

RESEARCH ARTICLE

DESIGN, DEVELOPMENT, CHARACTERIZATION AND COMPARISON OF CALCIUM SILICATE AND CHOLESTYRAMINE BASED ELETRIPTAN HYDROBROMIDE FLOATING MICROSPHERES**Saleha, K. Shravan Kumar,* D. Prabhakar, U. Ashok kumar**

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Corresponding Author's Email: shravankonda@yahoo.com*ABSTRACT:**

Studies were carried out to develop, characterize and compare oral floating microspheres for Eletriptan Hydrobromide using Ion exchange resin like Cholestyramine and low density porous carrier like calcium silicate so as to provide extended gastric retention. The prepared resinate were studied for the effect of pH and drug resin ratio on drug loading and is similar with calcium silicate. Both the formulations were evaluated for drug entrapment, *in vitro* floating behavior, *in vivo* buoyancy and *in vitro* drug release studies. Dissolution study of Eletriptan hydrobromide microspheres with both the calcium silicate and cholestyramine was able to sustain the release of the drug. The study suggests that the floating microspheres of Eletriptan hydrobromide provide sustained release over 24 h and also showed *in vivo* buoyancy for more than 10 h in rabbit.

Keywords:**1. INTRODUCTION:**

The word new or novel in the relation to drug delivery system is a search for something out of necessity. An appropriately designed sustained or controlled release drug delivery system can be major advance toward solving the problem associated with the existing drug delivery system^{1,2}. Various attempts have been made to prolong the gastric residence time of dosage form in the stomach. Floating drug delivery system have a bulk density less than gastric fluids and so remains buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from stomach.

This result in an increased gastric residence time and a better control of the fluctuation in plasma drug concentration³. Single unit formulations are associated with problems such as sticking together or being obstructed in the gastrointestinal tract, which may have a potential danger of producing irritation. On the other hand a floating system made of multiple unit forms has relative merits compared to a single unit preparation. Indeed the gastric emptying of a microparticulate floating system would occur in consistent manner with small individual variations on each subsequent gastric emptying sunken particles will spread out over a large area of absorption sites, increasing the opportunity of drug release and absorption in a more or less predictable way. Moreover, since each dose consists of many subunits, the risk of dose dumping is reduced⁴. Floating microspheres provide a constant and prolonged therapeutic effect which will reduce dosing frequency.^{5,6} Eletriptan Hydrobromide is an antimigraine drug; its mechanism of action is explained by two theories to explain the efficacy of 5-HT receptor agonists in migraine. One theory suggests that activation of 5-HT1 receptors located on intracranial blood vessels, including those on the arterio venous anastomoses, leads to vasoconstriction, which is correlated with the^{2,3,2}.

relief of migraine headache. The other hypothesis suggests that activation of 5-HT1 receptors on sensory nerve endings in the trigeminal system results in the inhibition of proinflammatory neuropeptide release. Inhibition of prostaglandin synthetase and its plasma elimination half life is 4 hrs and in order to maintain therapeutic plasma level drug must be administered at least twice a day⁷.

The aim of this study was to prepare Eletriptan Hydrobromide floating microspheres containing hydrophobic polymer ethyl cellulose along with low density calcium silicate porous carrier and ion exchange resin Cholestyramine to achieve better encapsulation efficiency, better buoyancy and sustained drug release profile suitable for oral administration. The influences of formulation variables on the microsphere properties were examined and the microsphere formulations suitable to achieve our goal were determined.

2. MATERIALS AND METHOD:**2.1. Materials:**

Eletriptan Hydrobromide was received as a gift sample from Finosa Pharmaceuticals, Hyderabad, India. Calcium silicate was procured from Johnson & George Chemical company, Mumbai, Ethyl cellulose was a gift sample from Merck, Mumbai, Acetonitrile, Dichloromethane and Light liquid paraffin and other chemicals were of analytical grade.

2.2. Methods:**2.2.1. Preparation of Eletriptan Hydrobromide adsorbed Calcium silicate:**

The porous carrier was dispersed into 10 ml water solution of drug (Eletriptan Hydrobromide). This solution was ultrasonicated to imbibe the drug solution inside the pores of porous carrier⁸.

Preparation of Eletriptan Hydrobromide – Cholestyramine complex:

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An accurately weighed amount of Eletriptan Hydrobromide (100 mg) was taken and added in 10 ml of distilled water. Then known weight of ion exchange resin was added to the solution and stirred on propeller stirrer. Resinate thus formed was washed with 0.1 N HCl to remove the unloaded drug. Resinate was dried overnight in an hot air oven at 50°C⁹.

2.2.3. Preparation of floating microspheres:

Microspheres were prepared using a modified water-in oil-in oil (W/O₁/O₂) double emulsion solvent diffusion method¹⁰. Briefly, for calcium silicate and cholestyramine based microspheres, the drug adsorbed calcium silicate and drug- cholestyramine complex was added respectively to the polymer solution of ethyl cellulose (EC) in acetonitrile and dichloromethane (CAN:DCM) (1:1) and stirred using a mechanical stirrer at 500 rpm. The resulting W/O primary emulsion was slowly added to 50 ml of light liquid paraffin, the second oil phase containing 0.5% span 80 as a surfactant while stirring by a paddle propeller at 1000 rpm. After 2 h, 10 ml of *n*-hexane (non-solvent) was added to harden the microspheres and stirring was continued for a further 1 h and the hardened microspheres were collected by filtration and washed thrice with 50 ml of *n*-hexane and air dried for 12 h. The effect of process variables like polymer concentration, stirring rate, temperature, concentration of aqueous phase on the particle size, buoyancy, drug entrapment efficiency, drug release, amount of porous carrier and ion exchange resin were studied.

Process variables: Amount of Polymer: 1000, 1500 mg; Amount of carrier: 150, 200, and 250.

3. Characterization of microspheres:

3.1. Micromeritic properties:

The microspheres were characterized by their micromeritic properties, such as particle size, true density, tapped density, compressibility index and flow properties. The size was measured using an optical microscope, and the mean particle size was calculated by measuring 200–300 particles with the help of a calibrated ocular micrometer. The tapping method was used to determine the tapped density and percent compressibility index¹¹ as follows:

Tapped density = Mass of microspheres / Volume of microspheres after tapping

$$\% \text{ Compressibility index} = (1 - V/V_0) \times 100$$

Here V and V₀ are the volumes of the sample after and before the standard tapping, respectively.

True density was determined using a benzene displacement method.

Porosity (ϵ) was calculated using the equation:

$$\epsilon = (1 - P_p/P_t) \times 100$$

where P_t and P_p are the true density and tapped density, respectively.

Angle of repose h of the microspheres, which measures the resistance to particle flow, was determined by a fixed funnel method.¹² and calculated as $\tan \theta = 2h/D$

Where 2h/D is the surface area of the free standing height of the microspheres heap that is formed on a graph paper after making the microspheres flow from the glass funnel.

3.2. Morphology:

The external and internal morphology of the microparticles and porous carrier were studied by scanning electron microscopy (SEM). The samples for SEM were prepared by lightly sprinkling the powder on a double adhesive tape stuck to an aluminum stub. The stubs were then coated with gold to a thickness of about 300 Å under an argon atmosphere using a gold sputter module in a high-vacuum evaporator. The coated samples were then randomly scanned and photomicrographs were taken with a scanning electron microscope (Jeol JSM-1600, Tokyo, Japan).

3.3. Determination of drug content of microspheres:

Drug amount in microspheres was determined by dissolving 10 mg of each sample in 100 ml dichloromethane. The drug concentration was determined spectrophotometrically (UV-160, Shimadzu, Japan) at 272.2 nm. All experiments were done in triplicate⁹.

3.4. Determination of production yield:

The production yield of the microparticles was determined by calculating accurately the initial weight of the raw materials and the last weight of the microspheres obtained¹³. All of the experiments were performed in triplicate

$$\% \text{ drug entrapment} = [\text{calculated drug concentration/theoretical drug concentration}] \times 100.$$

$$\% \text{ yield} = [\text{total weight of floating microparticles} / \text{total weight of drug, polymer, porous carrier/resin (if added)}] \times 100.$$

3.5. *In-vivo* floating behavior:

Microspheres (50mg) were spread over the surface of a USP XXIV dissolution apparatus type II filled with 900 ml of 0.1 N Hydrochloric acid. The medium was agitated with a paddle rotating at 100 rpm for 12 h. The floating and the settled portions of microspheres were recovered separately. The microspheres were dried and weighed. Buoyancy percentage was calculated as the ratio of the mass of the microspheres that remained floating and the total mass of the microspheres¹⁴.

$$\text{Buoyancy} = W_f / (W_f + W_s) \times 100$$

Where W_f and W_s are the weights of the floating and settled microparticles, respectively. All the determinations were made in triplicate.

3.6. *In-vitro* release studies:

The drug release rate from floating microspheres was determined using USP XXIII basket type dissolution apparatus. A weighed amount of floating microspheres equivalent to 20 mg drug was filled into a capsule and placed in the basket. 0.1 N HCl was used as the dissolution medium and maintained at 37±0.5°C. at a rotation speed of 100 rpm. Perfect sink conditions prevailed during the drug release studies. Five ml sample was withdrawn at each 30 min interval, passed through a membrane filter (Millipore), and analyzed spectrophotometrically at 272.2

nm to determine the concentration of drug present in the dissolution medium. The initial volume of the dissolution fluid was maintained by adding 5 ml of fresh dissolution fluid after each withdrawal. All experiments were conducted in triplicate.

3.7. *In-vivo* floating behaviour:

Barium sulphate loaded microspheres were prepared by adopting the procedure as described before except for using barium sulphate instead of drug. Healthy rabbit weighing approximately 2.3 Kg was used to assess *in vivo* floating behaviour. Ethical clearance for the handling of experimental animals was obtained from the SLS/2012/10/5/2(1047/ac/07/CPCSEA), constituted for the purpose. The animal was fasted for 12 h and the first X-ray photographed to ensure absence of radio opaque material in the stomach. The rabbit were made to swallow barium sulphate loaded microspheres with 30 ml of water. During the experiment rabbit were not allowed to eat but water was provided. At predetermined time intervals the radiograph of abdomen was taken using an X-ray machine¹⁵.

3.8. Accelerated stability studies:

Drug decomposition or degradation occurs during storage, because of chemical alteration of the active ingredients or due to product instability, leading to lower concentration

of the drug in the dosage form, hence the stability of pharmaceutical preparation need to be evaluated. The objective of stability studies is to predict the shelf life of a product by accelerating the rate of decomposition, preferably by increasing the temperature and relative humidity (RH) conditions. Stability studies were carried out at 40±2 °C and 75±5% relative humidity for 90 days¹⁶.

RESULTS AND DISCUSSIONS:

4.1. Formation of microspheres:

Microspheres were formed after a series of steps like solvent extraction and solvent evaporation and addition of non-solvent. Acetonitrile is a unique organic solvent which is polar, water miscible and oil immiscible. All other polar solvents are oil-miscible and do not form emulsions of the polymer solution in oil¹⁷. Dichloromethane is non-polar and oil miscible. Using acetonitrile alone as a solvent did not ensure formation of a stable emulsion, and non-polar solvent such as dichloromethane was included to decrease polarity of the acetonitrile solution¹⁸. Therefore, during the formation of microspheres, dichloromethane is extracted by liquid paraffin and acetonitrile is evaporated during stirring. The incorporation of drug adsorbed calcium silicate or drug – cholestyramine complex into the formulation may produce porous structure within the microspheres. The compositions are showed in Table.1.

Table 1: Composition of floating microspheres of Eletriptan hydrobromide

EC: Ethylcellulose, (ACN: DCM): Acetonitrile: Dichloromethane

Formulation	Drug (mg)	EC (mg)	Calcium silicate (mg)	Cholestyra-mine (mg)	ACN:DCM(1:1)(ml)
CS1A	100	1000	150	-	20
CS1B	100	1000	200	-	20
CS1C	100	1000	250	-	20
CS2A	100	1500	150	-	20
CS2B	100	1500	200	-	20
CS2C	100	1500	250	-	20
CH1A	100	1000	-	150	20
CH1B	100	1000	-	200	20
CH1C	100	1000	-	250	20
CH2A	100	1500	-	150	20
CH2B	100	1500	-	200	20
CH2C	100	1500	-	250	20

4.2. Micromeritic properties:

The mean particle sizes of calcium silicate powder was 142 ± 02µm, while that of microsphere formulations containing calcium silicate in the range of 150 to 250mg measured 650 ± 12µm to 828 ± 12µm when compared to cholestyramine measured 605±15µm to 813±14µm. the particle size of microsphere formulation without buoyant material was found to be 180±08µm. The tapped density values of calcium silicate ranged from 0.33±0.04g/cm³ to 0.65±0.06g/ cm³ that of tapped density values of cholestyramine ranged from 0.43±0.09g/ cm³ to 0.68±0.07g/ cm³, while true density of calcium silicate ranged between 1.66±0.12g/ cm³ and 1.84±0.1g/ cm³ and cholestyramine ranged between 1.89±0.15g/ cm³ and

2.11±0.5g/ cm³. The significant difference in the densities may be caused by the presence of low density calcium silicate and cholestyramine particles in the microspheres. The porosity of all the microsphere formulations was found to be in the range of 70.6%±2.5% to 90.0%±4.0%. The compressibility index of calcium silicate based formulations ranged between 14.73%±2.2% and 24.6%±3.1% while that of calcium silicate based formulations ranged between 15.12%±4.2% and 28.71%±4.3%. All formulations of calcium silicate showed excellent flow ability as expressed in terms of angle of repose (<40°) except formulation CS2C, probably due to higher content of calcium silicate, while in cholestyramine based formulations expressed flow ability in terms of angle of repose (<46°) except formulation CH2C, probably due

to higher content of cholestyramine. The better flow property indicates that the floating microspheres produced are non-aggregated.

4.3. Morphology:

Calcium silicate and cholestyramine based Ethyl cellulose microspheres were predominantly spherical in appearance; however some were found to be elongated. The porous nature and spherical shape of the microspheres are evident from their SEM photomicrographs Fig. 1, Fig. 2. As can be seen in the photomicrograph, there are many pores and cavities in the microspheres. Low-density drug adsorbed FLR particle is clearly visible inside the microsphere in Fig. 3 and Fig. 4, which make them float on the simulated GIT fluids shows the surface morphology of microsphere at a higher magnification.

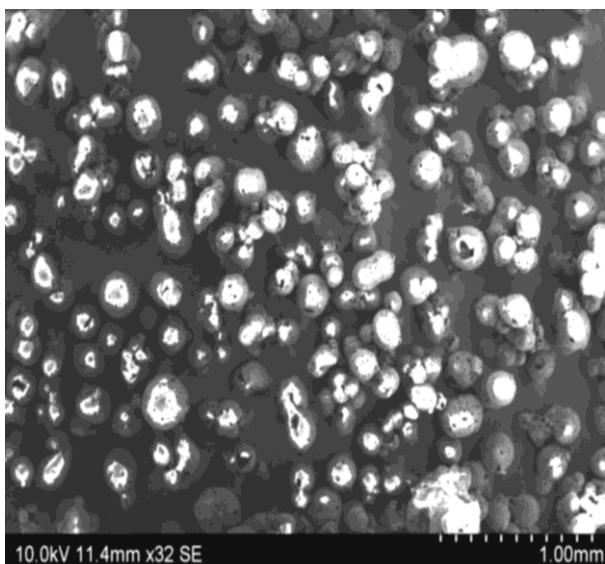


Fig. 1: SEM photomicrographs showing porous nature and spherical shape of calcium silicate based microspheres.

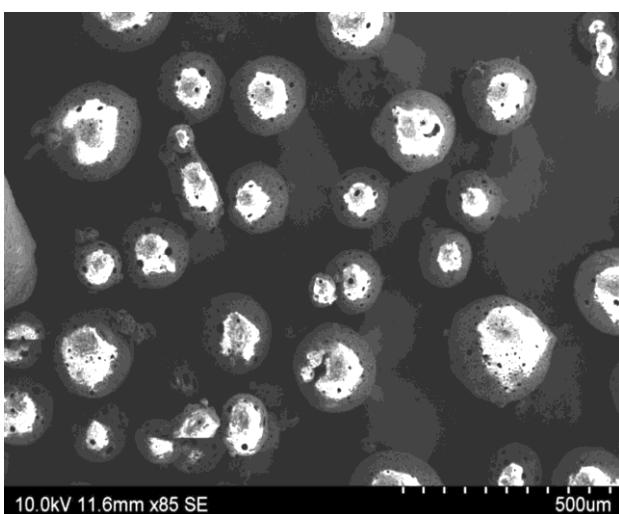


Fig. 2: SEM photomicrograph depicting many pores and cavities in the cholestyramine based microspheres.

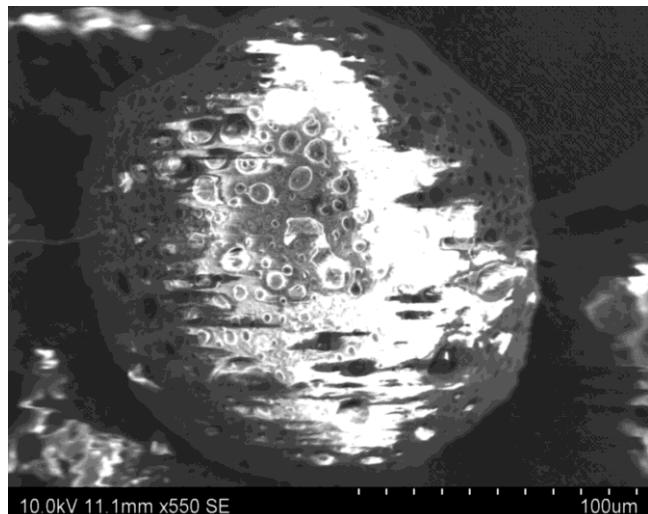


Fig. 3: SEM photomicrograph showing low-density drug adsorbed calcium silicate particle is clearly visible inside the microsphere.

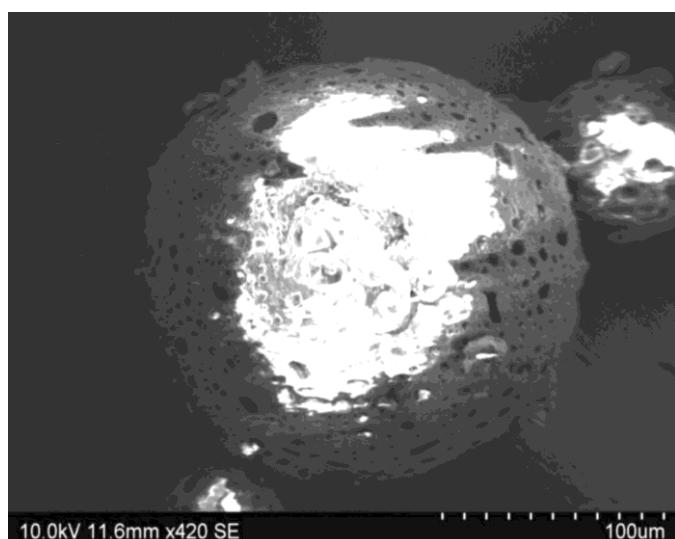


Fig. 4: SEM photomicrographs showing porous nature and spherical shape of cholestyramine based microspheres.

Percentage buoyancy and drug entrapment:

In Vitro Buoyancy percentage of the microspheres calcium silicate based Eletriptan hydrobromide was in the range of $76.15 \pm 0.55\%$ to $93.80 \pm 1.75\%$ at the end of 12 h above 88 %) and that of cholestyramine based Eletriptan Hydrobromide 77.54 ± 1.73 to $91.83 \pm 1.74\%$ at the end of 12 h as shown in Table. 2. Good *in vitro* floating behavior was observed for all the microsphere formulation. This may be attributed to the low density calcium silicate within the system.

The percent drug entrapment of calcium silicate based Eletriptan hydrobromide in all the formulations was in the range of $53.02 \pm 4.97\%$ to $75.29 \pm 1.93\%$ found to be good at all levels of drug loading and that of cholestyramine based microspheres was in the range of $19.96 \pm 1.73\%$ to $56.91 \pm 4.49\%$ as in Table.3. The extent of loading influenced the particle size distribution of microspheres. When the loading was high, the proportion of larger particles formed was also high. With 75%

entrapment, most of the particles (calcium silicate based) were in the size range of 84-100 micrometer, suitable for oral administration and with 57% entrapment, most of the particles (cholestyramine based) were in the size range of 58.5-68.9 micrometer. As the concentration of total amount of polymer was increased, drug entrapment efficiency (drug content) was also increased. Formulation CS2B showed good % drug entrapment ($73.10 \pm 1.93\%$).

Table 2: In-vitro buoyancy studies of Calcium silicate and Cholestyramine based Eletriptan Hydrobromide floating microspheres.

Formulation	Total floating time(hr)	% of Buoyancy
CS1A	>24	76.15 ± 0.55
CS1B	>24	86.81 ± 0.96
CS1C	>24	89.43 ± 4.43
CS2A	>24	86.21 ± 1.12
CS2B	>24	93.80 ± 1.75
CS2C	>24	90.96 ± 1.21
CH1A	>24	77.54 ± 1.73
CH1B	>24	80.49 ± 1.57
CH1C	>24	86.12 ± 0.97
CH2A	>24	82.77 ± 0.48
CH2B	>24	85.82 ± 1.20
CH2C	>24	91.83 ± 1.74

Table 3: Drug entrapment of floating microspheres

Formulation code	% Drug entrapment
CS1A	53.02 ± 4.97
CS1B	40.10 ± 9.62
CS1C	61.87 ± 0.57
CS2A	68.08 ± 0.98
CS2B	75.29 ± 1.93
CS2C	70.98 ± 0.59
CH1A	19.96 ± 1.73
CH1B	21.27 ± 0.63
CH1C	24.08 ± 0.45
CH2A	42.40 ± 1.77
CH2B	46.99 ± 0.79
CH2C	56.91 ± 4.49

4.4. Production yield:

The percentage yield of floating microspheres of formulations (CS1A to CS2C) was found to be in the range of 94.64 to 98.37% and 96.936 to 98.86% in cholestyramine based formulations (CH1A to CH2C)

4.5. In-vivo floating behavior:

The *in vivo* floating behavior of formulation (CS2B and CH2C) hollow microspheres loaded with barium sulphate was investigated by radiographic images (X-ray photographs) of rabbit's stomach at specific periods. The amount of X-ray opaque material in these hollow was sufficient to ensure visibility by X-ray but at same time the amount of barium sulphate (100 mg) was low enough to enable the hollow microspheres to float. The hollow microspheres did not adhere to the gastric mucous and floating on the gastric fluid for about more the 12 h. This

formulation CH2C hollow microsphere loaded with barium sulphate at 1st hour. was evident by the X-ray photographs taken at 1 h, & 9 h. It is shown in Fig. 5, Fig. 6, Fig.7 and Fig.8.

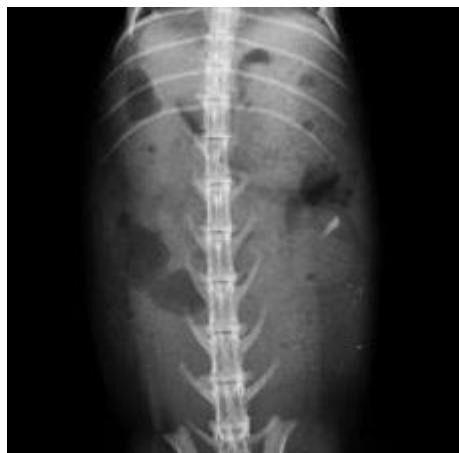


Fig 5: Radiographic images (X-ray photographs) of rabbit's stomach to investigate *in vivo* floating behavior of formulation CS2B hollow microspheres loaded with barium sulphate at 1st hour.



Fig 6: Radiographic images (X-ray photographs) of rabbit's stomach to investigate *in vivo* floating behavior of formulation CS2B hollow microspheres loaded with barium sulphate at 9th hour.



Fig 7: Radiographic images (X-ray photographs) of rabbit's stomach to investigate *in vivo* floating behavior of



Fig. 8: Radiographic images (X-ray photographs) of rabbit's stomach to investigate *in vivo* floating behavior of formulation CH2C hollow microspheres loaded with barium sulphate at 9th hour.

Release of Eletriptan Hydrobromide from calcium silicate and cholestyramine based microspheres was evaluated in pH 2.0 as shown in Table. 4 and Table. 5. Calcium silicate based floating drug delivery system provides the possibility of enhancing the bioavailability and control the release of Eletriptan Hydrobromide exhibiting absorption window by prolonging the gastric emptying time of the dosage form, ensuring availability of drug at the absorption site for the desired period of time. The calcium silicate microsphere with adsorbed drug and polymer coating showed a drug release ranging from 92.08 ± 3.59 to 98.05 ± 1.99 in Fig.9, when compared to cholestyramine based floating microspheres with drug release ranging from 92.60 ± 3.92 to 98.28 ± 1.60 as in Fig.10. The release of optimized formulations CS2B and CH2C is depicted in Fig.11. From the mathematical modeling of dissolution profiles, as shown in Table. 6, CS2B showed higher regression coefficient 0.9898 following first order non-fickian diffusion kinetic model.

4.6. *In-vitro* drug release study:

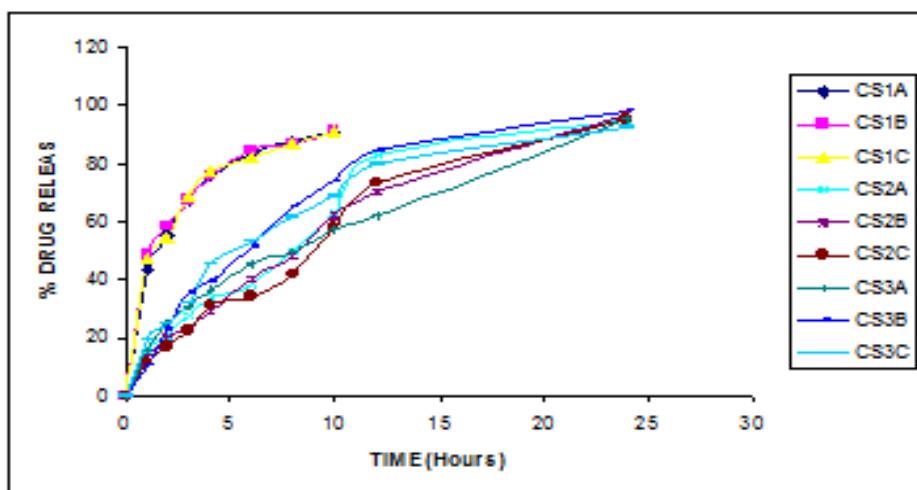


Fig 9: Cumulative percentage drug release in all Calcium silicate based microspheres

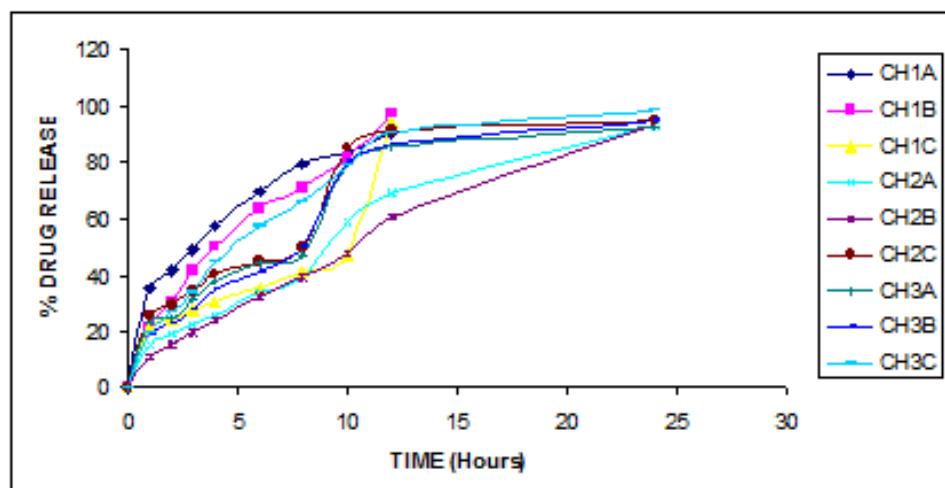
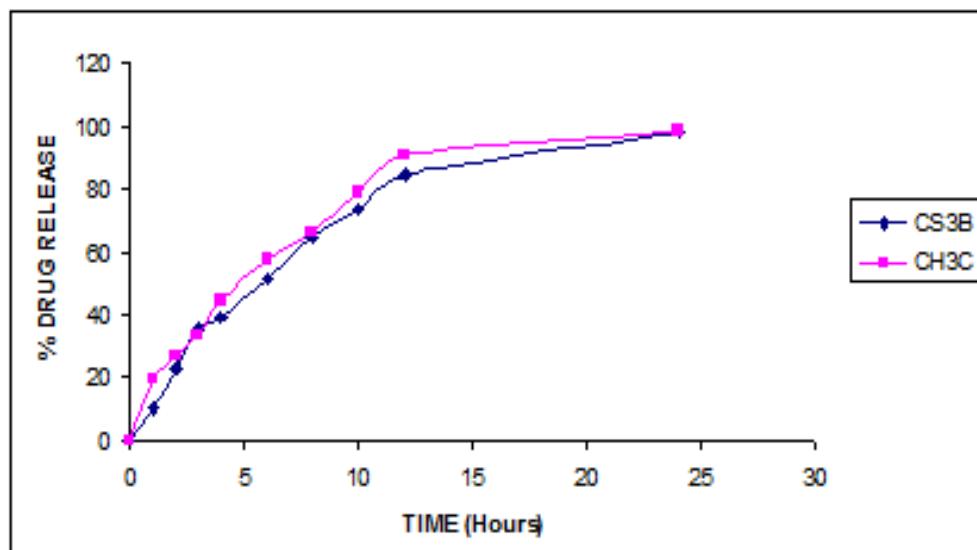


Fig 10: Cumulative percentage drug release in all Cholestyramine based microspheres.

**Fig 11:** Cumulative percentage drug release in optimized formulations.**Table 4:** Percentage drug release of Calcium silicate based Eletriptan Hydrobromide microspheres

Time (Hours)	CS1A	CS1B	CS1C	CS2A	CS2B	CS2C
0	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
1	15.96 ± 4.33	13.73 ± 2.17	12.06 ± 0.09	16.19 ± 3.58	10.69 ± 1.02	19.47 ± 2.55
2	20.80 ± 7.51	19.81 ± 2.18	17.25 ± 2.16	25.41 ± 0.77	23.25 ± 1.36	25.08 ± 4.14
3	27.92 ± 9.49	23.79 ± 4.36	22.47 ± 2.16	30.67 ± 5.87	35.37 ± 1.54	31.97 ± 5.00
4	33.82 ± 11.35	29.55 ± 4.39	31.22 ± 2.15	36.59 ± 4.57	39.32 ± 1.59	45.77 ± 3.39
6	38.50 ± 11.41	39.96 ± 6.57	34.14 ± 4.32	45.54 ± 4.56	51.16 ± 1.70	53.39 ± 4.72
8	49.84 ± 8.01	48.68 ± 4.45	41.83 ± 6.78	49.91 ± 5.93	64.82 ± 1.81	61.31 ± 3.19
10	63.24 ± 8.04	62.07 ± 5.75	57.68 ± 8.34	57.31 ± 2.24	73.67 ± 1.86	68.77 ± 4.20
12	82.58 ± 2.20	70.28 ± 5.78	73.12 ± 4.22	62.25 ± 0.09	84.34 ± 1.92	79.77 ± 6.26
24	95.28 ± 6.02	96.91 ± 2.12	95.40 ± 4.65	95.34 ± 7.51	98.05 ± 1.99	92.08 ± 3.59

Table 5: Percentage drug release of Cholestyramine based Eletriptan Hydrobromide microspheres

Time (Hours)	CH1A	CH1B	CH1C	CH2A	CH2B	CH2C
0	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
1	15.49 ± 8.73	11.19 ± 2.18	25.81 ± 5.34	23.31 ± 4.17	19.24 ± 5.48	19.75 ± 5.71
2	19.20 ± 6.40	15.50 ± 0.03	29.58 ± 4.65	24.31 ± 4.29	22.47 ± 4.03	27.11 ± 5.13
3	21.93 ± 5.79	19.84 ± 2.17	33.99 ± 7.48	30.95 ± 9.85	27.59 ± 5.88	33.38 ± 10.13
4	25.43 ± 7.12	23.82 ± 4.34	40.30 ± 11.04	37.87 ± 11.59	34.74 ± 1.80	44.44 ± 3.71
6	33.69 ± 6.94	32.20 ± 4.37	44.65 ± 11.72	44.07 ± 11.81	41.31 ± 1.95	57.43 ± 9.06
8	39.37 ± 8.06	39.01 ± 7.42	49.39 ± 12.66	47.44 ± 11.93	50.41 ± 3.23	65.87 ± 9.81
10	58.46 ± 2.31	47.47 ± 2.27	84.91 ± 0.80	79.45 ± 3.20	79.93 ± 6.31	78.98 ± 5.40
12	69.41 ± 5.15	60.73 ± 0.12	91.37 ± 1.13	85.63 ± 1.81	86.62 ± 5.91	90.41 ± 2.92
24	93.16 ± 2.49	93.43 ± 2.96	94.74 ± 1.53	92.60 ± 3.92	94.84 ± 0.95	98.28 ± 1.60

Table 6: Regression coefficient (R^2) values of Eletriptan Hydrobromide floating microspheres for different kinetic models

Formulation	Zero-order	First-order	Higuchi	Korsmeyer-Peppas	
	R^2			n	
CS1A	0.7697	0.963	0.9645	0.7262	0.2937
CS1B	0.7435	0.9513	0.9492	0.0016	0.0518
CS1C	0.7508	0.9525	0.9336	0.7121	0.3271
CS2A	0.8963	0.9676	0.9617	0.5794	0.5043
CS2B	0.9415	0.9506	0.9786	0.5985	0.4657
CS2C	0.9381	0.9589	0.9641	0.637	0.5819
CS3A	0.918	0.948	0.9961	0.65	0.5477
CS3B	0.8426	0.9898	0.9671	0.6927	0.628
CSC	0.8589	0.9858	0.9706	0.6829	0.523
CH1A	0.8853	0.9668	0.9859	0.6721	0.3118
CH1B	0.9593	0.8651	0.9916	0.6877	0.522
CH1C	0.8414	0.6018	0.7873	0.4446	0.3557
CH2A	0.9444	0.9629	0.9509	0.5421	0.4125
CH2B	0.9793	0.9389	0.962	0.591	0.5242
CH2C	0.8016	0.8804	0.639	0.5982	0.3578
CH3A	0.8285	0.9195	0.921	0.5708	0.3507
CH3B	0.8447	0.9446	0.9202	0.6349	0.4684
CH3C	0.8187	0.9847	0.9592	0.6772	0.4734

Table 7: Stability study for drug content of prepared CS2B and CH2C microspheres

Sampling (days)	Drug content (%) CS2B	Drug content (%) CH2C	Stability condition
0	75.29 \pm 1.93	56.91 \pm 4.49	40 °C/75% RH
7	75.25 \pm 1.24	56.75 \pm 3.98	
15	75.21 \pm 1.87	56.63 \pm 1.55	
30	75.18 \pm 1.85	56.56 \pm 1.98	
60	75.16 \pm 1.72	56.35 \pm 2.11	
90	75.11 \pm 1.22	56.14 \pm 1.65	

4.7. Accelerated Stability studies:

The objective of stability studies is to predict the shelf life of a product by accelerating the rate of decomposition, preferably by increasing the temperature and RH. The RSM containing selected formulation CS2B and CH2C was subjected to stability studies carried out by storing at 40°C/75% RH for 3 months (climatic zone IV condition for accelerated testing) to assess their stability. These samples were analyzed and checked for changes in physical appearance and drug content at regular intervals. The obtained data is presented in Table 7. From the table, it is clear that the formulation did not undergo any chemical changes/interaction during the study period.

5. CONCLUSION:

The present formulation study of Eletriptan Hydrobromide was performed in an attempt to prepare floating drug delivery system consisting of floating multiple unit system. Incorporation of Calcium silicate in the microspheres proved to be an effective method to achieve the desired

release behavior and buoyancy than incorporation of cholestyramine. The performance of these formulations was evaluated and the effect of various formulation variables was studied. The designed system, combining excellent buoyant ability and suitable drug release pattern, could possibly be advantageous in terms of increased bioavailability of Eletriptan Hydrobromide. Major advantages of the system include: (i) ease of preparation, (ii) good buoyancy, (iii) high encapsulation efficiency, and (iv) sustained drug release over several hours.

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CONFLICTS OF INTEREST:

The authors declare that they have no conflicts of interest.

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Figure legends