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FORMULATION AND EVALUATION OF SUMATRIPTAN SUCCINATE MICROSPHERES BY USING DIFFERENT POLYMERS

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ABSTRACT

In the present work, Microspheres of Sumatriptan Succinate using Sodium alginate, Chitosan, Eudragit as polymers were formulated to deliver Sumatriptan Succinate via oral route. The results of this investigation indicate that solvent evaporation method can be successfully employed to fabricate Sumatriptan Succinate microspheres. FT-IR spectra of the Drug and optimised revealed that the drug is compatible with the Excipients used. Micromeritic studies revealed that the mean particle size of the prepared microspheres and are suitable for bioadhesive microspheres 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 microspheres of Sumatriptan Succinate using sodium alginate as polymer adhered to the mucus to a greater extent than the microspheres of Sumatriptan Succinate using Chitosan as polymers. The *invitro* drug release decreased with increase in the polymer concentration. Analysis of drug release mechanism showed that the drug release from the formulations followed zero order kinetics. Based on the results of evaluation tests formulation coded T3 was concluded as best formulation.

KEYWORDS: Sumatriptan Succinate, Sodium alginate, Chitosan, Eudragit, Microspheres.

INTRODUCTION

Oral route drug administration is by far the most preferable route for taking medications. However, their short circulating half life and restricted absorption via a defined segment of intestine limits the therapeutic potential of many drugs. “Microspheres can be defined as

solid, approximately spherical particles, ranging in size from 1 µm to 1000 µm containing dispersed drug molecules either in solution or in crystalline forms".[1,2]

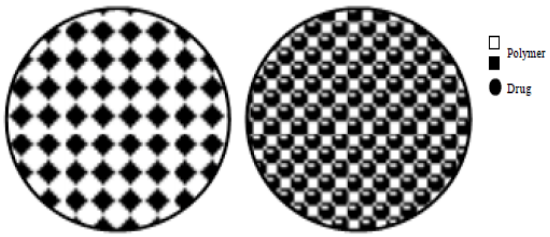

Fig. 1: Structure of Microspheres.

There are two types of microspheres[3]

Microcapsules and Micromatrices, which are described as, Microcapsules are those in which entrapped substance is distinctly surrounded by distinct capsule wall and Micromatrices in which entrapped substance is dispersed throughout the matrix. Microspheres are sometimes referred to as Microparticles. Microspheres can be manufactured from various Natural and Synthetic materials. Microspheres play an important role to improve bioavailability of conventional drugs and minimizing side effects.

Types of Microspheres[4]

1. Bioadhesive microspheres
2. Magnetic microspheres
3. Floating microspheres.
4. Radioactive microspheres
5. Polymeric microspheres.[5]

i) Biodegradable polymeric microspheres

ii) Synthetic polymeric microspheres

Methods of preparation[6]

1. Spray Drying.
2. Solvent Evaporation.
3. Single emulsion technique.
4. Double emulsion technique.
5. Phase separation coacervation technique.
6. Spray drying and spray congealing.
7. Solvent extraction.

8. Quassi emulsion solvent diffusion.

Sumatriptan Succinate is the 5-HT1B and 5-HT1D receptors function as auto receptors, which inhibit the firing of serotonin neurons and a reduction in the synthesis and release of serotonin upon activation. After sumatriptan binds to these receptors, adenylate cyclase activity is inhibited via regulatory G proteins, increases intracellular calcium, and affects other intracellular events. This results in vasoconstriction and inhibtion of sensory nociceptive (trigeminal) nerve firing and vasoactive neuropeptide release.

MATERIALS AND METHODS

Materials

Sumatriptan Succinate was procured from Sun Pharmaceuticals Pvt Ltd. Vadodara, India, provided by SURA LABS, Dilsukhnagar, Hyderabad. Sodium Alginate, Chitosan, Eudragit, Methanol, Sodium lauryl sulphate, Dichloro methane was purchased from Merk specialiities Pvt Limited, Mumbai.

Methods

Preformulation Studies

Spectroscopic Studies :Preparation Of 0.1n Hcl (pH 1.2)

Take 8.6ml of HCl in a 1000ml volumetric flask and make up the volume with distilled water.

Determination Of λ Max

Weigh 10mg of Sumatriptan Succinate and transferred into 10ml volumetric flask and dissolved in 10ml methanol (stock-I) to get concentration of 1000 µg/ml. From the stock-I take 1ml solution and make up 10ml with 0.1N HCL. From the second stock take 1ml solution and make up to 10ml with 0.1N HCL to get 10 µg/ml. Then scan from 200-400nm.

Preparation Of Standard Calibration Curve Of Sumatriptan Succinate

- 10 mg of Sumatriptan Succinate was accurately weighed and dissolved in 10ml of methanol (Stock Solution – I) to get a concentration of 1000 µg/ml.
- From the stock solution- I,1ml of aliquots was taken and suitably diluted with 0.1N HCl (Stock Solution-II) to get concentrations of 100µg/ml.
- From the stock solution- II, aliquots were taken and suitably diluted with 0.1N HCl (pH 1.2) to get concentrations in the range of 2 to 10µg/ml. The absorbance of these

samples were analyzed by using UV-Visible Spectrophotometer at 260nm against reference solution 0.1N HCl (pH 1.2). the procedure repeated to pH 6.8 phosphate buffer and pH 7.4 phosphate buffer.

Method of Preparation

Solvent Evaporation Method

Microspheres were prepared using Sodium Alginate, Chitosan, Eudragit and distilled water as continuous phase by solvent evaporation technique. Initially dichloromethane (DCM) and methanol was mixed uniformly at room temperature, then Sodium Alginate, Chitosan, Eudragit in various proportions was dissolved in the above solution. To this mixture, a drug solution corresponding was added and mixed thoroughly and injected drop wise in to the continuous phase consisting of 100mL of 0.2% (w/v) SLS (sodium lauryl sulphate) at 250 rpm. The microspheres obtained was washed for 2-3 times with distilled water and dried at room temperature. Different concentrations and ratios of polymers used in the formulation of microspheres are mentioned in Table No.1.

Table 1: Prepared formulation of Microspheres.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Sumatriptan Succinate	25	25	25	25	25	25	25	25	25	25	25	25
Sodium Alginate	25	50	75	100	-	-	-	-	-	-	-	-
Chitosan	-	-	-	-	25	50	75	100	-	-	-	-
Eudragit	-	-	-	-	-	-	-	-	25	50	75	100
Methanol	10	10	10	10	10	10	10	10	10	10	10	10
Sodium lauryl sulphate	10	10	10	10	10	10	10	10	10	10	10	10
Dicloro methane (mL)	10	10	10	10	10	10	10	10	10	10	10	10

Micromeritic Properties

The microspheres were characterized by their micromeritic properties such as particle size, bulk density, tapped density, compressibility index, Hausners ratio and angle of repose.

1. Bulk density

In this method floating microspheres are transferred to a measuring cylinder and is tapped manually till a constant volume is obtained. This volume is bulk volume and it includes true volume of the powder and the void space among the microspheres.

2. Tapped density

The ratio of mass of microspheres to volume of microspheres after tapping gives tapped

density floating microspheres.

Percent Compressibility index was determined by using the formula,

Carr's Index = (tapped density – bulk density) x 100 / tapped density

3. Hausners ratio

Hausners ratio of microspheres was determined by comparing tapped density to bulk density using the equation,

Hausner ratio = tapped density / bulk density

4. Angle of repose

Angle of repose (θ) of the microspheres, which measures the resistance to particle flow, was determined by a fixed funnel.

5. Percentage yield

The percentage of production yield was calculated from the weight of dried microspheres recovered from each batch and the sum of the initial weight of starting materials.

6. Drug entrapment efficiency

Weighed amount of microspheres (100 mg) with phosphate buffer pH 7.4 (10 ml) was added in a vial. The solution was stirred vigorously for 24 hours with mechanical stirrer. Supernatent was collected by centrifugation and drug content in supernatent was determined by using UV spectrophotometer at wavelength 260nm.

7. *In vitro* drug release study

The dissolution studies were performed in a fully calibrated eight station dissolution test apparatus (37 ± 0.5^0C, 50 rpm) using the USP type – I rotating basket method in simulated gastric fluid pH 1.2 (900ml) for 2 hours then replace the media with pH 6.8 phosphate buffer for 3 hours, then replace the media with pH 7.4 Phosphate buffer. A quantity of accurately weighed microspheres equivalent to 100mg Sumatriptan Succinate 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 260nm. At the same time the volume withdrawn at each time intervals were replenished immediately with the same volume of fresh pre-warmed simulated gastric fluid pH 1.2 maintaining sink conditions throughout the experiment.

8. In-Vitro Drug Release Kinetics

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.

Table 2: *In-Vitro* Drug Release Kinetics.

Release exponent (n)	Drugtransport 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 diffusion is Fickian.

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

Fourier Transform Infrared (FTIR) spectroscopy

The physical properties of the physical mixture were compared with those of plain drug. Samples was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in Agilent spectrophotometer and the IR spectrum was recorded from 4000 - 5000 cm^{-1}. The resultant spectrum was compared for any spectrum changes.

RESULTS AND DISCUSSION

Preformulation studies

Table 3: Calibration curve data for Sumatriptan Succinate in simulated gastric fluid pH 1.2.

Concentration (µg /ml)	Absorbance(nm)
0	0
10	0.114
20	0.234
30	0.331
40	0.441
50	0.539

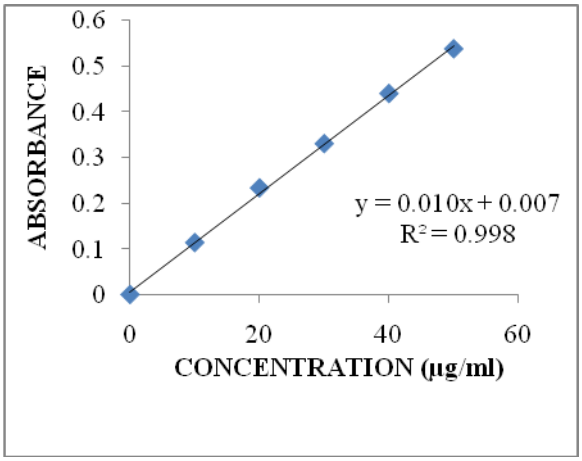

Fig. 2: Standard graph of Sumatriptan Succinate in simulated gastric fluid pH 1.2.

Table 4 shows the calibration curve data of Sumatriptan Succinate in pH 7.4 phosphate buffer at 262nm. Fig. 8.2 shows the standard calibration curve with a regression value of 0.999, slope of 0.011 and intercept of 0.003 in simulated gastric fluid pH 1.2. The curve was found to be linear in the concentration range of 10-50µg/ml.

Table 4: Calibration curve data for Sumatriptan Succinate in pH 7.4 phosphate buffer.

Concentration (µg /ml)	Absorbance
0	0
10	0.126
20	0.237
30	0.341
40	0.468
50	0.586

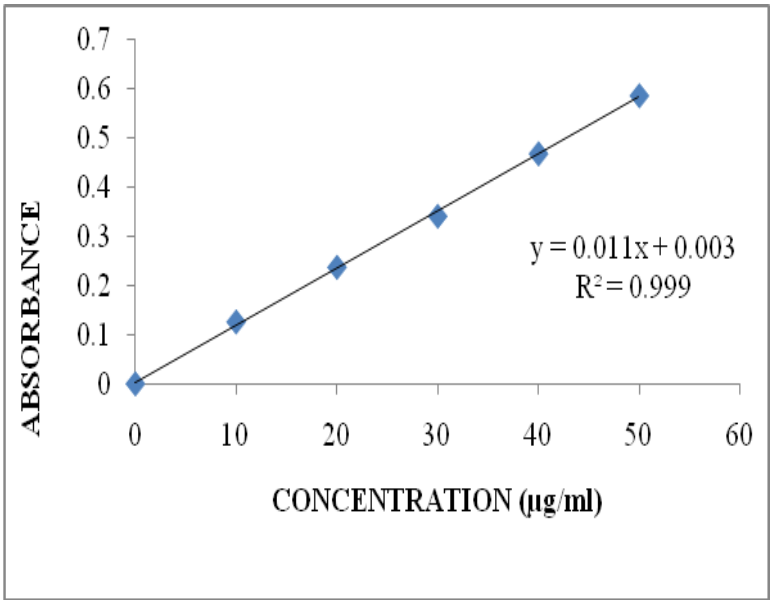

Fig. 3: Standard graph of Sumatriptan Succinate in pH 7.4 phosphate buffer.

Evaluation And Characterisation of Microspheres

Micromeritic Properties

The mean 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 microspheres size. Microspheres containing Sodium Alginate as a polymer had a size range of 314.26±1.68 µm to 487.3±2.71 µm. microspheres containing Chitosan as polymer exhibited a size range between 410.31±1.42 µm to 461.2±1.17µm. Microspheres containing Eudragit as copolymer had a size range of 361.12±2.14 µm to 428.41±3.47 µm.

The bulk density of formulation F1 to F12 containing Sodium Alginate, Chitosan, Eudragit formulation was in the range of 0.291 ±0.01 to 0.417 ±0.02 gm./cm^3 (as shown in table 8.3), tapped density 0.304 ± 0.01 to 0.430 ± 0.02 and hausners ratio 1.026 ± 0.01 to 1.045 ± 0.01.

The carr's index of formulation F1 to F12 containing different grades of Sodium Alginate, Chitosan, Eudragit 1.037 ± 0.01 to 4.309 ± 0.03 respectively. The angle of repose of formulation F1 to F12 containing Sodium Alginate, Chitosan, Eudragit formulation was in the range <23 respectively. The values of carr's index and angle of repose indicate good flow properties.

Table 5: Micromeritic property of floating microspheres of Sumatriptan Succinate.

Formulation code	Mean partical size	Bulk density ((gm./cm3))	Tapped density (gm./cm^3)	Hauseners ratio	Carr's index	Angle of repose
F1	314.26±1.68	0.351 ±0.01	0.364 ± 0.01	1.037 ± 0.01	3.571 ± 0.02	20.321 ±0.16
F2	415.9±1.18	0.291 ±0.01	0.304 ± 0.01	1.045 ± 0.01	4.309 ± 0.03	23.942 ±0.15
F3	391.64±2.19	0.373 ±0.01	0.383 ± 0.01	1.026 ± 0.01	2.610 ± 0.01	20.120 ±0.12
F4	487.3±2.71	0.318 ±0.01	0.329 ± 0.01	1.034 ± 0.01	3.459 ± 0.02	17.108 ±0.15
F5	410.31±1.42	0.417 ±0.02	0.428 ± 0.02	1.026 ± 0.01	2.570 ± 0.01	16.926 ±0.13
F6	461.2±1.17	0.386 ±0.01	0.398 ± 0.01	1.031 ± 0.01	2.917 ± 0.02	17.181 ±0.13
F7	432.1±1.27	0.307 ±0.01	0.318 ± 0.01	1.037 ± 0.01	3.611 ± 0.01	21.170 ±0.12
F8	448.31±1.55	0.406 ±0.02	0.419 ± 0.02	1.032 ± 0.01	3.102 ± 0.02	16.812 ±0.12
F9	398.58± 2.64	0.383 ±0.01	0.397 ± 0.01	1.036 ± 0.01	3.429 ± 0.02	16.909 ±0.13
F10	378.12±1.25	0.327 ±0.01	0.339 ± 0.01	1.037 ± 0.01	3.539 ± 0.01	16.537 ±0.09
F11	428.41±3.47	0.416 ±0.02	0.430 ± 0.02	1.034 ± 0.01	3.258 ± 0.02	16.921 ±0.11
F12	361.12±2.14	0.372 ±0.01	0.387±0.01	1.040 ± 0.01	1.037 ± 0.01	17.103 ±0.12

Percentage yield

It was observed that as the polymer ratio in the formulation increases, the product yield also increases. The low percentage yield in some formulations may be due to blocking of needle and wastage of the drug- polymer solution, adhesion of polymer solution to the magnetic bead

and microspheres lost during the washing process. The percentage yield was found to be in the range.

Drug entrapment efficiency

Percentage Drug entrapment efficiency of Sumatriptan Succinate ranged from 62.15 to 95.18 % for microspheres containing sodium alginate, Chitosan and Eudragit polymer, The drug entrapment efficiency of the prepared microspheres increased progressively with an increase in proportion of the respective polymers. Increase in the polymer concentration increases the viscosity of the dispersed phase. The particle size increases exponentially with viscosity. The higher viscosity of the polymer solution at the highest polymer concentration would be expected to decrease the diffusion of the drug into the external phase which would result in higher entrapment efficiency. The % drug entrapment efficiency of the prepared microspheres is displayed in Table 6, and displayed in Figures.

Table 6: Percentage yield and percentage drug entrapment efficiency of the prepared microspheres.

S. No.	Formulation code	% yield	Drug Content (mg)	% Drug entrapment efficiency
1	T_1	91.88	98.12	74.75
2	T_2	92.11	99.64	91.14
3	T_3	91.69	96.15	70.16
4	T_4	94.78	99.67	85.77
5	T_5	95.41	97.48	92.68
6	T_6	91.25	99.81	68.48
7	T_7	90.23	99.34	95.18
8	T_8	96.11	98.60	77.85
9	T_9	92.17	99.11	62.15
10	T_{10}	93.64	95.92	85.61
11	T_{11}	90.12	98.29	90.49
12	T_{12}	86.31	99.83	78.25

Swelling studies

The swelling ratio is expressed as the percentage of water in the hydrogel at any instant during swelling. Swell ability is an important characteristic as it affects mucoadhesion as well as drug release profiles of polymeric drug delivery systems. Swellability is an indicative parameter for rapid availability of drug solution for diffusion with greater flux. Swellability data revealed that amount of polymer plays an important role in solvent transfer. Thus we can say that amount of polymer directly affects the swelling ratio. As the polymer to drug ratio increased, the percentage of swelling increased from 29 to 60% for microspheres containing

sodium alginate as polymer, 59 to 73% for microspheres containing Chitosan as polymer. The percentage of swelling of the prepared microspheres is displayed in Figures. Containing Eudragit as polymer.

Table 7: Swelling studies.

S. No.	Formulation Code	Initial (Wt.)	Final (Wt.)	Percentage Swelling
1	T_1	10	11.21	29
2	T_2	10	13.54	49
3	T_3	10	18.61	71
4	T_4	10	16.91	60
5	T_5	10	19.75	73
6	T_6	10	17.61	67
7	T_7	10	14.99	59
8	T_8	10	18.42	71
9	T_9	10	19.22	90
10	T_{10}	10	17.24	87
11	T_{11}	10	18.31	48
12	T_{12}	10	16.54	83

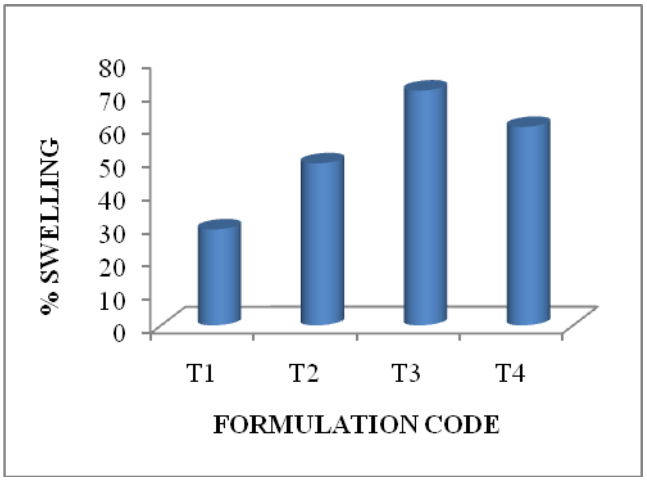

Fig. 4: Percentage swelling of microspheres containing sodium alginate.

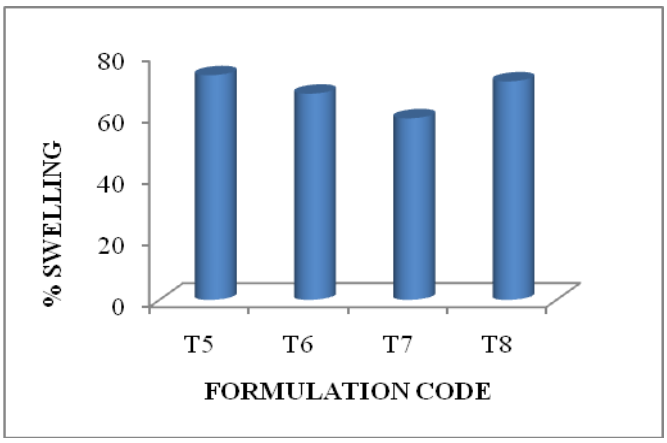

Fig. 5: Percentage swelling of microspheres containing Chitosan.

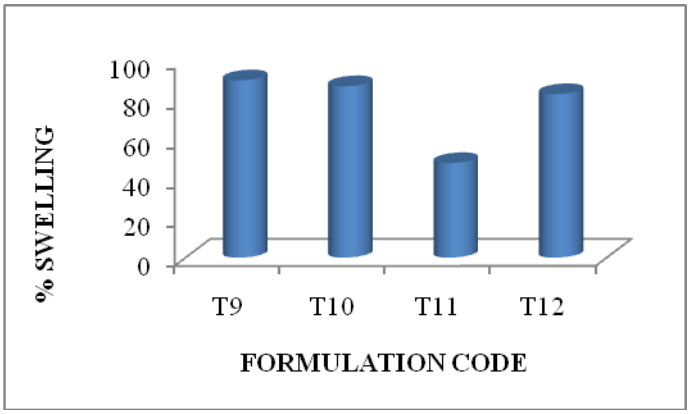

Fig. 6: Percentage swelling of microspheres containing Eudragit.

In-Vitro Mucoadhesion Test

As the polymer to drug ratio increased, microspheres containing sodium alginate exhibited % mucoadhesion ranging from 69 to 91%, microspheres containing Chitosan exhibited % mucoadhesion ranging from 76 to 91% and microspheres containing Eudragit exhibited % mucoadhesion ranging from 58 to 79%.

Table 8: Percentage mucoadhesion of the prepared microspheres.

S. No.	Formulation Code	No. of Microspheres		Percentage Mucoadhesion
		Initial (Wt.)	Final (Wt.)	
1	T_1	20	14.61	60
2	T_2	20	11.39	59
3	T_3	20	16.20	72
4	T_4	20	15.84	91
5	T_5	20	19.95	83
6	T_6	20	18.32	76
7	T_7	20	15.42	83
8	T_8	20	12.65	91
9	T_9	20	18.72	79
10	T_{10}	20	15.68	63
11	T_{11}	20	17.84	58
12	T_{12}	20	14.26	73

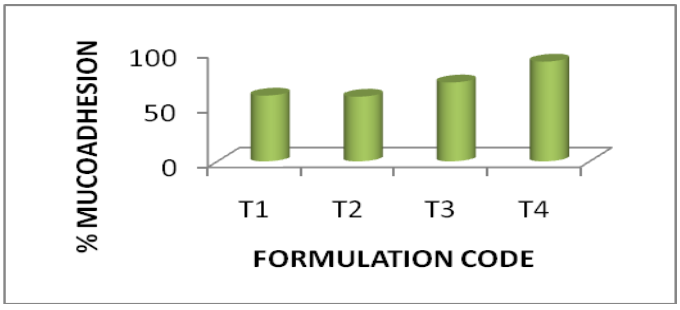

Fig. 7: Percentage mucoadhesion of microspheres containing sodium alginate.

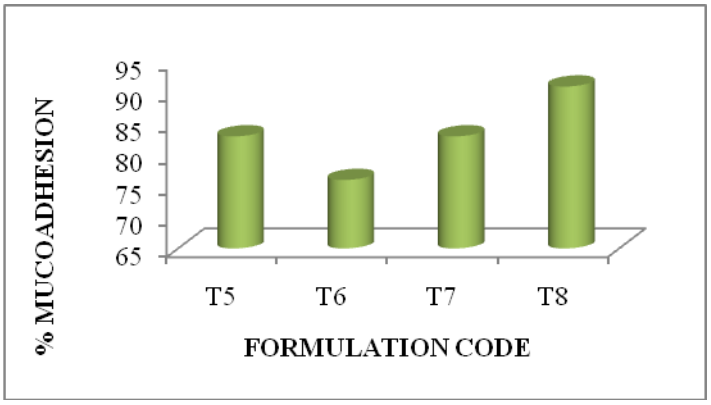

Fig. 8: Percentage mucoadhesion of microspheres containing Chitosan.

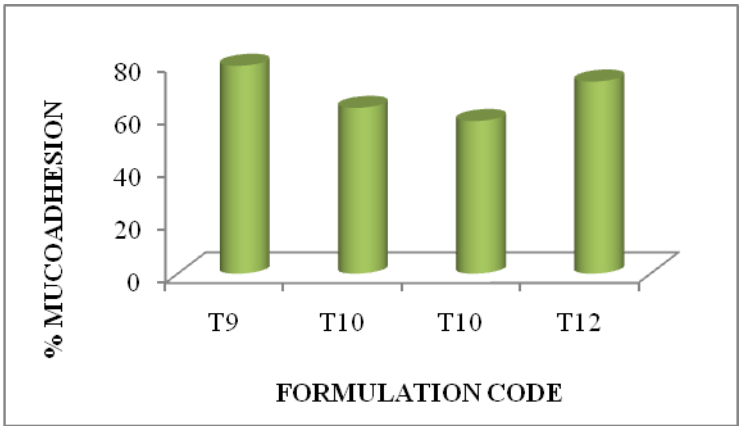

Fig. 9: Percentage mucoadhesion of microspheres containing Eudragit.

IN-VITRO Drug Release Studies

Dissolution studies of all the formulations were carried out using dissolution apparatus USP type I. The dissolution studies were conducted by using dissolution media, pH 1.2. The results of the in-vitro dissolution studies of formulations T1 to T12 are shown in table. The plots of Cumulative percentage drug release Vs. Time. Figure shows the comparison of % CDR for formulations T1 to T4, figure for formulations T5 to T8 and T9 to T12.

The formulations T_1, T_2, T_3 and T_4 containing Sodium Alginate showed a maximum release of 96.73% at 8 hours, 97.76% after 10 hours, 99.12% 12 hours and 91.47% after 12 hours respectively.

The formulations T_5, T_6, T_7 and T_8 containing Chitosan polymer showed a maximum release of 95.18% after 9 hours, 96.18% after 11 hours, 98.10% after 12 hours and 94.68% after 12 hours respectively.

The formulations T_9, T_{10}, T_{11} and T_{12} containing Eudragit showed a maximum release of 93.97% after 12 hours, 95.53% after 12 hours, 97.47% after 9 hours and 98.66% after 10 hours respectively.

This shows that more sustained release was observed with the increase in percentage of polymers. As the polymer to drug ratio was increased the extent of drug release decreased. A significant decrease in the rate and extent of drug release is attributed to the increase in density of polymer matrix that results in increased diffusion path length which the drug molecules have to traverse. The release of the drug has been controlled by swelling control release mechanism. Additionally, the larger particle size at higher polymer concentration also restricted the total surface area resulting in slower release.

Table 9: In-*Vitro* drug release data of Sumatriptan Succinate microspheres containing sodium alginate.

Time (h)	Cumulative Precent of Drug Released			
	T_1	T_2	T_3	T_4
0	0	0	0	0
1	21.12	19.25	15.48	14.97
2	33.61	23.14	21.91	22.54
3	45.59	33.27	34.48	28.16
4	56.46	46.80	39.16	36.73
5	60.28	53.96	48.10	44.97
6	75.92	64.91	51.22	53.87
7	87.89	68.75	60.11	60.17
8	96.73	74.13	67.81	67.98
9		82.94	77.43	72.55
10		97.76	82.66	81.70
11			91.84	84.10
12			99.12	91.47

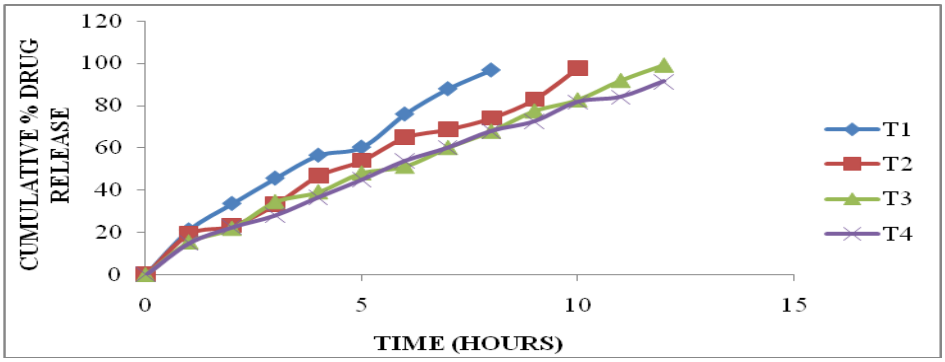

Fig. 10: In-Vitro drug release profile of Sumatriptan Succinate microspheres containing sodium alginate.

Table 10: *In-Vitro* drug release data of Sumatriptan Succinate microspheres containing Chitosan.

Time (h)	Cumulative Precent of Drug Released			
	T_5	T_6	T_7	T_8
0	0	0	0	0
1	22.87	15.74	13.94	11.31
2	32.11	26.22	22.67	20.76
3	42.62	30.51	35.72	28.41
4	53.92	43.96	44.14	32.93
5	65.09	56.15	54.18	45.72
6	72.87	62.85	62.90	52.84
7	82.19	69.49	71.98	59.36
8	87.67	73.65	76.16	65.84
9	95.18	77.95	81.74	72.20
10		86.83	89.50	77.89
11		96.18	92.14	86.24
12			98.10	94.68

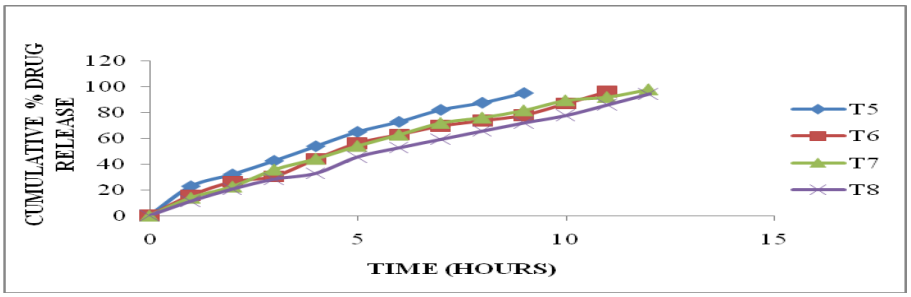

Fig. 11: *In-Vitro* drug release profile of Sumatriptan Succinate microspheres containing Chitosan.

Table 11: *In-Vitro* drug release data of Sumatriptan Succinate microspheres containing Eudragit.

Time (h)	Cumulative Precent of Drug Released			
	T_9	T_{10}	T_{11}	T_{12}
0	0	0	0	0
1	29.10	16.44	28.19	22.19
2	37.34	25.53	36.75	44.41
3	38.63	26.54	52.24	52.68
4	41.12	33.85	69.45	67.03
5	47.38	37.63	75.28	73.93
6	62.59	47.35	80.23	81.03
7	68.74	54.5	89.06	87.92
8	73.33	67.34	92.16	92.41
9	81.25	73.93	97.47	95.94
10	87.12	75.51		98.66
11	91.68	86.82		
12	93.97	95.53		

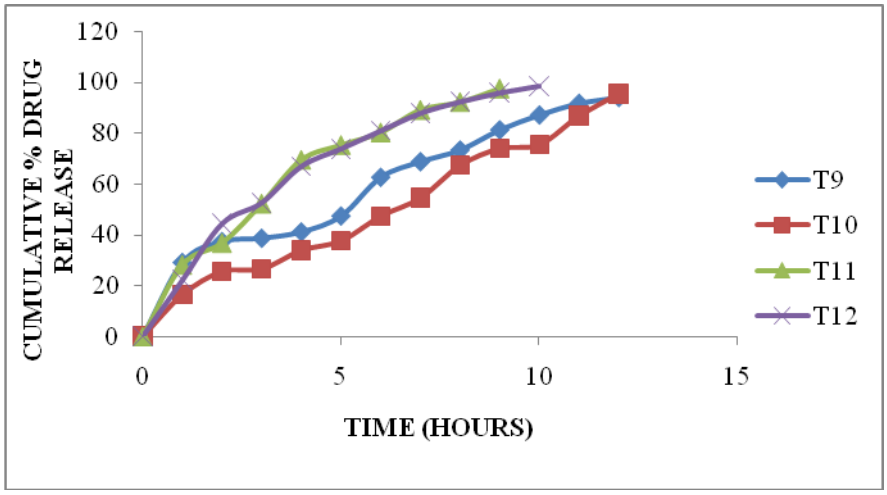

Fig. 12: *In-Vitro* drug release profile of Sumatriptan Succinate microspheres containing Eudragit.

In-Vitro Drug Release Kinetics

For understanding the mechanism of drug release and release rate kinetics of the drug from dosage form, the in-vitro drug dissolution data obtained was fitted to various mathematical models such as zero order, First order, Higuchi matrix, and Krosmeyer-Peppas model. The coefficient of determination (R2) 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 zero order release kinetics whereas release exponent value (n) ranged from 0.992. From the coefficient of determination and release exponent values, it can be suggested that the mechanism of drug release follows zero order release kinetics along with non-Fickian diffusion mechanism which leading to the conclusion that a release mechanism of drug followed combination of diffusion and spheres erosion.

Table 12: Release Kinetics Studies of the Optimized Formulation (T3).

Cumulative (%) Release Q	Time (T)	Root (T)	Log (%) Release	Log (T)	Log (%) REMAIN	Release Rate (Cumulative % Release / t)	1/Cum% Release	Peppas log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	**0**	0			2.000				100	4.642	4.642	0.000
15.48	1	1.000	1.190	0.000	1.927	15.480	0.0646	-0.810	84.52	4.642	4.389	0.253
21.91	2	1.414	1.341	0.301	1.893	10.955	0.0456	-0.659	78.09	4.642	4.274	0.367
34.48	3	1.732	1.538	0.477	1.816	11.493	0.0290	-0.462	65.52	4.642	4.031	0.610
39.16	4	2.000	1.593	0.602	1.784	9.790	0.0255	-0.407	60.84	4.642	3.933	0.709
48.1	5	2.236	1.682	0.699	1.715	9.620	0.0208	-0.318	51.9	4.642	3.730	0.911
51.22	6	2.449	1.709	0.778	1.688	8.537	0.0195	-0.291	48.78	4.642	3.654	0.988
60.11	7	2.646	1.779	0.845	1.601	8.587	0.0166	-0.221	39.89	4.642	3.417	1.225
67.81	8	2.828	1.831	0.903	1.508	8.476	0.0147	-0.169	32.19	4.642	3.181	1.461
77.43	9	3.000	1.889	0.954	1.354	8.603	0.0129	-0.111	22.57	4.642	2.826	1.816
82.66	10	3.162	1.917	1.000	1.239	8.266	0.0121	-0.083	17.34	4.642	2.588	2.053
91.84	11	3.317	1.963	1.041	0.912	8.349	0.0109	-0.037	8.16	4.642	2.013	2.628
99.12	12	3.464	1.996	1.079	-0.056	8.260	0.0101	-0.004	0.88	4.642	0.958	3.683

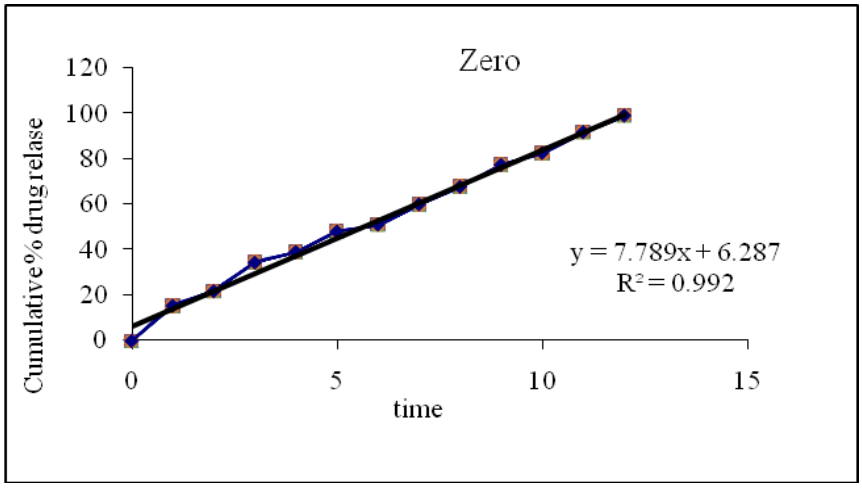

Fig. 13: Graph of zero order release kinetics of optimized formula.

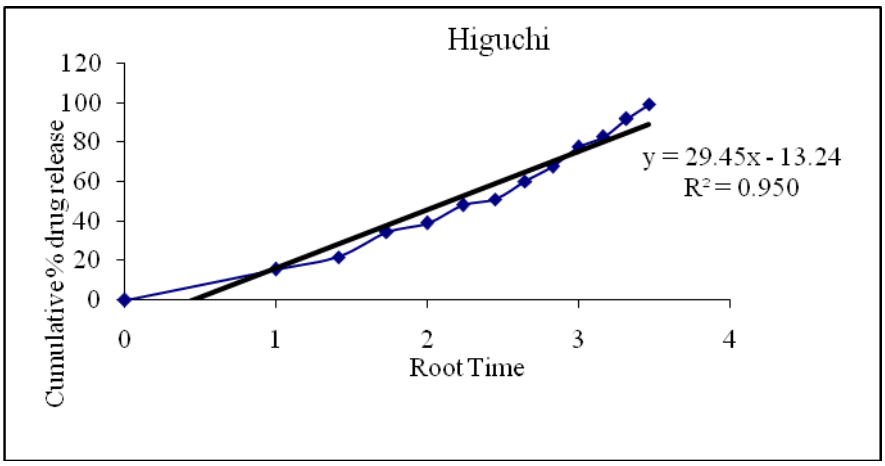

Fig. 14: Graph of higuchi release kinetics of optimized formula.

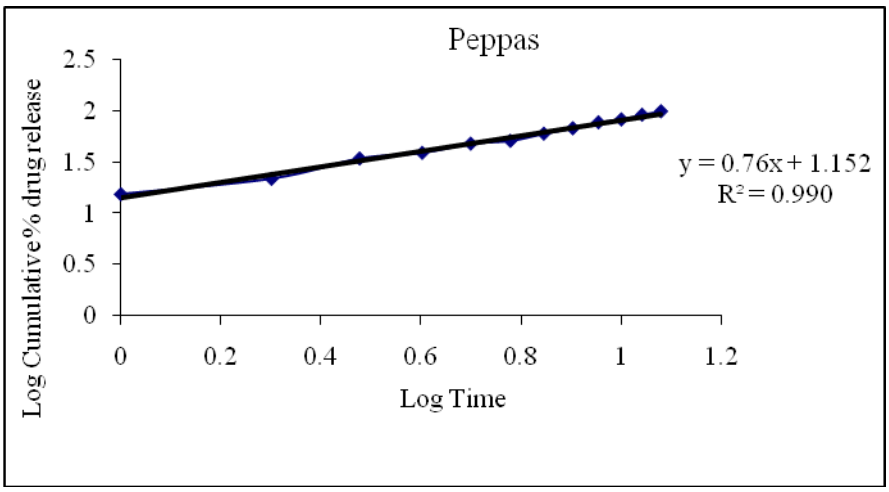

Fig. 15: Graph of peppas drug release kinetics of optimized formula.

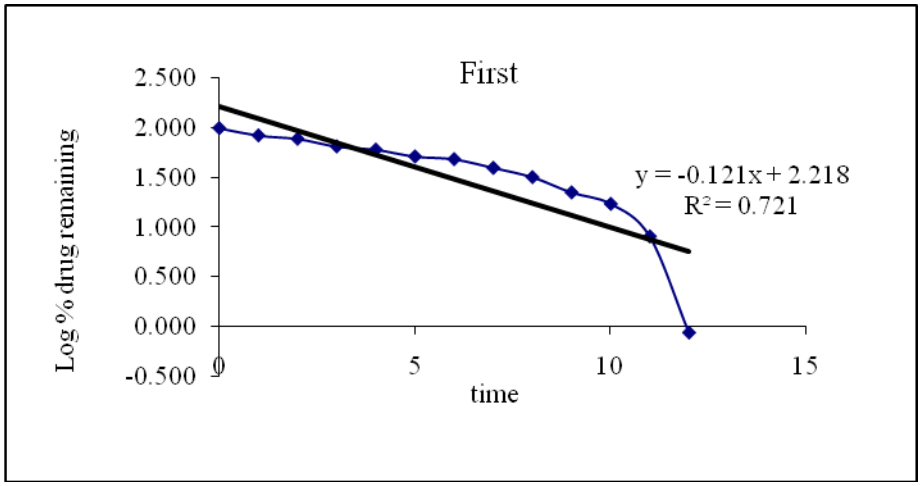

Fig. 16: Graph of first order release kinetics of optimized formula.

Optimised formulation F3 was kept for release kinetic studies. From the above graphs it was evident that the formulation F3 was followed zero order release kinetics.

Compatibility Studies

Drug polymer compatibility studies were carried out using Fourier Transform Infra Red spectroscopy to establish any possible interaction of Drug with the polymers used in the formulation. The FT-IR spectra of the formulations were compared with the FTIR spectra of the pure drug.

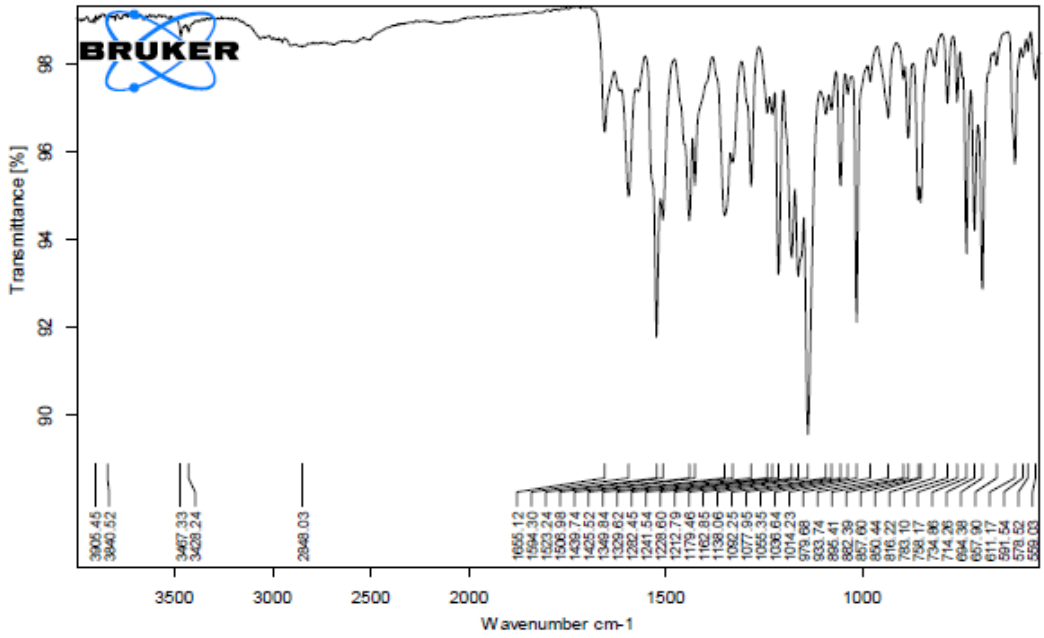

Fig. 17: FT-IR spectra of Pure drug.

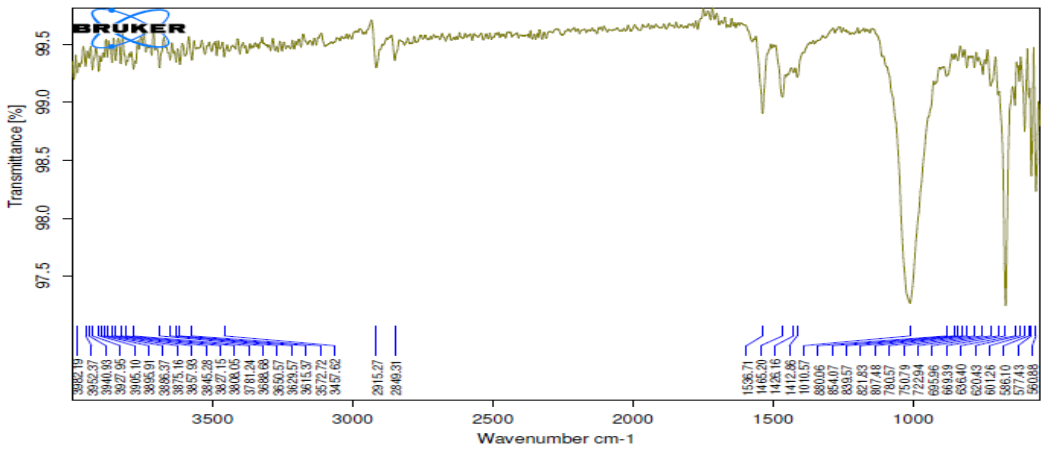

Fig. 18: FT-IR spectra of Optimised formulation SEM.

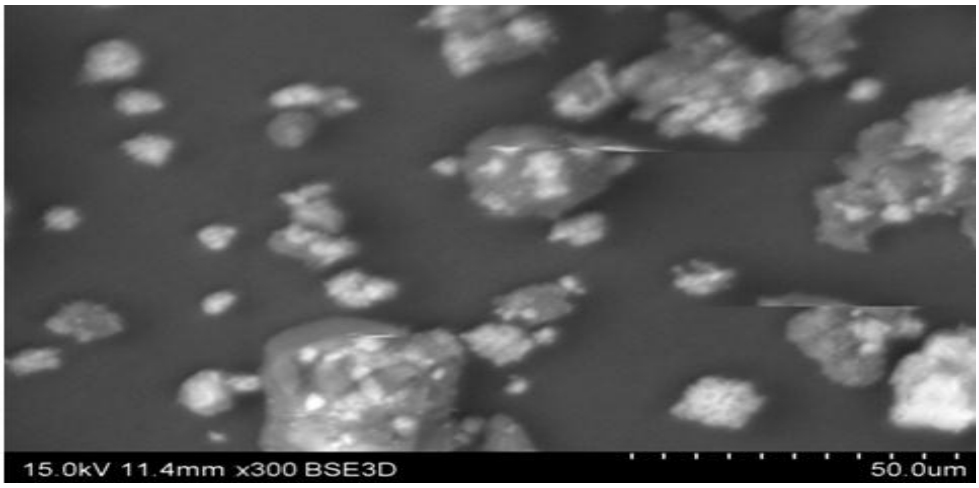

Fig. 19: SEM of Optimised formulation.

CONCLUSION

In the present work, bioadhesive microspheres of Sumatriptan Succinate using Sodium alginate, Chitosan, Eudragit as polymers were formulated to deliver Sumatriptan Succinate via oral route. From the study following conclusions could be drawn:-

- The results of this investigation indicate that ionic cross linking technique solvent evaporation method can be successfully employed to fabricate Sumatriptan Succinate microspheres. The technique provides characteristic advantage over conventional microsphere method, which involves an “all-aqueous” system, avoids residual solvents in microspheres. Other methods utilize larger volume of organic solvents, which are costly and hazardous because of the possible explosion, air pollution, toxicity and difficult to remove traces of organic solvent completely.

- Micromeritic studies revealed that the mean particle size of the prepared microspheres was in the size range of 314.26±1.68 µm to 487.3±2.71 µm and are suitable for bioadhesive microspheres for oral administration.
- Increase in the polymer concentration lead to increase in % Yield, % Drug entrapment efficiency, Particle size, % swelling and % Mucoadhesion.
- The *in-vitro* mucoadhesive study demonstrated that microspheres of Sumatriptan Succinate using sodium alginate, Chitosan, Eudragit as polymer adhered to the mucus to a greater extent than the microspheres of Sumatriptan Succinate.
- The *invitro* drug release decreased with increase in the polymer concentration.
- Based on the results of evaluation tests formulation coded T_3 was concluded as best formulation.
- Analysis of drug release mechanism showed that the drug release from the formulations the best fit model was found to be zero order release kinetics.

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