INTRODUCTION

Oral directions of drug administration have broad recognition of up to 50-60% of whole dosage forms [1]. Oral drug delivery (i.e.: tablets, capsule, powders, emulsions, suspensions, etc.) is considered as the most common, most popular, convenient and safe (when compared to parental route) [2]. Solid dosage forms are more popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance [3-5]. The majority accepted solid dosage forms are tablets and capsules; one of the important drawbacks of solid dosage forms is compliance [3-5]. The majority accepted solid dosage forms are tablets and capsules; one of the important drawbacks of solid dosage forms is the frequency of administration and as an alternative for administration of a single dose and as an alternative for multiple dosage, having a benefit that the drug release was long-term and it has been noticeable to pharmaceutical manufacturing [11-15]. LTD is a lipophilic, non-sedating H1 blocker and used to treat seasonal allergic rhinitis having low bioavailability (40%) and biological half-life (8 h). So, patients can avoid frequent administrations in a day [16-20]. Such frequent drug administration may reduce patient compliance and therapeutic effectiveness [21-25]. To overcome the above-mentioned problems it is required to convey the single dose for an extended period. Besides, LTD shows the greatest solubility at acidic pH and it is an appropriate candidate for the expansion of gastroretentive drug delivery systems (GRDDS). The aim of extended release (ER) DDS is to be customized in such a method with the intention; extra residence time in the stomach to release the drug before the absorption window. The goal of GRDDS is to provide a beneficial quantity of the drug to the appropriate location in the body and sustain the required drug concentration. To avoid the problems associated with the delivery of LTD, we planned to formulate LTD in an extended-release floating matrix formulation. This will allow us to reduce the frequency of administration and enhances patient compliance. To achieve the goal we have used low-density lipids or floating aids like compritol and precirol that can avoid the first-pass metabolism and will improve the bio-availability of the formulation.

MATERIALS AND METHODS

Materials

Loratadine received as a gift sample from Hetero Labs Ltd, Hyderabad, India. HPMC K15 M and HPMC K100 M procured from B and K Technologies, China. Compritol and precirol were purchased from Gattefosse, Germany. MCC-(Avicel PH 200), Aerosil and Magnesium stearate from SD Fine Chemicals Ltd, Mumbai. Hydrochloric acid from Merck specialities Pvt. Ltd. Mumbai, India

Methods

Pre-compression characterization

Drug excipient compatibility studies

Fourier transform infrared spectroscopy (FTIR)

The drug excipient compatibility study was carried out by FTIR with in the frequency range of 4000-400 cm⁻¹ and 4 cm⁻¹ resolution. The IR spectra for the test samples were obtained using the KBr disk method using an FTIR (Star Tech Labs Pvt. Ltd, Hyderabad) [26].

Differential scanning calorimetry (DSC)

The differential thermal analyzer was used to find out the presence of any interaction among drug and excipients. About 5-15 mg of the sample was taken in pierced DSC aluminium pan and scanned in the temperature range of 50-300 °C and the heating rate was 10 °C/min; nitrogen served as purged gas and the system was cooled down by liquid nitrogen [27].

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ABSTRACT

Objective: The main objective of the research work is to develop a single unit non-effervescent drug delivery system of Loratadine (LTD) by direct compression process to prolong the gastric residence time (GRT).

Methods: LTD non-effervescent floating tablets were prepared with different polymers like hydroxypropyl methylcellulose (HPMC) K15M, HPMC K100M (i.e.: 1:1, 1:2, 1:3) as release retardants. Glycerol behenate (Compritol 888 ATO) and Glycerol palmitostearate (Precirol ATO 5) were used (1:1, 1:2, 1:3) as low-density lipids to impart buoyancy for longer period.

Results: The drug (LTD) and excipient (i.e. HPMC, low-density lipid aids, etc.) interaction studies were carried out by Fourier Transform Infrared Spectroscopy (FTIR) and there was no likely interaction involving them. The developed LTD floating matrix tablets were characterized by pre and post-compression parameters and all results were found within the pharmacopoeial limits. The cumulative percentage of drug release ranges from 56.87±0.25 % (F12) to 99.87±0.09 % (F2). The drug release profiles of the all formulations (F1 to F12) were subjected to various pharmacokinetic models.

Conclusion: Hence, from all evaluation studies, it was evident that F3 formulation was optimized (99.82±1.63 % drug release in 12 h).

Keywords: Buoyant, Non-effervescent, Low-density lipids, Direct compression

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Flow properties of the powder blend

The powder mixtures of different formulations were evaluated for angle of repose (\(\theta\)), bulk density (gm/cm\(^3\)), tapped density (gm/cm\(^3\)), Carr’s index or compressibility index (%) and Hausner’s ratio [28]. The evaluation test results are shown in table 2.

Angle of repose (\(\theta\))

The fixed funnel method was employed to measure the \(\theta\) and it was determined by below formula

\[ \theta = \tan^{-1}(h/r) \]

Here \(\theta\) is the angle of repose, \(h\) is the height of the pile and \(r\) is the radius of the base.

Carr’s index or compressibility index (%)

Bulk density (BD) and tapped densities (TD) were determined by the following formulas.

\[ \text{BD} = \frac{\text{Weight of the sample}}{\text{Volume of the sample}} \]

\[ \text{TD} = \frac{\text{Weight of the sample}}{\text{Tapped volume of the sample}} \]

The carr’s index was calculated by the following formula

\[ \text{Carr’s index} = \frac{\text{TD} - \text{BD}}{\text{BD}} \times 100 \]

Hausner’s ratio

Hausner’s ratio was calculated by the following formula

\[ \text{Hausner’s ratio} = \frac{\text{TD}}{\text{BD}} \]

Construction of loratadine calibration curve

The study started with the construction of a standard calibration curve of Loratadine. The standard graph of LTD with 0.1N hydrochloric acid (HCl) was plotted by taking concentration ranging from 5µg/ml to 45µg/ml on X-axis and absorbance values on Y-axis [29-30].

Preparation of LTD non-effervescent floating matrix tablets

Floating tablets containing LTD were prepared by a direct compression technique [31]. Polymers and floating aids ratios were taken as 1:1, 1:2, and 1:3 (table 1). LTD and all other additives are precisely weighed and sieved through 44 mesh.

The LTD was well mixed with a magnitude of necessary polymers (HPMC K15M, HPMC K100M), floating aids (Compritol 888 ATO and Precirol ATO 5), MCC (Avicel PH 200) in geometric proportions. After that the blend was lubricated with previously weighed, sieved magnesium stearate and aerosil. Finally, about 100 mg of the lubricated blend was subjected to compression by using a 6 mm circular standard flat-faced punch on 10 stations rotary tablet punching machine (i.e. Karnavathi, Gujarat, India) [32].

| *Formulation (mg/tablet) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 | F12 |
|--------------------------|----|----|----|----|----|----|----|----|----|-----|-----|-----|
| Drug [LTD]                | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10  | 10  | 10  |
| HPMC K15M                | 10 | 20 | 30 | -  | -  | -  | -  | -  | -  | -   | -   | -   |
| HPMC K100M               | -  | -  | -  | 10 | 20 | 30 | -  | -  | -  | -   | -   | -   |
| Compritol 888 ATO       | 10 | 20 | 30 | -  | -  | -  | 5  | 10 | 15 | 5   | 10  | 15  |
| Precirol ATO 5          | -  | -  | -  | 10 | 20 | 30 | 5  | 10 | 15 | 5   | 10  | 15  |
| Avicel PH 200           | 65 | 45 | 25 | 65 | 45 | 25 | 65 | 45 | 25 | 65  | 45  | 25  |
| Tak                     | 2  | 2  | 2  | 2  | 2  | 2  | 2  | 2  | 2  | 2   | 2   | 2   |
| Aerosil                 | 2  | 2  | 2  | 2  | 2  | 2  | 2  | 2  | 2  | 2   | 2   | 2   |
| Magnesium stearate     | 1  | 1  | 1  | 1  | 1  | 1  | 1  | 1  | 1  | 1   | 1   | 1   |
| Total weight            | 100| 100| 100| 100| 100| 100| 100| 100| 100| 100 | 100 | 100 |

*Each value represents mean±SD (n=30)

Post-compression characterization

The above-compressed LTD floating tablets should be characterized by several specifications, which include weight variation, thickness, friability; hardness and drug content uniformity, etc., were shown in table 3.

Weight variation (mg)

The weight of the prepared LTD floating tablets (i.e. n=20; randomly from every batch, then average weight should be well-thought-out) determined by using an electronic balance (Shimadzu, AUX220, Japan) [33].

Thickness (mm)

The thickness of the prepared LTD floating tablets (i.e. n=20) measured by, vernier calipers, tablet thickness is reliable from batch to batch or within a batch only if the tablet granulation or dust mix is satisfactorily dependable on particle size and size distribution, if the punch tooling is of regular length, and the tablet press is clean and in good working order. Thickness must be controlled for consumer acceptance of the product, and to facilitate packaging [34].

Friability (%)

The friability test was performed with prepared LTD floating tablets (i.e. n=20; unintentionally from the entire batches) by placing in Roche friabilator and allowed to make 100 revolutions (i.e. 25 rpm for 4 min).
time (FLT) and the total duration of tablet float on the surface is called as total floating time (TFT) [38].

**In vitro dissolution (%)**

The drug release or *in vitro* dissolution studies (i.e. n=6) of LTD non-effervescent floating tablets were carried out with USP dissolution type-II (i.e. paddle) method at 50 rpm in 900 ml of 0.1N HCl as dissolution medium, maintained at 37 °C±0.5 °C. About to 5 ml of aliquot (i.e. sample) was withdrawn at predetermined time intervals for every 1 hour up to 12 h and replaced with 5 ml of fresh medium (i.e. 0.1N HCl) each time. The samples were analyzed by using a double beam UV visible spectrophotometer (Elico, SL210, Hyderabad) at 280 nm. By using a standard calibration curve, calculate the cumulative percentage of drug release [39-40].

**In vivo buoyancy studies (h)**

*In vivo* gastric retention time (GRT) was determined by X-ray procedure in healthy human volunteers (n=3). The procedure of the radiographic studies was approved by the institutional human ethical committee (IHEC). For *in vivo* study (i.e.: Proposal no. IRB-AGI/2018-19/11), Barium sulphate (BaSO₄) containing LTD floating tablets were prepared by a similar method as described in the formulation. In this revision, part of the LTD was replaced using BaSO₄, each one of the ingredients remained equivalent [41].

**Mechanism of drug release kinetics**

The drug release data of LTD prepared floating matrix tablets were fitted into different kinetic models representing Zero order, First order, Higuchi and Peppas model to know the release mechanism [42-45].

**RESULTS AND DISCUSSION**

**Construction of loratadine calibration curve**

The maximum concentration (λ<sub>max</sub>) of LTD in 0.1N HCl was scanned and found to have the maximum absorbance at 280 nm. The standard graph of LTD in 0.1 N HCl was shown in fig. 1 by taking concentration ranging from 5µg/ml to 45µg/ml and a good correlation was obtained with a regression coefficient (R<sup>2</sup>) value of 0.998.

![Standard graph of loratadine](image)

*Fig. 1: Standard graph of LTD; (n=1)*

![FTIR spectrum of the pure drug](image)

*Fig. 2: FTIR spectrum of the pure drug; (n=1)*
Pre-compression characterization

Drug excipient compatibility studies

The drug excipient compatibility study was carried out by using DSC and FTIR. FTIR is one of the most powerful analytical techniques when it comes to the determination of the presence of various functional groups and DSC is a thermo analytical method in which the differentiation in the sum of heat required to raise the temperature of the sample and reference is precisely the same.

Fourier transform infrared spectroscopy (FTIR)

The spectral laboratory analysis of pure drug (LTD) and optimized formulation (F3) as shown in fig. 2 and fig. 3 correspondingly; principle peaks at similar wave-numbers and in an optimized formulation (F3) some different wave numbers observed. However, these additional peaks were observed with physical mixtures, which could be due to the occurrence of polymers. The results advise that there is no reaction connecting the drug and polymers used in the current study.

Differential scanning calorimetry (DSC)

The thermal properties of the drug and the mixture of drugs and excipients are of important interest since this can help to assess the interaction among different components of the formulations (i.e., drug and other additives). Pure drug (LTD) and optimized formulation (F3) were subjected to DSC analysis.

The DSC curve of a pure drug (i.e. fig. 4) showed a sharp endothermic peak at 136.11 °C. The optimized formulation (F3) drug and Compritol 888 ATO showed a sharp endothermic peak at 135.10 °C (i.e. fig. 5). From the results, it was concluded that the drug was compatible with excipients used in formulations.

Flow properties of the powder blend

All prepared LTD powder blends are subjected to various parameters. The angle of repose ranges from 21.23±1.08 (F2) to 31.40±1.05 (F8); Carr’s index ranges from 10.12±0.36 (F11) to 15.36±0.47 (F4); Hausner’s ratio values ranges from 1.06±1.01 (F9) to 1.26±0.55 (F7). From the above results, the powder blends (i.e. F1 to F12) showed well to excellent flow properties [46].
Table 2: Pre-compression characterization of LTD floating matrix tablets

| Formulation code | Angle of repose (θ) | Carr’s index (%) | Hausner’s ratio | Flowability |
|------------------|---------------------|------------------|-----------------|-------------|
| F1               | 26.51±1.26          | 12.38±1.04       | 1.12±0.44       | Very good   |
| F2               | 21.23±1.08          | 10.54±0.89       | 1.10±0.38       | Excellent   |
| F3               | 25.34±0.54          | 14.79±0.63       | 1.12±1.06       | Very good   |
| F4               | 23.71±0.82          | 15.36±0.47       | 1.14±0.89       | Very good   |
| F5               | 27.34±0.09          | 13.79±1.02       | 1.08±0.61       | Good        |
| F6               | 23.23±0.06          | 14.54±0.68       | 1.17±0.74       | Very good   |
| F7               | 21.34±0.04          | 12.79±1.09       | 1.26±0.55       | Good        |
| F8               | 31.40±1.05          | 12.08±0.53       | 1.23±1.08       | Good        |
| F9               | 28.52±1.02          | 15.32±1.27       | 1.06±1.01       | Excellent   |
| F10              | 25.26±0.93          | 14.36±0.84       | 1.17±0.82       | Very good   |
| F11              | 25.78±0.64          | 10.12±0.36       | 1.14±0.64       | Very good   |
| F12              | 24.61±0.14          | 12.09±0.52       | 1.19±0.76       | Very good   |

*Each value represents mean±SD (n=3)*

Post-compression characterization

Weight variation (n=20)

The above-prepared formulations, 20 tablets from each batch (i.e. F1 to F12) were individually weighed in milligrams (mg) on electronic balance (Shimadzu, AUX 220, Japan) and results in ranges from 96.86±1.61 mg (F10) to 100.08±0.01 mg (F4).

Thickness (n=20)

Thickness is the only dimensional variable related to the compression process and is measured for all formulations (i.e. F1 to F12) by Vernier calipers and results range from 2.75±0.76 mm (F11) to 3.05±0.48 mm (F4).

Friability (n=20)

Initially, weigh the tablets (i.e. total weight of the tablets is W1) and after 100 revolutions, de-dusted and reweighed (i.e. total weight of the tablets is W2) then worked at percentage weight loss and found the range from 0.12±0.65 % (F10) to 0.49±0.07 % (F4). Friability test of each one formulation (F1 to F12) was found satisfactory (i.e.<1%) and viewing sufficient struggle to the mechanical shock and abrasion.

Hardness (n=6)

The hardness of the tablet was maintained for every batch, was instructed to play downwards on drug release because the effect of polymer concentration is the only area of interest and it was found between 4.27±1.08 kg/cm² (F5) to 6.09±1.10 kg/cm².

Drug content uniformity (n=6)

The drug content was estimated by using UV visible spectrophotometer and the drug released from the entire prepared non-effervescent floating matrix tablets ranges from 96.16±1.15 % (F8) to 99.81±1.54 % (F7).

In vitro buoyancy studies (n=3)

All prepared LTD floating matrix tablet formulations (F1 to F12) were evaluated for buoyancy; 0.1N HCl used as medium and lipid aids used to float the tablet without using any gas generating agents such as sodium bicarbonate, citric acid, and tartaric acid etc.. To develop the desired non-effervescent floating matrix tablets of LTD, it was needed to optimize the buoyant properties and release rates. The floating aids (Compritol 888 ATO and Precirol ATO 5), slow down the water diffusion and results in the buoyancy of dosage form over an encoded time. There was no FLT, (i.e. all prepared LTD non-effervescent floating matrix tablets buoyant was zero seconds) which means by floating aids the prepared tablets directly float on the surface of the medium (i.e. 0.1N HCl) and the TFT of all prepared LTD formulations (i.e. F1 to F12) showed ≥12 h [47, 48]. The in vitro buoyancy was shown in fig. 6 and fig. 7.
Table 3: Post-compression characterization of LTD floating matrix tablets

| Formulation code | Weight variation a (mg) | Thickness a (mm) | Friability a (%) | Hardness b (Kg/cm²) | Drug content b (%) | Matrix integrity |
|------------------|-------------------------|-----------------|-----------------|---------------------|-------------------|-----------------|
| F1               | 98.88±1.01              | 2.97±0.61       | 0.22±1.25       | 4.95±0.71           | 97.25±0.87        | Good            |
| F2               | 98.5±1.09               | 2.95±0.52       | 0.29±0.87       | 5.07±0.85           | 96.93±1.07        | Very Good       |
| F3               | 99.0±1.03               | 2.85±0.63       | 0.41±0.35       | 5.12±0.59           | 99.86±1.54        | Very Good       |
| F4               | 100.0±0.01              | 3.05±0.48       | 0.49±0.07       | 6.01±1.63           | 98.33±0.15        | Excellent       |
| F5               | 99.5±1.25               | 2.89±0.31       | 0.21±1.15       | 4.27±1.08           | 97.90±1.09        | Very Good       |
| F6               | 98.7±1.91               | 2.95±0.74       | 0.14±0.98       | 5.37±0.58           | 97.40±0.54        | Excellent       |
| F7               | 98.8±1.02               | 3.04±0.79       | 0.21±0.56       | 5.32±1.53           | 99.8±1.54         | Good            |
| F8               | 99.8±0.95               | 2.85±0.93       | 0.23±1.05       | 4.96±1.43           | 96.16±1.15        | Very Good       |
| F9               | 98.0±1.06               | 3.01±0.67       | 0.15±1.54       | 5.61±1.12           | 98.31±0.76        | Excellent       |
| F10              | 96.8±1.61               | 2.79±0.31       | 0.12±0.65       | 4.35±1.56           | 98.16±0.65        | Good            |
| F11              | 98.9±0.75               | 2.75±0.76       | 0.24±1.34       | 6.09±1.10           | 98.83±0.20        | Excellent       |
| F12              | 98.9±1.36               | 2.96±0.27       | 0.20±1.14       | 4.38±1.12           | 96.31±1.85        | Excellent       |

*Each value represents mean±SD (n=20); b Each value represents mean±SD (n=6)

Fig. 6: Top views of in vitro buoyancy studies of optimized formulation (F3), a) at zero time b) at 3 h c) at 6 h d) at 12 h; (n=3, mean±SD)

Fig. 7: Front view of in vitro buoyancy studies of optimized formulation (F3), a) at zero time b) at 3 h c) at 6 h d) at 12 h; (n=3, mean±SD)

Fig. 8: Cumulative percentage drug release profiles of LTD prepared floating matrix tablets (F1 to F6); (n=6, mean±SD)
**In vitro** dissolution (n=6)

The prepared LTD floating tablets were exposed to dissolution medium (i.e. 0.1N HCl), the medium penetrates the free spaces, hydrating the polymer and lipid aid. Finally, it forms a gel-like consistency, from which the drug releases slowly for a prolonged time [49]. The cumulative percentage of drug releases was shown in fig. 8 and fig. 9. The most promising formulation was F3 because it cumulative percent of drug release was about 99.82±0.29 % in 12 h.

**In vivo** buoyancy studies (n=3)

The optimized formulation (F3) was prepared with the same compression force as BaSO₄. All the physicochemical properties were within the pharmacopoeial limits [50]. In vivo, radiographic studies were conducted on 3 healthy male human volunteers with a glass of water and a standard diet was provided to find out the GRT of the tablets. X-ray pictures were taken at different time intervals such as 1, 3 and 6 h.

The X-ray image shows that tablets remain in the stomach for about 6 h and which indicate the good floating property (shown in fig. 10). These studies revealed that the mean GRT was found to be ±0.5 h.

**Mechanism of drug release kinetics**

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release, the dissolution data were fitted into zero-order, first order, and Higuchi and Korsmeyer Peppas models. In all formulations (F1 to F12), the diffusion exponent value was>5. The correlation coefficient (R²) and diffusion exponent (n) of release data of all prepared LTD non-effervescent floating tablets (i.e. F1 to F12 formulations) were calculated. The optimized formulation F3 followed the Peppas model (R² =0.996) with the non-Fickian mechanism and it was shown in table 4.

![Graph: Drug release profiles of LTD floating matrix tablets (F7 to F12)](image1.png)

Fig. 9: Cumulative percentage drug release profiles of LTD prepared floating matrix tablets (F7 to F12); (n=6, mean±SD)

![X-ray images of optimized formulation (F3)](image2.png)

Fig. 10: X-ray images of optimized formulation (F3); a) at 30 min; b) at 3 h; c) at 6 h (tablet position was indicated with the circle and arrow mark); (n=3, mean±SD)

| Formulation code | Zero-order | First-order | Higuchi | Hixon crowell | Korsmeyer peppas |
|------------------|------------|-------------|---------|---------------|------------------|
| F3               | 0.978      | 0.869       | 0.914   | 0.862         | 0.996            |

*Each value represents mean±SD (n=6)*
CONCLUSION

The LTD non-effervescent floating tablets were developed by using HPMC K15, HPMC K100 as release retardants and Compritol 888 ATO, Precirol ATO 5 were used as floating aids. From the above DSC and FTIR results, there was no drug and excipient interaction found. The LTD non-effervescent floating tablets were developed by using HPMC K15, HPMC K100 as release retardants and Compritol 888. The LTD non-effervescent floating tablets were developed by using HPMC K15, HPMC K100 as release retardants and Compritol 888.

AUTHORS CONTRIBUTIONS

All authors have contributed equally

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest

REFERENCES

1. Shweta P. Matrix tablet formulation: design, evaluation, and scaling up. J Pharm Pharmacol 2011;43:425-40.
2. Shah R, Patel S, Patel H, Pandey S, Shah S, Shah D. Development of extended release matrix tablets with different tablet hardness. Int J Pharm Sci 2013;8:946-51.
3. Nachaegari SK, Bansal AK. Co-processed excipients for solid dosage forms. J Indian Pharm Sci 2011;43:365-70.
4. York P. Solid-state properties of powders in the formulation and processing of solid dosage forms. Int J Pharm 2006;285:141-52.
5. Radhakrishnan P, Singh SK, Verma PR. Pharmaceutical formulations to increase gastric residence time: concepts and strategies. Drug Delivery Lett 2017;7:190-200.
6. Jadi RK, Tatikonda A, Reedy PR, Venisetty RK. Design and characterization of pregabalin swellable core osmotic pumps. Int J Pharm Sci Res 2016;5:8-15.
7. Togaru V, Venisetty RK, Bakhshi V, Jadi RK. Formulation development and in vitro evaluation of propranolol hydrochloride extended-release matrix tablets. Emergent Life Sci Res 2017;3:38-47.
8. Roy H, Parida KR, Nandi S, Panda SK, Mohapatra DK. Design of fast dissolving amiodipine besylate tablet formulations. Asian J Pharm 2014;6:51-9.
9. El Ragely NA, Badawy AM, Khateeb SE. Stability indicating methods for the determination of loratadine in the presence of its degradation product. J Pharm Biomed 2002;27:694-8.
10. Yeleken G, Kotlovska H, Sztovikova M, Golenia E, Ustenova G. Development of direct compressed loratadine mini-tablets. Int J Pharm Sci Res 2017;9:401-6.
11. Kumar AD, Rani JM, Sudhakarababu AM, Rao VP. Formulation optimization and evaluation of loratadine gastroretentive tablets. Int J Bio Pharm Res 2013;4:190-5.
12. Bommra R, Naidu RS, Yamsani M, Veerabhara K. Development and evaluation of gastroretentive norfloxacin floating tablets. Acta Pharm 2009;59:21-1.
13. Guguloth M, Bomma R, Veerabhara K. Development of sustained-release floating drug delivery. J Pharm Technol 2011;65:198-206.
14. Dudyipala N, Narula A, Janga KY, Bomma R. Amoxicillin trihydrate floating-bioadhesive drug delivery system for eradication of helicobacter pylori: preparation, in vitro and in vivo evaluation. J Bioequivalence Bioavailability 2016;8:18-24.
15. Prasad RR, Kumar JR, Vasudha BA, Chettupalli AK. Formulation development and evaluation of allopurinol solid dispersions by solvent evaporation technique. Int J Appl Pharm 2018;10:168-71.
16. Shrivankar RM. Advances of hydrazine linkers in polymeric drug delivery. J Crit Rev 2019;6:1-4.
17. Van Lenthe E, Ehlers A, Baerends EJ. Geometry optimizations in the zero-order regular approximation for relativistic effects. J Phys Chem A 2009;113:10504-10.
18. Shimakawa Y. New approaches to enhance gastric retention for prolonged drug delivery. J Pharm Invest Dev 2017;7:101-11.
19. Jadi RK, Tatikonda A, Reedy PR, Venisetty RK. Design and characterization of pregabalin swellable core osmotic pumps. Int J Pharm Sci Res 2016;5:8-15.
43. Dash S, Murthy PN, Nath L, Chowdhury P. Kinetic modeling on drug release from controlled drug delivery systems. Acta Pol Pharm 2010;67:217-3.
44. Singhvi G, Singh M. In vitro drug release characterization models. Int J Pharm Stud Res 2011;2:77-84.
45. Costa P, Lobo JM. Modeling and comparison of dissolution profiles. Eur J Pharm Sci 2001;13:123-33.
46. Lopes CM, Bettencourt C, Rossi A, Buttini F, Barata P. Overview on gastroretentive drug delivery systems for improving drug bioavailability. Int J Pharm 2016;510:144-58.
47. Bera H, Boddupalli S, Nandikonda S, Kumar S, Nayak AK. Alginate gel-coated oil-entrapped alginate-tamarind gum-
magnesium stearate buoyant beads of risperidone. Int J Biol Macromol 2015;78:102-11.
48. Satishbabu BK, Sandeep VR, Ravi RB, Shrutinag R. Formulation and evaluation of floating drug delivery system of famotidine. Int J Pharm Sci 2010;72:738-44.
49. Adel S, ElKasabgy NA. Design of innovated lipid-based floating beads loaded with an antispasmodic drug: in vitro and in vivo evaluation. J Liposome Res 2014;24:136-49.
50. Jadi RK, Bomma R, Sellappan V. Development of a new single unit dosage form of propranolol HCl extended-release non-effervescent floating matrix tablets: in vitro and in vivo evaluation. J Appl Pharm Sci 2016;6:112-8.