Role of Pharmaceutical Excipients in Solid Oral Dosage Forms (Tablets)

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Introduction

Excipients are classified as substances other than the Active Pharmaceutical Ingredients (APIs) used in the formulation of a Pharmaceutical product for long-term stabilization. Excipients are the constituents that are added in the formulation for the specific purposes. They play the integral role in the formulation of a stable medicinal product and its administration. Ideally, an excipients does not demonstrate any medicinal property but facilitates the absorption of the drug. Since excipients are an important part of the drug development process, it is necessary to choose the right excipients (or combination of excipients) for the drug in focus. Some of the major roles that excipients have are:

- Accelerating the process of drug delivery by aiding the manufacturing process
- Enhancing and safeguarding the stability of the drug
- Supporting the identification of the product while enhancing its safety
- Enhancing the effectiveness and delivery of the drug
- Maintaining the integrity of the drug product

Even though the excipients are inert substances in the drug product, they still may lead to adverse effects, if not used correctly. Therefore, identifying, analyzing and using the right excipients is necessary to ensure safe outcome of the drug.

Base requirements for an excipients

An excipients shall meet the following basic requirements to qualify the suitability needs:

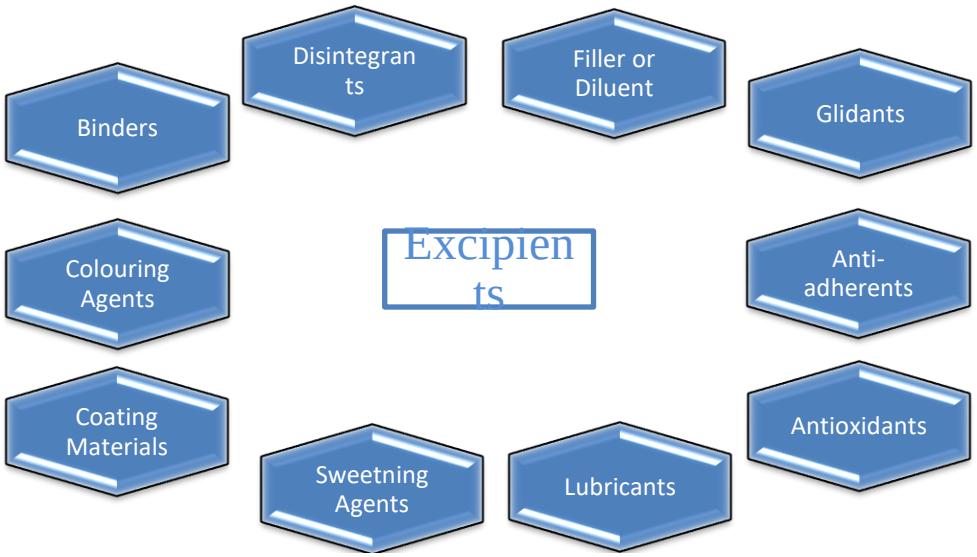
- Shall be Pharmacologically safe and inert
- Shall be compatible with the API, other components, and packaging material
- Shall support the shelf life of the pharmaceutical product
- Shall be cost effective
- Shall be taste, odor and color compliant
- Shall be GMP and Regulatory compliant

Functions of excipients

In many products, excipients make up the bulk of the total dosage form. Function of excipients include diluents or fillers, binders, disintegrates, lubricants, coloring agents and preservatives.

- Diluents or fillers are inert ingredients that can significantly affect the chemical and physical properties of the final tablet thus affecting the biopharmaceutical profile.
- For manufacturing technology functions binders, glidants, lubricants shall be used.
- For optimum or modified drug release, disintegrates, hydrophilic polymers, wetting agents, biodegradable polymers shall be used.
- Stability enhancers like antioxidants or UV absorbers shall be used.
- Unique identifiers like colorants can be used.
- For patient compliance flavors and sweeteners can be added.

Common excipients used in Oral Solid Dosage Forms (Tablets)



i) **Fillers or Diluents:** Essential excipients for tablets to increase the weight or volume. Also help in improvement of flowability and cohesion.
Examples of Fillers or Diluents- Starch, Lactose, Microcrystalline Cellulose (MCC), Dibasic calciumphosphate, Mannitol, Sucrose, Cellulose etc.

ii) **Binders or adhesives:** Necessary excipients for tablets to facilitate the agglomeration of powder into granules.
Examples of Binders or adhesives–Starch paste, Polyethylene-glycol, Gelatin, Tragacanth, Glucose, Cellulose derivatives, Polyvinylpyrrolidone(PVP)

iii) **Disintegrants:** Vital excipients for tablets to assist dosage form's breakup or disintegration into small fragments.
Examples of Disintegrants –Starch, Cross povidone, Polyvinylpyrrolidone, Carboxymethyl-cellulose (CMC), Sodium-starch-glycolate (SSG)

iv) **Lubricants:** Vital excipients for tablets to decrease the frictional forces between particles as well as particles and metal-contact surfaces.
Examples of Lubricants – Magnesium Stearate, Talc, Colloidal Silicon dioxide, Liquid paraffin, Propylene glycol(PEG), Stearic acid, Sodium Lauryl Sulfate (SLS) etc.

v) **Glidant:** To stimulate the flow properties of tablet granules or power materials.
Examples of Glidants – Talc, Corn starch, Colloidal silicon dioxide

vi) **Coloring agent:** to give a color or identification of the tablets as either pigment or coating materials.
Examples of Coloring agents - Red Ferric Oxide, Titanium Oxide, Lead Oxide, Copper Sulfate, and Carbon Black

vii) **Flavoring agents:** Used specifically in tablets such as chewable tablets or dispersible tablets or in coating solution for masking bad smell.
Examples of Flavoring agents – Lemon oil, Citric acid, Glycerol, Orange oil, Menthol, Vanillin etc.

viii) **Sweetener or Sweetening agent:** Especially used in the chewable, dispersible, sublingual tablet.
Examples of Sweetener or Sweetening agent–Dextrose, Sucrose, Lactose, Mannitol, Aspartame, Saccharine etc.

ix) **Surfactant:** Used for low solubility tablets to improve wetting and disaggregation of drug particles to get a rapid and improved dissolution.
Examples of Surfactants - Ethylene, Propylene oxide, Sorbitan esters, Ethoxylates, and Copolymers

x) **Release-Modifying Agents:** especially used to control drug release in modified-release formulations (prolonged-release or controlled-release tablet).
Example of Release-Modifying Agents - Hydroxypropyl Methylcellulose (HPMC), Xanthan Gum, Chitosan, Collagen, Hydroxy propyl cellulose (HPC) etc.

xi) **Coating materials:**
Film former which may be enteric or non-enteric, Solvent, Plasticizer, Colorant, Opaquing-Extender, Miscellaneous coating solution components, taste maskers, odor maskers.
Examples of Coating materials –
Polymers (immediate release)- Hydroxy Propyl Methyl Cellulose (HPMC), Hydroxy Propyl Cellulose (HPC), Ethyl Cellulose (EC), Methyl Cellulose, polyvinyl pyrrolidone, Eudragits
Polymers (Enteric Coating)– Cellulose acetate phthalate (CAP), Cellulose acetate trimellitate (CAT), Hydroxy Propyl Methyl Cellulose Acetate Succinate (HPMCAS), Hydroxy Propyl Methyl Cellulose phthalate (HPMCP), Polyvinyl acetate phthalate (PVAP), Shellac.
Polymers (Sustained Release) – Shellac, Zein, Ethyl cellulose
Plasticizers - Diethyl phthalate (DEP), Dibutyl phthalate (DBP), Dibutyl sebacate (DBS), Triethyl citrate (TEC), Acetyl triethyl citrate (ATEC), Acetyl tributyl citrate (ATBC), Tributyl citrate (TBC), and Triacetin (glyceryl triacetate; TA), castor oil.
Colorants –Water soluble dyes, FD&C lakes, D&C lakes, Inorganic pigments, Natural colorants.
Solvents/ Vehicles–Acetone, Methanol, Ethanol, Isopropyl Alcohol, Methylene chloride.

In most of the cases, it is not mandatory to use all the excipients for the tablets because some excipients providemore than one functions. For example, starch is a multi-functional excipient for tablets. It can serve as diluent, binder, and disintegrating agent. Likewise, the function of some excipients not necessary in some formulation. For example, a sweetener is necessary for chewable tablets, sublingual tablets, dispersible tablets, but not required for film-coated tablets.
Due to the considerable impact of excipients on the pharmaceutical formulations, selecting the suitable ones, is considered an important step in the drug manufacturing process that should be meticulously examined.
A precisely chosen excipient may reduce manufacturing expenditures by being multifunctional or may improve patient's experience by offering a better palatability.The API properties, process, and target formulation should also be considered, so that the excipients selected best suit the formulation, while they provide a balance between time efficiency, cost efficiency and anticipated product quality.Excipients play a vital role in the quality of dosage forms.

References:

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5) USP <1078>Good Manufacturing Practices for Bulk Pharmaceutical Excipients
6) Annex 5, WHO Technical Report Series 885, supplementary guidelines for the manufacture of pharmaceutical excipients.
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