Current Trends in Biotechnology and Pharmacy
Vol. 19(2) 2282-2293, April 2025, ISSN 0973-8916 (Print), 2230-7303 (Online)
DOI: 10.5530/ctbp.2025.2.15

Chronomodulated Therapy for the Treatment of Type II Diabetics by Using α-Glucosidasel Inhibitor

M. Sreelatha*[1], P.V. Swamy[2], P. Shailaja[3]

[1]Dept. of Pharmaceutics, Vagdevi College of Pharmacy, Gurazala, Andhra Pradesh.
[2]Dept. of Pharmaceutics, Shri Vishnu College of Pharmacy, Bhimavaram, Andhra Pradesh.
[3]Dept. of Pharmaceutics, A.U College of Pharmaceutical Sciences, Andhra University, Visakhapatnam, Andhra Pradesh.

*** Corresponding author**: msreelatha9@gmail.com

Abstract

Miglitol is an Anti-diabetic having a place with the class of α-glucosidase inhibitors, it has ability to bring down the postprandial glucose level in type-II diabetic patients. The present work was aimed to prepare miglitol pulsincaps to reduce the dose frequency and increase the patient compliance. Arrangement of pulsicapsules is associated with the four distinct stages: First stage involved preparation of immediate release granules and optimization of immediate release granules which were prepared by using crospovidone as superdisintegtrant in different conc. (MCM1-MCM6) by wet granulation method and granules were evaluated for the flow properties, drug content and *in-vitro* dissolution. Based on the results MCM5 was optimized to prepare the pulsincaps. In the second stage insoluble bodies of the capsules was prepared by treating with the formaldehyde solution. Third step was preparation of hydrogel plugs with 6 hr. lag time and the final stage was assembling of pulsincaps with three pulses of immediate release granules (MCM5) which were separated by two hydrogel plugs. The prearranged pulsincaps were assessed for *in vitro* drug release in three distinctive dissolution media. From the results CDC8 was optimized based on the predetermined lag time and drug release. Stability studies led at 40±2˚C/75±5% RH showed no note worthy changes inferring that an effective pulsatile drug delivery system of Miglitol was designed.

Keywords: Miglitol, α-glucosidase inhibitor, Pulsincaps, Crospovidone, Accelerated stability Studies.

Introduction

Most convenient route of drug administration is oral route due to its large surface area. Conventional drug delivery approaches are afflict by issues pertaining to the systemic toxicity and repeated dosing (1).

The classical drug delivery system has many limitations such as (2); (i) An improper time of drug release, (ii) Ultimate side effects on the body.

To avoid the all above snags and to meet the following requirements like: (i) Improve the site-specific targeted drug delivery, (ii) Correlation of the drug release process with the patient circadian rhythm, (iii) A careful control delivery of the highly toxic drugs, (iv) Use of more drugs in one system like pulsatile and controlled release drug delivery systems.

In the instances mentioned above, it is

better to optimize the drug release from a dosage form that will supply the necessary drug concentration at a certain time only (3).

Nonetheless, in the field of present day's drug treatment, developing considerations have been centered around pulsatile delivery of the drug for which ordinary controlled drug release framework with a ceaseless delivery are not great but rather a requirement for a beat of remedial focus in the intermittent way goes about as a push for the improvement of "Pulsatile Drug Delivery System''. In these systems a predetermined amount of the drug was released rapidly and transiently within short time period following a predetermined lag time (3).

Diabetes mellitus (DM) is one of the most serious health crises of the 21st century, and the majority of ministries and public health authorities are focusing on the disease's contemporary impact and consequences. Only in 2012, it was reported that at least 1.5 million people died as a results of diabetes. Diabetic patients are estimated to number around 642 billion by 2040 (4).

Diabetes mellitus necessitates long term therapy with medications such as sulfonylureas, which may harm the pancreas quickly with the immediate release dosage form. Finally, medicines that cause tolerance should not be given at a constant rate because the drug's effect dimishes at a constant dose level. Furthermore, when a drug level is kept constant, drug toxicity may grow with the time. In some instances, it is advisable to use a dosage form that will deliver the desired medication concentration at a certain time point only (5).

Miglitol (6) is a newer class of α- glucosidase inhibitor which is derived from 1- deoxy-nijirimycin structurally related to glucose. It is completely absorbed from GI tract with fewer side effects when compared to the acarbose.

MGL competitively inhibits the glycosidase at the small intestine brush borders, which is responsible for the breakdown of the complex polysaccharides in to simple glucose. This results in decrease in the postprandial glycaemia. Due to its short biological half-life (2-3 h), there is a need to develop pulsatile drug delivery system which can overcome its multi-dosing per a day and to increase the patient compliance, and reduce drug toxicity.

Materials and Methods

Material

MGL was obtained as gift sample from Mylan laboratories limited, Kazipally, Hyderabad, India. Crospovidone and Aerosil from Otto Chemical biochemika reagents. Mumbai. Metalose was a gift from Signet Chemical Corporation Pvt. Ltd, Mumbai. Sodium Carboxy Methyl Cellulose was obtained from Excel Fine Chemical, A.P., Magnesium Stearate was obtained from S.D Fine Chem Ltd, Mumbai, Methanol and other reagents used were standard analytical grade.

Methods

Formulation and evaluation of miglitol immediate release granules:

Miglitol immediate release immediate release granules were prepared by wet granulation process, by using various proportions of crospovidone as superdisintegrant were added to MGL and MCC along (3% w/v 50% methanol) to get the wet mass. The coherent mass was passed through the sieve no.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 poly-bag for further use. Formulation of MGL immediate release core granules was given in the Table-1.

Current Trends in Biotechnology and Pharmacy
Vol. 19(2) 2282-2293, April 2025, ISSN 0973-8916 (Print), 2230-7303 (Online)
DOI: 10.5530/ctbp.2025.2.15

Table -1: Different formulations of Miglitol immediate release granules

Ingredientsiforigranulesiinimg	Formulation code					
	MCM1	MCM2	MCM3	MCM4	MCM5	MCM6
Miglitol	25	25	25	25	25	25
Crospovidone	0	2	4	6	8	10
Micro crystalline cellulose ((MCC)	42	40	38	36	34	32
PVPiK30	5	5	5	5	5	5
Methanol	Qs	Qs	Qs	Qs	Qs	Qs

Flow properties of granules

Bulk density (7)

It is mathematically expressed as:

$$\text{Bulk density} = \frac{\text{Weight of thr granules (w)}}{\text{Bulk volume of the granules } (V_0)}$$

Procedure

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

Hausner's ratio (8)

The hausner's ratio <1.25 show free flowing of granules and > 1.25 indicates poor flow properties of granules.

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

Carr's compressibility index (8)

It indicated the compressibility of powder or granules. Powder or granules which have smaller the Carr's index value it has good compressibility.

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

Angle of repose (9)

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

$$\tan \theta = \frac{h}{r}$$

Where
θ = Angle of repose
h = height of pile
r = Radius of the base of the pile

Drug content (9)

Drug content was measured by dissolving the 10 mg of granules in 10 ml methanol and the solution was filtered and 1 ml filtrate was diluted with suitable dissolution medium. The diluted sample absorbance was measured at 210 nm using UV-Visible spectrophotometer. The results were given in the Table-3.

In-vitro Dissolution studies of immediate release granules (9)

Immediate release granules dissolution studies were carried out by using USP II dissolution apparatus (Dissolution model: 8 VDA). The test was carried out by taking granules equivalent 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 2 h and paddles were rotated at a speed of 75

rpm. A sample of 5 ml dissolution medium was withdrawn at predetermined time interval (5, 10, 15, 30, 45, 60, 90 and 120 min). Samples were suitably diluted and analyzed UV-Visible spectrophotometer at 210 nm. Three trails were done and mean % drug release was calculated.

Preparation of Pulsincaps

Solubility modification of hard gelatin capsules (10)

About 200 capsules of '0' size were taken. Bodies and caps were separated. The separated bodies were kept on the wire mesh placed in the desiccator 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 vapours 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 poly bags for future use.

Evaluation of treated bodies (11)

Qualitative Analysis for formaldehyde content

Preparation of formaldehyde standard solution

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

Preparation of test sample

Twenty five treated bodies were taken and cut into small pieces and dissolved in 40 ml of distilled water 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 4 ml of distilled water and 5 ml of 99.5% v/v acetyl acetone were added. Then this solution was heated for 40 min at 40˚C. At the same time 1 ml 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.

Preparation of hydrogel plugs (12)

Two polymers like Metalose 90SH 4000, 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 ratios, 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 6 mm 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/ Plug	Metalose 90 SH 4000	Sodium CMC	MCC	DCP	Aerosil	Magnesium stearate	Total Wt Ofi plug mg
MMC1	50	….	48	….	1	1	100
MDC2	50	….	….	48	1	1	100
MMC3	75	….	23	….	1	1	100
MDC4	75	….	….	23	1	1	100
CMC5	….	50	48	….	1	1	100
CDC6	….	50	….	48	1	1	100
CMC7	….	75	23	….	1	1	100
CDC8	….	75	….	23	1	1	100

Physicochemical characterization of Hydrogel plugs (13)

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.

Preparation of pulsicapsules (14)

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 pulsicapsules. Then the pulsicapsules 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 pulsicapsules contained three doses of Miglitol granules and two hydrogel plugs.

***In-vitro* dissolution studies of pulsicapsules (15)**

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 were goes into intestine which having the basic pH. Then pH 7.4 phosphate buffer (900 ml) was used for next 3 h transit time of small intestine. After 3 h 7.4 buffer was replaced with pH 6.8 phosphate buffer to maintain the colonic pH for remaining 13 h. Paddles were rotated at 75 rpm and temperature was maintained at 37±0.5˚C. 5 ml of sample was withdrawn from the dissolution basket and replaced with the same volume with respective dissolution medium to maintain the sink conditions. Samples were analyzed at 210 nm by using UV-Visible spectrophotometer.

Stability studies (16)

Stability studies were conducted to predict the shelf life of a product. The optimized formula was exposed to different conditions in stability chamber and analyzed for appearance, drug content and *in-vitro* dissolution drug release. The obtained results were compared with initial month results.

Results and Discussion

Flow properties of 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 in the range of 99.26 ± 0.82 to 99.85 ± 0.11 and results were given in the Table 3.

In-vitro Dissolution studies of immediate release 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 the Tables 4, 5 & 6 and Figures 1, 2 &3.

Table 3: Flow properties of immediate release core granules:

Formulation Code	Bulk density (g/cm³)	Tapped density (g/ml)	Compressibility Index (%)	Hauser's ratio	Angle ofi 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

All values were expressed mean±s.d., n=5

Table 4: The *in vitro* drug release profile for immediate release granules in 0.1N HCl

Time (min)	Cumulative% Drug Release*					
	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	

All values were expressed as mean±s.d., n=3

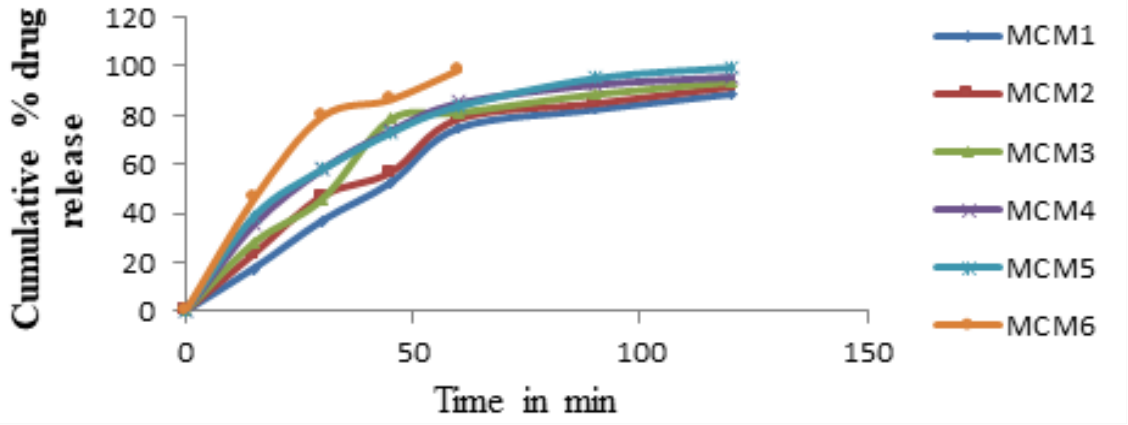

Fig.1: Comparative %drug release profile for immediate release granules of MCM1-MCM6 in 0.1N HCl

Table 5: The *in-vitro* drug release profile for immediate release granules in pH 7.4iPhosphateiBuffer

Time (Min)	Cumulative % Drug Release*					
	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	

All values were expressed as mean±s.d., n=3

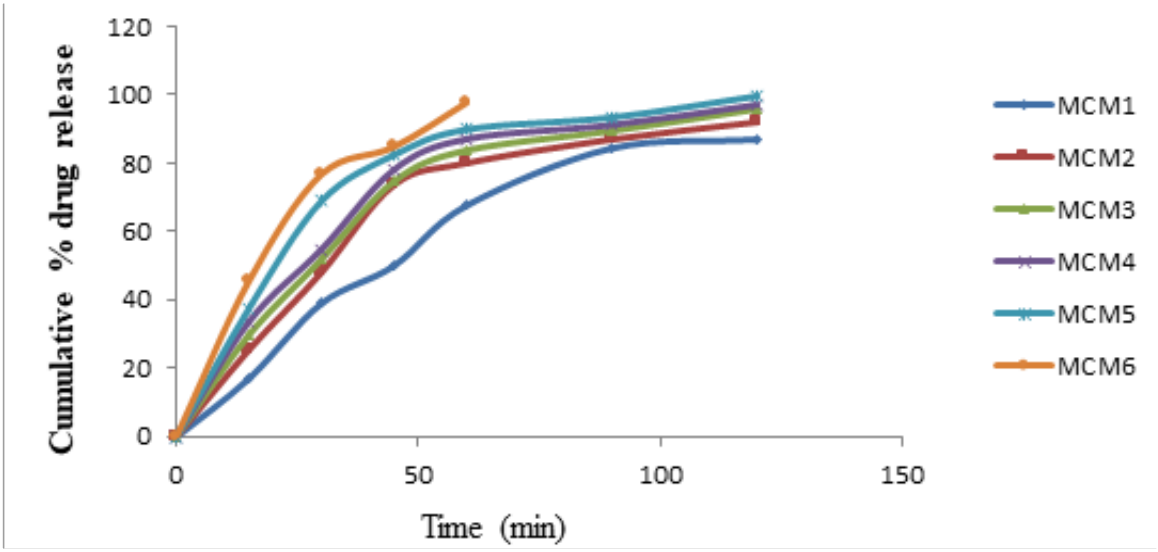

Fig.2: Comparative % drug release profile for immediate release granules of MCM1-MCM6 in pH 7.4iPhosphateiBuffer

Table 6: The *in-vitro* drug release profile for immediate release granules in pH 6.8 Phosphate Buffer

Time (min)	Cumulative % Drug Release*					
	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	

All values were expressed mean±s.d., n=3

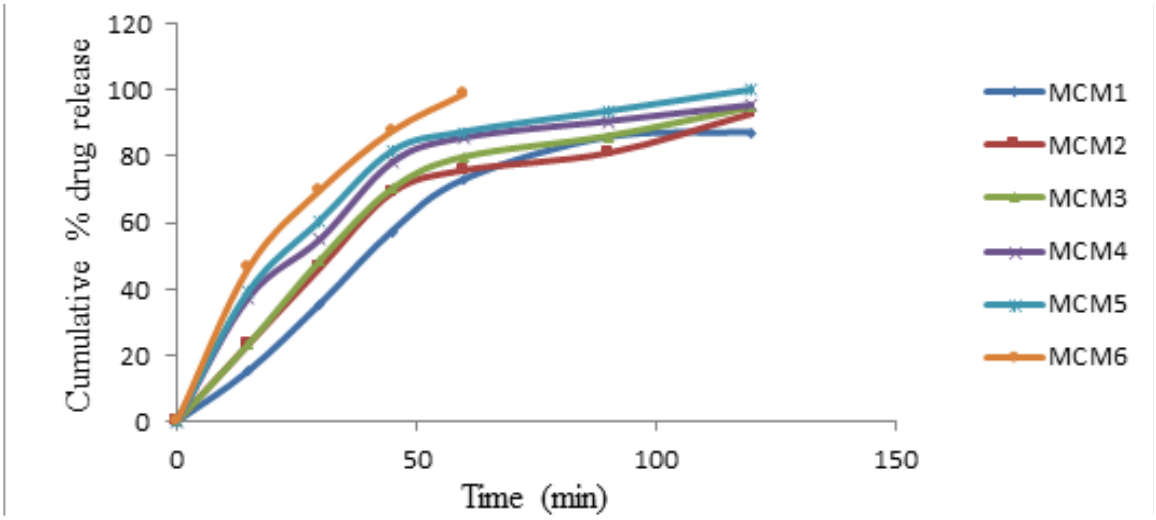

Fig.3: Comparative %drug release profile for immediate release granules of MCM1-MCM6 in pH 6.8iPhosphateiBuffer

Post compression characterization of hydrogel plugs:

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 ofihydrogeliplugs

Hydrogel plug code	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm²)	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
CMC5	101.1±0.02	3.42±0.78	4.1±0.05	4.45
CDC6	100±0.23	3.41±0.91	4.3±0.98	5.15
CMC7	100±0.54	3.41±0.45	4.5±0.01	5.45
CDC8	99.5±0.65	3.42±0.91	4.7±0.01	6.00

All values were expressed as mean±s.d., n=6

*All values were expressed as mean±s.d., n=3

Pulsincaps In-vitro dissolution studies:

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

All these 8 pulsincaps 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 pulsicapsules shown the desired drug release in 0.1N HCl for first 2 h, nearly 100% release which was first pulse.

The formulations MMC1, MDC2, MMC3, MDC4 pulsicapsules prepared with Metalose 90 SH 4000 as hydrogel plug shows minimum lag time of 2 h 30 min and maximum lag time of 4 h 15 min. In these formulations the second pulse starts 6 h 30 min which is not desirable.

Formulations CMC5, CDC6, CMC7, and CDC8 prepared with sodium carboxy methyl cellulose as hydrogel plug shown maximum lag time of 6 h, which was a predetermined lag time. CDC8 formulation was optimized because of its predetermined lag time of 6 h. CDC8 formulation contains 1:3 ratio of drug: polymer and DCP as diluents. Its maximum drug release of 99.79% in first pulse which was rapid, the second pulse release was started at 8th h (98.97%) and third pulse release was started at 16th h (99.87%). Hence the formulation CDC8 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 & Figures 4 and 5.

Table 8: The *in vitro* drug release profiles of pulsincaps formulations Metalose 90 SH 4000.

Buffer	**Time(h)**	**Cumulative % drug release***			
	Formulation code				
	MMC1	**MDC2**	**MMC3**	**MMD4**	
0.1 N HCl	0	0	0	0	0
0.15	38.87±0.27	35.98±0.24	31.09±0.45	36.76±0.57	
0.30	57.96±0.98	49.34±0.46	48.87±0.65	51.97±0.34	
0.45	72.98±0.67	71.29±0.89	60.88±0.45	68.34±0.75	
1	83.88±0.56	85.93±0.32	85.83±0.56	81.08±0.72	
2	99.37±0.43	99.23±0.78	99.23±0.82	99.45±0.21	
pH 7.4	3	0	0	0	0
phosphate	0	0	0	0	
buffer	37.56±0.89	20.78±0.98	0	0	
4					
5					
pH 6.8	6	82.92±0.45	64.96±1.22	15.47±2.42	0
phosphate	0	99.01±0.98	65.24±2.34	35.76±2.34	
buffer	0	0	99.45±0.43	66.35±0.76	
7	0	0	0	0	
8	40.67±2.45	22.34±1.09	0	0	
9	81.89±0.34	65.92±0.56	0	0	
10	….	99.57±0.53.	26.45±1.56	0	
11	….	….	63.45±1.09	37.97±1.45	
12	14	….		78.9±0.21	69.99±0.21
13	14.15	….	….	98.97±0.98	76.98±0.56
	14.30	….	….		87.90±0.78
	14.45	….	….		98.68±0.96

Allivaluesiwereiexpressedias mean±s.d., n=3

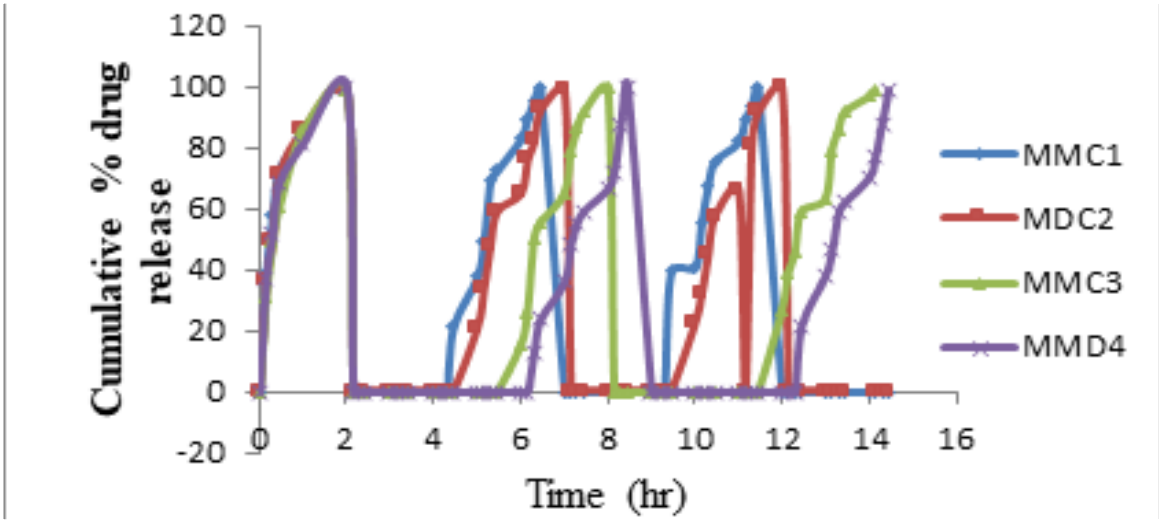

Fig.4: Cumulative % drug release profile of Miglitol pulsicapsules formulations MMC1, MDC2, MMC3, MDC4.

Table 9: The *in-vitro* drug release profile of pulsicapsule of formulations sodium carboxy methylcellulose

Buffer	**Time (h)**	**Cumulative % drug release***			
		Formulation code			
		CMC5	**CDC6**	**CMC7**	**CDC8**
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

*All values are expressed as Mean ± SD, n=3

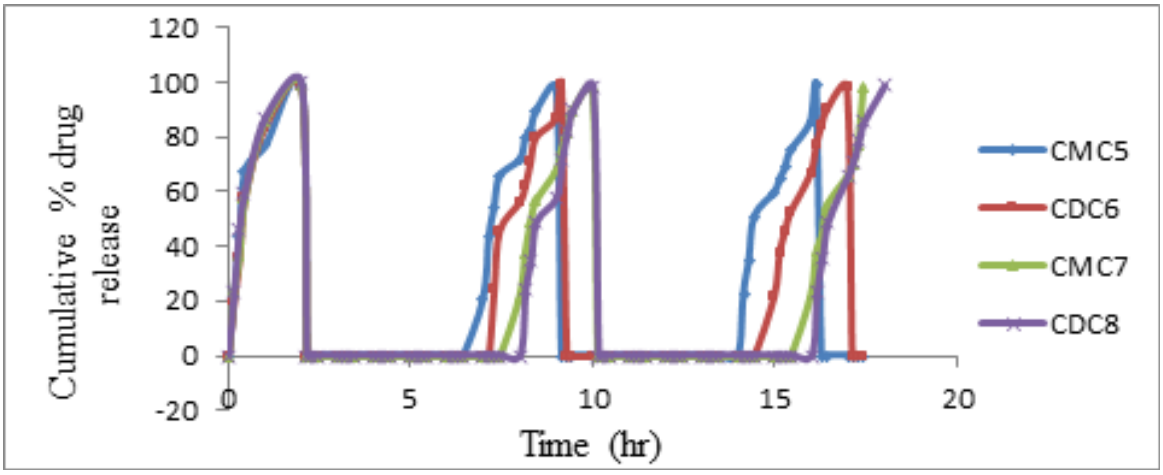

Fig.5: Cumulative % drug release profiles of miglitol pulsicapsules CMC5, CDC6, CMC7, and CDC8.

Stability studies:

The optimized formulation CDC8 was subjected to accelerated stability studies at 25±2º C/60±5% RH, 40±2º C/74±5% RH for 6 months and monitored the appearance, drug content and *in-vitro* drug release profile. The stored formulation tested after 3 months and 6 months for appearance, drug content and *in-vitro* profile. There were no note-worthy changes in appearance. Based on the statistical data analysis the t-test value was found to be -2.49 which indicate there was no significant changes in 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 CDC8 before and after storage

Test	**Initial**	**Storage conditions**			
		25±2ºC/60±5% RH		**40±2ºC/74±5%RH**	
		3 months	**6 months**	**3 months**	**6 months**
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

All values were expressed as mean±s.d., n=6.

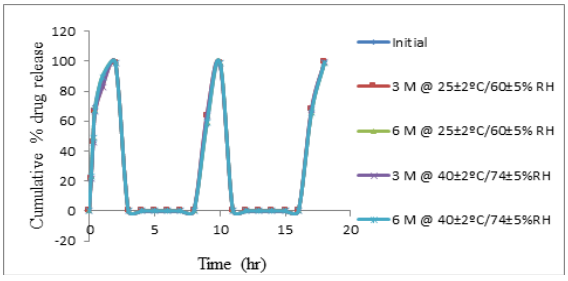

Fig.6: Comparative dissolution profiles of optimized formulationCDC8 before

And after storage at 25±2ºC/60±5% RH, 40±2ºC/74±5%RH

Conclusion:

From the present studies it can be concluded that the prepared Miglitol pulsicapsules has displayed promising *in vitro* characteristics. This will provide an ideal dosage regimen to reduce the dose frequency and drug toxicity with more patient compliance. The CDC8 (optimized formulation) has the 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 postprandial glucose level in type-II diabetes.

References:

1. Nokhodchi A, Raja S, Patel P, Asare-Addo K. The role of oral controlled release matrix tablets in drug delivery systems. BioImpacts: BI. 2012;2(4):175-87. doi: 10.5681/bi.2012.027.
2. Li J, Mooney DJ. Designing hydrogels for controlled drug delivery. Nature Reviews Materials. 2016;1(12):1-7. doi: 10.1038/natrevmats.2016.71.
3. Survase S, Kumar N. Pulsatile drug delivery: Current scenario. CRIPS. 2007; 8(2):27-33
4. Mehmet EO, Ioannis DK, Panoraia IS. Diabetes Mellitus: A Review on Path physiology, Current Status of Oral Medications and Future Perspectives. Acta Pharm. Sci. 2017, 55(1),61-82. DOI: 10.23893/1307-2080.APS.0555
5. Pozzi F, Furlani P, Gazzaniga A, Davis SS, Wilding IR. The time clock system: a new oral dosage form for fast and complete release of drug after a predetermined lag time. Journal of controlled release. 1994; 31(1):99-108. doi.org/10.1016/0168-3659(94)90255-0.
6. Reddy, V. S., Sahay, R. K., Bhadada, S. K., Agrawal, J. K., &Agrawal, N. K. Newer oral anti-diabetic agents. Journal, Indian Academy of Clinical Medicine. 2000;1(3);245-251. doi: 10.1007/s11739-011-0677-5.https://www.scribd.com/document/522301984/02.
7. Indian Pharmacopoeia New Delhi, Ministry of Health and Family Welfare, Govt. of India, Controller of publications, vol.-II, 1996; Page No. 734-736.
8. Banker GS, Anderson NR. Tablets. In: Lachman L, Liberman HA, Kanig JL. eds. The Theory and Practice of Industrial Pharmacy. Mumbai, India Varghese Publishing House; 1987:293–345.
9. 9. United States Pharmacopoeia 29-NF 24.The Official Compendia of Standards. Asian ed. Rockville, MD: United States Pharmacopoeia Convention Inc. (2006), 2679-2681.
10. Krögel I, Bodmeier R. Pulsatile drug release from an insoluble capsule body controlled by an erodible plug. Pharmaceutical research. 1998;15(3):474-81. doi: 10.1023/a:1011940718534.
11. Sandeep M, Kishore VS, Sudheer B, Ershad S, Adithya K. Design and development of chronopharmaceutical drug delivery of lansoprazole. Asian Journal of Pharmaceutical Research and Development.2013 Sep 1:63-70.
12. Shamima Nasrin Ashima Aziz, Mohiuddin Ahmed Bhuiyan. Design, formulation and in vitro evaluation of sustained release pulsatile capsule of metoprolol tartrate, IJPSR 2015; 6(7): 2755-2761.doi:10.13040/IJPSR.0975-8232.6(7).2755-61. https://www.researchgate.net/publication/279479968
13. Ashwini, M., & Ahmed, M. G. Design and evaluation of Pulsatile drug delivery of Losartan Potassium. Dhaka University Journal of Pharmaceutical Sciences 2014; 12(2): 119–123. https://doi.org/10.3329/dujps.v12i2.17610.
14. Ross AC, Macrae RJ, Walther M, Stevens HN. Chronopharmaceutical drug delivery from a pulsatile capsule device based on programmable erosion.Journal of pharmacy and pharmacology. 2000; 52(8):903-9. doi: 10.1211/0022357001774787.
15. 15..Sai Krishna MV, Saikishore V, Sravani SL, Rudrama Devi G. Design and characterization of pulsatile drug delivery of metaprolol tartrate. Indo Am J P Sci, 2017. 2017; 04(05):1052-1059. DOI:10.13040/IJPSR.0975-8232.11(1).358-64
16. ICH Harmonized Tripartite guidelines on “Stability Testing of New Drug Substances and Products Q1A(R2)”,6 February, 2003.