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A Brief Review on Formulation and Evaluation of Effervescent Tablet

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Abstract
Effervescent tablet is an widespread oral drug delivery system. Some drugs shows slow absorption of drug and slow onset of action, to overcome such problem, gastro retentive drug delivery system provides the prolonged and predictable drug delivery. From GRDDS, effervescent tablet act as an alternative option which provides effective therapeutic drug delivery. The fundamental contribution of this work is to provide prolonged action of drug and easy administration for the pediatric and geriatric patients. This review summarizes the key facts about selection of suitable drug and excipients, selection of method of formulation and evaluation test. This study shall help to choose best criteria of ingredients and method of formulation like wet granulation ,dry granulation , roller compaction, direct compression and fusion method while formulating effervescent tablet.

Keywords
Effervescent tablet, Gastro retentive drug delivery system , Prolonged drug delivery system , Floating drug delivery system.

Introduction

Oral dosage form is the agreeable drug delivery system due to its ease of administration, although it have some disadvantages like slow absorption and thus onset of action is time consuming. This can be avoided by administering the drug through gastro retentive drug delivery system which acts as an alternative dosage form.[4]

GRDDS: Gastro retentive dosage forms are drug delivery systems which remain in the stomach for an extended period of time and allow both target specific and controlled release drug delivery system. After administration of gastro retentive delivery, drug swells and remain floating in the stomach for a prolonged period of time, while it continuously releases drug in the upper intestinal tract with target drug delivery. Floating drug delivery system categorizes into effervescent system and non effervescent system .Detail classification of GRDDS is shown in fig1.[15]

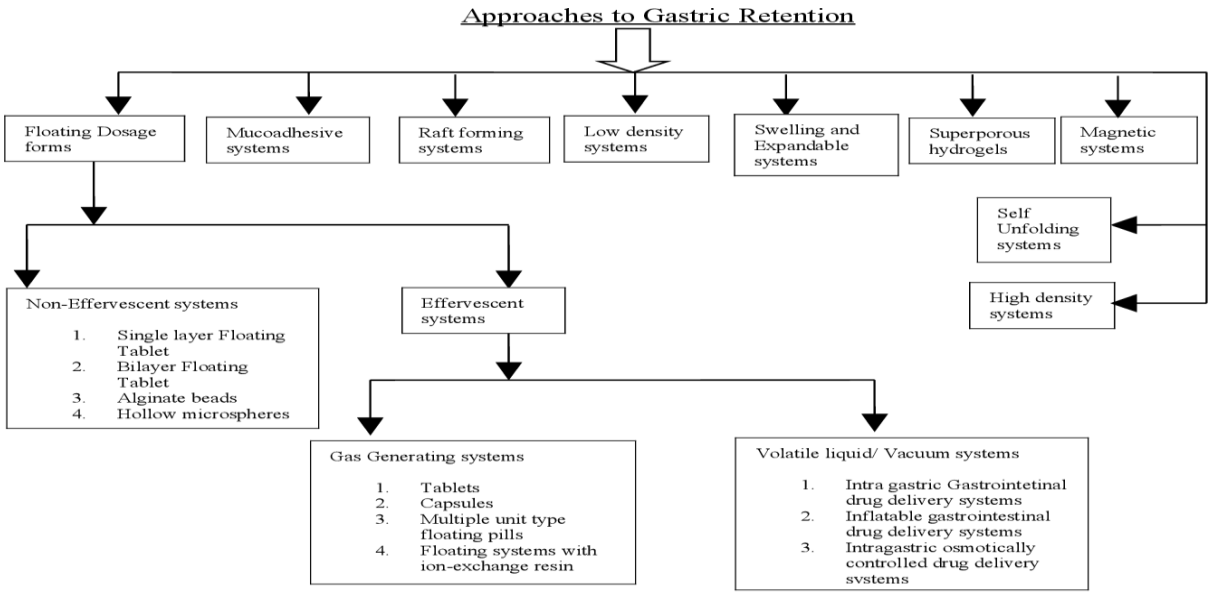


Figure No. 1[15]: Approaches to gastric retention

Effervescent tablets are dissolved in water before administration. The tablet is broken apart due to the internal release of CO 2 in water and the CO2 liberation is created by an interaction of acid and alkali in the presence of the water. Effervescent tablets are uncoated tablets and do not require any disintegrants, because tablet disintegrates due to the release of carbon dioxide when comes into the contact of water.[3] Effervescent floating drug delivery system produces CO2 gas, which reduces the system's density and allows it to stay buoyant in the stomach for a long time, allowing the drug to be given slowly and at a controlled rate.[4]

Figure No. 2 : showing dissolving effervescent tablet in a glass of water

The floating drug delivery systems result in long lasting intra-gastric buoyancy which may not only provide a sustained but also site specific action with reduced side effects for better patient compliance.[5]

Advantages Of Effervescent Tablets [7,8,9,10]

- Drug releases slowly at a desired rate, results in increased gastric retention and control on fluctuation in plasma drug concentration.
- Patient compliance is improved due to the convenience of administration.
- Reduces the frequency of dosing.

- Enhances absorption of drug and site specific drug delivery.
- Carbonation helps to mask the objectionable taste of drug.
- Treats gastric related disorder.

Disadvantages of Effervescent Tablet [1,7,10,11,12,13]

- Excipients and manufacturing methods used are expensive.
- Some API have disagreeable and irritating taste, that taste cant masked by using flavors
- Its high proportion of sodium and potassium make it unsuitable for cardiac disease patients.
- Special packaging materials and production facilities are essential.

General components used in effervescent tablet[1,10,16,17,18]

Acidifying agent	Citric acid , Tartaric acid , Malic acid , Fumaric acid, Ascorbic acid, Adipic acid
Alkalizing agent	Sodium bicarbonate, Sodium carbonate, Sodium sesquicarbonate , Potassium Bicarbonate , Potassium carbonate, Calcium carbonate, Sodium glycine carbonate
Lubricants	PEG 4000, PEG 6000, Sodium benzoate, sodium lauryl sulphate, Sodium acetate, Alanine, Glycine
Binders	PVP, PEG 6000, Mannitol
Swelling agent	Cross povidone, micro-crystalline cellulose, HPMC
Sweetening agent	Aspartame, Acesulfum potassium

Mechanism of Action[1]

The reaction between acid and base such as Citric acid and Sodium bicarbonate & Tartaric acid and Sodium bicarbonate, which results in liberation of carbon dioxide shown as follows:

$$C_6H_8O_7.H_2O + 3NaHCO_3\ (aq) \rightarrow Na_3C_6H_5O_7 + 4H_2O + \mathbf{3CO_2}\ (g) \uparrow$$

Citric acid + Sodium bicarbonate → Sodium citrate + Water+ Carbon dioxide

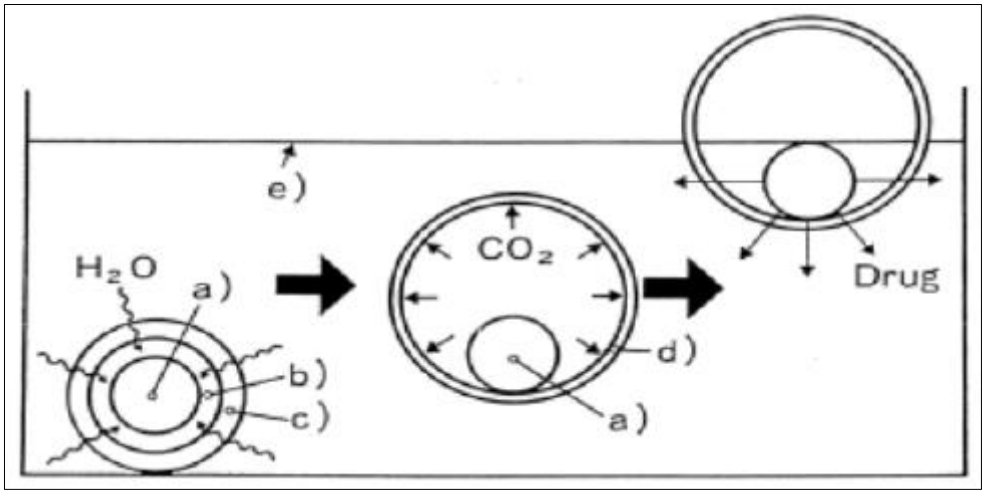
$C_4H_6O_6 + 2\ NaHCO_3 \rightarrow Na_2C_4H_4O_6 + 2H_2O + \mathbf{2CO_2}\ (g) \uparrow$

Tartaric acid + Sodium bicarbonate → Sodium Tartrate +Water + Carbon dioxide

From the above balanced equation we got the acid base ratio for the effective effervescent tablet

Citric acid : Tartaric acid : Sodium Bicarbonate

1 : 1 : 5



Steps Involved in Formulation of Effervescent Tablet

1. Selection of drug candidates for effervescent tablet.

2. Solubility study of drugs.

3. Construction of calibration curve of drug.

4. Selection of suitable excipients

5. Drug excipients compatibility study (FTIR)

Method of Formulation

1. Wet Granulation[1]

Wet granulation is the most widely used process of agglomeration of granules. It involves wet massing of the powder blend using a granulating liquid, wet sizing and drying.

Steps involved in the wet granulation

Mix all the API(s) and excipients by adding binder solution to form wet mass. Drying is carried out by using hot air oven or sunlight. Mix these prepared granules with disintegrants , glidant and lubricant. Now final granules compressed into tablets.

Merits:

- Enhance uniformity of powder density.
- Enhance flow property of an powder by improving the size and shape of powder (Spherical shape enhances flow of powder).
- Mechanical handling provides safe handling of powders without loss of mixture quality.

Demerits:

- Loss of material during manufacturing.
- Expensive process

2. Dry Granulation[1]

In dry granulation powder mixture is compressed into tablets without the use of solvent and heat. In this method two procedures are involved in the formation of a compact of material by compression and then milling of obtained compact for obtaining granules.

Two methods are commonly used in dry granulation.

1. Slugging: Powder is recompressed and the resulting tablets are milled to yield the granules.
2. Second method is to recompress the powder granules with pressure rolls using a machine called as Chill-sonator.

Finally, granules are compressed into tablets.

3. Roller Compaction[1]

In roller compaction the compaction of powder is done by using a pressure roll, accomplished by a machine called chill sonator. Chill-sonator turns out a compacted mass in a steady continuous flow. The powder flows down between the rollers from the hopper which containing a spiral auger to feed the powder into the compaction zone. Slugs or aggregates are milled for production into granules Now, obtained granules are compressed into tablets.

Use

- Provides higher manufacturing efficiency
- Used in the granulation of dry herbal material and inorganic materials.
- For the production of sustained release tablets as well as immediate release tablets.
- For the compaction of drugs and their formulations.
- In the production of direct-compressible excipients

5. Fusion Method[17]

All ingredients were weighted accurately and were mixed in a tumbling cubic blender. Then, the obtained resulting mixture was placed in an oven. The powder was mixed periodically until the crystallization water of acid was released as binder factor. After obtaining an aided pasty mass, this wet mass was passed through sieve and the obtained granules were dried in an oven. After drying, again sieving is carried out. In the next stage, sweeteners and flavors were added with the above prepared granule mass and mixed with other material. Finally, the lubricants were added and mixed with other material. The granule mixture is then compressed into tablets by using a single-punch press (KILIAN & CO. Germany). Finally, they were dried and packed. These are the 5 methods which are used in the manufacturing of an effervescent tablet[5].

Evaluation Test

Precompression Test [21,22,23,24]

1. Angle of repose:

Angle of repose is used to measure frictional forces between powders and granules. It is the maximum angle between the surface of pile and horizontal plane. Angle of repose is measured using fixed funnel method. In this method graph paper is placed on a flat horizontal surface, on which funnel fixed with its tip at height ‘’H’’ Now granules are poured carefully through the funnel until conical pile of granules just touches to the tip of funnel. The formed pile gives us diameter and radius from the graph paper. From the obtained

radius and height of the pile, angle of repose is calculated using given formula.

tan θ = h / r

Where, θ= angle of repose

h=Height of pile

r=Radius of pile

Indication of powder flow with relate to angle of repose:

Angle of repose	Type of flow
Less than 20	Excellent
20 to 30	Good
30 to 40	Passable
More than 40	Very poor

2. Bulk Density

Accurately weigh the given sample of granules. Carefully pour the weighed granules into the measuring cylinder using funnel. Without disturbing the measuring cylinder, level is observed & noted as apparent volume(v_0)and bulk density is calculated using given formula.

Bulk density =M/V_0

Where,

M=Mass of powder

V_0=Apparent volume

3. Tapped density

After measuring the bulk density, the same measuring cylinder is tapped for 750 times and level observed on measuring cylinder, noted as tapped volume. Now tapped density is calculated using given formula,

Tapped density = M/V

Where,

M=weight of powder

V=tapped volume

4. Carr's index

It is the method of measuring powder flow from tapped density and bulk density.

Carr's index =(Tapped density - Bulk density / Tapped density) ×100

Carr's index as an indication of powder flow.

Carr's index (%)	Flow pattern
5 to 15	Excellent
12 to 16	Good
18 to 21	Fair to passable
23 to 35	Poor
33 to 38	Very poor
More than 40	Extremely poor

5. Hausner's ratio

This method is developed to determine the compressibility strength of powder. Hausner's ratio is used to estimate flow property of granules.

Hausner's ratio= Tapped density/Bulk density[15]

Post Compression Test [1, 25,26,27,28,29,30,31]

1. Weight variation:

As per USP, 20 tablets were selected then weighed individually and calculate average weight. Percentage of weight variation is determined by using above formula.

% weight of variation = Individual weight-Average weigh/Average weight

IP/BP	Limit	USP
Less than 80mg	10%	Less than 130mg
80mg-250mg	7.5%	130mg-324mg
More than 250mg	5%	More than 324mg

not more than two individual tablet deviate more than 5% deviation.

2. Thickness and diameter

The thickness of arbitrarily chosen tablet is measured by using screw gauge and vernier caliper.

3. Friability

Take randomly 20 tablets, weigh it properly which is considered as initial weight (W_0) ,then deposited it in Friabilator. The Friabilator is rotated at 25 rpm for 4 minutes. After tablets were detached, again tablets were weighed after friabilation which is considered as (W_f).

The percentage of friability is calculated by,

$$\%F = (W_0 - W_f)/W_0 \times 100$$

Where,

%F= Percentage of friability

W_0= Initial weight

W_f=Final weight

It was carried out by placing one tablet in a 250 ml beaker. Total effervescence time was carried out by placing a tablet in beaker containing about 250 ml water at 20^0C to

USP limit is 0.5-1%.

4. Hardness

It is defined as force required breaking the tablets. The hardness of tablet is carried out using 'Monsanto Hardness Tester' and which is expressed in Kg/cm^2. Hardness for uncoated tablets that is effervescent tablets is 3-5kg/cm2 is considered to be satisfactory.

5.Floating lag time

It is the time period taken to start floating when it comes into contact with water.

6. Effervescence lag time

Time period taken to start effervescence after tablet comes in contact with water.

7. Total effervescence time

30^0C. Gas bubbles were evolved. Repeat this operation for 6 tablets. Tablet passes this test if it disintegrates within 3 minutes as prescribed.

8. Measurement of CO2 content

Dissolve the single tablet in 100 ml of 1N sulphuric acid solution. Weight variation is calculated from the weights of before and after dissolution. Obtained weight difference shows amount (mg) of CO_2 per tablet.

9. Water Content

10 tablets dried for 4 hours in desiccator containing silica gel. The percentage of water content is calculated using above formula

wt. of tablet before drying – wt. of tablet after drying/wt. of tablet before drying×100

Water content of 0.5% or less is acceptable.

10. Drug content

Ten tablets were triturated and from the fine powder weigh about equivalent to 1 tablet. Transfer that weighed powder into 100 ml of volumetric flask containing 50ml of water. Ensure absolute solubility of drug into the water. Adjust the volume up to 100 ml in volumetric flask. Now absorbance is checked UV-visible spectrophotometer.

11. Disintegration

Place one tablet in a 250 ml beaker containing water at 20^0C -30^0C,several gas bubbles have formed. When the gas surrounding the tablet or its fragment has stopped, the tablet will have disintegrated, been dissolved or distributed in the water, leaving no agglomerates of particles.

Conclusion

From the above it was concluded that the effervescent tablet is an widespread oral drug delivery system. Some drugs shows slow absorption of drug and slow onset of action, to overcome such problem, gastro retentive drug delivery system provides the prolonged and predictable drug delivery.

References

1. *Eichman, JD; Robinson, JR (June 1998). "Mechanistic studies on effervescent-induced permeability enhancement". Pharmaceutical Research. 15 (6): 925–30.*
2. *Yeniocak, Selman; Tatli, Ozgur; Cansu, Aysegul; Erturk, Engin; Erol, Mehmet Muharrem; Turedi, Suleyman (September 2010). "Acute severe respiratory distress secondary to misuse of an N-acetylcysteine effervescent tablet". The American Journal of Emergency Medicine. 28 (7): 842.*
3. *Begley, CG; Paragina, S; Sporn, A (March 1990). "An analysis of contact lens enzyme cleaners". Journal of the American Optometric Association. 61 (3): 190–4.*
4. *Andersen, MP (1992). "Lack of bioequivalence between disulfiram formulations. Exemplified by a tablet/effervescent tablet study". ActaPsychiatricaScandinavica.Supplementum. 369: 31–5.*
5. *Patil JS, Hydrogel System: An Approach for Drug Delivery Modulation, Advance Pharmacoepidemiology and Drug Safety, 2015; 4:135. 3*
6. *Patil JS, Novel Tubercular Therapeutic Agents: Need of the Day, Advance Pharmacoepidemiology and Drug Safety, 2015; 4:137.*
7. *Obara T, Prevalence, Determinants, and Reasons for the NonReporting of Adverse Drug Reactions by Pharmacists in the Miyagi and Hokkaido Regions of Japan, Advance Pharmacoepidemiology and Drug Safety, 2015; 4:191.*
8. *Teoh BC, et al. Perceptions of Doctors and Pharmacists towards Medication Error Reporting and Prevention in Kedah, Malaysia: A Rasch Model Analysis. AdvPharmacoepidemiol DrugSaf. 2015; 4:192.*
9. *United States Pharmacopeia 31/National Formulary 26. Rockville MD USA: United States Pharmacopeial Convention; 2008.*

10. *Yanze FM, Duru C, Jacob M, A process to produce effervescent tablets: Fluidized bed dryer melt granulation. Drug Development & Industrial Pharmacy, 2000; 26(11):1167-76.*

11. *Simona B, Tanja R, Using different experimental designs in drug excipient Compatibility Studies during the Preformulation development of a stable solid dosage formulation, ActaChimicaSlovenica, 2010; 57:895-903.*

12. *Larry LA and Stephan WH, Pharmaceutical Dosage Form: Tablets 3rd edition Vol. 1: 465.*

13. *Aboud HM, Elbary A, Ali AA, Enhanced dissolution of meloxicam from orodispersible tablets prepared by different methods, Bulletin of Faculty of Pharmacy, Cairo University, 2012;50:89–97.*

14. *Ahmed I, Aboul-Einien M, In vitro and in vivo evaluation of a fast disintegrating lyophilized dry emulsion tablet containing griseofulvin, European Journal of Pharmaceutical Sciences. 2007; 32:58–68.*

15. *Dhakar RC, Maurya SD,Dangi G, Kumar G , Gupta M, Kiroriwal S, Buccal Adhesive Dosage Forms As A NISDD: A Pharmaceutical Review, Research Pharmaceutica, 2010; 1(1): 46-59.*

16. *Aly AM, Amro BI, Hajji FD, Preparation and Evaluation of Rapidly Disintegrating Glimepiride Tablets. International Journal of Pharmaceutical Sciences and Nanotechnology, 2011; 3(4):1220-1229.*

17. *Ashish P, Harsoliya MS, Pathan JK, Shruti S, A ReviewFormulation of Mouth Dissolving tablet, International Journal of Pharmaceutical and Clinical Science, 2011; 1(1):1- 8.*

18. *Sandhyarani G, Kumar KP, Formulation and evaluation of fast dissolving Tablet of imidapril, Indian Journal of Pharmaceutical Science& Research, 2017;4(3):147-150.*

19. *Dhakar RC, Maurya SD, Gupta AK, Siddiqui AW, Interpenetrating polymeric network hydrogel for stomachspecific drug delivery of clarithromycin: Preparation and evaluation, Asian Journal of Pharmaceutics, 2010; 4(4): 184- 189.*

20. *Dhakar RC, Maurya SD, Aggarawal S, Kumar G, Tilak VK, Design and evaluation of SRM microspheres of Metformin hydrochloride, PharmacieGlobale(IJCP), 2010; 1(07):1-6.*

21. *Dhakar RC, Maurya SD, Sagar BPS, Prajapati SK, Jain CP, Variables influencing the drug entrapment efficiency of microspheres: a pharmaceutical review, Der Pharmacia Lettre, 2010; 2(5): 102-116.*

22. *Sastry SV, Nyshdham JR, Fix JA, Recent technological advances in oral drug delivery: A review. Pharmaceutical Science and Technology Today, 2000; 1(3): 38-45.*

23. *Maurya SD, Tilak VK, Dhakar RC, Verma KK, Soni U, Gupta, Preparation and evaluation of floating tablet of famotidine through solid dispersion, International Journal of Current Research and Review, 2011; (2)1: 21-30.*

24. *Thoke SB, Sharma Y., Rawat S, Nangude, SFormulation development & evaluation of effervescent tablet of Alendronate sodium with vitamin D3, Journal of Drug Delivery & Therapeutics; 2013; 3(5):65-74.*

25. *Abolfazl A, Formulation, Characterization and Physicochemical Evaluation of Ranitidine Effervescent Tablets, Advanced Pharmaceutical Bullet in, 2013; 3(2): 315-322.*