Formulation and Evaluation of Microsphere Based Nicorandil Sustained Released Tablet

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Abstract

The aim of the present work was to develop once-daily sustained release microsponge formulations of Nicorandil, a potent potassium channel opener used in cardiovascular diseases and it has low oral bioavailability (70%) and half-life 1 h. So, it is good candidate for sustained release formulations based on microsphere technology. The microsponges were prepared by using quasi-emulsion solvent diffusion method. Scanning Electron Microscopy (SEM) revealed that the microsponges of nicorandil with Eudragit - RSPO and HPMC K100M were smooth, porous, glossy and discrete spherical. The actual drug content and encapsulation efficiency of batch M1 to M9 were obtained in range of 62.05 ± 0.31 to 80.69 ± 0.43 and 64.41 ± 1.71 to 70.58 ± 1.12, respectively. The microsponges formulations were subjected to in-vitro release studies and the results were evaluated kinetically and statically. The best fitted model was found to be Korsmeyer - Peppas model (R² = 0.9992) for M6 batch. The ‘n’ value for Korsmeyer - Peppas model was between 0.5 and 1.0 which is indicative of non-Fickian diffusion. Statistical analysis using ANOVA yielded a p value of 0.572 for all the formulations, indicating that there was no significant difference among them.

Keywords: Nicorandil; Microsphere; Sustained release tablet; Korsmeyer-Peppas equation.

1. Introduction

Hypertension and angina pectoris, the most common cardiovascular diseases, require constant monitoring. Potassium channel openers are presently considered an important class of drug for hypertension and angina pectoris. The first therapeutic drug shown to possess an ability to hyperpolarize smooth muscle cell membranes is nicorandil, a potent coronary vasodilator [1]. Although nicorandil is one of the emerging molecule in the case of hypertension and angina [2,3], successful treatment means maintenance of blood pressure at a normal physiological level, for which a constant and uniform supply of drug

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is necessary [4]. Nicorandil has low oral bioavailability (70 %) and a short half-life just 1 hr, so the usual oral dosage regimen is 5 to 40 mg used 2 to 4 times a day. To reduce the frequency of administration, to improve patient compliance and reduce side effects [5], a once-daily sustained release formulation of nicorandil is desirable. The drug is freely soluble in water, and hence judicious selection of release-retarding system is necessary to achieve a constant in-vivo input rate of the drug.

Over the last few years, extensive efforts have been focused on targeting a drug or drug delivery system in a particular region of the body for extended period of time, not only for local targeting of drugs but also for better control systemic drug delivery [6]. The drug delivery technology area has become highly competitive and rapidly growing. More and more developments in delivery systems are being integrated to optimize the efficacy and cost-effectiveness of the therapy. New generation of pharmaceuticals, biopharmaceuticals are stimulating the rapid evolution of drug delivery technology. In the current years the development of new drugs is not sufficient for the drug treatment. But it also involves the development of suitable drug delivery system at site of action. The biggest challenge up to date is to control the delivery rate of the medicaments by various modern technologies met by extensive research [7]. Various multiparticulate approaches include formulation in the form of pellets; granules have been developed to achieve targeted and sustained release of drugs in the colon. They provide many advantages over single-unit systems because of their small size [8].

The aim of this work was to develop nicorandil - loaded sustained release microsponges for better effect. Microsponges are one of the most useful devices to deliver material in an effective prolonged and safe manner [9–11]. It was found that microsponges have unique dissolution and compression properties due to presence of sponge like texture. Microsponge drug delivery system has many favorable properties which make it suitable as a drug delivery carrier such as enhance stability due to high degree of cross-linking, reduce side-effects due to targeted and modify drug-release, and also it protects the entrapped active ingredients from physical and environmental degradation. These are also capable to deliver pharmaceutical active ingredients efficiently at the minimum dose at targeted site which reduce severe systemic side effects [12,13]. Current survey showed that microsponge offers a novel approach for drug targeting because there is no chemical modification of the active agent and this system is potentially applicable to a large group of chemically diverse agents for selective drug delivery to the target. Moreover, in -vitro studies have indicated that the microsponge system enhances the rate of dissolution of water-insoluble drugs [14].

2. Materials and Methods

2.1. Materials

Nicerandil was receives as gift sample from Alkem Research Lab. Mumbai (India). Eudragit RSPO, Eudragit RLPO, and Eudragit S100 were gifted by Emcure. Vadodara (India). HPMC (100,000 cps) and HPMC (15,000 cps) were also gifted by FMC
biopolymer, Mumbai (India). Tablettose™ and Avicel™ PH-102 were gifted by Meggle GmbH, Wasserburg, (Germany) and FMC International, Little Island (Cork), respectively. Starch 1500™ was generous gift from Colorcon Ltd., Goa (India). Isopropyl alcohol (IPA) and Dichloromethane, were used of S. D. Fine chemicals, Mumbai (India). All other chemicals were used of analytical grade.

2.2. Quasi-emulsion solvent diffusion method [15,16]

The microsponges containing Nicorandil were prepared by quasi emulsion solvent diffusion method using the different polymer amounts (Fig. 1). To prepare the internal phase, polymers were dissolved in mixture of IPA and dicloromethane (50:50). Then, Nicorandil was added in addition to magnesium stearate (0.5 % w/v), and dissolved under ultrasonication at 35°C at 70 - kHz frequency for 2 min. The internal phase was then poured into previously cooled (10 ± 0.5º C) liquid paraffin (300 mL) with constant stirring (1000 rpm) for 6 hr, the external phase. The prepared O/O emulsion was heated at 35 ± 2°C with constant stirring at 1000 rpm for another 90 min. During this time, the IPA and dicloromethane were completely removed by diffusion into liquid paraffin and evaporation through the air/liquid interface. The solidified microsponges were filtered and washed six times with 50 mL of n-hexane. The microsponges were dried in an air-heated oven at 40°C for 12 h and packed in air tight container for further study. The same procedure was followed for all the preparations and the composition of various microsponge formulations is given in Table 1.

Table 1. Composition of various microsponge formulations.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>M1</th>
<th>M2</th>
<th>M3</th>
<th>M4</th>
<th>M5</th>
<th>M6</th>
<th>M7</th>
<th>M8</th>
<th>M9</th>
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<tbody>
<tr>
<td><strong>Internal phase (mg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Nicorandil</td>
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<td>1500</td>
<td>1500</td>
<td>1500</td>
<td>1500</td>
<td>1500</td>
<td>1500</td>
<td>1500</td>
</tr>
<tr>
<td>HPMC K15M</td>
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<td>250</td>
<td>250</td>
<td>--</td>
<td>--</td>
<td>--</td>
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<td>250</td>
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<tr>
<td>Eudragit S100</td>
<td>250</td>
<td>--</td>
<td>--</td>
<td>250</td>
<td>--</td>
<td>--</td>
<td>125</td>
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</tr>
<tr>
<td>Eudragit RLPO</td>
<td>--</td>
<td>250</td>
<td>--</td>
<td>--</td>
<td>250</td>
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<tr>
<td>Eudragit RSPO</td>
<td>--</td>
<td>--</td>
<td>250</td>
<td>--</td>
<td>250</td>
<td>--</td>
<td>--</td>
<td>125</td>
<td>--</td>
</tr>
<tr>
<td>Magnesium Stearate</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
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<td>IPA (mL)</td>
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<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
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<tr>
<td>DCM (mL)</td>
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<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
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<td>10</td>
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<tr>
<td><strong>External phase (mL)</strong></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liquid Paraffin</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
</tr>
</tbody>
</table>

2.3. Fourier transform infrared (FTIR) spectral study

Fourier transform infrared (FTIR) spectral data were taken on a Shimadzu (model FTIR-8300, Tokyo, Japan) instrument to find out the chemical stability of the excipients. FTIR spectra of the Nicorandil, microsponge of batch F6 (having drug: polymer ratio 3:1) and physical mixture (drug + HPMC K100M + Eudragit RSPO) in the same ratio were
obtained. All the samples were crushed with potassium bromide to get pellets at 1 ton/cm². Spectral scanning was done in the range between 4000–400 cm⁻¹.

2.4. **Differential scanning calorimetry (DSC) study**

Different scanning calorimetry (DSC) was performed on Nicorandil and microsphere of batch F6 (Shimadzu DSC-60, Tokyo Japan). Approximately 2 mg of sample was weighed into a 40 µL aluminum pan and compressed in a dry air atmosphere. Pans were then sealed hermetically and run at a heating rate of 20ºC/min over a temperature range 40-400ºC.

2.5. **Scanning electron microscopy (SEM) study**

The detailed surface topography of the selected microsponges was observed using a scanning electron microscope (JEM-6400, Jeol Ltd, Japan). The microsphere sample was attached to the specimen holder using a double-coated adhesive tape and was gold-coated (20 nm thickness) under vacuum using a sputter coater for 5–10 min at 40 mA and then investigated at 30 Kv [17].
2.6. Determination of production yield

The production yield of the microsponges was determined by calculating accurately the initial weight of the raw materials and the final weight of the microsponge obtained, as the following equation.

\[
\text{Production yield} = \frac{\text{Practical mass of microsponges}}{\text{Theoretical mass (drug + polymer)}} \times 100
\]

2.7. Particle size analysis

Particle size and size distribution of microsponge particles was determined using optical microscope. The values were given for the formulations in the form of mean particle size [18].

2.8. Actual drug content and encapsulation efficiency

In 100 mL volumetric flask, 100 mg of crushed microsponges were taken and dissolved with small quantity of ethanol and volume was made up to mark with phosphate buffer pH 6.8 and stirred for 12 hours. After stirring, the solution was filtered through whatman filter paper and from the filtrate, appropriate dilutions were made and absorbance was measured at 262 nm by using UV/Vis Spectrophotometer (Shimadzu 1601, Tokyo, Japan). The encapsulation efficiency (%) of the microsponges can be calculated according to the following equation [19,20].

\[
\text{Actual drug content (\%) = \frac{\text{Actual drug content in microsponges}}{\text{Total amount of the microsponges}}} \times 100
\]

\[
\text{Encapsulation efficiency (\%) = \frac{\text{Practical drug content in microsponges}}{\text{Theoretical drug content in microsponges}}} \times 100
\]

2.9. In-vitro drug release studies of microsponge formulations

The microsponges (120 mg) containing 80 mg of nicorandil were subjected to in-vitro drug release studies after filling in 0 size capsule. The In-vitro drug release studies were carried out using USP apparatus (model TDT-60T, Electrolab) fitted with paddle (50 rpm) at 37 ± 0.5°C. Initial drug release was carried out in 900 mL of simulated Gastric intestinal fluid (SGF, pH 1.2) for 2 h, followed by 900 mL of simulated intestinal fluid (SIF, pH 6.8) for next 10 h. At a predetermined time interval, 10 mL samples were withdrawn, filtered through a 0.45 μm membrane filter, and assayed at 262 nm by using UV/Vis Spectrophotometer (Shimadzu 1601, Tokyo, Japan) to determine the percentage drug released. The same volume (10 mL) of fresh dissolution medium was replenished immediately after the sample was withdrawn. Dissolution tests were performed in triplicate for each sample [1].
2.10. Kinetic data analysis

To analyze the in-vitro release data various kinetic models were used to describe the release kinetics. The zero order describes the systems where drug release rate is independent of its concentration. The first order describes the release from system where release rate is concentration dependent. Higuchi described the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion. The following plots were made: cumulative % drug release vs. time (zero order kinetic models); log cumulative % drug remaining vs. time (first order kinetic model); cumulative % drug release vs. square root of time (Higuchi model), and log % drug release vs log time (Korsmeyer - Peppas model) [21].

2.11. Manufacturing of tablets containing microsponges

Direct compression method was used to demonstrate the compressibility and the tableting performance of the developed microsponges. Batch M6 microsponges containing 80 mg nicorandil (≈ 120 mg microsponges) were mixed with calculated quantity of directly compressible ingredients like Tablettose, Avicel PH102 and Starch 1500 according Table 2 for 5 min. The blend was mixed with magnesium stearate and talc for 2 min. The final mixture was directly tableted (300 mg) on a Rimex ten station rotary tablet machine using 10 mm diameter flat-faced punches (Cadmach Machinery Private Ltd., Ahmedabad). The tablets were evaluated for weight variation, crushing strength (kg/cm²), friability, and in-vitro drug release.

<table>
<thead>
<tr>
<th>Ingredient (mg)</th>
<th>NM1</th>
<th>NM2</th>
<th>NM3</th>
<th>NM4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microsponges of Batch M6</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>Tablettose</td>
<td>90</td>
<td>80</td>
<td>70</td>
<td>60</td>
</tr>
<tr>
<td>Avicel PH102</td>
<td>70</td>
<td>80</td>
<td>90</td>
<td>100</td>
</tr>
<tr>
<td>Starch 1500</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Magnesium Stearate</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Talc</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>300 ± 9</td>
<td>300 ± 11</td>
<td>300 ± 7</td>
<td>300 ± 10</td>
</tr>
</tbody>
</table>

2.12. Short-term stability study

The formulation showing optimum drug release was subjected for to a short-term stability study. According to ICH guideline, a selected formulation was kept in a closed glass container for 3 months at 40±2 °C at 75±5 % RH. Formulation was evaluated at periodical intervals of one month for the pattern of drug release.
3. Results and Discussion

3.1. Preparation of microsponges

The nicorandil loaded microsponges were prepared by quasiumulsion solvent diffusion method because this method was found to be very simple, reproducible, and rapid method. Moreover, it has advantage of avoiding solvent toxicity [22]. The drug and polymer in the ratio 3:1 was taken; in each formulation, the amount of magnesium stearate (100 mg), IPA and dichloromethane (10 mL) were kept constant. The microsponge formulations were prepared using mechanical stirrer (Remi 5 – MLH) at a stirring rate of 1000 rpm for 6 hr. The composition of various microsponge formulations are presented in Table 1. The effect of various variables like amounts and different grade of HPMC and Eudragit was studied.

3.2. Fourier transform infrared (FTIR) spectral study

Analysis of the FTIR spectra (Fig. 2) of the nicorandil, physical mixture of drug, HPMC K100M and Eudragit RSPO, and microsponge formulation batch F6 indicate a characteristic peaks at 3243 cm\(^{-1}\) (N-H amide stretching), at 2850 cm\(^{-1}\) (C-H aliphatic stretching), at 1562 cm\(^{-1}\) (N-H amide bending), at 1427 cm\(^{-1}\) (C-H bending) and 1361 cm\(^{-1}\) (NO\(_2\) stretching) for the drug, and at 1726.17 cm\(^{-1}\) (C = O stretching) around for Eudragit RSPO [23]. All the characteristic peaks of Nicorandil were observed in the spectra of physical mixture as well as microsponge formulation (Batch F6), thus indicating that no chemical interaction or changes took place during the development of the formulations and that the drug was stable in all the formulations.

![Fig. 2. FTIR spectra of Nicorandil, Physical mixture of Nicorandil, HPMC K100M and Eudragit RLPO and Microsponge formulations (Batch F6).](image-url)
3.3. Differential scanning calorimetry (DSC) study

In the DSC studies (Fig. 3), the thermogram of the nicorandil alone showed a sharp endothermic peak at 95.52°C which corresponds to the melting point of drug in the crystalline form. In each of the DSC thermograms of the microsponge formulations (F1 – F9) the characteristic endothermic peak at 96.25°C of the drug was also observed, thus indicating that there was compatibility between the drug and polymers used.

![DSC thermograms of pure nicorandil and microsponge formulations (Batch F6).](image)

3.4. Scanning electron microscopy (SEM) study

The morphology of the microsponges was studied by scanning electron microscopy (SEM). The representative photographs of the microsponges are shown in Fig. 4. The microsponges were observed to be spherical and uniform with no drug crystals on the surface.

![SEM photograph of nicorandil microsponge formulation (Batch F6).](image)

3.5. Evaluation of nicorandil microsponges

Production yield, average particle size, actual drug content and encapsulation efficiency of batch M1 to M9 are presented in Table 3. The production yield and average particle size of all the batches were found between 71.00 ± 0.73 to 80.93 ± 1.12 and 321.4 ± 0.21 to 401.1 ± 2.24, respectively. The actual drug content and encapsulation efficiency of batch M1 to M9 were obtained in range of 62.05 ± 0.31 to 80.69 ± 0.43 and 64.41 ± 1.71 to
70.58 ± 1.12, respectively. On subjecting the data obtained for various formulations in respect to production yield, actual drug content, and encapsulation efficiency to t-test at 95% level of significance, no significant difference in relation was observed amongst the formulations (p < 0.05). Among all formulations batch M6 showed maximum production yield (80.93 ± 1.12), highest actual drug content (80.69 ± 0.43) and encapsulation efficiency (70.58 ± 1.12).

Table 3. Evaluation of nicorandil microsponges.

<table>
<thead>
<tr>
<th>Batch Code</th>
<th>Production Yield (% ± SD)</th>
<th>Average Particle Size (μm ± SD)</th>
<th>Actual Drug Content (% ± SD)</th>
<th>Encapsulation Efficiency (% ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>78.19 ± 1.31</td>
<td>321.4 ± 0.21</td>
<td>62.05 ± 0.31</td>
<td>64.41 ± 1.71</td>
</tr>
<tr>
<td>M2</td>
<td>79.12 ± 1.37</td>
<td>321.7 ± 0.41</td>
<td>64.06 ± 0.85</td>
<td>65.94 ± 1.42</td>
</tr>
<tr>
<td>M3</td>
<td>71.00 ± 0.73</td>
<td>365.7 ± 1.31</td>
<td>66.37 ± 0.99</td>
<td>67.06 ± 1.32</td>
</tr>
<tr>
<td>M4</td>
<td>75.20 ± 1.01</td>
<td>401.1 ± 2.24</td>
<td>67.94 ± 0.74</td>
<td>66.40 ± 1.22</td>
</tr>
<tr>
<td>M5</td>
<td>74.33 ± 0.97</td>
<td>398.7 ± 1.75</td>
<td>75.32 ± 0.88</td>
<td>67.71 ± 1.51</td>
</tr>
<tr>
<td>M6</td>
<td>80.93 ± 1.12</td>
<td>376.9 ± 1.89</td>
<td>80.69 ± 0.43</td>
<td>70.58 ± 1.12</td>
</tr>
<tr>
<td>M7</td>
<td>80.00 ± 0.79</td>
<td>325.4 ± 1.42</td>
<td>62.40 ± 0.95</td>
<td>66.65 ± 0.95</td>
</tr>
<tr>
<td>M8</td>
<td>76.00 ± 1.22</td>
<td>369.7 ± 1.67</td>
<td>70.12 ± 0.12</td>
<td>68.93 ± 0.95</td>
</tr>
<tr>
<td>M9</td>
<td>73.00 ± 1.14</td>
<td>364.89 ± 1.52</td>
<td>72.40 ± 0.52</td>
<td>69.21 ± 1.10</td>
</tr>
</tbody>
</table>

n = 3, S. D. means Standard Deviation

3.6. In-vitro drug release study

The release profiles obtained for the microsponge formulations are presented in Figs. 5 and 6. The profiles showed a biphasic release with an initial burst effect. In the first hour, about 9 – 13% of the drug was released. Cumulative release for the microsponges after 12 h ranged from 47.1 to 56.28%. Maximum drug release (98.4%) within 24 h was observed from M6 microsponges formulation followed by M8 (95.99%) and M9 (93.9%) formulations. In-vitro drug release data of all the microspoge formulations was subjected to goodness of fit test by linear regression analysis according to zero order equation, first order, Higuchi, Hixon - Crowell model and Korsmeyer - Peppas models to ascertain the mechanism of drug release. The values of the linear regression analysis including regression coefficient ($R^2$) and diffusion exponent (n) are summarized in Table 4. The results showed that the release kinetics on the basis of the highest $R^2$ values best fitted a Zero order kinetic model. The best fitted models were found to be Korsmeyer - Peppas model for M6 and zero order for M2, M5 and M8. The ‘n’ value for Korsmeyer - Peppas model was between 0.5 and 1.0 which is indicative of non-fickian diffusion. Statistical analysis using ANOVA yielded a p value of 0.572 for all the formulations, thus indicating that there was no significant difference among them.
Table 4. Kinetic values obtained from different plots of batch M1 – M9.

<table>
<thead>
<tr>
<th>Batch Code</th>
<th>Zero order plots* (R^2)</th>
<th>First order plots! (R^2)</th>
<th>Higuchi plots† (R^2)</th>
<th>Korsmeyer plots‡ (n)</th>
<th>Korsmeyer plots‡ (R^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>0.9977</td>
<td>0.9540</td>
<td>0.9897</td>
<td>0.687</td>
<td>0.9972</td>
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<tr>
<td>M2</td>
<td>0.9981</td>
<td>0.9643</td>
<td>0.9918</td>
<td>0.628</td>
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<td>M3</td>
<td>0.9933</td>
<td>0.9730</td>
<td>0.9903</td>
<td>0.603</td>
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<tr>
<td>M4</td>
<td>0.9970</td>
<td>0.9583</td>
<td>0.9940</td>
<td>0.680</td>
<td>0.9966</td>
</tr>
<tr>
<td>M5</td>
<td>0.9983</td>
<td>0.9579</td>
<td>0.9951</td>
<td>0.613</td>
<td>0.9960</td>
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<tr>
<td>M6</td>
<td>0.9955</td>
<td>0.9379</td>
<td>0.9952</td>
<td>0.714</td>
<td>0.9992</td>
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<td>M7</td>
<td>0.9978</td>
<td>0.9591</td>
<td>0.9893</td>
<td>0.655</td>
<td>0.9971</td>
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<tr>
<td>M8</td>
<td>0.9982</td>
<td>0.9592</td>
<td>0.9913</td>
<td>0.619</td>
<td>0.9977</td>
</tr>
<tr>
<td>M9</td>
<td>0.9979</td>
<td>0.9525</td>
<td>0.9937</td>
<td>0.632</td>
<td>0.9973</td>
</tr>
</tbody>
</table>

*Zero order equation, C = Co + Ko t
†First order equation, Log C = Log Co – Kt / 2.303
‡Higuchi’s equation, Q = Kt^{1/2}
§Korsmeyer – Peppas equation, M_t / M_α = Kt^n

3.7. Short term stability study

The stability studies were applied on formulation M6 because of their good encapsulation efficiency. The nicorandil microsponges were stored in glass bottles at 40±2°C temperature for three months and evaluated at the interval of 1 month for any change in percentage drug content. The actual drug content varied from 80.69 ± 0.43 to 79.88 ± 0.07. The decrease in drug content was found but it is in prescribed limits as per degradation phenomena. Thus, it was found that the optimized formulation M6 was stable under storage conditions.

3.8. Evaluation of microsponge tablets

Controlled release tablets were prepared from the optimized formulation M6. The formulated tablets were subjected to various quality control tests like Hardness (4.4±0.279 to 4.8±0.137 Kg/cm^2), Friability (0.323±0.07 to 0.459±0.12) and percentage drug release after 24 h (92±0.17 to 93.75±0.21). All the tablets complied with the pharmacopoeial standards.

Fig. 5. The in vitro drug release profile of nicorandil from M1-M5 formulations.
Fig. 6. The in vitro drug release profile of nicorandil from M6 - M9 formulations.

4. Conclusion

The study conclusively demonstrated that nicorandil can successfully encapsulated into microsponge by Quasi-emulsion solvent diffusion technique using Eudragit and HPMC as polymer for controlling the release rate upto 24 h. The satisfactory compressibility of microsponges offers an alternative way for producing mechanically strong tablets. The production of novel once daily tablets of nicorandil microsponges with controlled release characteristics.

References