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Electrolytes effervescent tablets - A review

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Abstract

The evolution of gas bubbles from a liquid as a result of a chemical reaction is called effervescence. Effervescent tablets contain unique characteristics for a medicinal application that allows for quick absorption of the desired medication. If a drug dissolves quickly in water and is present in a suitable amount, it can be absorbed rapidly and effectively in this way. Citric, malic, tartaric, adipic, and fumaric acids are common acids used in effervescent processes. Citric acid is the most often utilized acid for this purpose, and it gives the products a citrus flavor. Due to their limited water solubility, tartaric, adipic, and fumaric acids are usually used in small amounts. Electrolytes Effervescent tablets are used to make dosing easier, ensure excellent compatibility, enhance superior and rapid absorption, boost a patient's liquid intake, and avoid swallowing large tablets.

KEYWORDS: Effervescent, Tablets, Electrolytes, Effervescent system.

INTRODUCTION

The oral dosage forms are the most common route of drug administration despite disadvantages like slow absorption, and thus the onset of action is prolonged. This will be overcome by administrating the drug in liquid form but, many APIs have a limited level of stability in liquid form. So, Effervescent tablets act as an alternative dosage form.[1,2]

"Effervescent tablets are tablets that are meant to be dissolved or dispersed in water before administration," according to the FDA's revised definition. in addition to the active ingredient, it usually contains a mixture of acids / hydrochloric acids (citric, tartaric, malic, or other suitable acids or acid anhydrides) and carbonates and bicarbonates (sodium, potassium, or other suitable alkali metal carbonates or bicarbonates).[3,4]When mixed with water, carbon dioxide is released. Sometimes the active ingredient can act as an acidic or primary metal compound required for the foaming reaction. Effervescent tablets are commonly uncoated tablets containing acids, carbonates, or bicarbonates, reacting quickly with water to release CO2. It must be dissolved or diluted in water before use. Some drugs are helpful for pharmaceuticals that damage the stomach or are susceptible to stomach pH, and medicines that are regularly prescribed in high quantities and can be taken as effervescent tablets.

Moreover, because effervescent tablets are administered in liquid form, they are easier to swallow than tablets or capsules with a problematic consumption for so many reasons.[5,6] One dose of an effervescent tablet, on the other hand, is often dissolved in 3-4 ounces of water. Effervescent products do not directly contact the gastrointestinal tract because they have been pre-dissolved in a buffer solution. As a result of the reduced gastrointestinal irritation can be tolerated well in the stomach and intestine.

Just before administration, the tablet is dissolved in a glass of water, and the resulting medication solution or dispersion is to be consumed immediately. Internal forces quickly break apart the tablet due to the interaction of tartaric acid and citric acid with alkali metal carbonates or bicarbonates in the presence of water. The dissolution of API in water and the taste-masking effect are both improved due to CO2 gas liberation. Compared to other oral dosage forms, the advantages of effervescent tablets include the ability of the formulator to enhance flavor, a gentler influence on the patient's stomach, and marketing considerations.

Acid or acid salts (citric, tartaric, malic, or any other suitable acid or acid anhydride) and carbonates or bicarbonates (sodium, potassium, or any other suitable carbonate or bicarbonate) are contained in uncoated tablets and known as effervescent tablets. Suitable alkali metal carbonate or hydrogen carbonate) that reacts

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

quickly in the presence of water to release carbon dioxide. As a result of CO2 gas liberation. API dissolution in water is improved, as is the taste masking effect.[7,8]

More than 2,000 milligrams of water-soluble active ingredients in a single dose can be contained in a standard effervescent tablet (1 inch in diameter, weighing five grammas in total Weight). A sachet (powder form) is a common means of delivery if the necessary dose is more significant than that. The effervescent items acquired a great deal of significance with the Alka Seltzer technology in the 1930s. Over the years, these mixtures have been moderately popular because they are attractive dosages and therapeutic activities for patients.

The aim of this study To enhance the bioavailability of drugs. To avoid the first-pass effect, they should have satisfactory properties, tablets with greater bioavailability than other dosage forms to achieve better patient compliance. It is possible to improve the stability of Effervescent tablets, and the bubbling tablets require a strictly humid control area. The Effervescent tablets can't be made in an average area where the humidity and temperature are not maintained.

Electrolytes

Electrolytes play a critical role in the body's maintenance of homeostasis. They have vital roles in such physiologic functions as maintaining intracellular and extracellular fluid distribution; energy production and utilization; electrical conductivity and muscular contraction in cardiac, skeletal, and vascular smooth muscle; and clot formation. Many disease processes can cause electrolyte abnormalities, including gastrointestinal disease, endocrine diseases like diabetes, hyper is, hypoadrenocorticism, thyroid disorders; renal and urinary disease; various neoplasms; sepsis; and skin disorders. Treatment interventions in critically ill animals can precipitate electrolyte disorders or clinically significant shifts in electrolyte distribution and levels within the body. Appropriate treatment of electrolyte abnormalities may lead to decreased morbidity and mortality. Many of the clinical signs of electrolyte abnormalities can be masked by or thought to result in the underlying disease state. The role of the astute critical care technician is to observe for potential sequelae of electrolyte abnormalities, appropriately obtain samples and use in-house analyzers, and During the stay, notify the doctor of any significant changes found on laboratory monitoring.[9]

Basic living processes such as maintaining electrical neutrality in cells and creating and conducting action potential in nerves and muscles require electrolytes. Sodium, potassium, and chloride are the many electrolytes, magnesium, calcium, phosphate, and bicarbonates. Electrolytes are found in both our food and our fluids.

These electrolytes can have an imbalance, resulting in either high or low levels. Electrolyte levels that are too high or too low can impair normal biological activities and possibly result in life-threatening issues.[11]

Electrolytes are minerals that have an electric charge and are found in your blood and other bodily fluids.

Electrolytes affect how your body functions in many ways, including:

- The amount of water in your body
- The acidity of your blood (pH)
- Your muscle function
- Other important processes

You lose electrolytes when you sweat. You must replace them with drinking fluids that contain electrolytes. Water does not contain electrolytes.

Common electrolytes include:

- Calcium
- Chloride
- Magnesium
- Phosphorus
- Potassium
- Sodium

Electrolytes can be acids, bases, or salts.

Reason for selection of Effervescent tablet-

- Fast onset of action. -Effervescent tablets have the most advantage in that the drug substance is already in solution at the instant it's absorbed; therefore, the absorption is easier and more effective than with traditional tables. Faster absorption means a quicker onset of action.

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Effervescent drugs are administered to the stomach at a pH that's good for absorption. Many medications pass slowly through the alimentary canal or have absorption impeded by food or other medicines.

- No need to swallow tablets - effervescent medicines are administered in liquid form so that the number of people who are unable to swallow tablets or who do not like swallowing pills and capsules is growing with an effervescent dosage form compared to tablets or capsules; one dose can usually be delivered in only 3 or 4 ounces of water
- Good stomach and intestinal tolerance - In a buffered solution, the effervescent tablets dissolve entirely. Buffering often prevents gastric acids from interfering with medications themselves, which can be a significant cause of stomach aches, and decreased localized contact in the upper gastrointestinal tract leads to less pain and better tolerability.[12]
- More portability-Effervescent tablets are more straightforward to carry than liquid medicine since no water is added before being ready to use.
- Improved palatability-drugs delivered with effervescent base taste better than most liquids, superior taste masking of mixtures and suspensions is achieved by limiting objectionable characteristics and complementing flavor and fragrance formulations. The effervescent tablet essentially includes flavoring to taste much better than a mixture of water powder non-effervescent.
- More reliable response drugs with effervescent technology have more consistent, predictable, and reproducible pharmacokinetics than tablets or capsules.[13]
- Accurate dosing - researchers have shown that, relative to traditional formulations, effervescent tablets increase the absorption of some active ingredients. This is because the carbon dioxide released by the effervescent reaction may boost the permeability of the active ingredient due to a paracellular pathway alteration. The paracellular pathway is the first route of absorption of hydrophilic active ingredients during which the solutes diffuse into the intercellular space between epithelial cells. it's postulated that the CO2 widens the intercellular space between cells, which results in more excellent absorption of active
- Ingredients (both hydrophilic and hydrophobic). The increased absorption of hydrophobic active ingredients might be thanks to the nonpolar CO2 gas molecules partition into the cell wall, thus creating an improved hydrophobic environment, which might allow the hydrophobic active ingredients to be absorbed.
- Conventional tablets are also associated with slower action onset, and the first-pass metabolism is often experienced. Effervescent tablets prevent the first-pass metabolism, and rapid action starts are also made. Oral liquid also provides fast onset of action; however, careful handling is required.[14]

FORMULATION

In addition to active ingredients, it generally contains a mixture of acids/acid salts, carbonate, and hydrogen carbonates that release CO2 when mixed with water.

DRUGS THAT ARE FORMULATED AS EFFERVESCENT TABLETS:

1. Difficult-to-digest or stomach-disrupting drugs:

When calcium carbonate is taken in an effervescent formulation, the calcium dissolves in water is readily available for the body to absorb, and there is no risk of excessive gas in the stomach or constipation due to a lower level of acid in the stomach.

2. pH-sensitive drugs, such as amino acids and antibiotics:

The effervescent formulation can buffer the water-active solution such that the stomach pH improves (becomes less acidic), preventing the destruction or inactivation of the active ingredient caused by low stomach pH.

3. Drugs that require a large dose:

A single dose of a standard effervescent tablet (1 inch in diameter, 5 g total weight) can contain more than 2 g of water-soluble active components. If the desired dose is higher, the sachet (powder form) is the usual administration method.[15]

EXCIPIENTS

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

1. Lubricants: The suitable effervescent lubricant (or auxiliary agent) is non-toxic, tasteless, and water-soluble. A lubricant consisting of 4% polyethylene glycol (PEG) 6000 and 0.1 percent sodium stearyl fumarate showed to be effective for ascorbic acid tablets manufactured via direct compression. On a small scale. Water-soluble lubricants such as sodium chloride, sodium acetate, and D, L-leucine have also been recommended for effervescent tablets. Metal stearates are present in short amounts. Surfactants like sodium lauryl sulfate and magnesium lauryl sulfate are lubricants as well.[16]
2. Antiadherents: Granule adherence is avoided by utilizing discs made of polytetrafluoroethylene or polyurethane.[17]
3. Disintegrants or dissolution aids;
Disintegrants are selected to obtain a clear solution within a few minutes of placing the tablet in cold water.[18]
4 . Surfactants; Surfactants are substances that help drugs to wet and dissolve more quickly.[19]
5. Antifoaming agent; Reduce the production of foam and, as a result, the tendency of medications to stick to the glass wall above the water level. Antifoaming agent polydimethylsiloxane is used.[20]
6. Sweeteners; Sucrose, saccharin, and other natural sweeteners were used as sweeteners.[21]
7. Flavors: Flavors are used to provide sweeteners an additive effect, masking the disagreeable taste.
8. Colors: To achieve a better appearance, water-soluble colors might be used.[22]
9. Binders: Binders usually are not used since they inhibit the effervescent tablet from dissolving quickly. Binders can, however, be used in the formulation of effervescent granules. With dehydrated alcohol as the granulating liquid, an exuberant granulation comprised of anhydrous citric acid and NaHCO3 was created. During the massing, a part of the citric acid dissolved and served as a binder. For the ascorbic acid effervescent tablet, maltitol worked well as a binder.
The formation of maltitol crystal bridges was thought to be the binding process.[23]

MANUFACTURING

Effective Tablet Manufacturing Requires Controlled Environmental Conditions. In the manufacturing of these tablets, humidity and temperature control in the production environment is essential.
Conditions of the Environment:
Low relative humidity (maximum of 25% or less) and moderate to cool temperatures (25 ° c) are necessary for the manufacturing areas to prevent granulations or tablets from sticking to the machinery and picking up moisture from the air, which may lead to to to product degradation.[24]

Methods For Manufacturing

The most common manufacturing method is to use high-speed rotary tablet presses. Various granulation technologies are available, including dry and wet granulation methods, two-step granulation (granulating the acid and alkali phases separately), and one-step granulation utilizing water or organic solvents.

Wet Granulation:

In the pharmaceutical industry, wet granulation is the most extensively utilized agglomeration method. The wet granulation method consists of wet massing the powder mixture with a granulating liquid, damp sizing, and drying.[25-32]
The wet granulation process has several necessary steps.

- The drug(s) and excipients are mixed.
- Getting the binder solution ready.
- To make a wet mass, combine the binder solution with the powder combination.
- Wet granules are dried.
- Disintegrant, glidant, and lubricant are mixed with screened granules.

Advantages

- Permits powders to be handled mechanically without losing mix quality;
- improves powder flow by increasing particle size and sphericity.
- Powder density homogeneity is increased and improved.

Wet granulation limitation

- The most significant disadvantage of wet granulation is its price. It is a costly procedure because of the labor, time, equipment, energy, and space required.
- Material loss at several phases of processing.

Dry granulation :

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

The powder combination is compressed without the use of heat or solvent in the dry granulation process. It is the least desirable of all granulation processes. The two main methods are compressing the material into a compact and then milling the compact to obtain granules. Dry granulation is done in two ways. Slugging is the more generally used process in which the powder is recompressed and the resulting tablet or slug is ground to produce the granules. Another option is to use a machine like the Chilosonator to recompress the powder with pressure rolls.[33-39]

Direct Compression:

To obtain a free-flowing, non-segregating, compressible combination, direct compression usually needs a careful selection of raw materials.

Tableting:

Tablets are prepared using single punch 8,9and rotary machines.

Effervescent Tablets Benefits[40]

1. Less discomfort and better tolerability
2. Swallowing is preventable.
3. More stability is obtained.
4. Enhanced palatability.
5. And more portability.
6. Enhanced therapeutic effect.

Drawbacks possible

1. Moisture-based reactions.
2. The expensive.
3. Special packaging is required.
4. Maintenance of specified moisture and humidity The temperature is difficult.

Effervescent Tablets Disadvantages:[41]

1. Unpleasant taste of certain active compounds.
2. Larger tablets need unique packaging materials.
3. Relatively costly to manufacture due to large amounts of more or less expensive excipients and special processing facilities.
4. Clear solution is preferred for administration, although a fine dispersion is now universally accepted.

EVALUATION OF EFFERVESCENT TABLET

Pre-compression evaluation:

1. Angle of repose(θ):

The angle of repose shall be specified as the maximum possible angle Between the surface and the horizontal plane of the powder pile. In a loose powder or granules, the frictional force can be determined by the angle of repose. This is an example of the flow characteristics of the powder.

$\tan \theta = H / R$

$\theta = \tan^{-1} (H/R)$

Where θ is the angle of repose

H is the height of the pile

R is the radius of the base of the pile

The powder mixture was allowed to flow through the funnel fixed to a stand (H). The rest angle was then measured by measuring the height and radius of the heap of powder formed. It was taken care to see that through the sides of the funnel, the powder particles slip & roll over each other. The relationship between the angle of repose and the property of powder flow.[42-44]

Table 1: Angle of repose as an indication of powder flow properties.

The angle of repose (degrees)	Type of flow
< 20	Excellent
20-30	Good
30-34	Passable
> 40	Very poor

2. Bulk density:

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

An accurately measured granulation sample was carefully transferred with the aid of a funnel to the measuring cylinder. Without compacting, the level was observed and noted as apparent volume (V0).[45-47]

By the formula as given, the bulk density was calculated Mentioned below:

Bulk density = M / V0

Where,

M = Mass of powder taken.

V0 = Apparent untapped volume.

3. Tapped Mass:

The cylinder was put on the tapped density tester (ETD 1060, Electrolab) after bulk density measurement and was mechanically tapped. Initially, the cylinder was tapped 500 times, and therefore the tapped volume (V1) was measured at the closest graduated units. The tapping was repeated 750 more times, and therefore the tapped volume (V2) most comparable to the graduated units was repeated.[48-50]

The density of tapping was measured by the formula as given below:

Tapped density = M / V2

Where,

M = Weight of powder.

V 2= Tapped volume.

4. Carr's Index;

Carr developed an indirect method of calculating powder flow from bulk densities. A direct measure of the percentage compressibility of a powder was a measure of the Power and stability of the potential powder arch or bridge.[51-53]

The Carr index of each formulation was determined according to the following equation;

% Compressibility = Df – Do / Df × 100

Where,

Df = Fluff or Poured bulk or bulk density.

Do = Tapped or Consolidated bulk density.

Table 2: Carr's Index as an indication of powder flow

Carr's index (%)	Type of flow
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-35	Poor
33-38	Very poor
>40	Extremely poor

5. Hausner's ratio:

Hausner showed that the ratio tapped density/bulk density was connected to inter-particle friction could be used to predict the properties of powder flow. He found that the low inter-particle friction powder had a ratio of approximately 1.2, where Hausner's ratio exceeds 1.6 as more cohesive, less free-flowing powders. Hausner's ratio of less than 1.25 indicates excellent flow.

Hausner's Ratio = Tapped density/bulk density.[54-57]

Post-compression evaluation:

1. The hardness of tablets.

In manufacturing, packaging, and shipping, tablets require a certain amount of strength or hardness and resistance to withstand mechanical shock from handling. Force on the anvils and the crushing pressure that just causes the tablets to break were observed between two anvils to perform this test tablet. To measure the hardness of tablets, the Monsanto Hardness Tester was used. The results were expressed in kg/cm2.[58-64]

2. Weight variation.

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Twenty tablets were weighed individually; the average Weight was calculated .and comparing the individual tablets' weights to the average. The tablets meet the test if no more than two tablets are outside the percentage limit and if no tablet differs by more than two times the percentage limit.[65-68]

Tabel:3:Weight variation specification

IP/BP	Limit	USP
80 mg or less	1.0%	130mg or less
More than 80mg or Less than 250mg	7.5%	130mg to 324mg
250mg or more	5%	More than 324mg

3. Thickness of tablet

During counting and shipping, variations in tablet thickness can cause problems. Using Vernier calipers, the thickness of the tablets was measured.[69-72]

4. Friability

A Roche friabilator performed this test. Samples of ten preweighed tablets were placed during a friabilator which was operated for 100 revolutions. The tablets were then being dusted and reweighed. Tablets that lose but 0.5–1.0% of their Weight were considered acceptable. Also, if capping occurs during friability testing, the tablets were rejected.[73-76]

$$F = \frac{W\ Initial - W\ Final}{W\ initial} \times 100$$

5. Solution PH

One tablet was dissolved in purified water. After complete dissolution, the solution pH was measured by a pH meter. This test was repeated three times for every formulation.[77-80]

6. Effervescent time

A tablet was put in a glass containing purified water, and a stopwatch measured effervescent time.[81-84]

7. Water content

Ten tablets were dried in a desiccator containing silica gel for 4 hours. The percentage of the content of water was calculated as.[85-87]

8. Co2 content

In 3 different beakers, three tablets were put in 100 ml of 1N sulphuric acid solution. The difference in Weight before and after the dissolution of the tablets was calculated to assess the amount of CO2 released (mg).[88-90]

9. Equilibrium moisture content

Three tablets were put at 18°C in three desiccators containing saturated saline solutions, relative humidity of potassium nitrate (RH, 90%), sodium chloride (RH, 71%), and sodium nitrite (RH, 60%). The percent equilibrium moisture content was determined after 1 and 7 days using the Karl-Fisher method using the Autotitrator instrument. [91-92]

10. Disintegration Time Measurement

At 15-25 °C, one tablet was dissolved in 200 mL filtered water, and the effervescent time was measured with a stopwatch. The effervescence time is over when a clear, particle-free solution is obtained. For each approach, the average of six measurements was calculated.[93-96]

11. Dissolution studies

the in vitro dissolution tests were carried out in the USP dissolution test apparatus type 2 (paddle). In a covered vessel, 900 ml of the dissolution media (phosphate buffer pH 6.8) was placed, and the temperature was kept at 37 0.5 ℃. The paddle's rotational speed was set to 50 rpm. At one-minute intervals, samples were taken. For each example, one ml of dissolving medium was removed and replaced with the same quantity of dissolution media at 37 ◦ c. The sample was filtered using Whatman filter paper and diluted with phosphate buffer to evaluate the UV spectrophotometer. The absorbance was recorded, and the total percent release was determined.[97-100]

APPLICATION OF EFFERVESCENT TABLET.[101-105]

1. Better stability and easy transporting.

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

2. Alternative to parenteral forms, where it is difficult to administer by parenteral route.
3. Zero-order releases are often achieved by incorporating low levels of effervescent mixtures within the tablet matrix.
4. It is helpful in the pulsatile system; a fast-releasing core was formulated to get rapid drug release after the rupture of the polymer coating.
5. Floating time in floating drug delivery systems is strongly influenced by the concentration of effervescent agents.
6. Programmed drug delivery is achieved.
7. For controlled release, effervescent osmotic pump tablets were used.
8. Cosmetic effervescent tablets were also available.
9. Effervescence-induced enhancement is seen as an opening of tight junctions and increases the hydrophobic nature of the cell wall across rats' and rabbits' intestines.

Conclusion

The action of an effervescent formulation is accelerated. Effervescent tablets can be made using the Dry, Wet, or Compression methods, with the Wet approach being the most common. Effervescent granules can be made using a wet process, such as the Fusion method, or a dry way, such as the hot-melt Extrusion method, with the Fusion method being the most important. As a result, the authors of this review article proposed that electrolyte effervescent tablets be utilized in the case of dehydration.

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Conflict of Interest

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