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Review Article

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A REVIEW ON EFFEREVESENT TABLETS
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ABSTRACT:

In the recent trend, the people are very busy with their schedules and have less time to care for health. Even in the treatment, they were searching for quick relief and easily administrable formulations. One such formulation is effervescent tablet. Effervescent tablet is a tablet intended to be dissolved or dispersed in water before administration. They show the special features like less irritation and greater tolerability, swallowing can be prevented; more stability is achieved, improved therapeutic effect. In this review formulation, manufacturing and applications of effervescent tablets were covered.

KEY WORDS: Efferevescent tablets, Floating tablets, Relative humidity, Palatability.

INTRODUCTION:

Effervescent tablet is a tablet intended to be dissolved or dispersed in water before administration. A typical effervescent tablet (1 inch in diameter weighting 5 grams in total weight) can include more than 2,000 milligrams of water soluble active ingredients in a single dose. If the required dose is larger than that, the sachet (powder form) is a common means of delivery. In the 1930s, the effervescent products gained much importance with the technology of Alka Seltzer. These mixtures have been moderately popular over the years since along with medicinal activity they are attractive dosage form for the patients. Some active ingredients are are difficult to digest in the stomach eg: calcium carbonate. In order to digest in the stomach these active ingredients needs more acids, but as age passes the acid in the stomach decreases gradually. Thus these active ingredients may pass

through the stomach without dissolving and may lead to constipation. Also the low pH in the stomach can cause active ingredients to become denatured. However, the effervescent formulation of calcium dissolves in water is readily available for the body to absorb and buffer the water active solution so that the stomach pH increases and thus prevent denaturation and therefore no risk of constipation.

FORMULATION:

It generally contains in addition to active ingredients, mixture of acids/acid salts and carbonate and hydrogen carbonates which release carbon dioxide when mixed with water.

DRUGS THAT ARE FORMULATED AS EFFERVESCENT TABLETS:

1. Drugs difficult to digest or disruptive to the stomach:

If the 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 and there is no constipation caused due to less amount of acid in the stomach.

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

Effervescent formulation can buffer the water-active solution so that the stomach pH increases (becomes less acidic) and thus prevent the degradation or inactivation of the active ingredient that is caused due to low PH in the stomach.

3. Drugs requiring a large dose:

A typical effervescent tablet (1 inch in diameter weighing 5 g in total weight) can include more than 2 g of water-soluble active ingredients in a single dose. If the required dose is larger than that, the sachet (powder form) is the common means of delivery

EXCIPIENTS¹:

The excipients used in the effervescent formulations are

1. Lubricants: A perfect lubricant (or auxiliary agent, in general) for effervescent products must be non-toxic, tasteless, and water-soluble. A combination of 4% polyethylene glycol (PEG) 6000 and 0.1% sodium stearyl

fumarate proved to be a good lubricant for ascorbic acid tablets made by direct compression on a small scale².

Sodium chloride, sodium acetate, and D, L-leucine (water soluble lubricants) also have been suggested for effervescent tablets³. Very low concentrations of metal stearates. Surfactants such as sodium lauryl sulfate and magnesium lauryl sulfate also act as lubricants.

2. Antiadherents: By using discs, such as polytetrafluorethylene or polyurethane, the adherence of the granules is prevented.

3. Binders: As binders prevent a rapid dissolution of the effervescent tablet usually not used. But effervescent granules may be formulated with binders. An effervescent granulation composed of anhydrous citric acid and NaHCO₃ was made with dehydrated alcohol as the granulating liquid. A portion of the citric acid dissolved during the massing and functioned as a binder⁴. Maltitol was a suitable binder for ascorbic acid effervescent tablets. Formation of crystal bridges of maltitol was the assumed binding mechanism.⁵

4. Disintegrants or dissolution aids: Disintegrants are selected such that a clear solution should be obtained within a few minutes after adding the tablet to a glass of cold water.

5. Surfactants: Used to increase the wetting and dissolution rates of drugs.

6. Antifoaming agents: To reduce the formation of foam, and consequently the tendency of drugs to stick to the wall of the glass above the water level. Polydimethylsiloxane is used as antifoaming agent⁶.

7. Sweeteners: Sweeteners like sucrose, saccharin and other natural sweeteners were used.

8. Flavors: Flavors are used for giving the additive effect for sweeteners to mask the unpleasant taste.

9. Colors: Water-soluble colors may be added to get the pleasant appearance.

EFFERVESCENT REACTION:

Effervescence is the evolution of gas bubbles of CO₂ due to reaction (in water) of acids and bases. Typical acids used in this reaction are citric, malic, tartaric, adipic, and fumaric. Typical bases used in the effervescent reaction are sodium bicarbonate, potassium bicarbonate, sodium carbonate, and potassium carbonate.

The most common reaction for pharmaceutical purpose is the acid base reaction between sodium bicarbonate and citric acid.



252g (3mol) 192g (1 mol) 54g (1 mol) 132g (3 mol) 258g (1 mol)

This reaction starts in presence of water, even with small amount as catalyzing agent, and because water is one of the reaction products, it will accelerate the rate of reaction, leading to difficulty in stopping the reaction. For this reason, the whole manufacturing and storage of effervescent products is planned by minimizing the contact with water.

MANUFACTURING:

Controlled environmental conditions is very important in effervescent tablet manufacturing. Humidity and temperature control in production area is an essential step in the manufacturing of these tablets.

Environmental Conditions: Low relative humidity (maximum of 25% or less) and moderate to cool temperatures (25°C) in the manufacturing areas are essential to prevent the granulations or tablets from sticking to the machinery and from picking up moisture from the air, which may cause product degradation.

Methods For Manufacturing

High-speed rotary tablet presses are mostly used . Different granulation technologies are available, ranging from dry granulation and wet granulation methods which include two-step granulation (granulating acid and alkali phase separately) to one-step granulation using water or organic solvents.

Wet Granulation:

The acid and carbonate parts of the effervescent formulation can be granulated either separately or as a mixture with water (crystal water of citric acid, liquid water, or water vapor), ethanol (possibly diluted with water), isopropanol, or other solvents.

When granulating either with solvents containing water or pure water, the effervescent reaction will start. Care must be taken to maintain adequate control of the process. Vacuum processing is often beneficial due to the ability to control the effervescent reaction and the drying process.

Citric acid is moistened and added to the NaHCO₃. Partial wet fusion occurs, and granules are formed by kneading in a suitable mixer. The granules are tableted while still damp, with the moist citric acid acting as a lubricant. The compressed tablets are transferred immediately and continuously to ovens where they are dried at 70–75C. Drying also hardens them. As soon as they leave the dryer, the tablets are packed in aluminum foil lined with polyethylene⁷.

Dry Granulation:

Slugging of the material is done by using heavy-duty tableting equipment or with roller compaction.

Direct Compression:

Direct compression normally requires careful selection of raw materials to achieve a free-flowing, non-segregating, compressible mixture.

Tableting:

By using single punch^{8,9} and rotary machines tablets are prepared.

COMMERCIALY AVAILABLE:

Commercially available effervescent tablets from brand leaders in INDIA.		
Name of product	Active ingredient	Manufacturer
Histac	Ranitidine HCl	Ranbaxy
Pepfiz-O&L	Papain ,Fungal diastase ,Simeticone	Ranbaxy
Effcal	CaCO ₃ , Vitamin D ₃	Ranbaxy
Tagamet	Cimetidine	Glaxo smithkline

Zantac	Ranitidine	Glaxo smithkline
Vitalmag	Magnesium citrate, Folic acid ,Vitamin B6	ICN Hungary
Calcium sandoz	Calcium	ICN Hungary
Ca-C 1000	Calcium,Ascorbic acid	ICN Hungary
Hangoverz	Aspirin, Caffeine	Pious Pharma. Ltd
Solpado	Paracetamol ,Codeine phosphate	Sanofi-aventis
Prolyte fizz	Glucose + Potassium Chloride +Sodium Bicarbonate + Sodium Chloride+ Anhydrous Citric Acid	Cipla

Advantages of Effervescent Tablets

1. Less irritation and greater tolerability.
2. Effervescent drugs are delivered to the stomach at a pH that is just right for absorption.
3. Swallowing can be prevented.
4. More stability is achieved.
5. Improved palatability.
6. More portability.
7. Improved therapeutic effect.

Possible Drawbacks

1. Reactions due to moisture.
2. Expensive.
3. Require special packaging.
4. Maintenance of specified humidity and temperature is difficult.

Packaging:

1. Packaging should be done in air tight containers.
2. The time and the conditions between the production of effervescent tablets and its packaging operation should be minimized to improve the stability of the product.
3. Package should be 0.001-inch-thick aluminum that completely blocks light, oxygen, and moisture.
4. The area within the packet should be large enough to hold the tablets without creating stress on the foil and as small as possible to minimize the amount of “room-air” that it can trap inside with the tablets.
5. Desiccants are used to “bind-up” any free moisture in the tablet or in the air to prevent the effervescent reaction from starting prematurely.

Labeling:

It should be labeled as

These products are not to be swallowed directly .

Not to open until time of use.

Storage:

Protect from excessive moisture.Desiccants are usually added to the containers.

Applications Of Effervescent Tablets

1. Better stability and ease of transporting.
2. Alternative to parenteral forms, where administration through parenteral route is difficult ¹⁰.
3. Zero order release can be achieved by incorporation of low levels of effervescent mixtures with in the tablet matrix¹¹.
4. It is helpful in pulsatile system; a quick releasing core was formulated in order to obtain rapid drug release after the rupture of the polymer coating ¹².
5. The concentration of effervescent agents significantly affects the floating time in floating drug delivery systems ¹³.
6. Programmed drug delivery can be achieved¹⁴.

7. Effervescent osmotic pump tablets were used for controlled release¹⁵.
8. Cosmetic effervescent tablets were also available¹⁶.
9. Effervescence induced enhancement is seen like opening of tight junctions and increase the hydrophobic nature of the cell membrane across rat and rabbits small intestine.

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