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Review article Granules

Comprehensive Review on Effervescent Granules Formulation

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ABSTRACT

The present work is based on the formulation of effervescent granules of Tinidazole and Ofloxacin and their comparative study. Seven such formulations were prepared using cetyl alcohol and tartaric acid and sodium bicarbonate as effervescent base at different ratios. The granules were prepared by the melt granulation method, and they were evaluated for flow property (such as angle of repose, bulk density, tapped density, and Carr's index), particle size, pH, effervescence time, in vitro dissolution studies, and drug content. Effervescence is defined as the evolution of bubbles of gas from a liquid as a result of a chemical reaction. Effervescent mixtures have been known and used medicinally for many years. Effervescent powders used as saline cathartics were available in the eighteenth century and were subsequently listed in the official compendia as compound effervescent powders. These were more commonly known as 'Seidlitz powders'.

Keywords: Formulation, Effervescent granules

INTRODUCTION

Effervescent granules are granular dosage form of drug in a dry mixture usually composed of effervescents like sodium bicarbonate, citric acid and tartaric acid. Effervescent granules when added to water, the acids and the base react to liberate CO_2, resulting in effervescence.

The choice of ingredients for effervescent granules depends both upon the requirement of the manufacturing process and the necessity of making a preparation which dissolves in water. The required ingredients are at least one acid and at least one base. The base must release carbon dioxide upon reaction with the acid.

Examples of such acids include tartaric acid and citric acid. Examples of bases include sodium carbonate, potassium bicarbonate, sodium bicarbonate.

Effervescent granules are usually prepared from a combination of citric and tartaric acid rather than from a single acid because the use of either acid alone causes difficulties.

When tartaric acid is the sole acid, the resulting granules readily crumble and lack mechanical strength. Citric acid alone results in a sticky mixture which is difficult to granulate during the manufacturing process.

Granules are preparations consisting of solid, dry aggregates of powder particles sufficiently robust to withstand handling. They are intended for oral administration. Some are swallowed as such, some are chewed and some are dissolved or dispersed in water or another suitable liquid before being administered.

For reasons of patient safety and to ensure the correct administration of the medicinal product, this term may also be used where very small tablets (rather than granules) are presented in a sachet, and where the entire contents of the sachet are intended for oral administration as a single dose.

Granules contain one or more active substances with or without excipients and, if necessary, colouring matter authorised by the competent authority and flavouring substances. Granules are presented as single-dose or multidose preparations.

Each dose of a multidose preparation is administered by means of a device suitable for measuring the quantity prescribed. For single-dose granules, each dose is enclosed in an individual container, for example a sachet or a vial.
Effervescent mixtures have been moderately popular over the years since along with the medicinal value of the particular preparation, they offered the public a unique dosage form that was interesting to prepare. In addition, they provided a pleasant taste due to carbonation which helped to mask the objectionable taste of the drugs.

TYPES OF DRUGS USED IN EFFERVESCENT GRANULES

Usually water soluble drugs
1- Alka seltzer: (Aspirin) minor aches, pains, inflammation, fever, headache.
2- Citro carbonate: Urinary pH modifiers and to treat gastric antacid.

MECHANISM OF EFFERVESCENCE

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

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

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

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

ADVANTAGES

1. Rapid onset of action (prepared as solution) rapid disintegration and dissolution.
2. Pleasant taste chemical reaction between acid and base lead to liberate CO2 which act as local anaesthetic effect of oral cavity so mask the undesirable taste.
3. Psychological effect, patient comfort to it.
4. Provide alkaline solution, neutralization of an acidic drugs as aspirin (alkalinization of urine and increase excretion of drug which is acidic).

DISADVANTAGES

1. Unstable (absorb the water [moisture] from the atmosphere).
2. Not accurate dose estimation because the one who estimate the dose is the patient himself.
3. Sodium overload (these granules are not suitable for hypertensive patients)
4. Have many drug-drug interaction.
5. It can be overcome by packaging and compressing into tablet dosage form and put them in aluminum foil (not in plastic foil because it allow the absorption of water from moisture).

SOURCES OF ACIDS USED IN EFFERVESCENT GRANULES

Formulation of effervescent preparation mainly consists of three components: Active ingredients (drug), acid source, and alkaline source constituted by carbonate and bicarbonate.
Acid substance and carbonates or a bicarbonate substance reacts rapidly in the presence of water by releasing carbon dioxide.
They are usually dissolved or dispersed in water before administration. They provide a pleasant taste due to carbonation which helps in taste masking of objectionable medicaments.
This is a unique advantage of this dosage form over other fast release dosage forms which required the use of method of taste masking. Other excipients are diluents, binders, disintegrating agent, sweetener, flavors, colors, surfactants, and antifoaming agents (if required).

The active ingredients are either present in the effervescent formulation as readily soluble compounds or they are solubilized by salt formation during the dissolution process. However, it is also possible to disperse poorly soluble active ingredients.
1. **Natural acids:** (citric acid, tartaric acid, malic acid ,fumaric acid). Highly soluble in water and thus widely use in preparation of effervescent.
2. **Anhydride acids:** (anhydrous citric acid and anhydrous tartaric acid) . when dissolved in water give hydrous acids.
3. **Salts acids:** (disodium dihydrogen phosphate ,and sodium disulfide). soluble at pH 4.5 otherwise they are strong acids.
4. **Effervescent base:** used mainly in the preparation of effervescent granules. Sources of acids Na2CO3 used instead of NaHCO3 but the last is more effective because it´s more soluble in water.

COMPOSITION

Citric acid - 1 part
Tartaric acid - 2 part
NaHCO3 - 3.44
Total - 6.44

Effervescent granules are usually prepared from a combination of citric and tartaric acid rather than from a single acid because the use of either acid alone causes difficulties.
When tartaric acid is the sole acid, the resulting granules readily crumble and lack mechanical strength. Citric acid alone results in a sticky mixture which is difficult to granulate during the manufacturing process. The reaction between citric acid, tartaric acid and sodium bicarbonate results in liberation of carbon dioxide.

TYPES OF METHOD FOR PREPARATION OF EFFERVESCENT GRANULES

- Wet method
- Fusion method(Dry)
- Hot extrusion method
- Non aqueos method
- Melt granulation method

HOT MELT EXTRUSION TECHNIQUE

First weigh the required quantity of ingredients and pass them through sieve no 18.Heat it a temperature of about 50 0C to 80 0C until a molten mass is obtained. Now cool down the mass at room temperature and then pass the mass through the sieve no8 or sieve no10 to obtain granules. Finally dry the granules at a temperature not exceeding 60 ºC.29-30

FUSION METHOD OR DRY METHOD

It is the most important method for the preparation of effervescent granules. In this fusion method compression step is eliminated. In this method the powders are heated using an oven or source of heat. Fusion method uses the water of crystallization present in the citric acids which acts as binding agent. The powdered mixture is stirred well to obtain a uniform mass and is passed through a sieve to obtain granules and is finally dried in an oven.

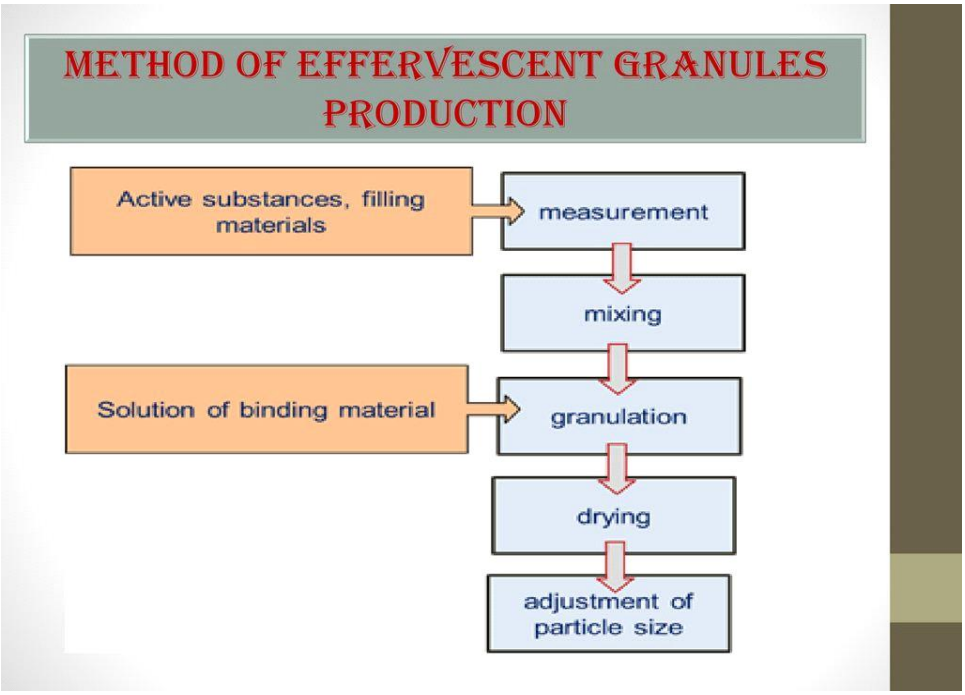
NON AQUEOUS METHOD

The ingredients are weighed and are taken into a china dish. To the ingredients add drop by drop alcohol (Ethanol) until it forms a mould. Pass the mould through the sieve no 10, granules are obtained & these granules are kept in an oven at an temperature of 55o C for 12 hours, the granules are again passed through the sieve to obtain uniform sized granules. These granules are further packed in Sachets and are stored for further use.

WET METHOD

It is the oldest method of granule preparation .Firstly all the ingredients are powdered and are gone through a sieve to induce uniform particle size. Wet massing is the most significant step within the wet granulation process. During this step to the powdered mixture a granulating agent is added. After the powdered mixture is moistened it is passed through a mesh screen to produce desired size granules. Later these granules are dried by using a hot air oven.

STEPS INVOLVED IN PREPARATION OF EFFERVESCENT GRANULES



EVALUATION TESTS FOR EFFERVESCENT GRANULES

The evaluation test carried out for Effervescent granules are

- Bulk density
- Tapped density
- Angle of Repose
- *Invitro*, dissolution studies
- Carr's index
- Stability studies.
- Effervescence cessation time

CONCLUSION

Effervescent granules are an effective and cost-saving preparation. This article explains about the composition and usage of the ingredients used in effervescent granules. It also provides information on its action and steps involved in effervescent granules preparation along with the advantages and disadvantages discussed.

REFERENCES

1. Ashika Advankar, Rahul Maheshwari, Vishakha Tambe 1, Pooja Todke, Nidhi Raval, Devesh Kapoor, Rakesh K. Tekade. Chapter 13 - Specialized tablets: ancient history to modern developments. Drug Delivery Systems. Advances in Pharmaceutical Product Development and Research. 2019: 615-664 https://doi.org/10.1016/B978-0-12-814487-9.00013-2.
2. Jinan Al-Mousawy, Zahraa Al-Hussainy, Maryam Alaayedi. Formulation And Evaluation of Effervescent Granules of Ibuprofen. Int J Applied Pharmaceutics. 2019; 11(6): 66-69. doi:10.22159/ijap.2019v11i6.34912
3. European Pharmacopoeia. Available from: https://www.fpharm.uniba.sk/uploads/media/Granules.pdf.
4. Available from: https://www.sciencedirect.com/science/article/pii/B9780128144879000132.
5. Palanisamy P, Abhishekh R, Yoganand Kumar D. Formulation and evaluation of effervescent tablets of aceclofenac. Int Res J Pharm. 2011;2:185-9.
6. Rajalakshmi G, Vamsi C, Balachandar R, Damodharan N. Formulation and evaluation of diclofenac potassium effervescent tablets. Int J Pharm Biomed Res. 2011;2:237-43.
7. CVS Subramanyam Unit operations text book. Effervescent granules by non-aqueous method pg-127.
8. Mohrle R. Exiciepient of tablets. In: Lieberman HA, Lachman L, Schwartz JB, editors. Pharmaceutical dosage form: tablets. 2nd ed. Vol. 1. New York: Marcel Dekker, Inc; 1989, Chapter 6.
9. Parikh DM. Handbook of pharmaceutical granulation technology. 2nd ed. Marcel Dekker; 2005. p. 365-83.
10. Hameed K. Available from: https://www.slideshare.net/kir2n/granules.
11. Thulluru A, Sai VK, M PK, B R. Effect of effervescence in combination with superdisintegrants in the formulation of propranolol HCl oral disintegrating tablets. Asian J Pharm Clin Res. 2017;10(3):227. doi: 10.22159/ajpcr.2017.v10i3.16096.
12. Diyya AS, Thomas NV. Formulation and evaluation of metronidazole effervescent granules. Int J Pharm Sci Res. 2018;9:2525-9.
13. Sandhya S, Gowthami G, Vinod KR, VidyaSravanthi E, Saikumar P. RaoKNVetal. Formulation and evaluation of herbal effervescent granules incorporated with Limnophila indica extract for bacillary dysentery. Annals Bio Res. 2012;3(1):63-72.
14. Raymond M. Effervescent tablets: Lieberman HA. Lachman L and Schwartz TB: pharmaceutical dosage forms. New York: Marcel Dekker, Inc, 2008; 2(1): 285-328.
15. Palanisamy P. Formulation and evaluation of effervescent tablet of aceclofenac. Int Res J Pharm. 2011;2(12):185-90.