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FORMULATION AND EVALUATION OF MUCOADHESIVE MICROSPHERES OF AN ANTI-MIGRAINE DRUG

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ABSTRACT

Objective: The objective of this research work is to develop and evaluate mucoadhesive microspheres of an anti-migraine drug for sustained release. **Materials and Methods:** Mucoadhesive microspheres were prepared by emulsification method using Sodium alginate (SA), polyvinyl pyrrolidone (PVP) and Chitosan in the various drug-polymer ratios of 1:1, 1:2 and 1:3. Nine formulations were formulated and evaluated for possible drug polymer interactions, percentage yield, micromeritic properties, particle size, drug content, drug entrapment efficiency, drug loading, swelling index, *In-vitro* wash off test, *in vitro* drug release, surface morphology and release kinetics. **Results:** The results showed that no significant drug polymer interaction in FTIR studies. Among all the formulations SF3 containing sodium alginate showed 77.18% drug release in 6hrs. **Conclusion:** Amongst the developed mucoadhesive microspheres, SF3 formulation containing sodium alginate exhibited slow and sustained release in a controlled manner and it is a promising formulation for sustained release of Sumatriptan succinate.

Keywords: Mucoadhesive microspheres**,** Sodium alginate, polyvinyl pyrrolidone, Chitosan**,** sustained release.

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INTRODUCTION

Mucoadhesive microspheres is one category of microspheres offers advantage of increasing the residence time, efficient absorption, enhanced bioavailability, much more intimate contact with the mucus layer and reduction in frequency of drug administration. Hence, in this study an effective attempt was made to formulate the mucoadhesive microspheres of sumatriptan succinate as a model drug whose half-life is 2.5hrs with poor bioavailability of 14% due to first pass metabolism. The drug was chosen with an objective to sustain the drug action and to enhance the bioavailability. In order to improve the bioavailability, localization of the active component to a specific site mucoadhesive drug delivery systems have been utilized for the designing of microspheres using, Mucoadhesive polymers. Mucoadhesive polymers are water-soluble and water insoluble polymers, which are swellable network, joined by cross linking agents. These polymers possess optimal polarity to make sure that they permit sufficient wetting by the mucus and optimal fluidity that permits the mutual adsorption and interpenetration of polymer and mucus.[1,2,3]. In this study sumatriptan succinate mucoadhesive microspheres are formulated and evaluated.

MATERIALS AND METHODS

Materials

Sumatriptan succinate was obtained as gift sample from Sunglow pharmaceuticals Pvt Ltd, Puducherry. Sodium alginate, PVP and Chitosan were obtained from Loba Chemie Pvt Ltd. The other solvents like acetic acid, liquid paraffin (light), span 80, glutaraldehyde and n-hexane were of Analytical Research (AR) Grade and obtained from Merck specialties Pvt. Ltd.

Pre-formulation studies:

Pre-formulation is considered as important phase where

researcher characterizes the physical, mechanical and chemical properties of new drug substance which helps to develop stable, effective and safe dosage forms. Not only for drug, but also they check possible interaction with various excipients.

Organoleptic properties:

- **Colour:** A small quantity of Sumatriptan succinate was taken in a butter paper and viewed in well-illuminated place.
- **Taste and Odour:** Very less quantity of Sumatriptan succinate was used to get the taste with the help of tongue as well as smelled to get the odour.

Solubility studies of Sumatriptan succinate [4]

An excess quantity of Sumatriptan succinate is taken separately and added in 10ml of different solutions (methanol, alcohol, phosphate buffer and water). The solutions are shaken well for few minutes. Then the solubility is observed. The absorbance is measured using UV visible spectrophotometer at respective λmax.

Analysis of sumatriptan succinate [4]

100mg of Sumatriptan succinate is accurately weighed and transferred into a 100ml volumetric flask which contains 50ml buffer solution and the volume is made up to the mark by using buffer solution.

From the stock solution, different concentrations of solutions are made and its absorbance is measured using UV visible spectrophotometer at respective λmax.

Compatibility study between drug and polymer [5]

The FTIR spectra of the drug (alone), polymer (alone) and the drug-polymer (mixture) were recorded by the potassium bromide pellet method. The pellets were scanned over a wave number range of 4000–400 cm^{-1} in a Thermo scientific, FTIR instrument.

Formulation of mucoadhesive microspheres

Preparation of mucoadhesive microspheres by Emulsification method:

An accurately weighed amount of drug is dispersed in an individual polymer solution namely Sodium alginate, Poly vinyl pyrrolidone and Chitosan. The drug polymer solutions are taken in the ratio of 1:1, 1:2, and 1:3 for all the three polymers. The dispersions are emulsified in liquid paraffin containing 2% v/v span 80 and the solution is stirred using a mechanical stirrer at 1500-2000 rpm for 1 hr. Cross linking agent (Calcium Chloride and Glutaraldehyde) is added to the emulsion slowly and stirring is continued for 2 hrs (For Sodium alginate and Chitosan). The prepared microspheres are collected by filtration and washed 3 times with suitable solvent to remove liquid paraffin. Then, the microspheres are lyophilized to dry.

Characterization of mucoadhesive microspheres

Percent yield

The prepared microspheres are evaluated for percentage yield. The percentage yield is calculated as per equation below,

$$\text{Percent yield} = \frac{\text{The amount of microspheres obtained (gms)}}{\text{The theoretical amount (gms)}} \times 100$$

Micromeritic properties:

The microspheres are characterized for micromeritic properties such as true density, tapped density, compressibility index and flow properties. The tapped density and compressibility index is determined by tapping method.

Bulk density

True density of microspheres is determined by pouring sample through a glass funnel into a graduated cylinder. The volumes occupied by the microspheres are recorded. True density is calculated.

$$\text{Bulk density (gm/ml)} = \frac{\text{Weight of microspheres in gms}}{\text{Volume occupied by the microspheres}}$$

Tapped density

Tapped density of microspheres is determined by pouring sample through a glass funnel into a graduated cylinder. The tapped volume occupied by the microspheres is recorded. Tapped density is calculated by using the formula

$$\text{Tapped density (gm/ml)} = \frac{\text{Weight of microspheres in gms}}{\text{Vol occupied by the microspheres (after taping)}}$$

Angle of repose

Flow ability of the prepared microspheres is determined by calculating angle of repose by fixed funnel method. A funnel with 10 mm inner diameter of stem is fixed at a height of 2 cm. over the platform. About 10 gm of sample is slowly passed along the wall of the funnel till the tip of the pile formed and touches the steam of the funnel. A rough circle is drawn around the pile base and the radius of the powder cone is measured. Angle of repose is calculated by using the following formula,

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

Where, θ = Angle of repose

h = Height of the pile

r = Average radius of the powder cone

Carr's Index

It is also one of the simple methods to evaluate flow property of powder by comparing the bulk density and tapped density. A useful empirical guide is given by the Carr's compressibility.

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Particle size analysis:

The Mucoadhesive microspheres are examined by optical microscope. The freshly prepared suspension of microspheres is examined on an optical microscope and size of the microspheres is measured by using a pre-calibrated ocular micrometer and stage micrometer.[6]

Drug entrapment efficiency:[7]

Drug loaded microspheres (100 mg) are powdered and

transferred into 100 ml volumetric flask dissolved in 10 ml of solvent and the volume is made up with suitable dissolution medium. The resultant dispersion was kept for 24 hrs for complete dissolution and filtered through a 0.45 µm membrane filter. The drug entrapment efficiency is determined spectrophotometrically after appropriate dilutions at respective λmax. The drug entrapment efficiency is calculated by the following equation, Drug Entrapment Efficiency = Amount of drug in microspheres / Amount of drug added initially × 100.

Determination of drug content in microspheres

Drug loaded microspheres (100 mg) are powdered and transferred into 100 ml volumetric flask dissolved in 10 ml of solvent and the volume is made up with suitable dissolution medium. The drug content is determined spectrophotometrically after appropriate dilutions at respective λmax. The drug content is calculated by the following equation,

Drug content = Amount of drug in microspheres / Amount of microspheres × 100

Determination of drug loading in microspheres

The drug loading in the microspheres is estimated by using the formula

$$L = Qm/Wm \times 100$$

Where,

L = Percentage of drug loading in the microspheres

Wm= Weight of microspheres in grams

Qm = Quantity of drug present in Wm grams of microspheres.

Swelling index: [8]

The swelling index is a property measured to know the behaviour of polymer in physiological solution. It is determined by keeping the microspheres in buffer solution for 24 h and washed. The swelling index is calculated using formula,

$$\alpha = \frac{W2 - W1}{W1}$$

Where,

α is swelling index, W1 is weight of microspheres before swelling and W2 is weight of microspheres after swelling.

***In-vitro* wash off test (mucoadhesion test):** [9]

The mucoadhesive properties of the microspheres were evaluated by in vitro wash-off test. A 4cm x 4cm piece of goat intestinal mucosa was tied onto the paddle bottom of a USP dissolution test apparatus - II using a thread. A weighed amount of microspheres, i.e. 100mg were spread onto the wet, rinsed tissue specimen. The dissolution test apparatus was operated such that the tissue specimen was rotated at a speed of 25 rpm in phosphate buffer (pH 7.4). At the end of 6th hour, the amount of microspheres still adhering onto the tissue was scrapped and weighed. The percentage mucoadhesion of the microspheres was determined using the following formula:

$$\text{Percentage mucoadhesion} = \frac{W2}{W1} \times 100$$

Where,

$W_1$is weight of microspheres applied

$W_2$is weight of microspheres still adhered

***In vitro* drug release study**

The drug release is studied by using USP type II apparatus at 37 ± 0.5^{0}C and at 100 rpm in phosphate buffer pH7.4. Five ml of the sample solution is withdrawn at predetermined time intervals, filtered, diluted suitably and analyzed spectrophotometrically. Equal amount of the fresh dissolution medium is replaced immediately after withdrawal of the test sample. Percentage drug dissolved at different time intervals is calculated using the Lambert-Beer's equation. The result is obtained in triplicate and the average value reported.[10]

***In-vitro* drug release study of selected mucoadhesive microspheres of sumatriptan succinate and marketed conventional tablets**

The *In-vitro* drug release values of selected mucoadhesive microspheres of sumatriptan succinate were compared with the marketed conventional tablet.

Surface topography by Scanning Electron

The surface morphology and structure are visualized by scanning electron microscopy (SEM) [10]

Release Kinetics Studies [11]

Drug release pattern from microspheres:

In order to understand the mechanism and kinetics of drug release, the results of the in vitro drug release study are fitted with various kinetic equations like zero order, first order and Higuchi model. In order to define a model which will represent a better fit for the formulation.

1. Zero – order model: Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the equation:

$Q_t = Q_0 + K_0t$

Where,

Q_t is the amount of drug dissolved in time t,

Q_0 is the initial amount of drug in the solution,

K_0 is the zero order release constant and

t is time in hours.

Expressed in units of concentration/time.

Graph: X- axis is time in hours and Y- axis is % cumulative drug release.

2. First order model: The release of the drug which followed first order kinetics can be expressed by the equation:

$\text{Log } Qt = \log Q_0 + Kt / 2.303$

Where,

Q0 is the initial concentration of drug,

Qt is cumulative amount of drug released per unit surface area,

k is the first order rate constant and

t is the time.

Graph: X- axis is time in hours and Y- axis is log % cumulative drug release.

3. Higuchi model: Higuchi model describes the drug release from several typed of matrices initially conceived for planar systems, then extended to different geometrics and porous systems. It was derived by higuchi in 1961. For higuchi release kinetics equation is,

$Q = KH\ t_0$.

Where,

Q is amount of drug released per unit surface area of the dosage form

KH is Higuchi release rate constant and

t is time.

4. Korsmeyer – Peppas model: Koresmeyer derived a simple relationship which describes drug release from a polymeric system. To find out the mechanism of drug release, first 60% drug release data was fitted in Koresmeyer – Peppas model equation,

(Mt/M) = Km tn

Where,

Mt is amount of drug released at time t,

M is total amount of drug in dosage form,

Km is kinetic constant,

n is diffusion and release exponent and t is time in hours.

RESULTS AND DISCUSSIONS

Pre Formulation Studies

Preformulation studies were performed for the drug to rule out the interaction with the Polymers used for formulating mucoadhesive microspheres. The various preformulation parameters like organoleptic characteristics, analysis of API and compatibility studies were studied and results were shown below.

Organoleptic properties:

- **Colour:** White to off-white.
- **Taste & odour:** Bitter taste and Odourless.

Analysis of Sumatriptan succinate:

Standard curve of Sumatriptan succinate:

The UV spectrophotometric method of analysis showed linearity range from 0-10 µg/ml for Sumatriptan Succinate in phosphate buffer pH 7.4 at 226nm wavelength. The regression coefficient ($R^{2)}$ of Sumatriptan Succinate in the solution was found to be 0.999 and was within the limits as shown in as shown in Table-1 and in Fig-1.

Table 1: Absorbance of Sumatriptan Succinate

S. No	Concentration (µg/ml)	Absorbance at 226 nm
1	0	0
2	2	0.250
3	4	0.545
4	6	0.810
5	8	1.120
6	10	1.420

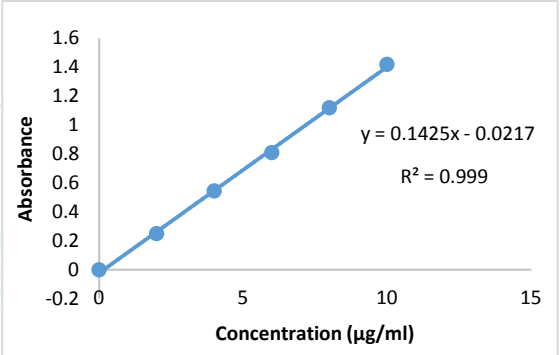

Figure 1: Calibration Curve of Sumatriptan Succinate

Compatibility study between drug and polymer by FTIR

The FTIR spectrophotometric method was used to study the compatibility between the drug and polymers. FTIR spectrum of pure drug, drug polymer mixture was taken and compared as shown in Fig-2 to 6. From the spectra it was analyzed that Sumatriptan Succinate showed characteristic bands at 3271cm^{-1} for N-H stretching, 1641cm^{-1} for N-H bending, 1300cm^{-1} for C-N vibration, 1121cm^{-1} for C-N stretching, 1077cm^{-1} for S=O Stretching.

On comparing the spectrum of pure drug with drug and polymer mixture all the characteristic peaks of drug were found to be similar with the IR spectra of drug polymer mixture indicated the absence of drug-polymer interactions and showed the suitability of the polymers used for the preparation.

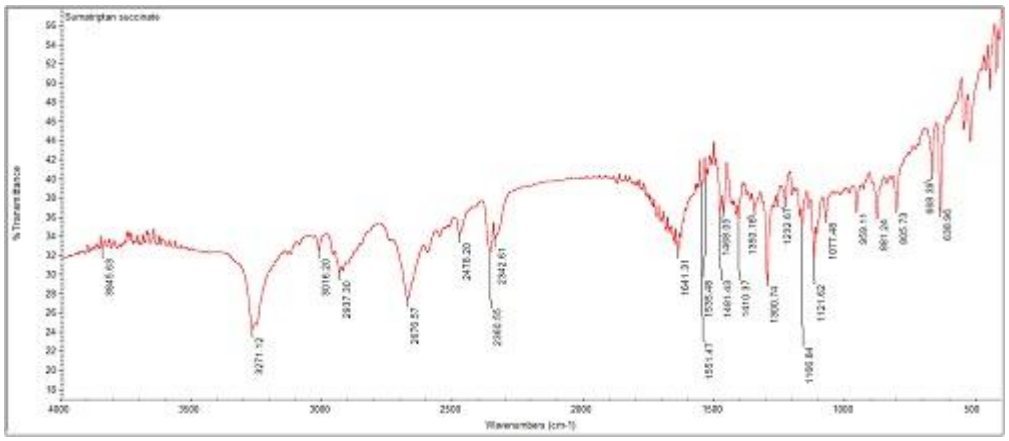

Figure 2: FTIR spectra of sumatriptan succinate

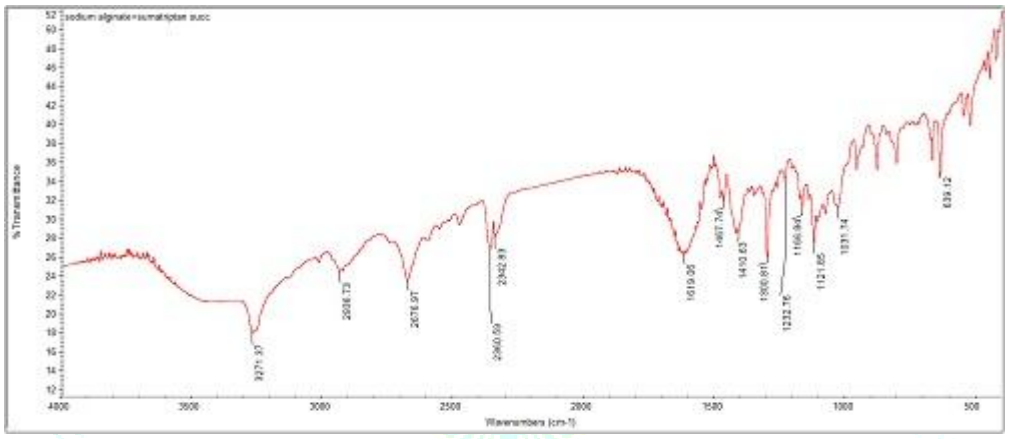

Figure 3: FTIR spectra of sumatriptan succinate and sodium alginate.

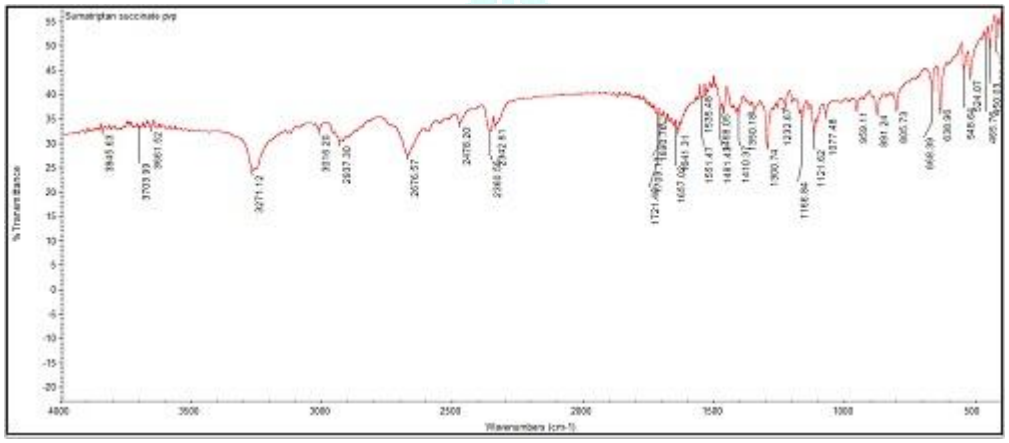

Figure 4: FTIR spectra of sumatriptan succinate and Polyvinylpyrrolidone.

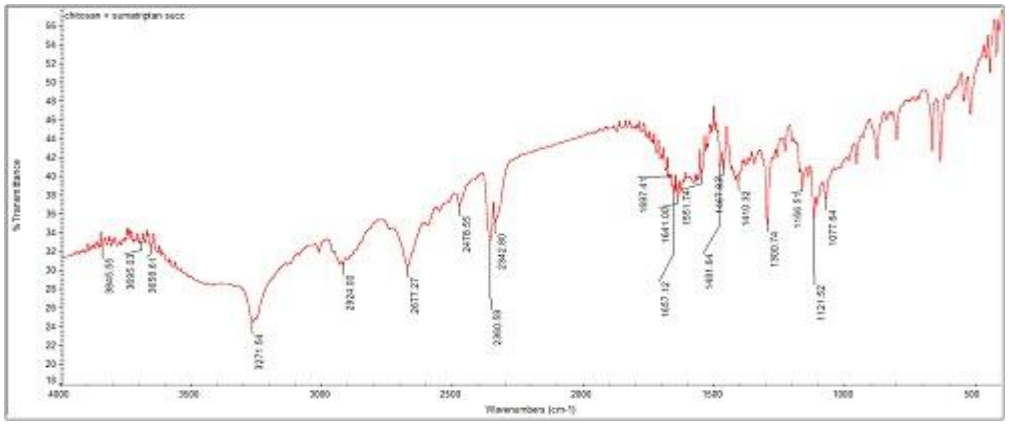

Figure 5: FTIR spectra of sumatriptan succinate and chitosan

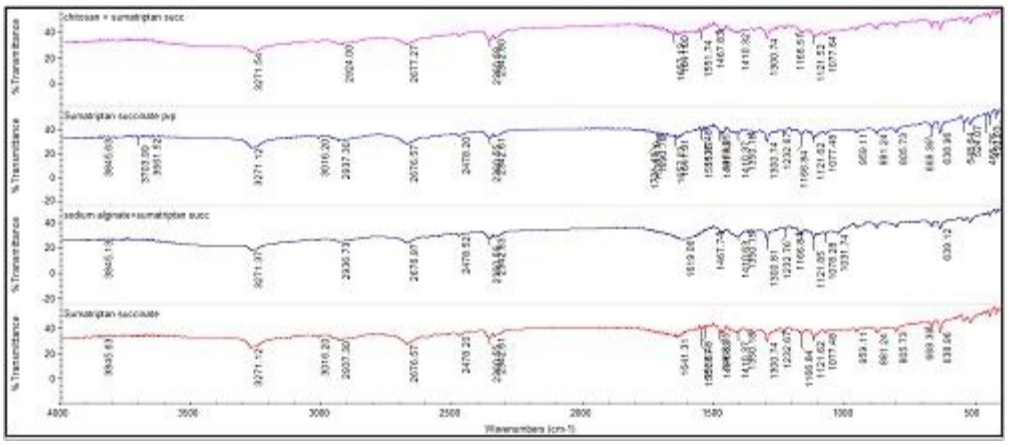

Figure 6: FTIR spectra of sumatriptan succinate with sodium alginate, Polyvinylpyrrolidone, and chitosan

Formulation of Mucoadhesive Microspheres

Preparation of mucoadhesive microspheres by Emulsification method:

Mucoadhesive microspheres of sumatriptan succinate were prepared by emulsification method using sodium alginate, poly vinyl pyrrolidone and chitosan. The drug-polymer solutions were taken in the ratio of 1:1, 1:2, and 1:3 respectively and were mentioned in Table-2.

Table 2: Formulation of Mucoadhesive Microspheres

Formulation Code	Drug (mg)	Polymer (mg)	Liquid paraffin (ml)	Span 80 (ml)	Calcium chloride (ml)	Glutaraldehyde (ml)
SF1	100	100	25	0.5	25	-
SF2	100	200	25	0.5	25	-
SF3	100	300	25	0.5	25	-
PF1	100	100	50	0.5	-	-
PF2	100	200	50	0.5	-	-
PF3	100	300	50	0.5	-	-
CF1	100	100	50	0.5	-	4
CF2	100	200	50	0.5	-	4
CF3	100	300	50	0.5	-	4

Characterization of Mucoadhesive Microspheres

Percentage Yield

The percentage yield of the mucoadhesive microspheres of sumatriptan succinate was calculated and the results were shown in the Table-3. From the result, it was observed that the percentage yield of all the preparations such as SF1, SF2, SF3, PF1, PF2, PF3, CF1, CF2, and CF3 was in the range of 87.5 to 98.62%. Further, it was observed that an increase in the polymer ratio in the formulation, the percentage yield also increased in all the formulations.

Table 3: Characterization of sumatriptan succinate mucoadhesive microspheres

S.no	Formulation code	Percentage yield (%)	Mean particle size (µm)	Drug Content (%)	Drug entrapment efficiency (%)	Drug loading Capacity (%)
1	SF1	90.54	31	81.68 ± 1.62	71.48 ±1.23	35.74 ±1.32
2	SF2	93.66	37.50	76.42 ±1..23	69.28 ±1.06	23.09 ±1.54
3	SF3	98.62	40.50	73.41 ±1.39	66.46 ±1.53	16.61 ±1.25
4	PF1	87.5	17.50	81.76 ±1.65	87.18 ±1.54	43.59 ±1.06
5	PF2	93	19.50	77.91 ±1.51	85.83 ±1.36	28.61 ±1.15
6	PF3	94.37	23	73.57 ±1.72	81.68 ±1.56	20.45 ±1.39
7	CF1	92.5	32.5	76.31 ±1.63	76.74 ±1.41	38.37 ±1.71
8	CF2	95	38.75	73.32 ±1.56	73.32 ±1.31	24.44 ±1.62
9	CF3	97.5	42.50	70.21 ±1.64	68.96 ±1.62	17.55 ±1.34

Mean±standard deviation (n=3)

Micromeritic properties

The micromeritic properties such as bulk density, tapped density, Hausne's ratio, compressibility index and angle of repose were carried out and the results were shown in the Table-4. From the study, it was observed that the bulk and tapped density, Hausner's ratio, Carr's index and angle of repose of all the preparations such as SF1, SF2, SF3, PF1, PF2, PF3, CF1, CF2, CF3 was in the range of 0.25 to 0.86 g/ml, 0.31 to 0.86 g/ml, 1.2 to 1.45, 16 to 30%, 2.90 to 11.75 θ respectively.

Further, it was observed that the values of bulk density and tapped density in all the formulations were within the limit, an increase in the Hausner's ratio was observed with mucoadhesive microspheres of sumatriptan succinate using Polyvinylpyrrolidone as polymer than with the other polymers may be due to its hydrophilic nature. The low values of angle of repose and Carr's index was observed in all the formulations of mucoadhesive microspheres of sumatriptan succinate may be due to more fineness of the formulation and mucoadhesive nature of the polymer.

Table 4: Micromeritic properties of sumatriptan succinate mucoadhesive microspheres

Formulation Code	Bulk density(g/ml)	Tap density(g/ml)	Hausner's ratio	Carr's index (%)	Angle of repose
SF1	0.41 ±0.24	0.51 ±0.21	1.24 ±0.09	19.60 ±0.8	8.65 ±0.15
SF2	0.52 ±0.59	0.65 ±0.25	1.25 ±0.04	20 ±0.6	9.51 ±0.31
SF3	0.55 ±0.45	0.66 ±0.65	1.2 ±0.02	16.66 ±0.7	11.75 ±0.25
PF1	0.58 ±0.26	0.85 ±0.95	1.45 ±0.06	30.90 ±0.6	2.90 ±0.61
PF2	0.63 ±0.65	0.86 ±0.18	1.39 ±0.06	28.14 ±0.8	3.87 ±0.18
PF3	0.66 ±0.57	0.83 ±0.56	1.33 ±0.05	26.01 ±0.4	3.95 ±0.24
CF1	0.25 ±0.43	0.31 ±0.21	1.24 ±0.09	19.35 ±0.9	5.59 ±0.35
CF2	0.28 ±0.19	0.36 ±0.36	1.28 ±0.08	22.22 ±0.5	6.51 ±0.26
CF3	0.32 ±0.32	0.40 ±0.41	1.25 ±0.05	20 ±0.8	7.54 ±0.15

Mean±standard deviation (n=3)

Particle Size Analysis

All the formulations were subjected to particle size analysis by optical microscopic method and the results were tabulated in the Table-3. From the study it was observed that the mean particle size was significantly increased with increase in the polymer concentration. The particle size in all the formulations was in the order of,

CF1-CF3> SF1-SF3 > PF1-PF3.

The small particle size was observed with mucoadhesive microspheres of sumatriptan succinate with PVP when compared with the other polymers may be due to the formation of unstable nuclei.

Drug content, Drug Entrapment Efficiency and Drug loading of mucoadhesive microspheres of sumatriptan succinate

The results of drug content, drug entrapment efficiency and drug loading of mucoadhesive microspheres of sumatriptan succinate were enlisted in Table-3. The percentage of drug content, drug entrapment efficiency and drug loading for all the formulations SF1-SF3, PF1-PF3, CF1-CF3 was in the range of 70.21% to 81.68%, 66.46 %to 87.18% and 16.61% to 43.59% respectively.

From the study it was observed that an increase in the concentration of polymer in all the formulations, results in decrease in the percentage of drug content, drug entrapment efficiency and drug loading. The reason may be due to loss of drug during washing, adherence of drug on the walls of the beaker and stirrer, addition of insufficient amount of cross linking agent and duration of stirring.

Higher percentage of drug content, drug entrapment efficiency and drug loading was observed with PVP mucoadhesive microspheres of sumatriptan succinate may be due to its hydrophilic nature.

Swelling index

The swelling index demonstrated the ability of the mucoadhesive microspheres to get swell at the absorbing surface by absorbing fluid at the site of absorption. It is also used to check the water absorption property of the polymers. The swelling index for all the formulation was calculated and results were shown in Table-5. From the study it was observed that the swelling index value was in the range of 1.1 to 2.94mg/ml, indicated that an increase in the concentration of polymer produced, an increase in the swelling property of microspheres. Among the polymers, swelling index value was high with sodium alginate formulations than with the other polymers. May be due to more water absorbing nature of sodium alginate which absorb water within its porous structure.

Table 5: Swelling index and percentage mucoadhesion of sumatriptan succinate mucoadhesive microspheres

S.no	Formulation	Swelling index (mg/ml)	Percentage Mucoadhesion
1	SF1	2.43 ±0.51	54 ±1.45
2	SF2	2.73 ±0.36	61 ±1.53
3	SF3	2.94 ±0.54	72 ±1.65
4	PF1	1.1 ± 0.56	21 ±1.34
5	PF2	1.31 ± 0.45	40 ± 1.26
6	PF3	1.42 ± 0.49	79 ± 1.47
7	CF1	1.24 ±0.42	45 ± 1.49
8	CF2	1.56 ±0.35	79 ± 1.58
9	CF3	1.75 ±0.52	85 ± 1.61

Mean±standard deviation (n=3)

SEM analysis

Morphological analysis of the mucoadhesive microspheres of sumatriptan succinate (SF3) was carried out using scanning electron microscopy (SEM) and the result were shown Fig-7.The SEM photographic result reveals that the microspheres were almost spherical in shape and rough surface.

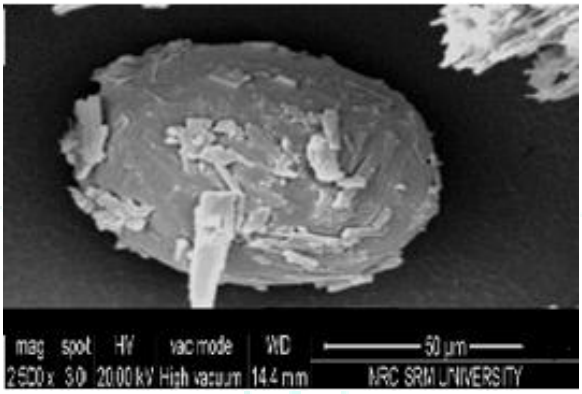

Figure 7: Scanning electron microscopy of mucoadhesive microspheres of sumatriptan succinate (SF3)

***In-vitro* wash off test (mucoadhesion test):**

In-vitro wash off test is used to determine the mucoadhesion behaviour of the polymers. The test was carried out for all the formulations and the result test was enlisted in Table-5. From the result it was found that the percentage of mucoadhesion for all the formulations was in the range of 21 to 85% showed good mucoadhesion nature and the values also indicated that an increase in the concentration of polymer resulted in an increase in the percentage of mucoadhesion of microspheres. Among the formulations the percentage of mucoadhesion was higher with chitosan microspheres due to strong electrostatic interactions of the Cationic polymers with the negatively charged mucin present in the mucosal layer whereas sodium alginate and PVP mucoadhesion with mucin mucosal layer is due to hydrogen bonding.

***In-vitro* drug release studies:**

The percentage cumulative drug release was calculated and the values were shown in Table-6 and in Fig-8.

At 8th hr the percentage cumulative drug release for SF1, SF2, and SF3 formulations was found to be 52.48%, 53.19%, 64.17%, respectively. For PF1, PF2, PF3 formulations, the percentage cumulative drug release was in the order of 30.29%, 35.48%, and 37.68% respectively and for CF1, CF2, CF3 formulations the percentage cumulative drug release was in the order of 40.64%, 32.75%, 29.34%respectively. Among all the formulations sodium alginate microspheres showed increased and sustained drug release. Further among the three sodium alginate microspheres, SF3 showed increased amount of percentage drug release due to increased drug polymer ratio and the mechanism of drug release is due to swelling and erosion.

The percentage cumulative drug release for PVP was less than sodium alginate microspheres of sumatriptan succinate may be due to its high viscous and mucoadhesive nature. The percentage cumulative drug release for chitosan microspheres was less than sodium alginate microspheres but greater than PVP microspheres due to its high mucoadhesion nature.

Hence among all the formulations, SF3 was chosen for further study due to its increased drug release.

Table 6: Cumulative percentage drug release for mucoadhesive microspheres of sumatriptan succinate

Time (min)	SF1	SF2	SF3	PF1	PF2	PF3	CF1	CF2	CF3
10	21.54 ±0.61	23.05 ±1.03	27.07 ±1.23	12.32 ±1.26	12.56 ±1.30	12.50 ±1.32	14.15 ±1.32	20.44 ±1.01	12.08 ±1.31
20	23.60 ±0.53	27.96 ±1.66	31.59 ±1.02	12.94 ±1.54	13.49 ±1.67	16.61 ±1.21	16.63 ±1.02	21.03 ±0.94	12.94 ±1.02
30	25.77 ±0.42	28.57 ±1.23	33.74 ±0.99	13.56 ±1.56	15.69 ±1.48	17.15 ±1.05	19.74 ±1.31	21.93 ±0.84	13.44 ±1.32
45	27.06 ±0.65	31.61 ±1.36	36.28 ±0.98	14.76 ±1.22	17.86 ±1.35	18.12 ±1.34	23.09 ±1.04	23.29 ±0.67	14.27 ±1.04
60	30.79 ±0.74	34.90 ±1.01	39.96 ±0.55	15.05 ±1.32	21.54 ±1.25	21.18 ±1.24	28.54 ±1.12	24.19 ±1.24	14.76 ±1.52
120	32.01 ±0.65	38.63 ±1.23	43.48 ±0.68	16.12 ±1.05	22.25 ±1.54	3.55 ±1.54	31.67 ±1.02	24.99 ±1.07	16.32 ±1.34
240	36.34 ±0.45	41.43 ±1.54	46.42 ±0.67	17.54 ±1.09	24.25 ±1.64	25.66 ±1.36	34.30 ±1.17	27.57 ±1.11	18.57 ±1.25
300	40.76 ±0.49	43.29 ±1.02	50.19 ±1.41	20.81 ±1.34	27.23 ±1.35	27.51 ±1.54	35.56 ±1.19	28.29 ±1.20	23.47 ±1.32
360	44.64 ±0.57	46.18 ±1.61	54.21 ±1.03	26.57 ±1.24	31.52 ±1.91	33.71 ±1.24	38.47 ±1.31	29.49 ±0.97	25.08 ±1.31
420	46.01 ±1.34	48.95 ±1.03	59.32 ±1.30	28.21 ±1.09	33.25 ±1.20	35.45 ±1.09	39.59 ±1.64	31.02 ±1.36	27.15 ±1.64
480	48.68 ±1.03	53.19 ±1.24	64.17 ±1.05	30.29 ±1.64	35.48 ±1.03	37.68 ±1.64	40.64 ±1.31	32.75 ±1.09	29.34 ±1.31

Mean±standard deviation (n=3)

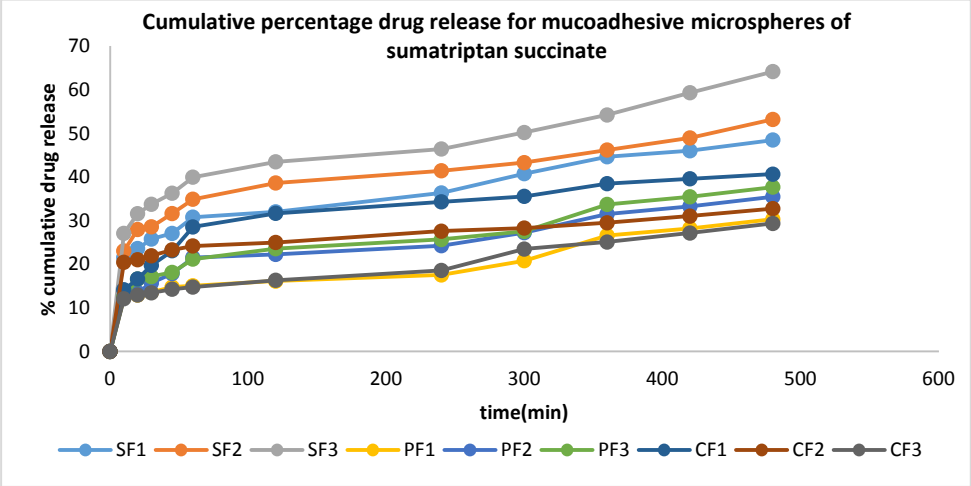

Figure 7: Cumulative percentage drug release for mucoadhesive microspheres of sumatriptan succinate

Table 7: Drug release kinetics data for mucoadhesive microspheres of sumatriptan succinate (SF3)

Formulation Code	Zero order R^2	First order R^2	Higuchi diffusion kinetics R^2	Korsmeyar-peppas		Hixson Crowell R^2
				R^2	n	
SF3	0.892	0.830	0.956	0.984	1.26	0.6791

***In-vitro* drug release of mucoadhesive microspheres of sumatriptan succinate (SF3) with marketed conventional tablets:**

The percentage cumulative drug release for mucoadhesive microspheres of sumatriptan succinate SF3) and marketed conventional tablets values were shown in Fig-9. The percentage cumulative drug release for the marketed tablets was 99% at 30 min while SF3 formulation showed 64.17% drug release at 8th hr.

Kinetics of Drug release

The kinetics of *In-vitro* drug release for mucoadhesive microspheres of sumatriptan succinate (SF3) was determined by applying the drug released data to various kinetic models such as zero order, first order, Higuchi

and Korsmeyer- Peppas. The result obtained was represented in Table-7 and in Fig-10.

In the present study, the release profile of the SF3 formulation follows Korsmeyar-peppas equation with the 'R^2' value-0.984. Further the 'n' values of Korsmeyar peppas was 1.26. Therefore the most probable mechanism of drug release was super case II transport.

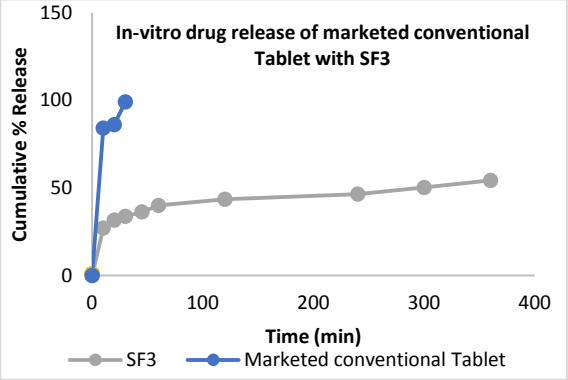

Figure 9: *In-vitro* drug release of mucoadhesive microspheres of sumatriptan succinate (SF3) with marketed conventional tablet

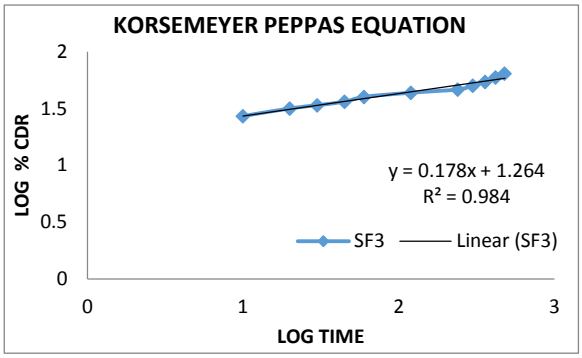

Figure 10: Korse-meyer Peppas Equation for mucoadhesive microspheres of sumatriptan succinate (SF3)

CONCLUSION

Varying degrees of sustained release was obtained from sumatriptan succinate mucoadhesive microspheres prepared from sodium alginate, PVP and chitosan by emulsification method. Among all the formulations developed sodium alginate mucoadhesive microspheres showed the most drug sustaining and it is promising for sustained release of sumatriptan succinate.

REFERENCES

1. Boddupalli BM, Mohammed ZN, Nath RA, Banji D. Mucoadhesive drug delivery system: An overview. J Adv Pharm Technol Res 2010; 1:381-7.
2. Alagusundaram M, Chetty MS, Umashankari K, Badarinath AV, Lavanya C, Ramkanth S. Microspheres as a novel drug delivery system: A review. Int J Chem Tech Res 2009; 1(3):526-534.
3. Venkatesh Gavini, B. Ragini and K. Kaumudi. Mucoadhesive microspheres-a novel approach of drug targeting. Wjpps. 2014; 3(10):310-335.
4. A. Madhusudhan Reddy, J. Sindhura, B. Naga Lakshmi, A. Abhishekar Reedy, D. Navya Sri, M. Nireekshan Kumar and P. Srinivasa Babu. Formulation and evaluation of bilayered tablets of sumatriptan succinate by using hydrophilic polymers. Der Pharmacia Lettre, 2016; 8(5):189-206.
5. R Indira Prasanna, P Anitha, and C Madhusudhana Chetty. Formulation and evaluation of bucco-adhesive tablets of sumatriptan succinate. Int J Pharm Investig. 2011; 1(3):182–191.
6. Atul Kumar, Shubhendra Jha, Ravindra Rawal, P.S.Chauhan, Sheo Datta Maurya. Mucoadhesive Microspheres for Novel Drug Delivery System: A Review. Am. J. PharmTech Res. 2013; 3(4) ISSN: 2249-3387:195-213.
7. Baby H. Dandge, M H G Dehghan and Varsha M. Gaikwad. Preparation and characterization of mucoadhesive microparticles of sumatriptan succinate for intranasal delivery. Journal of Pharmacy Research 2009; 2(9):1536-1539.
8. Dada Khalandar K S, Yajaman Sudhakar, KN Jayaveera. Chitosan Based Nasal Microspheres of Sumatriptan: Formulation and In-Vitro Evaluation. Res. J. Pharma Bio & Chem Sciences. 2011; 2(3):489-498.
9. Engla G., Soni L., Dixit V. Sustained release delivery of repaglinide by biodegradable microspheres. Journal of Drug Delivery and Therapeutics, 2017; 7(7):77-80. https://doi.org/10.22270/jddt.v7i7.1593
10. Carol Mattson Porth, Glenn Matfin, Pathophysiology Concepts of Altered Health States Eighth edition. Lippincott Williams & Wilkins, 2009; 1251-1253.
11. Korsemeyer R.W et al. Mechanism of solute release from porous hydrophilic polymer. Int. J. Pharm. 1983; 15: 25-35.