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A review on Effervescent Tablets

K. Munirajalakshmi*, P. Keerthana, O. Koushik, G. Himabindhu, T. Usha kiran Reddy, G. Sindhu, CH. Apparao

S V University College of Pharmaceutical Sciences, S V University, Tirupati-517502, A.P, India

A B S T R A C T

Oral dosage forms are the most popular way of taking medication, despite having some disadvantages compared with other methods like risk of slow absorption of the medicament, which can be overcome by administering the drug in liquid form, therefore, possibly allowing the use of a lower dosage. However, instability of many drugs in liquid dosage form limits its use. Effervescent technique can be used as alternate to develop a dosage form which can accelerate drug disintegration and dissolution, is usually applied in quick release preparations. Along with the development of new pharmaceutical technique, effervescent tablets are more and more extensively to adjust the behaviour of drug release, such as in sustained and controlled release preparations, pulsatile drug delivery systems.

Keywords: Oral dosage, medication, pulsatile drug delivery systems, liquid dosage form

A R T I C L E I N F O

Corresponding Author
K. Munirajalakshmi
S V University College of Pharmaceutical Sciences,
S V University, Tirupati-517502, A.P, India

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1. Introduction

Effervescent tablets are the uncoated tablet formulations where the drugs are made to be easily dissolved in the water. They are the mixture of carboxylic acid and carbonate hydrogen carbonates. They are the dosage forms that are to be administered by dispersing the drug in the water even before the administered in the body[23]. Effervescent products are those formulations where they are able to releasing carbon dioxide (sodium carbonate and sodium bicarbonate) and an agent that induces releases of CO2 (adipic acid, malic acid, tartaric acid, ascorbic acid, fumaric acid, maleic acid, succinic acid, or citric acid)[24]. The active pharmaceutical ingredient is present either in the effervescent granules or may be present in the salt form at the time of dissolution. Effervescent tablets are formulated by mixing these active drug substances along with binders, diluents, and lubricants, and then compressing them into tablets[25]. Water-soluble lubricants are used such as sodium benzoate, polyethylene glycol, and adipic acid. Effervescent tablets do not need disintegrants incorporated into their formulations as the evolution of in situ CO_2 facilitates the disintegration process [24].

Effervescence reaction

$3NaHCO_3$ (aq) + H3C6H5O7 (aq) → 3H2O (aq) + 3CO2 (g)+ 3Na3C6H5O7 (aq) Effervescence reaction equation[25].

The two aspects that decides the choice of ingredients in the formulation of an effervescent preparation are:

Manufacture process requirements and the requirement to prepare a dosage dissolving in the water

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

Acids: Acids include citric acid, Tartaric acid, Malic acid, Adipic acid and Fumaric acid[25].

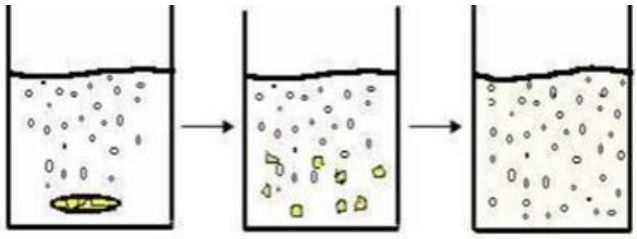
Bases: Bases include Sodium carbonate, Sodium hydrogen carbonate, Potassium bicarbonate, Sodium sesquicarbonate[25].

Sweetener: Mannitol, Sucrose.

Binding Agent: Starch paste

Solvent: Ethanol (non-aqueous method)

Effervescent preparations mostly contain and include the active pharmaceutical ingredient and the acid/acid salts (citric, tartaric and malic acids), and also hydrogen carbonate salts or carbonate salts (sodium, potassium carbonate or hydrogen carbonate). All the materials in the pharmaceutical preparations include the substances that releases the carbon dioxide when dissolved in water or also when directly put in the water[27]. Effervescent tablets also include various ingredients like lubricants, binders, flavours, and fillers and sweeteners. Sweetening agents are very important in these formulations. As sucrose is hygroscopic(which absorbs water easily) it could be the major reason for the increase in the mass of the tablet, hence other sweeteners like aspartame, mannitol and sucralose are often used[28].



Dissolution of tablets

Materials used for the preparation of effervescent powders[15]:

- Citric Acid
- Tartaric Acid
- Malic Acid
- Fumaric Acid
- Adipic Acid 4598
- Sodium Bicarbonate
- Sodium Carbonate
- Sodium Sesquicarbonate
- Potassium Bicarbonate

Advantages of Effervescent Tablets:

- Effervescent preparations are mostly fast in their onset of action[16].
- The tablets are not needed to be swallowed.
- Good in the intestine and stomach and much better tolerance.
- They are portable.
- Improved palatability.
- Since they can release the carbon dioxide in the water and they are solid dosage forms they are very good in stability[16].
- They can be incorporated with large amounts of doses than normal dosages
- They are the perfect dosage forms when as they can release sustained and consistent release of the drugs.
- Accurate Dosing.

Disadvantages of Effervescent Tablets:

- Some of the dosage forms have bad tase and smell and that will make it difficult for the tablets or powders to be administered and prepared[17].
- Larger tablets would need different kinds of packing materials.
- Relatively expensive to produce due to large amount of more or less expensive excipients and special production facilities[16].

METHODS

FORMULATION OF EFFERVESCENT POWDERS

Wet method:

At first the ingredients are powdered and then they are taken into the sieving process inorder to produce desired size of the particles. Wet messing is the most famous process used in the formulations.[1] The powdered drug binder material is added with granulating agents where it helps in granulating the drug substance and then after that it is cooled and then it is made into solid granules.[4]

Dry granulation:

Dry granulation is a process in which there is no presence of heat or solvent inorder to prepare granules[2]. It is the least used method among all the granulation methods. it includes two processes where the drug is first taken into the compaction process and then its milled to form granules. There are two methods of formulation, Slugging is the most common way. Where the compaction is made and then the milling takes place where the granules get separated.[1]

Wet Granulation:

In this method first the material is weighed and then all the weighed material is sifted with the sieve No.60 and then the sifted material is transferred to a Rapidmixer Granulator, where it is mixed for 5 mins slow speed and then the binder solution is added to it. The solution is then mixed for two minutes at a high speed[3]. After this, the solution is passed in to a sieve and dried at 70^{o} C using tray drier, and then they are made into tablets where this is called slug. After this the milling process continues where the tablets are converted into granules. An alternative method involves recompressing the powder with pressure rolls.[3]

Roller compaction:

Compaction of powder by means of pressure roll can also be accomplished by a machine called Chilsonator. Unlike tablet machine, the chilsonator turns out a compacted mass in a steady continuous flow[4]. The powder is fed down between the rollers from the hopper which contains a spiral auger to feed the powder into the compaction zone. Like slugs, the aggregates are screened or milled for production into granules[5].

Advancement in Granulations

Steam Granulation:

It is modification of wet granulation. Here steam is used as a binder instead of water. Its several benefits includes higher distribution uniformity, higher diffusion rate into powders, more favourable thermal balance during drying step, steam granules are more spherical, have large surface area hence increased dissolution rate of the drug from granules, processing time is shorter therefore more number of tablets are produced per batch, compared to the use of organic solvent water vapour is environmentally friendly, no health hazards to operators, no restriction by ICH on traces left in the granules, freshly distilled steam is sterile and therefore the total count can be kept under control[4].

Melt Granulation / Thermoplastic Granulation:

In this type of granulation, the granules are obtained by adding mouldable binder. Where the binder is solid in room temperature and it gets converted to liquid in temperature ranging from 50 - 70 and this is ultimately used as binding liquid[5]. In this method the drying process is not required since the material gets dried by cooling as the binder is solid in room temperature [5].

FORMULATION OF EFFERVESCENT TABLETS

Tablet Compression: Compression of effervescent tablets is very much different from compression of normal traditional tablets, a general effervescent tablet should have very low moisture content i.e., 0.3%, whereas the remaining drugs would require 2% moisture content in the compression[20]. An additional drawback is that, typically, these types of formulations contain only small amounts of binders in order to facilitate easy dissolution and disintegration of the drug in the water[21]. In some cases, the tablet compression is provided with moisture content of 2-3% in order to maintain trouble free compression but eventually it is reduced to 0.3% after the compression by drying to maintain stability of the drug. Additionally, it's important that there is a seamless connection between the drying step, the compression step and the post-drying step as any delays could destabilize the formulation [21].

Lubricants

Lubricant addition to a medicament is a most common practice in the tablet production, the most commonly used substance is magnesium stearate. The lubrication in the formulation is important to improve the flow of the tablet, this is very much important to improve the flow because the tablets dyes are filled with the bulk volume. The second function is to prevent the tablet sticking to the dyes at the time of punching. During the effervescent preparations the tablets should not be used with lubricants such as magnesium stearate as they are not soluble in water, they could form a thin film on the layer. The theory to prevent this phenomenon is to use lubricants that are soluble in water [22].

2. Evaluation of Effervescent Powders

Angle of repose:

The granules that are already prepared are poured from 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 if the pile and the radius of the pile are calculated with the help of the below formula[6].

$\tan \Theta = h/r$

$\Theta = \tan^{-1} (h/r)$

Here, h= height of the powder pile
r = radius of the powder pile [6]

S.no	Type of cohesion	Measure of angle of repose
1	**Very low Cohesion**	**Less than 30°**
2	**Low Cohesion**	**30 to 38°**
3	**Passable**	**38 to 45°**
4	**Cohesive**	**45 to 55**

Bulk density

The bulk density is obtained by dividing the bulk mass with the volume in cm^3. The sample of the substance of 50 cm^3 which is already passed into the sieve no. 20 was carefully taken into a 100ml graduate cylinder[7]. The cylinder was dopped at 2-second intervals 3 times on a hard wooden plankfrom a height of 1 inch from the wooden plank. The bulk density of the formulation can be obtained by dividing the weight of the sample in grams to the final volume obtained in cm^3 in the container after 3 consecutive tapping. It is calculated by using equation below [6]:

$D_f = M/V_p$

Where

D_f = bulk density

M = weight of samples in grams

V_p= final volumes of granules in cm3

Tapped density:

The tapped density is obtained by dividing the bulk mass with the volume in cm^3. The sample of the substance of 50 cm^3 which is already passed into the sieve no. 20 was carefully taken into a 100ml graduate cylinder [7]. The cylinder was dopped at 2-second intervals 100 times on a hard wooden plank from a height of 1 inch from the wooden plank. The tapped density of the formulation can

be obtained by dividing the weight of the sample in grams to the final volume obtained in cm^3 in the container after 100 consecutive tapping. It is calculated by using equation below[7]:

$D_o = M/V_p$

Where

D_o= bulk density

M = weight of samples in grams

V_p = final volumes of granules in cm3

Weight Variation

Weight variation is a method of evaluation to maintain tablet uniformity, each tablet is weighed and the tablet weight is noted down separately [9]. Then the individual tablet weight is compared with the standard weight of the tablets. The tablets pass the test when they do not cross the percentage limit i.e., none of the tablets should have the % weight greater than 2 times the % limit[9].

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 [10].

pH:

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 [11].

Moisture Content

10 tablets were taken and weighed and are put in a desiccator for 4hrs and are weighed again after removing, the difference between the weight weighed before and after gives us the moisture content[14]. Moisture content of 0.5% or less is acceptable

Friability

The tablets' friability was measured using an instrument called Roche's friabilator at 25 rpm for duration of 4 minutes[12]. The final weight of the tablets was noted and compared to their initial weights for Friability studies[13].

Dissolution studies

The tablets were weighed and dissolved in a dissolution medium, (0.1 N Hydrochloric acid) at a temperature of 37 ± 0.5℃ the time of dissolution was noted and then the test samples are collected and observed under Ultra violet -Visible spectroscopy on regular intervals [11].

Packaging

When the material is pressed in the tablets the surface area of the tablet is eventually reduced, which means that the rate of absorption of moisture from the air in the granules is also reduced significantly. Consequently, the dehumidification of the environmental air is now less critical.

Storage & Labelling:

Effervescent formulations should be stored in a place away from moisture content they have to be stored in a closed packs preventing air entering the pack and they had to be kept away from atmospheric moisture content. These should be labelled that these products are not allowed to be swallowed directly but had to be dissolved in water before consumption. The label should also mention that the tablets should not open until the time of dissolving them into the water if they are packed separately.

2. Conclusion

The Effervescent tablet of Sodium Alendronate and Vitamin D3 is a new pharmaceutical formulation to be taken orally and offering a considerable advantage: avoidance of gastro-intestinal disorders, to the limits of the possible. Another aspect of this invention is that the absorption of the active ingredient is faster when compared to the tablet form; consequently, an enhanced bioavailability of the active ingredient is probable.

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