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 of powder particles that may contain one or more APIs, with or without other ingredients. 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 medicines 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, gentile on the digestive tract, it is better tasting, and more stable than liquid dosage form. With advantages, there are some disadvantages also these are – cannot be given to the children due to the possibility of gas (CO₂) 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-\(\text{-}\)isobutyl phenyl propanoic acid \((\text{CH}_3)_2\text{C}_6\text{-H}_2\text{CH}\text{-CH}_2\text{CO}_2\text{H}\) 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 in efervescent granules 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 efervescent 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.

\[
\text{Angle of repose} \theta = \tan^{-1}\left(\frac{h}{r}\right)
\]
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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.

\[ \text{Bulk density} = \frac{\text{Weight of powder taken}}{\text{Bulk volume}} \]  

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:

\[ \text{Tapped density} = \frac{\text{Weight of granules}}{\text{Tapped volume}} \]

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

\[ \text{Carr’s index ratio} = \left( \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \right) \times 100 \]

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.

\[ \text{Hausner’s Ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \]

Effervescence time
In vitro effervescence 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 effervescence 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.

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

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) CH₂        | 3044.39         |
| C=O              | 1707.00         |
| O-H              | 2988.29         |

*The unit of wavenumber is cm⁻¹, No. indicates number

Fig. 1: Fourier transform infrared spectra of ibuprofen
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The 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 evolve 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.

**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

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### Table 3: Composition of formulations

| S. No. | Ingredient          | Formulations |
|-------|---------------------|--------------|
| 1.    | Ibuprofen           | 0.25 g       |
| 2.    | Citric acid         | 1.00 g       |
| 3.    | Tartaric acid       | 2.00 g       |
| 4.    | Sodium bicarbonate  | 3.00 g       |
| 5.    | Potassium bicarbonate | -           |
| 6.    | Croscarmellose      | 1.00 g       |
| 7.    | Cross-povidone      | 1.00 g       |
| 8.    | Hydroxypropyl methylcellulose | 0.50 g   |
| 9.    | Mannitol            | 0.25 g       |
| 10.   | Lactose             | 1.00 g       |
| 11.   | Methanol            | 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/cm³) | Tapped density (g/cm³) | 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 | 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

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

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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 or 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.

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