Granules

Granules are defined as a dosage form composed of dry aggregates of powder particles that may contain one or more APIs, with or without other ingredients. They may be swallowed as such, dispersed in food, or dissolved in water. Granules are frequently compacted into tablets or filled into capsules, with or without additional ingredients.

Reason For Granulation

1. To prevent segregation of the constituents of powder Mix
2. To improve the flow properties of the powder mix
3. To improve the compaction characteristics of powder mix
4. Granules have higher porosity than powders
5. To improve the compressibility of powders.
6. The granulation of toxic materials will reduce the hazard of generation of toxic dust, which may arise during the handling of the powders.
7. Materials, which are slightly hygroscope, may adhere & form a cake if stored as a powder.
8. good tasting, sparkling drinks containing ingredients which do not normally taste good in liquid form
9. high dose products where large conventional tablets would have to be swallowed
10. quicker and more complete absorption of dosages
11. compounds normally not stable or soluble in liquid form

Effervescent Granulated

An effervescent dosage form, frequently tablets or granules, contains ingredients that, when in contact with water, rapidly release carbon dioxide. The dosage form is dissolved or dispersed in water to initiate the effervescence prior to ingestion.

- Effervescent salts are granules or coarse to very coarse powders containing a medicinal agent in a dry mixture usually composed of sodium bicarbonate, citric acid, and tartaric acid. When added to water, the acids and the base react to liberate carbon dioxide, resulting in effervescence. The resulting carbonated solution masks undesirable taste of any medicinal agent.

- ❖ Using granules or coarse particles of the mixed powders rather than small powder particles decreases the rate of solution and prevents violent and uncontrollable effervescence. Sudden and rapid effervescence could overflow the glass and leave little residual carbonation in the solution.
- ❖ Using a combination of citric and tartaric acids rather than either acid alone avoids certain difficulties. When tartaric acid is used as the sole acid, the resulting granules readily lose their firmness and crumble. Citric acid alone results in a sticky mixture difficult to granulate.

Limitations of effervescent formulations

1. It cannot be given to the children because of possibility of gas (CO2) toxicity.
2. If packaging is not done properly then there are chances of degradation by environmental moisture.
3. It has shorter shelf life as compared to other solid dosage forms.
4. It requires special machinery requirements for manufacturing.
5. This dosage form is costly then tablets.

Preparation of Effervescent Granulation

It has been found that citric acid monohydrate and tartaric acid used in the ratio of 1:2, respectively, produces a powder with good effervescent properties. The amount of sodium bicarbonate to be used may be calculated from the reaction which occur when the granules come in contact with water. The reaction equation between citric monohydrate and sodium bicarbonate is given below:

$$3NaHCO_3 + HO-\underset{\underset{CH_2-COOH}{|}}{\overset{\overset{CH_2-COOH}{|}}{C}}-COOH \cdot H_2O + 4H_2O \rightarrow HO-\underset{\underset{CH_2-COONa}{|}}{\overset{\overset{CH_2-COONa}{|}}{C}}-COONa + 3CO_2\uparrow + 8H_2O$$

$(3 \times 84g) \quad (1 \times 210g)$

Setting up a proportion to determine the amount of sodium bicarbonate that will react with 1 gm of citric acid, one has:

$$\frac{1 \times 210g \text{ citric acid monohydrate}}{3 \times 84g\ NaHCO_3} = \frac{1.0g \text{ citric acid monohydrate}}{Xg\ NaHCO_3}$$

$X = 1.2g$ sodium bicarbonate to react with 1.0g of citric acid monohydrate

Similar calculations show that 2.24 gm of sodium bicarbonate react with 2 gm of tartaric acid.

$$(2 \times 84g) \quad (1 \times 150g)$$

$$\frac{1 \times 150g \text{ tartaric acid}}{2 \times 84g \ NaHCO_3} = \frac{2.0g \text{ tartaric acid}}{Xg \ NaHCO_3}$$

$$X = 2.24g \text{ sodium bicarbonate to react with } 2g \text{ tartaric acid}$$

Thus, with the acids in a ratio of 1:2, it has been calculated that 3.44 g (1.2 g + 2.24 g) of sodium bicarbonate is necessary to react stoichiometrically with the 3 g of combined acids. To enhance the flavor, the amount of sodium bicarbonate may be reduced to 3.4 gm to allow for a small amount of unreacted acid to provide a tart taste.

Method of preparation

Dry or Fusion Method

In the fusion method, the one molecule of water present in each molecule of citric acid acts as the binding agent for the powder mixture. Before mixing the powders, the citric acid crystals are powdered and then mixed with the other powders of the same sieve size to ensure uniformity of the mixture.

- The sieves and the mixing equipment should be made of stainless steel or other material resistant to the effect of the acids.
- The mixing of the powders is performed as rapidly as is practical, preferably in an environment of low humidity to avoid absorption of moisture and a premature chemical reaction.
- After mixing, the powder is placed on a suitable dish in an oven at 34 C to 40 C. During the heating process, an acid resistant spatula is used to turn the powder. The heat releases the water of crystallization from the citric acid, which, in turn, dissolves a portion of the powder mixture, setting the chemical reaction and consequently releasing some carbon dioxide.

- This causes the softened mass of powder to become somewhat spongy, and when it has reached the proper consistency (as bread dough), it is removed from the oven and rubbed through a sieve to produce granules of the desired size. A No. 4 sieve produces large granules, a No. 8 sieve prepares medium size granules, and a No. 10 sieve prepares small granules.
- The granules are dried at a temperature not exceeding 54 C and are immediately placed in containers and tightly sealed.

Wet Method

The wet method differs from the fusion method in that the source of binding agent is not the water of crystallization from the citric acid but the water added to alcohol as the moistening agent, forming the pliable mass for granulation. In this method, all of the powders may be anhydrous as long as water is added to the moistening liquid. Just enough liquid is added (in portions) to prepare a mass of proper consistency; then the granules are prepared and dried in the same manner as previously described.

H.W. Calculate the amount required from CaCO3 and KaHCO3 with citric acid and tartaric acid instead of NaHCO3?

Procedure

1. Weight 2.5 gm of citric acid and 4 gm of tartaric acid and 7 gm of NaHCO3.
2. Triturate the mixture using pestle and mortar
3. Transfer the content into beaker and heat it on the heater
4. Mix the contents properly
5. Sieve the mixture using NO. 8 sieve
6. Store it in sealed package to prevent premature effervescent