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Preparation And Evaluation Of Aspirin Granules Prepared By Wet Granulation Technique, By Using Different Types Of Binders

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ABSTRACT:

Aspirin tablet is prepared by wet granulation method. Aspirin belonging to the class of NSAID having analgesic, antipyretic, anti-inflammatory and antiplatelet activity at systematic standard doses. In this Lubricants in combination leads to better drug release kinetic. The Prepared Tablet is Evaluated In terms of bulk density, tapped density, the angle of repose, Carr's Index and, hardness test, weight variation test, friability test and in vitro study. The result associated with optimized batch is good satisfactory and having better drug release kinetic. The in-vitro dissolution studies we got result our formulation follow Zero Order Kinetics with the effect of lubricants using in combination for better kinetic drug release.

Introduction:

Granules are produced to enhance the uniformity of the API in the final product, to the density of the blend so that it occupies less volume per unit weight for better storage and shipment, to facilitate metering or volumetric dispensing , to reduce dust during granulation process to reduce toxic exposure and process-related hazards, and to improve the appearance of the product. Consequently, the ideal characteristics of granules includes spherical shape for important flow, marrow particle size distribution for content informatiyand volumetric dispensing, sufficient fines to fill void spaces between granules for better compaction and compression characteristics, and adequate moisture and hardness to prevent breaking and dust formulation during process.

Granulation is an exemplary of particle design and the properties of the particles acquired after graduation depend on particle size of the drug and excipients, the type, concentration, and volume of Binders and / or solvents, granulation time, type of granulatior, drying rate etc . The primary method by which the agglomerated granules are formed include solid bridges, sintering, chemical reation, crystallization and deposition of colloidal particles. Besides, binding can also be accomplished through adhesive and cohesive forces by utilising high viscous binders. The series of mechanisms by which granules are formed from the powder particles encompass wetting and nucleation, coalescence or grwth, consolidation and attrition or breakage.

WHAT IS GRANULATION

Granulation may be defined as a size enlargement process which converts fine or coarse particles into physically stronger and larger agglomerates having good flow property better composition characteristics and uniformity. The art and science for science for process and production of granules are known as granulation technology. GreanulationTechnology can be broadly classified into 2 types based upon the type of processing involved.

DRY GRANULATION

Dry Granulation involved granule formulation without using liquid solution as product may be sensitive to moisture and heat. In this process dry powder particles may be brought together.

WET GRANULATION

Wet granulation is the most widely used process of Granulation in the pharmaceutical industry. It involves addition of a liquid solution to powder, to from a wet mass or it forms granules by adding the powder together with an adhesive, instead of by compaction.

The wet mass is dried and then sized to obtained granules.The liquid added bindds the moist powered particles by a combination of capillary and viscous forces in the wet state.Morepermanentl bonds are formed during subsequent drying which leads to the formation of agglomerates.

Although the process is most widely used in the pharmaceutical industry, the conventional wet.

Greanulation process has following merits and demerits.

FlUID BED GRANULATION

Fluidization is the operation by which fine solids are transformed into a fluid like state through contact with a gas. At certain gas velocity , the fluid will support the particles giving them free mobility without entrapment.

Fluid bed processing of pharmaceuticals was first reported by Wurster, by using air suspension technique to cost tablets later used this technique in Granulation and drying of pharmaceuticals for the preparation of compressed tablets.

SPRAY DRYING

Spray drying as a process has been used to produce microcapsule, food ingredients, food ingredients, flavours ,and various biotechnological preparations. This process differs from the methods discussed above in that it is a continuous process in which a dry granular product is made from a solution

Or a suspension rather than initially dried the primary powder particles. The solution or suspension may be a drug alone,a mixture of different excipients or a complete formulation. As long as the liquid solution or suspension feed to the drying system, dry powder products continues to be produced. Represent the configuration of spray dryer of open-mode design with single point powder discharge.

EXCIPIENTS

Typically, a wet granulation formulation will contain one or more diluents for bulk or to aid processing, a binder to facilitate granule growth and to aid compaction into hard tablet, a disinterested and a lubricant. Additionally wetting agents, stabilising agents and colourants are used as required. Table 1 show commonly used key excipients for low to medium dose drug the diluents are likely to make up majority of tablet. But diluent do more provide bulk and some properties of

Commonly used diluents are discussed below.

BINDER

These are the dry powder or liquid which are added during wet granulationto promote granules or to the tablet. Binders can be in powder form and liquid form. Example of Binders are powder binders: cellulose, methyl cellulose, polyvinyl pyrrolidine, PEG solution binders:gelatine, PVP, HPMC, PEG, sucrose, starch. Binders can be added in the following ways to the formulation added as poelwder before wet agglomeration so that the binder is evenly distributed. As solution from it is used as agglomeration liquid in the wet granulation. It is called as liquid binder.

Excipient categoy	Functions	Working principle	Examples
Binders and Adhesive	Impart Cohesive Qualities To Powdered Material.	Improves free Flow Qualities By Formulation Of Granules To Desired Hardness And Size.	Acacia, Gelatin,SarchPaste, Polyvinyl , pyrrolidone, Glucose, CarboxymethylCellulose, Povidone.

Table no –01 : Binders used in solid dosage forms.

TYPES OF BINDERS:

Classification On The Basis Of Their Source:

1. **Natural polymers:** Starch, pre gelatinized starch, gelatin, acacia, tragacanth and gums
2. **Synthetic polymers:** PVC, HPMC, methyl cellulose, ethyl cellulose, PEG.
3. **Sugar:** glucose, sucrose, sorbitol.

Classification On The Basis Of Their Application:

1. **Solution binders:-**
   These are dissolved in a solvent. Examples including gelatin, cellulose, cellulose derivatives, polyvinyl pyrrolidine, starch, sucrose and polyethylene glycol.
2. **Dry binders**
   These are added to the powder blend, either after a wet granulation step, or as part of a direct powder compression formula. Examples include cellulose, methyl cellulose.

   AIM, OBJECTIVE AND PlAN OF WORK

   Aim – preparation and evaluation of aspirin granules prepared by wet granulation technique by using different types of Binders.

   Objective –
   - To study the effect of binders.
   - To study properties of granulation technique.
   - To study bulk density.
   - To study tap density.
   - To study moisture content.

Plan of work –

- **Selection of drug**
  - Aspirin
- **Selection of granulation method**
  - Wet granulation
- **Selection of binders**
  - Tragacanth
  - Gum acacia
  - Sucrose
  - Starch
- **Excipient**
  - Citric acid

- Calacium carbonate
- Saccharin sodium

- **Evaluation method**
- Bulk density
- Bulk volume
- **Tap density**
- Tap volume
- Carr's index
- Hausners ratio
- Angle of repose
- Moisture content

Material and methods (experiental)

Glassware's – measuring cylinder, beaker, mortar and pestle, standard sieve set.

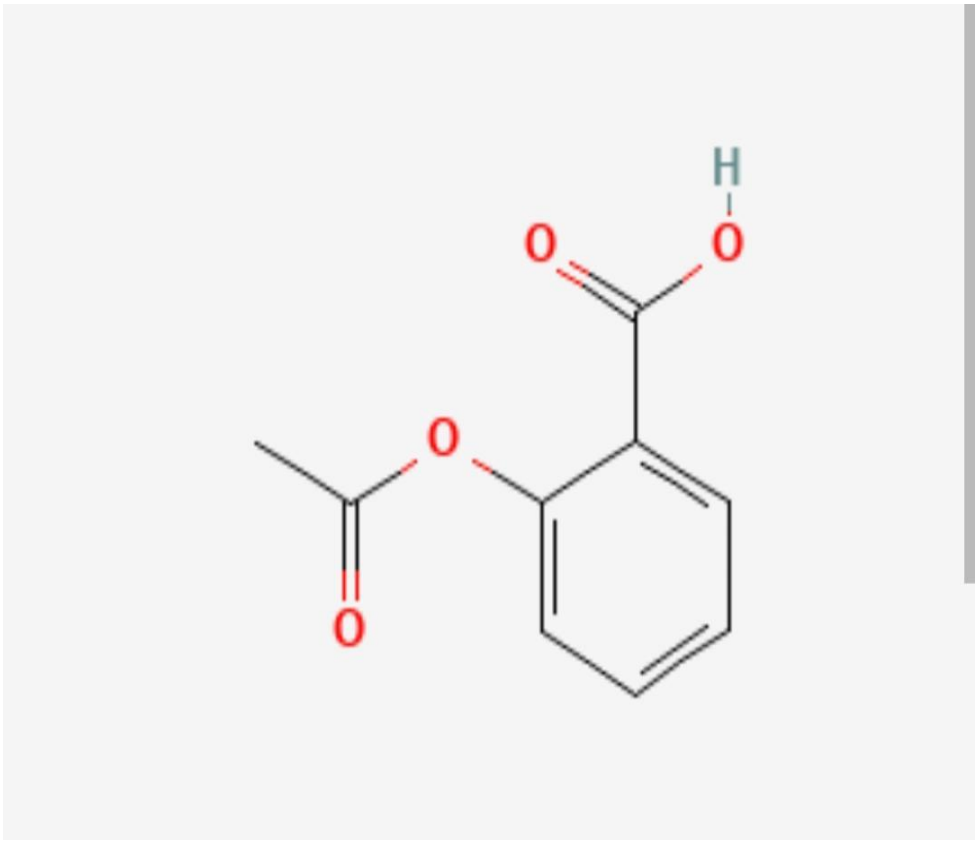
Procedure

1. Weigh and pass aspirin powder through 60# sievs.
2. Mix all the above ingredients talc, (binder) and magnesium stearate.
3. Compress into slug using 18 mm flat face punishes
4. Grind the slugs using 20 mesh screen.
5. Transfer into polybag and add the reminder disintegration and lubricant, mix for 10 minutes.
6. Store prepared granules in well closed and labelled container

SELECTION OF DRUG

Aspirin (Acetylsalicylic Acid)

Fig- 2 Aspirin



Molecular formula: c9H8O4

Molecular Weight/Molar Mass: 180.159 g/mol

Melting point : 136° C

Density: 1.40 g/cm3

Boiling Point: 1.40°c BH

Selection of binder-

TRAGACNTH

Tragacanth is a natural gum obtained from the dried sap of several species of Middle Eastern legumes of the genus Astragalus, including . The gum is sometimes called Shiraz gum, gum elect or gum dragon. T

Gum Acacia –

The structure of acacia gum is complex and ill-known. The main structure features is a backbone of beta -glactopyranose units with 1,3 bonds and side chains of 1,6 – linked galactopyranose units terminating in B-D-glucrronopyanose and 4-O-methyl – B-D-glucoronopyranose.

Sucrose –

Sucrose is a type of sugar made up of one molecule of glucose and one molecule of fructose joined together. It is a disaccharide, a molecule composed of two monosacharide: glucose and fructose. Sucrose is produced naturally in plant , from which table sugar is refined.

Starch-

Starch is a soft, white, tasteles powder that is insoluble incold water, alcohol, or other solvents. Starch is a polysaccharides comprising Glucose monomers joined in Alpha 1,4linkages

The simplest from of starch is the linear polymer amylose: amyllopectin is the breached from.

EVALUATION METHODS

1. **Bulk density –**
   Bulk density is an indicator of soil compaction. It is calculated as the dry weight of soil divided by its volume. This volume includes the volume of soil particles

and the volume of pores among soil particles. Bulk density is typically expressed in g/cm3.
Bulk density= mass / volume.

2. **Tap volume –** The ratio of the mass of the powder to the volume occupied by the powder after it has been tapped for a defined period of time.

3. **Hausners ratio –** The Hausner ratio is a number that is correlated to the flowabilityof a powder or granular material. It is named after the engineer Henry. The Hausner ratio is not an absolute property of a material iths value can vary depending on the methodology used to determine it.

Hausners ratio = tapped density/ poured or bulk density.

4. **Carr's index –**carr's index = bulk density – tapped density / tapped density.
5. **Tap density –** Tapped density of a powder is the ratio of the powder to the volume occupied by powder after it has been tapped for a defined period of time. **Tap density = mass / volume**
6. **Angle of repose –** Under the static balance, the angle between the slope of a powder the horizontal plane is Angle of Repose. It is measured when the powders fall to a surface via gravity and from a cone.

   Angle of repose = ()= tan -1 h/r

7. **Bulk volume –** Term used relative to the density and volume of a porous solid, such as a reference brick It is defined as the volume of the solid material plus the volume of the sealed and open pores present.
   Bulk volume = powder+ space between powder particles.

8. **Moisture content –** Moisture contact is, simply, how much water is in a product. It influence the physical properties of a substance, including weight, density, viscosity, conductivity, and others. It is generally determined by weight loss upon drying.
   Moisture content = after drying / before drying × 100

Methods	Standard value

Bulk density	1.33 g/cm^3- 2.65 g/cm^3
Bulk volume	0.18ml – 1.25 ml
Tap density	< 0.72g/ ml
Tap volume	< 49 m^3
Carr's index	5- 16
Hausners ratio	1.0- 1.11 w/v
Angle of repose	< 25
Moisture content	8.5 % - 8.10 %

Table –Standard value of evaluation of aspirin granules by wet granulation.

RESULT –

Sr. No.	Parameter	B1	B2	B3	B4
1	**Bulk density**	**0.32 g/ml**	**0.35 g/ml**	**0.38 g/ml**	**0.39 g/ml**
2	**Bulk volume**	**0.25 ml**	**0.18 ml**	**0.22 ml**	**0.24 ml**
3	**Tap density**	**0.41 g/ml**	**0.42 g/ml**	**0.44 g/ml**	**0.43 g/ml**
4	**Tap volume**	**39 m^3**	**33 m^3**	**35.1 m^3**	**40 m^3**
5	**Carr's index**	**8.76 %**	**6.52 %**	**7.2 %**	**12 %**
6	**Hausners ratio**	**1.06 w/v**	**1.12 w/v**	**1.03 w/v**	**1.02 w/v**
7	**Angle of repose**	**22.36**	**20.1**	**25.64**	**22.30**
8	**Moisture content**	**8.5%**	**8.2 %**	**8.8 %**	**8.6%**

Conclusion

Wet granulation is possible the most frequently used means of producing a compression mix for tablets, and a process that is applicable to just about any drug, but the downside is that numerous formulation and process factors and their interaction results in complex development programmeeven for apparently simple formulations. Nevertheless, on a practical level there are some guidelines that seem to be generally applicable.Greanulation tends to improve powder flow and worsen compact ability, therefore concentrate on developing a light, granule with sufficient flow for tableting. Including at least 50% of the disintegration in the intragranular portion of the formulation. Stabilising agents may be more effective when used wet greanulation than in dry processing. Minimise the potential for size segregation of granules in downstream operations to avoid potential tablet inhomogeneity.

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