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Review Article

A Comprehensive Review on Effervescent Tablets

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Abstract

Effervescent tablets are becoming increasingly popular due to their ease of administration and rapid onset of action. They typically contain acidic materials and carbonates or bicarbonates that react quickly in the presence of water, releasing carbon dioxide and improving API solubility and flavour masking. However, effervescent tablets can be bulky, and the reaction rate is difficult to control due to water's catalytic effect. This article discusses the advantages and disadvantages of effervescent tablets, common effervescent reactions, active ingredients that can be formulated, and the preparation and manufacturing process. It also evaluates effervescent granules and tablets and explores the latest advancements in effervescent technology. Overall, effervescent tablets offer a promising option for drug delivery, and ongoing research will undoubtedly yield even more advanced formulations in the future.

Keywords: Effervescent granules, Effervescent tablets, Hot melt granulation, Carbon dioxide content, Water activity

Introduction:

For decades, oral drug administration has been acknowledged as the most widely used mode of administration among all techniques employed for the central administration of drugs through several pharmaceutical items in varied dose forms. The popularity of the oral route can be attributed in part to its simple and straightforward administration. Future market trends predict that the worldwide oral solid-dosage pharmaceutical formulation business will rise from 489.5 billion dollars in 2017 to 925.5 billion dollars by 2027.[1] In terms of physical, chemical, and microbiological properties, solid tablets are the most durable oral dose form when compared to oral liquids, capsules, solutions, or suspensions.[2] There are various sorts of tablets in the market, each with its own set of drawbacks. Slow absorption is a significant drawback because it prolongs the start of the effect. This issue could be handled by producing effervescent tablets.[3]

According to Indian Pharmacopoeia, effervescent tablets are tablets without coatings that include acidic materials and both carbonates/ bicarbonates that react quickly in the prevalence of water and release CO_2, and authorized flavouring ingredients. They are designed for dissolution or distributed in water before being administered.[4] Saline cathartics became the first effervescent formulations to be produced in the eighteenth century.[5,6]

Effervescent tablets typically contain acids or acid salts such as citric acid, tartaric acid, malic acid, or any other appropriate acid or acid anhydride and carbonates/ bicarbonates such as sodium, potassium, or any other appropriate alkali metal carbonate or hydrogen carbonate, which rapidly react in contact of water via releasing the carbon dioxide. API solubility in the water and flavour masking are both improved on account of CO_2 gas liberation.[3,7–11]

Typically, acid-base neutralisation reactions occur in effervescent formulations by releasing effervescence of CO_2 and producing buffered salt as a product of the reaction. The interaction between citric acid and the sodium salt of bicarbonate is the most prevalent effervescent reaction.

As water is present to catalyse the reaction, even in little amounts, the reaction proceeds more quickly. All moisture-sensitive or effervescent items are kept in a moisture-free environment since water catalyses the reaction.[9,12,13]

Pros of effervescent tablets:

Popular dosage forms that have several advantages over other methods of pharmaceutical delivery include effervescent formulations. The following are some pros of effervescent formulations:

- Faster onset of action: In contrast with medicine types, effervescent formulations quickly dissipate in water and are absorbed by the body. This may lead to a quicker start to action and quicker symptom relief.[6]
- Better bioavailability: Effervescent preparations may improve a drug's bioavailability, which is the amount of

the active component that is absorbed by the body and is readily available to have a therapeutic effect.[6]

- More feasible: Patients who struggle to swallow will find effervescent formulations more convenient because they can be dissolved in water.[14]
- Better taste: Effervescent formulations frequently have a tasty flavour, which can increase patient compliance and drug adherence.[14]
- Reduced gastrointestinal irritation: By buffering the stomach acid, effervescent formulations might lessen the gastrointestinal irritation brought on by some drugs.[15]
- Improved portability: When compared to liquid dose forms, effervescent tablets are easier to store and transport because of their compact form.[10]
- Increased palatability: Flavouring agents are frequently used in the formulation of effervescent tablets to enhance their flavour and increase patient acceptability. This might be especially helpful for children and older people who may have trouble swallowing regular tablets or capsules.[9]
- Good stability: Effervescent pills have good stability in general. This is a consequence of the tablet packaging shielding the active chemicals from the outside environment, preventing them from being exposed to oxygen or moisture, which may lead some medications to deteriorate and become ineffective.[8]
- Improved absorption: Effervescent formulations have been prepared to dissolve fast in the water[16], which can help the active components be absorbed more readily. This is so that the medication will be spread more equally and have a larger surface area during the effervescence process, which will make it easier for the body to absorb it.[17,18]
- Prevents first-pass metabolism: Effervescent tablets have the ability to prevent first-pass metabolism, which is the liver's breaking down of a drug before it enters the bloodstream. This is an instance of medication's direct bloodstream absorption from the digestive system, avoiding the liver.[11]
- Can include a high amount of active ingredient: Effervescent formulations can contain lots of active compounds, which may be very helpful for drugs that need greater doses. This is so because, in comparison to other medicine forms, the effervescent tablets matrix may hold a greater volume of active chemicals.[14]
- Exact dosing: Effervescent tablets deliver an exact quantity of active components on account of the available tablet dosage form.[11]
- Possibility of a therapeutically-appropriate combination of numerous active ingredients: Effervescent tablets can combine more than one active component if doing so is therapeutically acceptable on account of the relatively large tablets.[17]

Cons of Effervescent tablets:

- Bigger tablets: Tablets that are effervescent are often larger in size than ordinary tablets, necessitating specific packaging.[3,9]
- Complex process: when compared to traditional tablets, this requires correct temperature and humidity conditions, making it a difficult moreover pricey procedure.[3,9]
- Sensitive packaging: because these tablets are prone to hygroscopicity, it requires sensitive packing that includes a desiccant.[3,9]
- Some active compounds have off-notes: some active compounds have off-notes that cannot be disguised by flavourings or sweeteners. This will result in an unsatisfactory product.[14]
- Required time for disintegration: the disintegration of tablets might take up to 5 minutes. This is mostly determined by the temperature of the water and active substances present.[14]

Common Effervescent reactions:

The interaction of citric acid with sodium bicarbonate is the most common effervescent reaction, and it's employed in the most effervescent formulations. In this reaction, 1 mol of citric acid reacts with 3 mol of the sodium salt of bicarbonate in the presence of water, yielding 1 mol of sodium citrate as a product and 3 mol of CO_2 in the form of effervescence and 3 mol of water as a by-product. (Figure 1)

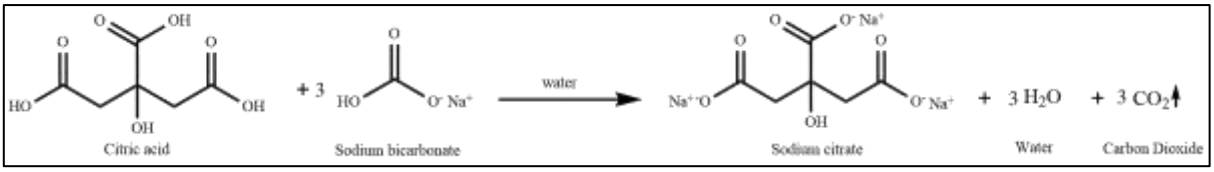

Figure 1: Reaction between citric acid and Sod. bicarbonate

The reason that sodium carbonate possesses a pH value that's greater than sodium bicarbonate[19], it is frequently substituted with sodium bicarbonate. In this reaction, 2 mol of citric acid reacts with 3 mol of the sodium salt of carbonate in the presence of water, yielding 2 mol of sodium citrate as a product while emitting 3 mol of CO_2 as effervescence and 3 mol of water as a by-product. (Figure 2)

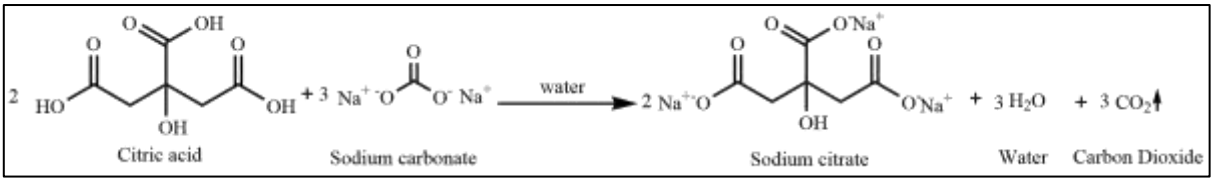

Figure 2: Reaction between citric acid and Sod. carbonate

Calcium carbonate i.e., $CaCO_3$ has poor water solubility, but when it interacts with citric acid, the result is water soluble, meeting the demand for effervescent formulations[19]. In this reaction, 2 mol of citric acid reacts with 3 mol of calcium carbonate in the presence of water, yielding 1 mol of calcium citrate as a product and 3 mol of CO_2 in the form of effervescence and 3 mol of water as a by-product. (Figure 3)

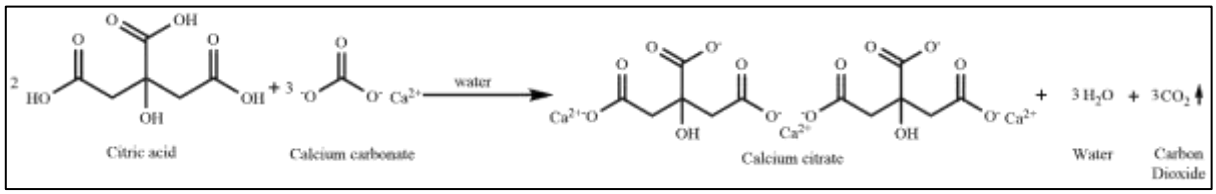

Figure 3: Reaction between citric acid and Cal. Carbonate

Tartaric acid, which is more water-soluble than citric acid, is also utilised in many effervescent compositions[19]. In this reaction, 1 mol of tartaric acid reacts with 2 mol of sodium bicarbonate in the presence of water, yielding 1 mol of sodium tartrate as a product and 2 mols of CO_2 in the form of effervescence and 2 mol water as a by-product. (Figure 4)

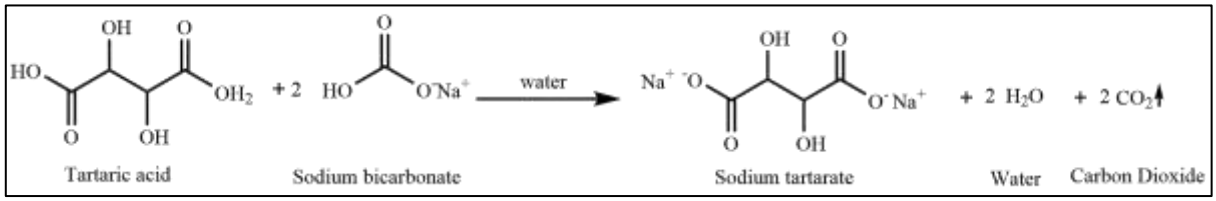

Figure 4: Reaction between tartaric acid and Sod. bicarbonate

Why are most effervescent tablets so large?

When studying the typical reaction between citric acid and the sodium bicarbonate, the cause of this can be understood.

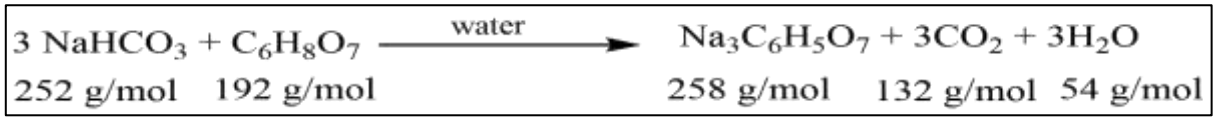

Figure 5: common effervescent reaction

If a placebo tablet containing 192 mg $C_6H_8O_7$ and 252 mg $NaHCO_3$ is considered to react when it dissolves in 100 ml of water, it will produce 258 mg $Na_3C_6H_5O_7$, 132 mg CO2 and 54 mg of additional H_2O. (Figure 5)

Given that 1 mol of CO_2 is equal to 22.4 mL under normal circumstances, 132 mg of CO_2 produced by the reaction of the tablet mentioned above is equivalent to 67.2 ml of gas. The fact that CO_2 dissolves in water at a temperature of 20 °C and 1 bar at a rate of 90 mg of CO_2 per 100 ml water, the amount of gas produced by this tablet will primarily dissolve in solution rather than form many bubbles. Therefore, larger tablets will be required to produce the desired effervescent reaction.[19–21]

Effect of water on effervescent formulations:

When water is present, even in little amounts as a catalysing agent, this reaction begins. Because water is one of the reaction products, water will speed up the reaction rate, making it complicated to halt. Due to this, minimal water interaction is incorporated into the entire manufacture and storage of effervescent items.[12,13,22]

Active ingredients that can be formulated in effervescent tablets:

- Drugs that are challenging to digest or have stomach disturbances:

Calcium carbonate tablets, the most popular type of calcium, are a prime illustration. The calcium salt of carbonate in a typical tablet or powder dissolves in the stomach's acidic pH and is then transported into the digestive tract for absorption. But when calcium carbonate dissolves in the digestive system, CO_2 is released, which typically results in gas within the stomach. However, as people get older, their stomach acid decreases, making it possible for a calcium carbonate tablet to pass through the stomach undissolved. Constipation may follow from that. However, calcium dissolves in water when taken as an effervescent formulation, making it easily accessible to the body.[14]

- pH-sensitive medications, including antibiotics and amino acids

Active substances may get denatured, lose action, or remain inactive due to the stomach's low pH. However, effervescent substances can prevent the water-active solution from degrading or inactivating by buffering it so that the stomach's pH rises to alkaline and becomes less acidic. The stomach is induced to empty quickly—typically within 20 minutes into the small intestine—resulting in optimum absorption of the active component because of this buffering effect due to carbonation.[14]

- Drugs that call for a high dose

A normal effervescent tablet with a diameter of around 1 inch and a weight of 5 g contains over 2 g of water-based active ingredients in a single dose. If the necessary dosage is higher then, it can be delivered in powder dosage form. E.g., N-acetyl cysteine effervescent tablets[23]

- Those who are sensitive to oxygen, dampness, or light.

This group includes a lot of vitamins. There is often less than 0.5 per cent free moisture in effervescent formulations. The material required for the packaging formulation should

consist of aluminium with a thickness of 0.001 inches. It must be capable of completely blocking light, oxygen, and moisture to ensure the preservation of the contents and prevent any damage from the surrounding environment.[13,14]

Drugs that can be incorporated in effervescent products:

Drugs that fit the description provided above can be produced in effervescent forms. Due to its benefits, effervescent delivery can be quite helpful for a variety of therapies. such as in the therapy of pain[24–28], ulcers[29], allergies[30,31], osteoporosis, arthritis, inflammation, antimicrobial infections[32–34] and many more conditions[35]. Acetylsalicylic acid, also known to be aspirin, paracetamol[26,36,37], ibuprofen[38], ascorbic acids and other vitamins[39–41], calcium carbonate, and other antacids like ranitidine[42,43], famotidine[29], etc. are examples of this. The effervescent mechanism is also utilised in gastro-retentive medication delivery, which involves preparing floating tablets to achieve retention in the gastric medium.[44–48]

Preparation of effervescent tablets:

The effervescent tablet is made up of three primary parts:

• Active component; • Acidic source; • Alkaline substances (mainly carbonates/ bicarbonates);

The acids and alkalis are the crucial components that cause the tablet to effervesce and disintegrate when it comes in contact with water. Citric acid[49,50], both hydrated and anhydrous, is the most widely utilised acidic component, but other edible acids such as tartaric acid[51], fumaric acid[52], adipic acid[53], and malic acid[54] can also be employed.[55] Acid anhydrides and salts of acids are also used as acidic sources.[56]

The carbonate, which is the source of the carbon dioxide that causes effervescence, is often a water-soluble alkaline carbonate. The carbonate employed is critical since, in addition to causing effervescence, it can affect the tablet's stability. Because it is highly soluble and inexpensive, sodium bicarbonate is one of the most commonly utilised carbonates.[44,55,57,58] Other alkaline or alkaline earth metal carbonates that are physiologically appropriate may be employed, such as potassium carbonate or bicarbonate, calcium carbonate or bicarbonate, sodium carbonate, sodium glycine carbonate etc.[36,59–65]

Diluents, buffering agents, ligands, sweeteners, colouring agents, flavouring agents, solubilizers, wetting agents, disintegrants, and other commonly used excipients may be included in the formulation or preparation of effervescent tablets. Effervescent tablet formulations may also include a lubricant, which must be selected from totally water-soluble compounds that produce a clear solution. Sodium acetate, sodium benzoate, fumaric acid, polyethylene glycol (PEG) greater than 4000, glycine, and alanine are examples of this type of lubricant. Effervescent tablets require the use of proper lubricants, even though formulations using tartaric acid are less adherent to tablet tools than those containing citric acid.[66] Effervescent products can contain natural water-soluble sweeteners like sucrose, lactose, xylitol, D-glucose, sorbitol, or mannitol, and approved artificial sweeteners such as saccharin, aspartame, Acesulfame K, or cyclamates.[67–69] Antifoaming agents are substances used to prevent foaming. They include alcohols like cetostearyl alcohol, insoluble oils such as castor oil, polydimethylsiloxanes, stearates, silicone derivatives, ethers, and glycols.[70] However, because acidic and alkaline components add bulk to the tablets, other excipients should be maintained to a minimum and used only when necessary.

Manufacturing of effervescent tablets:

Effervescent tablet manufacturing is similar to regular tablet production but requires controlled environmental conditions. Temperature and humidity must be carefully regulated to prevent the raw materials from absorbing moisture and initiating the effervescent reaction. Low relative humidity (maximum of 25% or less) and moderate to cool temperatures (25°C) are necessary to prevent product degradation and sticking to machinery.

The most popular method to produce tablets with desirable properties is granulation. There are many different granulation processes available, ranging from one-step granulation utilising water or organic solvents to two-step granulation such as granulating the acid and alkali phases separately.

1. **Wet granulation:**

The most recommended approach for effervescent granulation is still wet granulation, despite significant drawbacks. This process produces uniform tablets, either in terms of weight or the amount of active component, and produces homogeneous granules suited for compression.[71]

1. Two-step granulation technique:

Before adding lubricant for tabletting, the acidic and basic components are separately granulated and then drily mixed using standard machinery like a fluid bed spray granulator, single pot, or high-shear granulator. Alternatively, one among the effervescent sources can be granulated and the other incorporated as a powder during final blending with additional chemicals like flavours and lubricants. This method boosts productivity and lowers costs by avoiding a full granulation stage.

2. One-step granulation technique:

The one-step granulation technique involves granulating acidic and alkaline components together using a small amount of water or organic solvents like alcohol, isopropanol, or other solvents with a binder. This technique produces dry effervescent granules instantly, regulating the effervescent reaction and leading to granule formation. It is essential for the effervescent and other components to be insoluble in the organic solvent used.

3. Fluidised bed granulation:

The components of an effervescent combination are all granulated in one step using fluid-bed granulator-dryer technology. With this technique, a fluidized bed is created by suspending a dry mixture of an acid source and a carbonate source in a heated air stream. When water, the most common granulating fluid, is injected in a little volume, it reacts briefly before being vaporised. When water is no longer sprayed and the drying phase is completed with warm dry air, the reaction is terminated.[72]

To create effervescent granules a rotor fluid bed spray-granulator can be used as an alternate approach. This technique reduces contact between two effervescent system components. This is a continuous two- or three-step technique for making effervescent granules. Granulating alkaline components in the rotary fluid bed is the first stage. In the following step, the granulating solution is sprayed along with acidic powders onto the alkaline spheres. This results in the formation of an outer acidic layer on the spheres, which is separated from the binder by a neutral layer. Agglomeration is finished, and then drying is initiated.[73]

4. High shear granulation:

It is conceivable to quickly switch from the granulation phase to the drying phase in high-shear granulator-dryer technology by creating a vacuum inside the bowl. This causes the water boiling point to decrease rapidly and the bowl is heated up to provide energy for evaporation. Within seconds, water on the surface of the wet granules is removed and the effervescent reaction stops. Microwave radiation combined with vacuum can also be applied to dry effervescent granules and stop the reaction.[74,75] TOPO granulation can be utilised for this type of granulation, where a vacuum can be applied to stop the reaction.[76]

2. **Dry granulation:**

The effervescent reaction is sparked by the wet granulation process, which degrades the substance. As a result, other options have been developed. One of these is dry granulation by slugging, which involves compressing big tablets or slugs using roller compactors or directly compressed other forms. These are the most successful alternatives to the wet granulation process.

a. Slugging:

To make slugs or large tablets, a roller compactor or chilsonator is often used to compress mixed powders between two counter-rotating rollers under higher pressure. The resulting slugs are then reduced to the appropriate size for tablet granulation. Lubrication may be necessary during the slug-making process. This technique is effective in producing effervescent tablets using dry granulation with acidic and basic substances. However, it involves the use of costly excipients and is only suitable for manufacturing small batches of tablets. The technique is simple, cost-effective, increase product throughput, and requires fewer operators and less space, but it also requires less air ventilation.

b. Direct compression:

Making effervescent tablets with acetylsalicylic acid has successfully used direct compression as an alternative way to dry granulation. Addressing problems with the process's operational effectiveness and stability is helpful with this procedure. However, on account of the need for complex raw material combinations that are compressible, free-flowing, and non-segregating, this technology can only be used in the most perfect of manufacturing environments, which limits its application in real-world applications.

c. Granulation by heating:

Dry granulation techniques, such as hot melt granulation[77,78], can be used as an alternative to wet granulation. In hot melt granulation, hydrated citric acid is melted to release the hydration water that serves as the granulating liquid, agglomerating the powder mixer's particles. The resulting granules are then chilled to achieve the required hardness and mechanical stability. Hot melt granulation can be accomplished using a high-shear granulator-dryer, or with low melting point polymers like PEGs as binders in a fluid bed spray-granulator. Hot melt extrusion is another unique technique that requires a hot-melt extrudable binder, extruders with temperature-controllable heating zones, and an extrusion die.[79,80]

Evaluation tests of effervescent granules:

1. Angle of repose:

Pouring the effervescent granules down a funnel onto the flat surface, generating a cone-shaped pile, is one way for measuring the angle of repose. The pile's height and radius are then measured, and the angle of repose is determined using the formula below. Another approach is to use a digital or mechanical angle of repose tester, which automatically calculates the angle of repose depending on the pile's height and radius. The angle of repose can be calculated using the formula below:

$$\tan \theta = h/r$$

where θ is the angle of repose, h is the pile's height, and r is the radius of the pile's base.[81]

Table 1: Standard values of angle of repose with respect to flowability

Angle of repose	Flowability
Less than 25^0	Excellent
Between 25^0 to 30^0	Good
Between 30^0 to 40^0	Fair
More than 40^0	Poor

2. Bulk density:

This density can be obtained by dividing the mass of the powder by its total volume., including the spaces between particles.[82] It is an important factor in the development of effervescent dosage forms as it affects flow properties, compressibility, and rate of dissolution. Measuring the bulk density ensures consistent dosing and optimal packaging.

3. Tapped density:

The powder density following tapping or compression is known to be tapped density of effervescent granules. It mimics the settling of powder during storage or transportation. Compared to bulk density, it is a more accurate indicator of powder packing behaviour. Tapped density is a crucial factor to take into account when developing effervescent dosage forms since it has an impact on the powder's uniformity and rate of dissolution. Calculating the tapped density involves dividing the granule mass by the powder's tapped volume. To obtain precise and repeatable readings, a calibrated tapping instrument should be employed. The standardised tapping conditions are specified in the USP or EP.[83]

4. Carr's index:

Carr's Index, also known as Carr's compressibility index, is a method for measuring powder flow indirectly by using a bulk density. It was created by Carr, and it establishes a powder's percentage compressibility, which reveals its potential strength and stability in the formation of bridges or arches. Carr's index of a formulation can be calculated using a specific equation that compares the poured bulk or bulk density to the tapped or consolidated bulk density. The equation involves subtracting the tapped density from the poured density, dividing the result by the poured density, and multiplying by 100 to obtain the percentage compressibility.[83]

5. Hausner's ratio:

A measurement of a powder's flowability known as Hausner's ratio is obtained by dividing the tapped density by the bulk density. The powder is put through standardised tapping to determine the values, and the bulk density is calculated by measuring the powder's volume and dividing it by its mass.[83]

Table 2: Standard values of Carr's index and Hausner's ratio with respect to flowability

Carr's index (%)	Flowability	Hausner's ratio
5-15	Excellent	1.05-1.18
12-16	Good	1.14-1.20
18-21	Fair- passable	1.22-1.26
23-35	Poor	1.30-1.54
33-38	Very poor	1.50-1.61
Greater than 40	Very-very poor	Greater than 1.67

Evaluation tests of effervescent tablets:

Pharmacopoeial evaluation criteria for effervescent tablets are identical to those for conventional tablets, although they all place a strong emphasis on the disintegration test.

They are evaluated using parameters such as disintegration time/effervescent time, dissolution time, weight variation, content uniformity, pH of the solution, hardness, friability, water activity, organoleptic properties, and carbon dioxide (CO_2) content.

1. Organoleptic properties:

The organoleptic qualities of effervescent tablets are assessed using different procedures, including visual inspection for colour, shape, and uniformity; odour assessment for the distinctive aroma of active components; and taste evaluation for effervescent reaction and overall palatability. These tests guarantee that the tablets satisfy the required quality standards and give consumers a positive sensory experience.

2. Weight variation:

The weight variation test is performed to make sure that each batch of effervescent tablets has weights that fall within a predetermined range. In this test, the weights of individual tablets are measured from a sample of tablets. The weights of the individual tablets are then contrasted with their combined weight. Typically, a percentage departure from the average weight is utilized to ascertain the allowable weight range. (**Table 3**) The test of weight variation is passed if the tablets fall within this range. If the tablets couldn't pass the test, additional analysis is needed to figure out what caused the variation and how to fix it.[84]

Table 3: Standard values weight variation test as per IP/BP and USP

Avg. weight of tablet as per IP/BP	% deviation	Avg. weight of tablet as per USP
Less than 80 mg	10 %	Less than 130 mg
80 mg to 250 mg	7 %	130 mg to 324 mg
More than 250 mg	5 %	More than 324 mg

3. Content of uniformity:

Evaluate the amount of the active ingredients in 10 units of a single-dose formulation to see if it is uniform. The composition of each unit should be between 85 and 115% of the average. The test is invalidated if one or more units fall outside of this range or outside of the range of 75 to 125%. Test 20 more units if one unit is between 75 and 125% but outside of the range of 85 to 115%. The test is considered acceptable if no more than one of the 30 total units falls outside of the range of 85-115% and no units fall outside of 75-125%.[85]

4. Disintegration time/ effervescent time:

As specified in IP, to test the disintegration of tablets, take a beaker with 250 ml of water at a temperature between 20°C to 30°C, add one tablet, and observe the release of CO_2 bubbles. The tablet should disintegrate within five minutes, leaving no clumps or particles. Repeat this process with five more tablets. The test is considered successful if all six tablets disintegrate within five minutes unless the specific rules of the tablet require otherwise.

5. Friability test:

For tablets that weigh 0.65 g or less on average, a sample of 6.5 g of whole tablets is obtained for testing, and for that tablet weight 0.65 g or more on average, a sample of 10 entire tablets is taken. The tablets are precisely weighed after being accurately dedusted, and then they are put in a drum and rotated 100 times. The tablets are cleansed of any loose dust after the rotation and precisely weighed one more. The test is run once, but if the weight loss exceeds the 1.0 % permissible limit, it is run twice, with the mean of the three tests being calculated. Following the test, if the sample has tablets that are clearly broken, chipped, or obviously cracked, the sample is considered a failure.[86]

6. Dissolution test:

In an effervescent tablet dissolution test, a tablet is drenched in a set amount of water at a specified temperature in dissolution equipment. The apparatus's paddle or basket rotates to induce agitation, and the drug concentration in the water is measured at regular intervals with a spectrophotometer or another technique. The test is carried out in triplicate, and the results are compared to the relevant quality and efficacy requirements.[82]

7. pH of the solution:

For quality control, the pH of effervescent tablet solution is critical. A stable pH throughout batches suggests that the raw ingredients are homogenous, whereas excessive fluctuation may indicate granulation or weighing difficulties. The taste of the tablet is also affected by the pH; acidic pH is preferable for antacids with citrus or berry flavours, whilst mint flavours are created at a neutral to slightly alkaline pH.[19] Because effervescent tablets change pH on standing due to the breakdown of carbonic acid and the presence of slowly soluble ingredients, pH can be determined using proper apparatus i.e., a pH meter at a given period.

8. Water activity:

The availability of unbound water for microbial growth is determined by water activity (aW), which is a crucial component in assuring food safety. Capacitance sensors and chilled-mirror dewpoint systems are utilised as the two measuring tools for aW. Hygroscopic polymer membranes are used in capacitance sensors whereas dewpoint sensors and infrared thermometers are used in chilled-mirror systems. Despite the advantages and disadvantages of each approach, both can measure aW precisely.[19,87]

9. Hardness and thickness:

Effervescent tablets must be strong enough to handle without chipping or breaking. Proper tool choices, like those with bevelled edges, can minimize these issues. A ratio of 1 between the thickness of the tablet and hardness is recommended for a strong tablet, though this can make packaging difficult due to increased thickness. Tablet height is also important for packaging, as it affects pack tightness.

Hardness can be calculated with standard testers like Monsanto's or Pfizer's hardness testers, Strong Cobb, or Schleuengir. Thickness can be evaluated with a vernier calliper.[88]

10. Carbon dioxide content:

Various methods can be used to measure the carbon dioxide released from effervescent tablets, including gravimetric, barometric[89,90], volumetric, gasometric, colorimetric, and balloon methods.[91] Every technique possesses its advantages and disadvantages. The gravimetric method calculates CO_2 released by determining the difference in sample weight before and after the reaction but is not very precise. The barometric method measures pressure and volume in a closed system. The volumetric method involves acid-base titration and is time-consuming. The gasometric method directly determines gas volume but is limited in adaptation for pharmaceutical use. The colorimetric method uses indicators to change colour intensity. The balloon method measures CO_2 by passing it into a balloon containing sodium hydroxide solution and titrating it with HCl.[92]

Advancements in effervescent technology:

Effervescent tablets are traditionally known for generating carbon dioxide when an acidic source reacts with alkaline carbonates. However, recent advances in this technology have produced the generation of hydrogen gas[93] and oxygen bubbles[94] through effervescence. This has opened up opportunities for topical drug delivery by combining mechanical and physiological characteristics.[95,96] Additionally, effervescent tablets have shown promise in oral hygiene and antimicrobial activity, owing to the progress of effervescent buccal and denture tablets.[97–99] These tablets are versatile and effective for delivering not only oral drugs but also herbal[100,101] and nutraceutical formulations.[102] Effervescent tablet formulations have also advanced in cosmeceuticals, such as pedicure, manicure, and bath bomb preparations.[103] Effervescent technology has the ability to be highly beneficial in drug delivery to the lungs.[104]

Conclusion:

Effervescent tablets are a popular dosage form that offers several advantages over other methods of drug delivery. They dissolve quickly in water and are absorbed by the body, resulting in a faster onset of action and better bioavailability. They are also more convenient for patients who have difficulty swallowing and have a better taste, which increases patient compliance. Effervescent tablets can also reduce gastrointestinal irritation, are easier to store and transport, and have good stability. They can improve absorption, prevent first-pass metabolism, and allow for precise dosing. Effervescent tablets can be formulated with a variety of active ingredients, including drugs that are challenging to digest or have stomach disturbances, pH-sensitive medications, drugs that require a high dose, and drugs that are sensitive to oxygen, moisture, or light. However, effervescent tablets have some drawbacks, such as their larger size, complex manufacturing process, sensitive packaging, and longer disintegration time. Despite these limitations, effervescent tablets have proven to be an effective and convenient dosage form for a variety of therapeutic purposes.

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