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Formulation and Evaluation of Indapamide Hemihydrate Sustained Release Tablets

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Abstract

The aim of the study is to formulate and to evaluate the indapamide SR tablet for the treatment of hypertension. Literature survey shows that indapamide is an anti-hypertensive and diuretic drug. The drug has been released up to 6–15 h, after taken orally. These tablets are absorbed into the systemic circulation and blood level shows the considerable peak of drug. It has been formulated as sustained release form for the betterment of therapeutic index and for maintaining constant blood levels. From the study, it has been concluded that HPMC shows the best results for the extending the release of drug. Wet granulation method is used for the preparation of these tablets. The compatibility study for optimized formulation shows satisfactory results. The evaluation of tablets was done for the hardness, friability, weight variation, thickness, drug content, *in vitro* buoyancy study, swelling index, *in vitro* dissolution studies, and stability study.

Keywords: Indapamide, Sustained release, Hypertension, *In vitro* dissolution, Wet granulation

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Introduction

Indapamide hemihydrate is a new class of drug used in the treatment of hypertension. This drug shows anti-hypertensive as well as used as diuretic effect. Studies show that indapamide shows the high peak concentration in blood within 2 h of administration.[1] Around 70–75% of dose has been eliminated by kidney and rest other is been eliminated by biliary route. The half-life is around 14–15 h. The peripheral blood may reverse the taken up of indapamide from erythrocytes.[2,3] The concentration may decrease after 8–9 h of administration. The blood/plasma ratio is about 6:1 when administer the drug. Plasma proteins may bind the indapamide formulation. These are the metabolized drugs. Only 7–8% of drug has been recovered from the urine.[4,5] 1.30 mg–10 mg of daily dose may show the antihypertensive effects.[6,7]

It is an indoline derivative of chloro-sulfonamide [Figure 1]. It does not contain any thiazide groups and has only one sulfonamide group. This may produce anti-hypertensive effect which is used for the improvement of compliances in atrial.[8,9] It is also used for the reduction of arteriolar peripheral resistance. It has two properties beyond diuresis. Vasodilation is observed and it also possesses high degree of antiarrhythmic effect.[10,11] These tablets lower the blood pressure within 24 h and are more lipid soluble.[12,13] These tablets are also used to overcome the problems such as hypokalemia, hyperglycemia, and hyperuricemia. They also have an effect on triglycerides serum, LDL cholesterol, and glucose tolerance.[14,15] The major challenges are lack of sufficient bonding and adhesion at the interface. The adjacent compacted layers which is often the result of an interfacial crack driven by residual stresses in the tablet propagating a finite distance within the tablet and leads to de-lamination (layer-separation) which may not always be apparent immediately after compaction.[16,17] Sustained release matrix dosage forms are designed to achieve a prolonged therapeutic action by continuous releasing medication over an extended period of time after administration of single dose.[18-20]

Materials and Methods

Indapamide hemihydrate of pharmaceutical grade and all grades of polymers was obtained as a gift sample. Analytical grades chemicals and reagents were used. Excipients used in this study are HPMC K4M, HPMC K100M, magnesium stearate, Aerosil, lactose monohydrate, starch, sodium bicarbonate, PVP K-30, talc, and isopropyl alcohol.

Method of Preparation of Tablet

For the preparation of tablets, indapamide hemihydrate and HPMC were mixed with other excipients. The powdered ingredients were mixed uniformly and subjected to wet granulation technique by using isopropyl alcohol. The wet mass was passed through the sieve no 16 and the resulting granules were dried into an oven at a temperature of 50°C. After the completion of drying, these granules were passed through sieve no. 12. Then around 5–8% magnesium stearate was mixed with these granules. The flat-faced punch rotary tablet machine was used for the compression of tablets. The formula for indapamide hemihydrate SR tablets is shown in Tables 1 and 2.

Standard Curve of Indapamide Hemihydrate

Stock solution of indapamide hemihydrate was prepared by weighing 15mg of indapamide hemihydrate drug powder in

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phosphate buffer with pH 7.2, transferred in 100 mL volumetric flask, diluting with the same solvent. From this stock solution, aliquots of 0.5–4.5 mL were withdrawn. Different concentrations 4–46 µg/mL were prepared by diluting up to 10 mL with pH 7.2 phosphate buffers. Absorbance was taken at λ_{max} 223 nm.

Pre-compression Parameters

Bulk density

A weighed quantity of powder was introduced in to the measuring cylinder and then the volume (v bulk) was noted. Bulk density (ρ bulk) was expressed in g/ml and determined by the following formula:

$$\rho\,\text{bulk} = \frac{m}{V\,\text{bulk}}$$

Tapped density

A weighed quantity of powder was introduced in to the bulk density apparatus. The cylinder was hit every 2 s from the height of 2.5 cm up to volume plateau. Tapped density (ρ tapped) was calculated from the following formula:

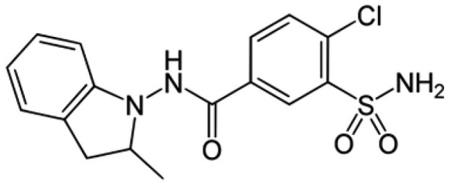

Figure 1: Structure of indapamide

$$\rho\,\text{tapped} = \frac{m}{V\,\text{tapped}}$$

Compressibility index

Compressibility index helps to explain the flow properties of the powders. It was expressed as percentage. It was calculated using the following equation:

$$\text{Compressibility index} = 100 \times \frac{\text{tappeddensity} - \text{bulk density}}{\text{Tappeddensity}}$$

Hausner's ratio

Hausner's ratio is used for the measurement of powder flow. It was calculated by the following formula: -

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Angle of repose

Fixed funnel method was used to measure the angle of repose. The funnel was attached in such a way that it just touches the apex of the heap of the drug powder. The height (h) and radius (r) were measured and angle of repose was calculated using the formula:

$$\text{Angle of repose } (\varnothing) = \tan^{-1}\left(\frac{h}{r}\right)$$

Post Compression Parameters

Weight variation test

To study weight variation, ten tablets were taken from each formulation and then weighted by electronic balance and mean ± SD was calculated.

Table 1: Composition of indapamide hemihydrate (F1 to F10)

Ingredients (mg)	*F1*	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*	*F9*	*F10*
Indapamide hemihydrate	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65
HPMC K4M	85	45	-	-	60	55	45	45	35	-
HPMC K100M	-	40	60	55	-	-	-	-	10	34
Magnesium stearate	1	1	1	1	1	1	1	1	1	1
Aerosil	1.35	1.35	1.35	1.35	1.35	1.35	1.35	1.35	1.35	1.35
Lactose monohydrate	110	110	110	110	110	110	110	110	110	110
Starch	5	10	20	-	25	-	30	-	35	-
Sodium bicarbonate	5	10	20	30	40	50	-	60	-	30
PVP K-30	-	-	-	5	-	10	-	15	-	20
Talc	1	1	1	1	1	1	1	1	1	1
Isopropyl alcohol	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

Table 2: Composition of indapamide hemihydrate (F11 to F20)

Ingredients (mg)	*F11*	*F12*	*F13*	*F14*	*F15*	*F16*	*F17*	*F18*	*F19*	*F20*
Indapamide hemihydrate	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65
HPMC K4M	40	60	40	60	40	60	40	60	-	40
HPMC K100M	10	-	25	-	20	05	30	15	65	30
Magnesium stearate	1	1	1	1	1	1	1	1	1	1
Aerosil	1.35	1.35	1.35	1.35	1.35	1.35	1.35	1.35	1.35	1.35
Lactose monohydrate	110	110	110	110	110	110	110	110	110	110
Starch	-	5	10	20	30	-	40	-	30	35
Sodium bicarbonate	5	10	5	10	30	50	20	60	-	-
PVP K-30	5	-	-	-	-	20	-	25	-	-
Talc	1	1	1	1	1	1	1	1	1	1
Isopropyl alcohol	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

Hardness

Hardness of the tablets indicates the ability to withstand mechanical shocks while handling and transportation. Monsanto hardness tester was used to check the hardness of the tablets. Formulations of tablets were randomly picked and use to determine the hardness of the tablets.

Friability test

Ten tablets were weighed and put into the friabilator and the process was continued for 4 min at 25 RPM. After that the tablets were then weighed again. The formula to calculate friability is as follows:

$$\text{Friability test} = \frac{\text{Weight of tablets before test} - \text{weight after test}}{\text{weight of tablets after test}} / 100$$

Acceptance of tablet is done when the maximum loss of weight is not greater than 1.0%.

Thickness

Vernier caliper was used to measure the thickness of each tablet. Calculation of average thickness of each tablet was done. If the tablets contain the deviated by ± 5%, it passed the test.

Drug content

Ten tablets were taken and crushed. With the help of sonication, drug of equivalent quantity was dissolved in 0.1N HCL and volume was made up to 100 ml. Using Whatman filter paper, solution was filtered. For obtaining the 10 µg/ml concentration, solution was treated with 0.1N HCl. By measuring the absorbance of solution, the drug content was calculated.

Disintegration test

Disintegration test apparatus is used for this test. It contains a basket rack as well as six glass tubes and the bottom of the glass it contains mesh sieve. 30–35 times per minute the basket was raised and lowered in 950 mL of water. It was maintained at a temperature of 37°C ± 2°C. In each tube, 5–6 tablets were placed and recorded the time. The time at which the tablet fragments passes through the mesh, is known as the tablet disintegration time.

Dissolution test

USP dissolution apparatus type II was used for the dissolution of different batches of the tablets. The dissolution study was performed out in pH 1.2 HCl buffer for the first 2 h, followed by phosphate buffer pH 7.2 for 3–16 h (900 ml). It was maintained at 37°C ± 0.5°C of temperature with 50 RPM stirring rate. Each sample was drawn at regular interval of time and the remaining volume was made up by fresh solvent. Whatman filter paper was used for filtration and by using UV-Visible spectrophotometer; observance was recorded against a blank.

Wetting time

A tablet was taken randomly and put into 2 layers of absorbent paper. Using pH 1.2 HCl buffer, absorbent paper was wetted and the unused buffer was drained out from the Petri dish. Stopwatch was used to record the time required for the buffer to diffuse from the wetted absorbent paper into the entire tablet. This test was performed in triplicate and mean ± SD was calculated.

Maximal water uptake capacity

Formulation of each tablet was weighed and put it into the desiccator for 4 h. Desiccator contained activated silica gel. Percentage of water contain was calculated by following equations: -

$$\text{Water content} = \frac{\text{weight before drying} - \text{weight after drying}}{\text{weight before drying}} / 100$$

Swelling index

In a dissolution test apparatus, tablet was placed for determining the swelling properties of tablet layer. It was conducted in a container capacity of 1000 ml of 0.1N HCl at 37 ± 0.5 °C. It was then rotated for 30 min at 50 rpm. Then, the tablets were removed from the medium, excess water was removed and weighed. According to the equation, swelling characteristics were expressed in terms of percentage water uptake (WU %).

$$\text{Swelling Index} = \frac{(\text{Weight of dry tablet} - \text{weight of swollen tablet}) \times 100}{\text{Weight}}$$

Drug release kinetics

Dissolution data were calculated by applying different type of kinetic models such as zero-order (cumulative amount of drug release vs. time), first order (log cumulative percentage of drug remaining vs. time), Higuchi equations (cumulative percentage of release vs. square root of time), and Peppas equations (log cumulative percentage of drug released vs. log time).

DSC study of sustained release layer

DSC is used for the formation of thermogram of sustained release tablet (indapamide hemihydrate). For the calibration of DSC temperature and enthalpy, indium was used. Samples were accurately weighed and used for DSC study. The heating rate of 10°C/min heating was maintained.

Results and Discussion

Standard curve of indapamide hemihydrate [Figure 2] was found to be linear (1–6 µg/mL) in pH 7.2 phosphate buffer.

Pre-compression parameters such as angle of repose, bulk density, tapped bulk density, compressibility index, and Hauser's ratio were calculated for all batches of indapamide hemihydrate [Table 3].

No change of peak was observed in sustained release tablet of indapamide hemihydrate and also there were no interactions between the drug and excipients which were used in the formulation. The thermogram is shown in Figure 3.

The post compression parameters such as weight variation, hardness, thickness, friability, swelling index, disintegration time,

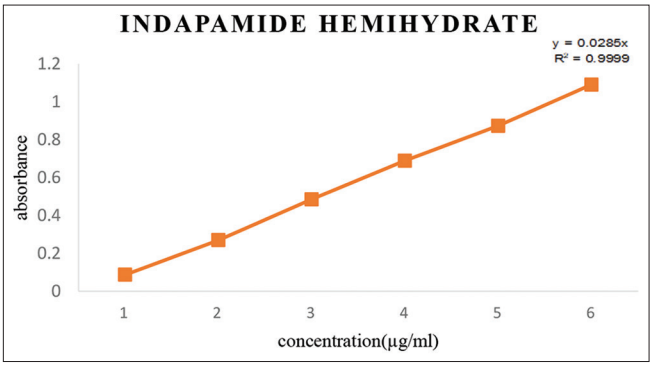

Figure 2: Standard curve of indapamide at phosphate buffer pH 7.2

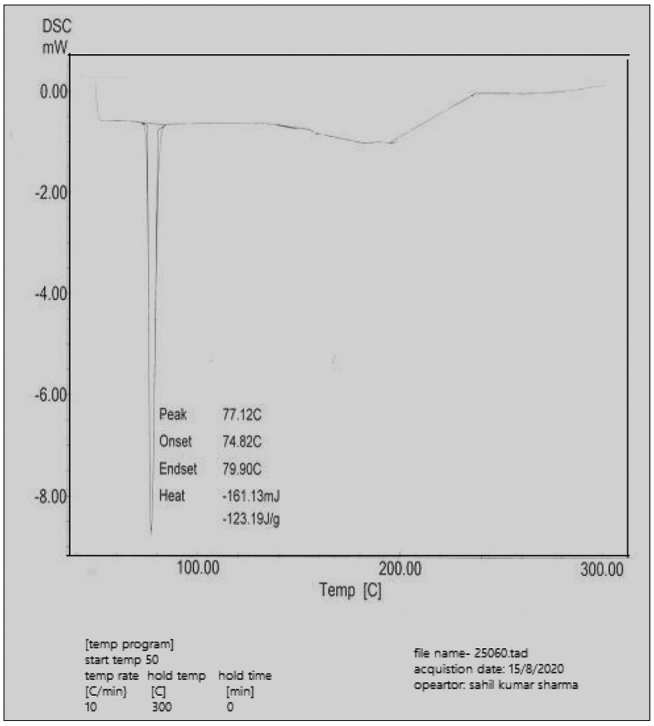

Figure 3: DSC of indapamide hemihydrate

duration of floating, and drug content of formulated matrix tablets were evaluated and were found to be satisfactory [Table 4]. All tablets comply with pharmacopoeia specifications for weight variation and friability. The formulations in all prepared batches contain Indapamide within 1.65 mg ± 5% of the labeled claim. The release of Indapamide from tablets was slow and extended over longer period of time. The *in vitro* release of SR tablets shows the effect of polymer concentration on the drug release and it was found that the drug release from the tablets was found to decrease with the increase of polymer concentration in the matrix. This may be due to the fact that high concentration of polymer in the tablets might have produced dense matrix around the drug particles, thereby providing more barriers for them to escape and dissolve.

The percentage of drug release after 16 h from HPMC K4M and HPMC K100M based polymer matrix tablet of formulations F-1 to F-20 was found to be in the range of 71.16–99.29% and as shown in Figures 4-7. From these release patterns, correlations were found between polymer ratio and drug release rate, and it was found that the release rate decreases with increasing polymer concentration. Formulations F-5, F-10, F-15, F-18, and F-20 were found effective in sustaining the drug release after 16 h. Finally formulation F-2 was selected as optimized formulation among them as it shows the best results.

Different kinetic models were used to study the release of drug from all the formulations as shown in Figures 8-11. The results of kinetic studies reflected that all 20 formulations followed zero-order kinetics as it gave the highest linearity (R^2: 0.97–0.99), which suggests simultaneous swelling and erosion as the mechanism of drug release from these matrix tablets. To further confirm the actual release mechanism, all the release results were extrapolated by Korsmeyer-Peppas model. According to this model, all the formulations exhibited super Case II transport mechanism as "n" value of all formulations was of >0.85. From all these release kinetics, it was decided that F-2 is the best formulation and it showed the best results as a purpose of sustaining drug release. That is why tablets of formulation F-2 were then decided to be kept for stability study according to ICH guidelines for 0 to 6 months at accelerated condition (40 ± 2°C/75 ± 5% RH). All data were evaluated [Table 5] and no considerable changes were found in any of the selected parameters [Figure 12]. Hydrophilic polymer

Table 3: Precompression parameters of indapamide hemihydrate powder blend

Batch	*Angle of Repose (°)*	*Bulk density (g/mL)*	*Tapped density (g/mL)*	*Compressibility index (%)*	*Hauser's ratio*
F1	27.36±0.17	0.478±0.15	0.192±0.28	9.25±0.17	1.10±0.23
F2	27.25±0.16	0.480±0.13	0.168±0.26	13.59±0.16	1.15±0.15
F3	28.45±0.15	0.481±0.12	0.195±0.35	18.48±0.15	1.20±0.16
F4	27.65±0.13	0.489±0.11	0.165±0.33	9.45±0.12	1.21±0.17
F5	29.98±0.12	0.258±0.14	0.178±0.22	8.48±0.11	1.25±0.01
F6	27.75±0.15	0.148±0.15	0.156±0.28	8.49±0.11	1.09±0.03
F7	30.65±0.16	0.359±0.12	0.264±0.26	10.2±0.17	1.45±0.05
F8	30.65±0.19	0.300±0.13	0.278±0.27	10.3±0.16	1.25±0.13
F9	29.34±0.17	0.245±0.14	0.233±0.29	10.56±0.15	1.35±0.12
F10	29.38±0.12	0.359±0.15	0.215±0.35	8.48±0.14	1.46±0.12
F11	28.45±0.14	0.350±0.13	0.150±0.33	10.12±0.12	1.04±0.10
F12	27.55±0.16	0.470±0.18	0.166±0.32	12.14±0.13	1.00±0.18
F13	29.40±0.15	0.472±0.17	0.175±0.31	13.15±0.11	1.06±0.17
F14	30.10±0.15	0.365±0.12	0.189±0.30	16.15±0.12	1.02±0.19
F15	26.55±0.13	0.160±0.13	0.199±0.32	10.13±0.10	1.26±0.21
F16	27.45±0.14	0.490±0.12	0.233±0.26	9.12±0.12	1.39±0.12
F17	28.10±0.13	0.495±0.11	0.240±0.29	15.15±0.14	1.40±0.18
F18	29.20±0.10	0.255±0.15	0.265±0.31	16.17±0.16	1.56±0.13
F19	30.45±0.11	0.267±0.14	0.269±0.33	17.21±0.13	1.55±0.11
F20	30.85±0.12	0.489±0.15	0.271±0.34	18.02±0.15	1.50±0.14

Table 4: Post-compression parameter of indapamide hemihydrate

Formulation	*Weight (mg)*	*Thickness (mm)*	*Hardness (kg/cm²)*	*Friability (%)*	*Disintegration time (s)*	*Drug content (%)*	*Swelling index in 1 h (%)*
F1	210±7.8	3.32±0.06	4.5±0.30	0.584	35.38±6.55	100.60±0.68	12.4
F2	220±6.5	3.25±0.05	5.0±0.05	0.623	53.18±13.99	101.9±0.58	12.8
F3	215±7.75	3.34±0.06	5.2±0.35	0.789	36.67±5.60	101.8±0.44	13.3
F4	205±6.9	3.45±0.05	5.3±0.45	0.654	55.52±35.25	102.6±0.56	13.4
F5	240±7.9	3.65±0.08	5.1±0.65	0.357	79.69±24.38	101.7±1.48	13.6
F6	230±4.3	3.35±0.06	4.1±0.35	0.458	54.85±16.19	100.8±0.50	13.8
F7	230±6.7	3.45±0.05	5.2±0.45	0.036	55.52±14.30	101.3±0.56	13.7
F8	235±6.9	3.36±0.08	4.6±0.25	0.458	55.56±34.2	100.9±0.67	13.5
F9	195±7.8	3.14±0.04	6.4±0.35	0.369	60.25±33.56	101.8±0.86	12.6
F10	200±5.9	3.63±0.06	4.4±0.65	0.753	65.89±33.86	101.9±0.82	12.7
F11	175±1.5	3.11±0.08	4.2±0.36	0.449	78.36±34.26	100.15±0.85	12.9
F12	190±1.4	3.25±0.09	3.5±0.35	0.552	75.25±33.52	101.59±0.83	12.5
F13	195±1.5	3.15±0.05	2.2±0.11	0.724	70.45±32.25	100.45±0.84	13.3
F14	205±1.4	3.29±0.07	3.6±0.22	0.706	75.20±29.45	101.15±0.80	13.4
F15	235±1.5	3.39±0.06	4.5±0.32	0.552	80.25±30.15	100.17±0.78	13.6
F16	200±1.6	3.19±0.05	3.4±0.31	0.451	82.10±29.45	101.1±0.75	13.4
F17	245.29±1.7	3.26±0.07	5.0±0.40	0.305	86.13±21.25	100.18±0.56	13.5
F18	275±1.6	3.60±0.08	3.4±0.15	0.203	84.25±19.45	101.20±0.42	12.2
F19	210±1.3	3.30±0.06	4.2±0.20	0.155	72.15±25.10	100.16±0.59	12.3
F20	220±1.2	3.31±0.02	3.1±0.30	0.683	74.36±24.59	101.25±0.65	13.4

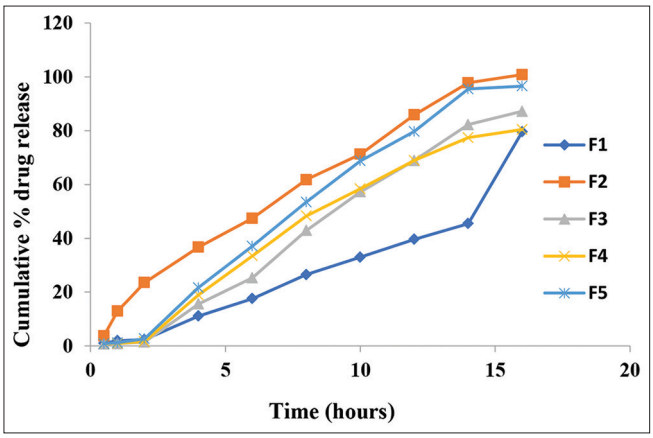

Figure 4: Dissolution profile of indapamide hemihydrate SR tablets (F1 to F5)

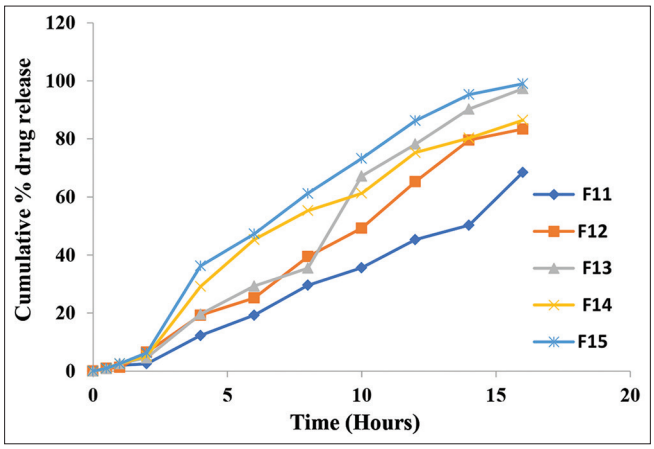

Figure 6: Dissolution profile of indapamide hemihydrate SR tablets (F11 to F15)

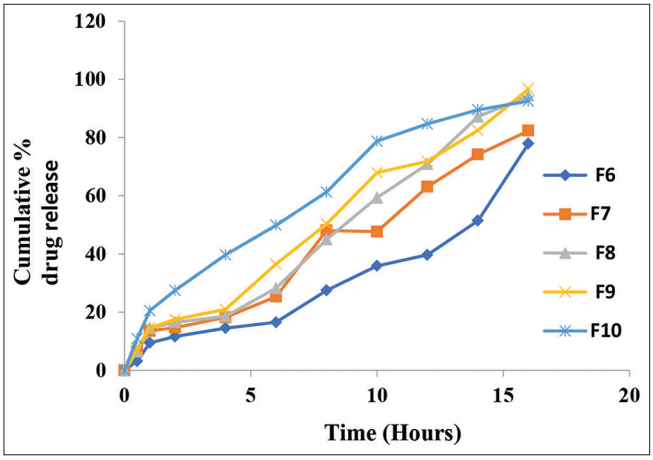

Figure 5: Dissolution profile of indapamide hemihydrate SR tablets (F6 to F10)

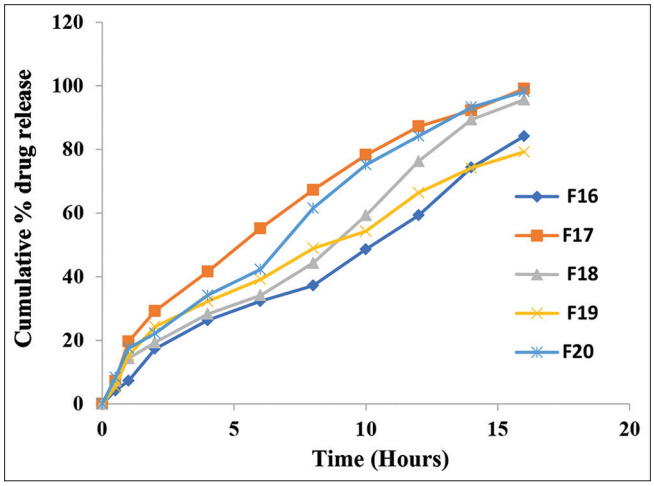

Figure 7: Dissolution profile of indapamide hemihydrate SR tablets (F16 to F20)

Table 5: Stability study data from 0 to 6 months

Time (month)	*Weight variation (mg)*	*Thickness (mm)*	*Hardness (Kg/cm2)*	*Friability (%)*	*Drug content uniformity (%)*
0	220±3.72	3.25±0.15	4.45±0.18	0.45	100.2 ± 0.9
1	220±2.65	3.24±0.17	4.86±0.19	0.44	100.2 ± 0.7
2	220±3.51	3.23±0.26	4.48±0.25	0.49	99.3 ± 0.6
3	220±2.84	3.25±0.27	4.47±0.34	0.44	99.1 ± 0.3
4	220±1.95	3.24±0.85	4.74±0.94	0.56	100±0.8
5	220±2.63	3.25±0.94	4.79±0.85	0.58	99±0.5
6	220±2.78	3.25±0.64	4.61±0.74	0.66	99±0.3

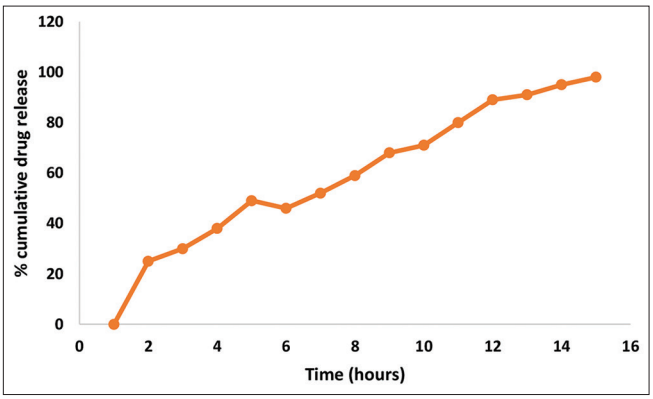

Figure 8: Zero-order kinetics of optimized formulation

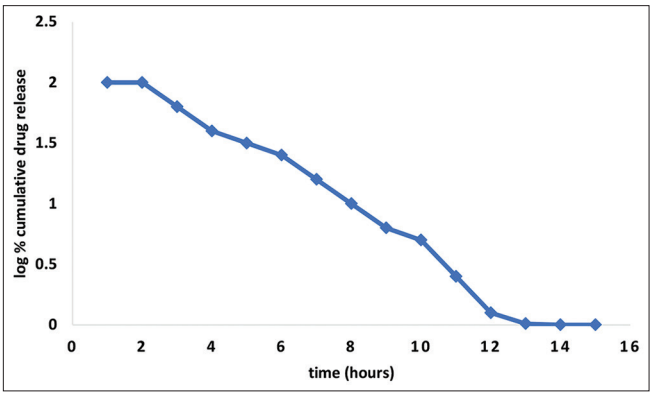

Figure 9: First-order kinetics of optimized formulation

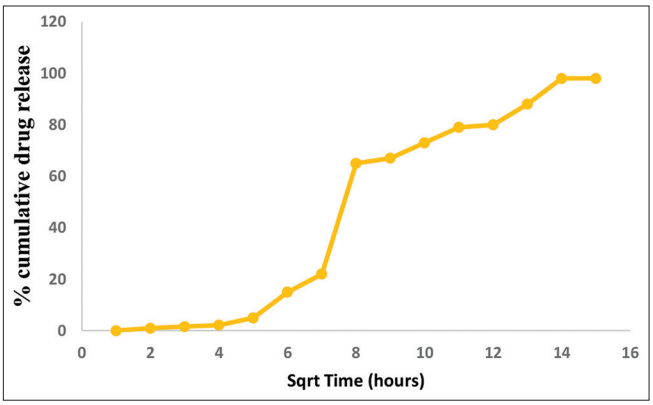

Figure 10: Higuchi release kinetics of optimized formulation

promotes desired sustained release of drug on hydration, swelling and gel formation when it interacts with gastrointestinal fluid.

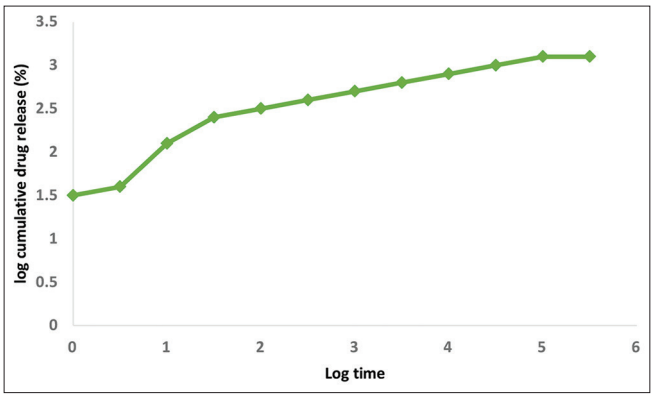

Figure 11: Peppas release kinetics of optimized formulation

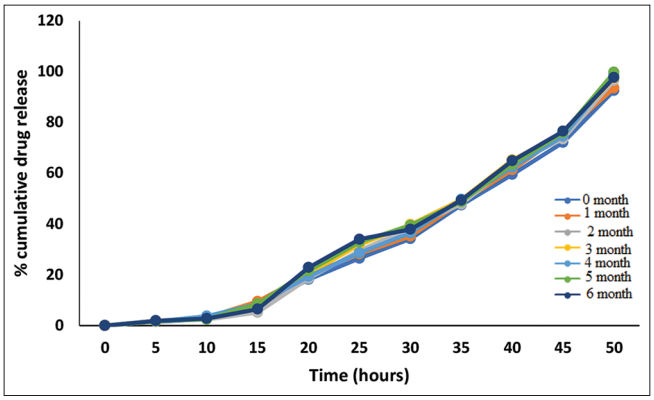

Figure 12: Indapamide hemihydrate release from bi-layer tablet after stability study

Results of the present study reveal that hydrophilic polymer based formulation F-2 of Indapamide hemihydrate 1.65 mg SR tablet fulfills all the requirements of sustained release dosage form.

Summary and Conclusion

The present study shows that for the control release of drug (indapamide hemihydrate) in the matrix system HPMC (sustained release polymer) shows a greater role. Result of pre-compression study shows that F2 granules of indapamide hemihydrate show good compressibility. The flow property of power was found to be good and in excellent range. The hardness and thickness was found to be in the range of 3–5 kg/cm^2 and 3–4 mm respectively. According to the ICH guidelines, the stability study was carried out and it was found that the batches were stable for 6 months. The statistical analysis shows that optimized formulation shows the improved bioavailability as compared to marketed formulation. The *in vitro* evaluation of all the batches shows that the floating

time was more than 23 h with 4–8 min of floating lag time. These tablets were sustained up to 16 h.

References

1. Yeole PG, Galgatte UC, Babla IB, Nakhat PD. Design and evaluation of Xanthan gum-based SR matrix tablets of Diclofenac Sodium. Indian J Pharm Sci 2006;68:185.
2. Pandey VP, Manavalan R, Hessian SM, Rao PL. Formulation and Development of Naproxen Conventional Tablets. Vol. 85. The Indian Pharmacist January; 2007.
3. Venkatesh, Nath BS. HPMC as wicking agent in Matrix tablets of Cetyl alcohol. Indian Drugs 1999;36:720.
4. Kumar MT, Srinivas G. HPMC based matrix tablets of atenolol and cisapride. Indian J Pharm Sci 2005;67:414.
5. Dhuikhel. Effect of Drug Solubility and polymer viscosity on *in-vitro* drug release from HPMC matrix tablets. Indian Drugs 2005;42:389-91.
6. Yu LX, Elison CD, Conner DP, Lesko LJ, Hussain AS. Influence of drug release properties of conventional solid dosage forms on the systemic exposure of highly soluble drugs. AAPS Pharm Sci 2001;3:24.
7. Rantanen J, Rasanen E, Tenhunen J, Kansakoski M, Mannermaa J, Yliruusi J. An evaluation of particle size and binder effects. Eur J Pharm Biopharm 2000;50:271-6.
8. Becker D, Rigassi T, Bauer-Brandla A. Effectiveness of binders using wet granulation. Drug Dev Ind Pharm 1997;51:356.
9. Rajnaik P, Stepanek F, Mancinelli C, Chern R, Farber L, Hill B. Experimental study of wet granulation in fluidized bed: Impact of the binder properties on the granule morphology. Int J Pharm 2007;334:92-102.
10. Chowdary KP, Ramya K. Pregelatinized starch: A potential pharmaceutical excipient. East Pharm 1999;42:199.
11. Streubel A, Siepmann J, Bodmeier R. Floating matrix tablets based on low density foam powder: Effects of formulation and processing parameters on drug release. Eur J Pharm Sci 2003;18:37-45.
12. Goole J, Vanderbist F, Aruighi K. Development and evaluation of new multiple-unit levodopa sustained-release floating dosage forms. Int J Pharm. 2007;334:35-41.
13. Ira IJ, Ahamed SK, Dewan SM, Moghal MM, Islam MA. Formulation and *in*-vitro evaluation of theophylline SR matrix tablets and comparison of release rate with marketed products dispensed in Bangladesh. Int J Pharm Ther 2013;4:91-7.
14. Rahela U, Moghal MM, Dewan SM, Amin MN. Formulation and evaluation of polymer effect on *in-vitro* kinetics of sustained release matrix tablets of carvedilol using model dependent methods. Int J Pharm Life Sci 2013;2:70-9.
15. Ashkari ST, Moghal MM, Dewan SM, Amin MN. Development of sustained release matrix tablets of carvedilol and evaluation of polymer effect on *in-vitro* release pattern. Int J Curr Pharm Clin Res 2013;3:18-22.
16. Williams RO 3rd, Reynolds TD, Cabelka TD, Sykora MA, Mahaguna V. Investigation of excipient type and level on drug release from controlled release tablets containing HPMC. Pharm Dev Technol 2002;7:181-93.
17. Chaffman M, Heel RC, Brogden RN, Speight TM, Avery GS. Indapamide. A review of its pharmacodynamic properties and therapeutic efficacy in hypertension. Drugs 1984;28:189-235.
18. Ayush G, Anshu S, Indrajeet S. Preparation and evaluation of film coated tablets of nitrofurantoin. Int J Res Pharm Pharm Sci 2016;1:47-53.
19. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanism of solute release from porous hydrophilic polymers. Int J Pharm 1983;15:25-35.
20. Ahmed M, Ahamed SK, Dewan SM, Moghal MM. Development of sustained release matrix tablets of ramipril and evaluation of polymer effect on *in-vitro* release pattern. Int J Pharm Sci Res 2013;4:1039-45.