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(REVIEW ARTICLE)

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Review on effervescent tablet

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Abstract

Effervescent tablet is a solid, compact form of medication or supplement that dissolves rapidly when exposed to water, releasing carbon dioxide and creating bubbles in the process. The tablet typically contains active ingredients such as vitamins, pain relievers, or minerals, alongside acid and carbonate compounds, which react with water to generate the effervescence. The bubbling effect not only makes the tablet easier to ingest but can also enhance the absorption of the active ingredients into the body. Effervescent tablets are often favored for their fast-acting delivery and ease of use, offering an alternative to traditional pill forms. The rapid dissolution in water also allows for quicker relief and a smoother experience for those who have difficulty swallowing pills.

Keywords: Effervescent tablet, Medication; Supplement; Dissolves in water; Carbon dioxide; Active ingredients; Fast-acting; Absorption; Alternative to pills

1. Introduction

For decades, oral drug delivery has been recognized as the most extensively used route of administration among all methods used for systemic drug delivery via diverse pharmaceutical products in various dosage forms. The reasons for the oral route's popularity may be traced in part to its ease of administration. Future market insights predict that the total worldwide oral solid-dosage pharmaceutical formulation business will rise from 489.5 billion dollars in 2017 to 925.5 billion dollars by 2027. In terms of physical, chemical, and microbiological properties, the solid tablet is the most durable oral dose form when compared to oral liquid capsules, solutions, or suspensions. 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 problem can be handled by producing effervescent tablets.

According to Indian Pharmacopoeia, effervescent tablets are tablets without coatings that include acidic materials and either carbonates or bicarbonates that react quickly in the presence of water and release carbon dioxide, as well as authorized flavouring ingredients. They are meant to be dissolved or distributed in water before being administered. Saline cathartics became the first effervescent formulations to be produced in the eighteenth century. Since then, numerous preparations based on effervescent technology have been developed, including stomach upset treatments such as Alka-Seltzer, vitamin supplements such as calcium, and analgesics. Because of their convenience of use, effervescent tablets have become increasingly popular in a range of industries, including vitamins and pharmaceuticals. Effervescent tablets are designed to dissolve into a solution when they come into contact with water or juice.

Effervescent tablets typically contain acids or acid salts such as citric acid, tartaric acid, malic acid, or any other suitable acid or acid anhydride and carbonates or bicarbonates such as sodium, potassium, or any other suitable alkali metal carbonate or hydrogen carbonate, which rapidly react in the presence of water by releasing carbon dioxide. API solubility in water and flavour masking are both improved as a result of CO_2 gas liberation.

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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 sodium bicarbonate is the most prevalent effervescent reaction.

$$C_6H_8O_7 + 3NaHCO_3 \xrightarrow{water} Na_3C_6H_5O_7 + 3CO_2 + 3H_2O$$

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.

Pros of effervescent tablet:

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

- Faster onset of action: Compared to other medicine types, effervescent formulations quickly dissolve in water and are absorbed by the body. This may lead to a quicker start to action and quicker symptom relief.
- 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.
- More feasible: Patients who struggle to swallow will find effervescent formulations more convenient because they can be dissolved in water.
- Better taste: Effervescent formulations frequently have a tasty flavour, which can increase patient compliance and drug adherence.
- Reduced gastrointestinal irritation: By buffering the stomach acid, effervescent formulations might lessen the gastrointestinal irritation brought on by some drugs.
- Improved portability: When compared to liquid dose forms, effervescent tablets are easier to store and transport because of their compact form.
- 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.
- Good stability: Effervescent pills have good stability in general. This is due to the fact that the tablet packaging shields 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.
- Improved absorption: Effervescent formulations are made to dissolve fast in the water, which can help the active components be absorbed more readily. This is so that the medication will be distributed more evenly and have a larger surface area during the effervescence process, which will make it easier for the body to absorb it.
- Prevents first-pass metabolism: Effervescent tablets have the ability to prevent first-pass metabolism, which is the liver's breakdown of a drug before it enters the bloodstream. This is due to the medication's direct bloodstream absorption from the digestive system, avoiding the liver.
- Can include a higher amount of active ingredient: Effervescent formulations can contain a lot of active substances, which can be very helpful for drugs that need greater doses. This is so because, in comparison to other medicine forms, the effervescent tablet matrix may hold a greater volume of active chemicals.
- Exact dosing: Effervescent tablets deliver exact amounts of active components because they are available in the tablet dosage form.

Possibility of a therapeutically-appropriate combination of numerous active ingredients: Effervescent tablets have the capacity to combine more than one active component if doing so is therapeutically acceptable because they are relatively large tablets.

2. Preparation of effervescent tablets

The effervescent tablet is made up of three primary parts:

- Active component;
- Acid source;
- Alkaline compound (mainly carbonate or bicarbonate);

The acid and alkali are the crucial components that cause the tablet to effervesce and disintegrate when it comes into contact with water. Citric acid, both hydrated and anhydrous, is the most widely utilised acidic component, but other edible acids such as tartaric acid, fumaric acid, adipic acid, and malic acid can also be employed.

The carbonate, which is the source of the carbon dioxide that causes the effervescence, is often a water-soluble alkaline carbonate. The carbonate employed are 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. 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, or sodium glycine carbonate etc.

Diluents, buffering agents, ligands, sweeteners, colouring agents, flavouring agents, solubilizers, wetting agents, disintegrants, and other commonly used excipients may be included in the formulation of effervescent tablets. Effervescent tablet compositions may also comprise a lubricant, which must be chosen from the completely water-soluble compounds generating a transparent solution. Sodium benzoate, sodium acetate, fumaric acid, polyethylene glycols (PEG) greater than 4000, alanine, and glycine are examples of this type of lubricant. However, because acidic and alkaline components add bulk to the tablets, other excipients should be maintained to a minimum and used only when necessary.

2.1. Acid source

Food acids, acid anhydrides, and acid salts are the three main acid sources.

2.1.1. Food acids

Food acids are the most widely used since they occur naturally and are ingestible.

Citric acid

Citric acid is the most commonly used food acid because it is abundant, relatively inexpensive, has good solubility, and has a pleasing flavour. Citric acid comes in both monohydrate and unhydrate forms. It is sold as colourless, transparent crystals or as white crystalline powder. Citric acid is widely accessible in fine granular, free-flowing powder forms with various particle sizes such as coarse, medium, fine, and so on. It has no odour and a harsh acidic flavour. It is soluble in both water and alcohol. It creates solutions with a citrus flavour. Because it is highly hygroscopic, efforts must be taken to avoid exposure during manufacturing and storage. The monohydrate form is more hygroscopic than the anhydrous form. When stored at humidity levels above 70% RH, the anhydrous form has a tendency to cake. Citric acid monohydrate absorbs insignificant amounts of moisture between 65 and 75% relative humidity, but significant amounts are absorbed above these humidity levels, whereas citric acid unhydrate absorbs insignificant amounts of moisture between 25 and 50% RH and significant amounts between 50 and 75% RH, with the formation of monohydrate form. The monohydrate melts at 100 °C and releases crystallisation water at 75 °C, making it suitable for use as a binder source in hot melt granulation.

Tartaric acid

Effervescent tablets frequently contain tartaric acid because it is an easily available commercial substance. With 1 part acid to less than 1 part water, it is more soluble than citric acid. It is offered as either white crystalline powder or colourless monoclinic crystals. It has no smell and a rather sour flavour. Additionally, it is more hygroscopic than citric acid and becomes deliquescent at RH levels above 75%. It is just as potent as citric acid, but because it is diprotic as opposed to triprotic, bigger doses must be required to reach equal acid concentrations in the effervescent process. Tartaric acid is similar to citric acid in terms of compressibility.

Ascorbic acid

Ascorbic acid is a white to light yellow, crystalline powder that has no fragrance and a harsh acidic taste. It is readily soluble in both alcohol and water (1 in 3.5). Ascorbic acid and anhydrous citric acid responded similarly when it came to the production of carbon dioxide from effervescent tablets based on these acids, ascorbic acid, tartaric acid, and sodium bicarbonate. The majority of carbon dioxide was produced by tartaric acid, although it took longer to disintegrate. The ascorbic acid gradually darkens when exposed to light. Since ascorbic acid is less hygroscopic than tartaric and citric acid, making effervescent tablets is made easier. Ascorbic acid usage reduces the necessity for strict air and temperature controls during manufacturing.

Fumaric acid

Fumaric acid is found as a crystalline powder or white, odourless or virtually odourless granules. It is a potent acid that is essentially non-hygroscopic and very cost-effective. It's extremely low water solubility (about 1 in 33 at 20°C) creates a challenge in the manufacturing of effervescent tablets. Salts with higher water solubility, like monosodium or potassium fumarate, can be utilised to make fumaric acid. Some formulations make use of fumaric acid's lubricating characteristics to reduce the need for additional lubricants.

Malic acid

Malic acid is sold as a crystalline white powder. It tastes very acidic and has a faint aroma. Additionally, it is easily soluble and hygroscopic. When mixed with a carbonate source, it has an acid strength that is lower than citric acid but strong enough to generate enough effervescence. Malic acid is more expensive than citric acid but can be employed in effervescent recipes for a smoother aftertaste.

Adipic acid

Adipic acid is sold as a white crystalline powder and is almost completely non-hygroscopic, but it also dissolves in water much less readily than citric acid. Additionally, it cost less and is less readily available. It has been claimed that this acid is having lubricating qualities.

Succinic acid

Succinic acid comes as shiny, odourless, white crystals or powder. It is also used as a flavouring agent. It is also dissolved in water but less readily than citric acid.

2.1.2. Alkaline compound

The alkaline substance is a crucial component of effervescent reactions in addition to the acidic source. Effervescence is provided by dry, solid carbonate and bicarbonate salts in most effervescent tablets. Bicarbonates are more reactive than carbonates and are utilized more frequently.

Sodium bicarbonate

Sodium bicarbonate has a saline, slightly alkaline taste and is an odourless, white crystalline powder. It comes in five different grades of particle size, ranging from tiny powders to freely flowing granules. At 20 °C, it dissolves in water 1 in 11 parts. It is abundant, cheap, and non-hygroscopic.Of all the sources of bicarbonate, it is the one that is utilised the most. It can be consumed and is frequently combined with other substances to act as an antacid. By weight, it produces around 52% carbon dioxide. With a pH of 8.3 in an aqueous solution with a 0.85% concentration, it is the least acidic of all alkalies. Due to its lack of elasticity, it causes issues when compressed. Spray-drying technology was employed in the manufacturing process to help sodium bicarbonate overcome its poor flowability and low compressibility. There is also immediately compressible sodium bicarbonate that has been spray-dried and contains additives like silicon oil and polyvinyl pyrrolidone. This product has good stability and compressibility.

If any moisture is present, normal sodium bicarbonate products, which are very unstable, will react with the acid component of an effervescent formulation. As a result, the manufacturing company faces a problem since it must handle, produce, and package the product in a humidity-controlled environment to reduce the risk of early effervescent reaction and ruination. The sodium bicarbonate must frequently be pre-dried before use in order to remove extra moisture and prevent reactivity. Many of these issues can be prevented by using Effer-Soda Sodium Bicarbonate. Effer-Soda It becomes a more stable form of sodium bicarbonate when it is dried and partially desiccated to boost its stability. It has a core of sodium bicarbonate and sodium carbonate as "desiccant skin" that has been added during manufacturing. In terms of bulk, this "desiccant skin" accounts for 8–12% of Effer-Soda. By absorbing moisture to create a hydrated salt (sodium sesquicarbonate), which is stable up to 70 °C, this sodium carbonate outer layer creates a barrier that safeguards the sodium bicarbonate core. The sodium carbonate outer layer dissolves when a lot of moisture is added to a glass of water by an effervescent tablet or powder, releasing the sodium bicarbonate for interaction with the acid component.

Sodium carbonate

In effervescent tablets, sodium carbonate, commonly referred to as soda ash, can serve as a source of carbon dioxide. Due to its high pH of 11.5 in an aqueous solution of 1% concentration, it is also employed as an alkalizing agent. It is very soluble in water. Commercially, sodium carbonate is offered in anhydrous, monohydrate, and decahydrate forms.

It is present in colourless, white crystals. Due to its capacity to absorb moisture and stop the start of an effervescent reaction, an anhydrous form is chosen. It also functions as a stabilising agent and is more *effervescent response resistant.*

3. Manufacturing of effervescent tablets

The manufacturing procedure for effervescent tablets is largely the same as that for normal tablets, but controlled environmental conditions are required. As a result, controlling humidity and temperature in the production environment is a crucial stage in the production of these tablets. Due to the hygroscopic nature of the raw materials employed in its production and the potential for the commencement of an effervescent reaction as a result of moisture absorption by these components, a regulated environment is necessary. In order to prevent the granulations or tablets from sticking to the machinery and from absorbing moisture from the air, which may lead to product degradation, low relative humidity (maximum of 25% or less) and moderate to cool temperatures (25^0C) are crucial in the manufacturing regions.

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.

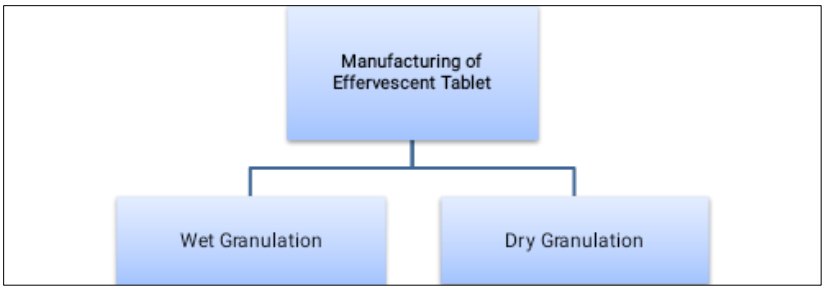

Figure 1 Types of Manufacturing of Effervescent Tablet

3.1.1. 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.

Two-step granulation technique

Before adding the lubricant for tabletting, the acidic and basic components are separately granulated, followed by a dry mixing process. This can be accomplished in a fluid bed spray granulator, a single pot, or a high-shear granulator (with subsequent drying). This process just needs standard machinery that can also be used for other materials' drying and granulation. An alternative method is to merely granulate one of the effervescent sources and incorporate the other as a powder during the final blending. It is blended with additional chemicals like flavours and lubricants. By avoiding the expense of a full granulation stage, this method boosts productivity and lowers costs.

One-step granulation technique

By granulating acidic and alkaline components together, the one-step granulation technique produces dry effervescent granules instantly. This is accomplished by using a small amount of water, which starts the effervescent reaction but regulates it, leading to the formation of granules. Organic solvents like alcohol (diluted with water), isopropanol, or other solvents with a binder can also be used for granulation. The formulation's effervescent and other components ought to be insoluble in an organic solvent.

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.

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. The next stage involves spraying the granulating solution together with acidic powders, which deposit on the alkaline spheres and create an exterior acid layer that is separated by a neutral layer of the binder. Agglomeration is finished, and then drying is initiated.

High shear granulation

It is possible 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 used to dry effervescent granules and stop the reaction. Topo granulation can be used for this type of granulation, where a vacuum can be applied to stop the reaction.

3.1.2. 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 other forms of direct compression. When compared to the wet granulation method, these are the most effective options.

Slugging

Obtaining slugs or huge tablets necessitates the use of robust tabletting machinery. One such device that compresses premixed powders between two counter-rotating rollers under intense pressure is the roller compactor, also known as a chilsonator. Depending on the roller configuration, this produces a brittle material that can be in the form of a ribbon, sheet, or piece. The resulting slugs are then shrunk down to the proper size for tablet granulation. During the slug-making process, lubrication could be required. This approach allows for the dry granulation of acidic and basic components either independently or jointly. It is especially helpful for materials that need precompression to boost density or get rid of trapped air owing to porosity but cannot be compressed using conventional wet granulation procedures. This method has the benefits of being straightforward, inexpensive, increasing product throughput, requiring fewer operators and less space, and requiring less air ventilation. The technique's main disadvantage, however, is the usage of pricey excipients, which limits its applicability to small-batch manufacturing of effervescent tablets.

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, due to 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.

Granulation by heating

As an alternative to wet granulation, dry granulation techniques such as heating can be used. By melting hydrated citric acid at a temperature of around 100 °C, which releases the hydration water that serves as the granulating liquid, the powder mixer's particles are agglomerated. In order to acquire the required hardness and mechanical stability, the resultant granules are chilled. Hot melt granulation and surface hot melt granulation are two methods that can be applied. In the process of surface hot melt granulation, all the ingredients are combined, dried in an oven, and then water is released from the citric acid and other ingredients to create granules. However, with a static bed dryer, this process is challenging to manage and has lower reproducibility. In a high-shear granulator-dryer, hot melt granulation is carried out. The bowl is heated to release the water of hydration from citric acid, and occasionally this sets off an effervescent reaction that results in the production of more water, which serves as a binding liquid. Low melting point polymers like PEGs have been employed as binders in a fluid bed spray-granulator where this procedure has also been applied. A hot-melt extrudable binder, such as PEGs with a molecular weight between 1000 and 8000 Da, as well as extruders with solid conveying zones, numerous distinct temperature-controllable heating zones, and an extrusion die, are required for the unique hot melt extrusion technique.

3.2. Marketed product

Figure 2 Types of Marketed Formulation of Effervescent Tablet

4. Conclusion

Effervescent tablets offer a unique and effective delivery method for medications, vitamins, and supplements. Their ability to dissolve quickly in water, releasing carbon dioxide and creating a bubbly solution, provides a faster onset of action compared to traditional pill forms. This form of medication is particularly beneficial for individuals who have difficulty swallowing tablets and those seeking a more convenient, quick-dissolving option. Additionally, the effervescence can aid in the absorption of active ingredients, enhancing their effectiveness. Overall, effervescent tablets combine ease of use with rapid action, making them a popular choice for many users seeking efficient and accessible health solutions.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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