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**Research Article**

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**FORMULATION AND IN-VITRO EVALUATION OF SUSTAINED RELEASE  
TABLET OF ISOSORBIDE -5- MONONITRATE BY  
POROUS OSMOTIC TECHNOLOGY**

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**Abstract**

The objective of the present study was to develop sustained release tablet of Isosorbide Mononitrate by porous membrane osmotic technology. The drug is mainly indicated for the treatment of Stable and unstable angina pectoris, acute myocardial infarction and heart failure. The tablets were prepared by wet granulation method. The granules were evaluated for angle of repose, bulk density, tapped density, compressibility index and Hausner ratio. The tablets were subjected to thickness, hardness, friability, weight variations, and drug content by assay and *in vitro* dissolution studies. The drug release from Isosorbide Mononitrate sustained release was carried out in 1.2 N HCl, 4.5 pH acetate buffer and 6.8 pH phosphate buffer for 24hrs. The granules showed satisfactory flow properties, compressibility index and drug content. All the tablet formulations showed acceptable pharmaceutical properties. Formulation variables like type (PVP, PEG 4000 and HPMC) and level of pore former (0-55%, w/w of polymer), percent weight gain were found to affect the drug release from the developed formulations. The optimized formulation showed the highest  $f_2$  ( $f_2 = 76.4$ ) value. The drug release from the developed formulation was independent of pH and agitational intensity. The similarity factor  $F_2$  was applied between the optimized formulation and the theoretical dissolution profile. The drug release data were plotted using various kinetic equations (Zero order, first order, Higuchi's kinetics, Korsmeyer and Peppas kinetics and Hixson and Crowell kinetics) to evaluate the drug release mechanism and kinetics. The formulations were found to be stable for after 2 months of accelerated stability studies.

**Keywords:** Coating; extended release; Isosorbide mononitrate; Osmotic pressure; Osmotic pump; Stability.

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**Introduction**

Conventional drug delivery systems have little control over their drug release and almost no control over the effective concentration at the target site. This kind of dosing pattern may result in constantly changing, unpredictable plasma concentrations.

Drugs can be delivered in a controlled pattern over a long period of time by the process of osmosis. Osmotic devices are the most promising strategy based systems for controlled drug delivery. They are the most reliable controlled drug delivery systems and could be employed as oral drug delivery systems.

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The present review is concerned with the study of drug release systems which are tablets coated with walls of controlled porosity. When these systems are exposed to water, low levels of water soluble additive is leached from polymeric material i.e. semi permeable membrane and drug releases in a controlled manner over an extended period of time. Drug delivery from this system is not influenced by the different physiological factors within the gut lumen and the release characteristics can be predicted easily from the known properties of the drug and the dosage form.

The various types of osmotically controlled drug delivery systems and the basic components of controlled porosity osmotic pump tablets have been discussed briefly. A controlled-porosity osmotic wall can be described as having a sponge like appearance. The pores can be continuous that have micro porous lamina, interconnected through tortuous paths of regular and irregular shapes. Generally, materials (in a concentration range of 5% to 95%) producing pores with a pore size from 10 Å -100 m can be used. This system is generally applicable for only water-soluble drugs. as poorly water soluble drugs cannot dissolve adequately in the volume of water drawn into the Osmotic Pump Tablet(OPT). Recently this problem can be overcome by adding agents like sulfobutyl ether--cyclodextrin (SBE)7m--CD or hydroxypropyl--cyclodextrin (HP--CD) as solubilizing and osmotic agents. Several approaches have been developed to prepare the porous membrane by spray coating using polymer solutions containing dissolved or suspended water-soluble materials. To carry out drug-excipients compatibility studies with excipients expected to be a part of final formulation. To develop and optimize proto type formulation for 20 mg dose. The aim of the work is to investigate the possibility of obtaining a prolonged, relatively constant level of isosorbide-5-mononitrate. Isosorbide -5-Mononitrate has long

elimination half life of 4-5 hours in comparison of isosorbide Di-nitrate. Despite of this long elimination half life, Isosorbide Mononitrate is prescribed 2-3 times/day for prophylactic treatment of angina leads to poor patient complaints and development of tolerance. Present studies investigate the possibility for the development of sustained release tablet of ISMN, to reduce the side effect, dosing frequency and improve patient compliance. Keeping these factors in view it is aim to formulate and evaluate SR tablet of 20 mg, to provide a controlled and predictable release of isosorbide-5-mononitrate, which is an organic nitrate used as anti-anginal drug for the treatment of stable and unstable angina pectoris, acute myocardial infarction for once daily administration.

The present study, aim towards the development of sustained release of drug from the tablet by using osmotic technology. Theoretically design zero – order delivery pattern for the release the drug from the formulation. Considering different formulation variables and the selection of the optimized formulation from the drug release profile, considering the cost of drug by reducing the drug dose and increasing its effectiveness and deliver drug at near constant rate. Evaluation for the stability of the formulation for 2 month

### Methods and materials

Isosorbide Mononitrate was procured by Sangrose Lab.PVT.LTD (Kerala., India), Lactose, Sodium Chloride and PVP was gifted by FMC Biopolymer (India), Colloidal Silicon Dioxide, Magnesium Stearate and Eudragit was gifted by HMS (India), HPMC, PEG 4000, Ethyl Cellulose and Propylene Glycol was gifted by Nice Chemicals (India) and other chemicals all gifted by Merck Limited, India.

**Table no: 1 Formulations of Core Tablets:**

| Serial No: | Ingredients            | Quantity for 1 tablet (150 mg) |
|------------|------------------------|--------------------------------|
| 1          | Isosorbide Mononitrate | 20.00                          |
| 2          | Lactose                | 65.00                          |
| 3          | Sodium Chloride        | 35.00                          |
| 4          | PVP                    | 10.00                          |
| 5          | Magnesium Stearate     | 2.00                           |
| 6          | Silicon dioxide        | 0.50                           |
| 7          | Eudragit               | 5.00                           |
| 8          | Isopropyl Alcohol      | q.s                            |

**Table no: 2 Development of various Tablet Formulations:**

| Ingredients      | F1    | F2    | F3    | F4    | F5    | F6    | F7    |
|------------------|-------|-------|-------|-------|-------|-------|-------|
| Ethyl Cellulose  | 3.95  | 3.66  | 3.30  | 3.00  | 2.74  | 2.74  | 2.74  |
| HPMC             | -     | -     | -     | -     | -     | 1.52  | -     |
| PEG 4000         | -     | -     | -     | -     | -     | -     | 1.52  |
| PVP              | -     | 0.37  | 0.82  | 1.20  | 1.52  | -     | -     |
| Propylene Glycol | 1.05  | 0.98  | 0.88  | 0.80  | 0.73  | 0.73  | 0.73  |
| Ethanol          | 38.00 | 38.00 | 38.00 | 38.00 | 38.00 | 38.00 | 38.00 |
| Dichloro methane | 57.00 | 57.00 | 57.00 | 57.00 | 57.00 | 57.00 | 57.00 |

### Evaluation of the sustained release developed formulations:

#### Weight Variation Test:

Twenty tablets were randomly selected and weighed to determine the average weight and were compared with the individual tablet weight. The percentage weight variation was calculated. As per Indian Pharmacopoeia Specification, the tablet with an average weight less than 80 mg, the percentage deviation should not be more than  $\pm 10\%$ , tablet with an average weight between 80- 250 mg, the percentage deviation should not be more than  $\pm 7.5\%$  and tablet with an average weight more than 250mg should not be more than  $\pm 5\%$ .

The results are given in Table no: 4

The thickness and diameter was calculated using the formula:

#### Hardness Test:

The hardness of tablet was carried out by using Monsanto type hardness tester. The hardness of the tablet in  $\text{kg}/\text{cm}^2$  was measured. The results are given in the Table no:17

#### Thickness and Diameter:

Control of physical dimensions of the tablets such as thickness and diameter are essential for consumer's acceptance and to maintain tablet to tablet uniformity. The dimensional specifications were measured using screw gauge. The thicknesses of the tablets are mostly related to the tablet hardness, can be used as an initial control parameter. The zero of the screw gauge was noted. Placed the tablet in gap and noted the reading on the main scale.

Reading = PSR + (Corrected HSR + Least count)

Where,

PSR = Pitch Scale Reading

HSR = Head Scale Reading.

#### Friability Test:

Weighed a sample of 20 tablets and placed it in the Roche Friabilator. Rotated the equipment for 100 revolutions at 25 rpm for 4 minutes. The tablets were dedusted and reweighed. The loss of weight was calculated from which the friability was obtained.

The friability was calculated from the following formula:

$$\% \text{ Friability} = \frac{\text{Loss in Weight}}{\text{Initial Weight}} \times 100$$

The results were given in the Table no: 4

#### Optimized Formulation:

The optimized formulation was selected by comparing the % drug release obtained by dissolution profile of all the formulation with the marketed formulation. The release profile from this formulation is shown in Figure 2. The formulation with maximum comparable %drug release from the developed formulation to the marketed formulation was considered as the optimizes formulation. Above all the formulation F5 shows maximum and comparable % drug release after 24hrs of dissolution studies. Therefore, F5 is taken as the optimized formulation.

#### In vitro drug release kinetics:

In vitro dissolution studies were carried out at  $37 \pm 5^\circ\text{C}$  in 900ml of 1.2 N HCl/4.5  $\text{P}^{\text{H}}$  acetate buffer/ 6.8  $\text{P}^{\text{H}}$  phosphate buffer in USP- 1 (Basket type apparatus). The rotation speed was kept at 100rpm.

The kinetic release mechanism was analyzed according to the following equation.

### Curve fitting Analysis:

For the determination of the drug release kinetics from the porous osmotic pump tablet, the *in vitro* release data were analyzed by zero order, first order, Higuchi and Korsmeyer and Peppas equations.

- Zero order release kinetic
- First order release kinetics
- Higuchi release model
- Korsmeyer and Peppas kinetics

### Stability protocol:

Accelerated stability studies have been carried out on optimized formulation batch of the product in ICH certified stability chamber maintained at  $25^{\circ}\text{C} \pm 2^{\circ}\text{C} / 75\% \pm 5\%\text{RH}$  and room temperature for 2 month. The tablets were drawn periodically and evaluated for drug release studies, hardness drug contents.

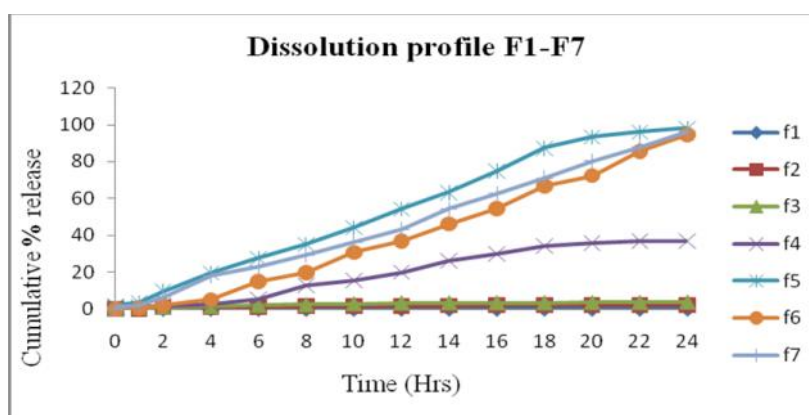
### Tablet storage condition and sampling plan for stability studies:

Accelerated Stability –  $40^{\circ}/75\text{RH}$   
 Room Temperature –  $25^{\circ}/70\text{RH}$   
 Stages – 30 Days, 60 Days

**Table no. 03: Cumulative %Drug Release profile of all tablets formulations:**

| Time(Hrs) | F1    | F2     | F3    | F4     | F5     | F6     | F7     |
|-----------|-------|--------|-------|--------|--------|--------|--------|
| 0         | 0     | 0      | 0     | 0      | 0      | 0      | 0      |
| 0.5       | 0     | 0      | 0.789 | 1.053  | 1.900  | 0.066  | 1.053  |
| 1         | 0     | 0.0657 | 0.987 | 1.514  | 3.600  | 0.789  | 2.303  |
| 2         | 0     | 0.921  | 1.25  | 1.842  | 9.804  | 2.237  | 6.580  |
| 4         | 0     | 1.054  | 1.580 | 2.566  | 19.708 | 5.198  | 17.964 |
| 6         | 0     | 1.25   | 2.039 | 5.462  | 27.612 | 15.003 | 23.189 |
| 8         | 0     | 1.383  | 2.500 | 13.029 | 35.214 | 19.872 | 29.283 |
| 10        | 0     | 1.58   | 2.961 | 15.595 | 44.318 | 30.796 | 36.389 |
| 12        | 0.061 | 1.8004 | 3.422 | 20.004 | 54.422 | 37.048 | 43.365 |
| 16        | 0.064 | 1.908  | 3.553 | 30.007 | 74.915 | 54.420 | 62.842 |
| 20        | 0.066 | 2.039  | 3.619 | 35.797 | 93.519 | 72.318 | 80.367 |
| 24        | 0.066 | 2.106  | 3.685 | 36.916 | 98.122 | 94.684 | 96.455 |

**Fig. 01: Cumulative % drug release of all formulations:**

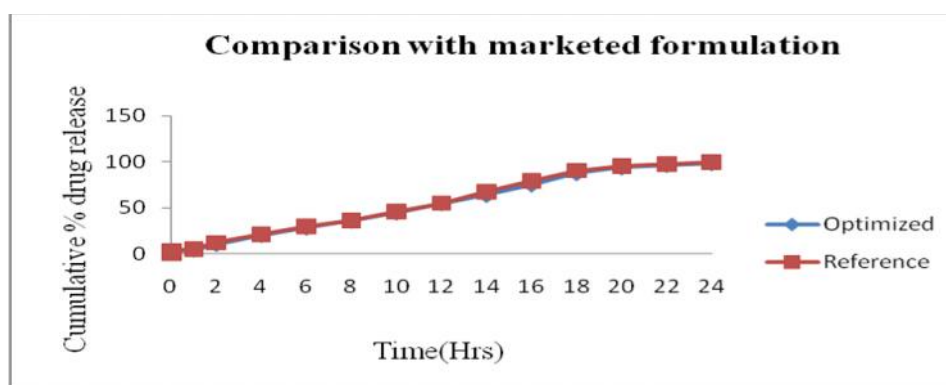


**Table no. 04: Evaluation of tablet formulations**

| Parameter                      | F1     | F2    | F3     | F4     | F5     | F6     | F7     |
|--------------------------------|--------|-------|--------|--------|--------|--------|--------|
| Uniformity of weight           | Pass   | Pass  | Pass   | Pass   | Pass   | Pass   | Pass   |
| Hardness (Kg/cm <sup>2</sup> ) | 6.82   | 7.24  | 7.63   | 7.31   | 7.35   | 7.39   | 6.87   |
| Thickness (mm)                 | 3.52   | 3.53  | 3.56   | 3.62   | 3.58   | 3.52   | 3.66   |
| Diameter (mm)                  | 6.51   | 6.50  | 6.52   | 6.51   | 6.50   | 6.49   | 6.50   |
| Friability (%)                 | 0.01   | 0.01  | 0.01   | 0.01   | 0.01   | 0.01   | 0.01   |
| Drug Content (%)               | 96.203 | 94.45 | 95.542 | 93.454 | 98.403 | 97.087 | 96.976 |

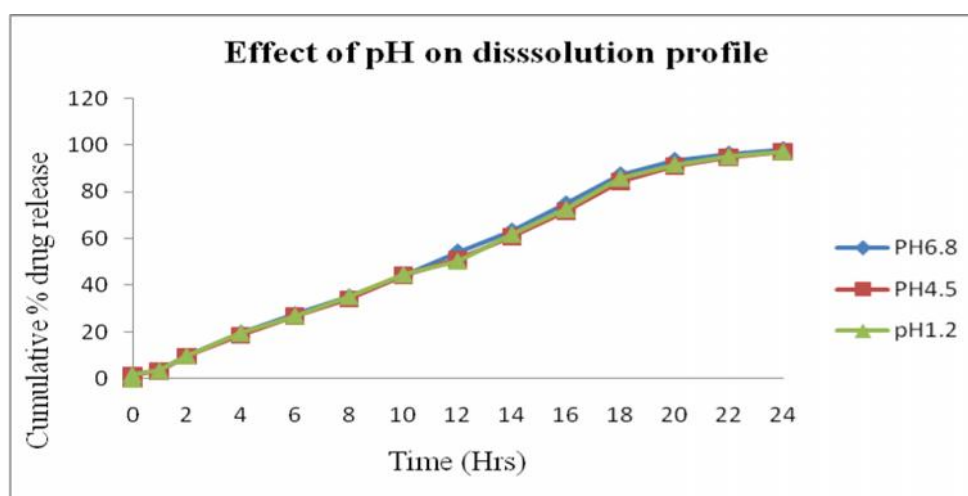
**Table no. 05: Comparison of Cumulative % Drug release of optimized formulation with marketed SR tablet (Monit SR)**

| Time(Hrs) | Marketed SR tablet (Monit SR) | Optimized formulation (F5) |
|-----------|-------------------------------|----------------------------|
| 0         | 0                             | 0                          |
| 0.5       | 2.8                           | 1.900                      |
| 1         | 4.7                           | 3.600                      |
| 2         | 11.5                          | 9.804                      |
| 4         | 20.9                          | 19.708                     |
| 6         | 29.3                          | 27.612                     |
| 8         | 36.1                          | 35.214                     |
| 10        | 45.9                          | 44.318                     |
| 12        | 52.9                          | 54.422                     |
| 16        | 72.45                         | 74.915                     |
| 20        | 88.26                         | 93.519                     |
| 24        | 100.03                        | 98.122                     |

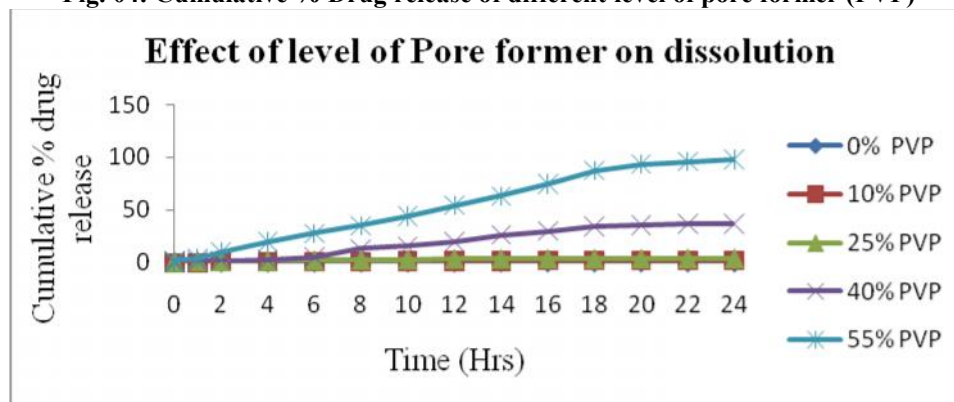
**Fig. 02: Cumulative % drug release of optimized formulation and marketed product:**

**Table no. 06: Cumulative % Drug release in different dissolution medium (F5):**

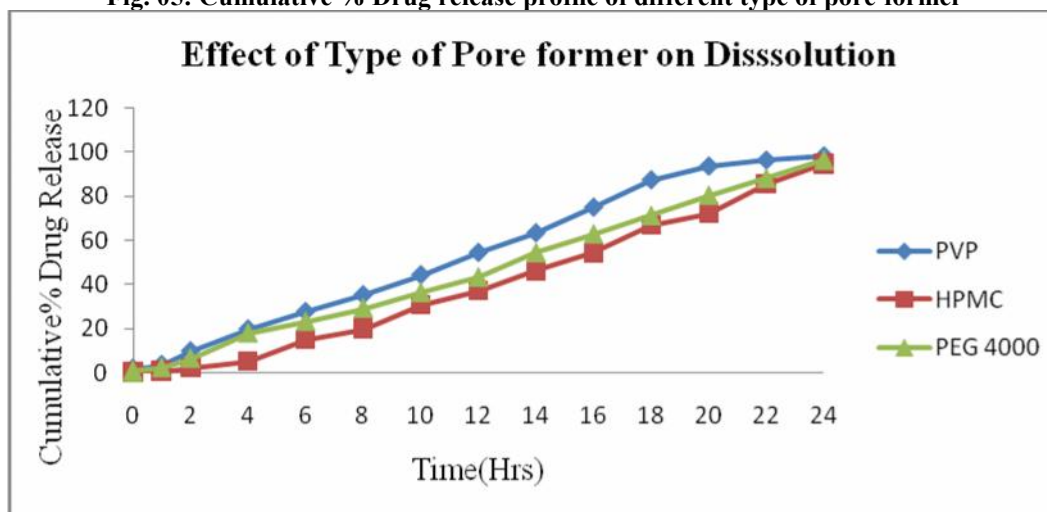
| Time(Hrs) | 1.2N HCl | 4.5 pH Acetate Buffer | 6.8 pH Phosphate Buffer |
|-----------|----------|-----------------------|-------------------------|
| 0         | 0        | 0                     | 0                       |
| 0.5       | 1.67     | 1.91                  | 1.900                   |
| 1         | 3.45     | 3.58                  | 3.600                   |
| 2         | 9.8014   | 9.976                 | 9.804                   |
| 4         | 18.613   | 19.645                | 19.708                  |
| 6         | 26.787   | 27.108                | 27.612                  |
| 8         | 34.187   | 35.256                | 35.214                  |
| 10        | 44.219   | 44.765                | 44.318                  |
| 12        | 50.156   | 50.387                | 54.422                  |
| 16        | 69.432   | 69.543                | 74.915                  |
| 20        | 84.889   | 86.698                | 93.519                  |
| 24        | 96.984   | 97.146                | 98.122                  |

**Fig. 03: Cumulative % drug release in different dissolution media****Table no. 07: Effect of level of pore former (PVP) on cumulative % drug release**

| Time(Hrs) | 0% PVP | 10% PVP | 25% PVP | 40% PVP | 55% PVP |
|-----------|--------|---------|---------|---------|---------|
| 0         | 0      | 0       | 0       | 0       | 0       |
| 0.5       | 0      | 0       | 0.789   | 1.053   | 1.900   |
| 1         | 0      | 0.0657  | 0.987   | 1.514   | 3.600   |
| 2         | 0      | 0.921   | 1.25    | 1.842   | 9.804   |
| 4         | 0      | 1.054   | 1.580   | 2.566   | 19.708  |
| 6         | 0      | 1.25    | 2.039   | 5.462   | 27.612  |
| 8         | 0      | 1.383   | 2.500   | 13.029  | 35.214  |
| 10        | 0      | 1.58    | 2.961   | 15.595  | 44.318  |
| 12        | 0.061  | 1.8004  | 3.422   | 20.004  | 54.422  |
| 16        | 0.064  | 1.908   | 3.553   | 30.007  | 74.915  |
| 20        | 0.066  | 2.039   | 3.619   | 35.797  | 93.519  |
| 24        | 0.066  | 2.106   | 3.685   | 36.916  | 98.122  |

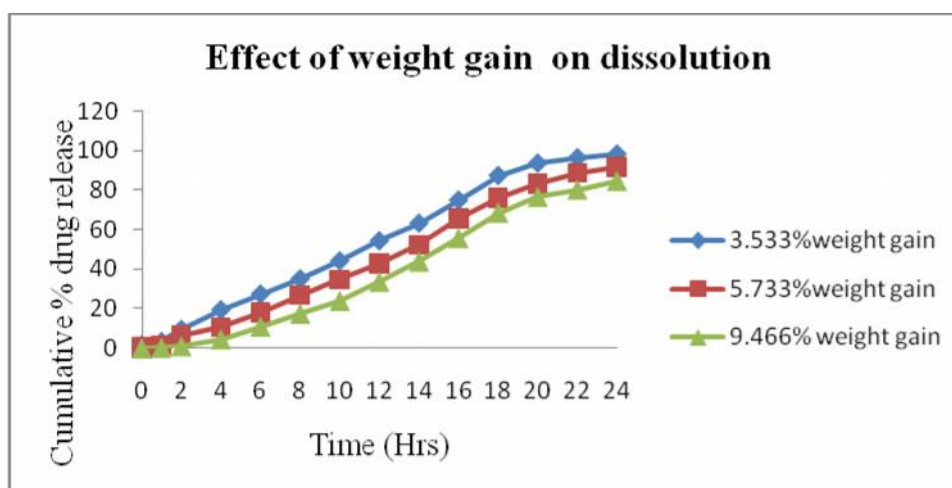
**Fig. 04: Cumulative % Drug release of different level of pore former (PVP)****Table no 08: Cumulative % Drug release profile of different type of pore former:**

| Time(Hrs) | PVP(F5) | HPMC(F6) | PEG4000(F7) |
|-----------|---------|----------|-------------|
| 0         | 0       | 0        | 0           |
| 0.5       | 1.900   | 0.066    | 1.053       |
| 1         | 3.600   | 0.789    | 2.303       |
| 2         | 9.804   | 2.237    | 6.580       |
| 4         | 19.708  | 5.198    | 17.964      |
| 6         | 27.612  | 15.003   | 23.189      |
| 8         | 35.214  | 19.872   | 29.283      |
| 10        | 44.318  | 30.796   | 36.389      |
| 12        | 54.422  | 37.048   | 43.365      |
| 16        | 74.915  | 54.420   | 62.842      |
| 20        | 93.519  | 72.318   | 80.367      |
| 24        | 98.122  | 94.684   | 96.455      |

**Fig. 05: Cumulative % Drug release profile of different type of pore former**

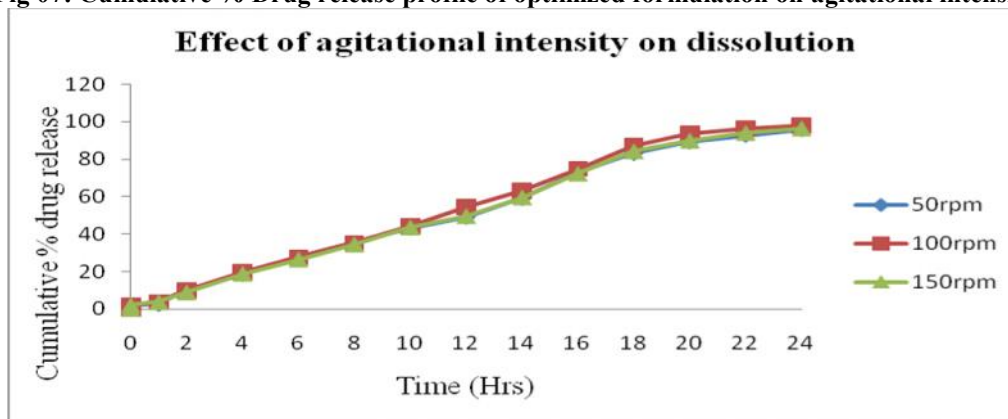
**Table no. 09: Cumulative % Drug release profile of weight gain on optimized Formulation:**

| Time(hrs) | 3.533% Weight gain | 5.733% Weight gain | 9.466% Weight gain |
|-----------|--------------------|--------------------|--------------------|
| 0         | 0                  | 0                  | 0                  |
| 0.5       | 1.900              | 0.945              | 0.066              |
| 1         | 3.600              | 1.78               | 0.466              |
| 2         | 9.804              | 6.456              | 1.194              |
| 4         | 19.708             | 10.795             | 4.743              |
| 6         | 27.612             | 18.413             | 11.105             |
| 8         | 35.214             | 26.962             | 17.643             |
| 10        | 44.318             | 34.845             | 24.143             |
| 12        | 54.422             | 42.832             | 33.745             |
| 16        | 74.915             | 63.642             | 51.695             |
| 20        | 93.519             | 79.304             | 70.543             |
| 24        | 98.122             | 91.783             | 84.651             |

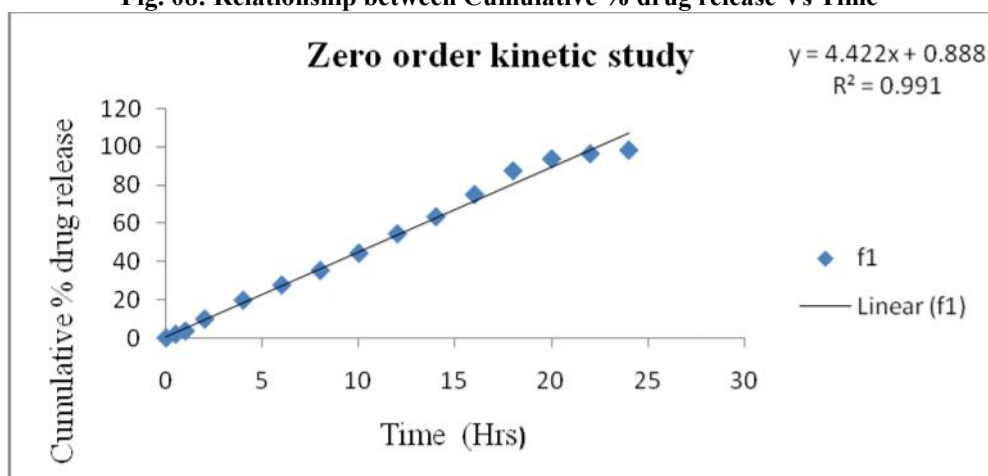
**Fig. 06: Cumulative % Drug release profile of weight gain on optimized Formulation****Table no. 10: Cumulative % Drug release profile of optimized formulation on agitational intensity**

| Time(Hrs) | 50 rpm  | 100 rpm | 150 rpm |
|-----------|---------|---------|---------|
| 0         | 0       | 0       | 0       |
| 0.5       | 1.87    | 1.900   | 1.92    |
| 1         | 2.58    | 3.600   | 3.65    |
| 2         | 9.79    | 9.804   | 8.8114  |
| 4         | 18.6988 | 19.708  | 18.7143 |
| 6         | 27.604  | 27.612  | 26.343  |
| 8         | 35.208  | 35.214  | 34.367  |
| 10        | 43.311  | 44.318  | 43.456  |
| 12        | 49.145  | 54.422  | 49.543  |
| 16        | 69.86   | 74.915  | 68.004  |
| 20        | 84.456  | 93.519  | 84.689  |
| 24        | 96.045  | 98.122  | 96.174  |



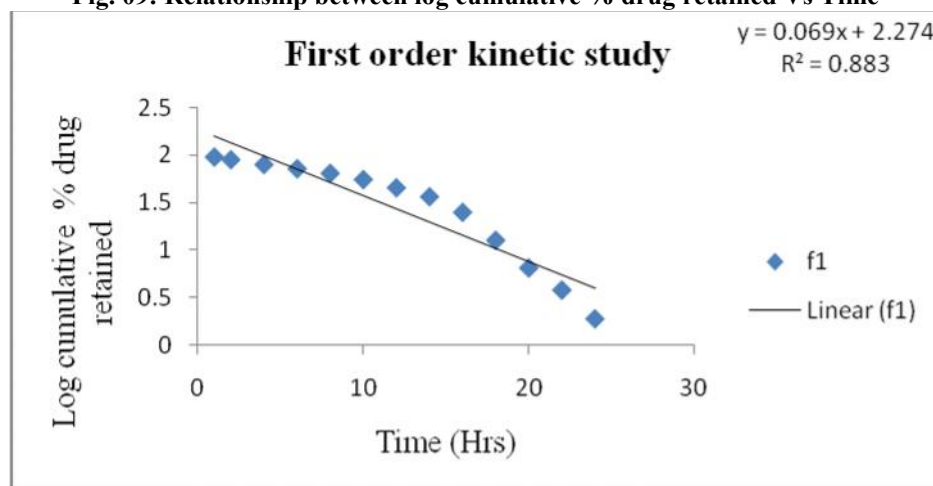
**Fig 07: Cumulative % Drug release profile of optimized formulation on agitational intensity****Kinetics of drug release****Label claim: 20 mg (F5 Formulation):****Zero Order kinetics (Cumulative % drug release Vs Time)****Table no. 11: Zero Order kinetics**

| S. No | Time(Hrs) | Cumulative %drug release |
|-------|-----------|--------------------------|
| 1     | 1         | 3.600                    |
| 2     | 2         | 9.804                    |
| 3     | 4         | 19.708                   |
| 4     | 6         | 27.612                   |
| 5     | 8         | 35.214                   |
| 6     | 10        | 44.318                   |
| 7     | 12        | 54.422                   |
| 8     | 16        | 74.915                   |
| 9     | 20        | 93.519                   |
| 10    | 24        | 98.122                   |

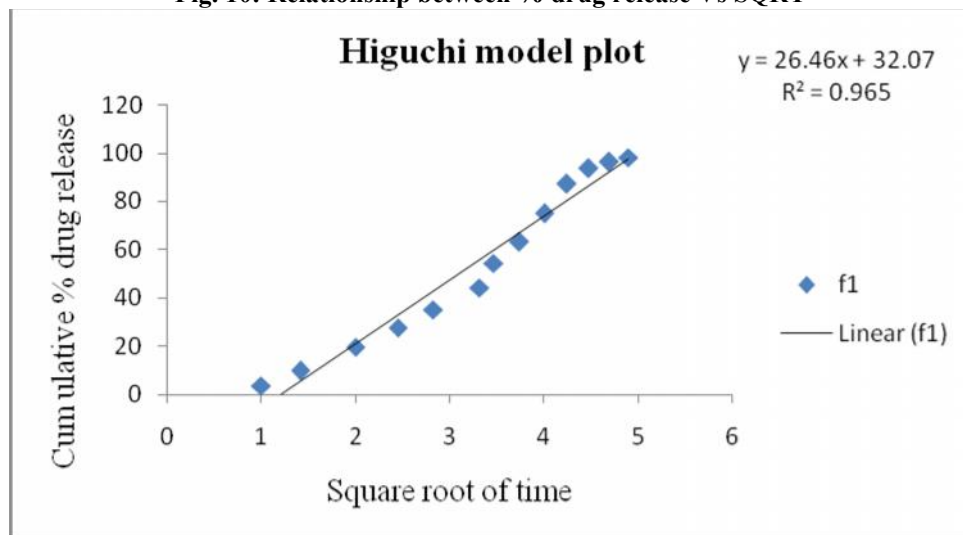
**Fig. 08: Relationship between Cumulative % drug release Vs Time**

**First Order Kinetics (Log Cumulative % drug remaining Vs Time****Table no. 12: First Order Kinetics**

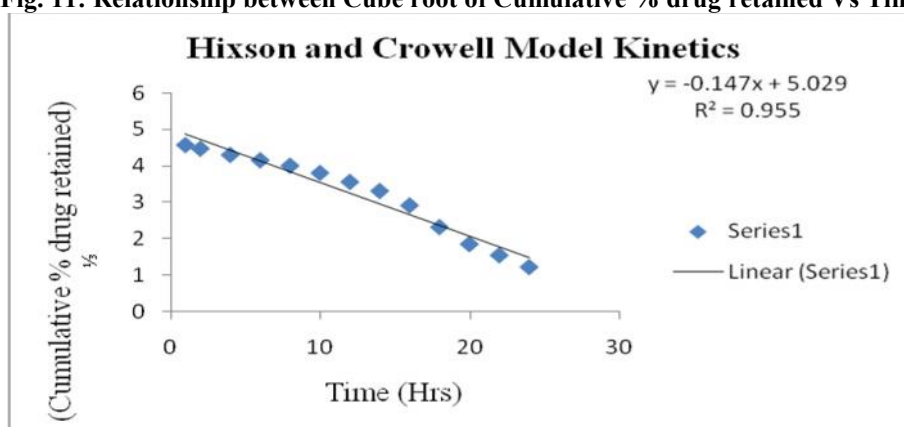
| S. No: | Time(Hrs) | Cumulative% Drug Release | Cumulative % Drug retained | Log Cumulative % Drug retained |
|--------|-----------|--------------------------|----------------------------|--------------------------------|
| 1      | 1         | 3.600                    | 96.4                       | 1.984                          |
| 2      | 2         | 9.804                    | 90.198                     | 1.955                          |
| 3      | 4         | 19.708                   | 80.296                     | 1.9046                         |
| 4      | 6         | 27.612                   | 72.394                     | 1.859                          |
| 5      | 8         | 35.214                   | 64.793                     | 1.8115                         |
| 6      | 10        | 44.318                   | 55.691                     | 1.7457                         |
| 7      | 12        | 54.422                   | 49.589                     | 1.6953                         |
| 8      | 16        | 74.915                   | 30.085                     | 1.47835                        |
| 9      | 20        | 93.519                   | 14.481                     | 1.160799                       |
| 10     | 24        | 98.122                   | 1.878                      | 0.27369                        |

**Fig. 09: Relationship between log cumulative % drug retained Vs Time****Higuchi Model (Cumulative % Drug release Vs SQRT)****Table no. 13: Higuchi Model Kinetics**

| S.No: | Time(Hrs) | SQRT   | Cumulative % Drug release |
|-------|-----------|--------|---------------------------|
| 1     | 1         | 1      | 3.600                     |
| 2     | 2         | 1.4142 | 9.804                     |
| 3     | 4         | 2      | 19.708                    |
| 4     | 6         | 2.449  | 27.612                    |
| 5     | 8         | 2.828  | 35.214                    |
| 6     | 10        | 3.162  | 44.318                    |
| 7     | 12        | 3.464  | 54.422                    |
| 8     | 16        | 4      | 74.915                    |
| 9     | 20        | 4.472  | 93.519                    |
| 10    | 24        | 4.898  | 98.122                    |

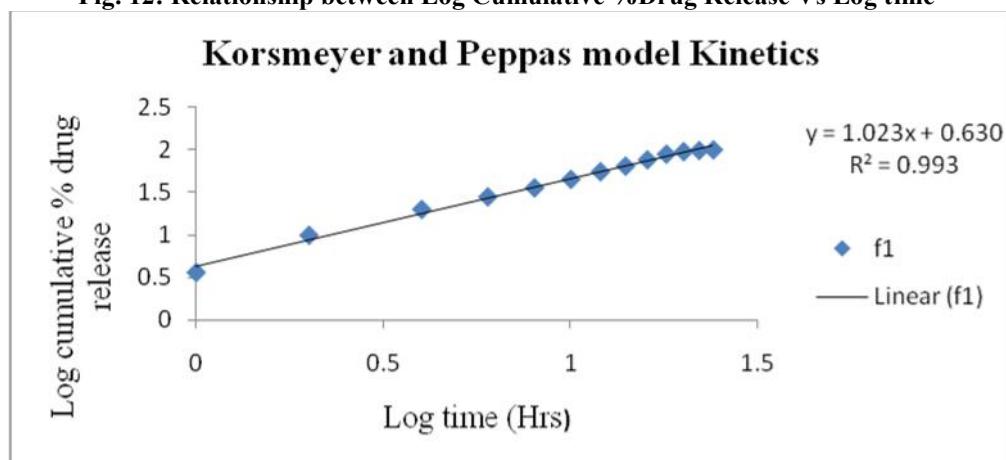
**Fig. 10: Relationship between % drug release Vs SQRT****Hixson and Crowell Model Kinetics:****Table no. 14: Hixson and Crowell Model Kinetics**

| S.No. | Time(hrs) | Cumulative % drug release | Cumulative% drug remaining | Cube root |
|-------|-----------|---------------------------|----------------------------|-----------|
| 1     | 1         | 3.600                     | 96.4                       | 4.585     |
| 2     | 2         | 9.804                     | 90.198                     | 4.4846    |
| 3     | 4         | 19.708                    | 80.296                     | 4.3141    |
| 4     | 6         | 27.612                    | 72.394                     | 4.167     |
| 5     | 8         | 35.214                    | 64.793                     | 4.0164    |
| 6     | 10        | 44.318                    | 55.691                     | 3.8188    |
| 7     | 12        | 54.422                    | 49.589                     | 3.5723    |
| 8     | 16        | 74.915                    | 30.085                     | 2.9273    |
| 9     | 20        | 93.519                    | 14.481                     | 1.8644    |
| 10    | 24        | 98.122                    | 1.878                      | 1.2337    |

**Fig. 11: Relationship between Cube root of Cumulative % drug retained Vs Time**

**Korsmeyer and Peppas Model Kinetics****Table no. 15: Korsmeyer and Peppas Model Kinetics**

| S.No. | Time(Hrs) | Log Time | Cumulative % Drug release | Log Cumulative % Drug release |
|-------|-----------|----------|---------------------------|-------------------------------|
| 1     | 1         | 0        | 3.600                     | 0.5563                        |
| 2     | 2         | 0.3010   | 9.804                     | 0.9913                        |
| 3     | 4         | 0.6020   | 19.708                    | 1.2945                        |
| 4     | 6         | 0.778    | 27.612                    | 1.4410                        |
| 5     | 8         | 0.9030   | 35.214                    | 1.5466                        |
| 6     | 10        | 1        | 44.318                    | 1.6464                        |
| 7     | 12        | 1.079    | 54.422                    | 1.7356                        |
| 8     | 16        | 1.2041   | 74.915                    | 1.8745                        |
| 9     | 20        | 1.3010   | 93.519                    | 1.9708                        |
| 10    | 24        | 1.3802   | 98.122                    | 1.9917                        |

**Fig. 12: Relationship between Log Cumulative %Drug Release Vs Log time****Linearity of Kinetics Models****Table no. 16: Linearity of Kinetics Models**

| S.No. | Kinetics Models          | R <sup>2</sup> |
|-------|--------------------------|----------------|
| 1     | Zero Order Kinetics      | 0.991          |
| 2     | First Order Kinetics     | 0.883          |
| 3     | Higuchi Model            | 0.965          |
| 4     | Hixson and Crowell Model | 0.955          |
| 5     | Korseny and Peppas Model | 0.993          |

**Stability studies**

The fabricated sustained release optimized formulation (F5) was subjected to stability studies at

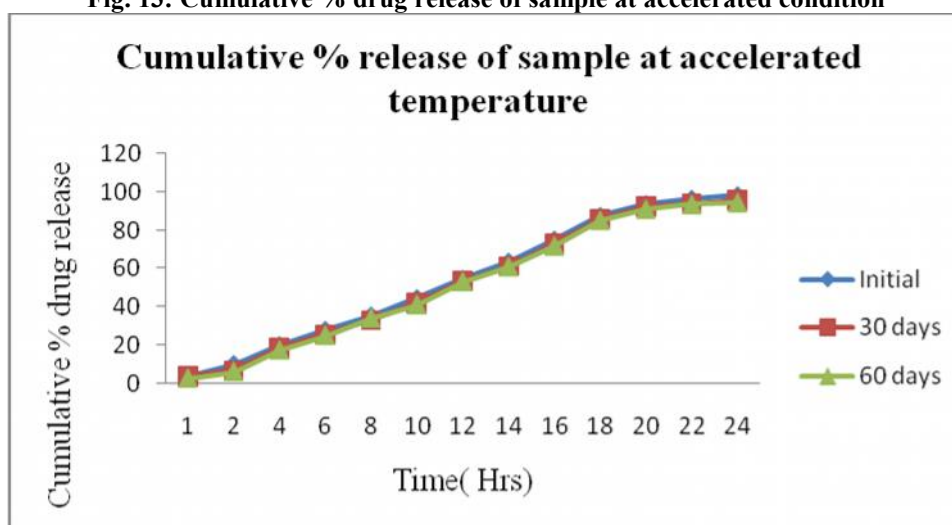
25°/60% RH and 40°/27% RH for 30 days. The product was evaluated for drug compatibility, drug content and drug release. The results were given in table no: 31, 33 and 34

**Storage Condition at 40°C ± 2°C/ 75% RH ± 5%:****a) Description:****Table no. 17: Description of drug**

| Test                       | Observation      | Inference                             |
|----------------------------|------------------|---------------------------------------|
| Description(Colour change) | No colour change | Complies with the stability condition |

**b) Dissolution data:****Table no. 18: Cumulative % drug release of stability samples stored at accelerated condition:**

| Time(Hrs) | Initial (0 days) | 30 days | 60 days |
|-----------|------------------|---------|---------|
| 1         | 3.600            | 3.66    | 2.599   |
| 2         | 9.804            | 6.76    | 6.068   |
| 4         | 19.708           | 18.702  | 17.287  |
| 6         | 27.612           | 25.599  | 25.087  |
| 8         | 35.214           | 33.184  | 34.086  |
| 10        | 44.318           | 42.264  | 41.169  |
| 12        | 54.422           | 53.414  | 53.285  |
| 16        | 74.915           | 72.908  | 71.869  |
| 20        | 93.519           | 92.458  | 91.175  |
| 24        | 98.122           | 96.098  | 96.99   |

**Fig. 13: Cumulative % drug release of sample at accelerated condition****Room Temperature (25°C ± 2°C/60% RH ± 5%)****a) Description****Table no. 19: Description of drug**

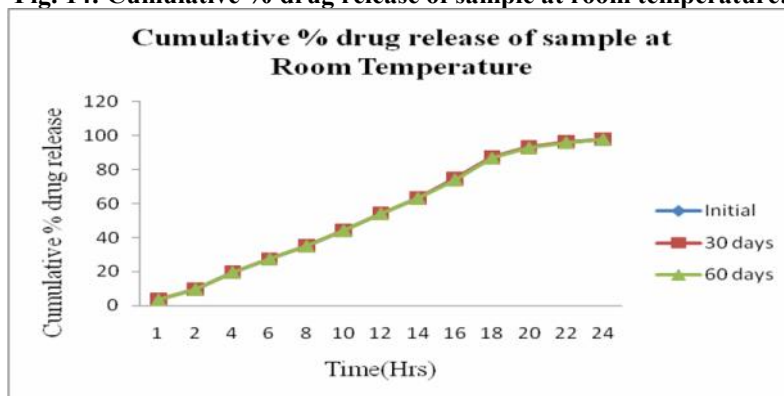
| Test                        | Observation      | Inference                             |
|-----------------------------|------------------|---------------------------------------|
| Description (Colour change) | No colour change | Complies with the stability condition |

## b) Dissolution data:

Table no. 20: Cumulative % drug release of stability of samples stored at room temperature

| Time(Hrs) | Initial<br>(0 days) | 30 days | 60 days |
|-----------|---------------------|---------|---------|
| 1         | 3.600               | 3.64    | 3.554   |
| 2         | 9.804               | 9.812   | 9.668   |
| 4         | 19.708              | 19.706  | 19.678  |
| 6         | 27.612              | 27.609  | 27.487  |
| 8         | 35.214              | 35.221  | 35.195  |
| 10        | 44.318              | 44.326  | 44.207  |
| 12        | 54.422              | 54.206  | 54.167  |
| 16        | 74.915              | 74.918  | 73.995  |
| 20        | 93.519              | 93.499  | 92.784  |
| 24        | 98.122              | 98.007  | 97.873  |

Fig. 14: Cumulative % drug release of sample at room temperature:

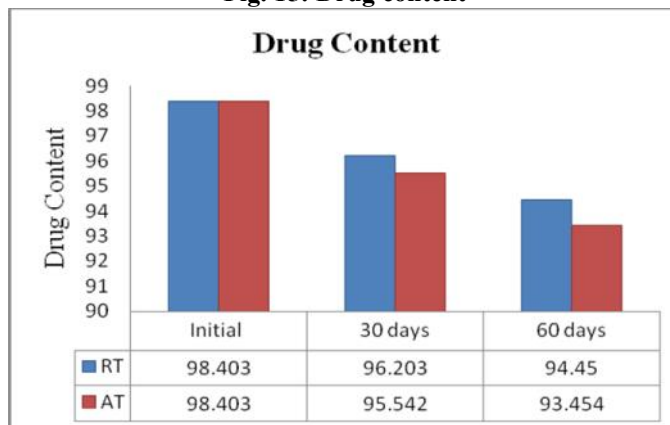


## Drug Content:

Table No. 21: Drug Content

| Room Temperature |         |        | Accelerated Temperature |         |         |
|------------------|---------|--------|-------------------------|---------|---------|
| Initial          | 30 Days | 60days | Initial                 | 30 Days | 60 Days |
| 98.403           | 96.203  | 94.450 | 98.403                  | 95.542  | 93.454  |

Fig. 15: Drug content



## Summary and conclusion

The present work have been made to formulate sustained release tablet of Isosorbide -5-Mononitrate based on porous membrane osmotic technology by using Sodium chloride as osmogen and different formulation variables. Isosorbide Mononitrate which is preferably used as anti anginal drug for the treatment of stable and unstable angina pectoris , acute myocardial infarction and heart failure. In the present study, an attempt was made to formulate 20mg sustained release tablet which can provide effective drug release for 24hrs. Sustained release tablets of Isosorbide Mononitrate were prepared by wet granulation technique. *In vitro* studies showed formulation F5 was well suited to be sustained release formulation. The coating solutions were prepared by using various polymers and pore formers, meets all the ideal characteristics to formulate in the form of sustained release drug delivery system. Under pre formulation study, the organoleptic properties were complied with the BP specification. Physical properties such as bulk density and tapped density were more in case of granules ready for compression than that of Isosorbide-5 Mononitrate raw powder. The compatibility evaluation was performed by FT-IR spectroscopy analysis. The study implies that the drug and polymers were compatible with each other. There were no interactions found between the drug and the polymers. F5 formulation was optimized as it complied with all the pharmacopoeial specifications. The physical parameters like thickness, diameter, hardness, friability, weight variations were carried out. The assay was carried out for optimized formulation and the result was found to be 98.403%. The drug release from the developed formulations was independent of pH and agitational intensity of the release media. It was found that the drug release increases with increasing the level of pore former (PVP), the membrane became more porous after coming in contact with the aqueous environment. The drug release was found to decrease with the increase in the weight gain of the membrane. The drug release was found to be more with PVP than with HPMC, Ethyl Cellulose and PEG4000. The similarity factor  $f_2$  was applied between the dissolution profile of optimized batch and the theoretical dissolution profile, which also indicate a decent similarity between both dissolution profiles. Stability studies were carried out by keeping the Sustained release tablets at room temperature ( $25^\circ\text{C} \pm 2^\circ\text{C}/ 60\% \pm 5\% \text{RH}$ ) and at accelerated temperature ( $40^\circ\text{C} \pm 2^\circ\text{C}/ 75\% \pm 5\% \text{RH}$ ) in stability chamber for 60 days. The result of stability studies conducted on F5 revealed no change in physical appearance, drug content and *in vitro* dissolution profile, hence F5 formulation was found to be stable at tested

temperature. Finally the drug release from the selected formulation (F5) fitted well in the Zero order kinetics. From the results obtained, it can be concluded that formulation F5 has achieved the objectives of sustained drug release, patient convenience and cost effectiveness as a single daily dose of the drug. It could be concluded that sustained release tablet may be formulated by employing osmotic technology.

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