

**FORMULATION AND EVALUATION OF PARACETAMOL
EFFERVESCENT TABLET**

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ABSTRACT

The oral dosage forms are the furthermost widespread way of taking medicine despite having around drawbacks like slow absorption and thus onset of action is delay. This can be overcome by administering the medication in liquid form but, many APIs consume limited level of constancy in liquid form. So, Effervescent Tablets turns as an alternate dosage form. The tablet is added into a glass of liquid just previously administration and the medication solution or dispersion is to be drunk instantly. The tablet is rapidly broken separately by internal release of CO₂ in water due to interface between tartaric acid and citric acid with alkali metal carbonates or hydrogen carbonate in existence of water. Due to release of CO₂ gas, the dissolution of API in water in addition to taste masking effect is enhanced. The advantages of effervescent

tablets associated with further oral dosage forms contains an prospect For formulator to expand taste, a added gentle action on patient's stomach and marketing characteristics. In present work an attempt has been made to formulate an effervescent tablet containing instant release of paracetamol by means of various acids and bases. In present work we are used different acids and bases in dissimilar concentration. In the preformulation study, compatibility evaluation was performed which implies that drug; acids, bases and other excipient are well-matched with each other. The formulation of tablets was done by using wet granulation technique. Then formulated tablets were evaluated for hardness, friability, weight variation, disintegration time and in-vitro drug release. From study it was concluded that F3 shows the better result than the F1 & F2.

KEYWORDS: Effervescent tablet, sustained release, wet granulation method.

INTRODUCTION

Oral drug delivery has been recognized for decades as the furthestmost broadly used route of administered amongst all the routes that have been working for the systemic distribution of drug via numerous pharmaceutical products of diverse dosage forms. The motives that the oral route attained such approval may be in part accredited to its ease of administration. Oral sustained drug delivery system is difficult by partial gastric residence times (GRTs). Speedy GI transit can avoid comprehensive drug release in the absorption region and decrease the effectiveness of the administered dosage.^[1]

Effervescence is described as exclusion of carbon dioxide gas from a fluid due to chemical reaction. This effect starts when preparation come in contact with water which works as catalyzing agent. Effervescent tablets need to be liquified in water before administration. The tablet is punctually broken down by releasing carbon dioxide in water. Carbon dioxide produces by effervescent reaction increases the penetration of active substance into the paracellular pathway and consequently their absorption. The effervescent formulation does not come in direct contact with the gastrointestinal tract and thus such dosage forms are useful for this kind of patient. It decreases the onset of action, due to faster absorption of formulation in liquid dosage form, as compared to tablet formulations.^[2]

Effervescent tablets were designed to supply solutions that release greenhouse gas simultaneously. Usually, these tablets are prepared by compressing the active ingredients with mixture of bicarbonate of soda and organic acids like citric and hydroxy acid. Generally, these tablets are included drugs that are solved rapidly when entered to water and that they are recommended as a transparent and palatable solution. So, they'll be prescribed to patients who suffered from swallow capsules or tablets. The main advantages of effervescent tablets are quick production of solution. Thus, it's faster and better to soak up. As a source of acid, acid is that the most used acid. Also, other acids like tartaric, fumaric, adipic, malic acid and anhydrides and salts of acid will be used. Potassium and washing soda, sodium and hydrogen carbonate, arginine carbonate are used as a sources of alkali sodium hydrogen carbonate is one amongst the foremost used carbonate due to high solubility, severe reaction and low cost. So, excipients like water soluble lubricants (e.g. PEG 4000, 6000 and sodium benzoate), sweeteners, flavourings and water-soluble colours (Placeholder1) are applied.^[3]

Benefits

1. Pleasant Taste Compared to Regular Tablets.

Effervescent tablet can be liquified in a liquid such as fruit juice or water, which is the main cause of their approval. Due to which their taste gets way improved than regular tablet.

2. Distributed More Evenly

The dissolution of predictable tablet is gradually in sometime and can sometime be gateway causing there to the motive of irritation in some cases, in difference the dissolution of effervescent tablet is comprehensive and even through the stomach which stops the accumulation of component in local area. This makes effervescent tablet taste better and fewer irritative and on effervescent method of ingestion of ingredient. Apart from providing nutritional benefit intended effervescent tablet also rise liquid consumption.

3. Increased Liquid Intake

Increased Liquid Consumption is more helpful during period of desiccation ill time and in less liquid ingestion.

4. Easy Alternative to Regular Tablets

Effervescent tablet can use in residence of regular tablet. Which cause trouble in swallowing either due to sickness or age, old age people who administer medicine or supplement on daily basis reports problem associated to swallowing of tablet to overcome these difficulties effervescent tablets are of great significance and can be on relaxed way to swallow a tablet.

5. To Sum Up

Effervescent tablets are receiving progressively popular and it's easy to work out why. They supply a way more effective way of taking supplements or medicine since being spread consistently and far faster than regular medicines.^[4]

Reason for selection of effervescent tablets of paracetamol

Fast onset of action

Effervescent tablet has main advantage that the drug product is already in solution on the time it is consumed. Therefore, the absorption is earlier and further complete than with predictable tablet. Earlier absorption means faster onset of action. Effervescent drug is distributed to the stomach at a pH that is just correct for absorption. Numerous medication

portable slowly through the stomach or have absorption that is hindered by food or another drug.

No need to swallow tablet - effervescent tablets are administered in liquid form so they easy to take as International Journal of Pharmaceutical Research & Development ISSN: 0974 – 9446 Existing online on www.ijprd.com 78 associated to tablets or capsule. The number of persons who cannot gulp tablet or who dislike swallowing tablet and capsule is rising. Through an effervescent dosage form, one dose can usually transport in just 3 or 4 ounces of water.

Good stomach and intestinal tolerance - effervescent tablet liquify completely in a buffered solution. Reduced localized contact in the upper stomach leads to fewer irritation and greater acceptability. Buffering also prevent intestinal acids from interrelating with drug themselves, which can be a main cause of stomach tolerance.

More portability - effervescent tablet is more simply delivered than liquid medication because no water is added until it is complete to use.

Improved palatability - drugs transported with effervescent base, taste improved than most liquids, mixture and suspensions. Greater taste masking is attained by limiting offensive characteristics and adding formulations with flavour and fragrances.

More consistent response - drugs delivered with effervescent technology have expectable and reproducible pharmacokinetics Profile that are considerably more consistent than the tablets or capsule.

Accurate dosing - researchers have been revealed that effervescent tablets improve the absorption of number of active constituents compared to predictable formulations. this is because the carbon dioxide formed by the effervescent reaction can increase active ingredient penetrability due to an change of paracellular pathway.^[5]

Table 1: Excipients used in Formulation.

Sr.No.	Category	Use	Example
1.	Diluents	Used to make up volume of tablet.	Lactose, Microcrystalline cellulose.
2.	Glidant	Helps in free flowing of granules from hopper to die cavity.	Colloidal silicon dioxide, starch, Talc.

3.	Binder	Used as binding agent in tablets.	Glucose, Lactose, Gelatin.
4.	Lubricant	Used to reduce the friction between die wall and tablet.	Stearic acid, Magnesium stearate, Talc, SLS.
5.	Disintegrant	Generally, not used in Effervescent tablet.	Sodium starch glycollate, Starch.
6.	Antiadherent	Prevents sticking of tablets	talc

Aim & Objectives

The aim of this study was to formulate effervescent tablet with sufficient mechanical integrity and to achieve faster disintegration in the water.

Objectives

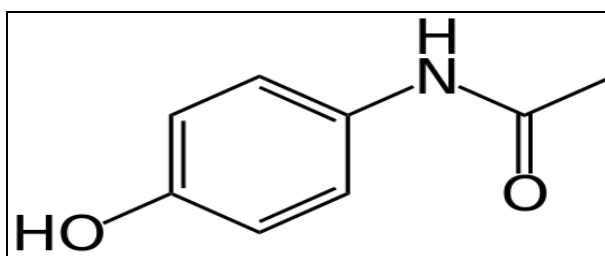
- To optimize formulation for effervescent tablet.
- To prepare effervescent tablet
- To evaluate various parameter for effervescent tablet.
- To generate information useful to the formulation in developing desired, stable and bioavailable dosage form.
- Fast onset of action.
- Rapid and enhanced absorption.

MATERIAL AND METHOD

Ingredients: paracetamol, citric acid, Sodium Bicarbonate, starch, talk, lactose.

Paracetamol: Paracetamol / acetaminophen is one of the greatest prevalent and most usually used analgesic.

Structure



Name	Paracetamol
IUPAC name	N-(4- hydroxyphenyl) ethanamide
Molecular formula	C ₈ H ₉ NO ₂
Molecular mass	151.163 gm/mol
Density	1.263 g/cm ³
Melting point	169° c

Boiling point	420 ⁰ c
Solubility in water	7.21g/kg (0 ⁰ c)

Table 2: Formula for preparation of effervescent tablet.

Sr No:	Ingredient	F1 (mg)	F2 (mg)	F3 (mg)
1.	Paracetamol	300	300	300
2.	Sodium bicarbonate	92	110	128
3.	Citric Acid	112	120	128
4.	Lactose	92	92	92
5.	Gelatin	18	18	18
6.	Starch	12	12	12
7.	Talc	22	22	22

METHOD

Drug (Paracetamol), sodium bicarbonate were sieve through sieve No: 40#. Granules prepared with ethanol to form damp mass and it was passed through sieve no. 40#.

Citric acids, sodium bicarbonate, spray dried lactose, starch, gelatine was blended & passes through sieve no: 40#. Granules prepared by using binding agent (ethanol) & dry at 60⁰c for 30 minutes. Both granules mix & dry at 60⁰c for 15 minutes. Granules were compressed into tablet by using single rotary tablet punching Machine.

Evaluation of Precompressed Blend**1. Angle of Repose (θ)**

The dry mixture powders were permitted to flow through the funnel immovable to a stand at certain height (h). The angle of repose was then considered by measure the height and radius of the heap of powders formed.

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

$$\theta = \tan^{-1} (h / r).$$

Where θ called as angle of repose, h and r were height and radius of the powder heap pleasingly. According to the conditions the angle of repose value less than 250 shows excellent flow whereas angle greater than 400 indicates poor flow.^[6]

2. Bulk Density

Apparent bulk density was resolute by pouring presieved drug excipient mixture into a graduated cylinder and measure the volume and weight “as it is”. It is expressed in g/ml and is specified by

$$Db = M / V_0$$

Where, M is mass of powder and V₀ is the Bulk volume of powder.^[7]

3. Tapped density

It is weight of granules divided by its tapped volume.

$$D_t = M / V_t$$

Where, M is mass of powder and V_t is the tapped volume of the powder.^[8]

4. Compressibility index

The % compressibility is determined by Carr's compressibility index.

The % Carr's index is calculated by means of the following formula:

$$\% \text{Carr's Index} = \frac{TD - BD}{TD} \times 100$$

Where, TD is tapped density and BD is bulk density.^[9]

5. Hausner's Ratio

It was calculated by following formula:

$$\text{Hausner's ratio} = \frac{\text{Tap density}}{\text{Bulk density}}$$

Hausner's ratio from 1.25 to 1.6 show moderate flowing properties. If ratio is more than 1.6 will show more cohesive powders.^[10]

Evaluation of tablet

Average thickness

The thickness of the tablets were determined using vernier Calliper. According to report tablet thickness would be precise within a $\pm 5\%$ variation of average value.

Hardness and friability

For each formulation, the hardness and friability of 20 tablets were determined using the Monsanto Hardness Tester and Roche Friabilator resp. Percentage friability of tablets was measured by using following formula,^[11]

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Disintegration time

This test performed on 6 tablets. For disintegration time, one tablet was positioned in the centre of the Petri dish (internal diameter 10 cm) comprising 10 ml of water and the time taken by the tablet to disintegrate totally was noted.^[12]

Weight Variation

Twenty tablets were selected casually. Tablets were weighed individually and mean weight was calculated. Then deviation of each tablet from average weight was calculated and percent deviation was calculated.

Content Uniformity

Used to ensure that every tablet contains the amount of drug substances certainly with little variation between tablets with in batch.^[13]

In vitro drug release studies

In vitro drug release studies were started using USP apparatus I (basket method). The dissolution media was 1000 mL of 0.1 N HCl at 37 °C for 30 minutes to signify the gastric medium where the tablets will disintegrate. In all experiments, 5 mL of sample was withdrawn at 5 min interval and replaced by means of fresh medium to keep sink condition. Samples were filtered and examined spectrophotometrically at 230 nm.^[14]

RESULT AND DISCUSSION

Table 3: Evaluation of Granules.

property	F1	F2	F3
Bulk density G/cm ³	0.75	0.72	0.73
Tapped density G/cm ³	0.86	0.81	0.85
Angle of repose (Degree c)	25.17	28.81	27.47
% Compressibility Hausner's Ratio	11.63 1.13	11.11 1.12	14.11 1.18

Table 4: Evaluation of Tablets.

Property	F1	F2	F3
Thickness (MM)	7.2	8.3	7
Disintegration Time (sec)	91 \pm 3	82 \pm 2	75 \pm 3
Hardness (kg/cm ³)	2.3	2.1	1.8
Friability Test (%)	Pass	Pass	Pass

Amount of drug content	76.5%	75%	76.6%
Weight variation	NMT 2 tablets out of range	NMT 2 tablets out of range	NMT 2 tablets out of range

From the evaluated data it has been observed that the F3 shows the better result than F1 & F2.

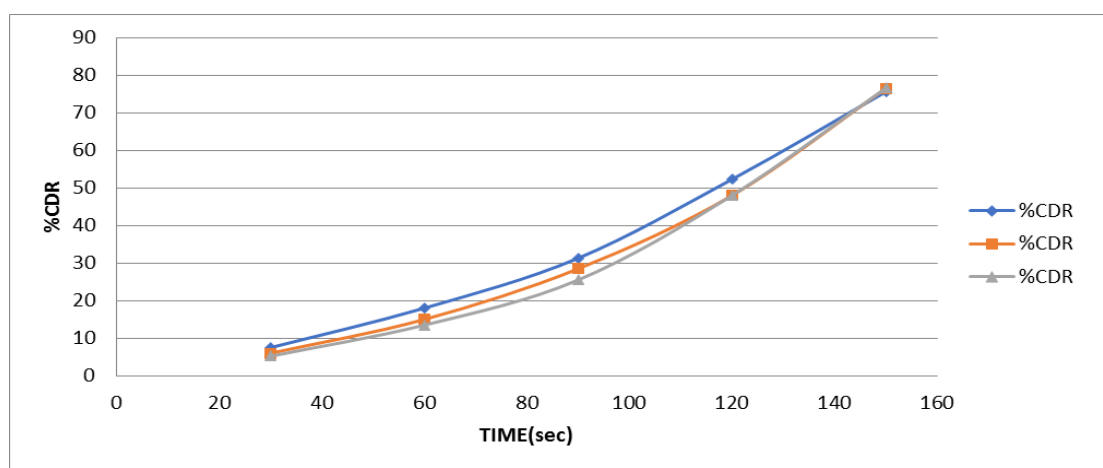


Fig: A. in vitro release of paracetamol effervescent tablet.

From above graph (Fig: a) F3 shows the more drug release as compared to F1 & F2. Therefore, it has been concluded that F3 shows better result.

SUMMARY AND CONCLUSION

The study was under taken with an aim to formulate effervescent tablets of analgesic and antipyretic drug (paracetamol).

The literature review showed that paracetamol having similar mechanism of action to aspirin because similarity in structure. Paracetamol act by reducing production of prostaglandin which involved in pain and fever process, by inhabiting the cyclo-oxygenase enzyme.

In present work an attempt has been made to formulate an effervescent tablet containing immediate release paracetamol using various acids and base. the effervescent tablets were prepared by wet granulation technique. Lactose as a binder and talc as lubricant were used. There are three formulations that content the citric acid and sodium bicarbonate were formulated.

These three formulations were evaluated for hardness, friability, weight variation, Disintegration time and in-vitro drug release. From above study it was concluded that F3 shows the better result than the F1 & F2.

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