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CELLULOSE ETHER HYDROGELS AS POTENTIAL CARRIERS FOR PULSATILE DRUG DELIVERY SYSTEM

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ABSTRACT: Hydrogels are cross-linked polymers with the capacity to bulge in an aqueous medium. Because of their extraordinary properties, these are utilized as brilliant drug delivery vehicles that particularly necessitate focusing on the drug to specific sites. On account of the eminent hydration and biocompatibility properties generally utilized in pharmaceutical field, especially cellulose derivatives. In oral medication, many advanced technologies are introduced. More recently pulsatile drug delivery system is meant for the release of drug followed by a predetermined lag time, which is an emerging approach in chronotherapeutics. In the current research work intended to formulate the pulsicapsules of miglitol by utilizing hydrogel plugs which were prepared by cellulose ethers like ethyl cellulose and sodium carboxymethyl cellulose in ratios of drug: polymer, *i.e.*, 1:2, 1:3. Zero size capsule bodies were treated with formaldehyde to adjust the solubility of capsules and pulsicapsules were prepared by filling the bodies with three dosages of immediate release granules of miglitol which were separated by two hydrogel plugs and closed with an untreated cap. The assembled pulsi capsules were assessed for *in-vitro* drug release in three diverse dissolution media. From the results, HP8 formulation (with the hydrogel plug composition of sodium carboxymethyl cellulose and dicalcium phosphate in 1:3 ratio) was optimized depending on the drug release pattern and predetermined lag time. At 40±2˚C/75±5% RH, accelerated stability studies were conducted and it showed no remarkable changes concluding that miglitol pulsicasules was developed successfully.

INTRODUCTION: Water with a cross-linked polymer network makes up hydrogels. Hydrogels have a solid-like appearance due to the cross-linked polymer network and can have various mechanical properties.

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Hydrogel features such as biocompatibility and environmental friendliness allow it to be employed in a wide range of applications. Recent advances in materials and processes hydrogel technology have allowed it to become more innovative to suit specific applications [1].

The pharmaceutical field has progressed in treating human disease, with the most recent triumph being drug administration using hydrogel as a carrier. The invention of these carriers allowed drugs to be delivered to target organs safely and without

causing harm [2]. 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 diminishes at a constant dose level. Furthermore, drug toxicity may grow with time when a drug level is kept constant. Sometimes, it is advisable to use a dosage form that will deliver the desired medication concentration at a certain time point only [3]. This type of disease needs a pulse of therapeutic concentration in a periodic manner because conventional controlled drug-release systems with a continuous release are not ideal. This a push for the development of "Pulsatile Drug Delivery Systems". Miglitol (MGL) [4] is a newer class of α- glucosidase inhibitors that is derived from 1- deoxynijirimycin structurally related to glucose. It is completely absorbed from GI tract with fewer side effects when compared to acarbose. MGL competitively inhibits the glycosidase at the small intestine brush borders, which is responsible for the breakdown of the complex polysaccharides into simple glucose; resulting in a decrease in the postprandial glycaemia. Due to its short biological half-life (2-3h), there is a need to develop a Chrono-therapeutics drug delivery system that can overcome its multi-dosing per day, increase patient compliance, and reduce drug toxicity.

MATERIALS AND METHODS:

Material: MGL gift sample was obtained from Mylan Laboratories Limited, Kazipally, Hyderabad, India. Crospovidone and Aerosil from Otto Chemical Biochemikareagents, Mumbai. India. Metalose was a gift from Signet Chemical Corporation Pvt. Ltd, Mumbai. Sodium carboxy-methylcellulose was procured from Excel Fine Chemicals, Andhra Pradesh, India. Magnesium tea rate was obtained from SD Fine Chem Ltd., Mumbai, India. Other reagents were standard analytical reagents grade.

Methods:

Preparation of Hydrogel Plugs [5]: Two polymers like, ethyl cellulose, and sodium carboxy-methylcellulose, were initially selected for the preparation of hydrogel plugs which were swellable polymers. The polymers were taken in two different drugs: polymer ratios, i.e., 1:2, 1:3, and these polymers were mixed with two diluents Di calcium phosphate (DCP) and microcrystalline cellulose (MCC).

To this, magnesium stearate and Aerosil were added to increase the flow properties of the powder and it was directly compressed with 6mm flat round punches in a tablet punching machine. Different formulations of hydrogel plugs are given in **Table 1.**

TABLE 1: DIFFERENT FORMULATIONS OF HYDROGEL PLUGS

Ingredients mg/tablet plug	Ethylcellulose	Sodium CMC	MCC	DCP	Aerosil	Magnesium stearate	Total Wt of plug
HP1	50	….	48	….	1	1	100
HP2	50	….	….	48	1	1	100
HP3	75	….	23	….	1	1	100
HP4	75	….	….	23	1	1	100
HP5	….	50	48	….	1	1	100
HP6	….	50	….	48	1	1	100
HP7	….	75	23	….	1	1	100
HP8	….	75	….	23	1	1	100

Physicochemical Characterization of Hydrogel Plugs [6]:

Weight Variation: Twenty hydrogel plugs were taken and the test was conducted according to IP standard procedure.

Thickness: Vernier caliper was used to measure the thickness of the hydrogel plugs.

Hardness test: The plugs hardness was measured using Monsanto's hardness tester and expressed in kg/cm [2].

Miglitol Immediate Release Granules Formulation and Preparation: Wet granulation method was used to prepare miglitol immediate release granules.

Various proportions of crospovidone as superdisintegrant were added to MGL and MCC (3% w/v PVP K30 in 50% methanol) to get the wet mass. The coherent mass was passed through sieve no. 22 (IP Standard) and the granules were dried at 60˚C for one hour using a 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 **Table 2.**

TABLE 2: DIFFERENT FORMULATIONS OF MIGLITOL IMMEDIATE RELEASE CORE GRANULES

Ingredients for granules in mg	Formulation code					
	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

Flow Properties of Granules [7]:

Bulk Density [7]: It is mathematically expressed as:

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

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

Hausner's Ratio [8]: The Hausner's ratio is a number that is correlated to the flow ability of a powder or granular material. The Hausner's ratioless than 1.25 indicates the 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 [7]: It indicates the compressibility of powder or granules. Powder or granules which have smaller Carr's index value (< 15) have good compressibility.

Carr's 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 [8]: 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 conical pile, r = Radius of the base of the conical pile

Drug Content [8]: 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 are given in **Table 3.**

***In-vitro* Dissolution Studies of Immediate Release Core Granules [9]:** Dissolution studies of immediate-release core granules were carried out by using the USP II dissolution apparatus (Veego Model: VDA-8D). The test was carried out by taking granules equivalent to 25 mg of drug and performed in three different dissolution media 0.1 N HCl, pH7.4 phosphate buffer, and pH6.8 phosphate buffer. The test was conducted at a temp. 37± 0.5°C by taking 900 ml of dissolution medium for 2h, and the paddle was rotated at a speed of 75 rpm. At predetermined time intervals (5, 10, 15, 30, 45, 60, 90, and 120 min) aliquots of 5 ml were withdrawn. At 232 nm the samples were analyzed after suitable dilution by using UV Visible spectrophotometer. Three trials were done, and mean % drug release was calculated.

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 and were 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 polybags for future use.

Evaluation of Treated Bodies [11]:

Qualitative Analysis for Formaldehyde Content:

Preparation of Formaldehyde Standard Solution: The suitable volume of formaldehyde was diluted with water to get a 20µg/ml concentration.

Preparation of test Sample: Twenty-five treated bodies were taken, cut into small pieces, and dissolved in 40 ml of distilled water by stirring with a magnetic stirrer for 1h to get excess formaldehyde. Then the solution was filtered, and the volume was 50 ml with distilled water.

Procedure for testing of Formaldehyde Concentration: One ml of test solution was taken to this added 4 ml of distilled water and 5ml of 99.5% v/v acetylacetone. Then this solution was heated for 40 min at 40°C. At the same time, 1ml of standard formaldehyde treated in the same manner was 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 Pulsicapsules [11]: Treated bodies and untreated caps of the '0' size capsules were taken for filling. Immediate release core granules formula MCM5 was selected as optimized for the preparation of miglitol pulsicapsules.

Then the pulsicapsules were assembled by taking 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.

Pulsicapsules *In-vitro* Dissolution Studies [12]: Alongthe GI tract to simulate the pH changes three dissolution media were used and dissolution was carried out by using USP II apparatus.

Acid Stage: The 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. Then pH 7.4 phosphate buffer (900 ml) was used for next 3 h which was 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 remaining 13 h.

Temperature was maintained at 37±0.5°C and Paddles were rotated at 75 rpm. Aliquots of 5 ml were withdrawn from the dissolution basket and replaced with the same volume of respective dissolution medium to maintain the sink conditions. By using a UV-Visible spectrophotometer, samples were analyzed at 232 nm.

Drug-Polymer Interactions: There is always a possibility of drug-polymer interaction in the formulation due to their intimate contact. Interaction studies were conducted on miglitol, crospovidone, hydrogel plug, and optimized formulations to study the drug-polymer interactions by using Fourier transform infrared spectroscopy (FTIR) and Differential scanning calorimetry.

Fourier Transforms Infrared Spectroscopy (FTIR): On Bruker spectrophotometer by using classic KBr pellet technique, FTIR spectra of Pure drug and samples were obtained and compared.

Differential Scanning Calorimetry (DSC): Five-nine mg samples were sealed in an aluminum pan and heated at a rate of 10° C/min at a temperature of 35 to 550° C in a nitrogen atmosphere at a . Samples thermograms were obtained using a Differential scanning calorimeter (HITACHI DSC 7020).

Stability Studies [13]: Stability studies were conducted to predict the shelf life of a product. The optimized formula was exposed to different conditions in the stability chamber and analyzed for appearance, drug content, and *in-vitro* dissolution studies. The obtained results were compared with the initial results.

RESULTS AND DISCUSSION:

Evaluation of Hydrogel Plugs: Hydrogel plugs were successfully prepared and evaluated for parameters like weight variation (%), thickness (mm) and hardness (kg/cm^2).

These parameters range from 99.5±0.65 to 101.1±0.02, 3.41±0.45 to 3.45±0.91, and 4.1±0.05 to 4.7±0.01, respectively. The results are given in **Table 3.**

TABLE 3: EVALUATION OF HYDROGEL PLUGS

Hydrogel plug code	Weight variation #(mg)	Thickness # (mm)	Hardness# (kg/cm^2)	Lag time*(h) Mean ± SD, n=3
	Mean ± SD, n=6			
HP1	100±0.54	3.45±0.89	4.6±0.02	7.30
HP2	100±0.23	3.44±0.45	4.2±0.03	8.00
HP3	100.5±0.17	3.41±0.78	4.2±0.01	8.30
HP4	99.5±0.65	3.45±0.91	4.5±0.03	9.30
HP5	101.1±0.02	3.42±0.78	4.1±0.05	4.45
HP6	100±0.23	3.41±0.91	4.3±0.98	5.15
HP7	100±0.54	3.41±0.45	4.5±0.01	5.45
HP8	99.5±0.65	3.42±0.91	4.7±0.01	6.00

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 99.85 ± 0.11, results were given in **Table 4.**

TABLE 4: MIGLITOLIMMEDIATE RELEASE CORE GRANULES FLOW PROPERTIES

Formulation code	Bulk density (g/cm^3)	Tapped density (g/ml)	Compressibility Index (%)	Hauser's ratio	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

All values were expressed Mean± SD, n=5

***In-vitro* Dissolution Studies of Immediate Release Granules:** Dissolution studies were carried out in three different media. Different concentrations of crospovidone result in a significant increase in drug release profile. The formulation MCM1 without crospovidone shows less % drug release, and the MCM2-MCM4 formulation released less % of the drug than MCM5 and MCM6 because these formulations contain a lower amount of superdisintegrant. The formulation MCM6 releases all the drugs within one hour due to the high amount of superdisintegrant. Hence MCM5 was considered an optimized formulation based on the flow properties, drug content, and drug release profile. The results were given in **Tables 5**, **6** & **7,** and **Fig. 1, 2** & **3.**

TABLE 5: THE *IN-VITRO* DRUG RELEASE 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	

TABL 6: THE *IN-VITRO* DRUG RELEASE DATA FOR 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	

TABLE 7: THE *IN-VITRO* DRUG RELEASE 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	

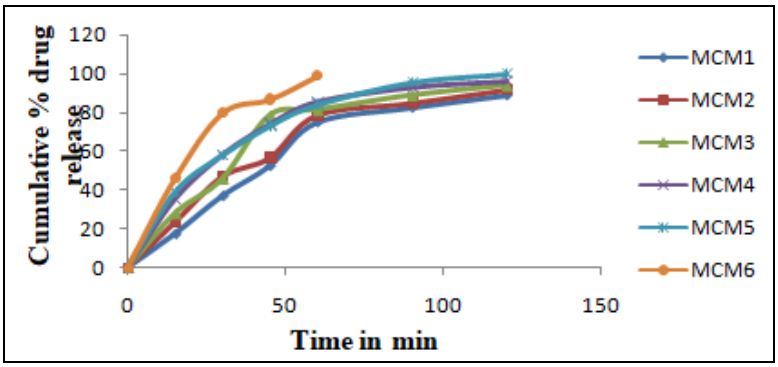

FIG. 1: COMPARATIVE %DRUG RELEASE PROFILE FOR CORE GRANULES OF MCM1-MCM6 IN 0.1N HCl

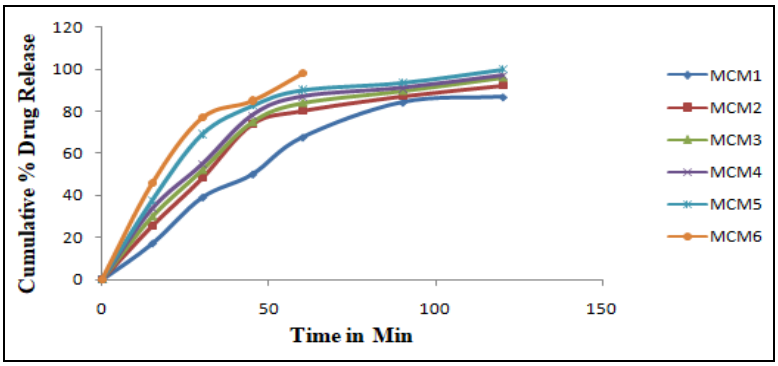

FIG. 2: COMPARATIVE % DRUG RELEASE PROFILE FOR CORE GRANULES OF MCM1-MCM6 IN PH 7.4 PHOSPHATE BUFFER

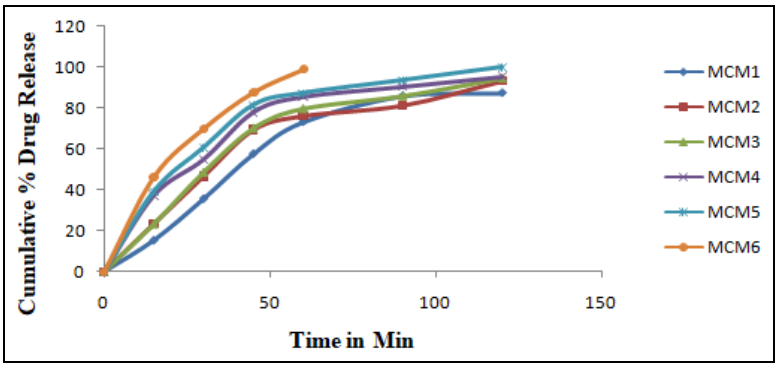

FIG. 3: COMPARATIVE % DRUG RELEASE PROFILE FOR CORE GRANULES OF MCM1-MCM6 IN PH 6.8 PHOSPHATE BUFFER

Pulsicapsules *In-vitro* Dissolution Studies: Dissolution studies revealed that there is no effect of dissolution media on drug release. All these 8 formulations of pulsicapsules were prepared with

two different polymers in two ratios 1:2 and 1:3, and two diluents were used, *i.e.,* MCC, which is hydrophilic in nature and another one is DCP which is hydrophobic in nature. All prepared pulsicapsules have shown the desired drug release in 0.1N HCl in the first 2 h (nearly 100% release), which was the first pulse. The formulations HP1, HP2, HP3 and HP4 prepared with ethyl cellulose as hydrogel plug showed a maximum lag time of 9.30h. Because of its hydrophobic nature, it took a long to get soft mass and ejection to release the undesirable second pulse. The remaining four formulations HP5, HP6, HP7, HP8 prepared with Sodium carboxymethylcellulose as hydrogel plug showed a maximum lag time of 6 h, which is a predetermined lag time. HP8 formulation was optimized because of its predetermined lag time of 6 h. HP8 formulation contains 1: 3 ratio of drug: polymer (*i.e.,* miglitol: Sodium carboxymethyl cellulose) and DCP as diluent. Its maximum drug release of 99.79% in first pulse was rapid, the second pulse release started at 8thh (98.97%) and the third pulse release started at 16th h (99.87%). Stability studies were conducted for optimized formulation (HP8). The results were given in **Tables 8 & 9** and **Fig. 4 & 5**.

TABLE 8: THE *IN-VITRO* DRUG RELEASE DATA OF PULSICAPSULE FORMULATIONS HP1-HP4

Buffer	Time (h)	Cumulative % Drug Release (Mean±SD, n=3)			
		Formulation code			
		HP1	HP2	HP3	HP4
	0.15	0	0	0	0
0.1 N HCl	0.30	19.90±0.45	20.34±0.56	20.11±1.34	20.87±0.98
	0.45	37.86±0.12	38.78±1.63	36.89±0.78	41.54±0.35
	1.00	53.45±0.78	69.97±0.86	58.90±0.45	64.67±0.12
	2.00	76.34±1.26	84.34±2.46	81.78±0.45	80.87±2.67
	3.00	95.68±3.46	97.45±1.56	97.89±0.98	98.89±0.89
pH 7.4 phosphate	4.00	0	0	0	0
buffer	5.00	0	0	0	0
	6.00	0	0	0	0
pH 6.8	7.00	0	0	0	0
phosphate	8.00	0	0	0	0
buffer	9.00	0	0	0	0
	10 .00	0	0	0	0
	11.00	43.57±0.56	0	0	0
	12.00	80.45±2.45	0	46.89±0.56	0
	13.00	0	62.45±0.65	79.08±0.76	27.09±0.46
	14.00	0	89.99±0.98	0	65.89±0.77
	15.00	0	0	0	0
	16.00	0	0	0	0
	17.00	0	0	0	0
	18.00	0	0	0	0

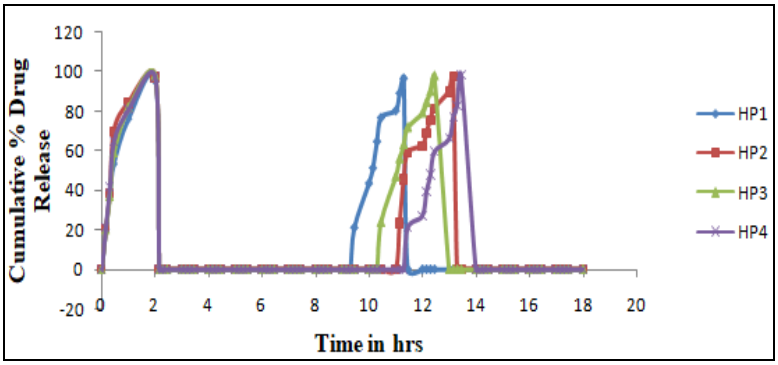

FIG. 4: CUMULATIVE % DRUG RELEASE PROFILE OF MIGLITOL PULSICAPSULE FORMULATIONSHP1, HP2, HP3, HP4

During the dissolution studies, the cap was dissolved within 5 min and the first dose was released initially and rapidly. Then the hydrogel plug was exposed to the dissolution medium and absorbed the surrounding medium, wetted and converted into the soft mass so that it was ejected

from the capsule body and released the second pulse. The same procedure was followed for the release of the third pulse. The formation of a soft mass of hydrogel depends on its nature and amount of polymer, and nature of diluents used.

TABLE 9: THE *IN-VITRO* DRUG RELEASE DATA OF PULSICAPSULE FORMULATIONS HP5-HP8

Buffer	Time (h)	Cumulative % Drug Release (Mean±SD, n=3)			
		Formulation code			
		HP5	HP6	HP7	HP8
	0.00	0	0	0	0
0.1 N HCl	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	3.00	0	0	0	0
buffer	4.00	0	0	0	0
	5.00	0	0	0	0
pH 6.8	6.00	0	0	0	0
phosphate	7.00	20.98±1.55	0	0	0
buffer	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

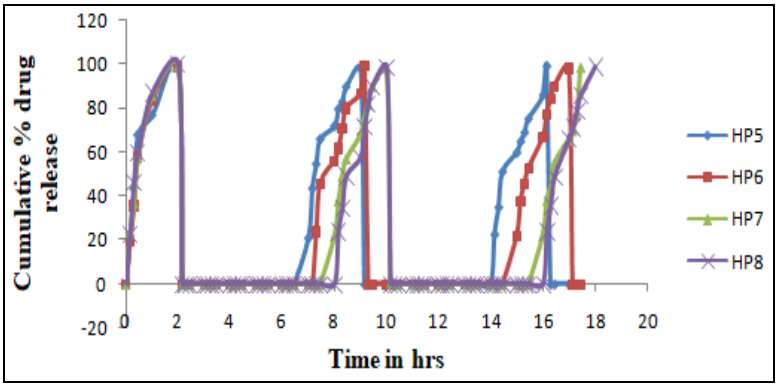

FIG. 5: CUMULATIVE % DRUG RELEASE PROFILE OF MIGLITOL PULSICAPSULE FORMULATIONS HP5, HP6, HP7 AND HP8

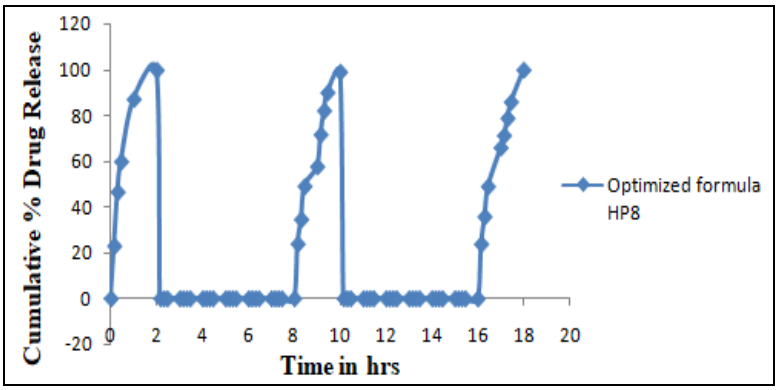

FIG. 6: CUMULATIVE % DRUG RELEASE OF OPTIMIZED FORMULA HP8

Drug-polymer Interaction Studies:

FTIR: Miglitol FTIR spectrum contains characteristic bands at 3865cm^{-1}, 2816 cm^{-1} and 1589 cm^{-1} which is C-H bending, C-H stretching, N-H stretching, respectively. All recorded FTIR spectra contain these characteristic bands, which confirm the compatibility between drug and polymers. All spectra were represented in **Fig. 7** to **11**

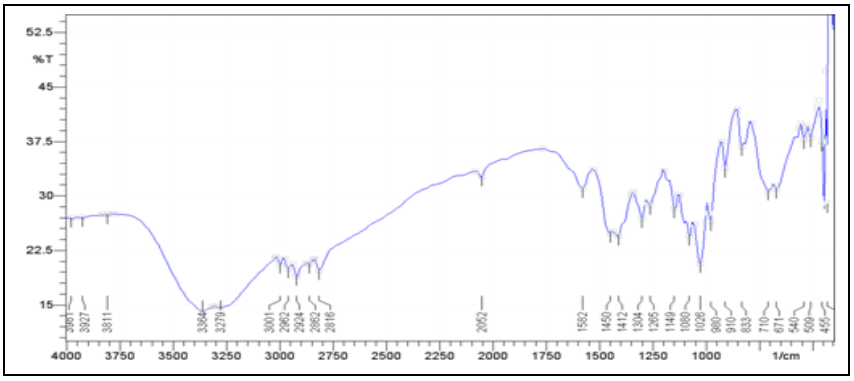

FIG. 7: IR SPECTRUM OF CROSPOVIDONE

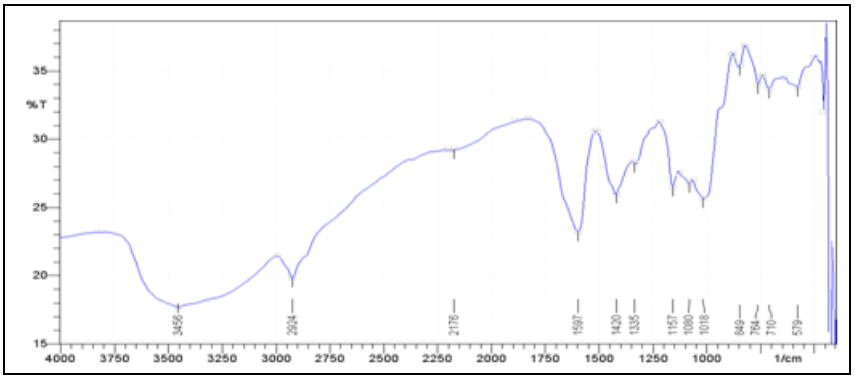

FIG. 8: MIGLITOL IR SPECTRUM

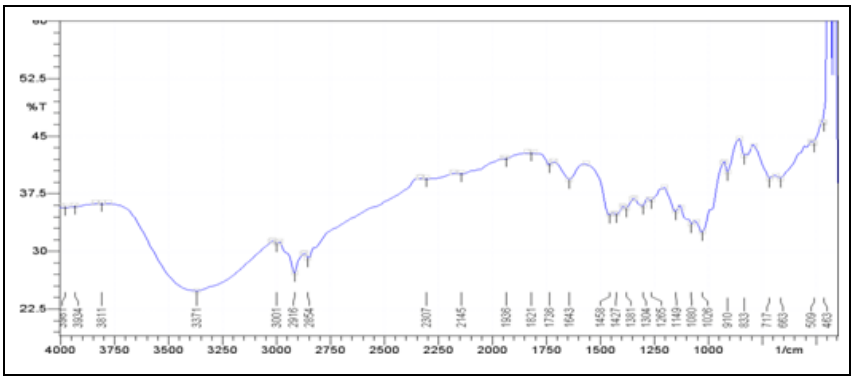

FIG. 9: IR SPECTRUM OF MIGLITOL-MCC

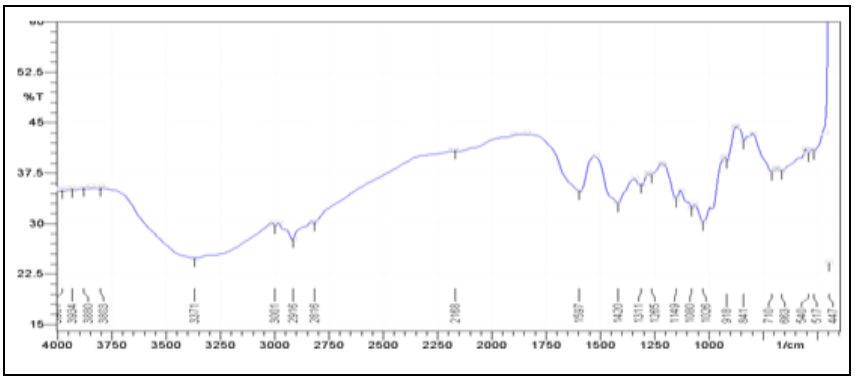

FIG. 10: IR SPECTRUM OF MIGLITOL-CP

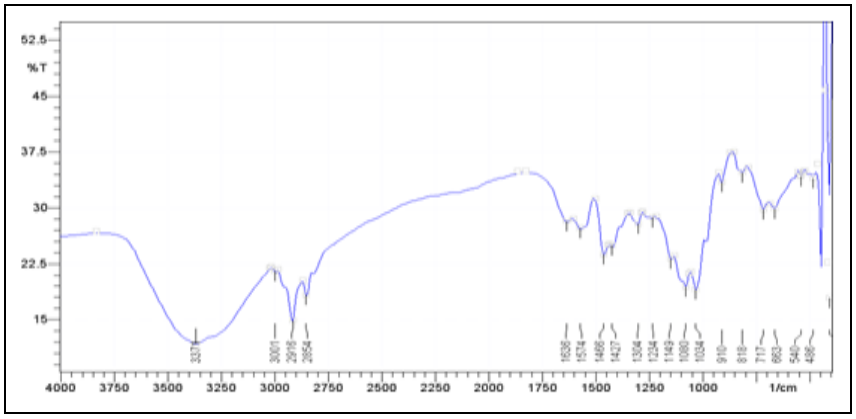

FIG. 11: FTIR SPECTRUM OF OPTIMIZED FORMULA (HP8)

DSC Analysis: Miglitol showed a single sharp endothermic peak at 147.17°Ccorresponding to the melting range of miglitol. Miglitol melting peak in optimized formulation was slightly shifted to left and melting peak was broadened to some extent, possibly due to changes in crystalline Compared to pure drug. The low melting point of the polymers might have influenced the shift in the melting point of the drug in the formulation. Thermal curves were given in **Figures 12** & **13.**

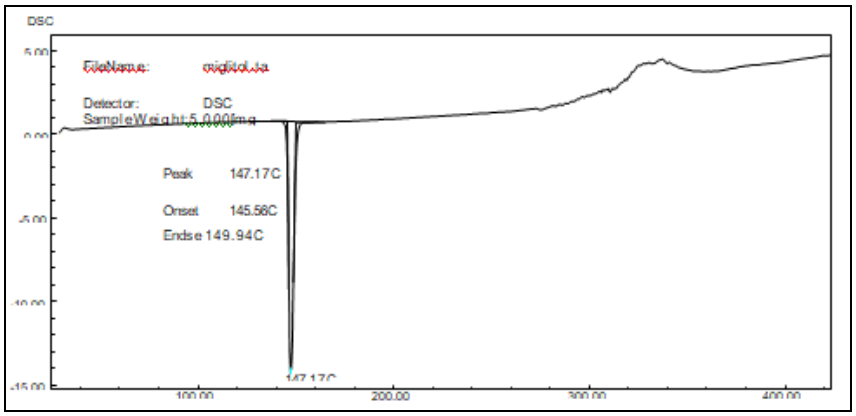

FIG. 12: DSC SPECTRUM OF MIGLITOL PURE DRUG

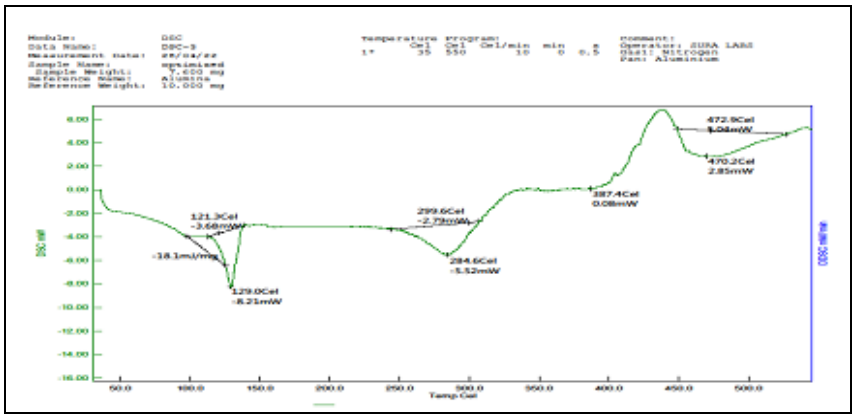

FIG. 13: DSC SPECTRUM OF OPTIMIZED FORMULA (HP 8)

Stability Studies: At 25±2ºC/60±5% RH, 40±2ºC/ 74±5% RH accelerated stability studies were conducted for optimized formulation HP8 for 6 months and monitored for the physical 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, indicating no remarkable changes in appearance, drug content and dissolution profile up to six months. In **Table 10** and **Fig. 14,** the results were given.

TABLE 10: STABILITY STUDIES DATA FOR OPTIMIZED FORMULATION HP8 BEFORE AND AFTER STORAGE

Test	Initial	Storage conditions			
		25±2˚C/60±5% RH		40±2˚C/75±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

* Mean ± SD, n=6.

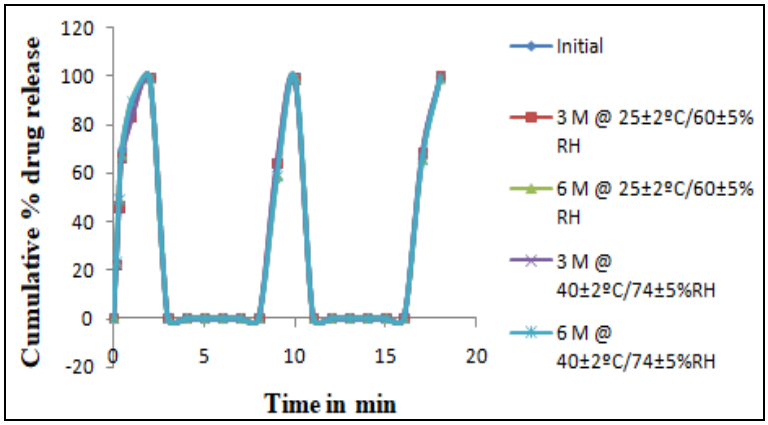

FIG. 14: COMPARATIVE DISSOLUTION PROFILES OF OPTIMIZED FORMULATION HP8 BEFORE AND AFTER STORAGE AT 25±2˚C/60±5% RH, 40±2˚C/75±5%RH

CONCLUSION: The results revealed that hydrogels, due to its eminent hydration and biocompatibility properties, are most widely utilized in the pharmaceutical field. In the present work miglitol pulsicapsules were prepared by using hydrogels as carriers to lower the postprandial glucose level were successful.

Thus, the optimized formulation HP8 can be considered one of the promising preparations to control the post-prandial glucose level in type-II diabetes. Because of their extraordinary properties, these hydrogels are utilized as brilliant drug delivery vehicles in different drug delivery systems.

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CONFLICTS OF INTEREST: Nil

REFERENCES:

1. Sarah Husnaini Zainal, Nurul Hanisah Mohd, Nabilah Suhaili, Farah Hannan Anuar, Azwan Mat Lazim and Rizafizah Othaman: Preparation of cellulose-based hydrogel: a review. Journal of Material Research and Technology 2021; 10: 935-52.
2. Ciolacu DE, Nicu R and Ciolacu F: Cellulose-Based Hydrogels as Sustained Drug-Delivery Systems. Materials 2020; 13(22): 5270-307.
3. Amritha R, Sivakumar R and Haribabu Y: A Review on Pulsatile Drug Delivery System: Drug Scheduling based on Biological Rhythm. Research Journal of Pharmacy and Technology 2022; 15(3): 1359-64.
4. Kusunoki M, Wakazono N, Tsutsumi K, Oshida Y and Miyata T: Combination Therapy of Alpha-Glucosidase Inhibitor, Thiazolidinedione and Sodium Glucose Co-Transporter-2 Inhibitor in Japanese Type 2 Diabetes Patients. Journal of Endocrinology and Metabolism 2020; 10(6): 167-72.
5. Zainal SH, Mohd NH, Suhaili N, Anuar FH, Lazim AM and Othaman R: Preparation of cellulose-based hydrogel: A review. Journal of Materials Research and Technology. 2021; 10: 935-952.
6. Kumar YG, Pulla RP, Ganesh A, Naresh G and Saleem A: Formulation and *in-vitro* evaluation of floating pulsatile drug delivery system of ivabradine. Journal of Drug Delivery and Therapeutics 2019; 9(3): 188-93.
7. Santosh Kumar Dash, Abdul Sayeed Khan, Ashutosh Padhan and Nabin Karna: Formulaton and evaluation of pulsatile drug delivery system of atenolol by using natural gum. IJPSR 2020; 11(7): 3229-3242.
8. Shajan A, Susan Raju, Surrayya Banu, Vidya Peter and Christina Das: Formulaton and evaluation of pulsatile drug delivery system containing domperidone and paracetamol. IJPSR 2017; 8(3): 1407-1412.
9. Pharmacopoeia of India. New Delhi: Ministry of Health and Family Welfare 1996; 2: 734-736.
10. Indrajeet S, Patil. Omkar A. Patil, Girish Chandra R, Mandake and Manoj M. Nitalikar: Development And Evaluation Of telmisartanpulsatile Drug deliveryby Using Surface Response Methodology, Asian J Pharm Res 2018; 8(4): 205-214.
11. Krishnan BV, Rao CB and Kishore VS: Design and characterization of chronopharmaceutical drug delivery of propranolol hydrochloride. IJPSR 2020; 11(1): 358-364.

12. Sai Krishna MV, Saikishore V, Sravani SL and Rudrama Devi G: Design and characterization of pulsatile drug delivery of metaprolol tartrate. IAJPS 2017; 4(5): 1052-9.

13. Zuthanpull F, Rajesh R and Ketal EK: A review on tability testing guidelines of pharmaceuctical products. Asian J Pharm Clin Res 2020; 13: 10:3-9.

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