AN OVERVIEW: EXCIPIENT USED IN TABLET DOSAGE FORM

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ABSTRACT

Excipients are all substances contained in a dosage form other than the active substances. Solvents used for the production of a dosage form but not contained in the final product are considered to be excipients. To produce a drug substance in a final dosage form requires pharmaceutical ingredients. The selection and testing of excipient in the design of drug dosage form present to the formulator the challenge of the predictive text. Many Formulators focussed their attention on the functionality of excipients to deliver a drug product of good quality. Excipients are manufactured from batch processes. This present review article focus on the role of excipient in solid dosage forms.

Keywords: Pharmaceutical Excipient, Solid dosage forms, Non-active ingredients.

INTRODUCTION

Pharmaceutical excipient are substances other than the pharmacologically active drug which are included in the manufacturing process or are contained in a finished pharmaceutical product dosage form. The word excipient is derived from the latin excipere, ‘meaning to except’, which is simply explained as ‘other than’. Pharmaceutical excipient are basically everything other than the active pharmaceutical ingredient. In the case of most dosage forms, the quantity of one or more excipient is greater than the quantity of the active pharmaceutical ingredients (APIs) present in them. Like APIs, excipient are also derived from natural sources, synthesized chemically, or prepared semi-synthetically starting from natural sourced material. They range from simple, usually well-characterized, organic or inorganic molecules to highly complex materials that are difficult to fully characterize. Excipients are included in drug delivery system to either aid the processing of the drug delivery system during its manufacture, protect, enhance stability, bioavailability, or patient acceptability, assist in product identification, or enhance any other attributes of the overall safety and effectiveness of drug delivery system during its storage or use (The International Pharmaceutical Excipient Council 1995). Many pharmaceutical scientists have focused their attention on the production of multifunctional excipient with enhanced performance to meet the need.
of formulation experts in term of cost of production, enhanced excipient functionality and quality of tablets. Excipients no longer maintain the initial concept of “inactive support” because of the influence they have both over biopharmaceutical aspects and technological factors. The desired activity, the excipients equivalent of the active ingredient’s efficacy, is called its functionality. The inherent property of an excipient is its functionality in the dosage form. In order to deliver a stable, uniform and effective drug product, it is essential to know the properties of the active ingredient alone and in combination with all other ingredients based on the requirements of the dosage form and process applied. Excipients are usually produced by batch processes; hence, there is a possibility of batch to batch variation from the same manufacturer[1].

**Functional use of excipient in tablet dosage form**: Excipient play a wide variety of functional roles in pharmaceutical dosage forms that include:

- Modulating solubility and bioavailability of active pharmaceutical ingredient.
- Increasing the stability of active ingredients in dosage form.
- Helping active ingredients to maintain preferred polymorphic forms.
- Acting as antioxidant, emulsifying agent, tablet binder, and tablet disintegrants.
- Modulating immunogenic responses of active ingredient.
- Maintaining the pH and osmolarity of the liquid formulations[2].

While selecting excipient for any formulation things should be considered wherever possible: keep the excipients to a minimum in number minimize the quantity of each excipients and multifunctional excipients may be given preference over unifunctional excipients. Fewer ingredients in the formulation are better for the following reasons:

- Excipients are not completely inert. Even commonly used excipients that are deemed to be pharmaceutically inactive and nontoxic may cause adverse reactions;
- Less ingredient variability to influence process and product consistency;
- Better economic efficiency in product manufacturing;
- Less probability of chemical or physical interaction between API and excipient and among excipients.
Approval of excipients: Under U.S law, an experiment, unlike an active drug substance has no regulatory status and may not be sold for use in food or approved drug unless it can be qualified through one or more of the three U.S. Food and Drug administration (FDA) approval mechanisms that are available for components used in food and or finished new drug dosage forms. These mechanisms are:

- Determination by FDA that the substance is “generally recognized as safe” (GRAS) pursuant to Title 21, U.S. Code of federal regulation, parts 182, 184, or 186 (21 CFR 182, 184 & 186);
- Approval of food additive petition as set forth in 21 CFR 171: or
- The excipient is referenced in, and part of, an approved new drug application (NDA) for a particular function in that specific product.

Excipients contained in (OTC) drug product subject to FDA monographs referenced in 21 CFR parts 331-358 must comply with the requirements in 21 CFR 330.1 (e) which reads as for “The product contain only suitable inactive ingredients which are safe in the amounts administered and do not interfere with the effectiveness of the preparation or suitable test or assay to determine if the product meets its professed standards of identity, quality, and purity. Colour may be used only in accordance with section 721 of the act[2].

Excipient present in a formulation must meet certain criteria which includes

- They must be nontoxic and physiologically inert.
- Cost must be low.
- Physically and chemically stable.
- Free from any unacceptable microbiological load.
- Colour compatible[7].

Classification of excipients in solid dosage forms

In addition to active ingredients, tablet contains a number of inert material known as additives or excipients. Different excipients are:

- Diluents & fillers
- Binders and adhesive
- Disintegrants
- Lubricants and glidants
- Colouring agent
- Flavouring agent
- Sweetening agents

**Role of each excipient in solid dosage forms:**

1. **Diluents & fillers:** Diluents are added where the quantity of active ingredient is small or difficult to compress. Where the amount of active ingredient is small, the overall tableting process are in large measure determined by the filler. Because of problems encountered with bioavailability of hydrophobic drugs of low water solubility, water – soluble diluent are used as fillers for these tablets. Diluents are used to provide better tablet properties such as cohesion & permit direct compression. Diluent used are Lactose, Spray dried lactose, Starch, Dextrose, Sucrose,Mannitol, Microcrystalline cellulose etc. A good filler must be inert, compatible with other components of the formulation, soluble, non-hygroscopic. Plant cellulose is a popular filler in tablets or capsules. Dibasic calcium phosphate is another popular tablet filler.

2. **Binders & adhesives:** Binder is added during granulation step to an API- filler mixture to ensure that granules and tablets can be formed with the required mechanical strength. Binders are usually starch, sugar, cellulose or modified cellulose such as microcrystalline cellulose, hydroxypropyl cellulose, lactose, sorbitol or mannitol. They are classified according to their applications:
   - Wet binders: These are dissolved in a solvent and used in a wet granulation process ex: gelatin, cellulose, cellulose derivatives, starch, sucrose, PVP.
   - Dry binders: These are added to the powder blend, either after a wet granulation step, or as a part of direct powder compression formula ex: Methylcellulose, cellulose, PVP[6, 8].

3. **Disintegrants:** Disintegrants expand and dissolve when wet causing the tablet to break apart in the digestive tract, releasing the active ingredients for absorption. Tablets must have sufficient strength to withstand the stresses of manufacturing processes, such as coating, packing, or distribution processes. To overcome the cohesive strength produced
by the compression process, and to break down the tablet into the primary particles as rapidly as possible, disintegrants are added to the tablet formulation. The commonly used disintegrants are: Starch USP (5-20% w/w), Starch 1500 (5-15% w/w), Microcrystalline cellulose (pH 101-102, 10-20% w/w), Ac-di-sol (1-3% w/w), Alginic acid (1-5% w/w) etc[6,8].

4. Lubricants & glidants: They are intended to reduce the friction during tablet ejection between walls of the tablet & die cavity ex. Mineral oil, Stearic acid, Talc. Lubricants are classified according to their water solubility i.e. water soluble and water insoluble. Selection of lubricant is depends partly on mode of administration, type of tablet, desired disintegration and dissolution properties. Water soluble lubricants are Boric acid, Sodium benzoate, Sodium oleate, Sodium lauryl sulphate, Sodium acetate & Water insoluble lubricants are Talc, Sterofex, Waxes, Stearic acid etc.

Glidants: - It is a substance that is added to a powder to improve its flow ability. A glidant will only work at a certain range of concentration. Above a certain concentration, the glidant will in fact function to inhibit flow ability. Ex of glidants include Magnesium stearate, Starch and Talc[5,6].

5. Colours, Flavours & Sweeteners: - Colours are used for product identification, production of more elegant product. Colours are added to improve the appearance of a formulation. Colour consistency is important as it allow easy identification of a medication. Colour used are Natural colours, FD&C and D&C dyes, lakes.

Flavours are used in chewable tablets or in mouth dissolving tablets. Flavours can be used to mask unpleasant tasting active ingredients and improve the likelihood that the patient will complete a course of medication. Flavouring may be natural (e.g. fruit extract) or artificial – a bitter product may use mint, cherry or anise.

Sweeteners are used in chewable tablets. Sweeteners are added to make the ingredient more palatable, especially in chewable tablets such as antacid or liquid like cough syrup. Various sugars are mannitol, saccharin, artificial sweeteners[8].

Preservatives: Antioxidants like vitamin A, vitamin C, retinylpalmitate and selenium, the amino acids cysteine and methionine. Synthetic preservatives like paraben, methyl paraben and propyl paraben.

Performance Characteristics of Excipients
Excipients can have profound effect on various aspect of the final dosage form. To make the final dosage forms with consistent quality, excipients should maintain the same performance qualification. Currently, all the excipients are characterized in pharmacopoeia by their chemical specification, instead of performance specification, mainly because of the difficulty in standardizing the performance criteria. The test of purity and identity described in pharmacopeia are generally very limited to their relevance to their formulation functionality (Banakar&Makoid, 1996). For example, excipients behave differently depending on the vendor to the extent that substitution from one source to the other is not possible. Since the same excipient may have very different physical properties, it is necessary to establish the performance standard of the basic properties such as flowability, binding ability, lubricity, disintegration property, etc. Physical properties such as particle size, roughness of the particle surface, density of the particles, compressibility, need to be standardized\(^{10}\).

**Search for New Excipients:**

- The growing popularity of the direct compression process and a demand for an ideal filler-binder that can substitute two or more excipient.
- Tableting machinery’s increasing speed capabilities, which require excipients to maintain good compressibility and low weight variation even at short dwell times.
- Shortcomings of existing excipients such as loss of compaction of microcrystalline cellulose (MCC) upon wet granulation, high moisture sensitivity, and poor die filling as a result of agglomerated.
- The ability to modulate the solubility, permeability, or stability of drug molecule.
- The growing performance expectations of excipients to address issues such as disintegration, dissolution and bioavailability\(^{11}\).

**CONCLUSION**

The success of any pharmaceutical excipient depends on quality, safety and functionality. There are large number of excipients which have been used in the solid dosage forms. Excipient possess some properties like disintegrating agent, binding agent, filler, sweeteners. The pharmacopoeias and international councils have spearhead some efforts to develop and harmonize the standards as well as to provide guidelines on good
manufacturing practices for excipients. Additional efforts are necessary to develop comprehensive and authoritative. The use of excipient is an excellent way to reduce time and cost in a well constructed formulation. Though considerable research has been done in recent years in the area of developing new excipients for tabletting. In summary, knowledge of excipient is a necessary prerequisite to the development of a dosage form that are stable and of good quality.

REFERENCES


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