**Development and Evaluation of Floating Microspheres of Sumatriptan Succinate using Ethyl Cellulose and Mucilage Extracted from Vigna Mungo**

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**Authors’ contributions**

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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**ABSTRACT**

**Aim:** The present investigation is to formulate and evaluate gastroretentive floating microspheres for sumatriptan succinate. Gastric retention is widely used approach to retain dosage form in stomach and to enhance absorption of drugs.

**Methods:** The gastroretentive floating microspheres was prepared by two different techniques as solvent evaporation and W/O/W multiple emulsion technique. Ethyl cellulose, HPMC K4M polymer and mucilage extracted from *Vigna Mungo* in various proportions were used for formulation of microspheres. Combination of ethyl acetate and acetone in different proportion was used as organic phase and the microspheres were characterized for particle size, shape, morphology, percentage yield, entrapment efficiency, drug loading, In-Vitro Floating/Buoyancy study, In-vitro Floating/Buoyancy study and release kinetics.

**Results:** The average particle size of all batches was found in the range 100 to 210 μm and the entrapment efficiency of all formulations was found in the range of 17.46 % to 59.28 %. Total...
floating time for Sumatriptan succinate floating microspheres was observed more than 12 h. The In-Vitro drug release study was performed for all formulations showed drug release in controlled manner.

**Conclusion:** The particle size was increased with increased polymer concentration and it showed that polymer concentration has an impact on the entrapment efficiency. Ethyl cellulose microspheres showed more entrapment and sustained delivery of sumatriptan Succinate than microspheres prepared by combination of Ethyl cellulose: HPMC K4M and Ethyl cellulose: *Vigna mungo* mucilage.

**Keywords:** Floating microspheres; sumatriptan succinate; solvent evaporation; *vigna mungo*.

1. **INTRODUCTION**

Oral drug delivery system is the most prominent and highly acceptable route of administration. Gastroretentive drug delivery system (GRDDs) is the most feasible controlled release system in which the drug delivery is prolonged by increasing gastric residence time. By increasing gastric residence time better control is achieved on fluctuation of plasma drug concentration. Floating drug delivery system is the hydrodynamically balanced system. As dosage form has low density which allows the system to remain buoyant for prolonged duration of time in gastric fluid and it is advantageous over immediate release system including the minimization of fluctuations and act for prolonged period of time [1,2]. Floating system is divided into two main types, one is effervescent system and other is non effervescent system. For floating dosage form desirable drugs are absorbed from stomach, having local action in stomach, poorly absorbed from alkaline pH, rapid absorption from GIT [1,2]. Sumatriptan succinate; selective agonist of 5 hydroxytriptamine, is a main choice of drug for migraine treatment. Sumatriptan succinate is effective in migraine attack in 70% of cases as well as used for treating headache, pain and other symptoms. Sumatriptan succinate does not cross blood brain barrier and has biological half life of 2.5 hr and its reported bioavailability is approximately 15% [3,4,5]. The *Vigna Mungo* mucilage has been used as binder, release retardant material in the development of dosage form. *Vigna Mungo* mucilage as a polysaccharide has excellent swelling capacity. So considering these advantages the work is initiated to develop microspheres containing *Vigna Mungo mucilage*. The main objective of the work is to develop microspheres as floating drug delivery as drug is rapidly and incompletely absorbed from gastrointestinal track. The drug has absorption from the stomach and upper part of small intestine [5-8]. Sustained release dosage form is mainly for better effect and longer duration of time. To allow absorption from stomach and upper part of small intestine, Sumatriptan succinate needs to be developed as Gastroretentive drug delivery system.

2. **MATERIALS AND METHODS**

2.1 **Materials**

Sumatriptan succinate was a gift sample from Emcure Pharmaceuticals, Pune. Hydroxy propyl methyl cellulose (K4M) was received as Gift sample from Colorcon India Ltd., Goa, India. Ethyl cellulose, calcium chloride, PVA was purchased from Research Lab fine Chem. Industries, Mumbai-400002, (India). Urad dal was purchased from local market of Pune, Maharashtra, India.

2.2 **Methods**

2.2.1 **Solubility estimation of sumatriptan succinate**

Sumatriptan Succinate (50 mg) was added to 50 ml of distilled water, acidic buffer pH 1.2, Phosphate buffer pH 6.8 and Phosphate buffer pH 7.4, respectively. The solutions were kept for stirring on mechanical shaker for 2 hrs at room temperature and the solutions were filtered by using 0.22 µ Whatman filter paper. Suitable dilutions were made and absorbance of final solutions was recorded using UV spectrophotometer at λmax 282 nm.

2.2.2 **Isolation/ extraction of mucilage [9-13]**

Urad dal (*Vigna Mungo*) Mucilage was isolated from freshly dried, coarsely powdered and dehusked seeds of *Vigna Mungo*. 20 g of Seed powder of *Vigna Mungo* was taken and added into 200 ml of cold distilled water. Slurry was prepared and then was poured into 800 ml of
boiling distilled water. The solution was boiled for 20 min in water bath under constant stirring. The resulting solution was kept overnight, so that most proteins and fibres settled down. The material was squeezed by using muslin bag to remove mark from filtrate and the filtrates were poured into twice volume of absolute ethanol with continuous stirring to precipitate mucilage. The mucilage was separated, collected and dried in an oven at 50°C for 24 hrs and the dried mucilage was powdered and passed through 40# sieve.

2.2.2.1 Physicochemical characterization of Vigna Mungo Mucilage

A. Phytochemical Testing:

- Molish Test: Alcoholic 1 ml solution of α Naphthol and few drops of conc. Sulphuric acid added to Mucilage Powder and formation of violet ring at the junction of liquids indicates presence of carbohydrates.
- Iodine Test: To the mucilage solution, 1 ml of iodine solution was added and appearance of reddish brown colour indicates presence of starch.
- Ruthenium Red Test: 0.5 ml of Ruthenium red reagent added to mucilage solution and appearance of pink colour specifies presence of mucilage.

B. Loss on drying:

500 mg of mucilage powder was weighed and placed in porcelain dish, kept in hot air oven at 105°C for 1h. Porcelain dish removed from oven and weighed again. The weight of mucilage powder determined and percentage LOD was calculated.

C. pH: The pH of mucilage powder was determined by using Digital pH meter. 1% w/v of mucilage solution prepared and pH observed.

D. Viscosity: 1% w/v solution of mucilage prepared and viscosity measured on Brookfield viscometer.

E. Swelling Index: 100 mg muclage powder weighed and kept in petri dish. Distilled water added into it. After 5 h, weight of mucilage determined and percentage of swelling with respect to time was calculated.

2.2.3 Preparation of floating microspheres by solvent evaporation methods [14-19]

Sumatriptan Succinate microspheres were prepared by varying the concentration of polymers in the formulation. The Ethyl acetate and acetone in various ratios in various ratios was used as organic phase and in aqueous phase comprises distilled water with emulsifier Tween 80. The composition of batches was given in Table 1. The polymer was dissolved in the organic solvent. Drug is dispersed in the organic phase containing polymers. The drug polymer solution is added dropwise to aqueous phase under continuous stirring. The resultant solution was stirred with a triple blade mechanical stirrer for 3 h to allow the solvent to evaporate. The microspheres formed were filtered, was washed with distilled water and dried overnight at room temperature.

2.2.4 Procedure of sumatriptan succinate floating microspheres by multiple emulsion technique

Different batches of Sumatriptan Succinate microspheres were prepared by varying the concentration of polymers in the formulation. The composition of batches was given in Table 2. The drug was dissolved in water forming W₁ solution. Polymer ethyl cellulose was dissolved in organic phase Ethyl acetate and acetone in various ratios. It is oil or organic phase (O) and the W₁ phase added into organic phase O. It formed W/O emulsion (Primary emulsion) and it is subjected to homogenization using probe sonicator. The external aqueous phase (W₂) was 10% calcium chloride solution containing 0.5% PVA. Emulsifying agent tween 80 added into it. The primary emulsion was injected into external aqueous phase to form W₁/O/W₂ emulsion. The resultant solution was stirred with a triple blade mechanical stirrer for 3 h to allow the solvent to evaporate. The microspheres formed were filtered, was washed with distilled water and dried overnight at room temperature.

2.2.5 Evaluation of floating microspheres [20-24]

2.2.5.1 Particle size, shape and morphology

The formed microspheres were characterized by optical microscopy for determination of particle size and size distribution. The eyepiece microscope was calibrated with stage micrometer. Randomly measured 100
microspheres and average particle size calculated. Edmondsons equation was applied.

\[ d_{\text{mean}} = \frac{\Sigma n d}{\Sigma n} \]

Where, \( n \) = the number of counted microspheres and \( d \) = mean size range

2.2.5.2 Percentage yield

Percentage yield of microspheres calculated by the using the formula

\[ \% \text{ Yield} = \frac{\text{Total weight of microspheres}}{\text{Total weight of polymer and drug}} \times 100 \]

2.2.5.3 Drug Entrapment efficiency and drug loading

The percent of drug encapsulated into the formulation is determined by drug entrapment efficiency method. The weighed amount of microspheres equivalent to 20 mg drug was crushed in the mortar and pestle. Then it was dissolved in methanol. The resultant solution was filtered by 0.22 \( \mu \) Whatman filter paper. After suitable dilution the absorbance was measured at 282 nm by UV Spectrophotometer. The entrapment efficiency and drug loading were calculated by using following formula.

\[ \% \text{ Entrapment Efficiency} = \frac{\text{Practical amount of drug content}}{\text{Total theoretical amount of drug content}} \times 100 \]

\[ \% \text{ Drug loading} = \frac{\text{Actual drug content}}{\text{Weight of microspheres}} \times 100 \]

2.2.5.4 Micromeritics study

To determine flow properties of microspheres, the micromeritic properties of microspheres such as bulk density, tapped density, angle of repose; compressibility index and Hausners ratio were performed.

### Table 1. Preparation of microspheres by solvent evaporation method

| Batch Code | Drug (mg) | Ethyl cellulose (mg) | HPMC K4M (mg) | Mucilage (mg) | Ethyl acetate (ml) | Acetone (ml) | Aqueous phase containing PVA and CaCl₂ (ml) | Tween 80 (ml) | RPM |
|------------|-----------|----------------------|---------------|--------------|-------------------|-------------|------------------------------------------|--------------|-----|
| F1         | 500       | 500                  | --            | --           | 10                | --          | 100                                      | 0.2          | 1000|
| F2         | 500       | 500                  | --            | --           | 10                | 2.5         | 100                                      | 0.2          | 1000|
| F3         | 500       | 500                  | 1000          | --           | 10                | 5           | 100                                      | 0.2          | 1000|
| F4         | 500       | 500                  | 1000          | --           | 10                | 2.5         | 100                                      | 0.2          | 1000|
| F5         | 500       | 500                  | 1000          | --           | 10                | 5           | 100                                      | 0.2          | 1000|
| F6         | 500       | 1000                 | 500           |             | 10                | --          | 100                                      | 0.2          | 1000|
| F7         | 500       | 1500                 | 500           |             | 10                | 2.5         | 100                                      | 0.2          | 1000|
| F8         | 500       | 1500                 | 500           | 80           | 10                | 5           | 100                                      | 0.2          | 1000|
| F9         | 500       | 1500                 | 500           | 80           | 10                | 2.5         | 100                                      | 0.2          | 1000|
| F10        | 500       | 1500                 | 500           | 80           | 10                | 5           | 100                                      | 0.2          | 1000|
| F11        | 500       | 1500                 | 160           | --           | 10                | --          | 100                                      | 0.2          | 1000|
| F12        | 500       | 500                  | 80            | --           | 10                | 80          | 100                                      | 0.2          | 1000|
| F13        | 500       | 1000                 | 80            | --           | 10                | 5           | 100                                      | 0.2          | 1000|
| F14        | 500       | 1500                 | 80            | --           | 10                | 5           | 100                                      | 0.2          | 1000|
| F15        | 500       | 1500                 | 80            | 160          | 10                | --          | 100                                      | 0.2          | 1000|
| F16        | 500       | 1500                 | 80            | --           | 10                | 5           | 100                                      | 0.2          | 1000|
| F17        | 500       | 1500                 | 80            | --           | 10                | --          | 100                                      | 0.2          | 1000|

### Table 2. Preparation of microspheres by multiple emulsion technique

| Formulation s | Drug (mg) | Ethyl cellulose (mg) | Ethyl acetate (ml) | Acetone (ml) | Aqueous phase containing PVA and CaCl₂ (ml) | Tween 80 (ml) | RPM |
|---------------|-----------|----------------------|-------------------|-------------|------------------------------------------|--------------|-----|
| F18           | 250       | 750                  | 10                | 5           | 50                                      | 0.5          | 700 |
| F19           | 250       | 1500                 | 10                | 0           | 50                                      | 0.5          | 700 |
| F20           | 250       | 1500                 | 10                | 5           | 50                                      | 0.5          | 700 |
| F21           | 250       | 2250                 | 10                | 5           | 50                                      | 0.5          | 700 |
Table 3. Composition of microspheres containing ethyl cellulose W/O/W emulsion

| Formulation | Drug (mg) | Ethyl cellulose (mg) | Ethyl acetate (ml) | Acetone (ml) | Aqueous phase (water) (ml) | Tween 80 (ml) | RPM |
|-------------|-----------|----------------------|-------------------|-------------|--------------------------|-------------|-----|
| F22         | 250       | 1500                 | 10                | 5           | 50                       | 0.5         | 100 |
| F23         | 250       | 2250                 | 10                | 5           | 50                       | 0.5         | 100 |

2.2.5.5 In-vitro floating/buoyancy study

The in-vitro floating ability of microspheres was carried out by using USP Dissolution apparatus II (Paddle type). Microsphere samples containing Sumatriptan Succinate: Ethyl cellulose (F 9 batch), Sumatriptan succinate: Ethyl cellulose: Vigna mungo Mucilage (F 13 batch) and Sumatriptan succinate: Ethyl cellulose: HPMC K4M (F 17 batch) samples were placed in 900 ml of 0.1 N HCl maintained at 37±0.5°C. The medium was agitated with paddle rotating at 50 RPM. After 6 h of revolution, both settled and floating microspheres collected separately. Those microspheres collected dried and washed. Percentage buoyancy is calculated by the formula:

\[
\% \text{ Buoyancy} = \frac{\text{Weight of floating microspheres}}{\text{Initial weight of floating microspheres}} \times 100
\]

2.2.5.6 In-vitro drug release study and release Kinetics study [25,26]

The In-vitro drug release study was performed using USP Type II dissolution test apparatus II. Microsphere samples containing Sumatriptan Succinate: Ethyl cellulose (F 9 batch), Sumatriptan succinate: Ethyl cellulose: Vigna Mungo Mucilage (F 17 batch) and Sumatriptan succinate: Ethyl cellulose: HPMC K4M (F 13 batch) samples were placed in 900 ml of 0.1 N HCl maintained at 37±0.5°C operated at 50 RPM. This study was performed till 6 hr. The sink condition is maintained throughout the experimentation. The samples were withdrawn for predetermined time interval. The released amount of sumatriptan succinate was analysed by using UV spectrophotometer at 282 nm. To study the drug release kinetics different mathematical models were employed as zero order, first order, Higuchi, Korsemayer- Peppas. The drug release behaviour is determined by these models. The regression coefficient was determined and comparing. The best fit model was selected based on the regression coefficient value.

2.2.5.7 Characterization of Microspheres by DSC, FTIR and FESEM studies

FTIR of Sumatriptan Succinate and microsphere formulations: The drug polymer samples were scanned on Shimadzu (FTIRNITY-1) with IR resolution software. It was scanned over wave number range of 4000–400 cm⁻¹ with diffraction reflectance scanning technique. The pure Sumatriptan Succinate, Ethyl cellulose, HPMC K4M, Vigna Mungo Mucilage, Microsphere samples containing Sumatriptan Succinate: Ethyl cellulose (F 9 batch), Sumatriptan succinate: Ethyl cellulose: Vigna Mungo Mucilage (F 17 batch) and Sumatriptan succinate: Ethyl cellulose: HPMC K4M (F 13 batch) were studied for FTIR.

DSC of Sumatriptan Succinate and microsphere formulations: Differential scanning calorimetric (DSC) measurements were carried out on a modulated DSC (Mettler Toledo). 2–10 mg samples were placed in aluminium pans and sealed. The probes were heated from 30 °C to 3000°C at a rate of 100 C/min under nitrogen atmosphere at the rate 40ml/min. The pure Sumatriptan Succinate, Ethyl cellulose, HPMC K4M, Vigna Mungo Mucilage, Microsphere samples containing Sumatriptan Succinate: Ethyl cellulose (F 9 batch), Sumatriptan succinate: Ethyl cellulose: Vigna Mungo Mucilage (F 17 batch) and Sumatriptan succinate: Ethyl cellulose: HPMC K4M (F 13 batch) samples were studied for DSC.

FESEM of sumatriptan succinate and microsphere formulations: Microsphere samples containing Sumatriptan Succinate: Ethyl cellulose (F 9 batch), Sumatriptan succinate: Ethyl cellulose: Vigna Mungo Mucilage (F 17 batch) and Sumatriptan succinate: Ethyl cellulose: HPMC K4M (F 13 batch) samples were studied for FESEM studies using NOVA NanoSEM 450, India. Plain Sumatriptan Succinate was studied using Scanning electron Microscope.
3. RESULTS AND DISCUSSION

3.1 Solubility Studies

Solubility study of Sumatriptan succinate showed that drug is freely soluble in water, soluble in Phosphate Buffer pH 7.4, acid buffer pH 1.2, and Phosphate Buffer pH 6.8.

3.2 Physicochemical Characterization of Vigna Mungo Mucilage

3.2.1 Phytochemical testing

The phytochemical testing of extracted Vigna Mungo mucilage through Molish test, Iodine test and Ruthenium red test confirms the extracted material/ mucilage was polysaccharide (Table 5 and Fig. 1).

Table 4. Solubility of Sumatriptan Succinate in different medium

| Medium                  | Solubility of drug in mg/ 50 ml |
|-------------------------|---------------------------------|
| Water                   | 37.05                           |
| Acidic Buffer pH 1.2    | 30.20                           |
| Phosphate Buffer pH 6.8 | 27.30                           |
| Phosphate Buffer pH 7.4 | 32.5                            |

Table 5. Phytochemical testing of Vigna Mungo mucilage

| Phytochemical Testing | Observation                                      | Inference          |
|-----------------------|--------------------------------------------------|--------------------|
| Molish Test           | Violet ring at the junction of two liquids       | Carbohydrate present |
| Iodine Test           | Reddish brown colour appeared                    | Starch present     |
| Ruthenium Red Test    | Pink colour appeared                             | Mucilage present   |

Fig. 1. Phytochemical tests of mucilage (A) Molish Test, (B) Iodine Test, (C) Ruthenium Red Test

3.2.2 Physicochemical testing

Table 6. Physicochemical testing of Vigna Mungo mucilage

| Parameter      | Result     |
|----------------|------------|
| Loss on drying (%) | 13.6 %     |
| pH             | 6.1        |
| Viscosity (cps) | 22.32 cps  |
| Swelling Index (%) | 45 %       |

3.2.3 Flow properties

Flow property of extracted mucilage was found to good as it is confirmed by estimation of angle of repose, bulk density, tapped density and Compressibility index (Table 7).
Table 7. Flow properties of Vigna Mungo mucilage

|                        | Bulk density (g/cm³) ±SD (n=3) | Tapped density (g/cm³) ±SD (n=3) | Compressibility index (%) ±SD (n=3) | Hausners ratio ±SD (n=3) | Angle of Repose (θ) ±SD (n=3) |
|------------------------|---------------------------------|-----------------------------------|-------------------------------------|-------------------------|-------------------------------|
|                        | 0.581 ± 0.02                    | 0.662 ± 0.02                      | 12.301 ± 1.6                        | 1.141 ± 0.02            | 28° ± 1.3 ± 1.47              |

3.3 Evaluation of Sumatriptan Succinate Floating Microspheres

Flow properties of Sumatriptan succinate floating microspheres: Bulk density of all formulations was found in the range of 0.434 to 0.740 g/cm³. Tapped density of all formulations was in the range of 0.520 to 0.804 g/cm³. It shows microspheres have low density than gastric fluid. (Density of gastric fluid is 1.064 g/cm³). It is better for floating ability. Compressibility index is in the range of 7.7 % to 22.5 %. Hausners ratio of microspheres was in the range of 1.08 to 1.29. Formulated microspheres showed angle of repose was in the range of 25 ° to 35 ° and it showed good flowing property.

3.3.1 Particle size and percentage yield

Microspheres particle size and shape studied by optical microscopy. Particles were uniformly distributed and spherical round in shape. The average particle size of all batches was found in the range 100 to 210 μm. The mean particle size of the microspheres was found to be increasing with increasing polymer concentration. The viscosity of the medium increased at higher polymer concentrations resulting in increased interfacial tension. Shearing efficiency decreased due to increased viscosity and thus particle size was increased with increased polymer concentration.

Percentage yield of different formulation batches in the range of 47.00 % to 87.88 %. Drug to polymer ratio 1:1 showed less percentage yield. As drug polymer ratio increased percentage yield is increased. This result showed that by increasing polymer concentration percentage weight increased. 800 to 1000 RPM is the optimum stirring speed of triple blade stirrer.

3.3.2 Entrapment efficiency and drug loading

The drug entrapment efficiency of microspheres varied from 17.46 % to 59.28 %. Result showed that as polymer concentration increased the entrapment efficiency get increased due to the higher polymer content, drug gets more surrounded by the polymer, thus polymer coating on drug increased and encapsulation of drug increased. The increased drug entrapment efficiency is attributed because of increased ethyl cellulose concentration. Microsphere batches prepared by Ethyl cellulose with HPMC K4M resulted decreased drug entrapment efficiency and drug loading. As HPMCK4M is hydrophilic polymer, it swells and erodes with time. HPMC could facilitate the diffusion of an entrapped drug to the surrounding aqueous medium during preparation of microspheres. So it cause decrease in entrapment of drug. Similar results were observed for the microspheres prepared by combination of polymer (ethyl cellulose) with Vigna Mungo mucilage. It is also attributed to water solubility of extracted mucilage. Entrapment efficiency is depending upon nature of drug, drug solubility, nature of polymer, polymer solubility, affinity between drug and polymer. Sumatriptan Succinate is hydrophilic drug, so aqueous solubility is more. During the microspheres preparation the drug diffusion in the aqueous medium was more. Leaching of drug to the external aqueous medium, which caused decrease in entrapment efficiency of Sumatriptan Succinate floating microspheres.

To overcome this problem, batch no. 18 to 21 prepared by multiple emulsion method. In this external aqueous medium was 0.5 % PVA solution with 10 % Calcium chloride. It was observed that there was no effective increase in entrapment and drug loading. Batch no. 22 and 23 contains combination of drug and ethyl cellulose in the ratio of 1:6 and 1:9 respectively. These microspheres prepared by w/o/w multiple emulsion method. As polymer concentration is more and primary aqueous medium W1 is less in amount, drug diffusion is less and encapsulation is more. Therefore batch no. 22 and 23 showed highest encapsulation efficiency.

3.3.3 Percentage buoyancy and total floating time

Buoyancy or floating ability of microspheres depends upon the apparent density and nature of polymer. The percentage buoyancy of all batches was above 65 %, which is studied for 12 h. The total floating time for all batches was
above 12 h. This result showed good floating ability of the Sumatriptan Succinate microspheres. It is observed that with increasing polymer concentration, percentage buoyancy increased.

3.3.4 *In-vitro* dissolution study

In-vitro drug release study of microspheres batches was performed in acidic buffer 0.1 N HCl. Dissolution study performed for 6 hrs. The % drug release from formulation batch of F9, F13 and F17 was 53.71 %, 72.12 % and 68.22 % at end of 6 hr respectively. From this observation it was concluded that as drug to polymer (ethyl cellulose) ratio increased the drug release rate decreased. The formulation batch F13 contains ethyl cellulose and HPMC K4M as polymers. The drug release rate of microspheres in presence of HPMC K4M polymer was increased. The F17 formulation batch contains ethyl cellulose and *Vigna Mungo* mucilage. Due to the presence of vigna mungo the drug release is little higher. *Vigna Mungo* is hydrophilic in nature, diffusion of drug increased.

| Batch No. | Percentage Yield (%) | Average Particle Size (μm) | Entrapment Efficiency (%) ± SD (n=3) | Drug Loading (%) ± SD (n=3) |
|-----------|----------------------|---------------------------|-------------------------------------|----------------------------|
| F1        | 47.00                | 111-125                   | 17.46 ± 0.08                        | 8.73 ± 0.04                |
| F2        | 50.40                | 96-125                    | 18.59 ± 0.16                        | 9.29 ± 0.08                |
| F3        | 48.60                | 103-125                   | 20.15 ± 0.28                        | 10.08 ± 0.14               |
| F4        | 54.67                | 131-150                   | 27.34 ± 0.59                        | 9.10 ± 0.20                |
| F5        | 52.00                | 111-130                   | 24.87 ± 0.27                        | 8.28 ± 0.09                |
| F6        | 54.13                | 151-170                   | 29.80 ± 0.42                        | 9.92 ± 0.14                |
| F7        | 64.30                | 170-190                   | 39.95 ± 0.77                        | 9.99 ± 0.19                |
| F8        | 61.40                | 151-170                   | 44.15 ± 0.27                        | 11.04 ± 0.07               |
| F9        | 76.80                | 170-190                   | 46.72 ± 0.79                        | 11.68 ± 0.2                |
| F10       | 53.06                | 155-170                   | 24.11 ± 0.19                        | 11.21 ± 0.09               |
| F11       | 60.95                | 177-192                   | 32.82 ± 0.13                        | 10.34 ± 0.04               |
| F12       | 65.87                | 177-200                   | 43.22 ± 0.30                        | 10.37 ± 0.07               |
| F13       | 69.72                | 185-200                   | 40.19 ± 0.27                        | 9.24 ± 0.06                |
| F14       | 56.76                | 155-171                   | 21.73 ± 0.17                        | 10.10 ± 0.08               |
| F15       | 62.47                | 151-175                   | 35.57 ± 0.07                        | 11.21 ± 0.02               |
| F16       | 69.33                | 177-192                   | 44.93 ± 0.41                        | 10.78 ± 0.10               |
| F17       | 73.38                | 185-200                   | 43.12 ± 0.13                        | 9.92 ± 0.03                |
| F18       | 63.50                | 126-150                   | 22.92 ± 0.77                        | 5.73 ± 0.19                |
| F19       | 62.40                | 155-170                   | 28.94 ± 0.84                        | 4.05 ± 0.12                |
| F20       | 71.09                | 150-170                   | 31.23 ± 0.79                        | 4.37 ± 0.11                |
| F21       | 77.08                | 176-200                   | 36.15 ± 1.39                        | 3.62 ± 0.14                |
| F22       | 82.29                | 160-190                   | 54.16 ± 0.47                        | 15.71 ± 0.14               |
| F23       | 87.88                | 191-210                   | 59.29 ± 0.68                        | 11.86 ± 0.14               |

Table 8. Evaluation of microspheres containing ethyl cellulose

![Fig. 2. In-vitro drug release study of floating microspheres formulations](image-url)
FTIR of sumatriptan succinate and microsphere formulations: The FTIR spectrum of pure Sumatriptan Succinate showed strong absorption bands at a wave number of 3374, 3200, 1556, 2990, 1132, 1082 cm\(^{-1}\), corresponding to N-H stretch, O-H bending, C=C stretch, C-H stretch, C-N stretch, S=O stretch respectively. The characteristic peaks confirmed the structure of Sumatriptan succinate. For ethyl cellulose absorption band at wave number of 1750, 3400, 1370 cm\(^{-1}\) corresponding to C=O stretch, O-H bending, C-H stretch respectively. 

*Vigna Mungo* Mucilage showed strong absorption band at wave number of 3479, 3400, 1600, 1250, N-H stretch, O-H bending, C=C stretch, C-N stretch, C=O stretch respectively. The FTIR spectrum of microsphere containing Sumatriptan Succinate: Ethyl cellulose (Part E Fig 3), Sumatriptan succinate: *Vigna Mungo* Mucilage (Part E Fig 3) and Sumatriptan succinate: Ethyl cellulose: HPMC K4M (Part E Fig 3) showed complete disappearance of characteristic wavenumber of 1708, 1556, 1132-1338, 1082 cm\(^{-1}\) observed in plain sumatriptan succinate. It suggests the drug is completely entrapped in polymer ethyl cellulose, Ethyl cellulose: *Vigna Mungo* Mucilage and Ethyl cellulose: HPMC K4M respectively for formulation.

DSC of sumatriptan succinate and microsphere formulations: DSC studies indicated a sharp endothermic peak at 170.49°C corresponding to melting point of pure Sumatriptan Succinate. The DSC endotherm of *Vigna Mungo* mucilage powder showed onset of endothermic peak at 72.38 °C. The DSC thermogram of microsphere containing Sumatriptan Succinate: Ethyl cellulose (Part E Fig 4), Sumatriptan succinate: Ethyl cellulose: *Vigna Mungo* Mucilage (Part F Fig 3) and Sumatriptan succinate: Ethyl cellulose: HPMC K4M (Part G Fig 3) does not show any melting endotherm corresponding to the pure drug. It suggests sumatriptan succinate in microspheres was in amorphous phase as a molecular dispersion or solid solution state in polymer matrix.

**Fig. 3.** FTIR of Sumatriptan Succinate (A), *Vigna Mungo* mucilage (B), Ethyl cellulose (C), HPMC K4M (D), Microsphere containing Sumatriptan Succinate: Ethyl cellulose (E), Sumatriptan succinate: Ethyl cellulose: *Vigna Mungo* Mucilage (F) and Sumatriptan succinate: Ethyl cellulose: HPMC K4M (G)
Fig. 4. DSC thermogram of Sumatriptan Succinate (A), Vigna Mungo mucilage (B), Ethyl cellulose (C), HPMC K4M (D), Microsphere containing Sumatriptan Succinate: Ethyl cellulose (E), Sumatriptan succinate: Ethyl cellulose: Vigna Mungo Mucilage (F) and Sumatriptan succinate: Ethyl cellulose: HPMCK4M (G)

Fig. 5. Microsphere containing Sumatriptan Succinate: Ethyl cellulose (Part A), Sumatriptan Succinate: Ethyl cellulose: Vigna Mungo Mucilage (Part B) and Sumatriptan succinate: Ethyl cellulose: HPMCK4M (Part C)
Surface morphology FESEM study of sumatriptan succinate and microsphere formulations: Formulation of microspheres depends on some factors like type, amount of solvent, polymer used and processing time. Found that solid microspheres were 100–1000μm in size shown in (Fig. 5 part A, B and C). Perforated spheres formed due to rapid evaporation took place during processing. The uniform stirring speed of mechanical stirrer makes the microspheres solids and spherical. During solidification process and cross linking leads to formation of voids, it may be related to mechanisms of air bubbles or entrapped fluid. Such spheres had possibility to achieve more space for interaction with dissolution media. It results in decreases in the sustained release property. The microsphere surface became smooth and non-porous, which was effective in delayed dissolution (Fig. 5 A). Furthermore, all three batches of microspheres had a regular spherical morphology (Fig. 5 Part A, B, C). The surface of microspheres containing Sumatriptan Succinate: Ethyl cellulose (Part A) was smooth with minimum perforation on surface. Remaining two batches of microspheres containing Ethyl cellulose: Vigna Mungo Mucilage (Part B) and Sumatriptan succinate: Ethyl cellulose: HPMC K4M (Part C) had regular spherical morphology with more pores, it suggest decrease in sustain release property.

4. CONCLUSION

The prepared microspheres were showed excellent micromeritic properties. The average particle size of all batches was found in the range 100 to 210 μm. Particle size of microspheres was changed. It is attributed with change in polymer concentration in prepared formulation batches. As polymer proportion is increased it leads to increase in particle size. The concentration of polymers has effect on the percentage yield. Drug to polymer ratio 1:1 showed less percentage yield. As the ratio of drug to polymer increased the percentage yield increased. The entrapment efficiency of all formulations was found in the range of 17.46 % to 59.28 %. The microsphere batch of Formula 9, Formula 13 and Formula F 17 showed 46.92 %, 40.19 % and 43.12 % of entrapment efficiency with corresponding drug loading of 11.68 %, 9.24% and 9.92 % respectively. More entrapment is attributed to greater proportion of polymer. Ethyl cellulose microspheres showed more entrapment than with HPMC K4M and Vigna Mungo mucilage. HPMC K4M and Vigna Mungo mucilage in microsphere formulation erodes with time. This is probable reason for less entrapment. Entrapment efficiency also depends upon of drug, drug solubility, nature of polymer, polymer solubility, affinity between drug and polymer. Sumatriptan Succinate is hydrophilic drug, so aqueous solubility is more. During the microspheres preparation the drug diffusion in the aqueous medium was more. Leaching of drug to the external aqueous medium, this resulted in poor entrapment efficiency for Sumatriptan Succinate. Entrapment efficiency was increased in W/O/W multiple emulsion method. All formulations showed good floating ability. Ethyl cellulose microspheres showed more entrapment and sustained delivery of sumatriptan Succinate than microspheres prepared by combination of Ethyl cellulose: HPMC K4M and Ethyl cellulose: Vigna mungo mucilage.

DISCLAIMER

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CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Sharma D, Sharma A. Gastroretentive drug delivery system-a mini review. Asian Pacific Journal of Health Sciences. 2014;1(2):80-89.
2. Niharika MG, Krishnamoorthy K, Akkala M. Overview on floating drug delivery system. International Journal of Applied Pharmaceutics. 2018;10(6):65-71.
3. Gururaj S, Kulkarni and D. Narasinha Reddy. Design, development and evaluation of sumatriptan succinate transdermal patches. International Journal of Pharmaceutical Science and Research. 2012;3(6):1656-1662.
4. Shivanand K, Raju S, Nizamuddin S, Jayakar B. In vivo bioavailability studies of sumatriptan succinate buccal tablets. Daru. 2011;19(3):224-30.
5. Arun KB, Mahalakshmi K, Rao VUM. Formulation and evaluation of gastro retentive floating microbeads of sumatriptan. International Journal of Pharmacy Review & Research. 2015;5(1):41-46.
6. Jagdale SC, Pawar CR. Application of design of experiment for polyox and xanthan gum coated floating pulsatile delivery of sumatriptan succinate in migraine treatment. Hindawi Publishing Corporation BioMed Research International; 2014. Article ID 547212:1-10.
7. Kumar GP, Venkata NSM, Krishn TM. Formulation, optimization and in-vitro evaluation of gastro retentive sumatriptan succinate tablets. European Journal of Pharmaceutical and Medical Research. 2017;4(2):347-365.
8. Pabbathi CS, Vattep B, Veerla V, Allakonda R. Design and characterization of gastro retentive floating tablets of sumatriptan Succinate. International Journal of Research in Pharmaceutical and Nano Sciences. 2017;6(6):287-293.
9. Yadav IK, Jaiswal D, Singh HP, Chandra D, Jain DA. Evaluation of seed mucilage of vigna mungo (L.) as a binder in tablet formulations. Journal of Pharmacy Research. 2009;2(8):1281-128.
10. Bodempudi S, Deveswaran R, Bharath S, Basavaraj BV, Madhavan V. Studies on Vigna Mungo mucilage as pharmaceutical excipient. Journal of Chemical and Pharmaceutical Research. 2011;3(2):118-122.
11. Gada SG, Anandkumar Y, Setty CM. Design and optimization of zidovudine loaded urid dall mucilage microspheres, using box behnken method. International Journal of Pharmaceutical Sciences and Research. 2019;10(4):1856-1864.
12. Ige PP, Gadgil PP, Sonawane RO. Use of black gram polysaccharide mucilage as release retardant in the development of sustained release matrix pellets of ciprofloxacin hydrochloride. Indian Journal of Pharmaceutical Education and Research. 2018;52(3):389-397.
13. Yadav IK, Jaiswal D, Ghosh N, Singh H, Mishra A, Bhattacharya A, Bajpai M. Evaluation of seed flour of vigna mungo (L.) based Sustained release matrix tablets of diclofenac sodium. Journal of Pharmacy Research. 2009;2(5):834-838.
14. Jadhao UT, Tekade BW, Bharambe GP, Vig V, Patil VR. Development and in-vitro evaluation of capecitabine microspheres by emulsification solvent evaporation method. Ijppr Human. 2017;10 (2):149-162.
15. Koppara S, Gande S. Development and evaluation of sustained release floating microspheres containing ropinirole HCl. International Journal of Pharmaceutical Sciences and Drug Research. 2018;10(3):158-164.
16. Kumbhar MD, Morey PH, Karpe MS, Kadam VJ. Development and characterization of gastroretentive floating microsphere for controlled release of metoclopramide hydrochloride. Indian Journal of Drugs. 2018;6(4):189-200.
17. Sharma D, Godbole MD, Burle S. Design optimize and evaluation of floating microspheres by solvent evaporation technique of antiulcer drug. World Journal of Pharmaceutical Research. 2017;6(3):1417-1433.
18. Sharma MK. Formulation and characterization of floating microspheres of acarbosse by solvent evaporation method. Mintage journal of Pharmaceutical & Medical Sciences. 2016;5(2):3-7.
19. Gattani YS, Kawtikwar PS, Sakarkar DM. Formulation and evaluation of gastro retentive multiparticulate drug delivery system of aceclofenac. International Journal of Chem Tech Research. 2009;1(1):1-10.
20. Khan R, Arora R, Ojha A, Chopra H, Upadhaya K. Formulation and evaluation of floating microspheres of levofloxacin. International Research Journal of Pharmacy. 2018;9(7):186-191.
21. Goyal M, Sharma P, Mehta SC. Formulation and characterization of calcium silicate based floating microspheres of famotidine for the
treatment of peptic ulcer. IJPSR. 2017;8(2):784-793.

22. Miranda FC, Kamath KK, Shabaraya AR. Development of gastro retentive floating microspheres of roxatidine acetate HCl by emulsion solvent diffusion technique. International Journal of Drug Delivery Technology. 2019;9(4):530-537.

23. Deepa MK, Karthikeyan M. Cefpodoxime proxetil floating microspheres: formulation and in-vitro evaluation. Iranian Journal of Pharmaceutical Sciences. 2009;5(2):69-72.

24. Goswami N, Joshi G, Sawant K. Floating microspheres of Valacyclovir HCl: Formulation, optimization, characterization, in-vitro and in-vivo floatability studies. J Pharm Bioall Sci. 2012; 4:8-9.

25. Higuchi T. Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. Journal of Pharmaceutical Sciences.1963;52(12):1145-1149.

26. Korsmeyer RW, Gurny R, Docler E, Buri P, Peppas NA. Mechanism of solute release from porous hydrophilic polymers. International Journal of Pharmaceutics. 1983;15(1):25-35.