DESIGN AND DEVELOPMENT OF ONCE DAILY PULSATILE DRUG DELIVERY SYSTEM OF MIGLITOL USING PULSINCAP TECHNOLOGY

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Abstract:

Diabetes mellitus belongs to the class of metabolic disorder, which is associated with high blood sugar level due to insufficient production of insulin by pancreas. Continuous, constant drug release was not suitable in case of Diabetes mellitus, but it needs a pulse of therapeutic concentration. In the present research work designed to develop the pulsatile drug delivery of miglitol. The solubility of capsule bodies was modified by treating with formaldehyde. The immediate release granules were prepared by wet granulation method and formulation was optimized based on the flow properties drug content and dissolution studies. Hydrogel plugs were prepared with two different cellulose ethers in 1:2 and 1:3 drug: polymer ratio's with predetermined lag time of 6 h. Pulsicaps were prepared by filling the treated bodies with three doses of miglitol immediate release granules which were separated by two hydrogel plugs then sealed with untreated caps. The prepared pulsicaps were evaluated for *in-vitro* drug release in three different dissolution media. From the results SDC4 formulation was optimized based on the drug release and predetermined lag time. The obtained results showed the capability of the system in drug release for a programmable period of time before and after lag time. Accelerated stability studies conducted at different humidity conditions showed no remarkable changes concluding that a successful pulsatile drug delivery system of Miglitol was developed.

Key words: Diabetes mellitus, pulsatile drug delivery, wet granulation method, cellulose ethers, and hydrogel plugs.

1.Introduction:

Diabetes mellitus belongs to the class of metabolic disorder, which is associated with high blood sugar level due to insufficient production of insulin by pancreas[1]. The patients suffering from diabetes are reported to have high blood sugar levels after meals compared to other timings. Diabetes mellitus requires long term treatment with sustained release formulations of drugs like sulfonylureas which may damage the pancreas.

Drug delivery has traditionally meant getting a simple drug absorbed predictably from the GIT or a site of injection. Second generations of drug delivery devices have been designed to administer drugs at a steady rate[2]. In early nineties efforts were made to design the drug delivery system which will release the drug at constant rate. In fact these systems turned to be one of the most successful delivery systems for effective drug delivery. But still for the many of the drugs these systems are not suitable. In this context, it is preferable to optimize the drug release from dosage form which will provide desired concentration of drug at a particular time only[3].i.e., chrono-pharmacotherapy of disease which shows circadian rhythms in their pathophysiology. In these types of diseases constant drug release is not preferred,but it needsa pulse of therapeutic concentrationin periodic manner which leads to development of Pulsatile Drug Delivery Systems.

Miglitol[4]is a novel type of glucosidase inhibitor produced from 1-deoxynijirimycin, which has a structure similar to glucose. There are less negative effects because it is completely absorbed from the GI tract. MGL inhibits glycosidase in the small intestine brush boundaries in a competitive manner. As a result, postprandial glycaemia is reduced. Because of its short biological half-life (2-3 hours), pulsatile drug delivery systems are needed to overcome multi-dosing per day, improve patient compliance, and reduce drug toxicity.

2. Materials and Methods

2.1 Material

MGL was obtained as gift sample from Mylan laboratories limited, Kazipally, Hyderabad, India. Crospovidone and Aerosil were from Otto Chemical Biochemika Reagents. Mumbai. Metalose was a gift from Signet Chemical Corporation Pvt. Ltd, Mumbai. Sodium carboxymethyl cellulose was procured from Excel Fine Chemicals, Andhra Pradesh, India. Magnesium Stearate obtained from S.D Fine Chem Ltd, Mumbai, methanol and other reagents used were of standard analytical reagent grade.

2.2 Methods

2.2.1 Formulation and preparation of Miglitol immediate release granules:

Miglitol immediate release core granules were prepared by wet granulation process. Various proportions of crospovidone as superdisintegrant was added to MGL and MCC along with (3% w/v PVP K30 in 50% methanol) to get the wet mass. The coherent mass was passed through the sieve #.22(IP Standard) and the granules were dried at 60˚C for one hour using hot air oven. Then the dried granules were packed in a polybag for further use. Formulation of MGL immediate release core granules was given in the Table-1.

Table-1: Different formulations of Miglitol immediate release core granules

Ingredients (mg/capsule)	**Formulationcode**					
	MCM1	**MCM2**	**MCM3**	**MCM4**	**MCM5**	**MCM6**
Miglitol	25	25	25	25	25	25
Crospovidone	0	2	4	6	8	10
Microcrystalline cellulose	42	40	38	36	34	32
PVP K30	5	5	5	5	5	5
Methanol	Qs	Qs	Qs	Qs	Qs	Qs

2.2.2 Flow properties of granules:

Bulk density[5]:

It is mathematically expressed as

Bulk density = Weight of the sample (g) / Volume of the sample (ml)

Procedure:

Accurately weighed granules were transferred in to measuring cylinder and the volume occupied by the granules in ml was noted down.

Hausner's ratio[6]:

The Hausner's ratio is a number that is correlated to the flow ability of a powder or granular material.The Hausner's ratio less than 1.25 indicates free flowing nature of granules and a value greater than 1.25 shows poor flow properties of granules.

Hausner's ratio = TBD/LBD

Where,
TBD = tapped bulk density
LBD = loose or aerated bulk density

Carr's compressibility index[6]:

It indicates the compressibility of powder or granules. Powder or granules which have smaller Carr's index value (< 15) have good compressibility.It is calculated as:

Carr's compressibility index, $C = (\rho_b - \rho_u)\ 100 / \rho_b$,

ρ_b=tapped bulk density

ρ_u= untapped bulk density (loose or aerated bulk density)

ConsolidationIndex(%)	Flow
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-35	Poor
33-38	Verypoor
>40	Very very poor

Angle of repose[7]:

Angle of repose was used to measure the flow properties. Angle of repose was measured by fixed funnel method of Banker and Anderson.

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

Where

θ = Angle of repose

h =height of pile

r = Radius of the base of the pile

Drug content[7]:

Drug content was measured by dissolving the 10 mg of granules in 10 ml methanol and the solution was filtered and 1ml filtrate was diluted with suitable dissolution media. The diluted sample absorbance was measured at 232 nm using UV Visible spectrophotometer (Elico SL-200). The results were given in the Table-3.

***In-vitro* Dissolution studies of immediate release core granules[7]:**

Dissolution studies of immediate release core granules were carried out by using USP II dissolution apparatus (VEEGO, Model: VDA-8D). The test was carried out by taking granules equivalent to 25 mg drug and performed in three different dissolution media like 0.1 N HCl, pH 7.4 phosphate buffer and pH 6.8 phosphate buffer. Test was conducted by taking 900 ml of dissolution medium at a temp. 37± 0.5˚C for 2h and paddle was rotated at a speed of 75 rpm. Aliquots of 5 ml were withdrawn at predetermined time intervals (5, 10, 15, 30,45,60,90 and 120

min). Samples were suitably diluted and analyzed in UV Visible spectrophotometer at 210 nm. Three trials were done and mean % drug release was calculated.

2.3 Preparation of Pulsicaps:

2.3.1 Solubility modification of hard gelatin capsules[8]:

About 200 capsules of '0' size were taken; bodies and caps were separated. The separated bodies were kept on the wire mesh and were placed in the desiccators which contained 25 ml of 37% v/v formaldehyde. To this a pinch of potassium permanganate was added and the desiccator was tightly closed. The bodies were exposed to formaldehyde vapors until proper solubility was achieved. Then the bodies were dried at room temp for 24 h to remove the excess formaldehyde. After drying the treated bodies were joined with untreated caps and kept in the polybags for future use.

2.3.2 Evaluation of treated bodies[9]:

2.3.2.1 Qualitative Analysis for formaldehyde content:

Preparation of formaldehyde standard solution:

Suitable volume of formaldehyde was diluted with water to get 20µg/ml concentration.

Preparation of test sample:

To 40 ml of distilled water add twenty five treated bodies cut into small pieces and dissolved it by stirring with magnetic stirrer for 1 h to get excess amount of formaldehyde. Then the solution was filtered and volume made up to 50 ml with distilled water.

Procedure for testing the concentration of Formaldehyde:

One ml of test solution was taken to this add 5 ml of 99.5% v/v acetyl acetone and 4 ml of distilled water. Then this solution was heated for 40 min at 40˚C. At the same time 1ml of standard formaldehyde was treated in the same manner taken as reference. Then the two solutions, i.e., test and reference samples were compared for color intensity. The color of the test sample was not more intensive than the reference sample.

2.3.3 Preparation of hydrogel plugs[10]:

Two polymers like Metalose 90SH 100000, Sodium carboxy methyl cellulose were initially selected for the preparation of hydrogel plugs which were swellable polymers. The polymers were taken in two different Drug: Polymer ratio's, i.e., 1:2 and 1:3 and these polymers were mixed with two diluents MCC and DCP. To this magnesium stearate and Aerosil were added to increase the flow properties of powder and it was directly compressed with 6mm flat round punches in punching machine. Different formulations of hydrogel plugs were given in the Table-2.

Table-2: Different formulations of hydrogel plugs

Ingredients mg/tablet plug	Metalose 90 SH 100000	Sodium CMC	MCC	DCP	Aerosil	Magnesium stearate	Total Wt
MMC1	50	….	48	….	1	1	100
MDC2	50	….	….	48	1	1	100
MMC3	75	….	23	….	1	1	100
MDC4	75	….	….	23	1	1	100
SMC1	….	50	48	….	1	1	100
SDC2	….	50	….	48	1	1	100
SMC3	….	75	23	….	1	1	100
SDC4	….	75	….	23	1	1	100

2.3.4 Preparation of pulsicaps[11]:

Treated bodies and untreated caps of the '0' size capsules were taken for filling. Immediate release core granules formula MCM5 was optimized for the preparation of Miglitol pulsicaps. Then the pulsicaps were assembled inside the treated bodies with three doses of optimized core granules and each dose was separated by hydrogel plug then closed with untreated caps. The assembled pulsicaps contained three doses of Miglitol granules and two hydrogel plugs.

2.4 Physicochemical characterization of hydrogel plugs[12]:

Weight variation:

Twenty hydrogel plugs were taken and test was conducted according to IP standard procedure.

Thickness:

Hydrogel plugs thickness was measured by using vernier calipers.

Hardness test:

Monsanto's hardness tester was used to measure the hardness of plugs. It was expressed in kg/cm^2.

2.4.3 *In vitro* dissolution studies of pulsicapsule[13]:

Dissolution studies were carried out by using USP II apparatus. Here three dissolution media were used to simulate the pH changes along the GI tract.

Acid Stage: Stomach has acidic pH this was maintained by using 0.1N HCl (900 ml) for first 2 h because it is average gastric emptying time. Then the acid was removed and refilled with phosphate buffer.

Buffer Stage: After gastric emptying the contents enter intestine which is having the basic pH. pH 7.4 phosphate buffer (900 ml) was used for next 3 h transit time of small intestine. After 3 h the pH 7.4 buffer was replaced with pH 6.8 phosphate buffer to maintain the colonic pH for the remaining 13 h. Paddles were rotated at 75 rpm and temperature was maintained at 37±0.5˚C.Aliquotes (5 ml) of samples were withdrawn from the dissolution basket at specified time intervals and replaced with the same volume of respective dissolution medium to maintain the sink conditions. Samples were analyzed at 210 nm by using UV Visible spectrophotometer.

2.5 Drug-Polymer interactions:

There is always a possibility of drug-polymer interaction in the formulation due to their intimate contact. Fourier transform infrared spectroscopy (FTIR),and differential scanning

calorimetry (DSC) studies were conducted on Miglitol, crospovidone, hydrogel plug and optimized formulations to study the drug-polymer interactions, if any.

Fourier transform infrared spectroscopy (FTIR):

FTIR spectra of samples were obtained on an IR spectrophotometer (Bruker Alpha II) using the KBr disc method. The scanning range was 500–3500 cm^{-1}.

Differential scanning calorimetry (DSC):

DSC was performed using a Differential scanning calorimeter (HITACHI DSC 7020) at a heating rate of 10° C/min from 35 to 550° C in nitrogen atmosphere

2.6 Stability Studies[14]:

Stability studies were conducted to predict the shelf life of a product. The optimized formulation was exposed to different conditions in stability chamber and these samples were analyzed for appearance, uniformity of content and *in vitro* dissolution performance. The obtained results were compared with the initial results.

3. Results and discussion:

3.1. Flow properties of Miglitol immediate release granules:

All prepared granules were uniform in size and flow properties of core granules of six formulations indicated that the granules were free flowing and drug content was found to be in the range of 99.26 ± 0.82 to 99.95 ± 0.11. The results were given in theTable-3.

Table-3: Flow properties of immediate release core granules (Mean±SD, n=5)

Formulation Code	Bulkdensity (g/cm^3)	Tappeddensity (g/ml)	Compressibility Index (%)	Hausner'sratio	Angle of Repose(°)	Drug Content(%)
MSM1	0.623±0.05	0.698±0.02	10.32±0.06	1.11±0.05	24.39±0.11	99.81±0.34
MSM2	0.634±0.03	0.704±0.05	10.78±0.05	1.12±0.07	24.17±0.81	99.32±0.17
MSM3	0.627±0.02	0.715±0.06	10.67±0.01	1.10±0.04	25.19±0.05	99.26±0.82
MSM4	0.642±0.04	0.745±0.03	10.45±0.04	1.12±0.03	27.03±0.11	99.88±0.21
MSM5	0.639±0.01	0.759±0.02	9.78±0.04	1.10±0.05	24.08±0.45	99.95±0.11
MSM6	0.645±0.06	0.773±0.08	10.05±0.07	1.09±0.02	24.11±0.87	99.83±0.56

3.1 Dissolution studies of Miglitol core granules:

Three different dissolution media was used in these studies. Different concentrations of crospovidone results in significant increase in drug release profile. The formulation MCM1 without crospovidone showed less % drug release and MCM2-MCM4 formulation released the less % of drug than MCM5 and MCM6 because it contains low amount of superdisintegrant. The formulation MCM6 drug release was completed within one hour due to high amount of superdisintegrant. Hence MCM5 was optimized based on the flow properties, drug content and drug release profile. The results were given in theTables-4,5&6 and Figures 1, 2&3.

Table-4: Dissolution data for Core Granules in 0.1N HCl

Time (min)	**Cumulative% Drug Release*(** Mean± SD, n=3)					
	MCM1	**MCM2**	**MCM3**	**MCM4**	**MCM5**	**MCM6**
0	0	0	0	0	0	0
15	17.46±0.87	23.42±0.93	27.97±0.23	35.44±0.56	38.87±0.51	46.03±0.73
30	36.98±0.56	46.98±0.47	45.76±0.96	58.09±0.71	57.96±0.37	79.83±0.27
45	52.44±0.43	56.65±0.63	78.41±0.57	73.87±0.23	72.98±0.34	86.78±0.41
60	74.83±0.87	78.64±0.43	81.23±0.47	85.34±0.63	83.88±0.75	98.98±0.67
90	82.34±0.56	84.86±0.95	88.75±0.68	92.87±0.61	95.37±0.56	
120	88.67±0.34	91.66±0.95	93.77±0.98	95.98±0.23	99.73±0.17	

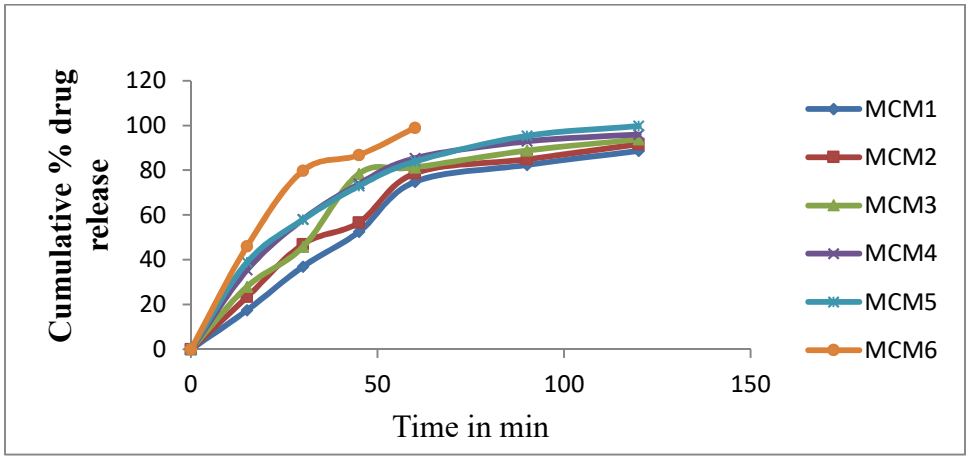

Fig.1: Comparative %drug release profile for Core granules of MCM1-MCM6 in 0.1N HCl

Table.5:Dissolution data Core Granules in pH 7.4 Phosphate Buffer

Time(Min)	**Cumulative % Drug Release*(** Mean± SD, n=3)					
	MCM1	**MCM2**	**MCM3**	**MCM4**	**MCM5**	**MCM6**
0	0	0	0	0	0	0
15	17.06±0.98	25.45±0.86	29.78±0.12	33.64±0.76	37.56±0.45	45.68±0.98
30	38.98±0.56	48.07±0.37	51.87±0.34	54.79±0.47	68.97±0.65	76.95±0.56
45	49.98±0.47	73.67±0.61	74.67±0.76	78.05±0.36	82.45±0.72	85.03±0.52
60	67.57±0.34	80.01±0.65	83.75±0.58	86.98±0.86	89.92±0.73	97.98±0.41
90	84.23±0.68	86.96±0.55	89.45±0.43	91.09±0.62	93.45±0.45	
120	86.76±0.23	91.97±0.78	95.78±0.94	96.98±0.89	99.67±0.91	

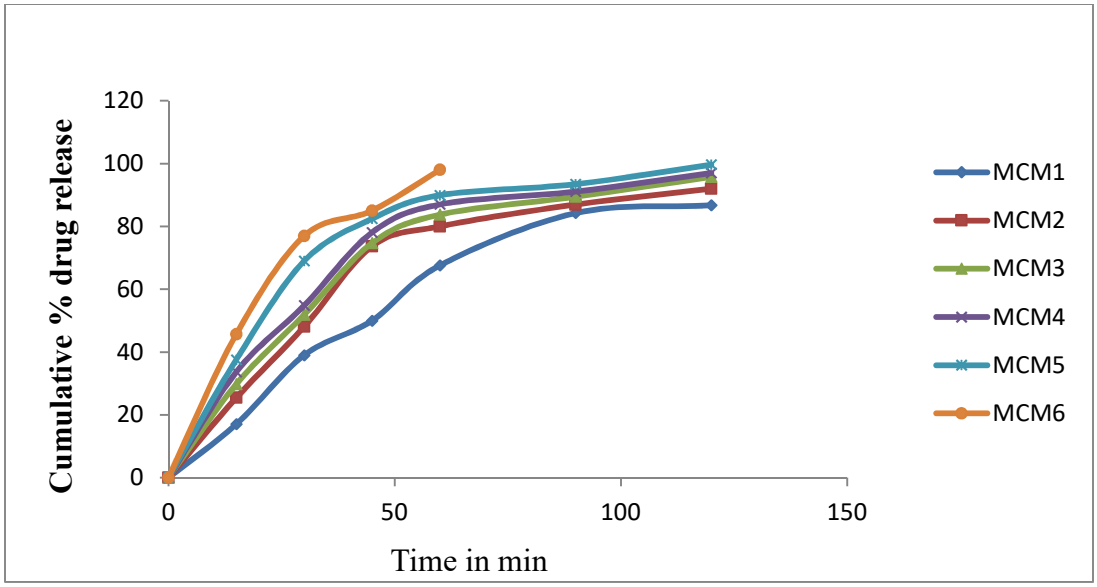

Fig.2: Comparative %drug release profile for Core granules of MCM1-MCM6 in pH 7.4 Phosphate Buffer

Table.6: Dissolution data for Core Granules in pH 6.8 Phosphate Buffer

Time(min)	Cumulative % Drug Release*(Mean± SD, n=3)					
	MCM1	MCM2	MCM3	MCM4	MCM5	MCM6
0	0	0	0	0	0	0
15	15.34±0.97	23.45±0.65	23.32±0.56	37.43±0.42	39.35±0.73	46.45±0.13
30	35.57±0.56	46.63±0.74	48.65±0.53	55.01±0.35	60.67±0.21	69.98±0.25
45	57.43±0.34	69.23±0.38	70.12±0.68	78.09±0.64	81.45±0.16	87.75±0.34
60	72.98±0.57	75.98±0.55	79.65±0.24	85.54±0.24	87.23±0.27	98.95±0.15
90	85.67±0.97	81.12±0.69	85.89±0.67	90.45±0.81	93.45±0.76	
120	87.12±0.97	93.02±0.85	94.56±0.62	95.32±0.36	99.87±0.13	

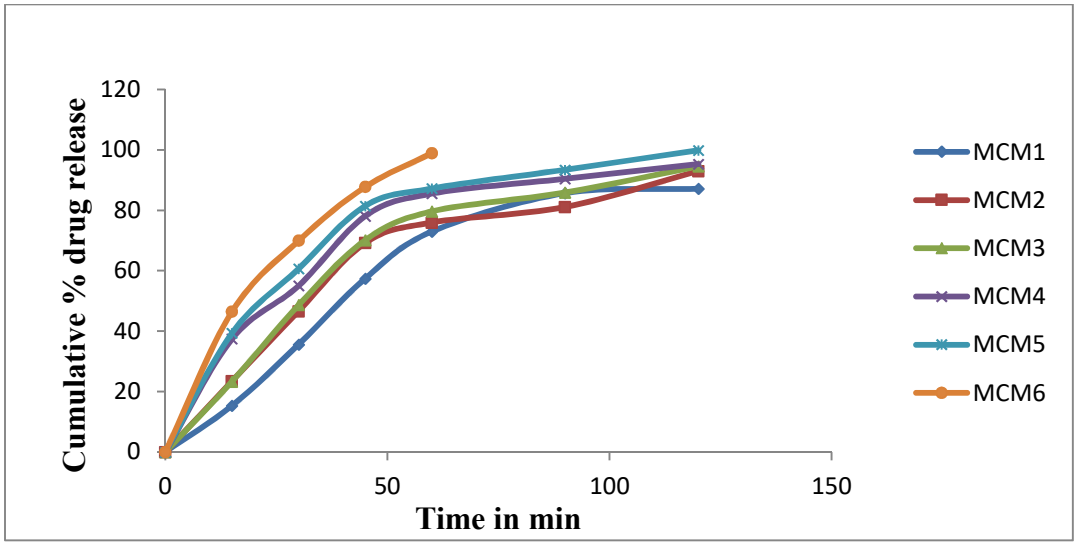

Fig.3: Comparative %drug release profiles for Core granules of MCM1-MCM6 in pH 6.8 Phosphate Buffer

1.3. Evaluation of hydrogel plug characteristics:

Hydrogel plugs were evaluated for post compression parameters like weight variation, thickness and hardness. This ranges from 98.89 ±1.15 to 101.1±0.02, 3.41±0.45 to 3.45±0.78 and 4.1±0.05 to 4.7±0.01 respectively. The results were given in the Table-7.

Table-7: Evaluation of Hydrogel plug characteristics

Hydrogel plug code	Weight variation# (mg)	Thickness* (mm)	Hardness* (kg/cm^2)	Lag time * (h)
MMC1	100±0.75	3.45±0.08	4.5±0.02	2.30
MDC2	99±0.98	3.42±0.78	4.3±0.01	2.45
MMC3	100±0.23	3.44±0.45	4.2±0.02	3.45
MDC4	98.89 ±1.15	3.45±0.78	4.7±0.01	4.15
SMC1	101.1±0.02	3.42±0.78	4.1±0.05	4.45
SDC2	100±0.23	3.41±0.91	4.3±0.98	5.15
SMC3	100±0.54	3.41±0.45	4.5±0.01	5.45
SDC4	99.5±0.65	3.42±0.91	4.7±0.01	6.00

#All Values Expressed as Mean±SD, n=10

*All Values Expressed as Mean±SD, n=3

3.4. Dissolution studies of pulsicaps:

Dissolution studies revealed that there is no effect of dissolution media on drug release.

All these 8pulsicapsules were prepared with two different polymers in two ratios 1:2, 1:3 and two diluents were used, i.e., MCC which is a hydrophilic in nature, and another one is DCP which is hydrophobic in nature.

All prepared pulsicaps have shown the desired drug release in 0.1N HCl in the first 2 h (nearly 100% release) which was first pulse.

The formulations MMC1, MDC2, MMC3, MDC4 pulsicaps prepared with Metalose 90 SH 100000 as hydrogel plug showed minimum lag time of 2 h 30 min and

maximum lag time of4 h 15 min. In these formulations the second pulse starts 6 h 30 min which is not desirable.

Formulations SMC1, SDC2, SMC3, and SDC4 prepared with sodium carboxy methyl cellulose as hydrogel plug shown maximum lag time of 6 h, which was a predetermined lag time. SDC4 formulation was optimized because of its predetermined lag time of 6 h. SDC4 formulation contains 1:3 ratio of drug: polymer and DCP as diluent. Its maximum drug release of 99.79% in first pulse which was rapid, the second pulse release was started at 8^{th} h (98.97%) and third pulse release was started at 16^{th} h (99.87%). Hence the formulation SDC4 was selected for stability studies.

During the *in-vitro* studies it was observed that the cap was dissolved within 5 min and first dose was released initially and rapidly then hydrogel plug was exposed to dissolution medium and absorbs the surrounding medium to get wetted and converted into soft mass, ejected from the capsule body and release the second pulse and same procedure was observed for release of third pulse. The formation of soft mass of hydrogel depends on its nature and amount of polymer and nature of diluents used. The results were given in the Tables-8, 9 and 7 & Figs-4 and 5.

Table 8: The *in-vitro* drug release profiles of pulsicaps formulations of Metalose 90 SH 100000.

Buffer	Time (h)	Cumulative % drug release*(Mean±SD, n=3)			
		Formulation code			
		MMC1	MDC2	MMC3	MDC4
0.1 N HCl	0.00	0	0	0	0
	0.15	23.45±1.34	21.90±0.34	19.67±2.23	24.45±0.09
	0.30	44.23±0.98	37.34±1.45	28.95±0.76	40.43±0.45
	0.45	58.67±0.67	49.98±0.56	45.76±0.56	68.09±0.28
	1.00	78.49±0.56	71.90±0.21	77.02±0.78	85.45±1.45
	2.00	99.56±0.12	98.97±0.67	99.05±0.07	99.78±0.21
pH 7.4 phosphate buffer	3.00	0	0	0	0
	4.00	0	0	0	0
	5.00	0	0	0	0
pH 6.8 phosphate buffer	6.00	0	0	0	0
	7.00	37.86±0.45	22.98±0.89	22.45±0.57	0
	8.00	75.93±0.98	69.45±0.65	69.56±0.98	62.65±1.45
	9.00	0	98.01±0.35	98.45±0.35	99.09±0.04
	10 .00	0	0	0	0
	11.00	0	0	0	0
	12.00	0	0	0	0
	13.00	0	0	0	0
	14.00	28.45±0.56	21.67±0.98	23.45±0.31	0
	15.00	73.34±0.76	63.57±0.34	69.45±0.12	49.00±3,45
	16.00	…	97.90±1.92	98.67±1.67	84.56±0.75
	16.15	…	…	…	98.69±0.78

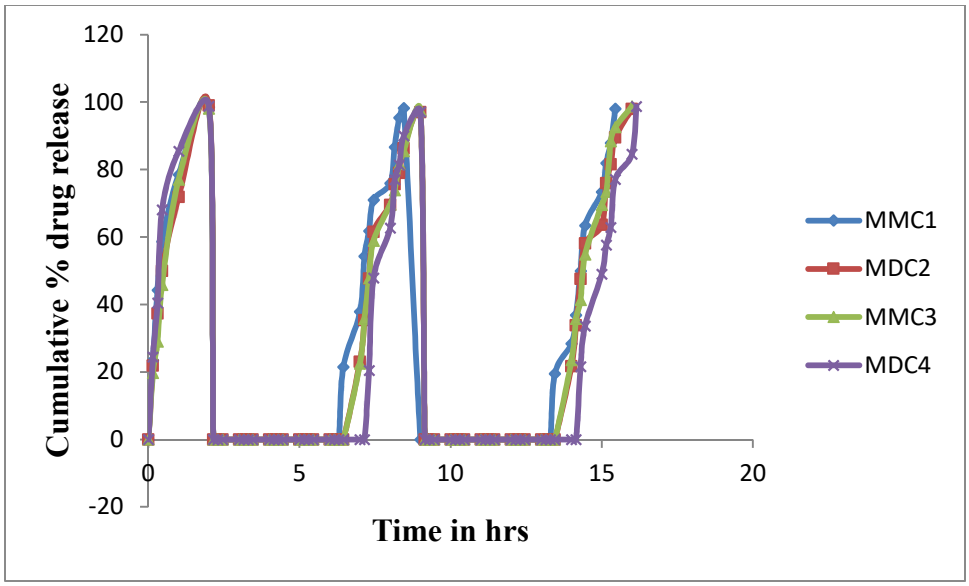

Fig.4: Cumulative % drug release profiles of Miglitol pulsicaps MMC1, MDC2, MMC3 and MMD4.

Table 9: The *In-vitro* drug release profile of Miglitol pulsicaps formulations of SMC1, SDC2, SMC3, SDC4

Buffer	Time (h)	Cumulative % drug release*(Mean±SD, n=3)			
		Formulation code			
		SMC1	SDC2	SMC3	SDC4
0.1 N HCl	0.00	0	0	0	0
	0.15	21.34±0.78	19.99±1.22	23.45±0.89	22.98±0.55
	0.30	43.57±0.57	35.78±0.76	36.78±0.23	46.56±0.45
	0.45	67.89±0.97	57.89±3.67	57.90±0.76	59.86±0,23
	1.00	76.86±0.45	83.55±0.89	85.78±0.64	87.09±0.87
	2.00	97.98±1.57	98.68±0.65	96.89±3.46	97.90±1.75
pH 7.4 phosphate buffer	3.00	0	0	0	0
	4.00	0	0	0	0
	5.00	0	0	0	0
pH 6.8 phosphate buffer	6.00	0	0	0	0
	7.00	20.98±1.55	0	0	0
	8.00	71.90±0.33	56.09±0.21	21.98±0.41	0
	9.00	98.59±0.67	86.75±2.45	67.93±0.96	57.67±0.72
	10 .00	0	0	97.01±2.67	97.87±0.92
	11.00	0	0	0	0
	12.00	0	0	0	0
	13.00	0	0	0	0
	14.00	0	0	0	0
	15.00	59.80±0.44	21.98±0.67	0	0
	16.00	85.86±0.24	66.68±0.21	22.09±0.67	0
	17.00	….	99.01±0.05	65.67±0.98	65.89±0.56
	18.00	….	….		99.87±0.23

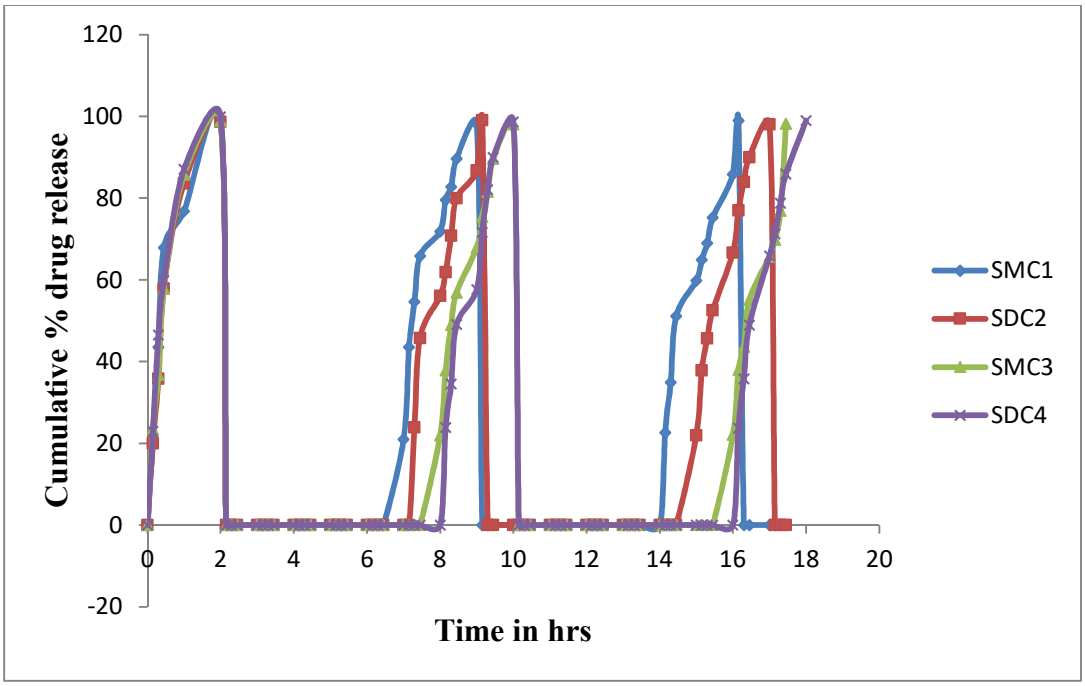

Fig.5: Cumulative % drug release profiles of Miglitol pulsicaps SMC1, SDC2, SMC3 and SMD4.

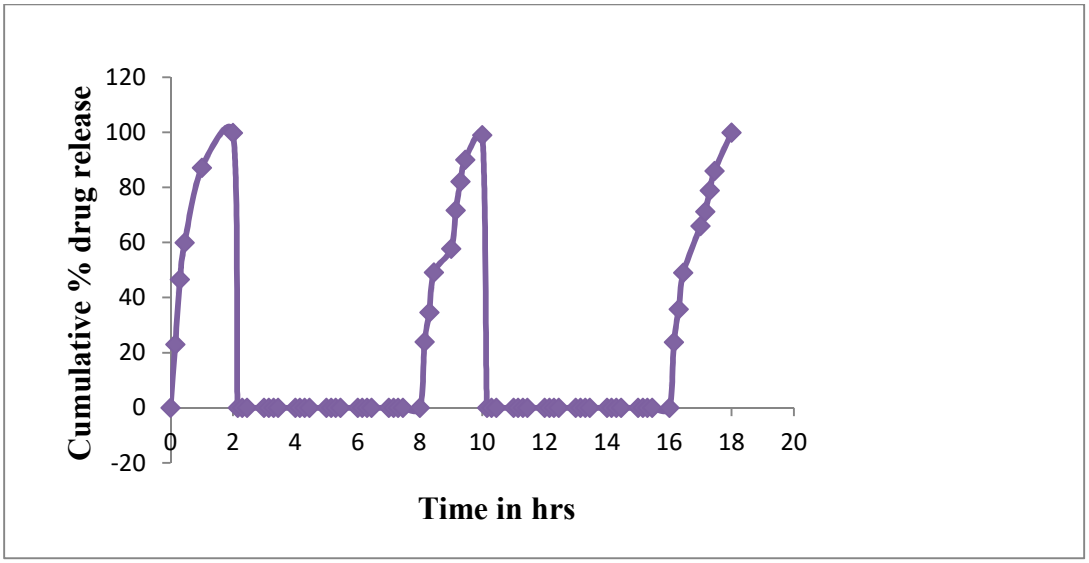

Fig.6: Cumulative % drug release of Optimized Formulation SDC4

3.5 Drug-polymer interaction studies:

3.5.1 FTIR

Miglitol FTIR spectrum contains characteristic bands at 3865cm^{-1} which is C-H bending 2816 cm^{-1} (C-H stretching) and 1589 cm^{-1}(N-H stretching). All the recorded FTIR spectra contain these characteristic bands which confirm the absence of chemical interaction between drug and polymers. The results were given in theFig.7, 8, 9,10,11,12.

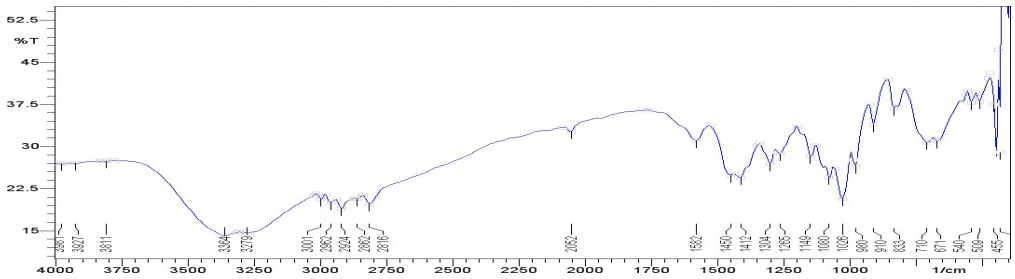

Fig.7: IR spectrum of Miglitol

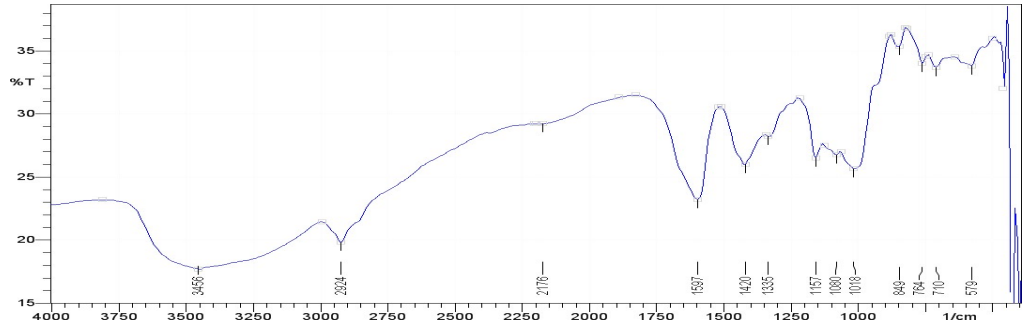

Fig.8: IR spectrum ofcrospovidone

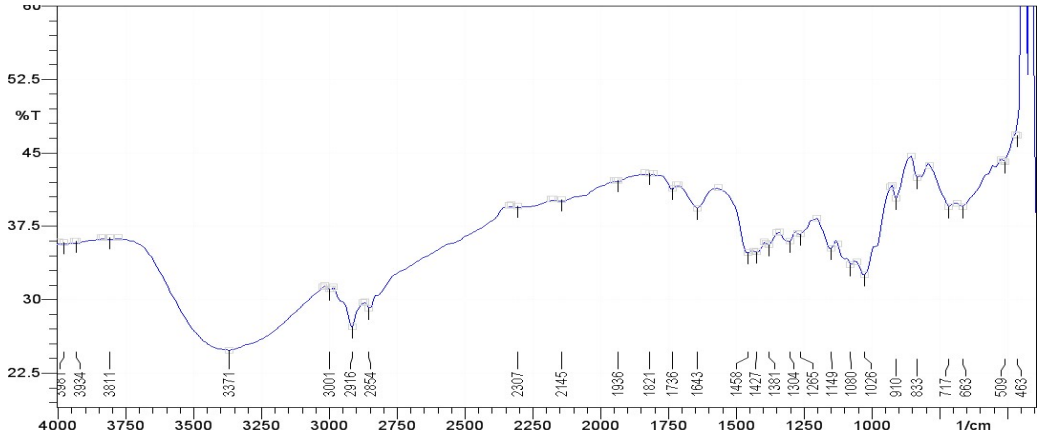

Fig.9: IR spectrum of Miglitol-MCC

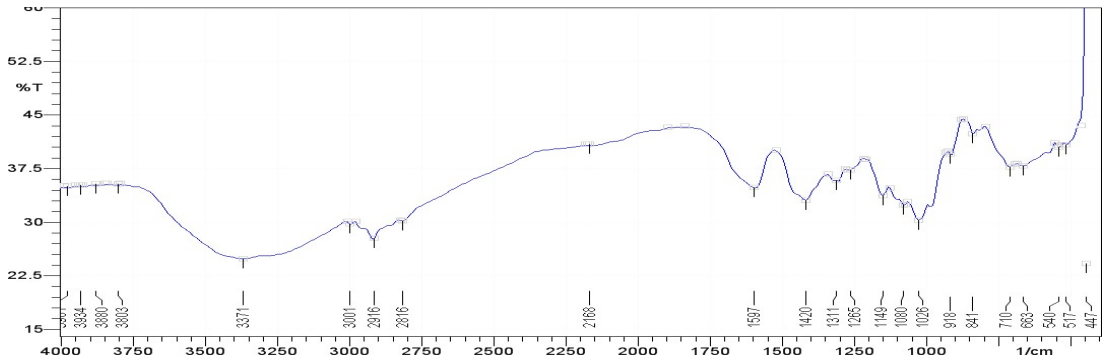

Fig.10: IR spectrum of Miglitol-CP

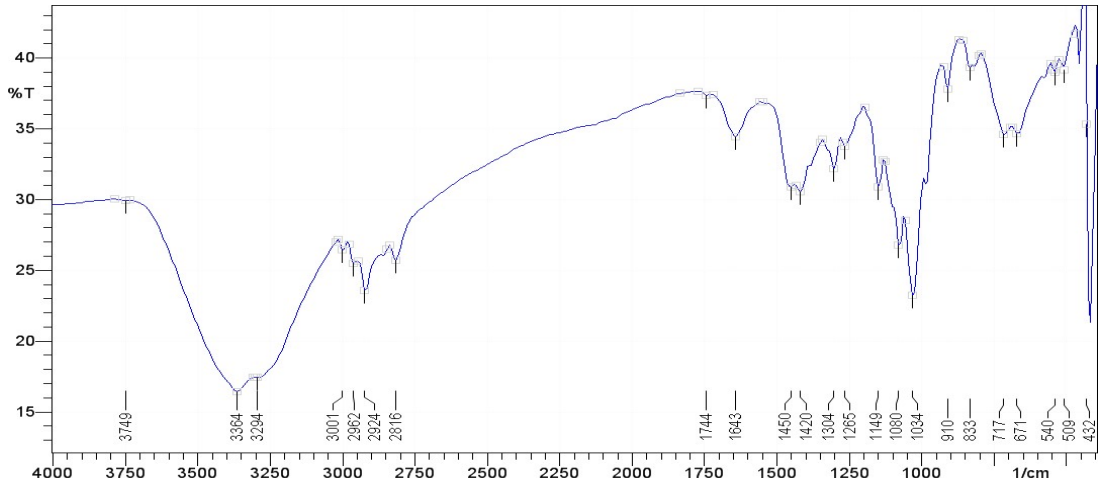

Fig.11: IR spectrum of Miglitol-sodium CMC

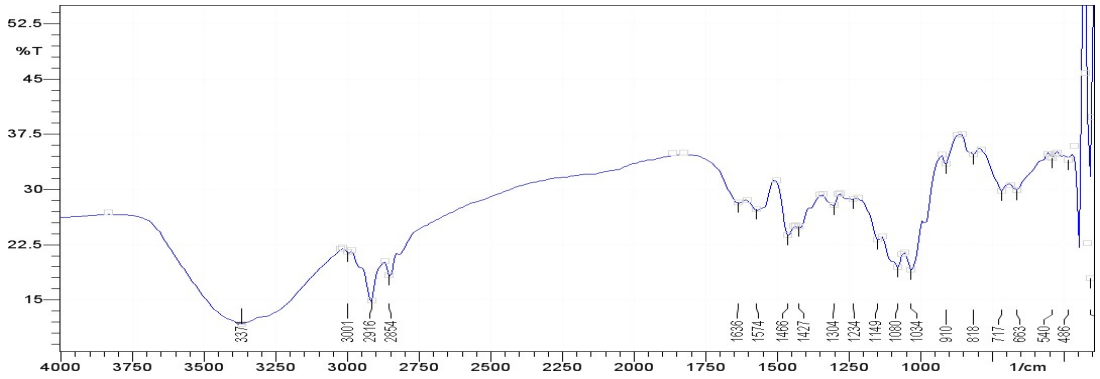

Fig.12: IR spectrum of optimized Formulation SDC4

3.5.2 DSC Analysis:

Miglitol showed a single sharp endothermic peak at 147.17˚Ccorresponding to the melting range of miglitol. Miglitol melting peak was slightly shifted to left for optimized formulation. Compared to pure drug the melting peak was broadened to some extent in the formulation which may be due to changes in crystalline form. The low melting point of the polymers might have influenced the shift in the melting point of drug in the formulation. The results were given in theFig.13, 14.

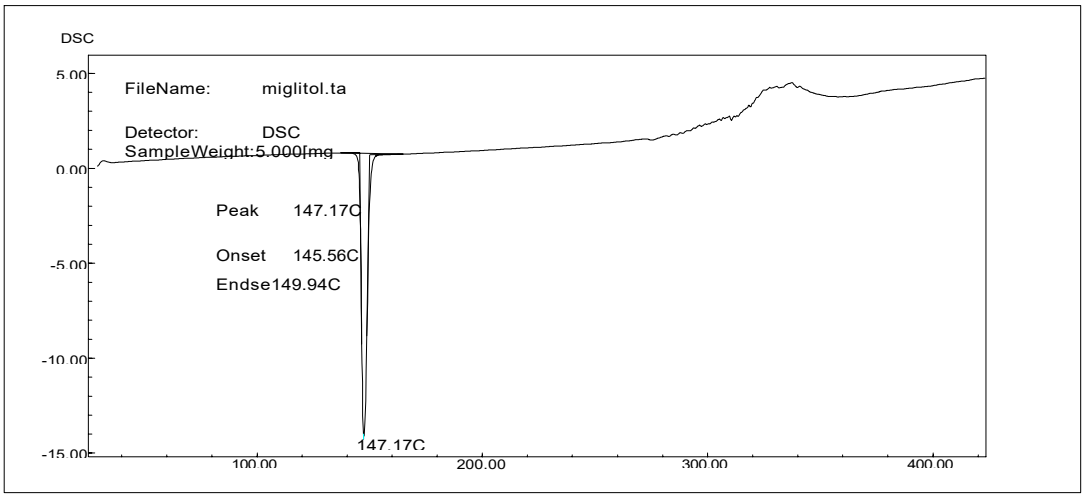

Fig.13: DSC endotherm of Miglitol pure drug

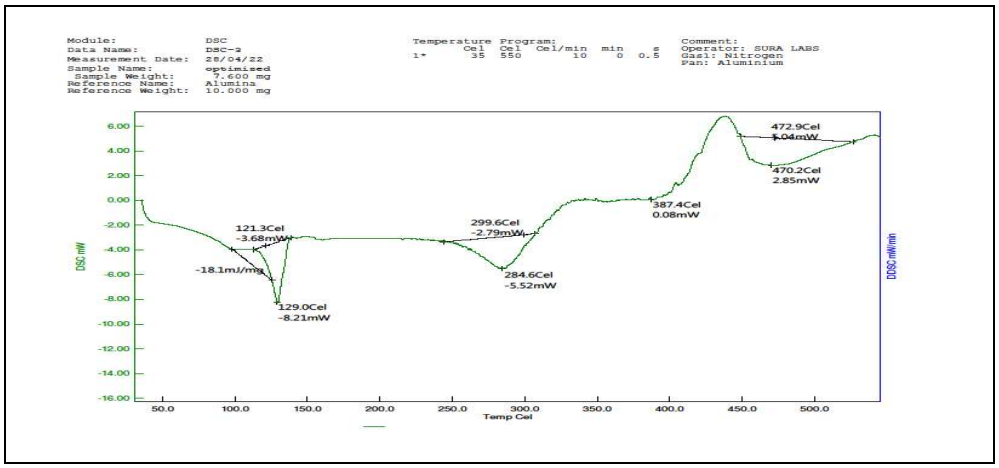

Fig.14: DSC endotherm of Optimized Formulation SDC4

3.6 Stability studies:

The optimized formulation SDC4 was subjected to accelerated stability studies at 25±2ºC/60±5% RH, 40±2ºC/74±5%RH for 6 months and monitored for the appearance, drug content and *in-vitro* drug release profile. The stored formulation was tested after 3 months and 6 months for appearance, drug content and *in-vitro* drug release profile. Based on the statistical data analysis the t-test value was found to be -2.49 which indicates that there were no significant changes in appearance, drug content and *in-vitro* profile up to six months. The results were given in the Table-10 and Fig.6

Table-10: Stability studies data for optimized formulation SDC4 before and after storage

Test	Initial	Storage condition			
		25±2°C/60±5% RH		40 ± 2ºC/75 ± 5% RH	
		3 months	6months	3 months	6months
Description	Complies	Complies	Complies	Complies	Complies
Drug content* (%)	99.98±0.2	100.03±0.3	99.42±4.13	99.28±2.25	99.11±1.23

***Mean ± SD, n=6.**

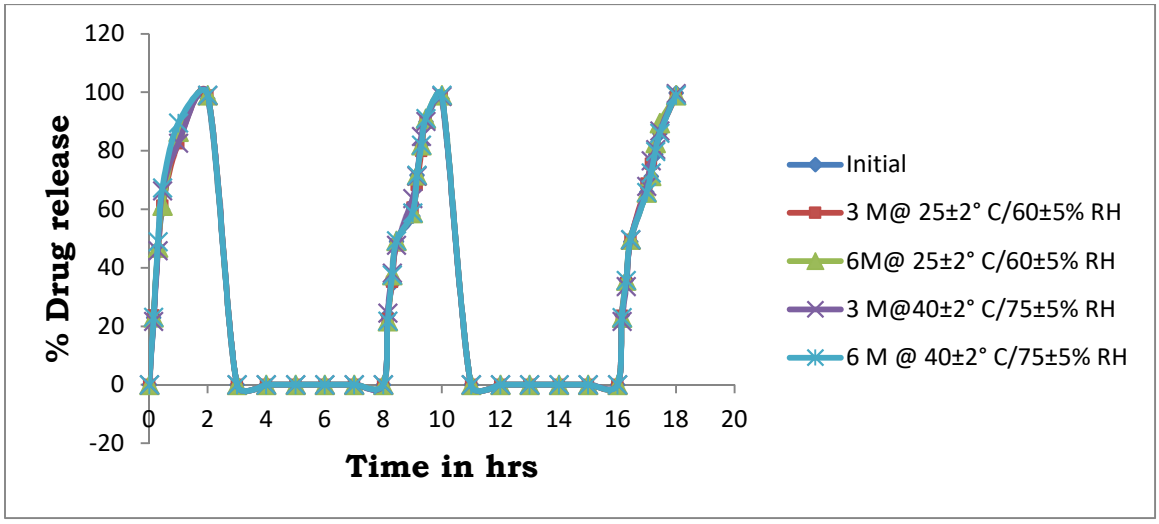

Fig.15: Comparative dissolution profiles of optimized formulation SDC4 before and after storage at 25 ± 2° C/60 ± 5% RH and 40 ± 2°C/75 ± 5% RH .

CONCLUSION

From results, it can be concluded that hydrogels offer a versatile platform for the therapy of diabetes. The prepared pulsicaps of miglitol with an aim to lower the postprandial glucose level were successful. This will provide an ideal therapeutic regimen to reduce the dose frequency with enhanced patient compliance and reduced drug toxicity. The optimized formulation (SDC4) exhibited good release profile up to 18 h with predetermined lag time of 6 h. Thus, the optimized formulation can be considered as one of the promising preparations to control the post-prandial glucose level in type-II diabetes.

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