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Review Article

REVIEW ON NOVEL PHARMACEUTICAL COPROCESSED EXCIPIENTS

PAWAR SARITA.B*, SAPANA. AHIRRAO, SANJAY. KSHIRSAGAR

Department of Pharmaceutics, MET's Institute of Pharmacy, Adgaon, Nashik,422003 Savitribai Phule Pune university, Pune, Maharashtra, India.

***For Correspondence:**
Department of Pharmaceutics, MET's Institute of Pharmacy, Adgaon, Nashik,422003 Savitribai Phule Pune university, Pune, Maharashtra, India.

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ABSTRACT

Excipients play an important role in formulating a dosage form. excipients are number more considered as inert ingredients of formulation, but have a well-defined functional role. the search for novel excipient consumes time and investment. coprocessed excipients on the other hand are the result of synergistic properties of existing excipients. coprocessed excipinets are a combination of two or more excipients designed to physical mixing and without significant chemical change. these Coprocessed excipients have high functionalies as compared to individual excipients like better flow property, compressibility, reduced lubricant sensitivity. these excipients are improved flowability, compressibility, tablet manufacturing by spray drying, solvent evaporation, speronization, melt extrution, granulation/agglomeration method. marketed product such as ludipress, celactose and prosolv etc. have already proven their worth in the market by reducing the cost the product and number of excipients yet maintaining efficacy of formulation. such excipients for some limitations due to their quality assessment and reproducibility of result.

KEY WORDS: Types of excipients, Coprocessed excipients, Method of coprocessing, marketed Coprocessed excipients, multifunctional excipients.

INTRODUCTION

In recent time, excipients are the largest components of any pharmaceutical formulation[(1).] The international pharmaceutical excipients council (IPEC) defined excipients as substances other than the API which have been properly evaluated for safety and are purposefully include in drug delivery system. [(2)]

- The processing of the drug delivery system during its manufacturing.
- Preserve, support or enhance stability, bioavailability, patient acceptability or performance of technological function.
- Improve in product identification or enhance any other quality of overall safety, effectiveness [(3)]

TYPE OF EXCIPIENTS:

1. Single entity excipients.
2. Mixtures/blends of multiple excipients.
3. Novel excipients or new chemical organization.
4. Co-process excipients.

1.Single entity excipients: It is defined as excipients containing one component which is the primary component called as single entity excipients[(2).]

2.Mixture/blends of multiple excipients: Simple physical mixtures of two or compendial /non-compendial excipients by means of low to medium shear process where the individual components are mixed together without significant chemical change for solid mixture/ blends the individual excipient remain physically separate at a particulate level [(3)].

3.Novel excipients or new chemical entities: It is defined as excipients which are chemically modified to form new/novel excipients. these are generally not listed in FDA inactive ingredient database. The new excipient means any inactive ingredient that are intentionally added to therapeutic and diagnostic products [(3)]

4.Co-process excipients: co-process excipients is 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[4].many different co-processing methods includes in pharmaceutical formulation development such as spray drying, solvent evaporation, crystallization, melt extrution and granulation/agglomeration[5].

Advantages of co-processed excipients: [4]

- Improving flow properties by controlled optimal particle size and size distribution.
- Improve compressibility, dilution potential, fill weight variation, flow properties, lubricant
- sensitivitiy.
- It can be also improving the tablet hardness and decrease disintegration time.

NEED OF CO-PROCESS EXCIPIENTS:[6]

Effective use of existing excipients: Recognition of new applications for the existing excipients is a inexpensive and less time involving process as compared to an absolutely new development. Excipients with desirable properties: the number of existing excipients which some of desirable properties required in some formulation. Drug developed by genetic engineering: As new drugs are being development, their compactibility with the existing excipients. Hence co-process excipient will be required to overcome these problems. Advances in production process and equipment: the development and improvements in pharmaceutical formulation process and equipments specifically increase in production rate at low cost. lead to the need for new co-process excipients.

The co-processed excipient involves actual process the following steps:(7,27)

1. Recognition the excipient group to be co-processed by carefully studying. the material characteristics and functionality required.
2. Select the proportions of various excipients.
3. Evaluate the particle size required for co-processsing. this is mostly important when one of the components is processed in a dispersed phase post processing, the particle size of the latter depends on its initial article size.
4. Selecting an appropriate drying process such as spray or flash drying optimization. Schematic representation of the co-processing method shown in figure.
5.

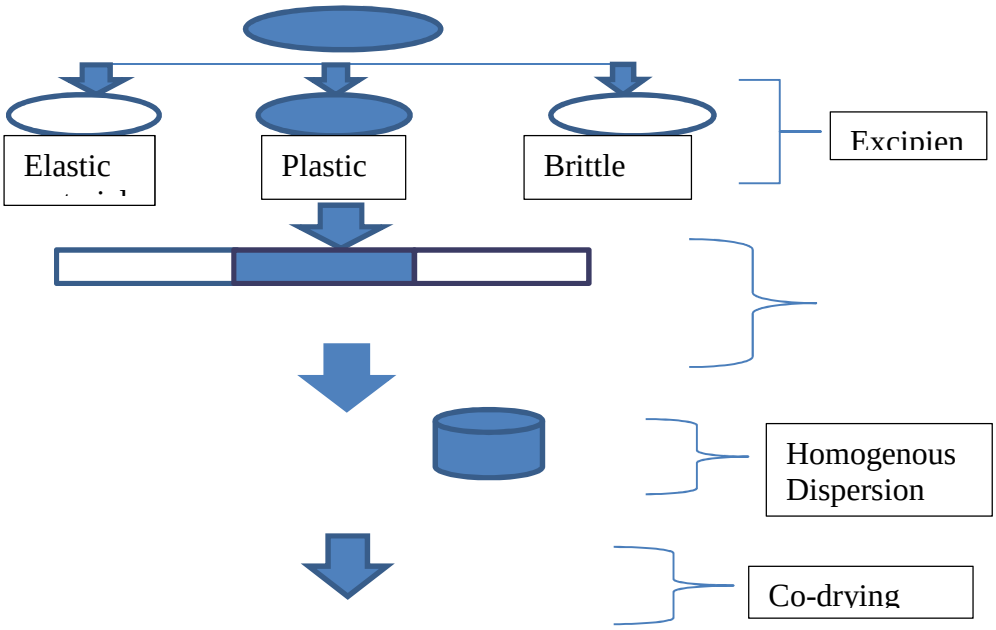

Figure: schematic representation co-processing method

METHODS OF COPROCESSING:

Method of co-process listed below

1. Spray drying
2. Solvent evaporation
3. Crystallization
4. Melt extrusion
5. Granulation/Agglomeration

1.spray drying:

This spray drying technique allow the conversion of feed from a fluid state into dried particulate form a fluid state into a hot drying medium. The feed can be a solution, suspension, dispersion or emulsion. the dried product can be form in the powders, granules or agglomerates .and these are depending upon the physical and chemical properties of feed and the dryer design final powder properties required.it is a continuous particle processing drying operation. the spray drying process parameter like inlet air temperature, atomization air pressure, feed rate, liquid viscosity, solid content in feed, disc speed can be help in design particle with desire characteristics. hence spray drying process can be desire as consisting of four steps[(8).]

a) Atomization of the liquid into droplets.
b) Contact of the droplet with the warm drying gas.
c) Fast evaporation of the droplets to form dry particles.
d) Recovery of the dry particles from the drying gas, using a cyclone.

Advantages of spray drying:

- Possibility to associated non-missible products in continuous operation.
- It allows blending and drying simultaneously soluble and insoluble compound.
- Provides opportunity to fix and protect sensitive active compound on natural carried.
- Improves hardness and compressibility.
- Enhances machine tableting speed,decreases disintegration time.

2.solvent evaporation:

the process is carried out in liquid manufacturing vehicle. the coating excipient is dissolved in a volatile solvent, which is immiscible with liquid manufacturing vehicle phase. a core excipient material to be microencapsulated is dissolved or dispersed in coating polymer solution with agitation. the core coating material mixture is dispersed in liquid manufacturing vehicle phase to obtain, the appropriate size microcapsule. the mixture is then heated to evaporated the liquid vehicle temperature is reduced to ambient temperature with continued agitation.at this stage 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.[(2)]

3.Crystallization :

Crystallization is the (natural or artificial) process of formation of solid crystals precipitating from a solution, melts or more rarely deposited directly from a gas. 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. Example: Sugar Tab [Sucrose, Invert sugar]. [(8,29)]

4.Melt extrusion:

Melt extrusion is a process of formation of small beads, pellets from the molten mass which is extruded through extruder. Extruders consist of four distinct parts: [(3)]

1. An opening though which material enters the barrel that may have a hopper that is filled with the materials to be extruded.

2. A conveying section (process section), which comprises the barrel and the screws that transport, and where applicable, mix the material.

3. An orifice (die) for shaping the material as it leaves the extruder.
4. Downstream auxiliary equipment for cooling, cutting and/or collecting the finished product. Example: Compressol S [Mannitol, Sorbitol] [8,29]

Advantages

- Excellent repeatibility.
- Complicate and intricate shapes are possible.
- Time required is less.

Disadvantages

- Equipment and die cost high.
- Minimum economic length high.[3].

5.Granulation/agglomeration:

Granulation is the process of forming or crystallizing into grains. granules have a size range between 0.2 to 4.0 mm depending on their use. synonym of granulation is "Agglomeration''. Agglomeration processes or in a more general term particle size enlargement technologies are great tools to modify product properties. Agglomeration of powders is widely used to improve physical properties like wettability, flowability, bulk density and product appearance.[2]

Advantages

- It eliminates the use of water or any other solvent.
- Short processing time.
- It can be suitable for conventional equipment.[10]

ADVANTAGES OF COPROCESSING [8,28]

- ✓ Controlled optimal particle size and particle size distribution ensure superior flow properties or coprocess excipients without to add glindents.
- ✓ Flow properties of silicified cellulose were studied in comparison with microcrystalline cellulose.
- ✓ Flow of Coprocessed excipients was better than the flow of simple physical mixtures.
  - ✓ **Improved compressibility**
  - Coprocessed excipient used mainly in direct compression because in this process there is increase in flow properties, which results in improved compressibility.
  - The pressure hardness relation of coprocessed excipients, when plotted and compared with simple physical mixtures, showed a marked improvement in the compressibility profile.
  - ✓ **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.
  - ✓ **reduced lubricant sensitivity**
  - Most co processed products consist of a relatively large amount of brittle material such as lactose monohydrate and a smaller amount of plastic material such as cellulose that is fixed between or on the particles of the brittle material.
  - The plastic material provides good bonding properties because it creates a continuous matrix with a large surface for bonding.
  - The large amount of brittle material provides low lubricant sensitivity because it prevents the formation of a coherent lubricant network by forming newly exposed surfaces upon compression, thus breaking up the lubricant network

EXAMPLES OF COPROCESSED EXCIPIENTS[26]

SR.NO.	COPROCESS EXCIPIENT	TRADE NAME	ADDED ADVANTAGES
1.	Lactose,3.2%Kollidon 30,Kollidon KL	Ludipress	Low degree of Hygroscopicity, good flowability, tablet hardness independent of machine speed.
2.	Lactose,25% cellulose	Cellactose	High compressibility,good mouthfeed,better tableting at low cost.
3.	Microcrystalline cellulose, silicone dioxide	Prosolv	Better flow, reduced sensitivity to wet granulation, better hardness of tablet,reduced friability
4.	Microcrystalline cellulose, guar gum	Avicel CE 15	Less gritiness, reduced tooth packing, minimal chalkiness,creamier mouth feed, improved overall palatability.
5.	Calcium carbonate, sorbitol	FormaXX	Controlled particle size distribution
6.	Microcrytalline cellulose, lactose	microcelac	Capable of formulating high dose, small tablet with poorly flowable active good flow.
7.	90%Microcrystalline cellulose,10% mannitol	Avicel HFE 102	Better Flow properties, better tabletability at slower speed
8.	Microcrystalline carboxy methyl cellulose	Avicel CL 611	Impart a thixotrophic viscosity profile, increase formulation stability across a wide range of PH use as stabilizer
9.	Starch w/w, gelatinisation aid & surfactant	Pregelatinised starch	Binder, diluent in oral capsule and tablet. having enhance flow and compression characteristics. tablet binder in dry compression.
10.	α-lactose monohydrate & β cyclodextrin	Not recognised	Good flowability, compressibility & compactibility. limitations of β cyclodextrin for it flowability & lubrication sensitivity is overcome.
11.	Lactose, Polyvinylpyrolidone	Crosspovidone/ ludipress	An excellent filler binder with very high dilution potential & good binding property .
12.	HPMC, lactose	Not recognised	Improve flowability,& compressibility
13.	Sucrose,3 % Dextrin	Dipac	Use for direct compressible tablet, improve flowability.
14.	Sucrose3%dextrin, mirocrystalline cellulose,silicon dioxide	Dipacprosolv	Directly compressible,better flow,reduced sensitivity to wet granulation,better hardness of tablet,reduced friability.
15.	95% β lactose,5% lactitol	Pharmatose dcl 40	High compressibility

16.	Orocell 200 with 90% mannitol Orocell 400 with 90% mannitol	Orocell 200 & orocell 400	A development filler binder with high dilution potential and good disintegrating property useful for oral disintigrating tablet
17.	Microcryatalline cellulose 89%,hidroxypropylmethyl cellulose2%,&crosspovidone 9%	panExcea^{TM}M C200G	Sronge intraparticle bonding bridges between the components,improved the blending,rapid disintegration time.
18.	I-O-Dglucopyranosyl,6-0-D glucopyranosyl D-sorbitol(1:3)particle size 90%,50%.	Isomalt galen IQ-721	Highly soluble agglomerated spherical isomer for fast dissolving and fast disintegration time
19.	Mannitol 84% crosspovidone 16% silicon dioxide < 1%	pharmaburst^{T} ^{M}CL	High compactibility,high loading insmall diameter tablets,smooth mouth feel,rapid disintegration time
20.	Mannitol particle size 60%	Manogem^{TM} EZ	Assist in formulating difficult to use non hygroscopoc orodispersible tablet containing find drug

REFERENCES

1. Gangurde.A.,Patole.R.K.,Sav.AK.,and Amin.P.D., 2013. A novel directly compressible Coprocessed excipient for sustained release formulation. Journal of Applied Pharmaceutical Science,3(9), pp.89-97
2. Chaudhari, P.D., Phatak, A.A. and Desai, U., 2012. A review: Coprocessed excipients–An alternative to novel chemical entities. International Journal of Pharmaceutical and chemical sciences, 1(4), pp.1480-1498.
3. Desai, U., Chavan, R., Mhatre, P. and Chinchole, R., 2012. A review: Coprocessed excipients. International Journal of Pharmaceutical Sciences Review and Research, 12(2), pp.93-105.
4. Uma.R.G.,2014.Overview of Coprocessed excipient use to improve tableting performance,Journal of advanced drug delivery,1(4).
5. Patil A,Kundu S,Shrinivasan G,2013,Review on coprocess excipients:A Novel Approach in formulation Development,International journal of pharmaceutical innovationas,3(5),pp.25-41.
6. Siraj, S.N., Kausar, S.H., Khan, G.J. and Khan, T., 2017. formulation and evaluation of oral fast dissolving tablet of ondansetron hydrochloride by coprocess excipients. Journal of Drug Delivery and Therapeutics, 7(5), pp.102-108.
7. Sharma, S.K., Alam, M.N., Jaimini, M., Chatterjee, A. and Mohan, S., 2013. Coprocessed excipients:A review.International Journal of Current Trends in Pharmaceutical Research,1(3),pp.205-214.
8. Nadavadekar, P. and Koliyote, S., 2014. Coprocessed excipients for orally disintegrating dosage form. International Journal of Pharma Research & Review, 3(4), pp.95-100.
9. Kumari, M.S., Prasanth, C.H., Bhargavi, C.S., Kumari, M.P. and Ushasri, S., 2013. Reassessment of novel co-processed multifunctional excipients. Int Res J Pharm App Sci, 3(4), pp.122-8.
10. priyanka.RP.,2016.directly compressible Coprocessed pharmaceutical excipients. international journal of pharmacy and technology.8(1),pp.3648-3670.
11. Chaudhari, S.P. and Patil, P.S., 2012. Pharmaceutical excipients: a review. Int. J. Adv. Pharm. Biol. Chem, 1(1), pp.21-34.

12. Jacob.S., Shirwaikar. A.A., Joseph. A. and Srinivasan.K.K., 2007. Novel co-processed excipients of mannitol and microcrystalline cellulose for preparing fast dissolving tablets of glipizide. Indian Journal of Pharmaceutical Sciences, 69(5), pp.633.
13. Uppuluri, P., Chakraborty, T., Devi, V.K. and Raichur, V., 2014.preparation of novel co-processed excipient-study of flow properties and compatibility.indo American journal of pharmaceutical research,4(10),pp.5074-5081.
14. Kucera, S.U., DiNunzio, J.C., Kaneko, N. and McGinity, J.W., 2012. Evaluation of Ceolus™ microcrystalline cellulose grades for the direct compression of enteric-coated pellets. Drug development and industrial pharmacy, 38(3), pp.341-350.
15. Saha, S. and Shahiwala, A.F., 2009. Multifunctional coprocessed excipients for improved tabletting performance. Expert opinion on drug delivery, 6(2), pp.197-208.
16. Gohel, M.C. and Jogani, P.D., 2005. A review of co-processed directly compressible excipients. J Pharm Pharm Sci, 8(1), pp.76-93.
17. Hadinugroho, W., Martodihardjo, S., Fudholi, A. and Riyanto, S., 2017. Evaluation of Polymers as binder on Coprocess of tablet. International Journal of ChemTech Research., 10(5), pp.46-51.
18. Gangurde, A., Patole, R.K., Sav, A.K. and Amin, P.D., 2013. A novel directly compressible co-processed excipient for sustained release formulation. Journal of Applied Pharmaceutical Science, 3(9), p.89.
19. Ahuja, R.K., Dhari, J., Goel, A., Kumar, V. and Sharma, R., 2015. Coprocessing of excipients: A review on excipient development for fast dissolving tablets. International Journal of Pharma Professional's Research, 6(3), pp.1264-1274.
20. Patel.H.,2016.A review on development of multifunctional Coprocessed excipient ,3(2),pp.48-52.
21. Allamneni, N. and Suresh, J.N., 2014. Co-processed excipients as a new generation excipients with multifunctional activities: An overview. IJPRJ(indian jornal of pharmaceutical science and research), 4(1), pp.22-25.
22. Nachaegari, S.K. and Bansal, A.K., 2004. Coprocessed excipients for solid dosage forms. Pharmaceutical Technology, 28(1), pp.52-65.
23. Bhagyashree.A.P,2014.Coprocessed excipients:An overview,world journal of pharmaceutical research,4(1),pp.454-469.
24. Kathpalia, H. and Jogi, K., 2014. Coprocessed excipients–a review. World J. Pharm. Res, 3(3), pp.3863-3885.
25. Preetha, P., Rao, A.S. and Priyanka, C.Y., 2015. formulation of direct compressed verampamil sustained release formulation using optimized co processed excipients. international journal of pharmaceutical sciences and research, 6(10), pp.4324-4335.
26. Mayur A.Deore,Prashant A.Deore,Pratik S.Chaudhari.,2017.Novel co-processess excipients to improve tabletting performance,European journal of biomedical and pharmaceutical sciences,4(3),pp.114-121.
27. Pooja M.A,Swati G.T,Ghanshyam C,Harshata B.S,Priti R.J,2014,Multifuctional excipients for solid dosage form,World Journal of pharmaceutical research,4(3),pp.575-591.
28. Maulin A.P,Prashant L.P,2014,high functionality Coprocessed excipients:A Review,world journal of pharmacy and pharmaceutical sciences,3(3),pp.795-806.
29. Harsha K, Kishori J,2014,coprocess excipients: A review,world journal of pharmaceutical research,3(3),pp.3863-3885.