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FORMULATION AND EVALUATION OF FLOATINGMICROSPHERES OF ESOMEPRAZOLE

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ABSTRACT

Floating drug delivery system is one of the novel drug delivery system. Floating drug delivery system have a bulk density less than gastric fluids and thus it remains buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time. Esomeprazole is proton pump inhibitor drug with short elimination half-life 1.5to3 hrs. Floating microspheres of Esomeprazole were prepared by Emulsion solvent evaporation method by using HPMC K4M, HPMC K15M, HPMC K100M, Ethyl cellulose as polymers. The floating microspheres were evaluated for micrometrics properties, particle size, percentage yield, *In-vitro* buoyancy, incorporation efficiency, drug polymer compatibility (IR study), scanning electron microscopy and in-vitro drug release. Results show that as the concentration of polymer increases it affects the particle size, percentage yield, in-vitro buoyancy and in-vitro drug release of microspheres. It was also found that cumulative drug release with different HPMC grade was found to be HPMC K4M ≥ HPMC K15M ≥ HPMC K100M. The micromeritic property was found to be good and scanning electron microscopy confirmed their hollow structure with smooth surface. Formulation F9 prepared with HPMC K100M: Ethyl cellulose exhibited excellent micromeritic properties, percentage yield, *In-vitro* buoyancy, incorporation efficiency and percentage drug release 94 % for a period of 12 hrs. The data obtained in this study thus suggest that floating microspheres of Esomeprazole are promising for sustained drug delivery, which can reduce dosing frequency.

KEYWORDS: Esomeprazole, Hydroxypropyl methyl cellulose, Ethyl cellulose,Floating microspheres.

INTRODUCTION

The oral route of drug administration is the most important method of administering drugs for systemic effects. The parental route is not routinely used or not possible to self-administration of medication. The topical route of administration has only recently been employed to deliver drugs to the body for systemic effects. It is probable that at least 90 % of all drugs used to produce systemic effects are administered by the oral route. When a new drug is discovered, one of the first questions a pharmaceutical company asks is whether or not the drug can be effectively administered for its intended effect by the oral route. If it cannot, the drug is primarily relegated to administration in a hospital setting or physician's office. Of drugs that are administered orally, solid oral dosage forms represent the preferred class of product. The reasons for this preference are well known.[1]

Oral Controlled Drug Delivery

Drug absorption at the desired rate means, first to reach the effective plasma level within an acceptable short time period; second, to avoid an overshoot in the case of rapidly absorbed drugs and third to maintain effective plasma levels over the desired time period. Although the intensity of pharmacological effect is related to the drug concentration at the site of action, which is in turn, related to the plasma drug concentration, an ideal situation is obtained when the concentration is continuously maintained between minimum effective and maximum safe levels (Therapeutic Index). Invariably, conventional drug dosage forms do not maintain the drug.[2] Controlled release (CR) DDS attempt to sustain drug blood concentration at relatively constant and effective levels in the body by spatial placement or temporal delivery. Thus CRDDS offer various advantages viz. reduce blood level fluctuations, minimize drug accumulation, employ less total drug, improve patient compliance, and minimize local and systemic side effects.[3-7]

OBJECTIVES

The aim of presented work is to develop the floating microspheres of Esomeprazole by emulsion solvent evaporation method Esomeprazole whose physiochemical properties and short half-life make it suitable candidate for floating drug delivery system.

To develop the floating microspheres of Esomeprazole by using different grades HPMC and ethyl cellulose as polymers.

To characterize prepared microspheres by Fourier Transform Infrared (FTIR) Spectroscopy.

Surface morphology of prepared microspheres can be studied by Scanning ElectronMicroscopy (SEM).

To evaluate the prepared floating microspheres for micrometric properties (particle size, bulk density, tapped density, compressibility index, hausnersratio and angle of repose), practical yield, drug incorporation efficiency, in- vitro buoyancy, in -vitro drug release study.

Esomeprazole is a proton pump inhibitor used to treat GERD, reduce the risk of NSAID associated gastric ulcers, eradicate H. pylori, and to treat conditions causing gastric acid hypersecretion.

Materials: Esomeprazole, Ethyl cellulose, HPMC K4M, HPMC K15M, HPMC K100M, Ethanol, Dichloromethane, Hydrochloric acid, Tween 80.

Preparation of floating microspheres of Esomeprazole[8,9]

The floating microspheres of Esomeprazole were prepared by emulsion solvent evaporation and emulsion solvent diffusion method using different polymers as follows:

Emulsion solvent evaporation[8,9]

The drug and polymer in different proportions are weighed (as shown in table 4) the polymer was co dissolved into previously cooled mixture of ethanol: dichloromethane at room temperature. The mixture was stir vigorously to form uniform drug polymer dispersion. The above organic phase was slowly added to 100 ml distilled water containing 0.01% tween 80 by maintain the temperature at 15 – 20°C and emulsified by stirring at 1200 rpm for 15 min. microspheres formed were filtered, washed with water and sieved between 50 and 30 mesh size, and dried overnight for 40°C.

Table 1: Formulation table of floating microspheres of Esomeprazole.

Ingredient(gm)	Formulation code					
	F1	F2	F3	F4	F5	F6
Ethyl cellulose	0.500	1.334	0.500	1.334	0.500	1.334
HPMC K4M	0.500	0.666	-	-	-	-
HPMC K15 M	-	-	0.500	0.666	-	-
HPMC K100M	-	-	-	-	0.500	0.666
Esomeprazole	1.000	1.000	1.000	1.000	1.000	1.000
Dichloromethane	30	30	30	30	30	30
Ethanol	30	30	30	30	30	30

RESULTS

Table 2: Standard calibration data of Esomeprazole in 0.1N HCl (max =330).

Sl.No	Concentration Mgc/ml	Absorbance (nm)
1	0	0
2	3	0.0729
3	6	0.1559
4	9	0.2339
5	12	0.3118
6	15	0.3798
7	18	0.4682

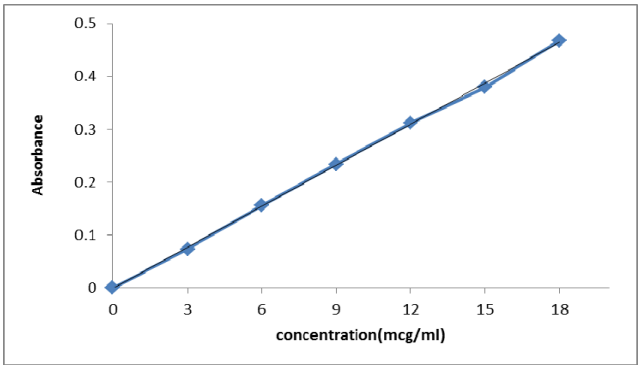

Figure 1: standard calibration curve of Esomeprazole in 0.1N HCl(max=330).

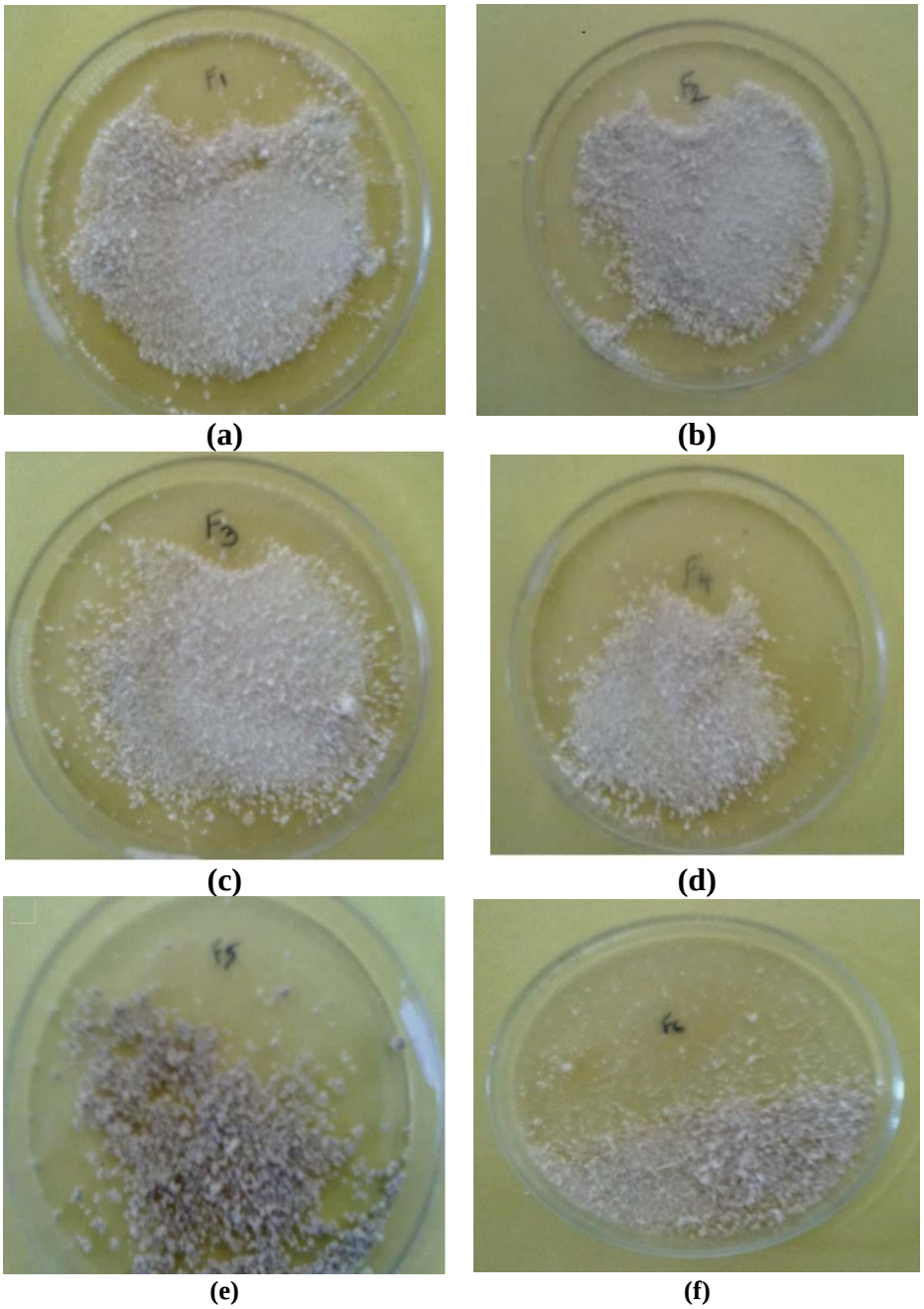

Figure 2: Image showing floating microspheres of Esomeprazole formulation (a)F1, (b)F2, (c)F3, (d)F4, (e)F5, (f)F6.

Figure 3: In-vitro buoyancy of floating microspheres of Esomeprazole formulation(a)F1,(b)F2,(c)F3.

Figure 4: In-vitro buoyancy of floating microspheres of Esomeprazole formulation(a)F4,(b)F5,(c)F6.

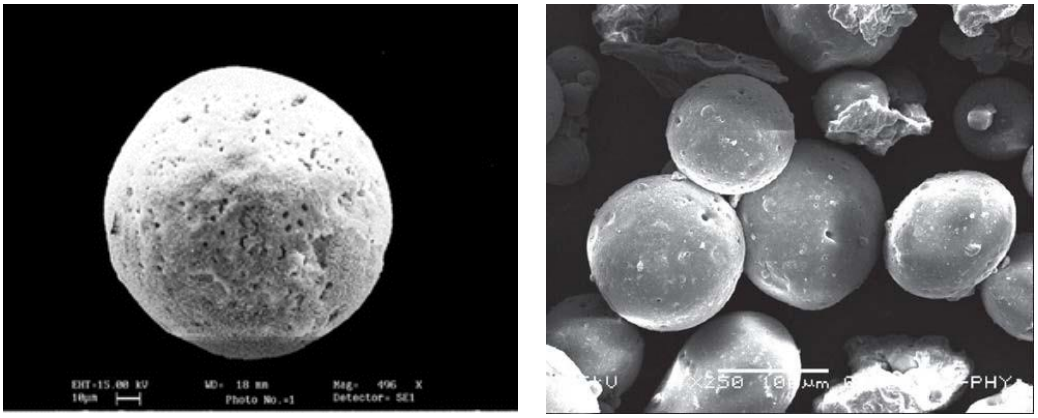

Figure 5: Scanning electron microphotograph of floating microspheres ofEsomeprazole F6.

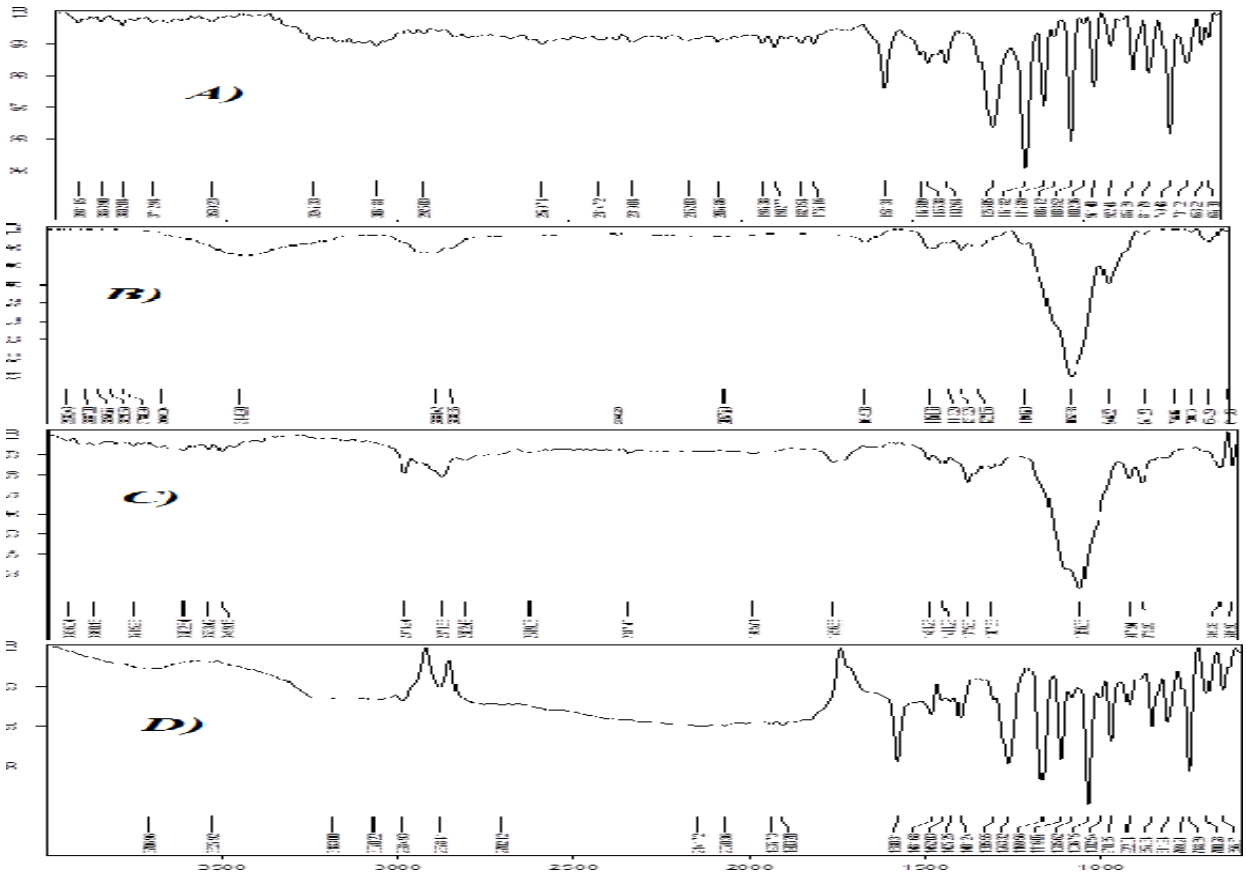

Figure 6: Image showing floating FTIR spectra floating microspheres of Esomeprazole (A) Esomeprazole (B) HPMC K4M, (C) ethyl cellulose, (D) mixture.

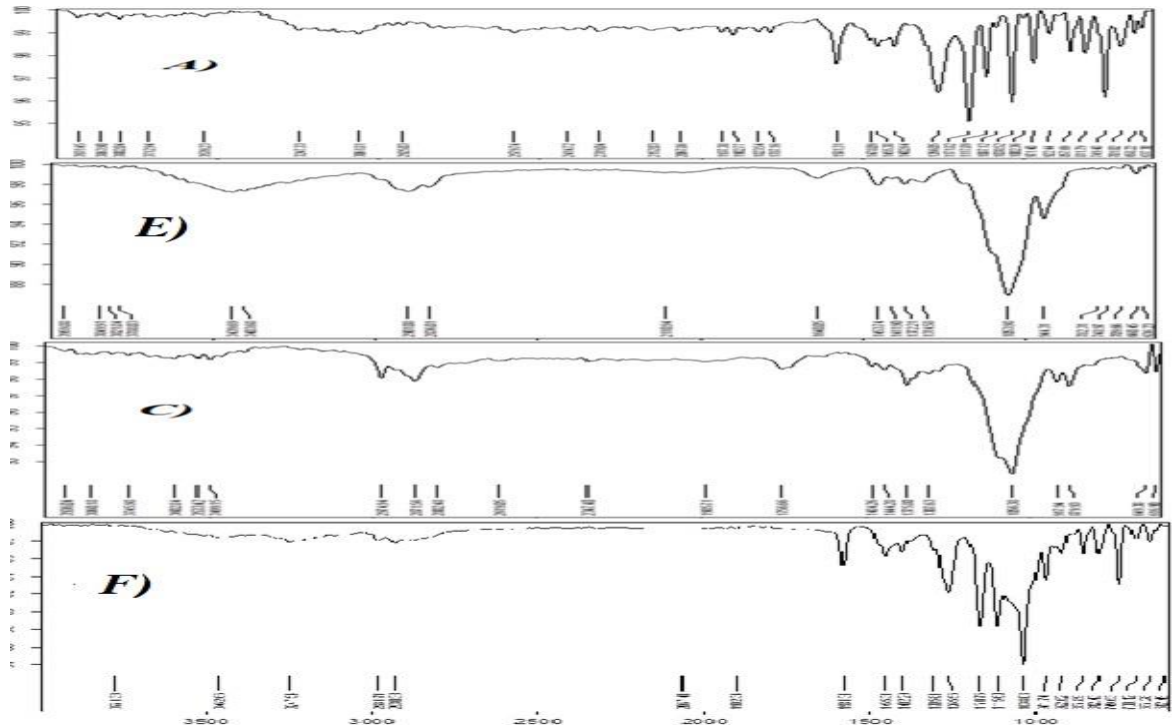

Figure 7: Image showing floating FTIR spectra floating microspheres of Esomeprazole (A) Esomeprazole (E)HPMC K15M, (C) ethyl cellulose,(F) mixture.

Table 3: Micromeritic property of floating microspheres of Esomeprazole.

Formulation code	Mean partical size	Bulk density (gm. /cm^3)	Tappeddensity (gm. /cm^3)	Hauseners ratio	Carrr's index	Angle of repose
F1	387.32±2.54	0.3572±0.010	0.4019±0.018	0.8902±0.04	11.13±0.11	32.49±1.71
F2	452.9±2.52	0.41240±0.012	0.4647±0.015	0.8840±0.05	12.03±0.64	27.72±1.89
F3	479.52±3.25	0.4308±0.007	0.4955±0.014	0.8681±0.03	13.46±0.24	31.88±2.78
F4	389.5±3.88	0.3575±0.014	0.4026±0.014	0.8879±0.01	11.3±0.33	27.00±1.93
F5	456.84±2.27	0.4150±0.015	0.4678±0.015	0.8871±0.02	11.4±0.26	26.02±1.80
F6	480.±2.25	0.4319±0.012	0.4973±0.021	0.8684±0.01	13.2±0.33	26.56±1.43

All values represented as mean ± standard deviation (n=3)

Table 4: Percentage yield, in-vitro buoyancy and incorporation efficiency of floating microspheres of Esomeprazole.

Formulation code	Percentage yield	*In-vitro* buoyancy (In hrs)	Incorporation efficiency (%)
F1	67.840.64	76.66±1.52	77.43±2.72
F2	85.59±0.69	82.39±2.07	87.34±2.84
F3	92.5±0.51	89.96±1.04	91.94±2.17
F4	70.67±0.66	75.43±2.02	67.11±3.01
F5	82.26±0.43	83.96±1.07	88.11±2.59
F6	89.84±0.72	90.39±2.00	92.30±2.88

All values represented as mean ± standard deviation (n=3)

Table 5: In-vitro drug release from formulation F1.

Time (hrs.)	Square Root of time	Log time	Cumulative drug release	Cumulative Percentage drug release	Cumulative Percentage drug remain	Log Cumulative Percentage drug release	Log Cumulative Percentage drug remain
1	1.000	0.000	0.138996	0.926641±0.21	99.07336	-0.03309	1.995957
2	1.414	0.301	1.111969	7.413127±0.49	92.58687	0.870001	1.966549
3	1.732	0.477	3.370811	22.47207±1.30	77.52793	1.351643	1.889458
4	2.000	0.602	4.935907	32.90605±3.64	67.09395	1.517276	1.826683
5	2.236	0.698	6.435097	42.90064±3.92	57.09936	1.632464	1.756631
6	2.449	0.778	7.660541	51.07027±2.80	48.92973	1.708168	1.689573

7	2.645	0.845	8.333398	55.55598±2.09	44.44402	1.744731	1.647813
8	2.828	0.903	8.974517	59.83012±1.69	40.16988	1.77692	1.603901
9	3.000	0.954	9.721969	64.81313±1.96	35.18687	1.811663	1.546381
10	3.162	1.000	10.71409	71.42728±2.1	28.57272	1.853864	1.455952
11	3.316	1.041	11.67297	77.81982±2.05	22.18018	1.89109	1.345965
12	3.464	1.079	12.73799	84.91995±1.10	15.08005	1.92901	1.178403

All values represented as mean ± standard deviation (n=3)

Table 6: In-vitro drug release from formulation F2.

Time (Hrs.)	Square Root of time	Log time	Cumulative drug release	Cumulative Percentage drug release	Cumulative Percentage drug remain	Log Cumulative Percentage drug release	Log Cumulative Percentage drug remain
1	1.000	0.000	0.138996	0.926641±1.18	99.07336	-0.03309	1.995957
2	1.414	0.301	3.301158	22.00772±0.28	77.99228	1.342575	1.892052
3	1.732	0.477	5.21251	34.75006±1.67	65.24994	1.540956	1.81458
4	2.000	0.602	7.370772	49.13848±1.11	50.86152	1.691422	1.706389
5	2.236	0.698	8.422703	56.15135±1.89	43.84865	1.74936	1.641956
6	2.449	0.778	8.923166	59.48777±1.53	40.51223	1.774428	1.607586
7	2.645	0.845	9.635676	64.23784±1.39	35.76216	1.807791	1.553424
8	2.828	0.903	10.45413	69.69421±1.61	30.30579	1.843197	1.481526
9	3.000	0.954	11.2739	75.15933±1.53	24.84067	1.875983	1.395163
10	3.162	1.000	11.88683	79.24556±1.47	20.75444	1.898975	1.317111
11	3.316	1.041	12.91853	86.12355±1.67	13.87645	1.935122	1.142278
12	3.464	1.079	13.67378	91.15856±1.20	8.841441	1.959797	0.946523

All values represented as mean ± standard deviation (n=3)

Table no. 7: In-vitro drug release from formulation F3.

Time (Hrs.)	Square Root of time	Log time	Cumulative drug release	Cumulative Percentage drug release	Cumulative Percentage drug remain	Log Cumulative Percentage drug release	Log Cumulative Percentage drug remain
1	1.000	0.000	0.173745	1.158301±0.38	98.8417	0.063821	1.99494
2	1.414	0.301	1.737452	11.58301±0.4	88.41699	1.063821	1.946536
3	1.732	0.477	3.614093	24.09395±1.54	75.90605	1.381908	1.880276
4	2.000	0.602	5.770656	38.47104±1.82	61.52896	1.585134	1.78908
5	2.236	0.698	7.062317	47.08211±3.5	52.91789	1.672856	1.723603
6	2.449	0.778	8.219459	54.7964±1.81	45.2036	1.738752	1.655173
7	2.645	0.845	8.859189	59.06126±1.95	40.93874	1.771303	1.612134
8	2.828	0.903	10.09236	67.28237±1.67	32.71763	1.827901	1.514782
9	3.000	0.954	11.22324	74.82162±2.1	25.17838	1.874027	1.401028
10	3.162	1.000	12.14768	80.98456±1.35	19.01544	1.908402	1.279106
11	3.316	1.041	12.93571	86.2381±2.35	13.7619	1.935699	1.138679
12	3.464	1.079	13.93448	92.89653±2.20	7.103475	1.967999	0.851471

All values represented as mean ± standard deviation (n=3)

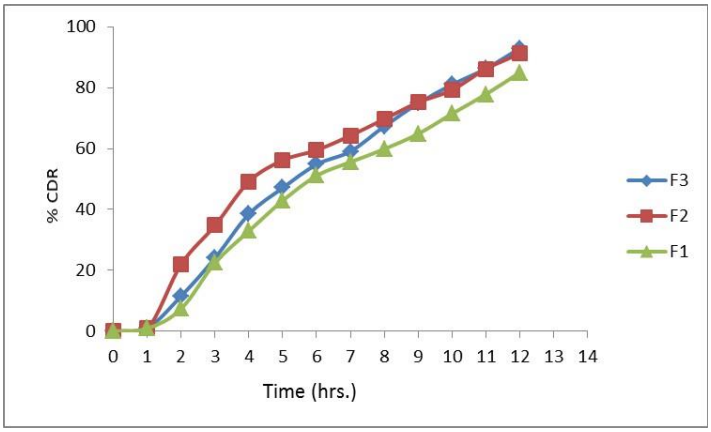

Figure 8: Cumulative percentage drug release of Esomeprazole fromformulation F1 to F3.

Table 8: In-vitro drug release from formulation F4.

Time (Hrs.)	Square Root of time	Log time	Cumulative drug release	Cumulative Percentage drug release	Cumulative Percentage drug remain	Log Cumulative Percentage drug release	Log Cumulative Percentage drug remain
1	1.000	0.000	0.138996	0.926641±1.18	99.07336	-0.03309	1.995957
2	1.414	0.301	1.355212	9.034749±0.28	90.96525	0.955916	1.958876
3	1.732	0.477	3.336062	22.24041±1.67	77.75959	1.347143	1.890754
4	2.000	0.602	4.901429	32.67619±1.11	67.32381	1.514231	1.828169
5	2.236	0.698	6.122857	40.81905±1.89	59.18095	1.610863	1.772182
6	2.449	0.778	7.660965	51.0731±1.53	48.9269	1.708192	1.689548
7	2.645	0.845	8.541931	56.9462±1.39	43.0538	1.755465	1.634011
8	2.828	0.903	9.252201	61.68134±1.61	38.31866	1.790154	1.58341
9	3.000	0.954	9.965135	66.43423±1.53	33.56577	1.822392	1.525897
10	3.162	1.000	10.9578	73.05199±1.47	26.94801	1.863632	1.430527
11	3.316	1.041	12.091	80.60669±1.67	19.39331	1.906371	1.287652
12	3.464	1.079	13.29556	88.63707±1.12	11.36293	1.947615	1.05549

All values represented as mean ± standard deviation (n=3)

Table 9: In-vitro drug release from formulation F5.

Time (Hrs.)	Square Root of time	Log time	Cumulative drug release	Cumulative Percentage drug release	Cumulative Percentage drug remain	Log Cumulative Percentage drug release	Log Cumulative Percentage drug remain
1	1.000	0.000	0.312741	2.084942±0.21	97.91506	0.319094	1.990849
2	1.414	0.301	1.181467	7.876448±0.49	92.12355	0.89633	1.964371
3	1.732	0.477	3.475251	23.16834±1.30	76.83166	1.364895	1.88554
4	2.000	0.602	5.492355	36.6157±3.64	63.3843	1.563667	1.801982
5	2.236	0.698	7.075135	47.16757±3.92	52.83243	1.673643	1.722901
6	2.449	0.778	8.078919	53.85946±2.80	46.14054	1.731262	1.664083
7	2.645	0.845	9.135344	60.90229±2.09	39.09771	1.784634	1.592151
8	2.828	0.903	10.26412	68.42749±1.68	31.57251	1.835231	1.499309
9	3.000	0.954	11.18667	74.57781±1.96	25.42219	1.87261	1.405213
10	3.162	1.000	11.90312	79.35413±2.10	20.64587	1.89957	1.314833
11	3.316	1.041	12.62181	84.145381.10	15.85462	1.92503	1.200156
12	3.464	1.079	13.75926	91.72839	8.271609	1.962504	0.91759

All values represented as mean ± standard deviation (n=3)

Table 10: In-vitro drug release from formulation F6.

Time (Hrs.)	Square Root of time	Log time	Cumulative drug release	Cumulative Percentage drug release	Cumulative Percentage drug remain	Log Cumulative Percentage drug release	Log Cumulative Percentage drug remain
1	1.000	0.000	0.277992	1.853282±0.38	98.14672	0.267941	1.991876
2	1.414	0.301	1.80695	12.04633±0.45	87.95367	1.080855	1.944254
3	1.732	0.477	3.822703	25.48468±1.54	74.51532	1.406279	1.872246
4	2.000	0.602	5.909961	39.39974±1.82	60.60026	1.595493	1.782474
5	2.236	0.698	6.889189	45.92793±3.50	54.07207	1.662077	1.732973
6	2.449	0.778	8.533205	56.88803±1.81	43.11197	1.755021	1.634598
7	2.645	0.845	9.138147	60.92098±1.95	39.07902	1.784767	1.591944
8	2.828	0.903	9.954479	66.36319±1.67	33.63681	1.821927	1.526815
9	3.000	0.954	10.91228	72.74852±2.10	27.25148	1.861824	1.43539
10	3.162	1.000	11.97587	79.83912±1.35	20.16088	1.902216	1.304509
11	3.316	1.041	13.28463	88.56422±2.35	11.43578	1.947258	1.058266
12	3.464	1.079	13.90062	92.67079±2.20	7.329215	1.966943	0.865057

All values represented as mean ± standard deviation (n=3)

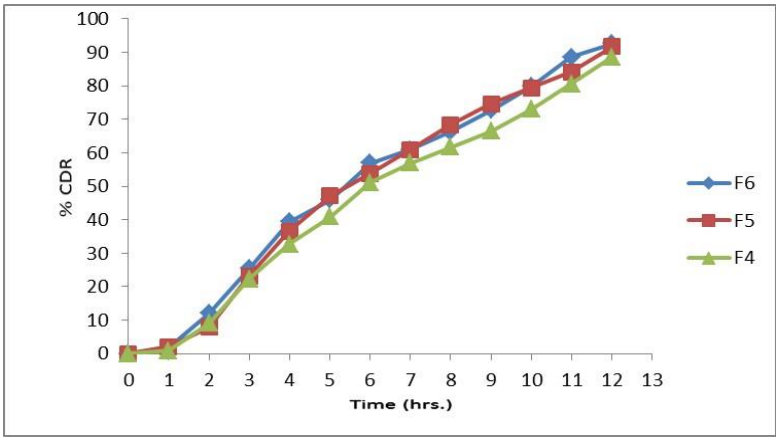

Figure 9: Cumulative percentage drug release of Esomeprazole fromformulation F4 to F6.

Table 11: kinetics data obtained from in-vitro release profile for floatingmicrospheres of Esomeprazole.

Formulation code	Zero-order kinetic data	Frist-order kinetic data	Huguchi matix data	Peppas kinetic data	
	Regression Coefficient(r)	Regression Coefficient(r)	Regression Coefficient(r)	Regression Coefficient(r)	n-value
F1	0.9767	0.9707	0.9927	0.8967	0.3349
F2	0.9360	0.9625	0.9811	0.7731	0.5642
F3	0.9816	0.9436	0.9965	0.8915	0.4540
F4	0.9850	0.9471	0.9944	0.8977	0.3542
F5	0.9760	0.9585	0.9929	0.9362	0.5244
F6	0.99804	0.9369	0.9954	0.9135	0.5728

DISCUSSION

Floating drug delivery system have a bulk density less than gastric fluids and thus it 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 results in an increased gastric residence time and a better control of the fluctuation in plasma drug concentration. Single unit formulations (floating tablet) 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 (floating microspheres) has relative merits compared to a single unit preparation. Floating microspheres provide a constant and prolonged therapeutic effect which will reduce dosing frequency.

The aim of present study was to develop floating microspheres of Esomeprazole by emulsion solvent evaporation method by using HPMC K4M, HPMC K15M, and HPMC K100M& Ethyl cellulose as polymers. Calibration curve for the estimation of Esomeprazole was constructed in 0.1N Hcl at 330 nm and 7.4 pH bufferat 284.6 nm, as shown in table-5,7 and figure-20, 22. The method obeyed Beer's Lambert law in the range of 0 to18mcg/ml. Floating microspheres of Esomeprazole using different grades of HPMC and ethyl cellulose as polymers prepared by emulsion solvent evaporation method as shown in table-4. In this method, the emulsion was stabilized by tween-80 and the volatile solvent get evaporated leaving a solidified thin film at the interface between aqueous phase and organic phase, where Esomeprazole get encapsulated in the core-coat of polymers.

Micromeritic properties

The mean particle size of the microspheres formulation F1 to F6 containing different grades HPMC & ethyl cellulose as in the range of 387.32±2.51 to 489.24±3.51 respectively (as shown in table 8). The effect of polymer concentration on the particle size of microspheres was determined. The mean particle size of the microspheres was found to increase with increasing ethyl cellulose concentration (as shown in table 8). The viscosity of the medium increases at a higher ethyl cellulose concentration resulting in enhanced interfacial tension. Shearing efficiency is also diminished at higher viscosities. This results in the formation of larger particles.

The bulk density, tapped density, hausners ratio of formulation F1 to F9 containing different grades of HPMC & ethyl-cellulose & formulation was in the range of 0.3572±0.02 to 0.5763± 0.03 gm./cm^3 (as shown in table 8).

The carr's index of formulation F1 to F6 containing different grades of HPMC & ethyl-cellulose 11.13±0.11 to13.46±0.24respectively. The angle of repose of formulation F1 to F6 containing different grades of HPMC & ethyl-cellulose & formulation was in

the range 26.02±1.71 to32.49±3.39 respectively (as shown in table 9) The values of carr's index and angle of repose indicate excellent flow properties.

Yield of floating microsphere

The percentage yield of floating microsphere formulation F1 to F6 containing different grades of HPMC & ethyl-cellulose & formulation was in range of 67.84±0.64 to93.78±0.35 (as shown in table 9). To observe the effect of polymer concentration on the percentage yield of the floating microspheres, formulations were prepared at varying concentration of ethyl cellulose (as shown in table 4). The yield ofthe floating microspheres increased with increasing polymer concentration. At low concentration of ethyl-cellulose part of the polymer solution aggregated in a fibrous structure, as it solidified prior to forming droplets or the transient droplets werebroken before solidification was complete due to poor mechanical strength resulting into low yield.

In-vitro buoyancy: The purpose of preparing floating microspheres was to extend the gastricresidence time of a drug. The buoyancy test was carried out to investigate the floatability of the prepared microspheres. The microspheres were spread over the surface of a simulated gastric fluid and the fraction of microspheres buoyant and settled down as a function of time was quantitated. The *In-vitro* buoyancy of formulation F1 to F6 containing different grades of HPMC & ethyl-cellulose &formulation was in range from 76.66±2.05 to 94.95± 1.07 respectively (as shown in table 9). Among all formulation F6 was found to be highest in-vitro buoyancy 94.95±1.07. The results also showed a tendency that the larger the particle size, the longer floating time.

Incorporation efficiency

The incorporation efficiency of formulation F1 to F6 containing differentgrades of HPMC & ethyl-cellulose & formulation was in the range of 77.43±2.72 to 96.38± 2.84 respectively (as shown in table 9) Among all formulation F6 96.38±2.84 Results demonstrated that increase in concentration of ethyl-cellulose increased the entrapment of the drug. The drug entrapment efficiency was found to be good in allthe formulation.

***In-vitro* drug release**

In-vitro drug release studies of Esomeprazole from floating microspheres were performed in pH 1.2 for12 hrs. In dissolution test apparatus. It was found that *In-vitro* drug release of formulation F1 to F containing ethyl-cellulose and various grades of HPMC.

F1, F2, F3, F4, F5, F6 show percentage drug release 84.91±0.95 to93.31±2.11 at end of 12 hours. Amongst the formulation F6 was found to be the best formulation as it releases Esomeprazole 94.06% in a sustained manner with constant fashion over extended period of time (after 12 hr.).

It was observed as the concentration of ethyl-cellulose was increased percent release of Esomeprazole decreases. The increase in ethyl-cellulose concentration leads to the increased density of polymer matrix into the microspheres which result in an increased diffusional path length. This may decrease the overall drug release from polymer matrix. Furthermore, smaller microspheres are formed at lower polymer concentration and have larger surface area exposed to dissolution medium. The r values of Zero order of the above 9 formulations were in the range of 0.8896 to 0.9954. Similarly, the R-value of first Order were in between 0.7581 to 0.0.9877 (as shown in table 19) Among the 9 formulations some formulations F3, F4, F6 release the drug by zero order kinetics and some are F1, F2, F5 release by first order kinetics. The results suggest that, the drug was released by mixed order kinetics. To ascertain, the drug release mechanism the in-vitro release data were also subjected to Higuchi's diffusion equation (Q=k.t1/2) the R-values of all the formulations of Higuchi's equations were 0.9800 and above (as shown in table 19). It suggests that the Higuchi diffusion plots of all the formulations were fairly linear and we can conclude that the drug released by Higuchi's diffusion mechanism. The formulations are also treated to Peppa;s plots by taking log percent versus log time. The plots are found to be fairly linear and the regression values (n value) of all formulations ranges from lowest 0.5004 to highest 0.6572 (as shown in table 19) which in the range of $0.45 < n < 0.89$. This suggests that the drug was released by non-Fickian control (Anomalous diffusion) with swelling. Four types of graphs i.e., cumulative percent drug release, first order, Higuchi diffusion and Peppa's exponential plots of all formulations were shown in figure 37-48.

Infrared spectroscopy (FTIR)

The prepared microspheres were characterized by FTIR spectroscopy to find out any chemical interaction between Esomeprazole and polymers used. The FTIR spectra of Esomeprazole, polymers and selected formulations is shown in the figure- 30,31,32 Our experimental results were assessed on the basis of physical data obtained for drug and polymers as well as formulations. The FTIR spectra of floating microspheres of Esomeprazole using ethyl cellulose and various grades of HPMC is as follows. The drug Esomeprazole has exhibited CH absorptions from 2729 $^{cm-1}$ to 3055 cm.$^{-1}$ indicating the presence of aromatic as well as aliphatic CH vibrations. The strong S=O absorption peak is noticed at 1266.05 cm^{-1}. The FTIR spectra show the pick at 339.33 cm^{-1} the pick in this range N-H stretching indicated that presence of amine group. The spectrum also shows the pick at 1581.31cm^{-1}. The pick in this range is due to C-N Stretching When the polymer ethyl-cellulose a single product was taken for IR measurements when strong hydroxyl primary OH peak was noticed and 3475 cm^{-1} may be due to the OH absorption which is present in the cellulose molecule. The aliphatic CH absorptions were noticed at 2974 cm^{-1} and 2874 cm^{-1}. The C=O peak was isolated has

given its absorption at 1747-1 cm^{-1}. Another polymer HPMC exhibited primary OH absorption at 3471 cm^{-1} due to the presence of anticipated functional group. In this case also the aliphatic OH absorption peaks were noticed 2978 cm^{-1} and 2879 cm^{-1}. This molecule showed C=O absorption peak at 1756 cm^{-1}. The IR spectrum obtained of Esomeprazole, ethyl cellulose and HPMC (formulation - F6, F3) were identical and there was no change in the functional group absorption of any molecule present in formulated product. The FTIR spectra were shown in fig no.30, 32, 32.

Scanning electron microscopy (SEM)

Morphology of microspheres was examined by scanning electron microscopy. The view of the microspheres showed a hollow spherical structure with a smooth surface morphology (Fig29) Some of the microspheres showed a dented surface structure but they showed good floating ability on the surface of the medium, indicating intact surface. The outer surface of the microspheres was smooth anddense, while the internal surface was porous. The shell of the microspheres also showed some porous structure (Fig.29). It may be caused by the evaporation of solvent entrapped within the shell of microspheres after forming a smooth and dense skin layer.

CONCLUSION

The data obtained from the study of "Formulation and evaluation of floating microspheres of Esomeprazole". Reveals following conclusion: Floating microspheres of Esomeprazole can be successfully prepared using HPMC and Ethyl cellulose as polymers by emulsion solvent evaporation. The percent yield of all floating microspheres formulation was more than 60% suggesting that the methods used for encapsulation was effective. The percent yield was significantly increased as the amount of polymer was increased in each preparation method. The entrapment efficiency was good in all the cases. This suggested that optimized parameters were used in the method of preparations. The in-vitro buoyancy was more than 70% after 12 hours indicated satisfactory performance of proposed formulations. The percent buoyancy increased significantly as the amount of polymer was increased in each preparation method. The mean particle size of microspheres was in the range of 102.33-420.53 µm depending upon the type of polymer used. The particle size increased significantly as the amount of polymer increased.

The flow properties of all the prepared microspheres were good as indicated by low angle of repose (<40º) and low compressibility index (I<25). The good flow properties suggested that the microspheres produced were non aggregated. In-vitro release of floating microspheres of Esomeprazole was found to be in following order. F3>F6>F5>F2>F4>F1. Among all formulations, F9 was found to be the best formulation as it releases Esomeprazole 94.60 % in a sustained manner with constant fashion over extended period of time (after 12 hrs.). *In-vitro* release data fitted into various kinetic models suggest that the release obeyed mixed order kinetic, higuchi diffusion mechanism and non fickian control (anomalous diffusion) with swelling.

Hence, finally it was concluded that the prepared floating microspheres of Esomeprazole may prove to be potential candidate for safe and effective sustained drug delivery over an extended period of time which can reduce dosing frequency.

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