ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 12, Issue 8, 2019

Online - 2455-3891
Print - 0974-2441

Research Article

PREPARATION AND EVALUATION OF IBUPROFEN EFFERVESCENT GRANULES

JUTI RANI DEVI[1]*, BIDYUT DAS[2]

[1]Department of Pharmacy, Pratiksha Institute of Pharmaceutical Sciences, Guwahati, Assam, India. [2]Department of Pharmacy, Girijananda Chowdhury Institute of Pharmaceutical Science, Guwahati, Assam, India. Email: jutiranidevi@gmail.com

Received: 08 May 2019, Revised and Accepted: 10 June 2019

ABSTRACT

Objectives: The aim of the present investigation is to prepare the effervescent granules of different formulations and evaluated for different parameters including drug release study.

Methods: The effervescent granules of five different formulations such as F1, F2, F3, F4, and F5 were prepared by the wet granulation method using different concentration of excipients including sodium bicarbonate and potassium bicarbonate. The prepared formulations were evaluated for different parameters including effervescent time as well as drug release study.

Results: After evaluating all the parameters, it has been found that the formulation F5 shows better drug release among all the formulation and least effervescent time. Where it can conclude that as the effervescent time is less, i.e., it quickly bursts and shows its effect quickly. Lesser the bursting time quicker the drug release.

Keywords: Ibuprofen, Nonsteroidal anti-inflammatory drugs, Osteoarthritis, Acid neutralizer, Effervescence, Effervescent granules.

 DOI: http://dx.doi.org/10.22159/ajpcr.2019.v12i8.33994

INTRODUCTION

Granules are a type of dosage form and composed of dry aggregates of powder particles that may contain one or more APIs, with or without other ingredients. Granules are frequently compacted into tablets or filled into capsules, with or without additional ingredients. Effervescence is the escape of gas from an aqueous solution and the foaming or fizzing those results in the release [1-3]. Effervescent granules are a combination of citric acid and tartaric acid, and when they come in contact in water, it causes effervescence of CO_2. This CO_2 helps as an excess acid neutralizer and taste masker. It also makes the drug more soluble. Effervescent granules are popular delivery systems due to their fast dissolving, highly soluble, and stable nature. Nowadays, many pharmaceutical products such as antacids, analgesics, and cough/cold are dispensed as effervescent granules. The dosage form is dissolved or dispersed in water to initiate the effervescence before ingestion [4-7]. The advantages of effervescent granules are easy to administer, onset of action is faster, easily portable, gentle on the digestive tract, it is better tasting, and more stable than liquid dosage form. With advantages, there have some disadvantages also these are – cannot be given to the children due to the possibility of gas (CO_2) toxicity. If the packaging is not done properly, then there are chances of degradation by environmental moisture. It has a shorter shelf life as compared to other solid dosage forms. Ibuprofen is chemically [(+/-) 2-(p-isobutyl phenyl propanoic acid $(CH_3)_2CHCH_2$-$C_6H_4CH_3CHCO_2H$] and is well known as nonsteroidal anti-inflammatory drugs, analgesic and antipyretic agent. It is a weakly acidic drug having high permeability through the stomach. The aim of the present investigation is to formulate five different formulations of ibuprofen with varying the concentration of excipients and evaluate for different parameters and select the best formulation among the prepared formulation and also determine the effect of polymers [8-10].

MATERIALS AND METHODS

Materials

Ibuprofen was procured by Alkem Pvt. Ltd.; citric acid, sodium bicarbonate, methanol, and cross-povidone were gifted by Merck Life Science Limited; and tartaric acid, potassium bicarbonate, mannitol, croscarmellose, lactose, and hydroxypropyl methylcellulose (HPMC) were gifted by Qualigens Fine Chemicals. In addition, an electronic balance (Shimadzu), a hot air oven (Labhosp), and ultraviolet (UV) chamber were used in this study.

Methods

Preformulation studies

The preformulation study is a branch of pharmaceutical sciences that use for the determination of physicochemical properties of a drug substance and other excipients used in the formulation. The goal of preformulation studies is to choose the correct form of the substance, evaluate its physical properties, and generate a thorough understanding of the material's stability. The use of preformulation parameters maximizes the chances in formulating an acceptable, safe, efficacious, and stable product. Preformulation studies encompass of organoleptic properties (color, odor, and taste), solubility studies (data are shown in Table 1), assay, melting point, determination of lambda max, preparation of calibration curve, and Fourier transform infrared (FTIR) studies (data are shown in Table 2 and Fig. 1).

Preparation of effervescent granules

The effervescent granules were prepared by the wet granulation method. All the ingredients were weighted properly. All the ingredients were powdered and sieved to get a proper uniform particle size. A clean china dish was taken and all the solid ingredients were transferred to it one by one. Add the solvent in proportions until a coherent mass was formed of uniform consistency. The coherent mass was dried at 30–40°C and then sieved through sieve no.16. The required quantity for different formula is given in Table 3.

Angle of repose

The prepared granules were allowed to pass through a funnel and the height of the pile (h) and radius of the pile (r) are measured [11]. From this, the angle of repose, i.e., the angle between the height of the pile and radius of the pile is calculated with the help of the following formula.

$$\text{Angle of repose } \theta = \tan\text{-}1(h/r) \quad (1)$$

Bulk Density [11]
A certain weight of granules was taken in a 100 ml measuring cylinder without compacting and maintain the proper level of granules and measure the volume, Vo (bulk volume) and calculated according to the formula given below.

Bulk density = Weight of powder taken/Bulk volume (2)

Tapped density
A certain weight of powder was taken in a 100 ml measuring cylinder and tapped for 100 times. The volume of the granules was measured after complete tapped and got tapped volume [11]. Calculate the tapped density according to the following formula:

Tapped density= Weight of granules/Tapped volume (3)

Carr's index ratio [12]
This was determined using bulk density and tapped density using the formula mention below.

Carr's index ratio = [(Tapped density–Bulk density)/Tapped density] × 100 (4)

Hausner's ratio
Hausner ratio is used to determine the flow property of powder [12]. Lower the Hausner ratio betters the flow property or vice versa. This was calculated from bulk density and tapped density using the formula given below.

Hausner's Ratio = Tapped density/Bulk density (5)

Effervescence time
In vitro, effervescent time is determined by taking a specific amount of the formulation and added to 150 ml of water and the effervescence time was determined [12,13]. Repeat the procedure for all the prepared formulations and measured the effervescent time for all the batches.

***In vitro* drug release study**
The dissolution studies were done to determine the amount of drug released during a specific period of time using USP type I dissolution apparatus (basket type) [12,14].

At first, 900 ml of dissolution medium (0.1 N HCl) was placed in the dissolution vessel. The granules were put inside the basket and the basket was covered with a clean and dried muslin cloth. The RPM was set at 100/min. About 5 ml of the sample was collected at an interval of 2 min and 5 ml of fresh dissolution medium was replaced in the dissolution basket. Thus, the sample collected at specified time intervals of 2, 4, 6, 8, and 10 min was subjected to UV analysis at a wavelength of 221 nm.

Table 1: Solubility data of ibuprofen

Solvent	Solubility
Water	Poorly soluble
Phosphate buffer 6.8	Slightly soluble
Phosphate buffer 7.2	Slightly soluble
Phosphate buffer 7.4	Slightly soluble
Methanol	Soluble

*Solubility of drug was performed in both polar and non-polar solvent

Table 2: Infrared study of ibuprofen (functional groups with its respective wavenumber)

Functional group	Wave no. (Cm-1)
C=O	1510.00
C-H	3184.40
(C-H) CH_2	3044.39
C=O	1707.00
O-H	2988.29

*The unit of wavenumber is cm^{-1}, No. indicates number

RESULTS AND DISCUSSION

After observing the organoleptic properties of effervescent granules containing ibuprofen drug was found to be white, slightly odor, tasteless, and crystalline in their properties. Drug ibuprofen is poorly soluble in a polar solvent and soluble in a non-polar solvent. Solubility data are given in Table 1. The melting point was found to be 75°C.

In FTIR study, the functional groups and wavenumbers shown by the drug ibuprofen are given in Table 2. This indicates that the drug ibuprofen shows a proper peek of C=O stretch at 1707.00/cm, O-H stretch at 2988.29/cm, (C-H) CH2 stretch at 3044.39/cm, and C-H stretch at 3184.40/cm; hence, it can conclude that the drug is pure (infrared spectra shown in Fig. 1).

The effervescent granules of five different formulations (F1, F2, F3, F4, and F5) were prepared by the wet granulation method by varying the concentration of ingredients. The detail compositions are given in Table 3. In these compositions, concentrations of polymers mainly potassium bicarbonate, croscarmellose, cross-povidone, and HPMC were changed and observed the data for different parameters. These polymers have an important role in bursting time as well as for drug release properties.

The prepared formulations were evaluated for flow property. Flow property is a very important factor for granules formulation. Proper

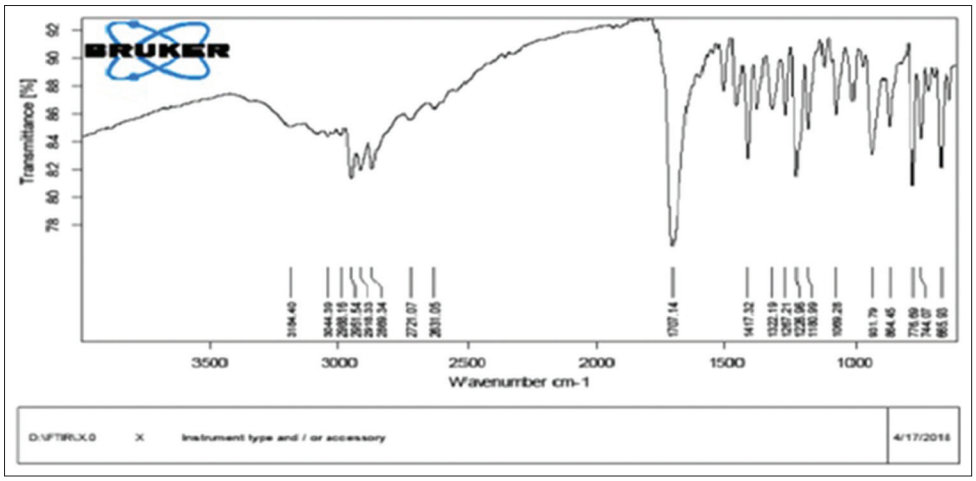

Fig. 1: Fourier transform infrared spectra of ibuprofen

Table 3: Composition of formulations

S. No.	Ingredient	Formulations				
		F1	F2	F3	F4	F5
1.	Ibuprofen	0.25 g	0.25 g	0.25 g	0.25 g	0.25 g
2.	Citric acid	1.00 g	1.00 g	1.00 g	1.00 g	1.00 g
3.	Tartaric acid	2.00 g	2.00 g	2.00 g	2.00 g	2.00 g
4.	Sodium bicarbonate	3.00 g	3.00 g	3.00 g	1.50 g	3.00 g
5.	Potassium bicarbonate	-	-	-	1.50 g	-
6.	Croscarmellose	1.00 g	2.00 g	-	1.00 g	1.00 g
7.	Cross-povidone	1.00 g	-	2.00 g	1.00 g	1.00 g
8.	Hydroxypropyl methylcellulose	0.50 g	0.50 g	0.50 g	0.50 g	1.00 g
9.	Mannitol	0.25 g	0.25 g	0.20 g	0.25 g	0.50 g
10.	Lactose	1.00 g	1.00 g	1.00 g	1.00 g	1.00 g
11.	Methanol	2–3 ml	2–3 ml	2–3 ml	2–3 ml	2–3 ml

*The weights of ingredients are in g except methanol, methanol is in ml

Table 4: Flow properties of formulations

Formulation	Angle of repose	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index	Hausner's ratio
F1	28.30	0.55	0.66	16.60	1.20
F2	29.12	0.53	0.61	13.11	1.15
F3	27.68	0.57	0.67	14.92	1.17
F4	28.03	0.54	0.63	14.20	1.17
F5	27.60	0.56	0.65	13.80	1.16

Table 5: Effervescent time of formulations

Formulation LATION	Effervescent time (min)
F1	1.22
F2	1.19
F3	1.11
F4	1.15
F5	1.09

*Bursting time is observed in minutes

Table 6: Percentage cumulative drug release study

Time (min)	% CDR of formulation				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
2	11.46	14.08	35.90	34.50	32.44
4	12.91	17.34	30.59	36.64	36.14
6	15.02	19.53	67.79	66.33	67.87
8	15.56	23.67	68.05	68.65	69.29
10	16.72	31.81	71.65	69.63	79.50

*CDR: Cumulative drug release

flow of granules gives a good release of drug from the formulations. Among all the prepared formulations, formulation F5 shows good flow property. All the data for the flow properties of all the formulations are shown in Table 4.

Effervescent time for effervescent granules was a very essential parameter for measuring the bursting time and also for the drug release parameter. For a good effervescent formulation, bursting time should be less, i.e., the granules should quickly evolute the bubbles of gas in a liquid. Among all the five formulations, F5 shows less effervescent time. All the data for an effervescent time are shown in Table 5 (Fig. 2).

In vitro drug release study was performed for all the prepared five formulations in 0.1 N HCl as dissolution media using USP type I dissolution apparatus (basket type). The dissolution studies were carried for 10 min for all five formulations. Among all the formulations, formulation F5 shows the highest drug release, i.e. up to 80%. All the data are summarized in Table 6. and graphical representation were shown in Fig. 3.

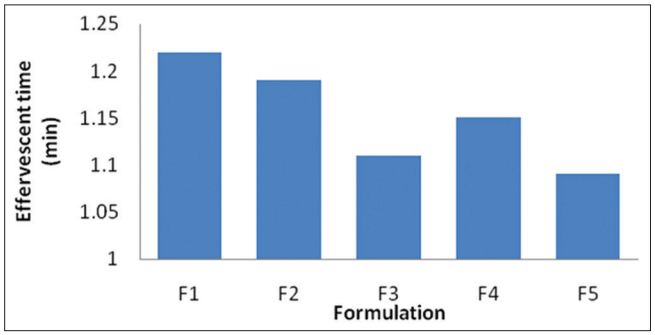

Fig. 2: Effervescent time (min) of different formulations

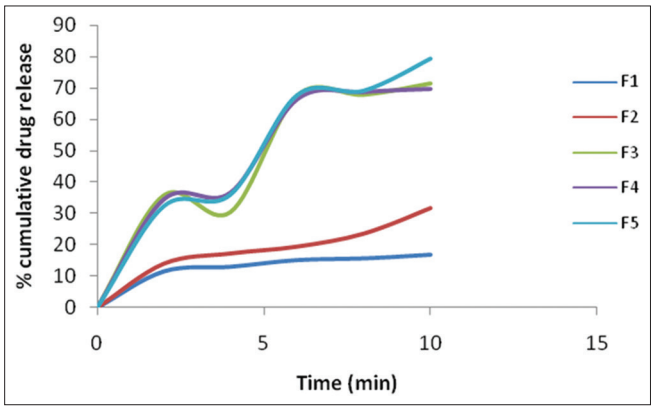

Fig. 3: *In vitro* drug release study of formulations

CONCLUSION

The present investigation of ibuprofen effervescence granules was prepared successfully by wet granulation method using a different concentration of polymers. After the preparation of five different formulations such as F1, F2, F3, F4, and F5 was evaluated for preformulation studies, formulation study, and *in vitro* evaluation study. Among all the five formulations, F5 formulation shows good results. After performing the entire test, it can be concluded that formulation

F5 containing all the ingredients except potassium bicarbonate shows satisfactory result and it can be used for further study.

ACKNOWLEDGMENTS

The authors are thankful to Girijananda Chowdhury Institute of Pharmaceutical Science, Guwahati, Assam-17, for providing facilities during the entire study and during the writing of the article.

AUTHORS' CONTRIBUTIONS

We herewith submit a manuscript entitled: "Preparation and evaluation of ibuprofen effervescent granules" author by Juti Rani Devi and Bidyut Das for consideration for publication as a research paper in the Asian Journal of Pharmaceutical and Clinical Research.

We hereby declare that the manuscript is not submitted or being considered to another journal in part of full for publication. The authors listed above are involved in the carrying out research work presented in the manuscript and that the research work was carried out at the address(es) listed in the title page of manuscript.

CONFLICTS OF INTEREST

The author(s) declare(s) that there are no conflicts of interest.

REFERENCES

1. Patel SK, Kumar D, Waghmode AP, Dhabale AS. Solubility enhancement of ibuprofen using hydrotropic agents. Int J Pharm Life Sci 2011;2:542-5.
2. Srinath KR, Chowdary CP, Palanisamy P, Vamsy KA, Aparna S, Ali SS, *et al*. Preparation and evaluation of effervescent tablets of paracetamol. Int J Pharm Res Dev 2011;3:76-104.
3. Satapathy SR, Patra M, Patnaik M. Process and variation in effervescent formulation: A review. Innov Int J Med Pharm Sci 2016;1:1-3.
4. Patel HK, Chuhan P, Patel KN, Patel BA, Patel PA. Formulation and evaluation of effervescent tablet of paracetamol and ibuprofen. Int J Pharm Res Sch 2012;1:1-2.
5. Bhattacharyya S, Swetha G. Formulation and evaluation of effervescent granules of fexofenadine hydrochloride. Pharm Innov 2014;3:1-8.
6. Banerjee N, Singh S. Formulation, evaluation and optimization of effervescent granules to be reconstituted into suspension of levetiracetam for sustained release. Int J Pharm Sci Rev Res 2013;20:181-6.
7. Maghrabi IA. Formulation of effervescent ibuprofen. Int J Pharm Sci Rev Res 2017;43:194-9.
8. Shet N, Vaidya I, Banerjee N. Formulation and evaluation of aceclofenac sodium effervescent taste masked granules. Int J Bio Pharm 2014;5:50-8.
9. Palanisamy P, Rabi A, Kumar DY. Formulation and evaluation of effervescent tablets of aceclofenac. Int Res J Pharm 2011;2:185-190.
10. Aslani A, Jahangiri H. Formulation, characterization and physicochemical evaluation of ranitidine effervescent tablets. Adv Pharm Bull 2013;3:315-22.
11. Thulluru A, Kumar VS, Kumar MP, Roshitha B. Effect of effervescence in combination with superdisintegrants in the formulation of propranolol HCl oral disintegrating tablets. Asian J Pharm Clin Res 2017;10:227-34.
12. Diyya AS, Thomas NV. Formulation and evaluation of metronidazole effervescent granules. Int J Pharm Sci Res 2018;9:2525-9.
13. Singh SK, Sharma V, Pathak K. Formulation and evaluation of taste masked rapid release tablets of sumatriptan succinate. Int J Pharm Pharm Sci 2012;4:168-74.
14. Mali AD, Bathe RS. Development and evaluation of gastro retentive floating tablets of a Quinapril HCL by direct compression technique. Int J Pharm Pharm Sci 2017;9:36-45.