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Review on Introduction to Effervescent Tablets and Granules

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Abstract

Effervescent granules and tablets are unique dosage forms having drug and effervescent base which is composed of sodium hydrogen carbonate, citric acid and tartaric acid, these combinations when added to water react to liberate CO2, resulting in effervescence. These granules have a wide application in day to day life. In this review it gives us information regarding the various ingredients used in preparation of effervescent granules and tablets. Effervescent granules can be manufactured by various methods like Wet method, dry method or Fusion method, Hot-melt extrusion method & Non- aqueous method. Effervescent tablets can be prepared by Wet granulation, dry granulation and compression.

Key Words: Effervescence, Fusion method, Hot melt extrusion, compression etc.

Introduction

Granules are a unique type of dosage form which are composed of dried aggregates of powder solid particles which contain one or more Active Pharmaceutical Ingredients, with or without other ingredients [1].Efferevescence is derived from a Latin word which means the escape of gas from an aqueous or water solution [2].

Effervescent granules are having high solubility, high stability, fast dissolving property and are also convenient dosage forms. Just before administration these granules are to be mixed in a glass of water and this solution or dispersion should be immediately drunk.The granules are quickly dispersed by the evolution of Carbon dioxide in water due to interaction between acid and base in the presence of water. Due to the liberation of Carbon dioxide gas, we observe the dissolution of the API in water as well as taste masking effect is also enhanced [3-4].

3NaHCO3 (aq)+ H3C6H5O7(aq) -----> 3H2O(aq) +3CO2+ 3Na3C6H5O7(aq)

Sodium bicarbonate Citric acid Water Carbondioxide Sodium citrate5

Advantages: Easy to administer, easily portable, onset of action is faster, gentle on the digestive tract, it is better tasting, and more stable than liquid dosage form, marketing aspects [6-9].

Disadvantages: It is not given to children due to C02 gas toxicity, if the packaging is not done properly then there might be chances of degradation, it has shorter shelf life compared to other dosage forms [10].

Granules shows better flowability, more uniformity in particle size, more stability and more wetting11.In addition to it due to carbonation they provide pleasant taste thereby masks the unpleasant taste of the drugs [12].

Generally Tablets are defined as the unit solid dosage form of medicament with excipients and are prepared by compression or by moulding. Effervescent tablet is a dosage form whichbefore administration gets dissolved in water [13]. The tablet is broken into pieces by the internal liberation of Carbondioxide in water which is obtained by the chemical reaction of Citric acid and Tartaric acid with metal carbonates or bicarbonates. Effervescent tablets generally consist of acids (COOH) and bicarbonates (HCO3) or carbonates (CO3) [14-15].

Advantages: Opportunity for formulator to improve taste, a more gentle action on patient's stomach and marketing aspects, greater bioavailability than other dosage form, better patient compliance and rapid onset of action [16].

Another main advantage of effervescent tablet is the exact quantity of the drug enters the GIT. The Carbondioxide which is obtained in an effervescence reaction increases the penetration of active material into the paracellular pathway and thereby increases their absorption rate [17-18].

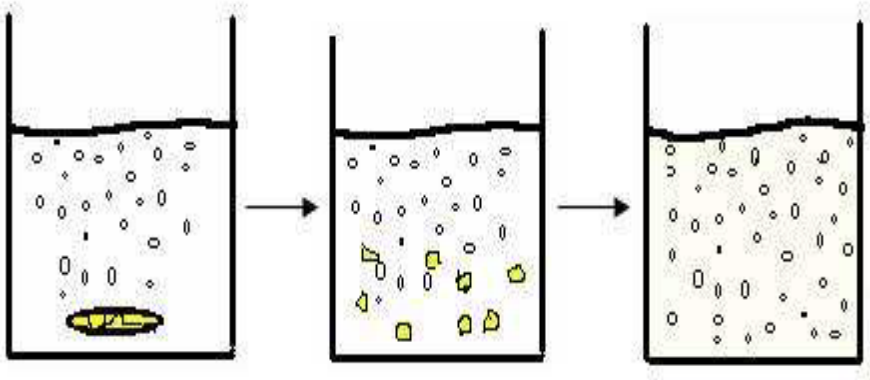
Mechanism of Effervescence:

$C_6H_8O_7.H_2O + 3NaHCO_3$ (aq) → $Na_3C_6H_5O_7 + 4H_2O + 3CO_2$ (g) ↑

Citric acid + Sodium bicarbonate → Sodium citrate + Water + Carbon dioxide

$C_4H_6O_6 + 2\ NaHCO_3 \rightarrow Na_2C_4H_4O_6 + 2H_2O + 2CO_2$ (g) ↑

Tartaric acid + Sodium bicarbonate → Sodium tartrate + Water + Carbon dioxide



Mechanism of Effervescence [19]

Fundamentals of Effervescent

The choice of ingredients for effervescent granules depends mainly on two aspects:

Requirement of the manufacturing process & the requirement of constructing a preparation which dissolves in water.

The required Ingredients are Acid &Base, additionally it also require a Sweetener and a Binding agent.

Acids: Samples of such acids include Citric acid, Tartaric acid, Malic acid, Adipic acid and Fumaric acid.

Bases: Samples of bases include Sodium carbonate, Sodium hydrogen carbonate, Potassium bicarbonate, Sodium sesquicarbonate.

Sweetener: Mannitol,Sucrose.

Binding Agent: Starch paste

Vehicle: Ethanol (non aqueous method) [20-22].

Effervescent tablets contain active pharmaceutical ingredients (API'S), compositions of acids/acid salts (citric, tartaric and malic acids), and hydrogen carbonate or carbonatesalts (sodium, potassium carbonate or hydrogen carbonate) and allof these ingredientsliberate Carbondioxide when combined with water [23].

Effervescent tablets also include various ingredients like lubricants, binders, flavors, and fillers and sweeteners.

To avoid the sticking of the tablet to the machine water soluble lubricants are used and it also prevents the formation of insoluble slurry on the water surface.

Sweetening agents are necessary in these formulations. As sucrose is hygroscopic(which absorbs water easily) it results in rise in tablet mass ,hence other sweeteners like aspartame, mannitol and sucralose are oftenly used [24].

Formulation Methodologies

The ratio of effervescent ingredients used for formulation of Effervescent formulations are (1:2:3.4) for the citric acid: tartaric acid: sodium hydrogen carbonate [25].

Effervescent Granules preparation

There are various methods of preparation of effervescent granules viz.

Wet Method, hot melt extrusion technique, Dry Method or Fusion method &Non aqueous method.

Wet Method

It is the oldest method of granule preparation .Firstly all the ingredients are powdered and are gone through a sieve to induce uniform particle size [26]. Wet massing is the most

significant step within the wet granulation process. During this step to the powdered mixture a granulating agent is added [27]. After the powdered mixture is moistened it is passed through a mesh screen to produce desired size granules. Later these granules are dried by using a hot air oven [28].

Hot Melt Extrusion Technique

Firstly weigh the required quantity of ingredients and pass them through sieve no 18.Heat it a temperature of about 50 0C to 80 0C until a molten mass is obtained.Now cool down the mass at room temperature and then pass the mass through the sieve no8 or sieve no10 to obtain granules.Finally dry the granules at a temperature not exceeding 60 ºC.29-30

Fusion Method or Dry Method

It is the most important method for the preparation of effervescent granules. In this fusion method compression step is eliminated. In this method the powders are heated using an oven or source of heat. Fusion method uses the water of crystallization present in the citric acids which acts as binding agent. The powdered mixture is stirred well to obtain a uniform mass and is passed through a sieve to obtain granules and is finally dried in an oven [31].

Non Aqueous Method

The ingredients are weighed and are taken into a chinadish. To the ingredients add drop by drop alcohol (Ethanol) until it forms a mould.Pass the mould through the sieve no 10, granules are obtained & these granules are kept in an oven at an temperature of 55o Cfor 12 hrs,the granules are again passed through the sieve to obtain uniform sized granules . These granules are further packed in Sachets and are stored for further use [32]

Effervescent Tablets Preparation

Generally Effervescent tablets can be prepared by Wet granulation, Dry granulation & Compression.

Wet Granulation

The wet granulation method is the most widely used method. The steps involved in the wet method are weighing, mixing, and granulation, screening the damp mass, drying, dry screening, lubrication and compression [33].

This method firstly involves weighing, sifting of the ingredients using sieve number 60, transferring the sifted material to Rapid Mixer Granulator, mixing it for five minutes at a slow speed and adding binder solution to it. The solution is then mixed for two minutes at a high speed. Following this, the mass is passed through a sieve and dried at 70°C using tray dryer. This is later compressed into tablets [34].

Direct Compression

The powdered mixture is directly compressed into tablets on a compression machine under 8000-12000lb of pressure.35

Dry Granulation

Dry Granulation does not involve the use of a solvent or a heat source.Out of all methods of granulation this method is the least used. The two fundamental procedures are, firstly, to create a compact of fibric by compression and then milling the compact to get granules. Two methods are used for dry granulation. Slugging is the most generally used method, where the powder is recompressed and the resulting tablets or slug are milled to yield granules. An alternative method involves recompressing the powder with pressure rolls, employing the use of a machine like a Chilosonator [36-43].

Evaluation of Effervescent Granules

[1] Angle of repose

The prepared granules were allowed to pass through a funnel and the height of the pile (h) and radius of the pile (r) are measured. From this, the angle of repose, i.e., the angle

between the height of the pile and radius of the pile is calculated with the help of the following formula.

Tan Θ = h/r

Θ = tan-1(h/r)

Here, h= height of the powder pile

r = radius of the powder pile

TYPE OF COHESION	MEASURE OF ANGLE OF REPOSE
Very low Cohesion	Less than 30°
Low Cohesion	30 to 38°
Passable	38 to 45°
Cohesive	45 to 55°

Table1: Standard limits for the measure of Angle of Repose

[2] Bulk density

A certain quantity of granules was taken in a measuring cylinder without compacting. The proper level of Granules was maintained, the volume V1 (bulk volume) was measured and calculated according to the formula given below:

Bulk density = Weight of the granules / V1

[3] Tapped density

A certain amount of granules was taken and tapped for 100 times in a measuring cylinder. Then the tapped volume (V2) is measured and calculated according to the formula given below:

Tapped density = Weight of the granules / V2

[4] Carr's Index

Carr's Index is determined by using a formula44

Carr's index ratio = [(Tapped density–Bulk density)/Tapped density] × 100

[5] Hausner's Ratio

Flow property of the powder can be determined using the Hausner's ratio. Lower the Hausner ratio betters the flow property or vice versa.Hausner's ratio is calculated by the formula.

Hausner's Ratio = Tapped density/Bulk density [45]

[6] Effervescence Time

In vitro effervescence time was measured by dissolving some quantity of the granules in a beaker containing 50 ml of Water. Granules were randomly selected from the batch and

In vitroeffervescence time was measured.Repeat the procedure for all the prepared formulations and measured the effervescent time for all the batches [46].

[7] Invitro Dissolution studies

The effervescent granules were placed inside the dissolution vessel. The USP TYPE II dissolution apparatus was used for this study of which paddle was set up at a speed of 75 rpm. Then the Samples of 1ml were withdrawn at time intervals 10, 20, 30, 40, 50 and 60 minutes. The volume of dissolution fluid is adjusted to 900 ml by replacing 1 ml of fresh dissolution medium after each sampling and thus sink condition was maintained.The dissolution media used is 0.1 N HCl and a temperature of 37 ± 0.5 0C was maintained in the apparatus [47].

Evaluation of Effervescent Tablets

Pre-compression studies

[1]Angle of repose

Angle of repose is measured to determine flow properties. A funnel is fixed and the granules are poured through the funnel

until the apex of the cone touches the tip of the funnel. Angle of repose is calculated by using a formula48:

Tan Ɵ = h/r

Ɵ = tan-1(h/r)

Where,

h = height of the cone

r = radius of the cone

[2]Bulk density

Granules are weighed accurately and added into the measuring cylinder. The level is observed and noted. Bulk density can be determined by the following formula:

Bulk density = M / V0

Here,

M = Mass of the powder

V0 = Apparent untapped volume

[3]Tapped density

After the measurement of bulk density, the cylinder is tapped for 500 times and the final volume is noted. The density after tapping can be determined by [49]:

Post-Tapping Density= M / V2

Where,

M= Mass of the powder

V2= Tapped volume

[4] Carr's Index

Carr's index ratio involves both then Bulk density and the Tapped density

Carr's Index = (Tapped density –Bulk density) / Tapped density × 100

[5] Hausner's Ratio

Hausner's ratio is the ratio of Tapped density to the Bulk density [50]

Hausner's Ratio = Tapped density / Bulk density

Post compression studies:

[1] Weight Variation

Weight variation was performed to know the tablet uniformity. 20 tablets were weighed individually and there average weight was also noted. Now the individual tablet weight is compared with the standard.The tablets pass the test if not more than two tablets are outside the % limit and none of the tablet differ by more than two times the % limit [51].

Indian Pharmacopoeia/British Pharmacopoeia	LIMITS	United States Pharmacopoeia
≤80mg	10%	≤130mg
80mg to 250mg	7.5%	130mg to 324mg
≥250mg	5%	>324mg

Table 2: Specification of weight variation.

[2] Thickness, diameter and hardness

The diameter and thickness of the tablet is tested using Vernier Callipers. Hardness of the tablet is tested using Monsanto Hardness tester [52].

[3] pH of the solution

pH of the solution can be determined using a pH Meter. Dissolve a tablet in 200ml of water at 20 ± 1 °C after immediate dissolution check the pH [53].

[4] Moisture Content

10 tablets were taken and weighed and are put in a dessicator for 4hrs and are weighed again after removing, the difference between the weight weighed before and after gives us the moisture content.

Moisture content of 0.5% or less is acceptable [51].

[5]Friability

The tablets' friability was measured using an instrument called Roche's friabilator at 25 rpm for duration of 4 minutes. The final weight of the tablets was noted and compared to their initial weights for Friability studies [54].

[6] Dissolution studies

The tablets were weighed and are dissolved in a dissolution medium (0.1 N Hydrochloric acid) at a temperature of 37 ± 0.5 ^{0}C. The time of dissolution was noted and at regular mean times test samples were collected and analysed under Ultraviolet-visible Spectroscopy [55].

Conclusion

An effervescent formulation produces quicker action. Effervescent tablets are prepared by Dry method, Wet method and Compression, in which Wet method is the most widely used for formulation of Effervescent Granules. Effervescent granules are prepared by Wet method, Fusion method or dry method, hot melt Extrusion method, in which the Fusion method is the most important method for the formulation of Effervescent granules.

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