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Effervescent Tablet: An Overview

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ABSTRACT

An effervescent tablet formulation typically comprises one or more active substances and other excipients that are required to enable the pharmacokinetic and mechanical properties of the final dosage form.

The oral dosage forms are the most popular way of taking medication despite having some disadvantages like slow absorption and thus onset of action is prolonged. This can be overcome by administering the drug in liquid form but, many APIs have limited level of stability in liquid form. So, effervescent tablets act as an alternating dosage form.

The tablet is added into a glass of water just before administration and the drug solution or dispersion is to be drunk immediately.

KEY WORD: Effervescent tablet

INTRODUCTION

Effervescent tablets are uncoated tablets that generally contain acid substances and carbonates or bicarbonates, and that react rapidly in the presence of water by releasing carbon dioxide. They are usually dissolved or dispersed in water before administration.

Effervescent tablets are a unique dosage forms having drug and effervescent base which is composed of sodium hydrogen carbonate, citric acid and tartaric acid, these base combinations when added to water react to liberate CO_2.[1]

ADVANTAGES

- Rapid medicinal effect.
- It provides hydration to the body.
- No harsh effect on the stomach.
- Improved bioavailability.
- No need to swallow tablets.
- More portability.
- Accurate dosing.
- Superior stability.
- Incorporation of large amounts of large ingredients.

DISADVANTAGES

- Expensive formulation.
- Not suitable for patients with hypertension and heart failure.
- Not for sustained or controlled release.
- Complex production process.

- Some active pharmaceutical ingredient have unpleasant taste which can't be masked.
- Proper storage is needed.[2]

PREFORMULATION

Preformulation may be defined as a stage of the research and development process where the preformulation scientist characterizes the physical, chemical, biopharmaceutical and mechanical properties of a new drug substance, in order to develop stable, safe and effective dosage form.

A) IDENTIFICATION AND CHARACTERIZATION METHOD OF TABLET

Physical appearance:

- Organoleptic properties of the candidate drug molecule, Eg: colour, odour and taste.
- Bulk characterization. Eg: particle size and surface area, powder flow properties, density, compressibility, crystallinity, polymorphism and hygroscopicity.

Solubility study:

Solubility study of a drug was prepared using 10ml of distilled water or any other organic solvent in 25ml volumetric flask. Precaution was taken so that the drug remains in medium in excess. Then by using mechanical shaker, the flask were for 24 hours. The sampling was done 24^{th} and 48^{th} hour. The sample withdrawn (1ml after filtration) was diluted with appropriate medium and was analysed using UV spectrophotometer.

Melting point determination:

Melting point of a drug was determined by taking a small quantity of drug in capillary tube sealed at one end and was placed in Thiel's melting point apparatus and temperature range at which the drug melted was noted. Average triplicate reading were noted.

Determination of λ_{max} :

In order to ascertain the wavelength of maximum absorption (λ_{max}) of the drug, different solutions of the drug (10 µg/ml or 20 µg/ml) in organic solvent of 200380nm against organic solvent as blank.

B) EXCIPIENT-DRUG COMPATIBILITY STUDY

Analytical Techniques Used to Detect Drug-Excipient Compatibility

Fourier Transform Infrared Spectroscopy (FT-IR):

FT-IR is another analytical technique used in compatibility assessment based on the same functional group change during drug-excipients interaction. If there is band shift and broadening in the functional groups as compared to spectrum of the pure active drug in the FTIR spectrum, there is an interaction between active drug and excipients. Fourier Transform Infrared Spectroscopy (FT-IR) Compatibility between the active drugs and worked excipients used were studied by using FTIR spectroscopy.

Thermal method of analysis

A) Differential scanning colorimetry (DSC):

DSC curves of pure components are curves obtained from 1:1 physical mixtures .A significant shift in the melting of the components or appearance of a new exo/endothermic peak and/or variation in the corresponding enthalpies of reaction in the physical mixture indicate incompactibility

B) Isothermal microcalorimetry:

It allows determination of minute amounts of evolved or absorbed heat. The activity of API, excipient and their mixtures are measured individually in the calorimeter and the thermal activity at a constant temperature is monitored.

C) Hot stage microscopy (HSM):

HSM is a visual thermal analysis technique, which allows efficient monitoring of solid state interactions that could be erroneously interpreted as compactibility by DSC. This technique only requires very small quantity of sample of sample when performing compactibility studies.

C) CRITERIA FOR EXCIPIENT SELECTION

Pharmaceutical excipients are substances other than the active pharmaceutical ingredient (API).that have been appropriately evaluated for safety and are intentionally included in a drug delivery system.

Criteria:

- They must be non-toxic.

- They must be commercially bioavailable in an acceptable grade in all countries where the product is to be manufactured.
- Low cost.
- They must be physiologically inert.
- They must be color compatible (not produce any off color appearance).
- They must have no deleterious effect on the bioavailability of the drugs in the product.

D) FORMULATION OPTIMIZATION TECHNIQUES

Optimization term is defined as "to make perfect" which means to make the perfect anything using different techniques and processes. Optimization techniques are used in the different formulations of drugs which help to make good products. It involves in the various form of drug product and their process. Optimization technique are used in the finding solution of a slew of issues relating to the pharmaceutical process and product such as new drug development selection of excipients, formulation, manufacturing and other pharmacy-related problems. Due to the optimization technique we examine the various problems that occur during research. Optimization technique are helpful to make easy the process and formulation of pharmaceutical products and processes.

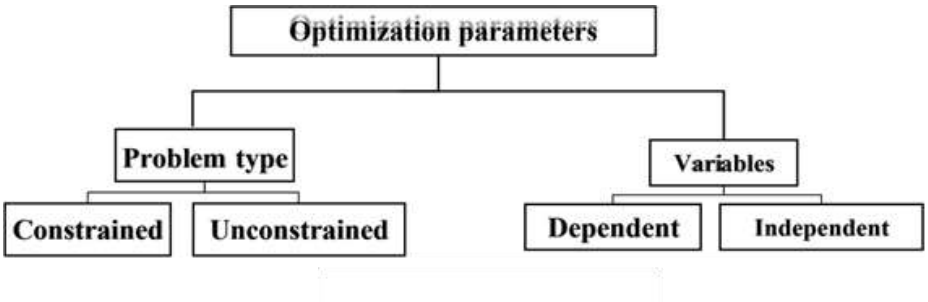

FIG.1: Optimization parameters

(I)Unconstrained

In this system, the restriction is not based on physical limitations. For example, one might want to make an uncoated tablet possible for a specific pharmaceutical system.

(II)Constrained

In this system the restriction is based on physical limitations. As a result, the constrained challenge is to make the uncoated tablet but is should not be Disintegrate in the stomach.

(III)Independent variables

This type of variable are come under the supervision of a formulator like the force of compression, lubrication level, binder level etc.

(IV)Dependent variables

The formulator has no direct control over this type of variable. They are reliant on an unrelated variable. These are responses like hardness, flow property, and friability, among others[3]

TABLET FORMULATION

Tablet Ingredients/ Excipients

In addition to active ingredients, tablet contains a number of inert materials known as additives or excipients.

Different excipients are:

1. Diluent
2. Binder and adhesive
3. Disintegrants
4. Lubricants and Glidants
5. Colouring agents
6. Flavouring agents

7. Sweetening agents
8. Acid agent
9. Alkaline agent

	EXCIPIENT	**USE**	**EXAMPLES**
1	Diluent	Used to increase weight and improve content uniformity	Anhydrous lactose, lactose monohydrate
2	Binder	Agents used to impart cohesive qualities to the powder material	Cellulose, methyl cellulose
3	Disintegrants	Used to promote the break-up of the tablet into smaller fragments in an aqueous	Carboxymethylcellulose(CMC), Hydroxypropylmethylcellulose(HPMC)
		environment	
4	Lubricants	Lubricants reduce the friction between the tablet and the die metal surface	Stearic acid ,magnesium stearate
5	Glidants	Glidants are intented to promote flow of granules or powder material by reducing the friction between the particle	Corn starch, talc, silica
6	Colouring agent	Used to impart appearance to the pharmaceutical dosage form	Red ferric oxide,Titanium oxide
7	Flavouring agent	Give a tablet an additional taste or flavour	Grape,Cherry,Honey,Raspberry
8	Sweetening agent	Used to impart sweetness to the product	Sucrose,Fructose,molasses
9	Acid agent	For the effervescence reaction	Citric acid, tartaric acid, fumaric acid, adipic acid, malic acid
10	Alkaline agent	For the effervescent reaction	Sodium carbonate, potassium carbonate, sodium bicarbonate, potassium bicarbonate

Table No. 1: Formulation of Effervescent Tablet

METHOD OF PREPARATION

The selected acid and alkali were placed on a heater at 54^0C to release the crystallization water of citric acid. The formed granules were then dried in an oven at 60^0C. Afterwards, the mixture of drug and the sweeteners was added. The powders were pressed in a single punch machine with a rod number 14. The tablets were again dried in an oven at 60^0C for 1 hour and finally packaged.[4]

EVALUATION OF EFFERVESCENT TABLETS

APPEARANCE

All tablets should have identical size, shape, thickness, color and surface markings. The general appearance of the tablet allows monitoring a lot-to-lot and tablet-to-tablet uniformity. Tight control of tablet thickness is required to ensure automated machine operations during its packaging and handling. Tablet-to-tablet thickness within a batch and average thickness of tablets across all batches are defined and controlled.

UNIFORMITY OF CONTENT

Potency of tablet is expressed in gm, mg of drug per tablet and is given as the label strength of product. This is usually tested by an analytical method for drug potency (such as high performance liquid chromatography) in a several individual tablets.

HARDNESS

Tablet hardness is the amount of force required to diametrically crush a tablet. It is representative of the tensile strength of a tablet and is determined by the cohesion characteristics of the powder blend. Tablet hardness impacts tablet disintegration, dissolution and friability. If tablets are too hard, they may not disintegrate within a reasonable period of time. This can leads to decreased bioavailability. If they are too soft, then they may not withstand the handling and shipping operations, leading to tablet breakage. Hardness is determined using Pfizer tester and Monsanto tester.

FRIABILITY

Tablets friability represents the tendency of a tablet to break into smaller pieces under mechanical stress, such as falling from a fixed distance. Friability is determined by using Roche friabilator, where the pre weighed tablets are placed in friabilator and operated 100 revolution.

Tablets drop from a fixed distance ie.6inch and the tablets are reweighed.

WEIGHT UNIFORMITY

Weight of tablet made is routinely measured to help ensure that a tablet contains proper amount of drug. Weighs 20 tablets selected randomly and determine the average weight. Then weighs each tablets individually and determine the weight variation of individual tablets from average weight.

DISINTEGRATION

Disintegration of tablets is evaluated to ensure that the tablet dissolves or breaks apart into smaller particles or granules on contact with water under agitation. Tablet disintegration is evaluated in a standardized apparatus that subjects six tablets to a defined mechanical stress in individual reciprocating cylinders in a suitable aqueous medium at 37^0C, to reflect

conditions on oral indigestion. The time it takes for the last of six tablets to disintegrate into smaller particles and disappear from the reciprocating cylinders is called disintegration time.

DISSOLUTION

In vitro drug release of the formulation was carried out using USP dissolution apparatus type

I paddle type under sink condition with rotating speed of. 50 rpm and at temperature of 37^0C. The samples were withdrawn at predetermined time intervals for period of 6 hours and the amount of drug in sample fluid were analysed using UV/Visible spectrophotometer.

CO_2 CONTENT

Three tablets were placed in 100 ml of sulphuric acid solution in 3 separate beakers. In order to determine the amount of released CO_2 (mg), the difference in weight before and after dissolving the tablets was calculated.

EFFERVESCENCE TIME

Three tablets were put in 3 beakers of water and the effervescence time was measured using a stopwatch. Effervescence time was defined as the moment when a clear solution was obtained.[5]

STABILITY STUDIES OF EFFERVESCENT TABLETS

Stability studies of pharmaceutical products may be expressed as the time during which the pharmaceutical products retain its physical, chemical, microbiological, pharmacokinetic properties and characteristics throughout the shelf life from the time of manufacture.

STABILITY TESTING METHODS

Stability testing is a procedure performed for all the pharmaceutical products at various stages of the product development.

Depending upon the aim, steps followed, the stability testing procedures have been categorized into four types and they are

1. Real-time stability testing
2. Accelerated stability testing
3. Retained sample stability testing
4. Cyclic temperature stress testing.

Real-time stability testing:

Real-time stability testing is normally performed for a long duration of time to allow significant degradation of the product under the storage conditions recommended. The period of time for the test of the product depends on the stability of the product which clearly tells that the product is not degraded or decomposed for a long time.

Accelerated stability testing:

This type of stability testing is done at higher temperatures and that decomposition the product is determined. The information is used to predict the shelf life or used to compare the relative stability of alternative formulations.

The accelerated stability studies are easily predicted by the Arrhenius equation

$$K = Ae^{-Ea/RT}$$

Where,

K= Specific rate constant

A= Frequency factor or Arrhenius factor

Ea= Energy of activation

R= Real gas constant 4.184 j/mol. k

T= Absolute temperature

In this method the drugs are stored at different temperatures such as 40°C, 60°C, 70°C, 80°C, 100°C etc.

Retained sample stability testing:

These studies are to be done at room temperature and at refrigerator temperatures.

In this type of testing, the stability is done by selecting one batch for a year. If the number of samples exceeds more than 50 then they are divided into two batches. The samples stability studies help to predict the shelf life. The maximum shelf life of every product predicted could be 5 years which is conventional to the test samples at 3, 6. 9, 12, 18, 24, 36, 48 and 60 months. This method of testing is also known as constant interval method

Cyclic temperature stress testing:

This method is not so much used to the sampling of the products. In this method, cyclic temperature stress tests are designed knowledge of the product so as to mimic likely conditions in the market place storage. In this testing the sampling is considered to be conducted by a cycle of 24 hours which is known as the rhythm of the earth is 24 hours.[6]

PACKAGING AND LABELLING OF EFFERVESCENT TABLET

PACKAGE

A Pharmaceutical Package container is an article or device which contains the pharmaceutical Product and the container may or may not in direct contact with the product.

The container which is designed for pharmaceutical purpose must be stable

TYPES OF PACKAGES

Primary Packaging: Primary packaging are those package which are in direct contact with the Pharmaceutical formulation. The main aim of primary package is to protect the formulation from environmental, chemical, mechanical and/or other hazards.

Secondary Packaging: The package external to Primary package is known secondary package. This package provide additional protection during warehousing and also provide information about drug product for e.g Leaflets.

Tertiary packaging: It is outer package of secondary packaging & prevents damage to the products. It is used for bulk handling and shipping. Examples: Barrel, crate, container, pallets, slip sheet.

TYPES OF PACKAGING FOR TABLETS

- Strip packing: It is unit dose packaging in which a pharmaceutical product is enclosed between two webs of heat-sealed flexible film.
- Blister packaging: Blister packaging is a type of packaging produced by heating a sheet of plastic and moulding it into shape to form a bubble or pocket the blister that completely covers the product.
- Tube packaging: Tablets are packaged in tight, moisture-free plastic or metallic tubes containing a desiccant.[7]

LABEL

Label is a display of written, printed or graphics upon a immediate container or wrapping of a drug package.

LEGAL REQUIRMENTS OF A LABEL:

- The name of preparation
- Strength and dosage form
- Quantity
- Instructions for the use
- Precautions & warnings
- Registration number
- Batch number
- Manufacturing date & Expiry date
- Price
- The name and address of pharmaceutical industry

CONCLUSION

A detailed study was conducted on effervescent tablets. Effervescent tablets are designed as to dissolve in water and release carbon dioxide. In this study we describe about the preformulation studies like identification and characterization method of drug, excipient drug compatibility studies, and criteria for excipient selection, formulation and optimization techniques and formulation were also studied. The method of preparation was studied and also it includes the evaluation, stability studies, packaging and labelling of effervescent tablets.

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