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INSIGHT IN TO USE OF CO PROCESS EXCIPIENTS IN ORAL DISINTEGRATING TABLETS-A REVIEW

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Abstract:
Fast Disintegrating tablets have started gaining popularity and acceptance as new drug delivery systems, because t hey are easy to administer. Recent development in fast disintegrating technology mainly works to improve the disint egration quality of these delicate dosage forms without affecting their integrity. Oral disintegrating dosage form have facing many challenges which can be overcome by upcoming newly emerging approach of use of coprocess adujants in it. The developments or improvements in pharmaceutical process and equipments, particularly increase in production rates at low cost, lead to the need for coprocess excipients excipients. This review highlight on various factors aspects of the oral disintegrating tablets with special emphasis on use of in it.coprocess excipients,
Keywords: *Coprocess,Fast disintegrating tablets,need, Diszntegration time, Super- Disintegrants etc.*

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INTRODUCTION:

The oral fastdisintegrating tablets is also known as fa st dissolve, rapid dissolve, rapid melt and quick disint egrating tablets. It is also know as rapid dissolve, rapid melt and quick disintegrating tab lets. However, the function and concept of all these d osage forms are similar. By definition, a solid dosage form that dissolves or disintegrates quickly in the ora l cavity, resulting in solution or suspension without th e need for the ministration of water, is known as an oral fast-dispersing dosage form. .According to Euro pean Pharmacopoeia, the ODT should disperse/disint egrate in less than three minutes. Difficulty in swallo wing (dysphagia) is common among all age groups[1 -2].

NEED TO FORMULATE MOUTH DISSOLVIN G TABLETS

1. The need for noninvasive drug delivery systems continues due to patient's poor acceptance and compliance with existing delivery regimes, limited market size for drug companies and drug uses coupled with high cost of disease management MDT is one such dosage form which is useful for Geriatric patients mainly suffering from conditions like hand tremors and dysphasia.
2. Pediatric patients who are unable to swallow easily because their central nervous system and interal muscles are not developed completely.
3. Traveling patients suffering from motion sickness and diarrhea that do not have easy access to water. Especially cancer patients after taking their chemotherapy Ideal properties of FDT5
4. Patients with persistent nausea for a long period of time are unable to swallow. [3-4].

IDEAL PROPERTIES OF ODT

1. Require no water for oral administration, yet dissolve /disperse/ disintegrate in mouth in a matter of seconds.
2. Have a pleasing mouth feel.
3.Have an acceptable taste masking property.
4. Be harder and less friable
5.Leave minimal or no residue in mouth after administration.
6. Exhibit low sensitivity [5].

CHALLENGES IN FORMULATION OF MOUT H DISSOLVING TABLETS

I.Mechanical strength and disintegration time MDTs are formulated to obtain disintegration time usually le ss than a minute.
While doing so, maintaining a good mechanical stren gth is a prime challenge. Many MDTs are fragile and there are many chances that such fragile tablet will break during packing, transport or handling by the patients. Tablets based on technologies like Zydis need special type of packaging. It is very natural that increasing the mechanical strength will delay the disintegration time.

ii.Taste masking- many drugs are bitter in taste. A tablet of bitter drug dissolving/ disintegration in mouth will seriously affect patient compliance and acceptance for the dosage form. So effective taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity.

iii) Mouth feel- MDT should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the MDT should be as small as possible. MDT should leave minimal or n o residue in mouth after oral administration. Moreover addition of flavours and cooling agents like menthol improve the mouth feel.

iv) Sensitivity to environmental conditions- MDT generally should exhibit low sensitivity to environme nt conditions such as humidity and temperature as most of the materials used in a MDT are meant to dissolve in minimum quantity of water.

v) Cost- The technology used for a MDT should be acceptable cost affordable to patient

Above challenges related to ODT can be solved by using coprocess excipients in manufacturing of ODT. [6-8].

PHARMACEUTICAL/ADDITIVES/NECESSITI ES/ADJUANTS/PHARMA AID /EXCIPIENTS

Pharmaceutical excipients are any substance other than the active drug product which has been appropriately evaluated for safety and is included in a drug delivery system to either aid processing of the system during manufacture or protect, support or enhance stability, bioavailability, or patient acceptability or assist in product identification or enhance any other attribute of the overall safety and effectiveness of the drug product during storage and use. According to International Pharmaceutical Excipient Council (IPEC), co-processed excipient is "a combination of two or more compendial or non-compendial excipients designed to physically modify their properties in a manner not achievable by simple physical mixing, and without significant chemical change. [9].

TYPES OF EXCIPIENTS

Generally types of excipients were classified into 4 types which were given below.

1.Single entity excipients.
2.Mixtures or blends of multiple excipients.
3.Novel excipients or new chemical entities.

4.Coprocessed excipients. [10-11].

CO-PROCESSED EXCIPIENTS.

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 individual4. Co-processing excipients leads to the formulation of excipient granules with superior properties compared with physical mixtures of components or individual components. The resulting engineered excipients are commonly known as "coprocessed," "high functionality," "multifunctional,"
"high functionality," "performance" excipients [12].

NEED OF CO-PROCESS EXCIPIENTS

1.**Effective use of existing excipients:** Identification of new applications for the existing excipients is a relatively inexpensive and less time involving process as compared to an entirely new development.

2. Excipients with desirable properties: There are a number of existing excipients which lack some of the desirable properties required in some formulations.

3. **Drugs developed by genetic engineering**: As new drugs are being developed, their compatibility with the existing excipients sometimes poses a big question. Hence, new excipients will be necessary to overcome these problems.

4. Advances in production process and equipment: The developments or improvements in pharmaceutical process and equipments, particularly increase in production rates at low cost, lead to the need for new excipients..

5.Patient or subject compliance: Some excipients, which are used now- a-days, are unacceptable for the reasons of patient safety and comfort. Lactose intolerance occurs in persons, who are deficient in the enzyme lactase, leading to abdominal cramps, diarrhea, distension and flatulence.

6. Specialized drug delivery systems: The development of novel or specialized drug delivery systems requires the use of special excipients. Metered dose inhalation devices require excipients of a particular size grade and development of oral strip preparations. [13-14].

CO-PROCESSING EXCIPIENT INVOLVES THE FOLLOWING STEPS:

1. Choice of excipients which should be combined
2. Choice of proportions of chosen excipients
3. Assessing the particle size required for co-processing.
4. Selecting a suitable process of drying such as spray or flash drying
5. Development of controlled production parameters to avoid batch to Batch variations. [15-16].

SIGNIFICANCE OF THE CO-PROCESSED EXCIPIENT

1. Enhancement in flow properties: Due to processing of excipients there is marked enhancement in flow property take place.

Controlled optimal particle size and particle-size distribution ensures superior flow properties of co-processed excipients without the need to add glidants

2.Absence of chemical change: Many detailed studies of an excipient‟s chemical properties after co processing have proven that these excipients do not show any chemical change. This absence of chemical change helps reduce company‟s regulatory concerns during the development phase.

3. Better dilution potential: Dilution potential is the ability of the excipient to retain its compressibility even when diluted with another material.Most active drug substances are poorly compressible, and as a result, excipients must have better compressibility properties to retain good compaction even when diluted with a poorly compressible agent. Cellactose is shown to have a higher dilution potential than a physical mixture of its constituent excipients.

4.Fill weight variation: In general, materials for direct compression tend to show high fill-weight variations as a result of poor flow properties, but coprocessed excipients, when compared with simple mixtures or parent materials, have been shown to have fewer fill-weight variation problems.

5.Reduced lubricant sensitivity: Most coprocessed products consist of a relatively large amount of brittle material such as lactose monohydrate. up the lubricant network.

6.Improved compressibility: Co-processed excipients like talc, Lactose have been used mainly in direct-compression tableting because in this process there is a net increase in the flow properties and compressibility profiles and the excipient formed is a filler–binder. 4.Better dilution potential: [17-19].

LIMITATIONS CO-PROCESSED EXCIPIENTS

1.Fixed ratio Major limitation of co-processed excipient mixture is that the ratio of the excipients in a mixture is fixed and in developing a new formulation, a fixed ratio of the excipients may not be an optimum choice for the API and the dose per tablet under development.

2.High cost Directly compressible co processed excipients are the specialized products which are produced by patented processes like spray drying, fluid bed drying, roller drying etc. Hence, these

products are relatively costly than their respective raw materials from which they are made.
3.Dilution potential up to 40% Most of the directly compressible co-processed excipients have a capacity to accommodate up to 40% of the poorly compressible active ingredients.
4.Lack of reworkability for spray dried co-processed excipients The original spherical nature of the excipient particles is lost if it is reworked hence loss of its intrinsic property and the increase in disintegration and dissolution profiles.
5. Lack of Pharmacopoeial acceptance Co-processed adjuvant lacks the official acceptance in pharmacopoeia. [20].

METHODS OF COPROCESSING

1) Spray Drying
2) Solvent Evaporation
3) Crystallization
4) Melt Extrusion
5) Granulation/Agglomeration [21].

EVALUATION OF MULTIFUNCTIONAL CO-PROCESSED EXCIPIENTS

1.Bulk density, Tapped density, True density, Hausner's ratio, Carr's index and angle of repose These parameters can be determined by USP method
2.Porosity Total intra-particle porosity, pore area, and pore size distribution are determined using a mercury porosimeter
3. Particle sizes analysis Mean particle size of co-processed excipient is analyzed by sieve analysis method
4. Percentage fines The percentage fine is defined as the percentage of the sample passed through a 200 mesh (74 mm) sieve. The sample is agitated on a sieve shaker on a 200 mesh for 5 min for finding percentage fines .
5. Morphology study Scanning electron microscopy is used to study morphology (Shapes, surface, etc) of co-processed excipients. SEM technology helps to understand adsorption or deposition of one excipient on second
6.Equilibrium moisture sorption The moisture sorption isotherm is determined by the gravimetric method
7.Loss on drying A sample of co-processed excipient is spread in a Petri dish, and the dish is placed in hot air oven at 100 °C for 3 hr. The percentage decrease in weight is noted to calculate loss on drying as per equation.
8.Compatibility of co-processed excipient The sample is compressed in a hydraulic press at compression forces of 0.5, 1.0, 1.5, 2.0 and 3.0 tons, using flat face punches. The hardness of each compact is measured using a hardness tester.
9.Heckel's plot The directly compressible adjuvant should exhibit good pressure- volume profile. The sample is compressed in a hydraulic press using and matching die at pressures of 1, 2, 3, 4, 5 and 6 tons for 1 min. [22].

EXCIPIENTS EXAMPLES OF CO PROCESSED DIRECTLY COMPRESSIBLE

Lactose, 3.2% Kollidon 30, Kollidon CL Calcium carbonate, Sorbitol Microcrystalline cellulose, Guar gum,starch ,pvp,crosspovidone,sodium starch glycolate, mannitol, Gellan Gum, Alginates, Indion 414. Ethyl cellulose, Methyl cellulose, HPMC, Sodium CMC, Cyclodextrin from starch [23].

FUTURE PROSPECTIVE

Natural polysaccharides are treated with water and co grinded further with Mannitol which exhibit super disintegration property. Growing demand of functional excipients, patent cliffs, increasing the demand of generics, and the emergence of new excipients in the market are the major factors driving the growth of the pharmaceutical excipients market.

CONCLUSION:

Fast Disintegrating tablets have started gaining popularity and acceptance as new drug delivery systems, because they are easy to administer. There are many challenges are present in development of oral disintegrating tablets. The developments or improvements in pharmaceutical process and equipments, particularly increase in production rates at low cost, lead to the need for coprocess excipients excipients..The Co-processing is the most widely explored method for the preparation of directly compressible adjuvants because it is cost effective and can be prepared in-house based on the functionality required
All coprocessed and modified excipients are playing very important role in the development of easy dosage form. Compared with existing excipients, the

improved physical, mechanical, and chemical properties of such excipients have helped in solving formulation problems such as flowability, compressibility, hygroscopicity, palatability, dissolu-tion, disintegration, sticking, and dust generation.Their is need to develop new specially designed equipment for evaluations of coprocess excipients& Coprocessed excipients have yet to find their way into official monographs, also we can explore coprocessed excipients in various drug deliveries.

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