FORMULATION AND DESIGN OF EXTENDED RELEASE MATRIX TABLETS OF ZIDOVUDINE HYDROCHLORIDE: A STUDY ON EFFECT OF VARIOUS GRADES OF ETHOCEL AND HPMC

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Received: 13 Feb 2017 Revised and Accepted: 01 Feb 2018

Objective: The current research was an attempt to formulate and design an extend release dosage form of zidovudine hydrochloride using various grades of ethyl cellulose (ethocel) such as ethocel 4CPS, ethocel 7 CPS and aqualon T10 Pharm EC with two grades of hydroxy propyl methyl cellulose (HPMCK4M and HPMC K15M).

Methods: Pilot scale batches of nine formulations were prepared using kollidon and adopting wet granulation technique. Physiochemical properties of tablet and granules were examined prior compression to get tablet. Tablets were characterized as drug content, percentage weight variation, thickness, Hardness, percentage friability and in vitro drug release pattern and studied for 12 hour in USP Type-II apparatus using 900 ml Phosphate buffer at 37 ± 0.5 °C. The dissolution release profile of drug in tablet was performed by various drug release kinetic modelling.

Results: The result revealed formulation F8 containing ethocel 7CPS and aqualon T10 was able to delay the pure drug release for 12 h and followed Higuchi pattern. Whereas; formulations containing only ethocel 4CPS provided earlier drug release. Dissolution data of promising formulation were analysed with innovator formulation for similarity factor (f2). Exhibited an acceptable value more than 50. FT-IR (Burrier-transform infrared spectroscopy) and DSC (differential scanning calorimetry) study revealed no such incompatibility found between the pure drug and polymers but slight change in crystallinity were observed in XRD study (X-ray diffraction). SEM (scanning electron microscope) study revealed very rare intragranular pore and cavity.

Conclusion: From that, it can be marked as viscosity and selection of ethocel have great importance in delay drug release.

Keywords: Zidovudine hydrochloride, Ethocel, Innovator, Compression, Hardness

INTRODUCTION

Oral drug delivery is that the most generally used routes for administration of medicine, which are explored for general delivery via numerous pharmaceutical products as completely different dose kind [1]. In long-run medical care for the treatment of chronic disorders, typical formulations are needed to be administered oftentimes in multiple dose regimens, and thus have many undesirable effects. therefore so as to cut back the disadvantage related to multiple dosing, controlled or sustained unleash solid unit dosage forms as tablets were developed [2]. They typically produces higher patient compliance, maintain uniform drug therapeutic level, price effectiveness, broad regular acceptance, cut back dose similarly as aspect effects and increase margin of error for top efficiency therapeutic agents [3].

HIV (human immune deficiency virus), the virus that causes AIDS, “acquired immunodeficiency syndrome” has become one in every of the world’s most serious health and development challenges. The primary cases were reported in 1981 and these days. There are unit roughly thirty seven million individuals presently living with HIV and tens of countless individuals have died of AIDS-related causes since the start of the epidemic. Whereas new cases are reported altogether regions of the globe, roughly two-thirds area unit in geographic region, with forty third of latest cases in eastern and Southern continent [4].

Zidovudine comes in category of drugs known as nucleoside reverse transcriptase inhibitors-NRTIs. This drug together with other concurrent HIV medicine to help control spreading of retroviral infection [5]. It helps to decrease the amount of spreading HIV infection in body so that our immune system does better. This lowers chance of getting HIV complications and improves patient quality of life. This drug has more contribution towards prevention of HIV infection from infected mother to newborn. However serious side effects also marked in certain cases such as lactic acidosis, myopathy, weakness, immune reconstitution inflammatory syndrome, blood anemia, unusual breathing, dark color urine, neutropenia, muscle pain etc [6]. Such above mentioned cases always associated in chronic administration of dosage. In order to reduce such kind of severe and ill effect to patients controlled and fabricated dosage form are always being proved one step forward in proving safety and efficacy. Very few literature studies have been reported in use of ethyl cellulose and hydroxyl propyl methyl cellulose (HPMC) in matrices drug delivery. Generally the controlled dosage forms or matrix tablets are fabricated by selecting suitable hydrophilic and hydrophobic polymer [7, 8]. Hence novelty of the proposed work is to use various grades of ethocel in combined use of HPMC in a matrix tablet of anti retroviral drug.

Thus, an attempt has been made to formulate the extended-release matrix tablets of zidovudine HCI and affect of various grades of ethocel such as ethocel 4CPS, ethocel 7CPS and aqualon T10 Pharm EC on release of zidovudine were also observed and studied. During the study various findings were observed and those interpretated data could be used in large scale production.

MATERIALS AND METHODS

Materials

Zidovudine HCI was received as gift sample from Cipla Ltd, Mumbai. Hydroxy-propyl methyl cellulose (HPMC K4M, HPMC K15M) and ethyl cellulose (ethocel 4CPS, ethocel 7CPS and aqualon T10 Pharm EC) were purchased from Loba Chemie, Mumbai, India. Dicalcium phosphate and polyvinyl pyrolidone (kollidon 30) were purchased from BASF Global (Germany). Colloidal silicon dioxide (aerosil-R 972) was received as gift sample from Ajanta Ltd, India. All remain high analytical grades of chemicals, solvent and iso propyl alcohol (IPA) was purchased from Merck chemicals, India.
Method for preparation of tablets
Zidovudine HCl, HPMC K4M, HPMC K15M, dicalcium phosphate, ethocul 4CPs, ethocul 7CPs aqualon T10 Pharm EC and kollidon CL-SF were passed through #70 mesh and collected separately in polyethylene bag (table 1). Wet granulation technique was applied for the batch preparation of matrix tablets. All the materials were sifted to rapid mixing pilot scale granulator (SSPM System and Engineers, India) and mixed for 30 minute at optimized speed. Kollidon-30 was dissolved in the mixture of iso propyl alcohol (IPA) and water [1:0.7] by the help of mechanical stirrer [9]. The above binder solution was added to dry mix and mixed for 20 minute to get wet mass. Then the resulted wet mass was dried at inlet temperature of 55 °C to 65 °C for 30 min and passed through multi mill (Bectoclean, Ahmedabad, India). The resulted dried granules were sifted through #14 mesh and milled through Multi mill. The comminated granules were lubricated with aerosil-R 972 for 10 min. Finally, the lubricated granules were compressed to formulate tablets using tablet compression machine (Cadmach Machinery Pvt. Ltd, Pune, India) with 10 mm spherical shaped punches [10, 11].

| S. No. | Ingredients                  | F1  | F2  | F3  | F4  | F5  | F6  | F7  | F8  | F9  |
|-------|-----------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 1     | Zidovudine Hydrochloride    | 250 | 250 | 250 | 250 | 250 | 250 | 250 | 250 | 250 |
| 2     | Dicalcium phosphate         | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 |
| 3     | Ethocul 4CPs                | 10  | -   | 5   | -   | 5   | -   | 5   | 10  |     |
| 4     | Ethocul 7 CPs               | -   | 10  | -   | 5   | -   | 5   | 10  |     |     |
| 5     | Aqualon T10 Pharm EC       | -   | -   | 10  | 5   | -   | 5   | 10  | -   | -   |
| 6     | HPMC K4M                   | 25  | 25  | 25  | 25  | 25  | 25  | 25  | 25  | 25  |
| 7     | HPMC K15M                  | -   | -   | 25  | 25  | 25  | 25  | 25  | 25  | 25  |
| 8     | Kollidon 30                | 40  | 40  | 40  | 40  | 40  | 40  | 40  | 40  | 40  |
| 9     | Isopropyl Alcohol          | q.s.| q.s.| q.s.| q.s.| q.s.| q.s.| q.s.| q.s.| q.s.|
| 10    | Aerosil R 972              | 5   | 5   | 5   | 5   | 5   | 5   | 5   | 5   | 5   |
|       | Total Weight (mg)           | 480 | 480 | 480 | 480 | 480 | 480 | 480 | 480 | 480 |

Micromeritic properties of prepared granules
Prior to compression, granules were evaluated for their characteristic parameters [12]. Angle of repose was determined by funnel method. Bulk density (BD) and tapped density (TD) were determined by cylinder method, and carr’s index (CI) was calculated using the following equation

CI = (TD-BD)/TD ×100 . . . . (1)

Haussner’s ratio (HR) was calculated by the following equation

HR=TD/BD . . . . . . . (2)

Physical characterization of matrix tablets
The physicochemical characteristics of tablets were analyzed such as Hardness, friability, weight variation thickness and assay of compressed matrix tablet for each formulation were determined. Tablet hardness test was determined for 20 tablets using tablet hardness tester (Pfizer Tester) and the data reported is the mean of triplicate. Friability test was assessed to measure the strength of tablets as result to withstand mechanical shock, wears and tears. Preweighed randomly selected ten tablets were placed in a Roche friability tester and operated for 100 rpm. As per the limit of standardization the difference in weight should not exceed 1%. The prepared tablets lies within the acceptable and passed US pharmacopoeia the maximum percentage friability should not exceed 1%. The prepared tablets lies within the acceptable and passed the friability test ranged from 0.17 to 0.45. All the tablets showed excellent uniform thickness and no such variation was found. Average

\[
R^2=50\times\log\left\{1+(1/n)\sum_{t=1}^{n}|f_t-T|\right\} \
\]

\[
HR=TD/BD . . . . . . . (2)
\]

Comparison of dissolution profile
The similarity factor (f2) given by scale up and post approval changes (SUPAC) guidelines [13] for a modified release dosage form was used as a basis to compare dissolution profile. The dissolution profiles are considered to be similar when f2 is between 50-100 and disimilarity factor (f1) lies below 15. The dissolution profiles of product was compared to Innovator (Zidine, Emcure-Innovator) using f2 and f1 which are calculated from the following formulae:

Micromeritic properties of granules
Micromeritic properties of precompressed granules were evaluated and cited in table 2. The angle of repose found to be within limit of 33±3.83 to 41±1.75. Tapped density was between 0.50 2 to 0.593

\[
\text{CI} = \frac{(TD-BD)}{TD} \times 100 . . . . (1)
\]

\[
HR = \frac{TD}{BD} . . . . . . . (2)
\]

RESULTS AND DISCUSSION
Micromeritic properties of granules
Micromeritic properties of precompressed granules were evaluated and cited in table 2. The angle of repose found to be within limit of 33±3.83 to 41±1.75. Tapped density was between 0.502 to 0.593 and bulk density was found between 0.415 to 0.467. The result cited in table indicated good flows as it varied from 33 to 41. In addition to that, carr’s index found to vary from 11.04 to 28.66, which indicates good compressibility [14].

Physical characterization of matrix tablets
Physicochemical characterization of tablets were studied and displayed in table 3. The hardness of tablets ranged from 4.9 kg/cm² to 5.9 kg/cm². During the study it observed that, formulations having ethocul grades of low viscosity have high crushing strength as compared to higher viscosity grades of ethocul as observed in aqualon T10 pharm EC. Formulation F1 exhibited higher crushing strength of 5.9 kg/cm² as it contained ethocul 4CPs and HPMC K4M. This is explained by the fact that ethocul of lower viscosity grades are more compressible and produced more harder tablet as observed during the study [15]. As per US pharmacopoeia the maximum percentage friability should not exceed 1%. The prepared tablets lies within the acceptable and passed the friability test ranged from 0.17 to 0.45. All the tablets showed excellent uniform thickness and no such variation was found. Average
During the study, it also observed formulations containing HPMC whereas F7 contained T10 pharma EC released only 7.2% on 12 h. Formulation F9 containing ethocel 4CPS at 2% released to 100%, progressively the drug release also extended as observed in F7 and F9. Formulation F1 and F2 contained HPMC K15M and HPMC K4M except F9, as the formulations contained only ethocel 4CPS. In this study an remarkable finding was observed that, though the variations in grades of ethocel the binder solution kollidon was fixed at maximum time period of 12 h as displayed in fig. 1. In all the dissolution studies were performed in Phosphate Buffer of pH 6.8 for were used to formulate zidovudine hydrochloride matrix tablet. The different grades of ethocel like ethocel 4CPS, 7CPS and aqualon T10 were used to formulate zidovudine hydrochloride matrix tablet. The dissolution studies were performed in Phosphate Buffer of pH 6.8 for maximum time period of 12 h as displayed in fig. 1. In all the formulations the percentage of ethocel were fixed at 2% but the varied in grades of ethocel. The binder solution kollidon was fixed at 8% in all formulation. During the study the effect of two grades of HPMC such as HPMC K4M and HPMC K15M with ethocel were also studied. Result showed time needed for 100% of drug release from F8 was 12 h, while F1 released 100% drug release within only 3 h. It also observed that formulation F6 prepared with ethocel 7 CPS and K15M delayed drug release as compared to formulations prepared by HPMC K4M except F9, as the formulation contained only ethocel 4CPS. From the experiment it can also be remarked that, as the polymer viscosity increases the extent of release also increases and vice versa. In this study an remarkable finding was observed that, though the formulations containing lower viscosity grades of polymer and have higher crushing strength but the polymers having higher viscosity such as HPMC K15M prolonged the drug release to certain extend [19].

The data obtained from in vitro dissolution studies were fitted to zero-order, first-order, and higuchi release kinetics. All formulations were best fitted either to zero order or higuchi. The best fit with higher correlation coefficient (r² >0.997) was found with higuchi’s equation for F8 and concluded the release of drug from tablet involves both dissolution and diffusion through polymers. To ascertain the exact mechanism of drug release, the data were fitted by korsemeyer-peppas equation. The “n” value lies between 0.41 to 0.51. Hence it can be inferred that the release was based on quasi fickian and the release of drug had great impact by those hydrophobic polymer. On the basis of the above results, F8 was selected and preceded for further study.

**Table 2: Micromeritic properties of prepared granules**

| S. No. | Formulation code | Bulk density (X±SD) | Tapped density (X±SD) | Hausner's ratio | Compressibility index (Carr’s index) | Angle of repose (X±SD) |
|--------|------------------|---------------------|----------------------|----------------|--------------------------------------|----------------------|
| 1      | F1               | 0.42±1.17           | 0.50±1.36            | 1.18           | 15.73                                | 40±1.58              |
| 2      | F2               | 0.42±2.11           | 0.58±2.63            | 1.35           | 26.33                                | 41±1.75              |
| 3      | F3               | 0.46±2.11           | 0.52±2.84            | 1.12           | 11.04                                | 37±2.84              |
| 4      | F4               | 0.41±2.15           | 0.58±2.49            | 1.37           | 27.19                                | 35±2.03              |
| 5      | F5               | 0.43±2.19           | 0.58±2.01            | 1.4            | 20.81                                | 35±1.06              |
| 6      | F6               | 0.42±2.16           | 0.57±2.39            | 1.34           | 25.69                                | 33±3.83              |
| 7      | F7               | 0.43±1.31           | 0.59±1.83            | 1.37           | 27.07                                | 38±2.94              |
| 8      | F8               | 0.43±2.12           | 0.59±1.52            | 1.4            | 28.66                                | 37±2.05              |
| 9      | F9               | 0.42±1.42           | 0.51±2.85            | 1.2            | 17.31                                | 39±2.52              |

Data are represented as mean±standard deviation (SD), n=3

**Table 3: Physical characterization of the designed formulations**

| S. No. | Formulation code | Average weight (mg) (X±SD) | Thickness (mm) (X±SD) | Crushing strength (Kg/cm²) | Drug content (%) (X±Sd) | Friability (%) |
|--------|------------------|---------------------------|----------------------|---------------------------|-------------------------|---------------|
| 1      | F1               | 480.1±0.53                | 4.27±1.01            | 5.4±2.45                  | 98.38±2.19              | 0.18%         |
| 2      | F2               | 481.3±2.29                | 4.17±1.12            | 5.2±1.46                  | 102.3±5.17              | 0.32%         |
| 3      | F3               | 482.0±1.27                | 4.18±2.23            | 5.6±2.55                  | 99.18±2.47              | 0.26%         |
| 4      | F4               | 481.6±0.29                | 4.3±1.27             | 5.4±3.06                  | 98.27±3.16              | 0.28%         |
| 5      | F5               | 482.1±0.28                | 4.2±0.98             | 5.2±2.72                  | 99.25±3.19              | 0.45%         |
| 6      | F6               | 480.5±1.15                | 4.2±0.35             | 5.0±3.25                  | 97.68±1.48              | 0.17%         |
| 7      | F7               | 482.1±1.07                | 4.27±0.87            | 4.9±3.14                  | 100.01±4.52             | 0.31%         |
| 8      | F8               | 480.6±0.57                | 4.2±1.17             | 5.1±2.45                  | 100.67±1.09             | 0.27%         |
| 9      | F9               | 480.2±1.12                | 4.2±1.12             | 5.4±2.78                  | 99.09±3.08              | 0.19%         |

Data are represented as mean±standard deviation (SD), n=3

**In vitro dissolution studies**

Different grades of ethocel like ethocel 4CPS, 7CPS and aqualon T10 were used to formulate zidovudine hydrochloride matrix tablet. The dissolution studies were performed in Phosphate Buffer of pH 6.8 for maximum time period of 12 h as displayed in fig. 1. In all the formulations the percentage of ethocel were fixed at 2% but the varied in grades of ethocel. The binder solution kollidon was fixed at 8% in all formulation. During the study the effect of two grades of HPMC such as HPMC K4M and HPMC K15M with ethocel were also studied. Result showed time needed for 100% of drug release from F8 was 12 h, while F1 released 100% drug release within only 3 h. It also observed that formulation F6 prepared with ethocel 7 CPS and K15M delayed drug release as compared to formulations prepared by HPMC K4M except F9, as the formulation contained only ethocel 4CPS. From the experiment it can also be remarked that, as the polymer viscosity increases the extent of release also increases and vice versa. In this study an remarkable finding was observed that, though the formulations containing lower viscosity grades of polymer and have higher crushing strength but the polymers having higher viscosity such as HPMC K15M prolonged the drug release to certain extend [19].

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**Fig. 1: In vitro dissolution study of all formulations, (Data are represented as mean±standard deviation (SD), n=3)**
Comparison of dissolution profile

The comparative results of the selected formulation batch F8 was compared with the theoretical dissolution profile (Zidine, Emcure-Innovator) using the similarity factor \( f_2 \) test and dissimilarity factor \( f_1 \) test. The results of the similarity tests showed that formulation F8 had \( f_2 \) value > 50 i.e. 64, indicating the closest fit to the dissolution profile of innovator.

Drug polymer interaction study

FT-IR study

Pure zidovudine HCl mixed with ethocel 4CPS, ethocel 7CPS, aqualon T10 pharm EC dicalcium phosphate separately with IR grade KBr and pellets were prepared by applying a pressure of 10 tons in a hydraulic press. The pellets were scanned over a wavelength range of 450 to 4,500 cm\(^{-1}\) using an FTIR IRSpirit, Schimazu. There was no chemical interaction between zidovudine hydrochloride and the polymers used which is obtained by employing I. R. spectral studies (fig. 2 and fig. 3). The characteristic peak of carbonyl group at 1685.84 cm\(^{-1}\) and azide group at 2083.19 cm\(^{-1}\) indicated the stability of drug before and after formulation.

DSC study

Differential scanning calorimetry (DSC) has shown to be an important tool to quickly obtain information about possible interactions between the active and the excipients, according to the appearance, shift or disappearance of endothermic or exothermic peaks. DSC study was performed using Perkin Elmer DSC to determine the drug excipient compatibility study. During study a sharp endothermic peak for zidovudine hydrochloride was obtained at 131.55 °C corresponding to melting point (fig. 4). But in the formulation there was a slight change in peak temperature such as 106 °C and 180 °C (fig. 5), also a slight change in peak area and peak shape changed, which might be due to reduction of the purity percentage of component, appearance of adjacent polymer and interaction with solvent excipients [20, 21].

![Fig. 2: FTIR spectrum of pure zidovudine hydrochloride](image)

![Fig. 3: FTIR Spectrum of formulation F8](image)

![Fig. 4: DSC curve of pure zidovudine hydrochloride](image)
XRD study

Change in crystallinity of drug can be determined by this technique. Pure drug and formulation components were analysed by the help of XRD 7000, Shimadzu [22]. Pure zidovudine HCl showed the classical diffractogram of the crystalline substance. The XRD pattern of the formulation showed slight change in peak and pattern, indicated slight loss of crystallinity (fig. 6 and fig. 7).

Fig. 5: DSC curve of formulation F8

Fig. 6: XRD of pure zidovudine hydrochloride

Fig. 7: XRD of formulation F8

Fig. 8: SEM study of formulation F8 granules
Authors Contributions

Author is a faculty in division of pharmaceutics and the work contributed on faculty development programme in the institution.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Chien YW. Novel drug delivery systems. 2nd ed. New York: Marcel Dekker; 1992.
2. Singh BN, Kim RH. Floating drug delivery system: an approach to oral controlled drug delivery via gastric retention. J Controlled Release 2000;65:235-59.
3. Brazel CS, Peppas NA. Temperature and pH-sensitive hydrogels for controlled release of antithrombotic agents. Mater Res Soc Symp Proc 1994;331:211-6.
4. https://www.webmd.com/drugs/2/drug-4386/zidovudine-oral/details. [Last accessed on 08 Sep 2017]
5. https://aidsinfo.nih.gov/drugs/4/zidovudine/0/patient. [Last accessed on 10 Sep 2017]
6. Santos JV, Pina ME, Marques MP, de Carvalho LA. New sustained release of Zidovudine Matrix tablets – cytotoxicity toward Caco-2 cells. Drug Dev Ind Pharm 2013;39:1154-66.
7. Ganesh S, Radhakrishnan M, Ravi M, Prasannakumar B, Kalyani J. In vitro evaluation of the effect of combination of hydrophilic and hydrophobic polymers on controlled release zidovudine matrix tablets. Indian J Pharm Sci 2008;70:461-5.
8. Kuksa A, Tiwary AK, Jain NK, Jain S. Formulation and in vitro, in vivo evaluation of extended-release matrix tablet of zidovudine.

Stability study of best batch

Long term, intermediate and accelerated stability testing study was carried out according to ICH guidelines considering 25±2 °C/60±5% RH, 30±2 °C/65±5% RH and 40±2 °C/75±5% RH respectively. One hundred tablets of batch F8 were securely packed in aluminium blister and placed in humidity chamber [24]. There was no such major significance change in hardness and drug assay at a regular interval of 3 mo during the study of 24 mo as shown in table 4.

Table 4: Stability study of best batch

| Month | Drug assay (%) | Crushing strength (Kg/cm²) |
|-------|----------------|---------------------------|
|       | Intermediate (30±2 °C and 65±5% RH) | Long term stability study (25±2 °C and 60±5% RH) |
| Month | Drug assay (%) | Crushing strength (Kg/cm²) | Month | Drug assay (%) | Crushing strength (Kg/cm²) |
|-------|----------------|---------------------------|-------|----------------|---------------------------|
| 3     | 100.07±3.15    | 5.8±1.69                  | 1     | 100.07±3.15    | 5.8±1.69                  |
| 6     | 100.34±2.11    | 5.8±1.8                   | 2     | 100.34±2.11    | 5.8±1.8                   |
| 9     | 100.31±2.02    | 5.8±1.77                  | 3     | 100.31±2.02    | 5.8±1.77                  |
| 12    | 99.90±1.02     | 5.7±2.35                  | 6     | 99.25±2.51     | -                         |
| 18    | 99.22±2.97     | 5.7±3.02                  |       |                |                           |
| 24    | 98.17±1.49     | 5.8±3.45                  |       |                |                           |

Data are represented as mean±standard deviation (SD), n=3

CONCLUSION

During this study extended release tablet of zidovudine HCl tablets were formulated. A total number of nine formulations were prepared by varying the amount of ethocel and HPMC. In this study the effect of various grades of ethocel with combination of HPMC studied. Result showed time took for F8 to release 100% drug was 12 hour. Moreover, it also observed that as viscosity of ethocel increased progressively extended the drug release. Formulation F8 compared with innovator and found to be providing satisfactory result. Furthermore, industrial grades of reproducible baches and in vivo pharmacokinetic study have to carry out.

Authors Contributions

Author is a faculty in division of pharmaceutics and the work contributed on faculty development programme in the institution.
21. Song SH, Chae BR, Sohn SI, Yeom DW, Son HY, Kim JH, et al. Formulation of controlled-release pebufiprofen tablet using Kollidon® SR. Int J Pharm 2016;511:864-75.

22. Ravala JA, Patela JK, Naihong L, Patela MM. Ranitidine hydrochloride floating matrix tablets. Asian J Pharm Sci 2007;2:130-42.

23. Khan GM, Meidan VM. Drug release kinetics from tablet matrices based upon ethylcellulose ether-derivatives: a comparison between different formulations. Drug Dev Ind Pharm 2007;33:627-39.

24. Guideline IH. Stability testing of new drug substances and products. Q1A(R2), current step; 2003. p. 4.