Formulation and evaluation of oral disintegrating tablets of furosemide

Manish Khadka*,1, Dharma Prasad Khanal1, Deepi Piya Baniya1, Prakash Karki1 and Saurav Shrestha2
1 Department of Pharmacy, Mannamohan Memorial Institute of Health Sciences, Tribhuvan University, Soalteemode-44600, Kathmandu, Nepal
2 Department of Pharmacy, Institute of Medicine, Maharajgunj Medical Campus, Tribhuvan University, Maharajgunj-44600, Kathmandu, Nepal

Abstract
Orally disintegrating tablets of Furosemide were prepared, evaluated and the comparison of the action of different concentrations of disintegrants on disintegration and dissolution of the tablets were studied. Direct compression method was used to prepare the orally disintegrating tablets containing 20 mg of Furosemide. The formulation was conducted using different concentrations of crospovidone, croscarmellose and sodium starch glycolate as superdisintegrants and their interactions with Furosemide were also evaluated using FTIR. FTIR studies using the drug and its mixtures with the excipients showed that the peaks correlate with one another which signify that there is no interaction between the drug molecule and the excipients used. The obtained results revealed that the disintegration time of ODTs were between 9 to 59 seconds. The percentage drug content of tablets in all the formulations was found between 91.51% to 106.69%, which complies with the limits established in pharmacopoeia. The in-vitro dissolution studies show maximum release of 89.47% in formulation F3 and minimum of 77.64% in formulation F12. Higher concentration of crospovidone and croscarmellose in formulations F3 and F6 showed better dissolution properties than SSG. So by varying the concentrations of super disintegrants, oral disintegrating tablets can be formulated.

Article History:
Received: 03.10.2021
Revised: 24.10.2021
Accepted: 02.12.2021

Keywords: Orally disintegrating tablet, Superdisintegrants, Furosemide, FTIR
*Corresponding Author
Manish Khadka
Email: maness.kdk@gmail.com
DOI: https://doi.org/10.37022/wjcmpr.v3i6.202

This article is licensed under a Creative Commons Attribution-Non-commercial 4.0 International License.
Copyright © 2021 Author(s) retain the copyright of this article.

Introduction
Orally disintegrating tablets are the dosage forms that get disintegrated when they come in contact with the saliva present in the oral cavity. The saliva penetrates the tablets and disrupts its structural integrity which results in the release of the drug from the dosage form [1]. The rapid disintegration of the tablets in the oral cavity may be rendered by the use of super disintegrants, such as crospovidone, croscarmellose and sodium starch glycolate, thus making the dosage form favorable for the pediatric population, geriatric population, bed-ridden patients and patients with dysphagia [2]. According to the United States Food and Drug Administration, an Oral Disintegrating Tablet is defined as “A solid dosage form which contains a medicinal substance or an active ingredient which rapidly disintegrates when placed upon the tongue, usually within matter of seconds [3]. The names such as rapid dissolving, mouth dissolving and fast melt tablets has also been given to the orally disintegrating tablets. The orally disintegrating tablets disperse and disintegrate when they come in contact with the saliva present in the oral cavity that omits the use of liquid to take the tablet, to swallow the whole dosage form or to chew the tablet. This dosage form is thus beneficial to the pediatric and geriatric patients and also to those who have swallowing difficulties including dysphagia and patients with psychiatric disorders [4]. Furosemide is a loop diuretic or often called as a high ceiling diuretic used in the treatment of edematous states which prevents and treats the fluid retention in the body. The usual dosage forms of furosemide available are 20 and 40 mg tablets. Chemically Furosemide is 5-(aminosulphonyl)-4-chloro-2-[(2-fuanylmethyl) amino] benzoic acid [5]. The Biopharmaceutics Classification System (BCS) classifies furosemide as a Class IV compound, which means that furosemide has a low solubility and a low permeability. The bioavailability of furosemide is found to be 37-70% with its peak plasma concentration (Cmax) found to be achieved within 60 to 90 min. The plasma half-life (11/2) of furosemide is 1.3±0.8 h in healthy subjects [6]. The purpose of this study is to formulate the ODTs of Furosemide and to perform the evaluation of those formulations for different parameters. The use of the superdisintegrants i.e. Crosspovidone, Crosarmellose sodium and Sodium starch glycolate and their effects on the tablets’ disintegration and dissolution has been studied.

Materials and Methods
Raw materials were obtained with coordination with the Department of Pharmacy MMIHS and Lomus and Qmed Pharmaceuticals. Furosemide, MCC, sucralose and mannitol

CODEN (CAS-USA): WJCMCF
Were obtained from Lomus Pharmaceuticals Pvt. Ltd., Gothatar, Kathmandu. Similarly, crospovidone, croscarmelose, SSG, talc and magnesium stearate were obtained from Qmed Pharmaceuticals Pvt. Ltd., Ghirling, Bhaktapur. All the other components used for the formulation were of Pharmaceutical grade.

**Preparation of Furosemide ODT**

Table 1: Direct compression method was used to prepare oral disintegrating tablet of Furosemide. At first all the ingredients excluding lubricant, glidant, sweetener and diluent (Mannitol) were passed through sieve of mesh size 30 and the remaining ingredients were passed through sieve of mesh size 50. Then all the ingredients except glidant and lubricant were weighed correctly and mixed thoroughly in a plastic pouch. Finally lubricant and glidant were added to the powder and mixed thoroughly to obtain uniform particle size. The prepared powder blend was then compressed with tablet compression machine using die of 7 mm diameter.

Table no. 1: Formulation of Furosemide ODTs.

| Formulation   | F1 (mg) | F2 (mg) | F3 (mg) | F4 (mg) | F5 (mg) | F6 (mg) | F7 (mg) | F8 (mg) | F9 (mg) | F10 (mg) | F11 (mg) | F12 (mg) |
|---------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|----------|----------|----------|
| Furosemide    | 20      | 20      | 20      | 20      | 20      | 20      | 20      | 20      | 20      | 20       | 20       | 20       |
| MCC           | 120     | 120     | 120     | 120     | 120     | 120     | 120     | 120     | 120     | 120      | 120      | 120      |
| Crospovidone  | 8       | 12      | 16      | -       | -       | -       | -       | -       | -       | -        | -        | -        |
| Croscarmelose | -       | -       | -       | 8       | 12      | 16      | -       | -       | -       | 8        | 12       | 16       |
| Sodium starch | -       | -       | -       | -       | -       | -       | 8       | 12      | 16      | 8        | 12       | 16       |
| Talc          | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5      | 2.5      | 2.5      |
| Magnesium stearate | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5     | 2.5      | 2.5      | 2.5      |
| Sucralose     | 2       | 2       | 2       | 2       | 2       | 2       | 2       | 2       | 2       | 2        | 2        | 2        |
| Mannitol      | 45      | 41      | 37      | 45      | 41      | 37      | 29      | 21      | 45      | 41       | 37       | 37       |
| Total         | 200     |         |         |         |         |         |         |         |         |          |          |          |

**Evaluation of pre-compression flow properties of powder blend**

**Organoleptic properties**

Organoleptic properties of API like color, odor and stability were observed and recorded. Solubility was observed in methanol and sodium hydroxide.

**Bulk Density**

Bulk density was measured using bulk density apparatus. Fixed weight of powder was poured in the measuring cylinder and volume was recorded.

\[
\text{Bulk density} = \frac{\text{Bulk weight}}{\text{Bulk volume}}
\]

**Tapped Density**

Fixed weight of powder was poured in the measuring cylinder and tapped 50 cycles multiple times. Volume was recorded after each 50 tapping cycles until fixed (concurrent) reading was obtained. The tapped density was obtained by using following equation:

\[
\text{Tapped Density} = \frac{\text{Bulk weight}}{\text{Tapped volume}}
\]

**Carr’s Index**

Carr’s index was obtained by using following equation:

\[
\text{Carr’s index (\%)} = \frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times 100
\]

Value less than 1.25 indicate good flow (=20% Carr), where greater than 1.25 indicates poor flow (=33% Carr) [7].

**Angle of Repose**

Fixed weight of powder was poured through funnel. The height and diameter of the power pile was noted. Angle of repose was obtained by using following equation:

\[
\text{Angle of repose} = \tan^{-1}\left(\frac{2h}{D}\right)
\]

Where, \(h\) = maximum cone height 
\(D\) = Average diameter

**Hausner’s ratio**

Flow properties of the powder can also be examined using hausner’s ratio. Hausner’s ratio was obtained by using following equation:

\[
\text{Hausner’s ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}
\]

CODEN (CAS-USA): WJCMCF
The value of ratio below 1.25 indicates good flow while above 1.35 indicates the poor flow [7].

**Post Compression Studies**

**Weight variation**
For each batch, 20 tablets were taken and weighed for weight of each tablet using a digital balance. The average weight of tablet for was determined and minimum and maximum deviation was calculated for each batch.

**Dimensions**
Dimension of 10 tablets for each batch was determined using vernier caliper and the average diameter and thickness was determined.

**Hardness**
Using Monsanto Hardness tester, the hardness of 10 tablets was measured and average hardness of tablets was determined.

**Friability**
The weight of tablets equal to 6.5 grams were taken and rotated for 100 cycles in a friabilator. After 100 revolutions, the tablets were weighed and percentage loss was calculated.

**Assay**
The assay of the tablets was determined using UV spectrophotometer, which was calibrated prior to its use.

**Preparation of sample for assay**
20 tablets were taken; they were weighed and then powdered. The quantity of powder containing 0.1g of Furosemide was taken and shaken with 150 ml of 0.1 M sodium hydroxide for 10 minutes. Sufficient quantity of NaOH was added to it to produce 250 ml volume and was filtered. 5 ml of this solution was diluted to 200 ml with 0.1 M NaOH and the absorbance of resulting solution was measured at maximum wavelength 274 nm [8].

**Preparation of standard for assay**
0.1g of standard Furosemide was weighed and shaken with 150 ml of 0.1 M sodium hydroxide for 10 minutes. Sufficient quantity of NaOH was added to it to produce 250 ml volume and was filtered. 5 ml of this solution was diluted to 200 ml with 0.1 M NaOH and the absorbance of resulting solution was measured at maximum wavelength 274 nm [8]. Amount of drug = (Abs. of Sample/Abs. of standard) x (wt. of standard/250) x (5/200) x (250/wt. of sample) x (200/5) x Avg. wt.

**Calibration**
The calibration of UV spectrophotometer was done with the help of standard Furosemide. At first 25 PPM solution was prepared by dissolving 6.25 mg of standard Furosemide in 250ml 0.1 M NaOH. Similarly, 20 PPM, 15 PPM, 10PPM, and 5PPM solutions were prepared by taking 40 ml, 30ml, 20 ml and 10 ml respectively of the prepared solution and making volume up to 50 ml. The absorbance of the solutions were measured at 274 nm.

**Disintegration Time**
The disintegration time of each batch of tablets was determined using USP disintegration test apparatus. To test the disintegration time, one tablet was placed in each small basket sinkers and the basket rack was positioned in a 1 liter beaker containing phosphate buffer of PH 6.8 at 37±0.5°C such that the tablet can remain 2.5 cm below the surface of liquid. The time taken for the completion of disintegration of tablet was noted.

**In-Vitro Dissolution test**
Dissolution of the Furosemide oral disintegrating tablets were performed using USP Type II Apparatus (Paddle Type) at 50 rpm. The dissolution flask was filled with 900ml of Phosphate buffer (pH 6.8) and was maintained at a temperature of 37±0.5°C. The dissolution apparatus was allowed to run for 30 minutes at a speed of 50 rpm after placing a tablet in the flask of the dissolution apparatus. At time interval of 5 minutes, 5 ml of dissolution medium was withdrawn, filtered and again replaced with 5 ml of fresh medium. The withdrawn dissolution medium was diluted to 50 ml and was analyzed spectrophotometrically at λ max is 274 nm using a UV-spectrophotometer. Finally the cumulative percentage release of drug was calculated.

Working formula:
Sample% =Absorbance of spl x wt of ref x 5 x 900 x Absorbance of ref 100 50 wt. of spl 5 x Purity %

**Results**

**Calibration Curve**
When absorbance v/s concentration was plotted, a straight line was obtained which suggests that the process used to measure the absorbance of sample is validated.

Table 2: Precompression Evaluation results

| Formulation | Bulk Density | Tapped Density | Angle of Repose | Carr’s Index | Hausner’s Ratio | Remarks |
|-------------|--------------|----------------|-----------------|--------------|----------------|---------|
| F1          | 0.5          | 0.681          | 32.9°           | 16.6°        | 1.2            | Good    |
| F2          | 0.5          | 0.74           | 35.4°           | 25.7         | 1.3            | Passable |
| F3          | 0.5          | 0.77           | 30.8°           | 23.9         | 1.32           | Passable |
| F4          | 0.5          | 0.75           | 34.5°           | 27.2         | 1.33           | Passable |
| F5          | 0.5          | 0.77           | 33.6°           | 23.3         | 1.3            | Passable |
| F6          | 0.5          | 0.698          | 31.3°           | 22.4         | 1.29           | Passable |
| F7          | 0.5          | 0.73           | 30.2°           | 21.3         | 1.27           | Passable |
| F8          | 0.5          | 0.717          | 31.2°           | 27.4         | 1.37           | Passable |
| F9          | 0.5          | 0.71           | 33.9°           | 20.9         | 1.26           | Passable |
| F10         | 0.5          | 0.694          | 34.2°           | 22.1         | 1.28           | Passable |
| F11         | 0.5          | 0.76           | 31.8°           | 27.6         | 1.37           | Passable |
| F12         | 0.5          | 0.691          | 33.1°           | 20.5         | 1.25           | Passable |
Batch Post compression Studies
limit and passable as per USP. The flow properties of powder

| F1    | 1.212 | 1.569 | 1.945 |
|-------|-------|-------|-------|
| F2    | 0.815 | 0.449 |       |

Concentration (PPM)

![Standard calibration curve of Furosemide](image)

**Fig 1:** Standard calibration curve of Furosemide

**General appearance**
Visual observation revealed that all the tablets of twelve formulations were round and flat.

**Precompression Studies**

Table 2: The Precompression studies’ result were within the limit and passable as per USP. The flow properties of powder blend was suitable for compression. Thus the study was further continued by compression of the powder blend into tablets.

**Post compression Studies**

Table 3: Post compression Evaluation results

| Batch | Weight Variation (mg±SD) | Average Diameter (mm±SD) | Average Thickness (mm±SD) | Average Hardness (kg/cm²±SD) | Friability (%) (<1% ) |
|-------|--------------------------|--------------------------|---------------------------|-----------------------------|------------------------|
| F1    | 0.1993±0.03422           | 7.21±0.02087             | 3.88±0.0689               | 3.5±0.357                  | 0.61                   |
| F2    | 0.1989±0.02573           | 7.25±0.02458             | 3.86±0.06323              | 3.3±0.25                  | 0.165                  |
| F3    | 0.1987±0.01997           | 7.22±0.03441             | 3.88±0.07542              | 3.2±0.41                  | 0.317                  |
| F4    | 0.1991±0.02231           | 7.26±0.02012             | 3.91±0.05253              | 3.5±0.26                  | 0.531                  |
| F5    | 0.1983±0.02231           | 7.23±0.05742             | 3.89±0.08002              | 3.7±0.29                  | 0.622                  |
| F6    | 0.2005±0.04224           | 7.26±0.02365             | 3.84±0.06537              | 3.3±0.15                  | 0.472                  |
| F7    | 0.1947±0.0452            | 7.23±0.06511             | 3.93±0.08184              | 4.0±0.13                  | 0.594                  |
| F8    | 0.1941±0.03243           | 7.24±0.03987             | 3.85±0.06357              | 3.8±0.25                  | 0.633                  |
| F9    | 0.1946±0.04332           | 7.22±0.03514             | 3.88±0.07350              | 3.6±0.25                  | 0.335                  |
| F10   | 0.1986±0.0278            | 7.24±0.03427             | 3.81±0.06782              | 4.3±0.25                  | 0.608                  |
| F11   | 0.1971±0.03567           | 7.29±0.06621             | 3.83±0.08244              | 4.1±0.30                  | 0.284                  |
| F12   | 0.1907±0.09002           | 7.27±0.03987             | 3.90±0.05311              | 3.5±0.35                  | 0.736                  |

**Table 4:** The disintegration time of the formulated batches was between 9 seconds to 59 seconds. The drug content of tablets was in between 93.22% to 106.69%. The content uniformity was in range of 79.68% to 114.38%.

**Table 4:** Post compression Evaluation results

| Batch | Disintegration time (Sec) (NMT 1min) | Assay (%) (90% to 110%) | Drug Content Uniformity (Q±15%) |
|-------|-------------------------------------|-------------------------|---------------------------------|
| F1    | 33                                  | 96.32                   | 88.23% to 97.36%               |
| F2    | 16                                  | 96.78                   | 89.32% to 101.2%               |
| F3    | 9                                   | 98.55                   | 91.78% to 100.18%              |
| F4    | 26                                  | 100.42                  | 82.54% to 103.1%               |
| F5    | 22                                  | 97.78                   | 88.52% to 96.69%               |
| F6    | 15                                  | 102.63                  | 89.19% to 101.7%               |
| F7    | 55                                  | 93.22                   | 79.68% to 99.70%               |
| F8    | 47                                  | 106.69                  | 84.82% to 105.72%              |
| F9    | 35                                  | 98.91                   | 81.41% to 109.37%              |
| F10   | 59                                  | 94.51                   | 77.4% to 96.83%                |
| F11   | 34                                  | 105.011                 | 79.71% to 109.25%              |
| F12   | 29                                  | 96.14                   | 83.62% to 114.38%              |

**In-Vitro Dissolution Studies**

Table 5: The dissolution of the formulation varied with variation in the concentration of the superdisintegrants. The in-vitro dissolution studies show maximum release of 89.47% in formulation F3 and minimum of 77.64% in formulation F12.

**Dissolution Profile of formulations F1 to F3**

| Time | F1 | F2 | F3 |
|------|----|----|----|
| 0    | 0.00| 0.00| 0.00|
| 5    | 36.58| 39.98| 42.56|
| 10   | 45.27| 49.57| 54.15|
| 15   | 53.90| 58.63| 61.25|
| 20   | 65.85| 69.33| 76.32|
| 30   | 81.69| 83.21| 89.47|
Fig 2: Comparison of cumulative amount of drug release vs time of formulations F1, F2 and F3

**Dissolution Profile of formulations F4 to F6**

| Time | F4  | F5  | F6  |
|------|-----|-----|-----|
| 0    | 0.00| 0.00| 0.00|
| 5    | 38.52| 36.32| 40.56|
| 10   | 51.21| 47.71| 51.27|
| 15   | 59.74| 51.68| 63.57|
| 20   | 67.13| 66.27| 71.21|
| 30   | 83.35| 82.84| 87.17|

Fig 3: Comparison of cumulative amount of drug release vs time of formulations F4, F5 and F6

**Dissolution Profile of formulations F7 to F9**

| Time | F7  | F8  | F9  |
|------|-----|-----|-----|
| 0    | 0.00| 0.00| 0.00|
| 5    | 32.56| 34.21| 38.47|
| 10   | 41.25| 48.86| 44.61|
| 15   | 53.14| 57.93| 57.32|
| 20   | 65.35| 70.31| 68.54|
| 30   | 78.91| 79.53| 81.26|
Fig 4: Comparison of cumulative amount of drug release vs time of formulations F7, F8 and F9

**Dissolution Profile of formulations F10 to F12**

**Table 8: Dissolution Profile of formulations F10 to F12**

| Time  | F10     | F11     | F12     |
|-------|---------|---------|---------|
| 0     | 0.00    | 0.00    | 0.00    |
| 5     | 31.89   | 33.56   | 29.43   |
| 10    | 43.53   | 45.36   | 41.54   |
| 15    | 51.24   | 53.75   | 50.39   |
| 20    | 65.44   | 64.23   | 61.27   |
| 30    | 79.36   | 81.66   | 77.64   |

Fig 5: Comparison of cumulative amount of drug release vs time of formulations F10, F11 and F12

**FTIR Results**

FTIR studies were done to evaluate whether there is any interaction between the active ingredient Furosemide and the excipients used in the formulations. The peaks of the active ingredient Furosemide and the mixture of excipients correlate with one another, the peaks positions are at the same wave number, however there is a broadband of amine group at 3340 cm⁻¹ which may probably be due to the interactions caused by intramolecular hydrogen bonding, other than that there are no other interactions between the active ingredient and the excipients used.
Discussion

The oral disintegrating tablets of Furosemide were formulated and evaluated. The use of superdisintegrants for the formulation of the ODTs was satisfactory and commercially feasible. The use of superdisintegrants caused quick disintegration and prompt dissolution of the tablet. The FTIR studies of the drug molecule and its mixture with the excipients were performed to confirm the compatibility of the drug molecule and the excipients. The FTIR peak of the drug molecule correlates with that of the mixture which confirms that the mixture is compatible and there is no interaction between the components [9].

The use of the superdisintegrants alone showed better results with better hardness, disintegration and dissolution, rather than combining them. This may be due to the fact that the concentration of superdisintegrants we used in combination was higher than the critical concentration which results in the retardation of water swellability of the superdisintegrants, which is reflected by our results [10].

The use of crospovidone and croscarmelose as superdisintegrants showed better results than sodium starch glycolate. These findings are also supported by other studies performed by Nagoba Shivappa, Warkari Rajan, Shimge Krishna, Gaikwad in Channabasweshwar Pharmacy College, Latur, India [11] and also by T.Gulsun, N.Ozturk, M.S. Kaynak, I.Vural, S.Sahin in İnönü University, Malatya, Turkey [12]. However the study conducted by Dr. Shahid Mohammed in Deccan School of Pharmacy, Hyderabad on Formulation and evaluation of Furosemide oral dispersible tablets showed better results in use of sodium starch glycolate as superdisintegrant [13].

This could be due to the reason that the ingredients used for trial formulations by Dr. Shahid Mohammed are different from ours. Dr. Shahid Mohammed primarily used mannitol as the fillers in tablets whereas MCC was used on our tablets as diluents. MCC is often used as a diluent and this excipient also possess the ability to improve the disintegration of the tablets [14].

The use of MCC and its property to act as a disintegrating agent and the different concentrations of the ingredients could be the reason for variation of our results from the results of research conducted by Dr. Shahid Mohammed.

Conclusion

The oral disintegrating tablets of Furosemide were prepared successfully by the use of direct compression method. Different formulations were designed to evaluate the influence of different concentrations of superdisintegrants on ODTs of Furosemide. Twelve formulations with different concentrations of superdisintegrants were prepared. FTIR studies using the drug and its mixtures with the excipients showed that the peaks correlate with one another which signify that there is no interaction between the drug molecule and the excipients used. The results justify that the increase in the concentration of superdisintegrants leads to the decrease in the disintegration time. The formulation prepared by using crospovidone as superdisintegrant has shown good in-vitro dispersion time. Among the formulations, the formulation as per batch F3 is found to be the most promising batch where 8% of crospovidone is used in each tablet as superdisintegrant, with the drug release of 89.47% within 30 minutes.

This suggests that the composition of Furosemide ODTs could be optimized so as to obtain rapid disintegration and drug dissolution along with acceptable tablets hardness and friability. This could be beneficial to improve the drug's...
absorption and bioavailability, which ensues better patient compliance and convenience.

**Acknowledgements**

The authors express their humble gratitude to Manmohan Memorial Institute of Health Sciences, Soalteemode Kathmandu, for providing the facilities for the research work.

**Conflict Of Interest**

The authors declare that there is no conflict of interest.

**References**

1. Abay FB, Ugurlu T. Orally Disintegrating Tablets: A Short Review. Journal of Pharmaceutics and Drug Development. 2015;3:3-303.
2. Tejas K, Ganesh D. A Review on Orodispersible Tablets: A Novel Approach. Research Journal of Pharmacy and Technology. 2019;12:8-3993.
3. Babu A, Akhtar M. Overview of formulation and evaluation of fast dissolving tablet: A promising tablet dosage form. Journal of Applied Pharmaceutical Research. 2020;8:3.
4. Hirani J, Rathod D, Vadalia K. Orally Disintegrating Tablets: A Review. Tropical Journal of Pharmaceutical Research. 2009;8:2.
5. Shende M, Chavan K. Formulation of Furosemide Oral Disintegrating Tablets Using Natural and Synthetic Superdisintegrants by SeDeM Expert Design System. Journal of Drug Delivery and Therapeutics. 2019;9:6.
6. Shariare M, Altamimi M, Marzan A, Tabassum R, Jahan B, Reza H et al. In vitro dissolution and bioavailability study of furosemide nanosuspension prepared using design of experiment (DoE). Saudi Pharmaceutical Journal. 2019;27:1.
7. Hao T. Understanding empirical powder flowability criteria scaled by Hausner ratio or Carr index with the analogous viscosity concept. RSC Advances. 2015;5:70.
8. Naveed S, Qamar F. Simple UV spectrophotometric assay of Furosemide. Journal of Innovations in Pharmaceuticals and Biological Sciences. 2014;01:06.
9. Bharate SS, Bharate SB, Bajaj AN. Interactions and incompatibilities of pharmaceutical excipients with active pharmaceutical ingredients: a comprehensive review. Journal of Excipients and Food Chemicals 2011;42:47.
10. Desai P, Liew C, Heng P. Review of Disintegrants and the Disintegration Phenomena. Journal of Pharmaceutical Sciences. 2016;105:9.
11. Nagoba Shivappa, Warkari Rajan, Shime Krishna, Gaikwad V. Formulation and Evaluation of Furosemide Oral Disintegrating Tablets. International Journal of Pharmaceutical Science Invention 2018;23:19.
12. Gulsun T, Ozturk M, Kaynak I, Vural S, Sahin S. Preparation and evaluation of furosemide containing orally disintegrating tablets by direct compression. International Journal of Pharmaceutical Sciences 2017;38:9.