Review Article

A Short Review on Formulation and Evaluation of Effervescent Tablets

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ABSTRACT

The most common pharmaceutical delivery technique is oral dose forms, although there are significant drawbacks compared to other delivery systems, such as the potential for drug absorption, which can be reduced by giving the medication in a liquid form. Reduced dose use is one potential advantage of doing this. Because some medications are unstable in their liquid dose form, there is a problem that limits the use of liquid dosage forms. There is a different approach that uses the effervescent process to create dose forms. This technique has the benefit of speeding up medication dissolution and disintegration. The product made using this technique is an example of the quick release preparations. A few of the products of this technique include pulsating drug delivery systems, sustained and controlled release preparations, and effervescent tablets, which play a large role in managing drug release behaviour. This review demonstrated how to use an effervescent tablet in a new way.

Keywords: Effervescent tablets, Oral dose form, Liquid dose form, Drug delivery system, Medication.

INTRODUCTION

Among all the ways that have been used for the systemic distribution of drugs via diverse pharmaceutical products of varied dose forms, oral drug delivery has long been recognised as the most frequently used route of administration. Its simplicity of administration may be part of the reason why the oral route attained such widespread acceptance[1-2]. Rapid GI transit can prevent full drug release in the absorption zone and lessen the effectiveness of the dose that was administered[3-4]. This can be overcome by administrating the drug in liquid from but, many APIs have limited level of stability in liquid form. So, effervescent tablets acts as an alternative dosage form[5]. Effervescence has been employed for years as an oral medicine delivery system in the pharmaceutical and dietary industries. As per revised definition proposed to US FDA, Effervescent tablet is a tablet intended to be dissolved or dispersed in water before administration. In addition to active ingredients, it generally contains mixture of acids/acid salts and carbonate and hydrogen carbonates which release carbon dioxide when mixed with water[6].

Effervescence is the evolution of gas bubbles from a liquid, as the result of a chemical reaction.

$$C_6H_8O_7\ (aq) + 3NaHCO_3\ (aq) \rightarrow Na_3C_6H_5O_7\ (aq) + 4H_2O + 3CO_2\ (g) \uparrow$$

Citric acid + Sodium bicarbonate → Sodium citrate + Water + Carbon dioxide[7]

Effervescence has been employed for years as an oral medicine delivery system in the pharmaceutical and dietary industries. Many different effervescent pills have been created over time. In addition to many preparations of prescription medications like antibiotics, ergotamine's, digoxin, methadone, and L-dopa, they also include dental enzyme compositions, contact lens cleaners, washing powder compositions, beverage sweetening tablets, chewable dentifrice, dental cleansers, and effervescent candies. Additionally, veterinary preparations have been created[7]. Effervescent tablets are favoured over tablets or capsules with a difficult consumption for some people since they are administered in liquid form and are simple to swallow. But one effervescent tablet dose is typically diluted in 3–4 ounces of water. The gastrointestinal system is not directly exposed to effervescent items since they have been dissolved in a buffer solution first. As a result of decreased gastrointestinal irritation, they might be well tolerated in the stomach and intestine. Another benefit of effervescent tablets is that when a patient takes one, exactly the prescribed dosage is absorbed by the stomach. Actually, the CO2 generated during an effervescence event improves the penetration of active compounds into the paracellular route and, as a result, their absorption[8,9].

EFFERVESCENT TABLETS BENEFITS OVER REGULAR TABLETS[10]:

Good taste:

Due to its ability to dissolve in a liquid, such as water or fruit juice, effervescent pills are particularly well-liked since they frequently taste better than ordinary tablets. Effervescent pills dissolve quickly, allowing you to benefit fully from the components while regular tablets dissolve slowly, which can result in reduced absorption rates.

Good distribution:

Imported regular tablets can occasionally be slightly distributed and dissolve slowly in the stomach, which can occasionally cause irritation. The benefit of an effervescent pill is that all of the contents entirely dissolve equally, so they cannot build up. This signifies not only the finest

flavour but also a lower risk of irritability and more effective ways to incorporate components.

More liquid intake:

Effervescent pills improve fluid consumption in addition to offering nutritional advantages. If you are sick or dehydrated and not taking in as much hydration, this is helpful. Effervescent pills, whether they are being used as a dietary supplement, herbal remedy, or for medical purposes, might be the greatest approach to rehydrate while still receiving the advantages of the medication.

Alternative to regular:

They are regarded as a terrific alternative for people who might have difficulty swallowing as a result of illness or advancing age. Effervescent tablets can make taking medication or supplements much easier for older adults who occasionally have trouble swallowing but still need to do so on a regular basis. Additionally, they are an excellent alternative to normal pills for those who have sore throats or medical conditions that make swallowing difficult because they can be a great way to take medication.

Simple and easy measurement:

Effervescent pills are uniform, blended, and ready to drink. They dissolve quickly into water or a liquid of your choosing. To prevent a lumpy bit, traditional tablets or powders must be measured and repeatedly agitated. Effervescent pills function best in situations where the drink is inconsistent and has bumps and bumps, despite stimulating and measuring. To guarantee you receive all the benefits of the pill and can properly consume it, simply install them and dispose of them completely and evenly.

FUNDAMENTALS OF EFFERVESCENTS[10]:

Effervescence consists of a soluble organic acid and an alkali metal carbonate salt, one of which is often the API. Carbon dioxide is formed if this mixture comes into contact with water. Typical examples of the acids and alkalis used include:

- Citric acid
- Tartaric acid
- Malic acid
- Fumaric acid
- Adipic acid
- Sodium bicarbonate
- Sodium carbonate
- Potassium bicarbonate
- Potassium carbonate
- Sodium sesquicarbonate

ADVANTAGES[11,12]:

- Fast onset of action.
- No need to swallow tablet.
- Good stomach and intestinal tolerance.
- More portability.
- Improved palatability.
- Superior stability.
- More consistent response.
- Incorporation of large amounts of active ingredients.
- Accurate Dosing.
- Improved Therapeutic Effect.
- In remote areas, especially where parenteral forms are not available due to prohibitive cost, lack of qualified medical staff, effervescent tablets could become an alternative.

DISADVANTAGES[13,14]:

- Unpleasant taste of some active ingredients.
- Larger tablets requiring special packaging materials.
- Relatively expensive to produce due to large amount of more or less expensive excipients and special production facilities.
- Clear solution is preferred for administration, although a fine dispersion is now universally acceptable.

FORMULATION:

It typically also comprises a combination of acids, acid salts, carbonate, and hydrogen carbonates, which when combined with water, generate carbonic acid gas.

Drugs that are formulated as effervescent tablets:

1. Medications that are hard to digest or that disturb the stomach: If the carbonate is consumed in an effervescent form, the calcium dissolves in water, is immediately absorbed by the body, and there is no risk of excessive gas in the stomach or constipation brought on by low stomach acid levels.
2. pH-sensitive medications, such as antibiotics and amino acids: Effervescent formulation can buffer the water-active solution, causing the stomach's pH to rise (become less acidic), preventing the active ingredient from degrading or becoming inactive due to the stomach's low pH.
3. A typical effervescent tablet (1 inch in diameter, 5 g total weight) can contain up to 2 g of water-soluble active components in a single dose of medication. The sachet (powder form) is the typical method of delivery if the prescribed dose is more than that.

FORMULATION METHODS:

Different Methods for formulation of Effervescent Tablet.

Wet granulation[15-27]:

Wet granulation is the agglomeration method that is most frequently utilised. Simple wet massing of a powder mixture with a granulating liquid, wet sizing, and drying constitute the wet granulation process. Wet granulation method further may be divided in two types looking on the amount of process steps- Important steps involved within the wet granulation.

- Drying of moist granules.
- Mixing of binder solution with powder mixture to make wet mass.
- Preparation of binder solution.
- Mixing of the drug(s) and excipients Mixing of screened granules with disintegrate, gliding, and lubricant.

Advantages:

- Permits mechanical handling of powders without loss of mix quality.
- Improves the flow of powders by increasing particle size and sphericity.
- Increases and improves the uniformity of powder density.

Disadvantages:

- Loss of fabric during various stages of processing.
- Two-step granulation method the best disadvantage of wet granulation is its cost.
- It's a fashionable process due to labour, time, equipment, and energy and space requirements.

Dry granulation[24-31]:

A dry granulation procedure involves pressing the powder combination without the use of heat or solvent. Nonetheless, is less preferred in all granulation techniques. Compressing and grinding a material compact to produce grains are two fundamental operations. There are two approaches to dry granulation. Slugging is the technique that is most frequently employed; when powder is present, it is crushed once more, and the tablet or slug that results is accessible to remove granules. Another method involves employing a device like a Chilosonator to reproduce the fine powder with pressure rolls.

Roller compaction[31-34]:

A device known as a chilsonator can be used for compression utilising a pressure roll. A chilsonator is weight mixed with continuous flow, unlike a tablet machine. From the hopper, which has a spiral auger feeding powder compaction region, the powder is fed between the rollers. Aggregates are screened to create granules, just like slugs.

Steam granulation[35,36]:

It alters the process of moist granulation. Instead of using water, steam is used here as a binding agent. Among its many advantages are its high uniform distribution, fast rate of powder distribution, favourable heat balance during drying, steam granules' rounded tops, and incomparison to the use of organic solvent vapour, water is more environmentally friendly, poses no health risks to workers, does not have ICH restrictions regarding the tracks left on the granules, and produces more tablets per set due to processing times being shorter and the steam being contamination- and sterility-free. Low dissolving rates can be utilised to prepare flavour granules without affecting drug availability, allowing the overall value to be kept under control.

Melt granulation[37-39]:

This method employs a mouldable binder to achieve granulation. The binder is solid at room temperature but melts between 50 and 80 degrees Celsius. Then, a binding liquid is created using this melted binder. There is no requirement for a drying phase in this procedure because granules can be dried by allowing them to cool to room temperature.

EVALUATION:

1. Angle of repose[40]:

The angle of repose is determined by using the funnel method. Effervescent Granules are poured from the funnel, that can be raised vertically until a maximum cone height, h, diameter of the heap, D, is measured. The repose angle θ is calculated by the formula

$$\tan \theta = 2h / D$$

2. Bulk density[41]:

Bulk density is determined by placing Effervescent Granules into a graduated cylinder and measuring the volume and weight.

3. Trapped density[41]:

Tapped density is determined by placing a graduated cylinder, containing a known mass of Effervescent Granules on mechanical tapping apparatus, which is operated for a fixed number of taps until the Effervescent Granules bed volume is reached a minimum. Using the weight of Effervescent Granules bed in a cylinder and this minimum volume, the tapped density is calculated.

4. Compressibility index and Hausner ratio[42]:

It is measured for the property of Effervescent Granules to be compressed. As such they are measured for the relative importance of inter particulate interactions. The compressibility index is calculated by the following equation:

{(Dt – Db)} × 100

Where Dt = Tapped Density.

Db = Bulk Density

Hausner ratio was calculated by the following equation

Dt / D0

Where Dt = Tapped Density.

D0 = Bulk Density.

Physicochemical Evaluation of the Effervescent Tablets:

1. Weight variation

Twenty Effervescent tablets are selected randomly and weighed individually. The average weight and standard deviation of all twenty Effervescent tablets are calculated[43].

2. Thickness

The thickness of the Effervescent Tablet is measured by using a sliding calliper scale, twenty Effervescent Tablets are selected randomly in a holding tray and total crown thickness is measured[43].

3. Hardness

The hardness of the Effervescent Tablet is measured using hardness testers.

4. Friability

Weighed twenty Effervescent Tablets are put into the Roche friabilator. With each revolution, the Effervescent Tablet is dropped six inches away at a speed of 25 rpm. After that, the Effervescent Tablets are reweighed and dusted[43].

5. Disintegration time:

A large number of gas bubbles are released when you place an effervescent tablet in a beaker with 200 ml of water at temperatures between 1500 and 2500 C. when there is no longer a clump of particles and the gas evolution surrounding the effervescent tablet ends in the water. Five further Effervescent Tablets are tested once again[44].

6. Solution pH

Solution of pH is measured with a digital pH meter in standardized water volume and temperature. Place an Effervescent Tablet in a beaker containing 200 ml of water at 1500C to 2500C. The pH is measured after complete disintegration of the Effervescent Tablet is done[45].

7. Drug content determination

Drug content is determined by dissolving the Effervescent Tablet in 200 ml of water. Determine Drug content absorbance of this solution, using UV Spectrophotometer to know how much drug is present in the tablet[46].

8. *In-vitro* drug release study

With the right dissolution media and a variety of instruments, in-vitro release tests were conducted. The dissolving medium's temperature was held constant at 37 0.5 °C. The release study takes 3.30 hours to complete. At a certain period, an aliquot of the dissolving medium is removed and filtered. Next, absorbance is calculated[46].

9. Measurement of CO_2 content

After one effervescent tablet has been completely dissolved in 100 ml of 1N sulphuric acid solution, weight changes are calculated. The weight differential that was found reveals how much CO2 (in milligrams) is in each tablet. Three measurements are averaged.

10. Evaluation of water content

10 tablets of the formulation are dried in a desiccator containing activated silica gel for 4 hours. The water content of 0.5 % or less is an acceptable parameter.

11. Uniformity of content

Ten tablets are chosen at random. Each tablet is put into a volumetric flask measuring 50 mL, where it is dissolved and diluted to that volume with phosphate buffer pH 6.8. This solution is diluted to a pH 6.8 of 100 ml from 1 ml using phosphate buffer. Each pill contains mg of the medication determined at 246 nm by UV spectroscopy.

IP: - Active less than 10 mg or 10 %,

BP: - Active less than 2 mg or 2 %,

USP: - Active less than 25 mg or 25 %.

12. Determination of the equilibrium moisture content

Saturated salt solutions of potassium nitrate (for creation 90% RH, at 18 °C), sodium chloride (for creation 71% RH, at 18 °C), and sodium nitrite (for creation 60% RH, at 18 °C) are made for three desiccators. Each formulation's three pills are put in desiccators. The Karl Fischer method and an auto titrator device are then used to determine the equilibrium moisture content on the first day and after seven days[47-48].

CONCLUSION

Regular tablets might be difficult to administer, therefore effervescent tablets are an excellent option.

Effervescent tablets can be taken with ease by the elderly or others who have difficulty swallowing because they must be taken after dissolving in water rather than being swallowed. Due to their high absorption, effervescent pills have a good therapeutic impact. Nowadays, more effervescent vitamins are produced since they are easier to take and improve patient compatibility. In addition to making administration easier, effervescent tablets also hide the taste of some components, reducing the need for flavouring additives. Effervescent tablets may help with issues with conventional tablets, such as stomach

compatibility. The person using effervescent tablets will feel better quickly because of their quick onset of effect.

The easiest way to hide the taste of the medication is to take effervescent pills, which also have a speedier onset of action, good compatibility, and a good therapeutic impact. The greatest part is that it enhances patient compliance.

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