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MULTIFUNCTIONAL EXCIPIENTS FOR SOLID DOSAGE FORM

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ABSTRACT

Drug products not only contain "actives" that confer the intended therapeutic benefits such as pain relief or act on particular part of the body, but contain other materials that are also "functional" with respect to the drug product. These are known as excipients and specific functionality which they confer to a particular product is independent upon the process used to add the excipient to the formulation and its exact location within the final dosage form. Development of new excipient entities and their evaluation is a costly procedure; modification of existing excipients is very easy, more economical and less time consuming. The development of excipients that are capable of fulfilling multifunctional roles such as enhancing drug bioavailability and drug stability as well as controlling the release of the drug according to the therapeutic needs is one of the most important prerequisites for further progress in the design of novel drug delivery systems. The main focus of this article is on multifunctional excipients that perform multiple functions in pharmaceutical formulations. Though there has been a Number of dosage forms available, solid dosage form remains the most widely preferred form.Direct compression method is a highly preferable method of tablet production because of its simplicity and cost effectiveness.

KEYWORDS: Direct compression, Co-processing, Multifunctional excipients.

INTRODUCTION

Solid medicaments may be administered orally as powders, pills, cachets, capsules or tablets. These dosage forms contain a quantity of drug which is given as a single unit and they are known collectively as solid unit dosage forms .Though many dosage forms are available

today, Tablets and capsules are the most preferred dosage forms of pharmaceutical scientists and clinicians because they can be accurately dosed and provide good patient compliance, they are easy for companies to manufacture, and they can be produced at a relatively low cost. This popularity of tablets coupled with an increased understanding of the physics of compression and of manufacturing process variables have matured the manufacture of tablets as a science in its own right.[1] Tablets are manufactured primarily by either granulation compression or direct compression. The latter involves the compression of a dry blend of powders that comprises drugs and various excipients. The simplicity and cost effectiveness of the direct-compression process have positioned direct compression as an attractive alternative to traditional granulation technologies. In a survey conducted in 1992 by Shangraw et al. concerning the process preferred by pharmaceutical manufacturers, nearly 41.5% indicated that direct compression was their process of choice, and 41.5% preferred both wet granulation and direct compression.[2] Only 17.2% indicated that they did not prefer direct compression as a tableting method. Most formulations (70–80%) contain excipients at a higher concentration than the active drug.[5] Consequently, the excipients contribute significantly to a formulation's functionality and processability. Now a days there has been a drift in the thought process among formulators, as formulas with a minimum number of components are finalized to prevent scale-up issues. Moreover, new tablet formats like Orally Disintegrating tablets (ODTs) are gaining popularity these days as they carry the promise of extending the market lifespan of the drug. The recent interest in demanding manufacturing processes and the focus on alternative delivery systems has led to increased demand of a range of specialty excipients collectively known as multifunctional excipients. Multifunctional excipients are a class of excipients that includes pre-processed and co-processed excipients that provide added functionalities to the formulation (for example, Silicified Micro-Crystalline Cellulose, which is a processed combination of MCC and colloidal silicon dioxide). These functionalities include flowability, compressibility, particle size distribution, shape, porosity, etc. The term multifunctional excipient is also extended to products that serve multiple roles in the formulation (for example, Ludipress, which is co-processed product containing lactose, Kollidon and Kollidon-CL, serves the role of DC diluent with binder and disintegrant properties).

Ways of achieving multifunctionality

Multifunctional excipients can be obtained by developing a new excipient (such as cross-linked polymers) or by developing new grades of existing excipients; modification in the

processing leads to changes in the particle size distribution, particle shape and morphology and porosity. Traditionally, industry stays away from developing a new excipient altogether, due to the cost involved and problems faced in getting regulatory approvals. Changing the manufacturing process of an excipient along with addition of minor amount of another known excipient results in a product that has enhanced physical characteristics leading to added functionality. Combining known excipients at sub-particle level (also known as co-processing) leads to excipients with modified properties like enhanced surface area, increased porosity, enhanced compressibility, good flow ability, etc. Co-processed excipients are also suitable for direct compression and thus help in simplification of tablet manufacturing. The reason for enhanced compressibility can be drawn from the fact that most of the co-processed excipients principally consists of a large amount of brittle material and a smaller amount of plastic material. Thus, a co-processed material displays the property, which is a combination of plasticity as well as brittleness.

There are also instances where pre-processing can lead to product with added functionality (for example, preprocessed partially pregelatinized starches result in better control of particle size distribution, which ultimately leads to lesser dust generation during tabletting and improvised flow of material). However, achieving multifunctionality through preprocessing is not too popular, as the functionality of the excipient can be improved only to a certain extent because of limited number of modifications possible.

Table: 1 Methods of preparing directly compressible excipients.

Method	Advantages and limitations	Examples
Chemical modification	Relatively expensive , Requires toxicological data, Time consuming	Ethyl cellulose, Methyl cellulose, Hydroxypropylmethylcellulose, carboxy methyl cellulose from cellulose , lacitol cyclodextrin from starch,
Physical modification Grinding /sieving	Relatively simple and economical compressibility may alter	Dextrose or Compressible sugar , Sorbitol, α-Lactose monohydrate, Dibasic calcium phosphate
Crystallization	Impart flowability to excipients, Requires stringent control on	β-Lactose, Dipac

	possible polymorphic conversions and processing conditions.	
Spray drying	Spherical shape and uniform size, good flowability, poor reworkability	Spray-dried lactose, Emdex, Fast Flo Lactose, Avicel pH, Karion Instant, TRI-CAFOS S, Advantose 100
Granulation / Agglomeration	Transformation of small, cohesive, poorly flowable powders into a flowable and directly compressible.	Granulated lactitol, Tablettose
Dehydration	Increased binding properties	Anhydrous α- Lactose

Co-processed excipients

Co-processing is another way that new excipients are coming to market without undergoing the rigorous safety testing of a completely new chemical. It can be defined as combination of two or more established excipients by using an appropriate process. Co processing of excipients could lead to the formation of excipients with excellent properties compared to the simple physical mixtures of their components. The main aim of co-processing is to obtain a product with added value related to the ratio of its functionality/price.[22]

Development of co-processed excipients starts with the selection of the excipients to be combined, their targeted proportion, selection of preparation method to get optimized product with desired physico-chemical parameters and it ends with minimizing avoidance with batch-to-batch variations.[23] An excipient of economical price has to be combined with the optimal amount of a functional material in order to obtain desire product, with excellent functionality than the simple mixture of components. Co-processing is interesting method because in this only physical modification of the products is occur without altering the chemical structure. A fixed and homogenous distribution for the components is achieved by embedding them within minigranules. Segregation is diminished by adhesion of the actives on the porous particles making process validation and in process control easy and reliable.[21]

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 improvements as well as masking the undesirable properties of individual excipients. The availability of a large number of excipients for co processing ensures numerous possibilities to produce tailor-made

"designer excipients" to address specific functionality requirements or enhancement of the desired properties of excipients.[24] For example, if a substance used as a filler–binder has a low disintegration property, it can be co processed with another excipient that has good wetting properties and high porosity because these attributes will increase the water intake, which will aid and increase the disintegration of the tablets. Manufacturing of 'ready-to-compress' powder mixtures for direct compression was performed by spray drying, without granulation, milling and/or blending steps in between spray drying and compaction.[25]

Co-processing of excipients

The main process of development of co processed excipient involves the following steps:

- Identification of the excipients group to be co-processed by carefully studying the material characteristics and functionality requirement.
- Chose the proportions of various excipients.
- Assessing the particle size required for co processing. This is especially important when one of the components is processed in a dispersed phase. Post processing the particle size of the latter depends on its initial particle size.
- Selecting a suitable drying process such as spray- or flash drying.
- Optimizing the process (because even this can contribute to functionality variations).

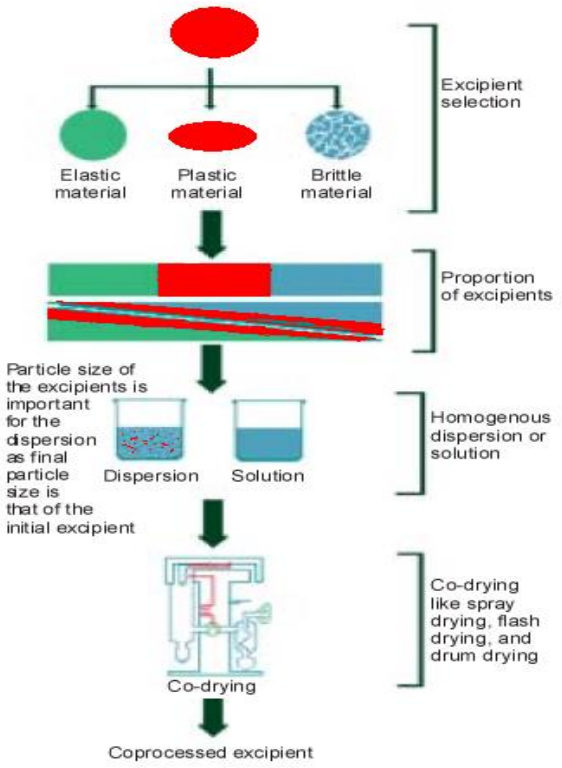

Figure: 1 Schematic representation of steps involve in co-processing.[20]

PROPERTIES AND ADVANTAGES OF THE CO PROCESSED EXCIPIENTS

(A) ABSENCE OF CHEMICAL CHANGE

Many detailed studies of excipients chemical properties after co processing have proven that these excipients do not show any chemical change. Detailed studies of X-ray diffraction analysis, solid-state nuclear magnetic resonance (NMR), IR spectroscopy, Raman spectroscopy, and C13 NMR spectroscopy have detected no chemical changes and indicate a similarity to the physicochemical properties of MCC. This absence of chemical change helps reduce a company's regulatory concerns during the development phase.[26]

(B) PHYSICOMECHANICAL PROPERTIES

(I) Improved flow properties

Controlled optimal particle size and particle-size distribution ensures superior flow properties of co processed excipients without the need to add glidants. A comparison of the flow properties of Cellactose was also performed. The angle of repose and the Hausner's ratio were measured, and Cellactose was found to have better flow characteristics than lactose or a mixture of cellulose and lactose. The spray-dried product had a spherical shape and even surfaces, which also improved the flow properties.

(II) Improved compressibility

The pressure–hardness relation of co processed excipients, when plotted and compared with simple physical mixtures, showed a marked improvement in the compressibility profile. The compressibility performance of excipients such Cellactose, and Ludipress have been reported to be superior to the simple physical mixtures of their constituent excipients.[26]

(III) Better dilution potential

Dilution potential is the ability of the excipient to retain its compressibility even when diluted with another material. Cellactose is shown to have a higher dilution potential than a physical mixture of its constituent excipients. Dilution potential can be defined as the amount of an active ingredient that can be satisfactorily compressed in to tablets with the given directly compressible excipient. A directly compressible excipient should have high dilution potential so that the final dosage form has a minimum possible weight. The dilution potential is influenced by the compressibility of the active pharmaceutical ingredient. A directly compressible excipient should be capable of being reworked without loss of flow or compressibility. On recompression, the excipient should exhibit satisfactory tabletting characteristics. The excipient should remain unchanged chemically and physically.[28]

(IV) Fill weight variation

Materials for direct compression tend to show high fill weight variations as a result of poor flow properties, but co processed excipients, when compared with simple mixtures or parent materials, have been shown to have fewer fill weight variation problems.[29] The primary reason for this phenomenon is the impregnation of one particle into the matrix of another, which reduces the rough particle surfaces and creates a near optimal size distribution, causing better flow properties. Fill weight variation tends to be more prominent with high-speed compression machines.[30]

(V) Other properties

Co processed excipients offer the following additional advantages:

- Pharmaceutical manufacturers have the option of using a single excipient with multiple functional properties, thereby reducing the number of excipients in inventory.
- Improved organoleptic properties such as those in Avicel CE- 15 (FMC Corp., Philadelphia, PA), which is a co processed excipient of MCC, and guar gum were shown to have distinctive advantages in chewable tablets in terms of reduced grittiness, reduced tooth packing, minimal chalkiness, better mouth feel, and improved overall palatability. Although co processing adds some cost, the overall product cost decreases because of improved functionality and fewer test requirements compared with individual excipients.
- They can retain functional advantages while selectively reducing disadvantages, co processed excipients can be used to develop tailor-made designer excipients. This can be helpful in reducing the time required to develop formulations. Co-proceseed excipients can be used as proprietary combinations, and in-house.
- Formularies can be maintained by pharmaceutical companies, which could help in developing a formulation that is difficult to reproduce and provides benefits in terms of intellectual property rights.

APPLICATIONS OF CO-PROCESING

- Improve the compressibility of various poor compressible drugs.
- These multipurpose excipients have dramatically reduced the number of incorporating excipients in the tablet.
- Co-processing is interesting because the products are physically modified in a special way without altering the chemical structure.
- We can achive the synergy of functionality by using co-processing.

- Co-processed excipients have an ability to modulate solubility and stability of the drug.

LIMITATION OF CO-PROCESSED EXCIPIENT

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. Co processed adjuvant lacks the official acceptance in pharmacopoeia. For this reason, a combination filler binder will not be accepted by the pharmaceutical industry until it exhibits significant advantages in the tablet compaction when compared to the physical mixtures of the excipients. Although the spray-crystallized dextrose-maltose (Emdex) and compressible sugar are co-processed products as single components and are official in USP/NF.[26]

A REGULATORY PERSPECTIVE OF EXCIPIENT MIXTURES

With the absence of a chemical change during processing, co- processed excipients can be considered generally regarded as safe (GRAS) if the parent excipients are also GRAS-certified by the regulatory agencies. Hence, these excipients do not require additional toxicological studies. Excipient 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. The mixture of excipients was presented as a topic to the National Formulary and was assigned a priority on the basis of the use of the mixture in marketed dosage forms in which processing has provided added functional value to the excipient mixture.

APPLICATIONS AND BENEFITS OF MULTIFUNCTIONAL EXCIPIENTS

Improvised flow: Co-processing of excipient with controlled particle size distribution and particle morphology results in product with superior flow. This has much to do with the spherical shape and even surfaces of the co-processed particles. The improved flowability of the material in turn helps decrease the weight variation problem encountered during the tabletting of a DC formula. This is advantageous especially when working on high-speed machinery. Enhanced compressibility: Co-processed excipients show remarkable improvement in the compressibility of the material. It is observed that the co-processed products have better compressibility as compared to the physical mixtures of the same components. The co-processed excipient also gives us the advantage of retaining the compactibility when diluted with another material (termed as dilution potential). Thus, co-processed excipients are an ideal choice for developing DC formulation of API with poor compressibility. In fact, some excipients (such as Pharmatose DCL 40) are so developed that

they can incorporate a large amount of drug without losing compactibility and hence are well-suited for high dose formulations.

Easy scale-up: Improved flow and good compactability coupled with multiple functions helps in developing formulas with a minimum of ingredients. Thus, such formulations show better adaptability to scale-up (especially on high-speed machinery) with minimum variation. The reduction in the number of ingredients in the inventory is also a welcomed change for industry, as it reduces the cost and time incurred during purchase and release of materials. In addition, it is a big relief for analysts, who can save time and the hassle of analyzing multiple excipients as per the specifications.

Special applicability: In ODT formats: Single-bodied multifunctional excipients like Ludiflash, F-MELT, Avicel CE-15 are especially developed for ODT formulations. They are tailor-made in order to give binding during compression (to produce a hard tablet at a minimum compression pressure) and show rapid disintegration when brought in contact with a medium. They are processed in such a way that they give a creamier mouthfeel on disintegration, thereby improving the overall palatability of the formulation. In some cases (like Ludiflash, which composes of around 90% mannitol) the excipient itself imparts a sweet taste to the product, cutting down on the need for sweetener in the formulation.

Other advantages: The use of multifunctionality excipients include reduced dust generation, easy flow of normal processing steps, reduced lubricant sensitivity, suitability of excipient for wet granulation, dry granulation and direct compression, robust tabletting at low compression pressure and IP benefits in terms of propriety.

RECENT STUDIES USING MULTIFUNCTIONAL EXCIPIENTS

Rice Germ Oil (RGO) as multifunctional excipient: Selfmicroemulsifying drug delivery system (SMEDDS) of tacrolimus (TAC) was formulated with RGO, an indigenous source of gamma-oryzanol. Modified Excipients in Novel Drug Delivery: Needof the Day Being the same biological source, RGO and rice bran oil (RBO) were compared and it was found that RGO have more solubilization potential for TAC (2.2-fold) as well as higher antioxidant activity (8.06-fold) than the RBO. TAC-SMEDDS was prepared using RGO/Capmul PG8 (2:3) as an oil phase, Cremophore EL as a surfactant, and Transcutol P as a cosurfactant. The in-vitro dissolution studies showed complete and rapid drug release in 30 min compared to a

plain drug (<5%) and marketed capsule (<50%). Thus, gamma-oryzanol-enriched RGO acts as a potential multifunctional excipient for lipid formulations.[8]

Sugar end-capped Poly-D, L-lactides as excipients: Sugar end-capped poly-D, L-lactide (SPDLA) polymers were investigated as a potential release controlling excipient in oral sustained release matrix tablets. The SPDLA polymers were obtained by a catalytic ring-opening polymerization technique using methyl α-D glucopyranoside as a multifunctional initiator in the polymerization. Polymers of different molecular weights were synthesized by varying molar ratios of monomer/catalyst. The matrixtablets were prepared by direct compression technique from the binary mixtures of SPDLA and microcrystalline cellulose, and theophylline was used as a model drug. The drug release was the fastest with the lowest molecular weight SPDLA grade, and the drug release followed zero-order rate. In conclusion, SPDLAs are a novel type of drug carrier polymers applicable in oral controlled drug delivery systems.[9]

O-Phospho-L-Serine, multi-functional excipient: Factor VIII (FVIII) is an important cofactor in the blood coagulation cascade. A deficiency or dysfunction of FVIII causes hemophilia A, a life-threatening bleeding disorder. FVIII circulates in plasma as a heterodimer comprising 6domains (heavy chain, A1-A2-B and light chain, A3-C1-C2). Replacement therapy using FVIII is the leading therapy in the management of hemophilia. This research work investigated the effect of O-phospho-L-serine (OPLS), which binds to the lipid binding region, on the immunogenicity of B domain deleted recombinant factor VIII (BDDrFVIII). Sandwich enzyme-linked immunosorbent assay (ELISA) studies showed that OPLS specifically bind to the lipid binding region. Overall, the study demonstrated that specific molecular interaction of BDDrFVIII occurs with OPLS resulting in less protein aggregation and less immunogenicity.[10]

Modification of the permeability of starch by processing with magnesium silicate: Starch processed with magnesium silicate, using co-precipitation or dry granulation, can be used as a multifunctional excipient with the required binding and disintegration properties. Powder compression using Kawakita analysis confirmed the higher plasticity and lower degree of rearrangement of starch- magnesium silicate resulting from co-precipitation compared to dry granulation. In addition, co-precipitation imparts high surface micro-irregularities as evidenced by SEM analysis. Formulation of a high strength model drug with starch-magnesium silicate illustrated the efficiency of the highly permeable starch- magnesium

silicate in attaining quick drug release when compared to formulations with commercially available modified starch.[11]

Co-processed MCC-Eudragit® E excipients for extrusion- e.spheronization: This study investigates the extrusion–spheronization performance of some mixtures of co-processed microcrystalline cellulose and Eudragit®E (as excipients) and sorbitol (as soluble filler-disintegrant. The pellets prepared with co-processed MCC-Eudragit_ E and sorbitol show a drug dissolution rate dependent on the content of Eudragit_ E in the co-processed excipient and on the proportion of sorbitol incorporated. Furthermore, the pellets made with co-processed MCC-Eudragit®E incorporating the higher proportion of sorbitol (50%) show a very high dissolution rate of hydrochlorothiazide (HCT) and undergo rapid disintegration in the dissolution medium.[12]

Modified celluloses- Multifunctional excipients: The assessment of different celluloses (native cellulose, powdered cellulose, UICEL B UICEL S, Microcrystalline cellulose, UICEL XL) with respect to their suitability as excipients in rapidly dissolving immediate release tablets was the main scope of this research work. Based on different models six celluloses were evaluated. All tested materials were suitable for rapidly dissolving immediate release tablets independent of the relative density and drug load.[13]

Chitin metal silicate (CMS) co-precipitate: The CMS co-precipitates have the potential to be used as a single filler tablet excipient with a multifunction action. This might make the formulation simpler by introducing one excipient with double or triple function instead of two or more excipients with less probability of incompatibility between formulation ingredients. The compressibility of poorly compressible drugs like Metronidazole and spironolactone was highly improved using CMS co precipitates.[14]

Selected polysaccharide hydrogels: Polysaccharide hydrogels from the seeds of Tamarindus indicia and from the trunk of PrunusAmygdalus were selected for physicochemical characterization and microbial load determination to establish them as pharmaceutical excipients. The Modified Excipients in Novel Drug Delivery: Need of the Day pharmaceutical properties such as density, porosity, packing arrangement, flow was found to be good for using them as pharmaceutical excipients. It was concluded that selected hydrogels had promising properties for application as multifunctional excipients.[15]

EXAMPLES OF INOVATIVE MULTIFUNCTIONAL EXCIPIENTS

GalenIQ™- The smart excipient: GalenIQ™- It is a novel multifunctional sugar free excipient. GalenIQ ™is white, odourless, water soluble, crystalline substance derived from sucrose. It has very low hygroscopic nature, excellent chemical stability. The direct compressible grades of GalenIQ™ have high tableting properties due to their excellent compactability. The main properties of direct compressible GalenIQ in tableting are excellent flow, unique morphology of GalenIQ™ ensures homogeneity of the mixture and content uniformity, function of binder and filler, very low compression of other binders is not required Moreover, the outstanding organoleptic and non-carcinogenic properties make it ideal for buccal applications, like chewable tablets or swallowable lozenges combines a multitude of outstanding characteristics and is suitable for a wide range of pharmaceutical applications. GalenIQ™ can be used as more than just a bulk excipient. It also serves as an anti-caking agent, anti-humectant, stabilizer or oral care and taste agent to mention just a few additional functions. GalenIQ™ (pharmaceutical grade isomalt) is a filler/binder, tablet &capsule diluent, coating agent& it complies with the isomalt monographs of the current Ph. Eur., BP, USP-NF and is approved for use in Japan and China. GalenIQ™ is manufactured under cGMP guidelines for pharmaceutical excipients (IPEC-PQG) & under its generic name, isomalt‟, GalenIQ™ is listed in all major reference books for pharmaceutical excipients Physicochemical properties of GalenIQ™ Different solubilities, very low hygroscopic, highly resistant against enzymatic and acidic degradation, heat stable; melting range: 145 to 150 °C, no reaction with amino groups, no incompatibilities with API‟s faced, unique morphology, equilibrated sweetness, non-carcinogenic.

MCC SANAQ®burst: MCC SANAQ®burst consists of 100%pure MCC (with no additional excipients).The fast disintegration is kept even after spheronization and extrusion. It is a unique multifunctional excipient act as binder, filler and superdisintegrant.

NEUSILIN: Neusilin® is a synthetic, amorphous form of Magnesium Aluminometasilicate (MAS). It is a multifunctional excipient that can be used in both direct compression and wet granulation of solid dosage forms. Neusilin® is widelyused for improvement of the quality of tablets, powder, granules and capsules. Neusilin® does not develop gels with aqueous solutions unlike other magnesium aluminium silicates (www.Neusilin.com). Neusilin®occurs as a fine powder or as granules of Magnesium Aluminometasilicate. Neusilin® is represented by an empirical formula Al2O3•MgO•1.7SiO2•xH2O.

Neusilin®is amorphous, possesses very large specific surface area and has high oil and water adsorption capacity. It is superior in compressibility. It makes hard tablets at low compression force and in addition, at low concentrations can improve the hardness of other filler and binder excipients. Compounding with Neusilin® helps to stabilize moisture sensitive as well as lipophilic API's. It is stable against heat and has a long shelf life.It is available in various grades. The grades differ in their bulk density, water content, particle size and pH [16]. It is used as excipient for direct compression, oil adsorption of poorly water soluble actives, improves powder flowability, anti-caking agent for hygroscopic powders, stabilization of deliquescent drugs, low friability and less tablet rejections and smaller tablets with relevant hardness.

SYLOID® FP Multifunctional excipients: SYLOID® FP silica is efficient in many pharmaceutical applications due to its unique morphology. It has a highly developed network of meso-pores that provide access to the large surface area that defines its performance. The result is a product that is easy to incorporate, providing more uniform dispersion of actives and improved content uniformity and high adsorptive capacity - both for hydrophilic and hydrophobic compounds.[17] It act as effective desiccant to increase the stability of moisture-sensitive active pharmaceutical ingredients (APIs),efficient conditioner for powder formulations used in suspensions, capillary wetting agent for better release and disintegration, contribution to the controlled release of active pharmaceutical ingredients and enhanced bioavailability. It is used as glidant, carrier for active ingredients, moisture scavenger/protector and used in tableting as well as Coating.

UNI-PURE™ WG Multifunctional Excipient: The optimum performance of UNI-PURE WG depends on several factors, including the physicochemical properties of the drug, the type of filler and the process used to make granules and tablet. In a given formulation, tablet performance is determinedly processing conditions. It Improves solid dosage formulations and simplifies processing, multifunctional excipient swells in cold water for better processing, improves compressibility, wet granulation binder, reduce disintegration time and enhanced tablet properties.

Pharmaburst™"Quick Dissolve": Pharmaburst is a co-processed excipient system with specific excipients, which allows rapid disintegration and low adhesion to punch faces. It is also said to be a "Quick Dissolve" delivery system. It is highly compactable, high loading in

small tablet, smooth mouth feel, standard temperature humidity and cooling, rapid disintegration, uses USP/EP excipients, produced under cGMP, cost effective.

Recombinant Albumin- rAlbumin: A multifunctional excipient, rAlbumin acts to stabilize the drug product by reducing aggregation, oxidation, and surface adsorption. Particularly valuable for liquid formulations, rAlbumin can significantly decrease the attrition rate in formulation development and provides increased freedom to choose the best candidate for further development Novozymes has developed a range of recombinant human albumins (rAlbumins) specifically for the pharmaceutical industry. Manufactured in an animal-free process to the highest quality standards, Novozymes' rAlbumins act as multifunctional excipients. Their use reduces the requirement for multiple excipients, such as SADs, and delivers a safe and consistent product that enhances the stability and performance of the customer's drug product. The functional properties of rAlbumin as an effective excipient in three areas commonly affecting product stability are: Aggregation, Oxidation and Nonspecific adsorption. It also provides a comparison of the physiochemical properties of a range of commercially available albumins through detailed product analysis[18] combinations.

A REGULATORY PERSPECTIVE OF MULTIFUNCTIONAL COPROCESSED EXCIPIENTS

With the absence of a chemical change during processing, co-processed excipients can be considered generally regarded as safe (GRAS) if the parent excipients are also GRAS-certified by the regulatory agencies [6].Hence, these excipients do not require additional toxicological studies. Excipient 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 marketplace. The mixture of excipients was presented as a topic to the National Formulary and was assigned a priority on the basis of the use of the mixture in marketed dosage forms in which processing has provided added functional value to the excipient mixture.[7] Although spray crystallized dextrose–maltose (EMDEX) and compressible sugars are co-processed, they are commonly considered as single components and are listed as such in the USP–NF. The third edition of the Handbook of Pharmaceutical Excipients has listed SMCC as a separate excipient.[8]

CONCLUSION

Multifunctional co-processed excipients have ability to improve the compressibility and flow ability of poor compressible drugs.Due to number of benefits co-processed excipients are

widely accepted in Pharma industry. Ready to compress multifunctional excipients save time and cost so it becomes economical for any pharmaceutical industry. Direct compression method is a highly preferable method of tablet production because of its simplicity and cost effectiveness.

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