical, physical exposure	HPMC, MC
Preservatives	Exert a wide spectrum of antimicrobial activity	propyl and methyl paraben
Sweeteners	Reduces the bitterness and increase patient compliance	saccharin, aspartame
Colours and Flavours	Improve appearance and mask taste, respectively	orange oil, menthol

Table 2: Liquid dosage form containing different excipients[12]

Excipient	Function	Examples
Vehicles	Means of solubilizing different components	Propylene glycol
Surfactants	Increase solubility of the drugs and stabilize the system	Polysorbate, Poloxamer
Antioxidants	Prevent oxidation	Butyl hydroxy toluene, butyl hydroxy anisole, ascorbic acid
Complexing agents	Binds reversibly with drugs to form stable complex	ß cyclodextrin
Tonicity modifiers	Maintain tonicity with the body's natural fluids	Dextrose, Glycerin
Buffers	Control the pH of liquid orals and important in storage	Acetate, Phosphate
Preservatives	Preserve the formulation	Benzyl alcohol, methyl paraben, chlorocresol
Sweetening agents	Impart sweetness to the formulation	Saccharin, Aspartame
Flavoring agents	Impart flavour to the formulation	Geraniol, Aromatic waters, Syrup
Colouring agents	Impart colour to the formulation	Amaranth, Erythrosin, Eosin, Tartarazine

Table 3: Semi-solid dosage form containing different excipients [13]

Excipient	Function	Examples
Semisolid bases	Base for dissolving drugs	Cocoa butter, glycerin, coconut oil, Propylene glycol
Hydrophilic solvents	Dissolve hydrophilic drugs	(Ethanol, water, Isopropanol, Propylene glycol)
Hydrophobic solvents	Dissolve lipophilic drugs	Mineral and vegetable oils, Benzyl benzoate
Emollients	Alter skin characteristics	Glycerin, mineral oil, isopropyl palmitate
Preservatives	Prevent microbial growth	Benzyl alcohol, methyl paraben, chlorocresol
Gelling agents	Formation of gel like structure	Pemulen, Carboxy methyl cellulose
Melting point modifier	Adjust melting point	Bees wax, white wax, yellow wax, lanoline
Emulsifiers	Reduce surface tension between two immiscible phases	(Sodium lauryl sulfate)
Solubilizers	Enhance solubility (Lanolin, cholesterol, or	(Lanolin, cholesterol, or cholesterol esters)
Viscosity modifiers	Adjust the viscosity	(Paraffin, Spermaceti, Lanolin)

Types of excipients: (based on their functions)

Excipients are classified according to their functions as:-Miscellaneous excipients used in the different dosage forms. They perform various functions such as:-binders, diluents, lubricants, disintegrants, plasticizers, etc. For

example: when 5% starch is used in the formulation, it serves as a binder for tablet formulations when used in dry form, it serves as the function of adisintegrants.[6]

Table 4: Types of excipients

Types of Excipients	Examples
Fillers	MCC, starch, sucrose, lactose, mannitol
Binders	Starch, Sucrose, Gelatin, methyl cellulose, PVP
Disintegrants	Alginates, Starch
Coating agents	HPMC,MC,HPC
Sorbents	Sawdust, Polyethylene, Nylon
Antiadherants	Magnesium stearate, Talc, Starch
Lubricants	Calcium stearate, glycerin, PEG, Mg. stearate
Glidants	Talc, starch, Mg stearate.
Preservatives	Methyl & Ethyl parabens, Propyl paraben, Benzoic acid and its salts, Sorbic acid and its salts.
Antioxidants	BHT(Butylated Hydroxy Toluene), BHA(Butylated Hydroxy Anisol), Sodium sulfite, Ascorbic acid.
Sweeting agents	Sucrose, Saccharine, Aspartame, Sorbitol etc.
Flavouring agents	Clove oil, citric and syrup, glycerin, rose oil, orange oil, menthol etc.
Colouring agents	Titanium dioxide, Amaranth Carmine, Indigo Carmine, Caramel
Solvents and co-solvents	Methanol, Chlordiazepoxide hydrochloride, glycerol, propylene glycol, ethanol, Oils, Sorbitol, Syrups
Chelating agents	EDTA, Calcium Disodium Edetate, Disodium Edetate
Buffers	Phosphate Buffer and acetate buffers
Viscosity imparting agents	Hydroxyethyl cellulose, Hydroxypropyl methylcellulose, Methylcellulose, Polyvinyl alcohol, PVP
Humectants	Calcium chloride, Sodium lactate, Glycerol, Sorbitol, mannitol
Surfactant	Polysorbate

- **Fillers**:

Fillers generally conjointly fill out the scale of a tablet or capsule, creating it sensible to supply and convenient for the buyer to use.

Function of fillers:

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

Typical features of fillers:

A good filler ought to generally be inert, compatible with the other parts of the formulation, non-hygroscopic, comparatively cheap, compactible, and ideally tasteless or pleasant tasting.

Examples:

Vegetable cellulose and dibasic calcium phosphate are commonly used as fillers. A variety of vegetable fats and oils can be used in soft gelatin capsules. Other examples of fillers are: lactose, sucrose, glucose, mannitol, sorbitol, calcium carbonate and magnesium stearate.[14]

- **Binders**:

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

Typical features of binders:

A binder must be compatible with otherformulation products and provide sufficient cohesion to the powders.

Classification and examples:

Binders are classified according to their application, Solvent 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 mix either after a wet granulation step or as part of a direct compression powder (DC) formulation. Examples are cellulose, methyl cellulose, polyvinylpyrrolidone and polyethylene glycol.[15]

- **Disintegrants**:

Disintegrants are substances or mixtures of substances added to drug formulations that facilitate the dispersion or fragmentation of tablet and capsule contents into smaller particles for rapid dissolution upon contact with water in the GIT.

Ideal properties of disintegrants:

- Good hydration capacity
- Low solubility
- Low gelling capacity.

Examples:

Polyvinylpyrrolidone, carboxymethyl cellulose, sodium starch glycolate etc.[1]

- **Coating Agent:**

Coating is a process whereby a substantially dry outer layer of coating material is applied to the surface of a

dosage form, and the agents used in this coating process are referred to as coating agents.

Types of coating agents:

Three types of coating agents are used pharmaceutically,

- Film coating.
- Sugar coating.
- Compression coating.

Function of coating agents:

- Protection of the tablet,
- Masking unpleasant taste and odour,
- Provide elegance to the dosage form,
- Easy to swallowing,
- Identification of the product. etc.

Examples:

HPMC, MC, HPC etc.[15]

- **Sorbents**:

Sorbents are substances that absorb 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:

Sorbents are used to prepare tablets/capsules against moisture by limiting liquid uptake (recovery of a liquid or gas either by absorption or adsorption) when dry.[15]

- **Antiadherents**:

Antiadherents or anti-sticking agents stop adhesion of the tabletsurface to the die walls and therefore the punches and as a consequence counter the selecting or projected of tablet.

Examples:

Water-insoluble lubricants such as magnesium stearate can be used as an anti-seize, as can talc and starch.[14]

- **Lubricants**:

Lubricants prevent ingredients from clumping and sticking to the tablet punch or capsule filling machine. Lubricants also ensure that tablet formation and ejection occurs with low friction between the solid and the mold wall.

Types:

- Hydrophilic: Generally poor lubricants, with no lubricating or seizing properties.
- Hydrophobic:The lubricants most commonly used today belong to the hydrophobic category. Hydrophobic lubricants are generally good lubricants and are usually effective at relatively low concentrations. Many have both non-stick and slip properties. For these reasons, hydrophobic lubricants are used much more frequently than hydrophilic compounds.Example include magnesium stearate.

Roles of lubricants:

1. True Lubricant role:
2. Anti-adherent role:
3. Glidant role.

Examples of lubricants:

Polyethylene glycol, Magnesium stearate, Stearic acid and it's derivatives.[15]

- **Glidants**:

A substance (e.g., colloidal silicon dioxide) that improves the flow of a granular mixture by reducing friction between the particles and is used in the pharmaceutical manufacture of tablets and capsules.

Functions of glidants:

Glidants are used to promote powder flow by reducing friction and cohesion between particles. They are used in combination with lubricants as they cannot reduce friction on the mold wall.

Examples:

Fumed silica, talc, and magnesium carbonate.[14]

- **Preservatives**:

Preservatives are substances commonly added to various foods and medicines to extend their shelf life.

Ideal properties of preservatives:

- In principle, the preservative system protects the product from microbial growth but does not affect product performance.
- In practice this means that it mustexert a broad spectrum of antimicrobial activity at low entrapment levels.
- Sustaining activity throughout product manufacture, lifetime and use.
- Do not compromise on the quality or performance of the product, packaging or delivery system.
- Do not compromise patient safety or product tolerability.

Examples:

Methyl & Ethyl parabens, Propyl paraben, Benzoic acid and its salts, Sorbic acid and its salts.[15]

- **Antioxidant**:

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

Ideal Properties of Antioxidants:

- Effective in low concentration and non-toxic.
- Stable and effective under normal conditions of use in a wide range of pH and temperature.
- Soluble in the required concentration.
- Compatible with a wide range of drugs and pharmaceutical excipients.
- Free of unpleasant odors and taste.
- Colorless in both the original and also in the oxidized form.
- Non-toxic both internally and externally at the required concentration.
- Reasonable cost.
- Does not react (adsorb, permeate or interact) with containers or closures.

Examples:

BHT (Butylated Hydroxy Toluene), BHA (Butylated Hydroxy Anisole), Sodium sulfite, Ascorbic acidetc.[14]

- **Sweetening agents:**

Sweeteners are used in liquid formulations specifically designed for oral administration to increase the palatability of the therapeutic agent.

Examples:

Sucrose, Saccharine, Aspartame, Sorbitol etc.[15]

- **Flavouring agents:**

Flavouring agents are added to increase patient acceptance. The four basic taste sensations are salty, sweet, bitter and sour. It has been proposed to use specific flavors to mask these specific taste sensations.

Examples:

Clove oil, Citric and syrup, Glycerin, Rose oil, orange oil, Menthol etc.[14]

- **Colouring agents:**

Dyes are pharmaceutical ingredients that provide the preferred color to the formulation.

There are two types of colouring agents

A. Natural (e.g., turmeric, Henna, indigo)
B. Synthetic(e.g., Fast green, Picric acid, Orange G)

Examples:

1. White: Titanium dioxide
2. Blue: Brilliant blue, Indigo carmine
3. Red: Amaranth Carmine
4. Yellow: Saffron
5. Brown: Caramel[15]

- **Solvent**:

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

Solvent classification:

Solvents can be broadly classified into two groups; They arePolar and Non polar

Typically, the solvation of a solvent depends on its classification. In general, the polar solvent is better at dissolving the polar compound and the non-polar solvent is better at dissolving the non-polar compound.

Example and uses of solvent:

The first choice for a solvent is water, in which the drug dissolves well. A water miscible solvent such as chlordiazepoxide hydrochloride can be used to improve solubility and stability.

Oils are used as emulsions, intramuscular injections and liquid fillers. Oral preparationaqueous methanol is commonly used in HPLC and is the standard solvent in sample extraction.

Other acceptable non-aqueous solvents are glycerol, propylene glycol, ethanol and are commonly used for lipophilic drugs.[14]

- **Co-solvent**:

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

Examples:

Sorbitol, Glycerol, Propylene glycol and Syrup.[14]

- **Chelating agent:**

The chelating agents are molecules capable of forming complexes with the drug, involving more than one bond, it is a complex compound containing one or more rings in its structure.

For example; ethylene diamine is bidentate and ethylene diamine tetra acetic acid is hexadentate.

Example and uses of chelating agent

- EDTA: Ethylenediamine tetraacetate is used to determine metal ions.
- EDTAH4: Ethylenediamine tetra acetic acid is used to soften water.
- Calcium disodium edetate: Used to treat heavy metal poisoning, mainly caused by lead states used. It is also useful in the treatment of cardiac arrhythmias.[14]

- **Buffering agent:**

These are materials that, when dissolved in solvent, allow the solution to resist any change in pH should an acid or base be added. The choice of the appropriate buffer depends on the pH value and the required buffering capacity.

Features of buffering agent:

It must have low toxicity, it must be buffered in the range of 7.4 as the body pH is 7.4, it must be non-irritating.

Examples of buffering agent:

Most buffer systems are based on carbonates, citrates, gluconates, lactates, phosphates or tartrates, etc.[14]

- **Viscosity imparting agents:**

These agents are used when it is desired to increase or decrease the viscosity of a liquid, either to serve as a palatability additive or to improve flow ability. They are also called thickeners.

Viscosity imparting agents are of two types:

A. Viscosity modifier: lowers the viscosity of a liquid to improve fluidity and make it tastier.
B. Viscosity enhancer: Increases the viscosity of a liquid to improve fluidity and make it tastier.

Most commonly used viscosity imparting agents are:

Hydroxyethyl cellulose, Hydroxypropyl methylcellulose, Methylcellulose, Polyvinyl alcohol, Polyvinylpyrrolidone.[14]

- **Humectant**:

A humectant attracts and retains moisture in the surrounding air by absorption by drawing water vapor into and/or beneath the surface of the organism/object. Humectants absorb water vapor from the atmosphere until a certain degree of dilution is reached. Aqueous solutions of humectants can reduce moisture loss.

Ideal properties of humectants:

- It must absorb moisture from the environment and hold at normal humidity levels.
- It should be colorless or not too intense in color.
- It should have a good smell and taste.
- It should not be toxic or irritating.
- Must not be corrosive to packaging materials
- It should not solidify under normal conditions.
- It should not be too expensive.

Humectant classification with examples:

There are three types of humectants such as:

A. Inorganic humectants
B. Metal-organic humectants, and
C. Organic humectants.

A. Inorganic humectants:

Their use in cosmetics is limited. Calcium chloride is an example. It has compatibility issues and is inherently corrosive. Therefore, it is not widely used in cosmetics.

B. Metal-organic humectants:

These have limited use in cosmetics due to compatibility issues, caustic nature and distinct taste. The example of this class is sodium lactate.

C. Organic humectants:

They are widely used in cosmetics. Includes polyhydric alcohols, their esters and ethers. The most commonly used organic humectants are Glycerin, Ethylene Glycol, Polyethylene Glycol (PEG), Diethylene Glycol, Triethylene Glycol, Propylene Glycol, Propylene Glycol, Glycerin, Sorbitol, Mannitol, Glucose.[14]

- **Surfactants**:

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

Properties of surfactants:

The surfactant must meet two structural requirements:

A. A surfactant must contain a lipophilic region.
B. A surfactant must contain a hydrophilic region.

In a surfactant, both the hydrophilic and lipophilic regions must be in balance, as then both regions will be concentrated at an interface, thus reducing surface tension.

Types of surfactants:

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

1. Anionic surfactants: Here the hydrophilic region is negatively charged, i.e.,an anion. Sodiumlauryl sulfates used as an excipient in some soluble aspirins and other fiber therapy capsules.
2. Cationic surfactant: Here the hydrophilic part is a positively charged cation. Cetyltrimethylammonium bromide (Cetrimide) is an effective antiseptic against bacteria and fungi.
3. Non-ionic surfactants: Tween 80 (polyoxyethylene sorbitan monooleate) – Polysorbate 80 is an excipient used to stabilize aqueous formulations of drugs for parenteral administration.
4. Amphoteric surfactant:Carrier helps with emulsification and encapsulation and is a good dispersing agent. e.g.,Lecithin.[14]

Production, Distribution and Use of Excipients

Most excipients are manufactured in large quantities in factories that do not manufacture them themselves. These plants work with continuous production cycles, which makes it difficult to trace the material, the quality of which is often not at pharmaceutical level. Others are isolated from plants or mineral raw materials instead of being produced by synthesis.[16]

The distribution phase of materials and finished products, if not controlled, can also be a source of poor quality, not to mention outright toxicity of the excipients. Contaminated glycerol has already been mentioned causing the deaths of eighty children due to anuric acute renal failure. From the manufacturer to the retailer and finally to the patient, this substance travels a long way, during which the properties of the excipient can be compromised due to inadequate storage and transport conditions, cross-contamination, labeling errors and batch traceability.[17]

When a generic drug is reformulated, the properties of the new excipients must be carefully evaluated, particularly in the case of modified-release formulations. Also, the use of injectables should be allowed. Only after careful verification of the chemical and physical compatibility of the active substances and their respective solutions.[18]

Advantages of excipients:

- Improves the moisturizing properties (surfactants).
- Hydrocolloids can serve as emulsifiers, binders and gelling agents.
- Improves the organoleptic properties.
- It serves as a vehicle for formulation.
- Patient compliance.[4]

Excipients interactions:

Excipients are considered inert substances, they tend to react with the components of the drug, other excipients and also with the packaging system. Excipients can also contain various impurities that can cause the degradation of the active pharmaceutical ingredients in the formulation and thus affect storage and shelf life of the formulation.

The different types of interactions that an excipient may experience are referred to as

- Drug-excipient interactions
- Excipient-excipient interactions
- Interactions between container and excipient.[6]

These interactions are analyzed in detail below: -

- **Drug-excipient interaction:**

In dosage forms, the active pharmaceutical ingredients are in close contact with the excipients contained in large quantities. Excipients and drugs may have certain incompatibilities that result in drug-excipient interactions. Excipients affect the physio-chemical properties of the (API) active pharmaceutical ingredient, which can lead to the formation of molecular complexes, acceleration of chemical degradation, etc. Drug-excipient interactions are further classified as

A. Physical interactions
B. Chemical interactions
C. Biopharmaceutical interactions

A. Physical interactions

Interactions alter dissolution rate, dose uniformity, etc. Physio-chemical interactions do not imply changes that allow the components of the formulation to retain their molecular structure. Physical interactions are difficult to see. Physical interactions can be beneficial or detrimental to product performance depending on the application.

B. Chemical interactions

Pharmaceutical active ingredients and excipients react with each other and form unstable compounds. Several chemical interactions between drugs and excipients have been identified and reported in the literature. In general, chemical interactions are detrimental to formulation, so these types of interactions should generally be avoided.

C. Biopharmaceutical interactions

These are the interactions observed after administration of the drug. The interaction within the body is between the drug and body fluids and affects the rate of absorption.[19]

- **Excipient–excipient interactions:**

Excipient-excipient interactions are observed very rarely, those are of top significance in figuring excipients can be considered. An essential part of pharmaceuticals and are present in most formulations in a larger proportion in relation to the active pharmaceutical ingredient, as they make up the majority of the formulation. It is always necessary to select an excipient that fulfills the ideal properties for a particular excipient. The Stableness of the dosage forms. Excipient–excipient interactions may be unwanted in addition to some interactions are used with inside the formulations to get the favored product attributes. Various excipients go through such type of interactions. Some excipients are formulated as combination in order to reap favored impact with inside the product; Such excipient-excipient interactions are useful for enhancing functional performances with inside the formulation. Interactions are observed very rarely, they are of paramount importance to calculate that excipients can be considered an essential part of pharmaceutical products and are present in most formulations in a higher proportion relative to the active pharmaceutical ingredient, since they constitute the bulk of the formulation. It is always necessary to select an excipient that meets the ideal properties for a given excipient. The stability of dosage forms. Preferred product attributes. Various excipients are subject to this type of interaction. Some excipients are formulated as a combination to achieve a beneficial effect in the product; Such excipient-excipient interactions are useful to improve functional performance within the formulation.[20]

- **Container-excipients interaction:**

The packaging of pharmaceutical products is an essential part of the processing steps of product formulation, i.e., in pharmacy it is important for the industry that properly selected packaging preserves the integrity of the products, so packaging selection begins with a physical identification of the products and chemical properties. They are need for protection and their marketing requirements. The container thus chosen must be of an inert nature, it must protect the product from external environmental factors, etc. Some commonly used as packaging material such as glass, plastic, metal, rubber, etc. these containers and closures react to some degree with the drug as well as with the excipient and lead to harmful effects, changing the stability of the product.[21]

II. CONCLUSION

Excipients are non-API substances that have been adequately evaluated for safety and that are intentionally incorporated into the manufacturing process or included in a dosage form of finished pharmaceutical products to alter function. The real importance of ensuring quality and performance is often underestimated. In fact, the functionality of the excipient can help determine whether a drug is successful or not, unwanted side effects and even serious side effects or patient death. To avoid these undesirable results, it is therefore very important to choose the right excipient for the formulation and to ensure its quality. Therefore, excipient selection should focus on biopharmaceutical, pharmaceutical, processing and stabilization perspectives. The various interactions of excipients such as drug-excipient interactions, excipient-excipient interactions, and container-excipient interactions can render the excipient deleterious for use in the formulation. To avoid using incompatible excipients ensure excipients are safe and stable for use in formulation design. The excipient included in a formulation must be highly stable, safe and effective, and most importantly, perform as expected function in the formulation.

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