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THE NEED OF MODIFIED EXCIPIENTS IN NOVEL DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

Therapeutic substances cannot be administered of their unique form, so they're modified into exceptional dosage forms to ensure affected person compliance, dose accuracy, and consistency. This helps enhance their bioavailability and aesthetics and decreases aspect outcomes. Excipients are the components of a formulation other than active elements. The improvement of recent or changed varieties of present excipients has been pushed through advances in method and drug shipping systems. Excipients are on the whole used as diluents, binders, disintegrants, adhesives, glidants and sweeteners in conventional dosage paperwork together with tablets and pills. Natural excipients are favored due to the fact they may be non-poisonous, less steeply-priced, and effortlessly available. The traditional idea of the excipient as an inert and reasonably-priced automobile has evolved into an important constituent of the components. This review presents an outline of excipients used in traditional dosage forms as well as novel drug shipping systems.

KEYWORDS: Novel drug delivery systems, Excipients, Dosage forms etc.

INTRODUCTION

Therapeutic moieties cannot be administrated as such, so they are modified to various dosage forms for the reasons of patient compliance, dose accuracy and consistency, improving bioavailability, aesthetics and reduction of side effects. Excipients are the fundamental requirements to these modifications allowing formulation scientists to achieve their

objectives. Excipients in brief can be defined as "The components of a formulation other than the active ingredient". As compounds become more challenging to formulate, new excipients are needed to enable the delivery, manufacture and development of these compounds. Conventional excipients have been replaced with sophisticated compounds that fulfill multifunctional roles in modern pharmaceutical dosage forms such as improvement of the stability and bioavailability of the active ingredient, enhancement of patient acceptability and performance of technological functions that ensure ease of manufacture.

Ideal characteristics of excipients

- Possessing chemical stability,
- Demonstrating non-reactivity,
- Exhibiting low sensitivity to device and processes
- Maintaining inertness inside the human body,
- Showing non- poisonous characteristic
- Having perfect sensory properties

Type of excipients

1. **Base on origin**

Type	Example
Animal	Lactose, Gelatine, Honey, bees wax
Vegetable	Starch, Turmeric, Acacia, Guar gum.
Mineral	Calcium phosphate, Lactic acid, Silica, Talc, Paraffin.
Synthetic	Boric acid, Lactic acid, povidone.

2. **Base on their function**

Type	Example
Lubricants	Talc, Stearic acid, Vegetables oil.
Diluent	Lactose, Sorbitol, Glucose, Starch paste
Binder and Adhesive	Acacia, Gelatine, Glucose, Starch
Disintegrant	Starches, cross link polymer, cellulose
Solvent	Water, Alcohol, Acetone, syrup
Buffer	Phosphate buffer, Acetate buffer
Preservative	Methyl paraben , Propyl Paraben
Sweeteners	Mannitol , Saccharine

Need of novel excipients

A. **Effective use of current excipients:** Using current excipients for brand spanking new programs is greater cost- powerful and much less time- ingesting than growing new ones. Chitosan, for example, has observed new programs in current years. Modified chitosan

with silicon dioxide is a brand new excipient advanced thru the coprecipitation of chitosan and silica and may be used as a top notch disintegrant.

B. **Excipients with acceptable homes:** There are numerous present excipients that lack a number of the acceptable homes required in a few formulations, viz., soluble tablets, wherein a really perfect lubricant have to be water soluble with effectiveness much like that of magnesium stearate.

C. **Drugs evolved with the aid of using genetic engineering:** As new pills are being evolved, their compatibility with the present excipients every now and then poses a huge question. Hence, new excipients could be essential to triumph over those problems. The pills of protein and peptide magnificence require stabilizers of a distinct nature while as compared to that of traditional oral strong dosage forms.

D. **Advances in manufacturing Technique and System:** New pharmaceutical manufacturing techniques and system require excipients with higher compressibility because of shorter live and make contact with times. This results in an boom in manufacturing quotes and a discount in costs.

E. **Patient or problem compliance:** Some excipients, which might be used nowa-days, are unacceptable for the motives of affected person protection and comfort. Lactose intolerance takes place in persons, who’re poor with inside the enzyme lactase, main to belly cramps, diarrhea, distension and flatulence.

F. **Specialized drug shipping structures:** The improvement of novel or specialised drug shipping structures calls for using unique excipients. Metered dose inhalation gadgets require excipients of a selected length grade and the improvement of mucoadhesive arrangements necessitated the usage of latest bio-adhesive polymers.

Advances in Formulations and Drug delivery systems

- Improvements to immediate and controlled release dosage forms
- Nanotechnology
- Specialized Delivery Systems
- Biologics

Excipients

1. **Synthetic excipients:** These are used in the manufacture of tablets to bind the tablet together, reduce die wall friction between the tablet and the tableting press, control pH balance, and to disintegrate the tablet in the stomach once it has been ingested. In parenteral, synthetic excipients are used as solubilization agents to make actives more soluble, and therefore, more deliverable.

2. **Multifunctional excipients:** Multifunctional excipients are a class of excipients that includes preprocessed and coprocessed 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).

Recent using multifunctional excipients

- Rice Germ Oil (RGO) as multifunctional excipient.
- Sugar end-capped Poly-D, L-lactides as excipients.
- O-Phospho-L-Serine, multi-functional excipient.
- Modification of the permeability of starch by processing with magnesium silicate-processed MCC-Eudragit® E excipients for extrusion spheronization.
- Modified celluloses- Multifunctional excipients.
- Chitin metal silicate (CMS) co-precipitate.
- Selected polysaccharide hydrogels.

3. **Herbal excipients:** Natural excipients such as cellulose, lactose, sucrose, glucose, and gelatin are used for filling and diluting. Microcrystalline cellulose is a common filler, binder, and disintegrant, used in concentrations of 10-30%. Natural polysaccharides are drastically used for the improvement of stable dosage forms. These polymers of monosaccharides (sugars) are cheaper and to be had in lots of systems with lots of properties. They are incredibly stable, safe, non-toxic, and hydrophilic and gel forming in nature. Pectins, starch, guar gum, amylase and karaya gum are some polysaccharides normally utilized in dosage forms. Non-starch, linear polysaccharides stay intact withinside the physiological surroundings of the belly and the small intestine, however are degraded through the bacterial population of the human colon which lead them to probably beneficial in focused transport structures to the colon.

Gums: Gums are translucent and amorphous materials produced through the plants. Usually pathological products, gums are produced while the plant is developing beneathneath unfavorable situations or while injured. Gums are plant hydrocolloids and can be anionic or non ionic polysaccharides. On hydrolysis gums yield sugar and salts of uronic acid.

Gums	Source	Family
Guar gum	The seed of cyamopsis tetragonolobus	Leguminosae
Gum acacia /Gum arabic	The dried gummy exudate obtained from the stem and branches of Acacia Senegal (Linne)	Leguminosae
Karaya gum	It is obtained from sterculia urens	Sterculiaceae
Xanthan gum	The fermentation of the gram-negative bacteria Xanthomonas campestris.	Leguminosae
Tragacanth	It is obtained from the branches of astragalus gummifer	Leguminosae

Volatile oils: Volatile oils are usually mixture of hydrocarbons and oxygenated compounds derived from those hydrocarbons. Many oils are terpenoid in origin; a number of them are fragrant derivatives combined with terpenes (e.g. cinnamon and clove). A few compounds (e.g. thymol and carvacrol) even though fragrant in structure, are terpenoid in origin's.

4. **Coprocessed excipients:** A coprocessed excipient is a combination of two or more copendial or non copendial excipients designed to physically modify their properties in manner not achievable by simple physical mixing and without significant chemical changes. Coprocessed excipient are used mainly in solid dosage liquid dosage and semisolid dosage.

Co-processed Excipients	Trede name	Manufacturer	Added advantage
Lactose, 3.2% Kollidon 30 Kollidon CL	Ludiptess	Basfag, Ludwigshafen Germany	Low degree of hygroscopicity, good flowability, tablet hardness independent of machine speed
Lactose 25% Cellulose	Cellactose	Meggle GmbH and co. Kg, Germany	Highly compressible, good mouth feel, better tableting at low cost
Sucrose 3% Dextrin	Dipac	Penwest pharmaceutical company	Directly compressible
Microcrystalline cellulose, Silicon dioxide	Prosolv	Penwest pharmaceutical company	Better flow, reduced sensitivity to wet granulation, better hardness of tablet,

			reduce friability
Microcrystalline cellulose, Guar gum	Avicel ce - 15	FMC corporation	Less grittiness, minimal chalkiness, overall palatability
Calcium carbonate, Sorbitol	Formaxx	Merck	Controlled practical size distribution
Microcrystalline cellulose, Lactose	Microlela	Meggle	Capable of formulating high dose, small tablet with poorly flow able active ingredients

Technologies used for coprocessed excipient

- ❖ Roller compaction
- ❖ Wet granulation
- ❖ Spray drying:

1. Concentration
2. Atomization
3. Droplet – air contact
4. Droplet drying
5. separations

- ❖ Co- spray drying
- ❖ Solvent evaporation
- ❖ Melt extrusion
- ❖ Crystallization
- ❖ Agglomeration

- ❖ **Roller compaction:** In the roller compaction procedure, powder blends first pass a feeding zone, in which maximum of the rearrangement occurs. The dense powders then undergo a compaction zone, in which growing pressure is being exerted through counter rotating rolls. As the stress is going up similarly into the compaction zone, the debris deform, fragment, and bond to shape ribbons. Roller compaction is broadly carried out to dry granulation. It gives many advanced traits e.g. proper manage of procedure and fee blessings in comparison to moist granulation. As no liquid or drying is involved, this procedure is greater appropriate for water or warmness touchy drugs. Compared to direct compression. Roller compaction can deal with excessive drug loading, enhance float and content material uniformity and save you segregation. Like every other processes, dry granulation has its very own issues, together with lack of compactibility of dissolution

problem. A systematic technique of formula and procedure improvement is the important thing to excessive nice drug products. At excessive drug loading, the compactibility and float cappotential of drug substance could be important for curler compaction and tableting processes. Different excipients want to be evaluated in formula improvement to acquire acceptable chemical stability, pill properties, and procedure manage.

- **Wet granulation:** Wet granulation is a procedure extensively used withinside the pharmaceutical industry. It has now no longer been changed via way of means of direct compression technology, in part due to improvement value issues and habits, and in part as it stays in a few instances an attractive technique. The procedure keeps till all of the powder has been agglomerated, and it wishes to be stabilized as some distance as moisture stability is concerned. The equilibrium might not be constant, however, because the moisture content material of the granules can be growing barely during the procedure, and the trajectories of the debris may also alternate with modifications withinside the density of the agglomerated powder mattress. Complete drying is quick carried out withinside the warm air movement while binder spraying is stopped. The drying step historically takes area after moving the damp mass into any other piece of equipment (fluid mattress dryer), however the use of single-pot technology (drying in area) is now spreading. The granules fashioned are understandably denser than the ones received in fluid mattress granulation.

Example

- Galeniqtm
- Neusilin
- Uni-Pure™ WG
- Captisol (Modified beta-cyclodextrin)

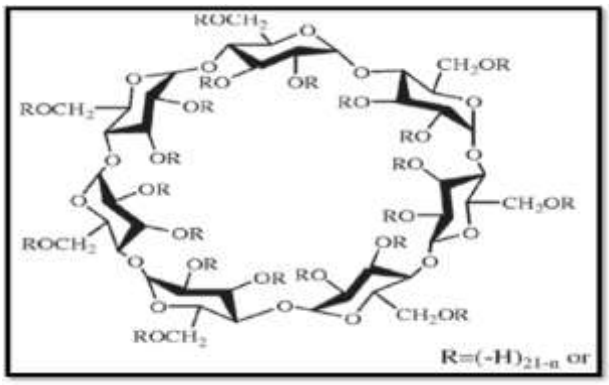

Fig:- Chemical structure of captisol.

Applications of novel excipients

1. Improved Solubility
2. Sustained and control release
3. Taste Masking
4. Drug Stability
5. Enhanced Drug Targeting
6. Incorporation of Biologics
7. Gene Delivery
8. Nano Particle formulation
9. Personalised Medicine
10. Modified Released System
11. Oral Thin Film
12. Nano medicine
13. Vaccine Formulation

CONCLUSION

The world of excipients has moved well beyond just improving the stability of drugs, to creating a total solution for manufacturers and ultimately, patients. Synthetic excipients represent a versatile class of materials that have been utilized in the development of different pharmaceutical formulations. Coprocessing could hold the key to a successful future for synthetic excipients by ushering in a new class of multifunctional compounds. Excipients can be physically modified to enhance its properties and to improve its performances. It can also be chemically modified to obtain a very wide range of new properties that can play an important role in the formulation of smart drug delivery systems.

REFERENCES

1. K. A. Abbas, S. K. Khalil and Anis Shobirin Meor Hussin ““Modified Starches and Their Usages in Selected Food Products: A review Study”, Journal of Agricultural Sciences, 2010; 2(2): P90.
2. Hoag, S.W., Excipient Variability and Functionality Testing. ExcipientFest, Baltimore, Maryland, 2011.
3. Carlin. B, Carter. D, Griffiths. M, Larner. G, Moore. K, Rothman. B, Schoneker. D, Sheehan. C, Uppoor. R, Walsh. P, Wiens. R, Joint position paper on pharmaceutical excipient testing and control strategies. Pharm. Technol, 2007.

4. Sheehan, C., USP Excipient Performance Chapter: Excipient QbD as it Relates to Performance and Functionality. ExcipientFest, Baltimore, Maryland, 2011.
5. Sheehan, C., Understanding the role of excipient functional category & performance-related tests in a quality-by-design framework. Drug Dev. Deliv, 2012.
6. Sheehan, C., Amidon, G.E., Compendial standards and excipient performance in the QbD era: USP excipient performance chapter. Am. Pharm. Rev, 2011; 14.
7. Wang, T., Alston, K.M., Wassgren, C.R., Mockus, L., Catlin, A.C., Fernando, S.R., Fernando, S., Basu, P.K., Hoag, S.W., The creation of an excipient properties database to support quality by design (QbD) formulation development. Am. Pharm. Rev, 2013.
8. Moreton, C., Functionality and performance of excipients in a quality-bydesign world, part VIII: excipient specifications. Am. Pharm. Rev, 2010; 13: 46-50.
9. ICH, Quality Risk Management Q, 2005; 9. http://www.ich.org/fileadmin/Public_-Web_Site/ICH_Products/Guidelines/Quality/Q9/Step4/Q9_Guideline.pdf.
10. ICH, 2009. Pharmaceutical Development Q8(R2). http://www.ich.org/fileadmin/ Public_Web_Site/ICH_Products/Guidelines/Quality/Q8_R1/Step4/Q8_R2_Guideline.pdf.
11. Marwaha, M., Sandhu, D. and Marwaha, R.K. "Co processing of excipients: a review on excipient development for improved tableting performance", International Journal of Applied Pharmaceutics, 2010; 2(3): 41-47.
12. Miller, R.W. "Roller compaction technology In: Handbook of Pharmaceutical Granulation Technology", Parikh D.M. (Ed.), Marcel Dekker, 1997; 100–149.
13. Pawar, S.K. and Vavia, P.R. "Rice Germ Oil as Multifunctional Excipient in preparation of SelfMicroemulsifying Drug Delivery System (SMEDDS) of Tacrolimus", American Association of Pharmaceutical Scientists, 2012; 13(1): 255-261.
14. Sene, C., Neun. D, Tan-sen hee, L. and Ulman, K. "Silicones as excipients for topical pharmaceutical applications". Dow corning internal document form, 2002; 52-1034-01.
15. Sene, C., Dupont, A. and Crowning, D. Characterising polymeric excipients. Innovations in Pharmaceutical Technology, 81-91.
16. Velagaleti, R. "Excipient Innovation and Regulatory Acceptance for Use in Drug Products– Solubilizer Solutol® HS 15 Case Study". Presented at: Annual Meeting of the American Association of Pharmaceutical Scientists. Los Angeles, CA, USA, November, 2009.
17. Vuorinen, S., Heinamaki, J., Antikainen, O., Lahcini, M., Repo, T. and Yliruusi, J. "Sugar End-Capped Poly-D, L-lactides as Excipients in Oral Sustained Release Tablets", American Association of Pharmaceutical Sciences, 2009; 10(2): 566-573.

18. Zeleznik, J.A. and Renak, J. “High Functionality Excipients (HFE) –PROSOLV® SMCC as an Effective Strategy for Generic Drug Formulation”, Business Briefing: Pharma Generics, 2004; 1-4.
19. Chaudhary, S.A., Chaudharya, A.B. and Mehta T.A. “Excipients Updates for Orally Disintegrating Dosage Forms”, International Journal of Research in Pharmaceutical Sciences, 2010; 1(2): 103-107.
20. Chougule, A.S., Dikpati, A. and Trimbake T. “Formulation development of coprocessed excipients”, Journal of Advanced Pharmaceutical Sciences, 2012; 2(2): 231-249.
21. Chaudhary, P.D., Pathak, A.A. and Desai, U. “A Review: Co processed Excipients-An Alternative to Novel Chemical entities”, International Journal of Pharmaceutical and Chemical Sciences, 2012; 1(4): 1480-1498.
22. S. jadhav. “A Review On Novel Excipients”. Article in International Journal of Research in Pharmaceutical sciences, 2023.
23. Krishna LN, Kulkarni PK, Dixit M, Lavanya D, Raavi PK. Brief introduction of natural gums, mucilages and their applications in novel drug delivery systems-a review. IJDFR, 2011; 2[6]: 54-71.
24. Guth, F., Schmeller, T., Kolter, K., 2011. Characterization Requirements for New Excipients, The international Pharmaceutical Excipients Council Europe Annual Seminar, Cannes.
25. Committee for Medicinal Products for Human Use. Guideline on excipients in the dossier for application for marketing authorisation of a medicinal product.
26. Bhattacharyya L, Schuber S, Sheehan C, William R. Excipients: background/introduction. In Excipient development for pharmaceutical, biotechnology, and drug delivery systems, 2006; 28: 21-22. CRC Press.
27. DeMerilis C., Goldring J., Schnoeker D: Inside IPEC: New Excipient Evaluation Procedure, Pharmaceutical Technology, 2008; 32.
28. DeMerlis, C.C., Goldring, J.M., Velagaleti, R. et al. Regulatory update: The IPEC novel excipient safety evaluation procedure. Pharm. Tech, 2009; 33[11]: 72–82.
29. Thompson, D.O. Cyclodextrins – enabling excipients: A case study of the development of a newexcipient – sulfobutylether ß-cyclodextrin CAPTISOL®, in Excipient Development for Pharmaceutical, Biotechnology and Drug Delivery Systems [ed. Katadare A.], Informa Healthcare USA, Inc., New York.
30. Saha, S. and Shahiwala, A. F. Multifunctional coprocessed excipients for improved tabletting performance. Expert Opinion on Drug Delivery, 2009; 6[2]: 197– 208.

31. Guidance for Industry: Non-Clinical Studies for the Safety Evaluation of Pharmaceutical Excipients, May, 2005; 3-4.
32. Santos H, Veiga F, Pina ME, Sousa JJ. Compaction compression and drug release properties of diclofenac sodium and ibuprofen pellets comprising xanthan gum as a sustained release agent. Int J Pharm, 2005; 295: 15-27.
33. Rajinikanth PS, Sankar C, Mishra B. Sodium alginate microspheres of metoprolol tartrate for intranasal systemic delivery: Development and evaluation. Drug Deliv, 2003; 10: 21-8.
34. USP Subcommittee on excipients. Pharm Forum, 1992; 18: 4387.