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Formulation and Evaluation of Mucoadhesive Microsphere of Esomeprazole and Domperidone

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Abstract:
Purpose: To prepare and evaluate mucoadhesive microsphere of esomeprazole and domperidone for the treatment of gastroesophageal reflux disease
Methods: The microspherewere prepared by solvent evaporation technique by using sodium carboxy methyl cellulose and sodium alginate as polymer. Esomeprazole and Domperidone was entrapped in the microsphere at various polymer. The microsphere were evaluated for their micromeretic properties and in- vitro release.
Results: The microspheres were discrete, spherical and showed good drug entrapment efficiency. Results indicate that the drug was compatible with the polymer used. Amongst all the formulations, F6 showed the most suitable sustain release properties with 97.75 % of drug released at the end of 24 hrs.
Conclusion: Microsphere prepared using sodium carboxy methyl cellulose and sodium alginate can be used as a sustained release delivery system for esomeprazole and domperidone.

Keywords: Microsphere, Solvent Evaporation, Esomeprazole, Domperidone, Sustain Release.

INTRODUCTION

MUCOADHESIVE MICROSPHERES

Recent advances in polymer science and drug carrier technologies have promulgated the development of novel drug carriers such as mucoadhesive microspheres that have boosted the use of bioadhesion in the drug delivery[4, 6].

Mucoadhesive microspheres include microparticles and microcapsules of 1 to 1000 µm in diameter consisting either entirely of mucoadhesive polymer or having an outer coating with adhesive property. Microspheres have the potential to be used for controlled as well as spatial drug delivery. Incorporating mucoadhesive ness to microspheres leads to efficient absorption and enhanced bioavailability of drug. Specific targeting of drug to the absorption site is achieved by using homing devices (ligand) like plant lectin, bacterial adhesion etc. on the surface of the microspheres. Mucoadhesive microspheres involve the use of polymer like sodium carboxy methyl cellulose and sodium alginate to adhere to mucosal linings of GIT and then processed to form microsphere through the technique solvent evaporation technique, thus offering the possibilities of localized as well as systemic absorption of drug in controlled manner [1, 7].

Advantages of mucoadhesive microspheres[2]

- Vaccine delivery for treatment of diseases like hepatitis, influenza, pertussis, ricin toxoid, diphtheria,

birth control. Microsphere in vaccine delivery have a specific advantage like improved antigenicity by adjuvant action, modulation of antigen release, stabilization of antigen[5].

- Mucoadhesive microspheres as a novel carrier system to improve drug delivery by various routes of administration like buccal, oral, nasal, ocular, vaginal and rectal, either for systemic or for local effects.
- Mucoadhesive microspheres are used as targeted drug delivery system for various diseases. Mucoadhesive microspheres are involved in various clinical as well as pharmaceutical aspects
- Efficient absorption and enhanced bioavailability of drug due to a high surface to volume ratio of microspheres.

Mucoadhesive drug delivery system also prolongs residence time of dosage forms at site of absorption to permit once or twice a day dosing[3].

Experimental Work

1. Organoleptic properties[10]

The color, odor and taste of the drug were recorded using descriptive terminology.

2. Solubility study

It is important to know about solubility characteristic of a drug in aqueous system, since they must possess some limited aqueous solubility to elicit a therapeutic response. The solubility of drug was recorded by using various descriptive terminologies.

3. Melting point determination

Melting point of the esomeprazole and domperidone was determined by using thieles tube method. 300ml of heavy paraffin was filled in thieles tube, the drug filled (small amount) in a capillary tube whose one end is sealed with the help of flame, was tied with a thermometer and was suspended in thieles tube filled with paraffin[10]. The heating was started and the point at which drug start melting was noted.

4. Partition coefficient determination

The partition coefficient is defined as the ratio of unionized drug distributed between the organic phase and aqueous phase at equilibrium. For a drug delivery system, lipophilic/hydrophilic balance has shown to be a contributing factor for the rate and extent of drug absorption. Partition coefficient provides a means of characterizing lipophilic/hydrophilic nature of drug. The measurement of drug lipophilicity and indication of its ability to cross the lipoidal cell membrane is the oil/water partition coefficient in systems such as octanol/water, octanol/0.1 N HCl etc[10, 11].

Procedure

The partition coefficient of drug was determined in solvent system Octanol/0.1 N HCl. Accurately weighed quantity of drug (10 mg) taken in one stoppered glass vial containing 5 ml of octanol, 5ml of 0.1 N HCl was added to the vial. Then the glass vial was kept to equilibrate by shaking in vortex mechanical shaker for 24 hours and after shaking, the vial containing materials were transferred into a separating funnel, kept overnight at room temperature for equilibrium. After appropriate dilutions, the aqueous phase was analyzed for drug against blank solution using shimadzu-1700 UV spectrophotometer at 242 λmax. The drug concentration in octanol phase was determined by subtracting the amount in aqueous phase from the total quantity of drug added to the vials. The partition coefficient value P was calculated by the following equation.

Po/w =(C organic/ C aqueous)

Pw/o =(C aqueous / C organic)

Where, Po/w is the partition coefficient of the oil in water
Pw/o is the partition coefficient of the water in oil
C organic is the concentration of drug in the organic phase
C aqueous is the concentration of drug in the aqueous phase

5. Development of standard curve esomeprazole and domperidone

Preparation of phosphate buffer pH 6.8: Dissolve 28.20 gm of disodium hydrogen phosphate and 11.45 gm of potassium dihydrogen phosphate in sufficient water to produce 1000 ml.

1) Preparation of standard solution for esomeprazole: Standard stock solution of Esomeprazole was prepared in Phosphate buffer pH6.8. 100 mg of Esomeprazole was accurately weighed into 100ml volumetric flask and dissolved in small quantity of buffer.

The volume was made up with water to get a concentration of 1000µg/ml. From this 10 ml solution was withdrawn and diluted to 100ml of phosphate buffer pH6.8 to get a concentration of 100µg/ml[12].

1. **Preparation of working standard solutions:** From standard solution take 0.3ml, 0.6ml, 0.9ml, 1.2ml, 1.5ml and 1.8ml were pipetted into 10ml volumetric flasks. The volume was made up with phosphate buffer pH6.8 to get the final concentrations of 3,6,9,12,15 and 18µg/ml respectively. The absorbance of each concentration was measured at 285nm.The data are compiled in Table and plotted a graph.λ Max :285nm.Beer's range: 3-18 µg /ml.
2. **Preparation of standard solution for domperidone**: 10 mg of domperidone was dissolved in 100 ml of Phosphate buffer pH 6.8 to give a concentration of 1 µg/ml.
3. **Preparation of stock solution:** From standard solution take 0.5, 1, 1.5, 2, 2.5 ml of solution in 10 ml of volumetric flask. The volume was made up to mark with Phosphate Buffer pH 6.8 to produce concentration as 5, 10, 15, 20, 25 µg/ml of domperidone respectively. The absorbance of prepared sample of domperidone was measured at 284 nm in Shimadzu UV spectrophotometer against Phosphate Buffer pH 6.8 as blank. By using same procedure Calibration curve of domperidone in Phosphate Buffer pH 6.8 was plotted[8]. The absorbance: λ max 284 nm Beers and Lamberts range: 5-25 µg/ ml.

6. PREPARATION OF MUCOADHESIVE MICROSPHERES BY EMULSION SOLVENT EVAPORATION TECHNIQUE

Drug loaded microsphere were prepared by water in oil (w/o) emulsification solvent evaporation method. For this, 100 mg of drug dissolved in 5 ml dimethyl sulfoxide, and then it was dispersed into 45 ml of 2% aqueous polymer solution[13]. A vortex homogenizer was used for rapid mixing of the drug solution into the aqueous polymer solution for 3 minutes. Then drug and polymer solution were added drop wise to 400 ml of the liquid paraffin containing 0.5 % span 20 as an emulsifying agent with constant stirring at 500 rpm. The constant stirring was carried out using magnetic stirrer. The beaker and its content were heated at 800C with constantstirring for 4.5 hrs until the aqueous phase was completely removed by evaporation[9, 14]. The liquid paraffin was decanted and collected microsphere were washed 5 times with 100 ml of n-hexane,filtered through Whatman's filter paper, dried in hot air oven at 500C for 2 hrs and stored in a desiccator at room temperature.

Table- 1:Composition of drug loaded microspheres of formulation F1, F2, F3, F4, F5 and F6

Formulation	Span 20 (%w/v)	Drug Esomeprazole (mg)	Drug domperidone (mg)	Sodium CMC (mg)	Sodium alginate (mg)
F1	1	100	50	200	-
F2	1	100	50	400	-
F3	1	100	50	800	-
F4	1	100	50	-	200
F5	1	100	50	-	400
F6	1	100	50	-	800

7. EVALUATION OF MICROSPHERES[15]

Appropriate assessment of a dispersed system requires characterization of both chemical and physical stabilities. Physical properties are very important with respect to the performance of dispersed systems.

7.1. Micromeritic Studies[16]

The prepared microspheres are characterized by their micromeritic properties such as microsphere size, tapped density, Carr's compressibility index, Hausner's ratio and angle of repose.

7.1.1. Bulk Density

The bulk density is defined as the mass of powder divided by bulk volume. The bulk density was calculated by dividing the weight of the samples in grams by the final volume in cm[9].

$$\text{Bulk density} = \frac{\text{Mass Of Microsphere}}{\text{Volume Of Microsphere Before Tapping}}$$

7.1.2. Tapped Density

Tapped density is the volume of powder determined by tapping by using a measuring cylinder containing weighed amount of sample. The cylinder containing Known amount of microspheres was tapped for about 1 minute on a tapped density apparatus until it gives constant volume.

$$\text{Tapped density} = \frac{\text{Mass Of Microsphere}}{\text{Tapped Volume Of Microsphere}}$$

7.1.3. Carr's Compressibility Index

This is an important property in maintaining uniform weight. It is calculated using following equation.

$$\% \text{ Compressibility Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Lower the compressibility values indicate better flow.

Table 2: Relationship between % Compressibility and Flowability

% Compressibility	Flowability
5-15	Excellent
12 – 16	Good
18 – 21	Fair to passable
23 – 35	Poor
33 – 38	Very poor
> 40	Extremely poor

7.1.4. Hausner's ratio

A similar index like percentage compressibility index has been defined by Hausner. Values less than 1.25 indicate good flow, whereas greater than 1.25 indicates poor flow. Added glidant normally improves flow of the material under study. Hausner's ratio can be calculated by formula,

Hausner's ratio = $= \frac{\text{Tapped density}}{\text{Bulk density}}$

7.1.5. Angle of Repose (θ)

Good flow properties are critical for the development of any pharmaceutical tablet, capsules or powder formulation. It is essential that an accurate assessment of flow properties be made as early in the development process as possible so that an optimum formulation can be quickly identified. Interparticle forces between particles as well as flow characteristics of powders areevaluated by angle of repose. Angle of repose is defined as the maximum angle possible between the surface and the horizontal plane[17].

Procedure: The angle of repose of each powder blend was determined by glass funnel method. Powders were weighed accurately and passed freely through the funnel so as to form a heap. The height of funnel was so adjusted that the tip of the funnel just touched the apex of the heap. The diameter of the powder cone so formed was measured and the angle of repose was calculated using the following equation,

$\tan \theta = h/r$

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

Where, θ = angle of repose

h = height of the pile

r = radius of the powder cone respectively

Angle of repose affects particle size distribution, as larger the particle size, it will flow freely and vice-versa. It is a helpful parameter to monitor quality of powdered or granular pharmaceutical formulations. For good flowing materials, the angle of repose should be less than 30°.

Table 3: Relationship between Angle of Repose and Flowability

Angle of Repose	Flowability
< 25	Excellent
25-30	Good
30-40	Passable
> 40	Very poor

7.2. Particle Size Determination[9]

Particle size distribution for the microspheres were measured by sieving method analysis, using set of standard sieves was weighed. Particles having size range between 50 and 1500 μm areestimated by sieving method. This method directly gives weight distribution. The sieving method is a useful application in dosage form development of tablets and spheres.

7.3. Percentage Yield

The total amount of dried microcapsules was weighed and the percentage yield was calculated by taking into consideration the total weight of the drug and polymer used for preparation of microspheres.

Percentage Yield = $\frac{\text{Practical yield}}{\text{Theoretical yield}}$X 100

7.4. Percentage moisture content

The drug loaded microspheres was evaluated to determine the percentage moisture content which sharing an idea about its hydrophilic nature. The microspheres weighed (w1) initially kept in desiccator containing Calcium chloride at 37º C for 24 hours. The final weight (w2) was noted when no further change in weight of sample was observed.

% Moisture Percentage= $\frac{W1-W2}{W2}$ X 100

7.5. Estimation of Drug Content

100 mg of microspheres was weighed and suspended in phosphate buffer pH 7.4. The suspension was suitably diluted with phosphate buffer pH 7.4 in 100 ml standard flask and filtered to separate the fragments. Drug content was analyzed after suitable dilution by UV spectrophotometer at a wavelength of 223 nm against phosphate buffer pH 7.4 as blank. All the studies were carried out in triplicate[18].

7.6. Drug Loading Capacity and Entrapment Efficiency (EE)[19]

Microspheres equivalent to 50 mg of the drug were taken for evaluation. The amount of drug entrapped was estimated by crushing the microspheres and extracting with aliquots of 0.1N HCl (pH-1.2) repeatedly. The extract was transferred to a 100 mL volumetric flask and the volume was made up using 0.1N HCl (pH-1.2). The solution was filtered and the absorbance was measured after suitable dilution spectrophotometrically at 212 nm against appropriate blank. The amount of drug loaded and entrapped in the microspheres was calculated by the following formulas:

% Entrapment Efficiency = Actual Drug Content / Theoretical Drug Content X 100

% Drug loading = $\frac{\text{Weight of the drug loaded in microsphere}}{\text{Total weight of the microsphere}}$X 100

7.7. In vitro drug release Study

The prepared microspheres were subjected to in vitro drug release sequentially in three different suitable dissolution media[20, 21]. USP type II dissolution apparatus was used. The dissolution medium for the first 2 hr was 900 ml of 0.1 N HCl (pH 1.2) and continued in phosphate buffer pH 6.8 for the next 7 hrs. The temperature of dissolution medium was maintained at 37 ±0.5 °C and the basket was rotated at 50 rpm. An aliquot of 5 ml was withdrawn at predetermined time intervals and replaced with an equal volume of the fresh dissolution medium to maintain sink conditions. The samples were analyzed at 272 nm, for thepercentage drug release using an UV Visible double beam spectrophotometer. The release study was performed in triplicates[22].

RESULT

1. Physicochemical parameters of drug

1.1. Organoleptic properties

Table 4: Organoleptic Character Of Esomeprazole And Domperidone

Characteristics	Esomeprazole	Domperidone
Odour	Odourless	Odourless
Colour	White	White and almost white
Nature	Amorphous	Crystalline

1.2. Solubility study

Table 5: Solubility Of Esomeprazole And Domperidone In Various Solvents

Name of solvent	Solubility	
	Esomeprazole	Domperidone
Distilled water	Practically insoluble	Slightly soluble
0.1N HCl	Slightly soluble	Soluble
0.1N NaOH	Slightly soluble	Soluble
Ethanol	Soluble	Slightly soluble
Methanol	Soluble	Freely soluble

1.3. Melting point determination

Melting point values of esomeprazole sample was found to be in range of 154º C to 169º C and domperidone sample was found to be in range 244°C - 248°C.The reported melting point for esomeprazole and domperidone was 155.2^0 C and 242.5^0 C. Hence, experimental values were same as official values.

1.4.Partition coefficient determination

Table 6: Partition coefficient of esomeprazole and domperidone in different O/W system

Sr. No	O/W System	Partition Coefficient	
		Esomeprazole	Domperidone
1	**Octanol/Water**	192	185
2	**Octanol/0.1 n HCl**	0.26	0.22
3	**Cyclohexane/Water**	0.35	031

1.5. Development of standard curve esomeprazole and domperidone

Table 7: Concentration And Absorbances OfEsomeprazole In 6.8 Ph Phosphate Buffer

Sr No.	Concentration	Absorbance
1	0	0
2	3	0.125
3	6	0.237
4	9	0.355
5	12	0.475
6	15	0.585

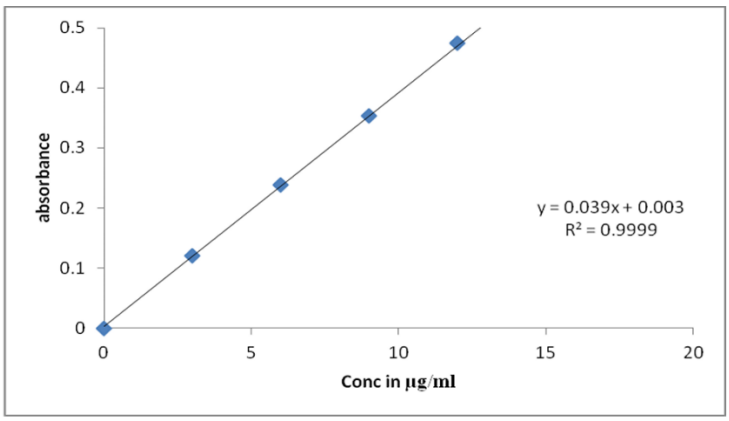

Figure 1: Calibration Curve Of Esomeprazole

Table 8: Concentration And Absorbances Of Domperidone In 6.8 Ph Phosphate Buffer

Sr No.	Concentration	Absorbance
1	0	0
2	5	0.121
3	10	0.210
4	15	0.305
5	20	0.423
6	25	0.510

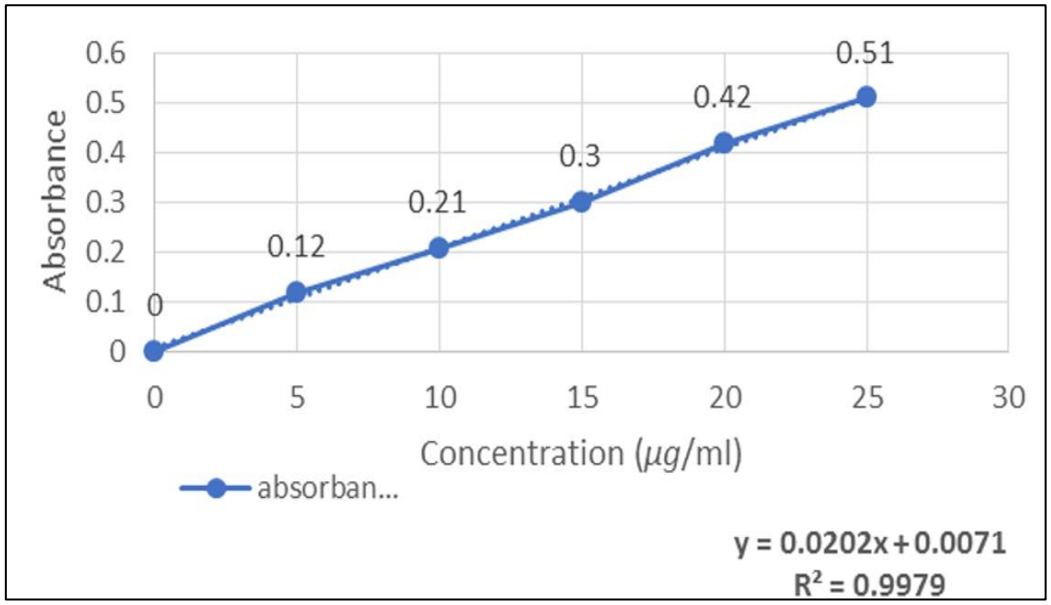

Figure 2: Calibration Curve Of Domperidone

2. Micromeritic Properties

The results of all formulations F1 to F6 of esomeprazole and domperidone microsphere are shown in Table10, which were evaluated for variable parameters such as bulk density, tapped density, % Compressibility index, Hausner's ratio and angle of repose. The % Compressibility index was in the range of 11-18 for all the formulations F1 to F6 indicating good flow property. The values of angle of repose for formulations F2,F3, F5 and F6 was found to be in the range of 25-30 which indicated the good flow potential.

Table 9: Micromeritic properties of esomeprazole and domperidone microspheres

Formulation Code	Bulk Density (g/cm3)	Tapped Density (g/cm3)	Compressibility Index (%)	Hausner's Ratio	Angle of Repose (θ)
F1	0.712± 0.008	0.845 ±0.005	15.73 ±1.17	1.186± 0.018	31.90 ± 0.33
F2	0.508 ±0.011	0.591±0.015	14.04 ±1.03	1.163±0.015	25.85 ± 0.22

F3	0.456 ±0.009	0.522 ±0.013	12.64 ±1.11	1.144 ±0.02	24.70 ± 0.19
F4	0.510 ±0.015	0.608±0.010	16.11 ±1.13	1.192 ±0.011	33.42 ± 0.68
F5	0.606 ±0.013	0.703 ±0.008	13.79 ±1.08	1.160±0.026	27.75 ± 0.15
F6	0.543 ±0.010	0.642 ±0.013	15.42 ±1.10	1.182 ±0.023	8± 0.25

3. Percentage yield

Table 10- Percentage Yield

Formulation	Theoretical yield (g)	Practical yield (g)	Percentage yield (%)
F1	0.340	0.275	80.88
F2	1.540	1.378	89.48
F3	2.0	1.892	94.60
F4	0.325	0.295	90.76
F5	0.620	0.595	95.96
F6	1.892	1.755	92.75

After the preparation of microspheres practical yield and percentage yield were calculated. It was found that percentage yield was in the range of 80.88 % to 95.96 %.

4. Particle Size Determination

Average particle size of microspheres was determined for all the formulations by sieving method analysis by using standard sieves. All the values were represented in table . From the values, the formulation F6 had given the less average particle size compared to all other formulation.

Table 11: Average Particle Size Of Microspheres

Sr. No	Formulations	Average particle size (µm)
1	**F1**	704.16
2	**F2**	624.34
3	**F3**	594.28
4	**F4**	690.45
5	**F5**	618.05
6	**F6**	585.85

5. Percentage moisture content

The percentage moisture content was calculated for all formulation (F1 to F6) by using desiccator containing calcium chloride at 37^0 C at 24 hrs. The final weight was determined and compared to initial weight. The values were represented in table

% Moisture Percentage= $\frac{W1-W2}{W2}$ X 100

Table 12: Percentage Moisture Content Of Microspheres

Sr. No	Formulations	Percentage moisture content (% ± S.D)
1	F1	5.173± 0.135
2	F2	2.629 ± 0.090
3	F3	1.316±0.210
4	F4	3.858 ± 0.175
5	F5	1.538 ± 0.115
6	F6	1.204 ± 0.110

By comparing all the values of all formulations, formulation F3 and F6 was found to be the best one. The formulation F6 showed less moisture content. The order was F6<F3<F5<F2<F4<F1.

6. Drug Loading Capacity and Entrapment Efficiency

The values of %drug loading and %entrapment efficiency are shown in Table14.As the polymer concentration was increased the %drug loading decreased and %entrapment efficiency was increased due to increase in the viscosity of the solution. This can be attributed to the permeation characteristics of each polymer used, that could facilitate the diffusion of part of entrapped drug to the surrounding medium during preparation of microspheres.

Table 13: Drug Loading and Drug Entrapment of Microspheres

Formulation Code	Actual Drug Content (mg)	Theoretical Drug Content (mg)	Total Weight of Microspheres (mg)	% Drug Loading	%Drug Entrapment
F1	18.95	24.65	50	37.12	75.29
F2	13.45	16.32	50	26.90	82.41
F3	11.25	12.85	50	22.5	87.54
F4	17.36	22.25	50	34.72	78.02
F5	14.85	16.50	50	29.70	90
F6	12.42	13.95	50	24.84	89.03

The percentage entrapment efficiency calculated for all microspheres ranged from 75.29 % to 90 %. The highest entrapment efficiency is found for the formulation F5. The percentage drug loading capacity of the microspheres was found to be in the range 22.5% to 37.12%.

7. In-vitro drug release studies

Dissolution studies on all the five formulations of esomeprazole and domperidone microspheres were carried out using a USP dissolution apparatus Type II. 0.1N HCl (pH 1.2) and pH 6.8 was used as the dissolution medium. The in-vitro drug release data of different formulations are shown in Table and Figure The cumulative percent drug release after 12 hours was found to be in the range of 69.85, 100.15, 89.25, 70.65, 82.06 and 85.77 for the formulations F1, F2, F3, F4, F5 and F5 respectively. The cumulative drug release significantly increased with increase in polymer concentration. The increased density of the polymer matrix at higher concentrations results in an increased diffusional path length. This may decrease the overall drug release from the polymer matrix. Furthermore, smaller microspheres are formed at a lower polymer concentration and have a larger surface area exposed to dissolution medium, giving rise to faster drug release.

Table 14: Cumulative percentage drug release of Formulation F1 to F6

Time (hours)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	6.85	9.35	8.95	7.58	9.95	10.24
2	12.55	19.24	14.81	13.28	14.45	17.85
3	18.58	25.65	22.28	22.32	24.50	24.55
4	23.65	32.55	27.92	28.05	31.62	33.28
5	28.15	38.52	31.92	36.32	37.85	38.85
6	35.45	46.98	39.85	42.00	45.14	42.66
7	39.22	53.17	49.35	50.29	49.65	53.25
8	44.75	80.32	59.76	55.25	59.39	58.45
9	51.86	86.35	69.35	61.52	69.55	65.75
10	55.95	94.03	78.90	79.44	70.54	70.45
11	69.85	100.15	89.25	70.65	82.06	85.77
24	74.22	-	93.65	74.88	100.35	97.75

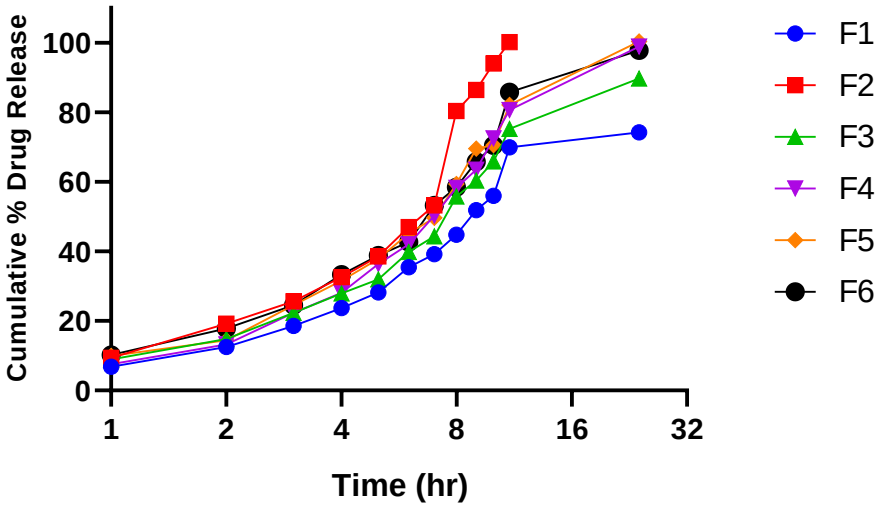

Figure 3-In vitro Drug Release Study of Formulations F1- F6

8. STABILITY STUDY

Stability study was carried out for the F3 formulation by exposing it to a temperature 40 ± 2C/ 75% relative humidity (RH) and percentage cumulative drug release (%CDR) for 2 months.The sample was analyzed for drug content at the regular intervals. It was found that no remarkable change in the drug content of F3 formulation. This indicates that F3 was stable for following temperature.

Table 15: Stability Study Data ForF5 Formulation

Sr. No	Days	% Drug content (w/w) 40± 2° C/ 75% RH	% CDR
1	**15**	86.65 ± 0.01	81.05± 0.02
2	**30**	82.95 ± 0.032	80.55± 0.01
3	**45**	88.28 ± 0.026	82.33± 0.015
4	**60**	87.852 ± 0.02	81.75± 0.025

SUMMARY

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body and also achieve and maintain the desired plasma concentration of the drug for a particular period of time. However, incomplete release of the dug, shorter residence times of dosage forms in the upper GIT leads to lower oral bioavailability. Such limitations of the conventional dosage forms have paved way to an era of controlled and novel drug delivery systems.

Esomeprazole and domperidone drug has been chosen as a model drug in the formulation of controlled drug delivery drug delivery systems for the present work. It is a drug of choice in treatment of antisecretory and antiemetic. However, it has been reported that absolute bioavailability of esomeprazole and domperidone when given orally is50-90 % and half life of 1- 1.5 hrs and for domperidone 7-12 hrs. A microparticulate drug delivery system was planned for Esomeprazole and domperidone as such a system when administered would remain adheres on the gastric mucosa for a prolonged period of time and drug would be available in the dissolved form. This would lead to improvement in the bioavailability of the drug. In this way, it stands an advantage over conventional dosage form.

CONCLUSION

The present study reports a novel attempt to formulate microspheres of the esomeprazole and domperidone by using natural gums like sodium carboxy methyl celluloseand sodium alginate as carrier. Microspheres of esomeprazole and domperidone were prepared by solvent evaporation method. Various evaluation parameters were assessed, with a view to obtain controlled release of esomeprazole and domperidone.

Details regarding preparation and evaluation of formulations have been discussed in previous chapters. From the study following conclusions could be drawn,

The evaluation parameters like morphological analysis, drug content, entrapment efficiency, drug loading capacity, invitro drug release and stability studies was done for the microspheres and found to be satisfactory. Good percentage of drug entrapment and practical yields were obtained with all the polymers. As the polymer concentration was increased the % drug loading decreased and % entrapment efficiency was increased due to increase in the viscosity of the solution.

Cumulative percentage drug release significantly decreased with increase in polymer concentration. Selected F1 and F6 formulated microspheres were stable and compatible at the selected temperature and humidity in storage for 60 days. From the stability studies it was found that there was no significant change. The stability study results shows that the formulation F3 was stable at temperature 40 ± 2˚C/75% RH and % CDR at the end of 2 months.

Among the mucoadhesive microspheres of esomeprazole and domperidone prepared using sodium carboxy methyl cellulose and sodium alginate polymers, the formulation F1, F2, F3 (containing sodium

carboxy methyl cellulose) and F4, F5, F6 (sodium alginate) showed reproducible results and the best mucoadhesive profile with good surface morphology. Among all the formulations of microspheres, formulation F2, F3 and F6 containing showed best sustained release effect.

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