

**A REVIEW ON “NEW GENERATION EXCIPIENTS OF  
MULTIFUNCTIONAL NOVAL DOSAGE FORM”**

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Article Received on  
02 July 2017,

Revised on 23 July 2017,  
Accepted on 12 August 2017

DOI: 10.20959/wjpr201710-9174

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**ABSTRACT**

In a Present Study of Pharmacy Co-processing is the way that new excipients approaching to the market without undergoing accurate safety testing of completely new chemical. It can be defined as combining two or more established excipients by an appropriate process. Co processing of excipients could lead to formation of excipients with greater properties compared to simple physical mixtures of their components. The main aim of co processing is to obtain product with an added value related to the ratio of its functionality price.

**KEYWORDS:** Co- Processed Excipients, Development, conventional excipients.

**INTRODUCTION**

Tablets are the most preferred dosage form of pharmaceutical professionals because they can be accurately dosed and provide good patient compliance. The ease of manufacturing, convenience in administration, accurate dosing, and stability compared to oral liquids, tamper proofness compared to capsules, Safe compared to parental dosage forms makes it a popular and versatile dosage form and can be produced at a relatively low cost. Tablet manufacturing techniques have undergone rapid change and development over last decades with the emergence of novel excipients, to justify the high rise in new drug development and high industrial output demand. new combinations of existing excipients are an interesting option for improving excipient functionality and to improve the tableting performance. This in turn

has lead to an increased research and detailed study for developing newer excipients by co processing technique which will improve the tablet manufacturing process. This review highlights the various co processed excipients which will be used to improve the tableting performance. A co-processed excipient is a combination of two or more compendia or non-compendia excipients designed to physically modify their properties in a manner not achievable by simple physical mixing, and without significant chemical change. Coprocessing offers many advantages such as improvising flow properties by controlled optimal particle size and particle-size distribution, compressibility, dilution potential, fill weight variation, flow properties, lubricant sensitivity. It can also improve the tablet hardness and decreases the disintegration time. The actual process of developing a co-processed excipient involves following steps such as identifying the group of excipients to be co-processed by studying the material characteristics and functionality requirements, selecting the proportions of various excipients assessing the particle size required for coprocessing, selecting a suitable process of drying and optimizing the process.

### **Advantages of Co-Processed Excipient**

The multifold advantages offered by co-processed excipient were given below.

- ☐ Provide a single excipient with multiple functionalities. Removal of undesirable properties.
- ☐ Overcome the limitation of existing excipient.
- ☐ Improvement of organoleptic properties.
- ☐ Production of synergism in functionality of individual components.
- ☐ Reduction of company's regulatory concern because of absence of chemical change during co-processing.
- ☐ Improvement in physico-chemical properties has expanded their use in the pharmaceutical industry.

### **Types of Excipient**

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

- ☐ Single entity excipient.
- ☐ Mixtures or blends of multiple excipient.
- ☐ Novel excipient or new chemical entities.
- ☐ Co processed excipient.

**Principle Involved In Co processing**

Solid substances are characterized by three levels of solid state: the molecular, particle and bulk level. These levels are closely linked to one another, with the changes in one level reflecting in another level. The molecular level comprises the arrangement of individual molecules in the crystal lattice and includes phenomena such as polymorphism, pseudo-polymorphism and the amorphous state. Particle level comprises individual particle properties such as shape, size, surface area and porosity. The bulk level is composed of an ensemble of particles and properties such as flow ability, compressibility and dilution potential, which are critical factors in the performance of excipient. Figure 1 shows the various levels of solid state and how a change at one level affects the other levels. This interdependency among the levels provides the scientific framework for the development of new grades of existing excipient and new combinations of existing excipient. The fundamental solid-state properties of the particles such as morphology, particle size, shape, surface area, porosity and density influence excipient functionalities such as flow ability, compact ability, dilution potential, disintegration potential, and lubricating potential. Hence, the creation of a new excipient must begin with a particle design that is suited to deliver the desired functionalities. However, particle engineering of a single excipient can provide only a limited quantum of functionality improvement. A much broader platform for the manipulation of excipient functionality is provided by co processing or particle engineering two or more existing excipient. Co processing is based on the novel concept of two or more excipient interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvements as well as masking the undesirable properties of individual excipient. The availability of a large number of excipient for co processing ensures numerous possibilities to produce tailor-made “designer excipients” to address specific functionality requirements.

**Methods of co processing were listed below**

- 1. Spray Drying**
- 2. Solvent Evaporation**
- 3. Crystallization**
- 4. Melt Extrusion**
- 5. Granulation/Agglomeration**

### 1. Spray Drying

This technique enables the transformation of feed from a fluid state into dried particulate form by spraying the feed into a hot drying medium. It is a continuous particle processing drying operation. The feed can be a solution, suspension, dispersion or emulsion. The dried product can be in the form of powders, granules or agglomerates depending upon the physical and chemical properties of the feed, the dryer design and final powder properties desired.

### 2. Solvent Evaporation

Solvent evaporation process involves the use of liquid manufacturing vehicle. The coating excipient is dissolved in a volatile solvent, which is immiscible with the liquid manufacturing vehicle phase. A core excipient material to be microencapsulated is dissolved or dispersed in the coating polymer solution. With agitation, the core coating material mixture is dispersed in the liquid manufacturing vehicle phase to obtain the appropriate size microcapsule. The mixture is then heated (if necessary) to evaporate the solvent. Once all the solvent is evaporated, the liquid vehicle temperature is reduced to ambient temperature (if required) with continued agitation. At this stage, the microcapsules can be used in suspension form, coated on to substrates or isolated as powders. The core materials may be either water - soluble or water - insoluble materials.

### 3. Crystallization

Crystallization is the (natural or artificial) process of formation of solid crystals precipitating from a solution, melt or more rarely deposited directly from a gas. Crystallization is also a chemical solid-liquid separation technique, in which mass transfer of a solute from the liquid solution to a pure solid crystalline phase occurs. Procedure: For crystallization to occur from a solution it must be supersaturated. This means that the solution has to contain more solute entities (molecules or ions) dissolved than it would contain under the equilibrium (saturated solution). This can be achieved by various methods, with (1) solution cooling, (2) addition of a second solvent to reduce the solubility of the solute (technique known as antisolvent or drown-out), (3) chemical reaction and (4) change in pH being the most common methods used in industrial practice. 4. Melt extrusion Melt extrusion is a process of formation of small beads, pellets from the molten mass which is extruded through extruder.

### Fast dissolving tablet

Drug delivery system is an efficient device for gaining market price, extending product life cycles and creating opportunities. Oral delivery is the gold standard in the pharmaceutical

industry where it is safest, most convenient and most useful method of drug delivery having the major patient fulfillment.<sup>[127]</sup> Some tablets are intended to melt in saliva remarkably quickly, within a few seconds and these are fast-dissolving tablets.

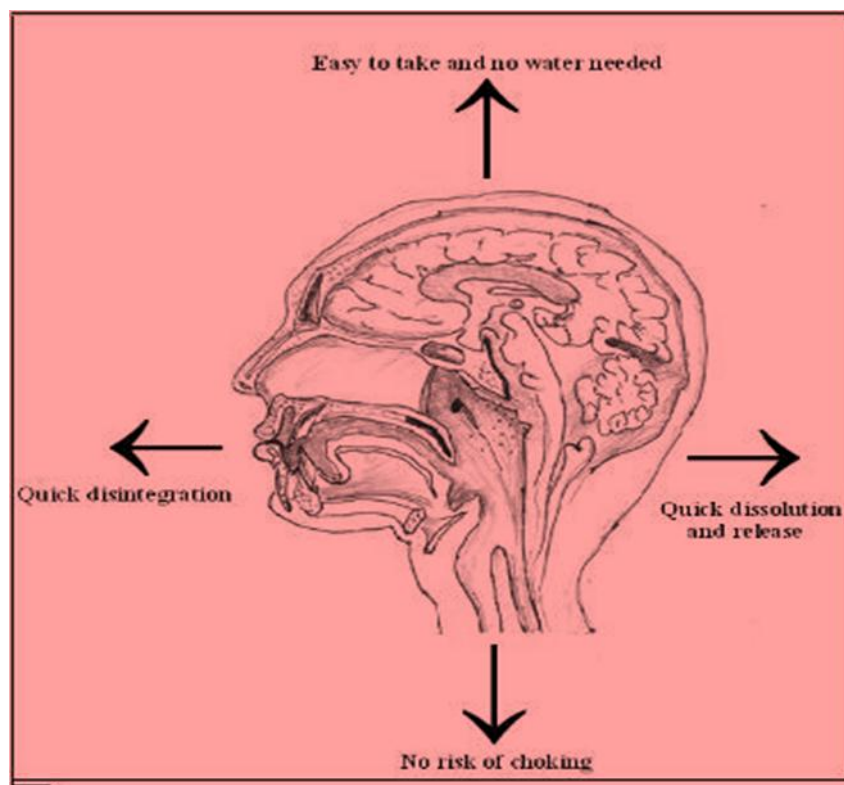
Fast dissolving tablets dissolve quickly in the mouth saliva without the of water. Others contain agents to improve the rate of disintegration in the oral cavity and are more properly termed fast disintegrating tablets, as they may take up to a minute to completely fall to pieces.

United States Food and drug administration (FDA) defined fast dissolving tablet (FDT) is a solid dosage form containing active ingredient which disintegrate speedily usually within a stuff of seconds when placed upon the tongue so called mouth-dissolving tablets, melt-in oral cavity tablets, rapimelts, porous tablets, etc.<sup>[129]</sup> This tablet format is designed to allow administration of an by word of mouth solid dosage form in the absence of water.

Fast dissolving tablets have been formulated for bedridden and geriatric patients and for active patients who are busy and traveling and may not have access to water. Such formulations provide an opportunity for product line extension in the many old persons who have difficulties in taking conventional oral dosage forms because of hand tremors and dysphagia. Swallow problems also are common in young individuals because of their undersized muscular and nervous systems. In some cases such as progress sudden episodes of allergic attack or coughing, and an unavailability of water, swallow conventional tablets may be difficult.

Children and elderly have difficulty in swallow unit dosage forms and so unable to take medicine as prescribed. Almost half of the population is affect by such problem, resulting in the high prevalence of noncompliance and ineffective therapy. Most pharmaceutical forms for oral administration are formulated for direct drinking, chewing, or for prior scattering and/or dissolution in water; some of them are immersed in the mouth (sublingual or buccal tablets).

To prevent the problems associated with regular dosage forms, verbally fast disintegrating tablets have been developed, which come together hardness, dosage uniformity, stability and other parameters, with extremely ease administration, since no water is required for swallowing the tablets and they are thus suitable for old, pediatric and traveling patients.



**Fig; 1 Mechanism of action FDT.**

### 1.1 Advantages of oral drug delivery system

1. The oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, short cost therapy, self medication and ease of administration leading to high level of patient requirement.<sup>[127]</sup>
2. The most well-liked dosage forms are being conventional tablets and hard gelatin capsules. One important problem of such dosage forms is difficulty in swallow for many patients; almost half of the population is affect by such problem. Hence they do not fulfill with prescription, which results in high occurrence of non-compliance and unsuccessful therapy.
3. Newly fast disintegrating drug delivery systems have started in advance popularity and acceptance as new drug delivery systems, because they are easy to administer and get better patient fulfillment.[Bandari S, Mittapalli RK].
4. In several cases such as action sickness, sudden episodes of allergic attacks or coughing and unavailability of water, swallowing conventional tablets may be difficult. Particularly the complexity is experienced by pediatric and elderly patients. To overcome such problems, fast disintegrating tablets have emerged as an alternative dosage forms.<sup>[130]</sup>

5. Current advances in novel systems (NDDS) aim for attractive the safety of a drug molecule while maintaining its therapeutic efficacy so as to attain better patient fulfillment.<sup>[127]</sup>

### 1.2 Advantages of fast dissolving tablet<sup>[128]</sup>

- ❖ Ease of swallowing: Dysphagic population constitute 35% of the general population since this disorder is associated with a number of medical condition such as stroke Parkinson's disease, AIDS, head and other neurological disorder.
- ❖ No water needed: These fast dissolve dosage forms do not need water for swallowing unlike conventional dosage form this is very convenient for patients who are travelling or do not have immediate access to water.
- ❖ Superior taste: most fast dissolve dosage form contains taste masked active ingredient usually sweetening agent and a flavor.
- ❖ Accurate dose: The fast dissolve dosage forms have the needed advantages of convenience and accurate dosing as compared to liquids.
- ❖ More rapid drug absorption through pre-gastric absorption form the mouth pharynx and esophagus.
- ❖ Quick drug therapy involvement is possible.
- ❖ Novel business opportunities like product differentiations line extension and life cycle management exclusivity of product promotion.

**Table 1: Various Therapeutic areas in which the fast dissolve dosage form are most applicable.**

Target Population	Therapeutic Areas
Pediatric	Antibiotics Anti-asthmatics Cough/Cold/Allergy Analgesic/Antipyretics
Adult and Elderly	Parkinson's Cough/Cold/Allergy Anti-migraine Alzheimer's Anti- emetics Cancer Diabetics AIDS Gastric Relief Psychotherapeutics Cardiovascular Analgesic/NSAIDs



### 1.3 Characteristics of an ideal orally disintegrating drug delivery system.

Orally disintegrating drug delivery system should possess following characteristics.

It should

- ❖ Require no water for oral administration.
- ❖ Dissolve / melt away/ disintegrate in mouth in a matter of seconds.
- ❖ Have a pleasing mouth sense and taste masking.
- ❖ Less friable and have sufficient hardness.
- ❖ Leave minimal in mouth after administration.
- ❖ Manufacturing using conventional manufacturing method.

### 1.4 Benefits of fast dissolving tablets are as follows.

- ✓ Administer without water, everywhere, any time.
- ✓ Easy for old patients, who experience difficulty in swallowing
- ✓ Beneficial for the other groups that may experience problems using conventional oral dosage form, due to being mentally ill, the developmentally immobilize and the patients who are uncooperative.
- ✓ Useful in motion sickness, sudden episodes of allergic attack or coughing, where an ultra rapid beginning of action required.
- ✓ An improved bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to fast disintegration and dissolution of these tablets.
- ✓ Stability for longer duration of time, since until it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

### Superdisintegrants

- ❖ In current years, several newer agents have been developed known as “Superdisintegrants”. A superdisintegrant is an excipient, which is added to tablet or capsule blend to aid in the disintegration of the compacted mass, when put into a fluid environment.
- ❖ This is especially important for immediate release product where quick release of the product is required.
- ❖ These newer substances are more efficient at lower concentrations with greater disintegrating efficiency and mechanical strength. The use of superdisintegrants is the basic approach in the progress of fast disintegrating tablets (FDTs).



- ❖ Superdisintegrants play a major responsibility in the dissolution and disintegration of the tablets. It is essential to choose an optimum concentration of superdisintegrants so as to ensure quick disintegration and high dissolution rates of tablets.
- ❖ Superdisintegrants provide rapid disintegration due to joint effect of swelling and water absorption by the formulation.
- ❖ Due to bulge of superdisintegrants, the wetted surface of the carrier increases, this promotes the wettability and dispersibility of the system, thus attractive the disintegration and dissolution.
- ❖ The best concentration of the superdisintegrant can be selected according to the decisive concentration of the disintegrant. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant, whereas higher than this concentration the disintegration time remains almost constant or even increases.

## CONCLUSION

Coprocessed excipients have yet to find their way into official monographs, which is one of the major obstacles to their success in the marketplace. The success of any pharmaceutical coprocessed excipient will depend on quality, safety and functionality. There is an increase in use of coprocessed excipients due to the improvement of functionality by overcoming the limitations with the single excipient. In day to day raising in development of new chemical entities, there is a huge scope for the development of coprocessed excipients. Development of new excipient requires safety evaluation which is expensive and time consuming. Instead of developing new excipient, coprocessing of existed approved excipients will reduce the safety evaluation. IPEC New Excipient Safety Evaluation Procedure should be used for co-processed excipients to reduce regulatory uncertainties.

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