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Development and Evaluation of Famotidine Floating Microsponges

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ABSTRACT:
Medications which are locally effective, have a brief window of absorbing in the stomach or upper small intestine, are destabilizing in the intestine or colonic environment, and then have lower solubility at higher pH levels are particularly interested in FDDS. A proprietary polymeric system made up of porous microspheres is called the Micro sponge Delivery System (MDS). These tiny, spherical particles, which resemble microscopic sponges, have a broad porous surface that allows the regulated release of active ingredients. They are made up of several interconnected voids inside a non-collapsible framework. To enhance the drug's site-specific absorption for the treatment of peptic ulcers, famotidine floating microsponges are created. To create the microsponges, a modified quasi-emulsion solvent diffusion approach has been applied. The produced microsponges had been tested for entrapment effectiveness, buoyancy, and cumulative drug release using various concentrations of EudragitS100 and Polyvinyl alcohol. For the F8 preparation, it was discovered that the entrapment efficiency was 99.8%, buoyancy was 81.2%, and CDR was 87.9%. In this work, a novel ulcer therapy strategy based on the flotation properties of microsponges is presented.

KEYWORDS: Microsponges, FDDS, Quasi emulsion solvent diffusion method.

I. INTRODUCTION:

Lower-density devices with appropriate buoyant for floating over the contents of the stomach and remained buoyant within without altering the gastric emptying rate for an extended length of time are known as floatable systems or hydrodynamically regulated systems [1]. The medicine is gradually withdrawn from the device at the proper pace while the body is floating on the content of the stomach. The stomach's residual system is emptied once the medication has been released. As a result, the GRT is elevated and the oscillations in plasma drug concentration are better controlled [2,3]. Various methods, such as bio-adhesive systems [4], bulging and swollen devices[5,6], floatable devices[7], and systems for prolonged gastric emptying [8], have been suggested to keep the dose form in the stomach.

Microsponges are proprietary, permeable, polymeric microspheres which are strongly cross-linked and have the flexibility to encapsulate a range of active substances. They are typically employed for sustained topical deliveryhowever recently oral administration has also been used [9]. Microsponges are made to distribute pharmaceutically active ingredients effectively at low doses, as well as to improve stability, beauty, and preparations flexibility, as well as to lessen adverse effects and alter drug release profiles [10].

A histamine H2 receptor antagonist is famotidine. It is used to treat Zollinger-Ellison syndrome, gastro-oesophageal reflux disease, duodenal ulcers, stomach ulcers, stress ulcers, and gastritis [11]. Famotidine has a poor bio-availability and a shorter biological half-life after oral treatment, which encourages the creation of controlled release formulations [12].

The goal of the current study is to create floating microsponges of famotidine that have undergone several assessment evaluations after being made utilizing the Quasi emulsion solvent diffusion technique and Eudragit S100.

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II. MATERIAL AND METHODS:

Materials:

We received a sample of famotidine as a gift from Hygia Laboratories, Uttar Pradesh India. Polyvinyl alcohol, dichloromethane, sodium chloride, and Eudragit S 100 were obtained from Hygia Institute of Pharmaceutical Education and Research, Lucknow.

Method:

By utilizing the Quasi emulsion solvent diffusion technique, microsponges were created. By diffusing Eudragit S100 in DCM in this approach, the inner organic phase was created, and the medication was added by dissolving in the solution while being sonicated. Water was used to dissolve polyvinyl alcohol in order to create the outer phase. The internal phase was then mixed with the external phase for three hrs. Filtered microsponges have been isolated, and they were seared in an air-heated oven for four hours at 400C [13,14].

III. CHARACTERIZATION:

Angle of Repose:

The graphic sheets were put on a horizontal surface, and the powders were let to fall over it via a duct that was held at a comfortable height to determine the angle of repose (about 2 cm). Following the measurement of the heap's height, a graph sheet was used to design the heap's base's circumference. The resulting circle's radius had been calculated [15]. It is calculated by following equation:

θ=tan-1 (h/r)

BULK DENSITY:

It is the proportion of the powder's complete volume to its bulk volume. The weighted powdershave been poured into a measuring cylinder, and the starting volume was recorded. Bulk volume refers to this initial volume. Three taps of the powder were necessary to reach a volume of bulk density that was steady. This information is used to compute bulk density using the below equation. It is calculated in g/ml and is supplied by

Pi = m/vi

TAPPED DENSITY:

Weighed API was kept into a graduated cylinder once the bulk density of the liquid being poured had been determined. Drug's volume usage was recorded [16]. The cylinder was then put through a tap density tests with 500, 750, and 1250 taps. The mixture, according to USP, underwent 500 taps. Calculated volume variation was sent through an additional 750 taps. Calculating % Variation

Pt = m/vt

COMPRESSIBILITY INDEX:

Weighted API has been moved to a graded 100ml cylinders and tested for tap density under 500, 750, and 1250 taps. Less than 2% should separate two taps from one another. Compressibility index percentage determined utilizing equation:

I = Vo-Vt/Vo x 100

HAUSNER'S RATIO:

It is a study of the drug's resistance to friction. The recommended scale is 1.2 to 1.5. The ratio of the tapped density to the bulk density is what determines it.

Hausner's ratio = ρt/ρd

PARTICLE SIZE ANALYSIS:

An optical microscope was used to analyze the particle size of the Microsponges formulation. The calibration factor was established after adjusting the stage and eye piece micro-metres. The size of the microsponges was then measured and notedafter they were placed on a slide [17].

Calibration Factor = Eye piece micro-meter division / stage micro-meter division X 10

ENCAPSULATION EFFICIENCY:

In 10ml of 0.1N HCl, 10milligrammes of the Microsponges preparation were weighted, quantified, and disintegrated. The mixture was then ultrasonically processed for 20 minutes at 250°C before being filtered and submitted to 266nm analysis [18].

% Encapsulation efficiency = (A/T) x 100

A = API in the weighted volume of microsponges, T = The quantity of medication that should be in microsponges.

IN VITRO DISSOLUTION STUDY:

The jar was filled with 900ml of 0.1N HCl Buffer, and the USP apparatus II (Paddle) was put together. The medium was given time to reach equilibrium at 37°C plus 0.5°C. The tank contained microsponges that were run at 50 rpm for 12 hours. Five milliliters of the receptor fluid were removed, filtered, and reintroduced at predetermined intervals. A UV spectrophotometer was used to do the necessary dilutions with receptor fluid and

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examine the results spectrophotometrically at 266 nm [19].

SCANNING ELECTRON MICROSCOPY:

SEM analysis was used to examine the surface properties of the pure medication and microsponges formulation. The sample has been mounted on a brass tub, then to create them conductive, they were thinly gold-coated. SEM pictures were then captured at a 15 Kev accelerating voltage [20].

IV. RESULT AND DISCUSSION:

DETERMINATION OF λ MAX:

Using a twin beam UV-Visible spectrophotometer, the lambda max of the pure medication was ascertained. It was discovered to be 266 nm.

FT-IR ANALYSIS:

We obtained the FTIR spectra of the medication and the improved formulae composition. There was no drug - polymer interaction, as evidenced by the distinctive peaks of the optimized preparation following a trajectory that was nearly identical with that of the medication and excipients separately.

MICROMERITIC PROPERTIES:[21]

The flow characteristics of the powder mixes of microsponges were assessed, and the findings were presented (table.5.2). The angle of repose ranged from 24 to 28, indicating adequate particle mobility with all preparations. Bulk density values have been discovered for being in the ranges of 0.38 to 0.53 gm/cm3. The density of the tapped material ranged from 0.37 to 0.56 gm/cm3. The results show that the microsponges' micrometric characteristics are within acceptable ranges and that they have adequate flow characteristics.

PARTICLE SIZE:

The microsponges' particle sizes vary from 93.1 to 132.7 m. When both Eudragit and PVA were present in large amounts, Formulation F8 showed a maximum particle size of 132.7 m. The microsponges F1, F5, and F9, with mean sizes of 93.1, 98.3, and 119.5, showed the effects of changing PVA at the same amount of Eudragit. As a result, the size grows as PVA levels rise.

SCANNING ELECTRON MICROSCOPY:

The porous surface of the microsponges is visible under scanning electron microscopy, which makes them excellent carriers and offers additional thesurface-active agents mixture coating's surface area. The SEM pictures of the microsponges may demonstrate the carrying microparticles' coating with the detergent solution.

ENTRAPMENT EFFICIENCY:

The higher entrapment efficiency was demonstrated by Preparation F8 (99.8%). The entrapment efficiency was unaffected by changing PVA at a fixed Eudragit amount. They demonstrated near capture rates of 81.6%, 78.4%, and 96.3%.

IN VITRO BUOYANCY:

In comparison to those created with less Eudragit, the microsponges formed with a greater amount were more buoyant. Less dense than those created with low levels of PVA were the microsponges made with high levels of PVA. As the density of the microsponges decreased, the buoyancy of the microparticles rose. Every formulation falls between 69% and 81%.

IN VITRO DRUG RELEASE:

The preparations created with low levels of Eudragit showed high% CDR for a given PVA level. F1: 93.6%, F5: 95.6%, and F7: 97.5%. Increasing the dose of Eudragit while keeping PVA constant results in bigger microsponges and a longer path for the medication to travel. The rate of medication release was decreased when Eudragit concentration rose. With 97.5%, Preparation F8 demonstrated the greatest release.

Table 1: Formulation Table for Famotidine Floating Microsponges:

Formulation code	Famotidine (mg)	Eudragit – S 100 (mg)	Dichloromethane (ml)	PVA (%)	NaCl (%)	Purified water (ml)
F1	110	450	10	1	1.2	Q.S.
F2	110	900	10	1	1.2	Q.S.
F3	110	1350	10	1	1.2	Q.S.
F4	110	1800	10	1	1.2	Q.S.
F5	110	450	10	1.5	1.2	Q.S.

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F6	110	900	10	1.5	1.2	Q.S.
F7	110	1350	10	1.5	1.2	Q.S.
F8	110	1800	10	1.5	1.2	Q.S.

Table 2: Pre-formulation experiments for floatable microsponges of famotidine

Formulation code	Bulk density (g/ml)	Tapped density (g/ml)	Angle of Repose (^{0})	Compressibility Index (%)	Hausner's Ratio
F1	0.38	0.43	24.31	19.36	1.21
F2	0.41	0.47	25.74	21.41	1.13
F3	0.39	0.41	23.19	24.10	1.31
F4	0.45	0.48	26.75	17.32	1.06
F5	0.46	0.49	27.42	18.19	1.42
F6	0.44	0.37	25.81	15.35	1.30
F7	0.48	0.51	26.31	18.67	1.51
F8	0.53	0.56	28.67	20.91	1.73

Table 3: Characterization of Famotidine floatable microsponges

Formulation code	Particle size (µm)	Entrapment efficiency (%)	Buoyancy (%)
F1	93.1	81.6	69.3
F2	97.2	89.4	71.4
F3	112.5	87.3	76.8
F4	98.3	78.4	73.6
F5	121.2	99.1	78.1
F6	124.8	96.3	71.3
F7	119.5	94.8	77.6
F8	132.7	99.8	81.2

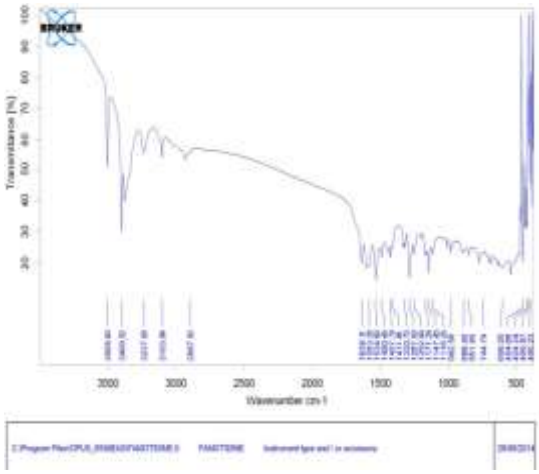

Fig 1: Pure Famotidine FT-IR

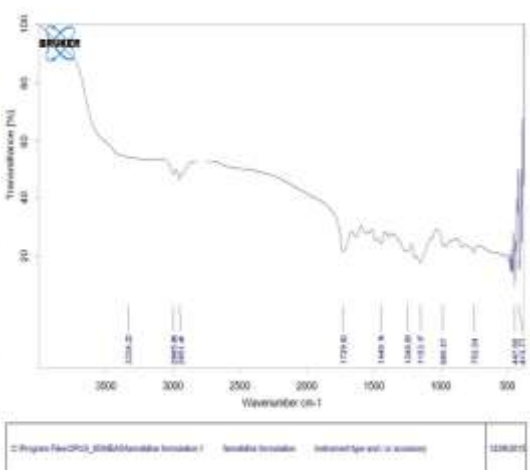

Fig 2: FTIR of Optimised Formulation

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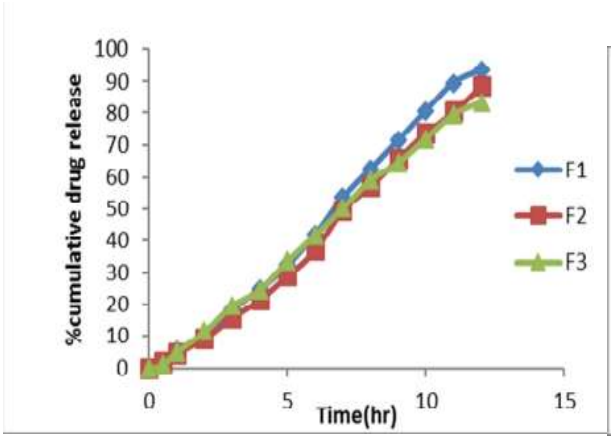

Figure 3: Famotidine in-vitro dissolution profiles using floatable microsponges (F1-F3)

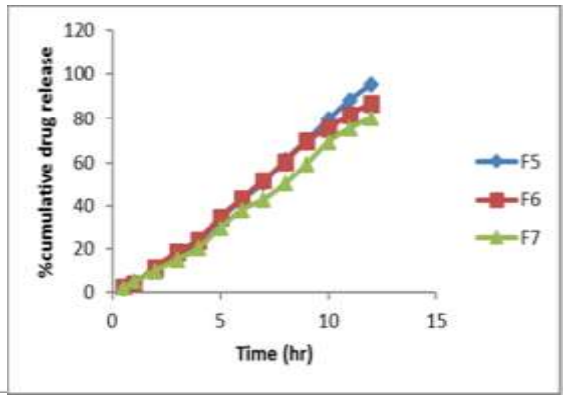

Figure 4: Famotidine in-vitro dissolution profiles using floatable microsponges (F5-F7)

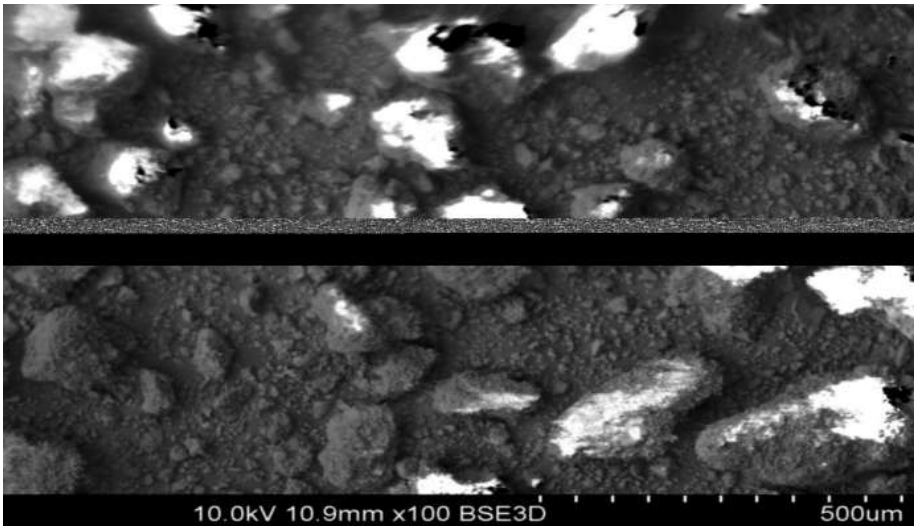

Fig 5: SEM analysis of optimized formulation (100X)

V. CONCLUSION:

It has been suggested that delivery system using polymer systems would predominate in the sort of CDDS both now and in the future. These administration methods offer potential benefits for both scientific and financial reasons, including increased treatment efficacy, consistent rate of release, degree of absorption, and patient acceptability. It was investigated if microsponges might be used as floatablegastro-retentive medication release systems. The research offers a novel method for treating ulcers based on the capacity of microsponges to float.

Conflict of Interest:

The authors have no conflict of interest.

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