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RESEARCH ARTICLE

CO-PROCESSED SUPERDISINTEGRANT A NOVEL APPROACH FOR REDUCING RISK IN DOSAGE FORM FORMULATION

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ABSTRACT

Several advantages offered by co-processed excipients such as production of synergism in functionality of individual components, reduction of company's regulatory concern because of absence of chemical change during co-processing and improvement in physico-chemical . The current review article is prepared to have a look over the recent development in excipient, co – processed excipients especially superdisintegrants and its composition & application for tablet manufacturing. With the ongoing demand of novel drug delivery, the Mouth dissolving tablet /sublingual /fast dissolving drug delivery system has become one of the mile stone of present research. There are many superdisintegrants, like polyplasdone, Sodium starch glycolate , kollidone CL, kollidone CLF, kollidone CL-SF, kollidone CL-M, starch 1500, etc. The search for newer disintegrating agent is ongoing and researcher are experimenting with multifunctional superdisintegrants due to its better disintegration, compact ability , mouth feel & flow property. Co-processed excipients especially superdisintegrants are reduce risk in early dosage form formulation due to its multifunctional property.

INTRODUCTION

According to "The International Pharmaceutical Excipients Council, 1995 " excipients is ''Substances, other than the active drug substance or finished dosage form, which have been appropriately evaluated for safety and are included in a drug delivery system to either aid the processing of the drug delivery system during its manufacture, protect, support, enhance stability, bioavailability, or patient acceptability, assist in product identification, or enhance any other attributes of the overall safety and effectiveness of the drug delivery system during storage or use''(1).

The US Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) defines, in the orange book, an oral disintegrating tablet as, "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue." At present, oral disintegrating tablets are the only quick-dissolving dosage form recognized by FDA and listed in the approved drug products with therapeutic equivalence evaluations (2-4).

These smaller tablets usually require disintegrants of much smaller particle size to guarantee content uniformity and to prevent the tablets from showing rough surfaces after storage.

Furthermore, in new drug delivery technologies such as oral dispersible tablets, fast disintegrants with very good mouth feeling are in strong demand. Based on these market trends, formulator / researcher will now require new disintegrants for their new applications.

Excipients balance the properties of the actives in fast-melting tablets. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives. The primary reason for lack of new chemical excipients is the relatively high cost involved in excipient discovery and development (5). Co-processed functional excipients offer a means to rapidly develop products for early human trials, while minimizing the risk to product quality.

In more recent years, several newer disintegrants have been developed, often called "superdisintegrants." These newer substances can be used at lower levels than conventionally used disintegrants (6). They have been used for a long time but have

certain disadvantages in terms of the amount that is needed to ensure disintegration. One particular disadvantage of disintegrants based on starch and of the cellulose derivatives is the increase of viscosity after disintegration. The first question is always related to the real effect of the disintegrant on the disintegration time (7) .

Superdisintegrants are used to improve the efficacy of solid dosage forms. This is achieved by decreasing the disintegration time which in turn enhances drug dissolution rate. Superdisintegrants are widely used in direct compression, wet granulation and capsule formulations. Superdisintegrants are generally used at a low concentration, typically 1-10% by weight relative to total weight of dosage unit (8) .

SELECTION OF SUPERDISINTEGRANT

Although the superdisintegrants primarily affects the rate of disintegration, when used at high levels it can also affect mouth feel, tablet hardness, and friability. Thus, several factors must be considered when selecting a superdisintegrants.

Disintegration : The disintegrant must quickly wick saliva into the tablet to generate the volume expansion and **Compact ability :** When manufacturing an Sublingual /Oral Mouth Dissolving Tablet (OMDT), it is desirable to have tablets with acceptable hardness at a given compression force to produce robust tablets that avoid the need to use specialized packaging while maximizing production speed. Thus, a more compactable disintegrant will produce stronger, less-friable tablets.

Mouth feel : To achieve patient compliance, MDTs must provide a palatable experience to the patient. Large particles can result in a gritty feeling in the mouth. Thus, small particles are preferred. If the tablet forms a gel-like consistency on contact with

The theory of disintegration of a tablet

Disintegrants are very hydrophilic → Spherical particles are uniformly distributed in the tablet → They swell during contact with water or other liquids → They significantly increase volume and disintegrate the tablet. In general, there is no perfect disintegrant. Disintegration is strongly dependent on the formulation of the tablet in terms of porosity, method of manufacture (wet or dry granulation) and the use of different actives and other excipients. Shown in table no. 1: Related research on Sublingual drug delivery system

water, however, it produces a gummy texture that many consumers find objectionable.

Flow : As with all direct compression tablet formulations, attaining good flow and content uniformity is important to achieving the required dosage per unit. In typical tablet formulations, superdisintegrants are used at 2–5 % weight of the tablet formulation. With OMDT formulations, disintegrant levels can be significantly higher.

MECHANISM OF ACTION OF SUPERDISINTEGRANT

By capillary action

By swelling

Because of heat of wetting

Due to release of gases

By enzymatic action

Due to disintegrating particle/particle repulsive forces

Due to deformation

FACTORS AFFECTING ACTION OF DISINTEGRANTS

Percentage of disintegrants present in the tablets.

Types of substances present in the tablets.

Combination of disintegrants.

Presence of surfactants.

Hardness of the tablets.

Nature of Drug substances.

Mixing and Screening.

TYPES OF SUPERDISINTEGRANT

Natural

Synthetic

Co-processed

Natural : These are various plant based material. Plant based material serve as an alternative to synthetic products because of following reasons is

Local accessibility

Eco-friendly

Bio-acceptable

Renewable source and low price as compared to synthetic products (27,28)

Shown in table no.3 literature Reviews On various Mucilages those are used as a Superdisintegrant (29-39)

SYNTHETIC

Advantages of Synthetic Super disintegrants

Effective in lower concentrations than starch

Less effect on compressibility and flow ability

More effective intragranularly

Limitations

Hygroscopic (may be a problem with moisture sensitive drugs)

Some are anionic and may cause some slight *in-vitro* binding with cationic drugs (not a problem *in-vivo*).

An acidic medium significantly reduces the liquid uptake rate and capacity of sodium starch glycol ate and croscarmellose sodium, but not crospovidone.

The degree of swelling of primojel1 (sodium starch glycol ate) and polyplasdone xl 101 (crospovidone) is minimized following wet granulation formulation. Finally, the medium ionic strength was found to have an adverse effect on the swelling capacity of croscarmellose (40-42) .

Table 3 shown Description And special feature of synthetic superdisintegrants (43-44)

CO-PROCESSED SUPER - DISINTEGRANTS

Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvement as well as masking the undesirable properties of individual. Co-processing excipients lead to the formulation of excipient granules with superior properties, compared with physical mixtures of components or individual components, like improved flow properties, absence of chemical changes, improved compressibility, better dilution potential, fill weight uniformity, and reduced lubricant sensitivity. Several co- processed superdisintegrants are commercially available: The use of co processing is a totally unexplored avenue in disintegrants. The widely used superdisintegrants are sodium starch glycolate, crospovidone, and croscarmellose sodium.

Hence, if a physical mixture of superdisintegrants is used in high-speed tableting, the problem of segregation of the disintegrants may be encountered. One of the reasons for preparing the co processed superdisintegrant was to avoid the problem of segregation. A blend of swelling and wicking types of excipient may also prove to be efficient because the medium (usually water) required for swelling will be brought into the tablet more easily if a wicking (hydrophilic) type of superdisintegrant is also present.

Table 5 : Description And Applications Of Co-Processed Excipients

CONCLUSION

The continued popularity of solid dosage forms create a radical change in tablet manufacturing due to the introduction of processes such as direct compression method and use of high-speed machines. The phenomenon of co-processed excipients is a field having vast scope for development of excipients with desirable property for direct compression as well as for specific

method and formulation. Excipients especially co- processed excipients play a vital role in the formulation of low weight solid dosage formulation. Excipients mixtures or co-processed excipients have yet to find their way into official monographs, which is one of the major obstacles to their success in the market place. Development of a number of new chemical entity rising day by day, which also increase the scope for further development and use of these excipients in future. Studies suggested that ease of availability of these co-processed excipients and its simplicity in the direct compression process developed more economical alternative in the preparation of oral drug delivery formulation than the patented techniques.

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