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Formulation and *In-vitro* evaluation of mucoadhesive nanospheres for an alpha glucosidase inhibitor

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Abstract
The aim of this study was to formulate and evaluate the release of Mucoadhesive nanosphere of Miglitol (half-life 2 hours) for the treatment of diabetes type 2 by combine the potential advantages of Mucoadhesive with controlled drug delivery using various ratios of different polymers. The results of this investigation indicate that ionic cross linking technique Ionotropic gelation method can be successfully employed to fabricate Miglitol nanosphere. The technique provides characteristic advantage over conventional nanosphere method, which involves an "all-aqueous" system, avoids residual solvents in nanospheres. FT-IR spectra of the physical mixture revealed that the drug is compatible with the polymers and copolymers used. The mean particle size of the prepared nanosphere was in the size range of 512.1±0.2to 903.6±0.4nm and is suitable for bioadhesive nanospheres for oral administration. Increase in the polymer concentration led to increase in % yield, % drug entrapment efficiency, particle size, % swelling and % mucoadhesion. The *in-vitro* mucoadhesive study demonstrated that nanosphere of Miglitol using sodium alginate along with Carbopol 934 as copolymer adhered to the mucus to a greater extent than the nanospheres of Miglitol using sodium alginate along with Carbopol 971 and HPMC K4M as copolymers. Analysis of drug release mechanism showed that the drug release from the formulations followed non-fickian diffusion and the best fit model was found to be Korsmeyer-Peppas. Based on the results of evaluation tests formulation coded T_4 was concluded as best formulation.

Keywords: Miglitol, kinetics, half-life, sodium alginate, dissolution, carbopol

Introduction
Type 2 diabetes mellitus (T2DM), known as non-insulin-dependent diabetes mellitus (NIDDM) is a chronic metabolic disease which is characterized by post prandial hyperglycemia (PPHG). Although recently, wide varieties of synthetic drugs are being used for the treatment of T2DM, most of them possess pronounced side effects in the long run particularly, drug resistance, hepatotoxicity, abdominal pain, flatulence and diarrhea. Therefore, there is a need for a search of an alternative agent possessing hypoglycemic effect on T2DM [1, 4].

Alpha-glucosidase enzyme is present ubiquitously throughout the lumen of the small intestine. It is responsible for the breakdown of complex into simple carbohydrates. Alpha-Glucosidase inhibitors such as Miglitol are drugs that have greater affinity towards this enzyme in comparison to carbohydrates. Miglitol regulates the postprandial glucose levels directly by inhibiting the enzyme reversibly and also indirectly by including the secretion of glucagon like peptide-1 (GLP-1) [5, 9]. Miglitol is a second generation alpha-glucosidase inhibitor. It is a derivative of 1-desoxynojirimycin, and binds reversibly to the brushborder alpha-glucosidase enzymes. In contrast to its parent drug (acarbose), Miglitol is almost completely absorbed in the small intestine [10].

Nanocarriers have emerged as an effective strategy for mucosa delivery of drugs, which possess a series of desirable properties, including small steric obstruction due to their nanometer size, and protection of cargo therapeutics at both the extracellular and intracellular levels [11]. However, one of the greatest challenges that limit the success of nanoparticles (NPs) is their ability to penetrate quickly through mucus to reach the underlying cells.

Mucus is a viscoelastic and adhesive hydrogel that covers in the surface of lung airways, gastrointestinal (GI) tract, female reproductive tracts, eye and other mucosa [12]. Mucus protects underlying epithelium by efficiently trapping pathogens and foreign particulates, then rapidly removing them. Therefore, mucus is not only vital for human health, but also represents a substantial barrier to mucosal drug delivery.

Mucus forms adhesive interactions with particulates via electrostatic interactions, vander Waals forces, hydrophobic forces, hydrogen bonding, and Chain entanglement [13, 14]. Mucoadhesive NPs is to prolong the retention time of particles in mucosal surface by maximize these interactions [15] which would undergo either direct transit or elimination. Different mucoadhesive systems have been well reviewed previously [16, 18]. Another strategy to overcome the mucus barrier and achieve longer retention time in cell surface is to develop a nanocarrier which can effectively penetrate the mucus layer and accumulate in epithelial surface. Justin Hanes and co-workers first proposed mucus penetrating particles (MPP) by mimicking the essential surface properties of viruses that allow them to avoid mucoadhesion, showing great promise in mucosal drug delivery. The aim of this work was to formulate mucoadhesive nanospheres of Miglitol by Ionotropic gelation method with a view to achieve controlled drug release, drug targeting to the specific site (gastric mucosa) and to increase the half-life and bioavailability of the drug.

Materials and methods

Materials

Miglitol, carbopol 934, 971 were received from M/s Baris pharmaceuticals Pvt. Ltd. Sodium alginate was obtained from Sisco Research Laboratory Pvt. Ltd. All other reagents and solvents used were of pharmaceutical or analytical grade.

Methods

Preformulation studies

Fourier Transform Infrared Spectroscopy Studies (FT-IR)

In order to check the integrity (Compatibility) of drug in the fo rmulation, FT-IR spectra of the formulations along with the drug and other excipients were obtained and compared using Shimadzu FT-IR 8400 spectrophotometer.

Formulation of Nanospheres

Batches of nanospheres were prepared by ionotropic gelation method which involved reaction between sodium alginate and polycationic ions like calcium to produce a hydrogel network of calcium alginate. Sodium alginate and the mucoadhesive polymers were dispersed in purified water (10 ml) to form a homogeneous polymer mixture. The API, Miglitol (100 mg) were added to the polymer premix and mixed thoroughly with a stirrer to form a viscous dispersion. The resulting dispersion was then added drop wise through a 22G needle into calcium chloride (4% w/v) solution. The addition was done with continuous stirring at 200rpm. The added droplets were retained in the calcium chloride solution for 30 minutes to complete the curing reaction. The suspension was allowed to suspend overnight and then probe sonicated for 3 min [19]. The above suspension was kept for freeze drying for 24 hrs. Twelve batches of nanospheres were prepared and labeled as T1 to T12 as shown in Table No. 01.

Table 1: Various Formulations of Miglitol Nanospheres

S. No.	Formulation code	Drug: Polymer Ratio	Polymer Ratio
1	T_1	1:2.5	Na alginate: Carbopol 934 (1.5:0.5)
2	T_2	1:3	Na alginate: Carbopol 934 (2:1)
3	T_3	1:3.5	Na alginate: Carbopol 934 (2.5:1)
4	T_4	1:4	Na alginate: Carbopol 934 (3:1)
5	T_5	1:2.5	Na alginate: Carbopol 971 (1.5:0.5)
6	T_6	1:3	Na alginate: Carbopol 971 (2:1)
7	T_7	1:3.5	Na alginate: Carbopol 971 (2.5:1)
8	T_8	1:4	Na alginate: Carbopol 971 (3:1)
9	T_9	1:2.5	Na alginate: HPMC K 4M (1.5:0.5)
10	T_{10}	1:3	Na alginate: HPMC K 4 M (2:1)
11	T_{11}	1:3.5	Na alginate: HPMC K 4 M (2.5:1)
12	T_{12}	1:4	Na alginate: HPMC K 4 M (3:1)

Characterization of nanospheres

Particle size analysis

The particle size and PDI of the Miglitol nanospheres were characterized using particle size analyzer (Malvern Zetasizer Nano S 90, UK) and distilled water was used as medium.

Scanning Electron Microscopy

Scanning Electron Microscopy was performed to characterize the surface morphology of the formed Nanospheres and this was done by using a JSM 6100 JEOC scanning electron microscope at 20kV.

Drug entrapment efficiency

Nanospheres equivalent to 15 mg of the drug Miglitol were taken for evaluation. The amount of drug entrapped was estimated by dissolving the freeze dried nanospheres in methanol to dissolve the coat of polymers. After 24 hours the solution was filtered and the absorbance was measured spectrophotometrically at 269 nm using UV Spectrophotometer. The amount of drug entrapped in the nanospheres was calculated by the following formula,

$$\% \text{ Drug Entrapment Efficiency} = \frac{\text{Experimental Drug Content}}{\text{Theoretical Drug Content}} \times 100$$

Swelling study

Swelling ratio of different dried nanospheres were determined gravimetrically in simulated gastric fluid pH 1.2 by compressing the nanospheres using inert diluent (microcrystalline cellulose) into tablet. The weight of individual tablet was taken prior to study (W0). The tablet were removed periodically from the solution, blotted to remove excess surface liquid and weighed on balance (Wt). Swelling ratio (% w/v) was determined from the following relationship:

$$\text{Swelling ratio} = \frac{(Wt - W0)}{(W0)} \times 100$$

Where W0 & Wt are initial weight and Final weight of nanospheres respectively.

Evaluation of mucoadhesive property

The mucoadhesive property of nanospheres was evaluated by an *in-vitro* adhesion testing method known as modified balance method. Freshly excised pieces of goat stomach was washed in 0.1N HCl (pH 1.2) and used immediately for the study. The mucosa was tied tightly with the mucosal side upwards to the block. This block was then lowered into the glass reservoir. The reservoir then filled with 0.1 HCl (pH 1.2). Such that surface of mucosal membrane is immersed into it to keep the surface moist. The nanospheres were compressed using inert diluent (MCC) into tablets to perform this study using the model. The tablets were sticked on the cork facing towards the mucosa and this whole assembly was placed on one side of the balance such that the tablet will adhere to the mucosa. To the other side of the balance water was added with burette slowly drop by drop into the beaker. The amount of water required to pull out the tablet from the mucosa represents the force required to pull the tablet against the adhesion.

Force of adhesion (N) = 0.00981W/2

W = weight of water

***In-vitro* drug release study**

The dissolution studies were performed in a fully calibrated eight station dissolution test apparatus (37 ± 0.5 ^{0}C, 50 rpm) using the USP type – I rotating basket method in simulated sodium phosphate buffer (900ml). A quantity of accurately weighed nanospheres equivalent to 15mg Miglitol each formulation was employed in all dissolution studies. Aliquots of sample were withdrawn at predetermined intervals of time and analyzed for drug release by measuring the absorbance at 269nm. The release data obtained was fitted into various mathematical models to characterize the type of release mechanism during the release process.

***In-vitro* drug release kinetics study**

The release data obtained was fitted into various mathematical models.The parameters 'n' and time component 'k', the release rate constant and 'R', the regression coefficient were determined by Korsmeyer-Peppas equation to understand the release mechanism. To examine the release mechanism of Miglitol from the nanospheres, the release data was fitted into Peppa's equation,

$Mt / M\infty = Ktn$

Where, $Mt / M\infty$ is the fractional release of drug, 't' denotes the release time, 'K' represents a constant incorporating structural and geometrical characteristics of the device, 'n' is the diffusional exponent and characterize the type of release mechanism during the release process (as shown in Table No. 02).

Table 2: The mechanism of drug transport – I

Release exponent (n)	Drug transport mechanism	Rate as a function of time
0.5	Fickian diffusion	$t^{-0.5}$
0.5<n<1.0	Anomalous transport or non-Fickian	t^{n-1}
1.0	Case-II transport	Zero-order release
Higher than 1.0	Super Case-II transport	t^{n-1}

If *n*< 0.5,

The polymer relaxation does not affect the molecular transport, hence diffus-ion is Fickian.

If n > 0.5, the solid transport will be non-fickian and will be relaxation controlled.

Other equations to study the drug release kinetics from dosage forms

a. Zero Order

% R = kt

This model represents an ideal release in order to achieve prolonged pharmacological Action. This is applicable to dosage Forms like transdermal systems, coated forms, osmotic systems, as well as Matrix tablets containing low soluble drugs.

b. First Order

Log (fraction unreleased) = kt/2.303

The model is applicable to hydrolysis kinetics and to study the release profiles of pharmaceutical dosage forms such as those containing water soluble drugs in porous Matrices.

c. Matrix (Higuchi Matrix)

% R = kt 0.5

This model is applicable to systems with drug dispersed in uniform swellable polymer matrix as in case of matrix tablets with water soluble drug.

d. Peppas Korsmeyer Equation

% R = kt n

Log % R = logk + nlogt

This model is widely used when release mechanism is well kn own or when more than one type of release phenomenon could be involved. The 'n' values could be used to characterize different release mechanisms as shown in Table No. 03.

Table 3: The mechanism of drug transport – I

Value of 'n'	Mechanism
0.5	Fickian Diffusion (Higuchi Matrix)
0.5<n<1	Anomalous Transport
1	Case – II transport (Zero Order Release)
n>1	Super Case Transport

Results and discussion

Preformulation studies

Fourier Transform Infrared Spectroscopy Studies (FT-IR):

The FT-IR spectra of the formulations were compared with the FTIR spectra of the pure drug. The results indicated that the characteristic absorption peaks due to pure Miglitol have appeared in the formulated nanospheres, without any significant change in their position after successful encapsulation, indicating no chemical interaction between Miglitol and Polymers as shown in Figure No. 01.

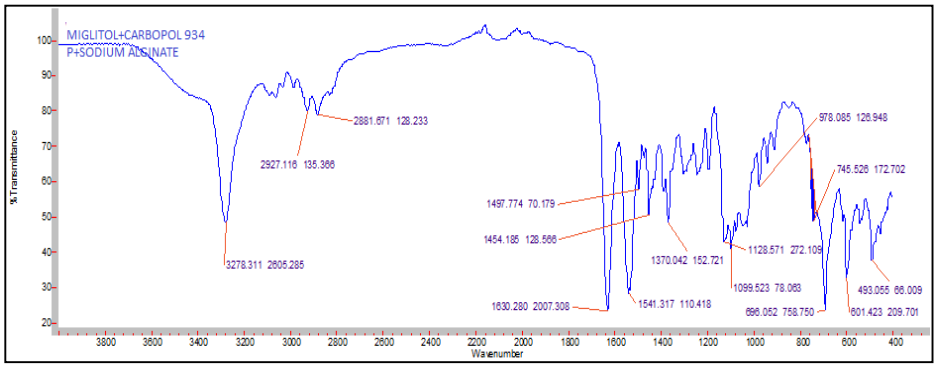

Fig 1: FT-IR spectra of Miglitol, Carbopol 934 and Sodium alginate

Particle Size

The mean particle size increased with increasing polymer concentration which is due to a significant increase in the viscosity, thus leading to an increased droplet size and finally a higher nanospheres size. Nanospheres containing sodium alginate along with various concentrations of polymers for all the batches from T1 to T12 are as shown in the Table No. 04 and Figure No. 02.

Table 4: The average particle size of formulations of T1 to T12

Formulation Code	Average particle size range (nm)	Formulation Code	Average particle size range (nm)
T_1	512.1±0.2	T_7	792.3±0.2
T_2	617.7±0.7	T_8	834.2±0.5
T_3	711.6±0.5	T_9	664.6±0.1
T_4	826.3±0.4	T_{10}	774.7±0.8
T_5	517.1±0.2	T_{11}	814.2±0.5
T_6	642.3±0.4	T_{12}	903.6±0.4

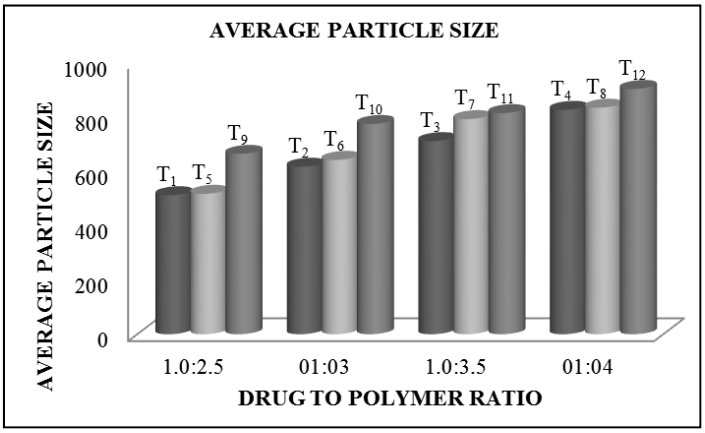

Fig 2: Comparison of average particle size of prepared nanospheres

Scanning Electron Microscopy

The SEM showed that the blend of sodium alginate and Carbopol 934 produced spherical with smooth surface nanospheres due to their high solubility in water. While sodium alginate nanospheres were of irregular shape with a rough morphology due to less water solubility and non-uniform evaporation of water from the surface of nanospheres as shown in the Figure No. 03 and 04.

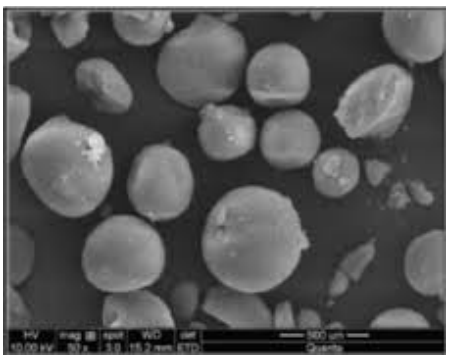

Fig 3: SEM of Miglitol nanospheres

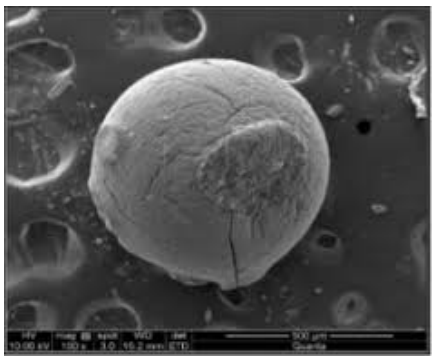

Fig 4: SEM of individual Miglitol nanospheres

Drug Entrapment Efficiency

The drug entrapment efficiency of the prepared nanospheres increased progressively with an increase in proportion of the polymers. Increase in the polymer concentration increases the viscosity of the dispersed phase. The particle size increases exponentially with viscosity. As the polymer to drug ratio increased, nanospheres containing sodium alginate along with carbopol 934 as copolymer exhibited % mucoadhesion ranging from 65 to 85%, nanospheres containing sodium alginate along with carbopol 971 as copolymer exhibited % mucoadhesion ranging from 60 to 75% and nanospheres containing sodium alginate along with HPMC K 4 M as copolymer exhibited % mucoadhesion ranging from 60 to 80%. The rank of order of mucoadhesion is carbopol 934 > HPMC K 4 M > carbopol 971 as shown in the Table No. 05 and Figure No. 05.

Table 5: Percentage mucoadhesion of the prepared nanospheres

Formulation Code	Percentage Mucoadhesion	Formulation Code	Percentage Mucoadhesion
T_1	65.25±0.51	T_7	70.52±0.43
T_2	70.36±0.25	T_8	75.48±0.28
T_3	75.32±0.21	T_9	60.34±0.41
T_4	85.41±0.16	T_{10}	70.21±0.51
T_5	60.28±00.56	T_{11}	75.62±0.43
T_6	65.37±0.68	T_{12}	80.23±0.41

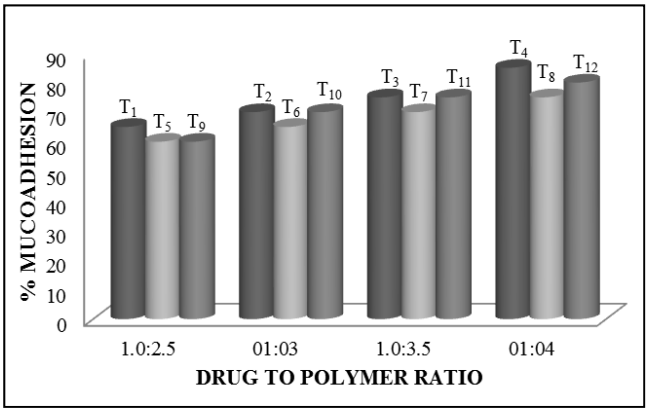

Fig 5: Comparison of percentage mucoadhesion of prepared nanospheres

Swelling Index

As the polymer to drug ratio increased, the percentage of swelling increased from 28 to 85% for nanospheres containing sodium alginate along with carbopol 934 as copolymer, 24 to 64% for nanospheres containing sodium alginate along with carbopol 971 as copolymer and 31 to 85 for nanospheres containing sodium alginate along with HPMC K 4 M as copolymer. The percentage of swelling of the prepared nanospheres is shown in Table No. 06 and Figure No. 06.

Table 6: Percentage swelling of the prepared nanospheres

Formulation Code	Percentage Swelling	Formulation Code	Percentage Swelling
T_1	12.8±0.25	T_7	15.5±0.39
T_2	14.2±0.35	T_8	16.4±0.52
T_3	16.2±0.53	T_9	13.1±0.21
T_4	18.5±0.61	T_{10}	15.3±0.51
T_5	12.4±0.29	T_{11}	16.7±0.54
T_6	13.9±0.37	T_{12}	18.5±0.36

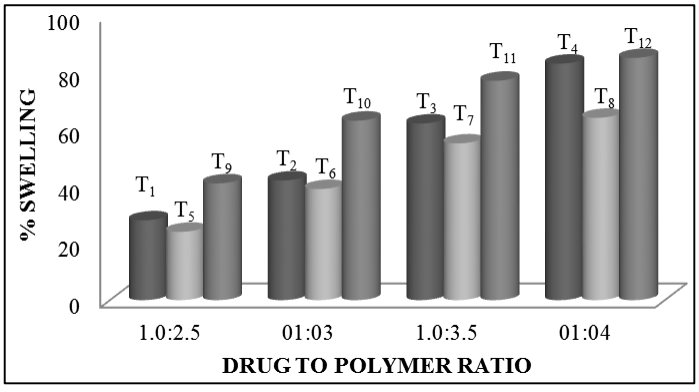

Fig 6: Percentage swelling of the prepared nanospheres

In-vitro drug release

The formulations T_1, T_2 and T_3 containing Sodium alginate along with Carbopol 934 as copolymer showed a maximum release of 92.66% after 9 hours, 90.66% after 10 hours, 90.6% after 11 hours and 94.66% after 12 hours respectively. The formulation T_4 containing Sodium alginate along with Carbopol 971 as copolymer showed a maximum release of 92.22% after 9 hours, 91.33% after 10 hours, 89.55% after 11 hours and 90.66% after 12 hours respectively. The formulation T_5 containing Sodium alginate along with HPMC K 4 M as copolymer showed a maximum release of 92.6% after 9 hours, 91.3% after 10 hours, 90% after 11 hours and 92.44% after 12 hours respectively. The results of the in-vitro dissolution studies of formulations are shown in Table No.07 and Figure No. 07 to 09.

Table 7: *In-Vitro* drug release data of Miglitol nanospheres of the formulations from T1 to T12.

Time (hrs)	Cumulative percentage drug release											
	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	T11	T12
1	24.88 ±0.02	21.11 ±0.03	18.66 ±0.32	15.88 ±0.06	27.77 ±0.02	22.44 ±0.03	18.44 ±0.06	17.11 ±0.11	25.77 ±0.11	21.55 ±0.11	18.66 ±0.03	16.44 ±0.12
2	31.55 ±0.03	31.55 ±0.09	25.11 ±0.10	24.22 ±0.07	36.44 ±0.05	32.22 ±0.04	29.33 ±0.04	26.44 ±0.06	35.33 ±0.23	31.77 ±0.09	26.55 ±0.10	27.11 ±0.20
3	42.44 ±0.03	39.77 ±0.02	35.44 ±0.05	32.66 ±0.06	43.77 ±0.02	40.88 ±0.01	39.55 ±0.03	37.55 ±0.10	43.55 ±0.16	40.44 ±0.14	36.55 ±0.10	36.44 ±0.18
4	53.55 ±0.03	47.77 ±0.05	40.66 ±0.03	39.33 ±0.03	54.66 ±0.04	48.66 ±0.02	45.55 ±0.04	46.88 ±0.08	54.25 ±0.11	48.44 ±0.03	43.66 ±0.13	45.55 ±0.21
5	62.00 ±0.21	56.66 ±0.09	52.22 ±0.05	47.55 ±0.07	64.01 ±0.07	57.55 ±0.02	57.33 ±0.12	55.77 ±0.03	63.55 ±0.16	57.11 ±0.02	54.55 ±0.09	55.33 ±0.11
6	74.66 ±0.06	62.44 ±0.28	57.33 ±0.06	55.77 ±0.09	75.77 ±0.06	63.55 ±0.04	65.33 ±0.09	63.55 ±0.04	75.33 ±0.05	63.11 ±0.16	62.33 ±0.11	63.11 ±0.21
7	83.55 ±0.12	69.55 ±0.16	63.11 ±0.07	61.77 ±0.02	84.65 ±0.02	70.44 ±0.01	71.55 ±0.11	71.33 ±0.06	84.09 ±0.03	70.22 ±0.06	67.68 ±0.09	71.55 ±0.16
8	89.33 ±0.03	75.33 ±0.20	69.11 ±0.06	69.55 ±0.04	90.01 ±0.04	76.55 ±0.03	77.56 ±0.10	75.77 ±0.05	89.77 ±0.05	76.21 ±0.18	73.55 ±0.12	76.44 ±0.09
9	92.66 ±0.02	84.66 ±0.30	75.33 ±0.04	77.55 ±0.06	92.22 ±0.01	85.55 ±0.04	81.55 ±0.09	79.77 ±0.06	92.66 ±0.21	85.11 ±0.16	78.55 ±0.08	80.66 ±0.08
10	85.55 ±0.04	90.66 ±0.17	82.66 ±0.05	85.55 ±0.07	84.88 ±0.03	91.33 ±0.03	83.33 ±0.13	82.44 ±0.04	85.11 ±0.18	91.33 ±0.09	83.66 ±0.08	85.55 ±0.11
11	80.22 ±0.01	84.22 ±0.15	90.66 ±0.04	90.66 ±0.05	79.55 ±0.04	85.77 ±0.01	89.55 ±0.11	86.88 ±0.01	80.66 ±0.10	85.33 ±0.08	90.23 ±0.20	89.55 ±0.21
12	78.88 ±0.03	80.88 ±0.31	89.55 ±0.06	94.66 ±0.04	77.55 ±0.02	81.11 ±0.06	87.55 ±0.06	90.66 ±0.11	78.09 ±0.13	81.11 ±0.11	87.55 ±0.10	92.44 ±0.08

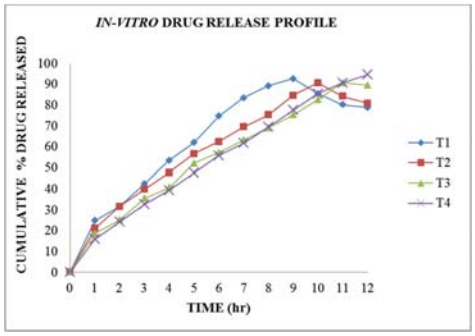

Fig 7: Comparison of *In-Vitro* drug release profile of Miglitol nanospheres containing sodium alginate along with carbopol 934 as copolymer

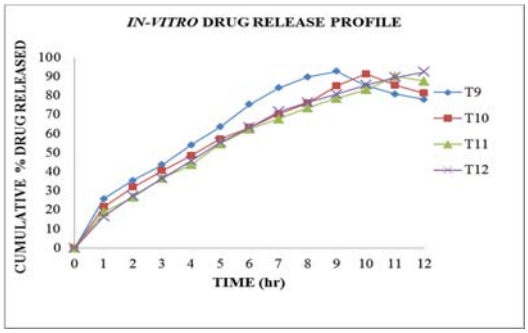

Fig 9: Comparison of *In-Vitro* drug release profile of Miglitol nanospheres containing sodium alginate along with HPMC K 4 M as copolymer

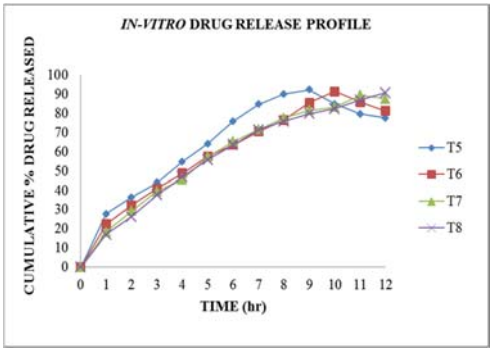

Fig 8: Comparison of *In-Vitro* drug release profile of Miglitol nanospheres containing sodium alginate along with carbopol 971 as copolymer

In-vitro drug release kinetics study

The coefficient of determination (R^2) was used as an indicator of the best fitting for each of the models considered. The kinetic data analysis of all the formulations reached higher coefficient of determination with the Korsmeyer-Peppas model (R^2 = 0.914 to 0.996) whereas release exponent value (n) ranged from 0.498 to 0.743. From the coefficient of determination and release exponent values, it can be suggested that the mechanism of drug release follows Korsmeyer-Peppas model along with non-Fickian diffusion mechanism which leading to the conclusion that a release mechanism of drug followed combination of diffusion and spheres erosion. Based on the results of evaluation tests formulation coded T4 was concluded as best formulation as per Table No. 08 and Figure No. 10 to 13.

Table 8: Release kinetics studies of the prepared formulations

Formulation code	Release model								
	Zero order		First order		Higuchi matrix		Koresmeyer-peppas		
	K	R^2	K	R^2	K	R^2	n	K	R^2
T_1	21.60	0.797	1.923	0.720	-0.313	0.912	0.556	1.388	0.925
T_2	16.39	0.908	1.991	0.890	-3.945	0.970	0.595	1.326	0.983
T_3	10.45	0.976	2.062	0.945	-8.966	0.975	0.673	1.233	0.991
T_4	7.434	0.990	2.118	0.914	-12.25	0.962	0.743	1.171	0.996
T_5	24.34	0.768	1.897	0.689	2.624	0.903	0.498	1.442	0.914
T_6	17.19	0.904	1.990	0.885	-3.333	0.971	0.579	1.346	0.981
T_7	14.53	0.936	2.018	0.985	-6.239	0.983	0.655	1.278	0.990
T_8	13.06	0.948	2.032	0.991	-7.587	0.984	0.690	1.241	0.991
T_9	23.20	0.783	1.909	0.704	1.336	0.909	0.526	1.418	0.925
T_{10}	16.73	0.906	1.992	0.885	-3.771	0.970	0.591	1.334	0.982
T_{11}	12.50	0.957	2.036	0.974	-7.640	0.982	0.667	1.253	0.993
T_{12}	11.94	0.959	2.061	0.982	-8.986	0.981	0.712	1.226	0.995

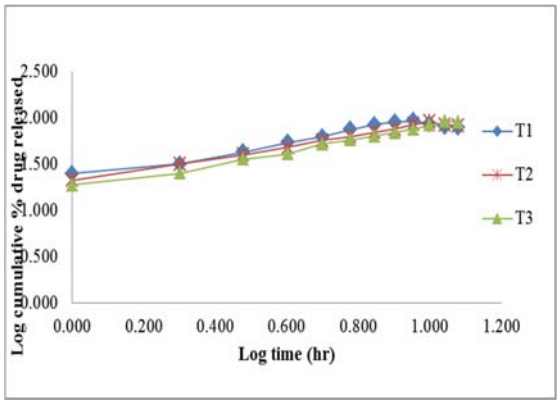

Fig 10: Korsmeyer-Peppas plots of Miglitol nanospheres formulations T_1, T_2 and T_3

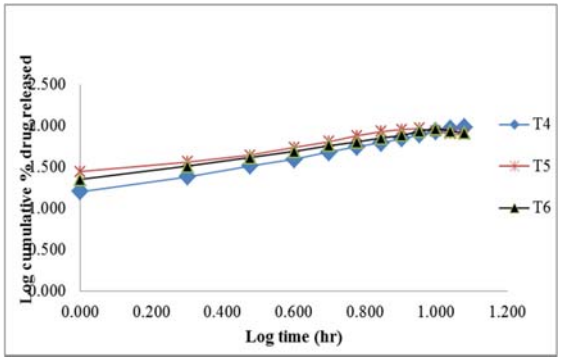

Fig 11: Korsmeyer-Peppas plots of Miglitol nanospheres formulations T_4, T_5 and T_6

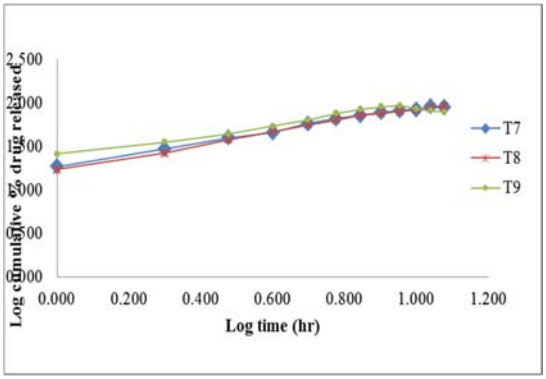

Fig 12: Korsmeyer-Peppas plots of Miglitol nanospheres formulations T_7, T_8 and T_9

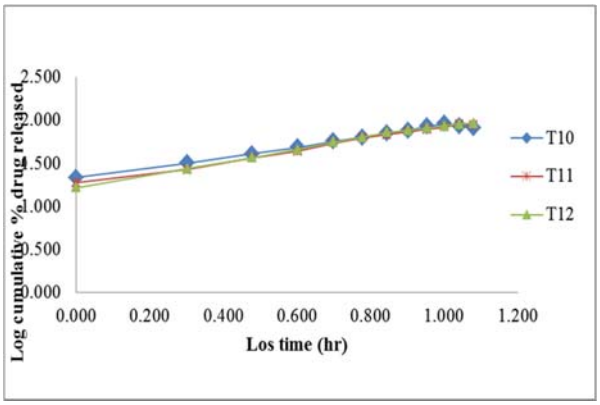

Fig 13: Korsmeyer-Peppas plots of Miglitol nanospheres formulations T_{10}, T_{11}, T_{12}

Conclusion

The results of the above investigation indicate that ionic cross linking technique Ionotropic gelation method can be successfully employed to fabricate Miglitol nanospheres. The technique provides characteristic advantage over conventional microsphere method, which involves an "all-aqueous" system, avoids residual solvents in nanospheres. Other methods utilize larger volume of organic solvents, which are costly and hazardous because of the possible explosion, air pollution and toxicity and difficult to remove traces of organic solvent completely. Micromeritic studies revealed that the mean particle size of the prepared nanospheres was in the size range of 512.1±0.2to 903.6±0.4nm and are suitable for bioadhesive nanospheres for oral administration. Increase in the polymer concentration led to increase in % yield, % drug entrapment efficiency, particle size, % swelling and % mucoadhesion. The in-vitro mucoadhesive study demonstrated that nanospheres of Miglitol using sodium alginate along with Carbopol 934 as copolymer adhered to the mucus to a greater extent than the nanospheres of Miglitol using sodium alginate along with Carbopol 971 and HPMC K4M as copolymers. The *in vitro* drug release decreased with increase in the polymer and copolymer concentration. Analysis of drug release mechanism showed that the drug release from the formulations followed non-Fickian diffusion and the best fit model was found to be Korsmeyer-Peppas. Thus, the formulated Miglitol nanospheres can achieve controlled drug release, drug targeting to the specific site (gastric mucosa) and increase the bioavailability of the drug.

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