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Research Article

EFFECT OF VARIOUS SURFACTANTS ON RELEASE BEHAVIOUR OF FUROSEMIDE FROM FLOATING TABLETS

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ABSTRACT

Generally from the last three decades various attempts has been made to develop a novel and efficient gastro retentive dosage forms which can retain in the stomach for an extended period of time in a predetermined manner. The main objective is to develop and evaluate a floating tablet of Furosemide with better solubility by using various surfactants with the use of different materials of surfactants and methods of direct compression technique. Thus the obtained formulations are to be evaluated by various parameters and results so obtained are to be tabulated. Many approaches are utilized in the development of gastric retention drug delivery systems via., hydro dynamically balanced systems, swelling, expanding, high density systems, super porous hydro gels, bio adhesive modified shapes etc. By utilising one of the above techniques it is possible to deliver drugs, which have narrow absorption window.

Keywords: Gastric floating systems, Surfactants, Furosemide, Release behaviour of Furosemide.

INTRODUCTION

The primary aim of oral controlled drug delivery systems is to achieve better bioavailability in which heterogeneous dispersion of particles of the agent in a solid polymer matrix controls the release of the agent by diffusion mechanism through the matrix and the dispersion of an agent in a water swelling hydro gel matrix has also been achieved by above mechanism1. In the same way the viscous solution of polymer of an agent also sometimes possible with liquid-liquid encapsulation2. The most accepted method is the process of chemical binding of an agent to a polymeric compound3. A prolonged gastric retention increases bioavailability, decreases wastage of drugs and increases solubility of drugs which are less alkaline in pH. These dosage forms prolong the gastric residence time enabling an extended absorption phase for the local treatment of drugs[4].

Floating drug delivery systems provides better bioavailability for the drugs that are unstable in intestinal and colonic environment. The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion, flotation, sedimentation, expansion, modified shape systems[5, 6].

The factors effecting the gastric retention include density, size and shape of dosage form, concomitant intake of food and drugs such as anticholinergic agents (eg.atropine, propantheline), opiates (eg.codeine) and prokinetic agents (eg.metoclopramide) and biological factors such as gender, posture, age, body mass index and disease state.(eg.diabetes). The prolongation of gastric residence time (GRT) by food is expected to maximize drug absorption from FDDS due to increased dissolution of drug and longer residence at the most favourable sites of absorption[7, 8]. GRT of a dosage form in the fed state can also be influenced by its size. The addition of a surfactant into a tablet formulation appears to be attractive method of improve the drug release rate. The improved release rate is often associated with the effect of surfactant increasing the hydrophilicity of the dosage form thereby promoting drug dissolution. It follows that the action of surfactant improving drug dissolution from tablets may be attributed to the action of surfactant producing fine disintegrated particles with correspondingly larger surface area for drug dissolution[9]. The presence of surfactants may lower the surface tension and increase the solubility of the drug within an organic solvent. The process of solubilisation involves the breaking of inter-ionic or intermolecular bonds in the solute, the separation of the molecules of the solvent to provide space in the solvent for the solute, interaction between the solvent and the solute molecule or ion[10]. The objective of the study is to design a floating tablet of Furosemide with different type of surfactants at various concentration like 5%, 6% and 7%. The main reason for addition of surfactants in this formulation to enhance the solubility of furosemide with release a drug at a controlled rate over a long period of time[11].

MATERIALS AND METHODS

Materials:

Furosemide was obtained as a gift sample from Fine Chemicals Group of Industries, Ankleshwar. HPMC K15M obtained from Shangai Shenmei Pharmaceutical Technology Co., LTD; Arlacel-60 obtained from Grant Industries In. All other chemicals and reagents were obtained of their analytical grade.

Methods:

The required quantity of Furosemide was taken in a mortar and pestle and triturate well and then passed through 100 mesh sieve, then the Furosemide was mixed with already sifted materials (100 mesh) of HPMC K15M, MCC, PVP and sodium bicarbonate. Then the resulting mixer was mixed with different percentage of various surfactants as per formula shown in Table 1; finally the blend was lubricated and compressed into a tablet by using 16 station compression machine13 (Manesty Machines Ltd.

FLOW PROPERTIES OF BLEND

Angle of repose

Angle of repose has been used as indirect methods of quantifying powder flow ability, because of their relationship with inter particle cohesion. A static heap will slide when the angle of inclination is large enough to overcome frictional forces and stop when gravitational forces balance the forces. The sides of heap will make an angle with horizontal which is called angle of repose[14].

Angle of repose=tan-1h/r

Where h is height of pile and r is radius of pile.

Bulk density

Bulk density is given by the mass "m" of the powder occupying a known volume 'v' according to the relationship[15].

Pb =(M/V)g/cc

It depends on particle size, shape, tendency of particle to adhere.

Tapped density

Weighed powder sample was transferred to a graduated cylinder and was placed on tapped density apparatus, was operated for a fixed number of taps (100).It is the ratio of weight of sample to tapped volume[16].

Tapped density=mass/tapped volume

Carr's Index

Based on the apparent bulk density and the tapped density , the percentage compressibility of the bulk drug was determined by using the following formula.

% Compressibility= tapped density-bulk density/tapped density X100

Hausner's Ratio

The ratio of tapped density to bulk density of the powders is called the Hausner's ratio.

Table 1: Formulation of furosemide floating tablets

S.No	Ingredients	A1	A2	A3	B1	B2	B3	C1	D
1.	Furosemide	60	60	60	60	60	60	60	60
2.	HPMC K15M	120	120	120	120	120	120	120	120
3.	MicrocrystallineCellulose	24.25	21.75	19.25	24.25	21.75	19.25	24.25	36.75
4.	NaHco3	25	25	25	25	25	25	25	25
5.	PVP	5	5	5	5	5	5	5	5
6.	SLS	12.5	15.0	17.5	-	-	-	6.25	-
7.	Arlacel-60	-	-	-	12.5	15.0	17.5	6.25	-
8.	Colloidal-Silicon-dioxide	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
9.	Magnesium stearate	2	2	2	2	2	2	2	2
Total wt per Tablet:		250mg	250mg	250mg	250mg	250mg	250mg	250mg	250mg

Table 2: Flow properties of the blend

Formulations	Bulk density (g/cm³)	Tapped density (g/cm³)	Compressibility Index C.I	Hausner ratio	Angle of repose (θ)
A1	0.40	0.50	20	1.25	32.50
A2	0.42	0.54	22.22	1.28	32.06
A3	0.44	0.57	22.80	1.29	31.65
B1	0.44	0.66	33.33	1.50	33.12
B2	0.50	0.68	26.47	1.36	33.65
B3	0.55	0.75	26.66	1.36	33.52
C1	0.42	0.58	27.58	1.38	32.86
D	0.33	0.50	34	1.51	28.56

EVALUATION OF FORMULATED TABLET

Tablet Hardness

The strength of tablet is expressed as tensile strength kg/cm2. The tablet crushing load, which is the force required to break a tablet by compression. It was measured using a tablet hardness tester (Pfizer Hardness Tester).**Weight variation test:**

Weight variation test is done by weighing 20 tablets individually, calculating the average weight and comparing the individual weight to the average.

Friability

Friability is performed to assess the effect of friction. Roche Friabilator was used for the purpose.

Buoyancy / floating test

The test was performed by placing one tablet from each formulation in USP type II dissolution apparatus containing 900 ml of pH 1.2 buffer using paddle at a rotational speed of 100 rpm. The temperature of the medium was maintained at37±0.5oC[19].

RESULTS AND DISCUSSION

The aqueous solubility of Furosemide was extremely low and could be improved by the addition of the various surfactants like SLS,Arlacel-60 at different concentrations like 5%,6% and 7%. Tablets were compressed and evaluated. All the parameters were within acceptable limits. The formulations containing surfactants compared with the formulation containing without surfactants. Totally eight formulation was formulated and evaluated. The formulated Floating tablets met the pharmacopoeial requirements of uniformity of weight. All the tablets conformed to the requirement of Assay as per IP. Hardness, Percentage Friability and thickness were all within acceptable limits.

The Floating lag time and Floating time was observed in simulated gastric fluid (pH 1.2). The formulation containing 5% Arlacel-60 (B1) showed better results and floated within 33 seconds. The formulation containing without surfactants (D) showed lowest results, it floated after 74 seconds. The floating time of all the formulations evaluated, the lowest floating time was observed in formulation containing without surfactant(D),that was < 10.

Table 3: Physical properties of tablets from various formulations

Formulations	Physical Parameters of each formulations					
	Average weight of tablets(mg)	Hardness Kg/cm²	Friability (Percentage)	Floating Lag time (Sec)	Total Floating Time (hours)	Thickness (mm)
A1	249	4.1	0.29	38	> 12	5.84
A2	250	4.3	0.27	45	> 10	5.85
A3	248	4.0	0.25	40	> 10	5.81
B1	250	4.2	0.24	33	> 24	5.82
B2	249	4.2	0.25	60	> 24	5.81
B3	248	4.3	0.24	30	> 24	5.79
C1	249	4.2	0.26	35	> 24	5.80
D	250	4.5	0.23	74	< 10	5.78

Table: 4 Swelling index and content uniformity for various formulations

Formulations	Swelling index(at the end of 8th hour)	Content Uniformity(%W/W)
A1	81	99.96
A2	92	98.65
A3	94	98.36
B1	127	89.95
B2	100	95.23
B3	114	99.89
C1	125	98.91
D	117	97.26

Table 5: Effect of Various surfactants on release rate (RPM: 50)

TIME (hrs)	% RELEASE OF VARIOUS FORMULATIONS IN PH 1.2							
	5%SLS (A1)	6%SLS (A2)	7%SLS (A3)	5% SPAN60 (B1)	6% SPAN60 (B2)	7% SPAN60 (B3)	WITHOUT SURFACTANT (D)	COMBI-NATION (C1)
0.5	35.48	13.91	10.27	22.38	17.44	24.16	6.42	26.91
1	38.23	15.81	18.39	23.81	21.75	29.23	12.44	30.05
2	39.79	20.05	20.67	28.25	25.93	31.27	25.17	32.19
4	43.29	22.29	22.76	29.92	28.98	37.43	36.83	35.94
6	45.29	28.19	33.23	31.59	30.34	39.10	40.08	37.44
8	45.95	35.67	35.28	32.18	32.43	42.08	44.45	39.02
12	63.52	51.51	51.59	46.86	51.27	54.27	52.13	50.85

Table 6: Effect of surfactants on release rate (RPM: 100)

SL.NO	TIME IN HOURS	PERCENTAGE DRUG DISSOLVED IN PH 1.2			
		Without surfactants (D)	5% SLS (A1)	7% Span-60 (B3)	Combination (C1)
1	0.5	17.29	28.67	17.91	27.53
2	1	20.35	29.46	19.99	29.76
3	2	24.05	34.56	25.76	34.09
4	4	31.46	37.35	37.76	38.95
5	6	34.18	43.32	43.84	45.20
6	8	56.23	67.14	60.75	53.12
7	12	90.59	98.44	93.05	86.68

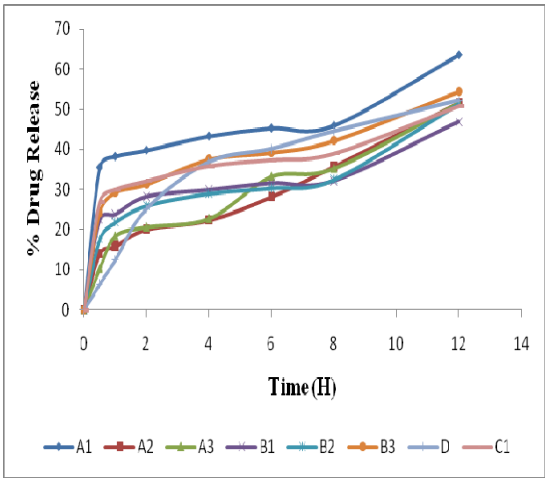

Fig. 1: Effect of various surfactants on release rate

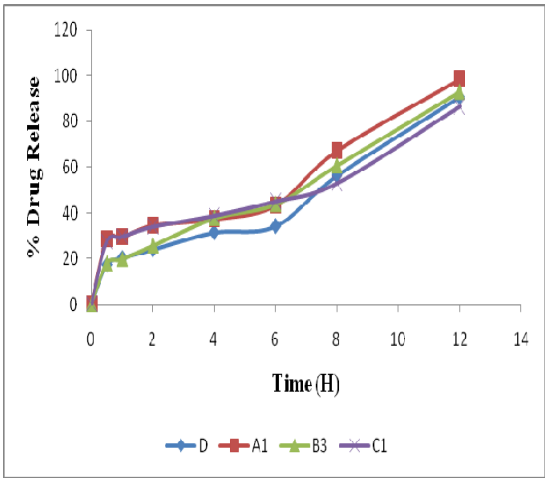

Fig. 2: Effect of surfactants and optimized formulations on their release rate.

The better floating time was observed in formulation containing various concentration of span-60 (B1, B2, B3) and formulations containing both surfactants (C1= 2.5% sls + 2.5% span-60) that showed > 24 hrs. Formulation containing 5% SLS (A1) showed > 12hrs.

The dissolution was carried out in simulated gastric fluid (pH1.2) by using type-II apparatus. The study was continued till 12th hours and the percentage drug release was calculated. Dissolution study was carried out at different RPM like 50 & 100 and the percentage drug release was noted. First the study was carried out at 50 rpm and the percentage was noted. In this rotational speed the highest percentage drug release (63.52%) was observed in A1(5% SLS) formulation. The lowest percentage drug release (46.86%) was observed in B1(5% Arlacel-60) formulation. Among the formulations performed at 50 rpm, the best three formulations was selected and dissolution was performed in same dissolution medium

but different rpm(100). When the rpm increased the percentage of drug dissolved also increased significantly. Among the three formulations (A1, B3, D), A1(5%SLS) showed highest percentage drug release(98.44%) at the end of 12th hour. During the dissolution study we observed that the place of tablet on the medium will also affect the drug release. The tablet sink in the medium was release the drug better than the tablets float on the medium.

CONCLUSION

The low aqueous solubility of furosemide was increased by incorporation of an-ionic and non-ionic surfactants like SLS and Arlacel-60 at different concentration and formulated as floating tablets. In this study the physical parameters and invitro drug release was estimated. Invitro dissolution was performed in simulated gastric fluid(pH 1.2) at different rpm like 50 & 100. Among the all formulations 5% SLS showed better dissolution(98.44%) at 100rpm. In this study we concluded the effect of SLS on the release of furosemide from floating tablet increase significantly and also the rpm, place of tablet on the medium will effect the release characteristics. The magnitude of the increase (or) decrease of release rate remarkably depends on the type of surfactants and on concentration. The results also showed that the surfactants are able to change the release rate of furosemide from floating tablets.

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