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Formulation and Comparative Evaluation of Nevirapine Floating Beads and Floating Gel

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ABSTRACT

The purpose of the study was to formulate floating alginate beads of Nevirapine (NVP), an Anti-HIV agent. Inspite of long half life (45 hrs) a Nevirapine controlled release once daily formulation could be used to maintain optimum peak plasma concentration for effective viral suppression. The floating bead formulations were prepared by dispersing Nevirapine together with Sodium bicarbonate in a mixture of sodium alginate and Hydroxypropyl methylcellulose solution and sunflower oil and then dripping the dispersion into an acidified solution of calcium chloride. Calcium alginate beads were formed, as the alginate underwent Emulsion gelation by calcium ions, and carbon dioxide developed from the reaction of carbonate salts with acid. The obtained beads were able to float due to CO_2 -gas formation and the gas entrapment by the polymeric membrane. The prepared beads were evaluated for percent drug loading, drug entrapment efficiency, morphology, surface topography, buoyancy, in-vitro release, and release kinetics. The beads containing higher amounts of calcium carbonate demonstrated an instantaneous, complete, and excellent floating ability over a period of 24 hours. And this floating beads are compared and evaluated with Nevirapine floaing gel, Good floating properties and sustained drug release were achieved. Finally, these floating beads seemed to be a promising gastro retentive drug delivery system.

Keywords: Gastro retentive Drug Delivery system, Nevirapine, Sustained release, Sodium alginate.

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INTRODUCTION

One approach for controlled release formulation of different therapeutic agents is the production of polymeric gel beads. The beads are discrete spherical microcapsules that serve as the solid substrate on which the drug is coated or encapsulated in the core of the beads. Beads can provide sustained release properties and a more uniform distribution of drugs include, within the gastrointestinal tract[1]. Furthermore, bioavailability of drugs formulated in beads has been enhanced .Numerous studies have been reported, concerning the use of alginate beads as a controlled release carrier. Alginate is a linear un branched polysaccharide composed of varying proportion of 1, 4- linked beta-D mannuronic acid (M) and alpha- L glucuronic acid (G) residues. Alginate has a unique gel- forming property in the presence of multivalent cations, such as calcium ions in an aqueous medium, which takes place mainly at junctions in the G-G sequence rich chain region known as egg box junctions. When divalent metal ions such as calcium, barium diffuse into an alginate solution, the rapid ion binding and formation of a polymeric network produces an inwardly moving gelling zone. In fact alginate moves from the gel core towards this gelling zone, leading to the deletion of the alginate within the core. Therefore, alginate is used as an immobilization matrix for cells and as pharmaceutical adjuvant2. Polymeric gel beads are used for controlled release of various therapeutic agents Nevirapine (NVP), a non-nucleoside reverse transcriptase inhibitor (NNRTI) of human immuno-deficiency virus type 1 (HIV-1), block polymerase activity after binding directly to the HIV-1 reverse transcriptase leading to disruption of the enzyme's catalytic site. NVP is a weak base with low water solubility, and belongs to BCS class II drug. In human, NVP is well absorbed orally with an estimated absolute bioavailability of about 90%. Floating drug delivery system is suitable for NVP as the absorption and solubility of NVP is high at pH<3 [2]. The absorption rate of NVP was decreased from upper part to lower part of GIT and from jejunum to descending colon. Thus, floating oral delivery system is expected to remain buoyant in a lasting way upon the gastric contents and enhance bioavailability. For this purpose calcium ions were used as cross linking agents in formulation of alginate beads by ionotropic gelation method. Next, characterization of the beads, drug entrapment within the beads and drug release kinetic were investigated. Results showed that the concentration of alginate was increased in the formulation the spherical shape of the beads was maintained and also more sustained action was observed.

MATERIALS AND METHODS

Nevirapine was a gift sample from Hetero drugs PVT LTD Hyderabad, HPMC (K100M) and

Sodium bicarbonate were purchased from Molychem laboratories, Mumbai. Sodium alginate, Guar gum were purchased from Finar reagents Ahmedabad, $Cacl_2$ was purchased from S.D. Fine laboratories, Mumbai. All reagents used were of analytical grade.

Compatability study

To determine the incompatibilities between drug & excipients, the Nevirapine, HPMC (K100M), Sodium alginate, Guar gum sodium bicarbonate, Sunflower oil were subjected to FTIR study.

Preparation of Floating Alginate Beads

Nevirapine floating beads were prepared using emulsion-gelation method and it is Effervescent system. Sodium alginate was dissolved in hot water by heating mantle by maintaining 40^0C then sodium alginate is kept for cooling later HydroxyPropylMethylCellulose (K100M)was dissolved in sodium alginate solution with stirring. Sunflower oil and sodium bicarbonate was added to polymer solution followed by Nevirapine is dissolved in 0.1N HCl. The homogenized mixture was extruded into calcium chloride solution at room temperature by using 2cc syringe by maintaining constant distance 5cm and speed 2ml per minute[3]. The formed beads were allowed to stand for varying times in the solution for curing then separated by filtration and dried at room temperature and used for further studies. Formulation data were tabulated in table 1.

Table 1: Formulation of Floating alginate Beads

	Drug(mg)	HPMCk100(mg)	Sodium alginate	Sodium Bicarbonate	Sunflower oil	Cacl2 50ml w/v
F1	50	50	1%	1%	1	7%
F2	50	50	2%	1%	1	7%
F3	50	50	3%	1%	1	7%
F4	50	50	1%	1%	1	8%
F5	50	50	2%	1%	1	8%
F6	50	50	3%	1%	1	8%
F7	50	50	1%	1%	1	9%
F8	50	50	2%	1%	1	9%
F9	50	50	3%	1%	3	9%
F10	50	50	1%	1%	3	7%
F11	50	50	2%	1%	3	7%
F12	50	50	3%	1%	3	7%
F13	50	50	1%	1%	3	8%
F14	50	50	2%	1%	3	8%
F15	50	50	3%	1%	3	8%
F16	50	50	1%	1%	3	9%
F17	50	50	2%	1%	3	9%
F18	50	50	3%	1%	3	9%
F19	50	50	1%	1%	5	7%
F20	50	50	2%	1%	5	7%
F21	50	50	3%	1%	5	7%

F22	50	50	1%	1%	5	8%
F23	50	50	2%	1%	5	8%
F24	50	50	3%	1%	5	8%
F25	50	50	1%	1%	5	9%
F26	50	50	2%	1%	5	9%
F27	50	50	3%	1%	5	9%

Preparation of Floating Gel

First of all, active material (Nevirapine) was passed from sieve # 22 while other inactive ingredients were passed form sieve # 40.Then Sodium bicarbonate and Nevirapine (50 mg) was added to it while stirring so that there was proper and homogenous dispersion of the active material in the solution. In around 30% water in other beaker was heated to NMT 60°C on hot plate and dissolved sodium alginate in it. Cool it to 40°C then guar gum is added by stirring. This solution was added to drug solution or vice-versa. This solution was mix well. Volume was adjusted to 100% with distilled water. Finally, the mixture was mixed well to get the final preparation. The formulation data of floating gel were tabulated in table 2.

Table 2: Formulation Table for Floating Gel

S.NO	Ingredients	G1	G2	G3	G4	G5	G6
1.	Nevirapine	50mg	50mg	50mg	50mg	50mg	50mg
2.	Sodium alginate	0.5%	1%	1.5%	2%	2.5%	3%
3.	Guar Gum	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%
4.	Sodium bicarbonate	2%	2%	2%	2%	2%	2%
5.	Purified water	100ml	100ml	100ml	100ml	100ml	100ml

EVALUATION OF FLOATING ALGINATE BEADS

Determination of the Beads Buoyancy

The Nevirapine beads (n = 20) were kept in a beaker filled with 50 ml of 0.1 M HCl. The floating ability of beads was measured by visual observation for the overall time period of 24h and floating lag time[5]. The beads that floated on the surface of the medium and those that settled down atthe bottom were recovered separately and the floating percentage (%buoyancy) was estimated .The integrity of the beads was also observed visually during the buoyancy test.The results of this parameters were shown in table 3

Percentage Yield

The total amount of beads was weighed and the percentage yield calculated by equation, taken into consideration the weight of drug and polymer. The results were shown in table 4

Percentage Yield = (Practical yield beads/Theoretical yield (Polymer + Drug) X 100.

Determination of actual drug content and entrapment efficiency

An accurately weighed amount of 10 mg of Nevirapine loaded beads was dissolved in 20ml of

0.1 M HCl solution. It was stirred for 2h using magnetic stirrer[8]. The resulting solution was then filtered and Nevirapine content was determined spectrophotometrically at 281 nm. Actual drug content (AC) and entrapment efficiency (EE) were calculated according to the following equations, the results were shown in table 4

Percentage of Drug Loading = Amount of drug in beads /total weight of beads×100

Entrapment efficiency = Actual drug content /theoretical drug content ×100

Differential Scanning Calorimetery (DSC)

The physical state of drug in the Nevirapine floating beads was analyzed by DSC. The thermograms of Nevirapine, Nevirapine floating beads with different polymers were obtained at a scanning rate of 10°C/min conducted over a temperature range of 120–300ºC,respectively.The DSC graphs of Nevirapine and optimized formulation were shown in figure 4,5 respectively.

EVALUATION OF FLOATING GEL

Determination of Drug Content

Accurately, 10 ml of in-situ gel from different batches were measured and transferred to 100 ml of volumetric flask. To this 50-70 ml of 0.1 N HCl was added and sonicated for 30 min. Volume was adjusted to 100 ml. Complete dispersion of contents were ensured, visually and filtered using Whatman Filter Paper. From this solution, 10 ml of sample was withdrawn and diluted to 100 ml with 0.1 N HCl. Contents of Nevirapine was determined spectrophotometrically at 281 nm using double beam UV-Visible spectrophotometer[9].The results were shown table 6

In-Vitro Floating Ability (In-Vitro Buoyancy)

The in-vitro floating study was carried out using 900 ml of 0.1N HCl, .The medium temperature was kept at 37^{o}C. Ten milliliter formulation was introduced into the dissolution vessel containing medium without much disturbance[10]. The time the formulation took to emerge on the medium surface (floating lag time) and the time the formulation constantly floated on surface of the dissolution medium (duration of floating) were noted. The results were shown table 6

Evaluation of In-vitro Drug Release Studies for Floating Beads and Floating Gel

In vitro dissolution studies of Nevirapine floating beads and floating gel were carried out in USP1 tablet dissolution test apparatus-II employing a basket at 50 rpm using 900ml of 0.1N HCl at 37±0.5ºC as dissolution medium. The results of floating alginate beads were shown in table 5, 6 and Floating gel release data were shown in table 8,9. At predetermined time intervals 5ml of the samples were withdrawn by means of a syringe fitted with a pre filter. The samples were analyzed for drug release by measuring the absorbance at 281nm using UV-Visible spectrophotometer after suitable dilutions[11]. All the studies were conducted in triplicate. The

results of in vitro release profiles obtained for all the Nevirapine formulations were fitted into four models of data treatment as follows zero-order kinetic model, first-order kinetic model, Higuchi's model, Korsmeyer-Peppas equation. The comparative evaluation of optimized formulations of floating beads and floating gel were shown in figure 9.

RESULTS AND DISCUSSION

Compatability study of Floating alginate beads and Floating Gel

FTIR spectrum of Nevirapine, Sodium alginate, HPMCK100, Guargum and Floating alginate beads formulations and Floating Gel formulations were shown in figures 1, 2, 3. FTIR spectrum peaks were observed with individual compounds have remain unaffected in Floating alginate bead formulations and floating gel formulations indicates Alginate beads and Gel formed were not a chemical reaction product, hence, the drug exists in original form and available for the biological action.

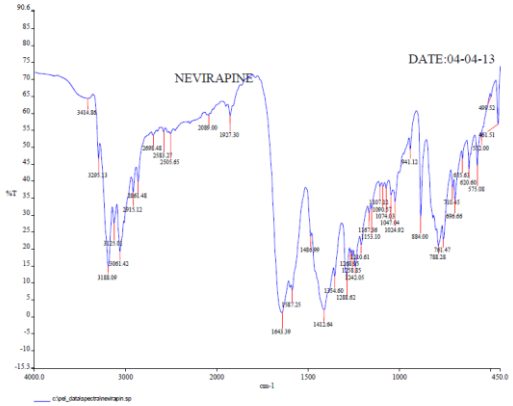

Figure 1 : FTIR of Nevirapine

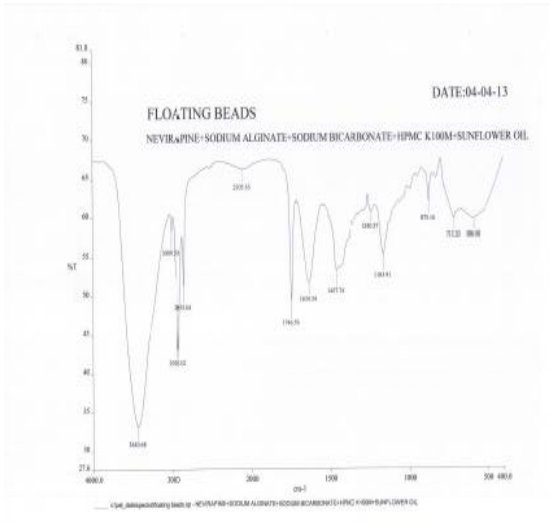

Figure 2: FTIR of Nevirapine Floating Beads

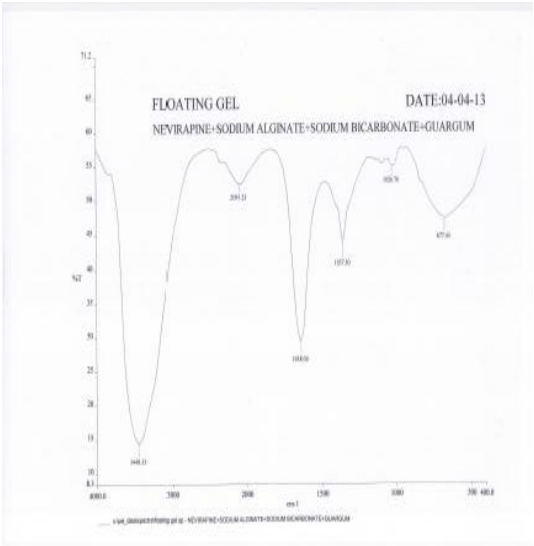

Figure 3 : FTIR of Floating Gel

Evaluation Parameters of Floating alginate beads

In vitro floating studies were performed by placing floating beads in the beaker containing 900 ml of 0.1N HCl maintained at a temperature of 37±0.5ºC. The floating lag time and floating time was noted visually. Floating lag time of Alginate beads ranges from 2min to 7 min6 seconds. All the formulations shown less lag time to float. This parameter is shown in table 3All the formulations designed and shown to float 24 hrs to increase drug release for extended period of time. It is shown in table 3 .All the formulations exhibited excellent floating ability, percentage ranges from 82.67±0.15 to 97.88±0.67. It is calculated by taking average of three determinations. It is shown in the table 3. the oil entrapped alginate beads containing sodium bicarbonate shown floating immediately and remained floating for 24 hours, but they have different floating lag time. The different lag time observed due to different polymer concentration and drug content of the beads. Increase in polymer concentration, floating lag time also increased.

Percentage yield of floating alginate beads ranges from 70.10±0.39 to 99.14±0.91.it is shown in table 4. F12 Shown good percentage yield.

Table 3: Evaluation Parameters of Nevirapine Floating Beads

FC	Curing Time(min)	Floating Lag time(min)	Floating Duration(hrs)	% of Bead Buoyancy
F1	20	3min 5 sec	24	92.41 ± 0.082
F2	20	3min 30sec	24	90.08 ±0.78
F3	20	4min 5sec	24	86.77 ±0.097
F4	15	3min 30 sec	24	93.76 ±0.17
F5	15	4min2sec	24	94.57 ±0.56
F6	15	5min6sec	24	90.78 ±0.091
F7	10	4min 7sec	24	92.45 ±0.76
F8	10	6min8sec	24	89.77 ±0.01
F9	10	8min3sec	24	82.67 ±0.15
F10	20	2min7sec	24	96.77 ±0.14
F11	20	2min	24	91.26 ±0.23
F12	20	3min8sec	24	87.98 ±0.54
F13	15	4min	24	94.75 ±0.34
F14	15	3min10sec	24	91.37 ±0.61
F15	15	5min	24	90.12 ±0.05
F16	10	5mn6sec	24	92.22 ±0.13
F17	10	6min8sec	24	89.17 ±0.56
F18	10	7min	24	87.89 ±0.45
F19	20	1min20sec	24	97.88 ±0.67
F20	20	3min8sec	24	94.55 ±0.054
F21	20	4min25sec	24	92.31 ±0.032
F22	15	2min6sec	24	93.77 ±0.17
F23	15	5 Min20sec	24	91.67 ±0.23
F24	15	7min6sec	24	89.67 ±0.29
F25	10	3min8sec	24	92.61 ±0.34
F26	10	4min7sec	24	90.14 ±0.19

F27	10	5min3sec	24	90.17 ±0.134

Table 4: Evaluation Parameters of Nevirapine Floating Beads

FC	Percentage yield	% Drug Loading	%Drug Entrapment
F1	91.27±0.13	4.14±0.42	90.10±0.86
F2	96.72±0.89	3.62±0.56	86.72±0.73
F3	93.61±0.34	3.36±0.78	93.71±0.91
F4	80.60±0.46	3.13±0.95	81.72±0.24
F5	91.07±0.57	3.24±0.37	84.61±0.57
F6	90.04±0.87	3.19±0.56	88.91±0.81
F7	93.45±0.68	3.76±0.83	83.61±0.46
F8	97.31±0.76	3.71±0.76	87.31±0.57
F9	93.68±0.47	3.62±0.23	82.36±0.51
F10	96.91±0.58	3.17±0.45	73.90±0.98
F11	91.78±0.56	3.15±0.67	77.56±0.49
F12	99.14±0.91	3.09±0.91	86.24±0.58
F13	93.01±0.86	3.89±0.45	81.24±0.91
F14	91.40±0.54	4.03±0.67	96.21±0.54
F15	86.88±0.13	2.92±0.98	71.42±0.56
F16	93.47±0.78	3.20±0.46	67.01±0.71
F17	89.86±0.56	2.97±0.73	69.56±0.98
F18	86.74±0.76	3.03±0.81	73.99±0.39
F19	92.03±0.65	4.05±0.99	90.05±0.58
F20	88.86±0.54	4.01±0.34	68.67±0.65
F21	90.39±0.38	2.81±0.54	68.07±0.17
F22	89.29±0.43	2.61±0.87	62.91±0.35
F23	91.32±0.59	2.72±0.34	69.71±0.76
F24	86.72±0.43	2.81±0.86	72.87±0.18
F25	93.61±0.76	2.36±0.45	66.71±0.67
F26	90.01±0.67	2.17±0.67	69.21±0.39
F27	70.10±0.39	2.18±0.56	72.62±0.56

Drug content and Drug entrapment was found in the range of 2.17 to 4.14 and 62.91 to 96.21 respectively, these parameters are shown in the table 4.Drug content and drug entrappement efficiency were also affected by various parameters. On increasing % concentration of sodium alginate and oil, the percentage of drug loading and entrapment efficiency increased, but not at all oil concentration.

Encapsulation efficiency and Drug loading was significantly increased by varying sodium alginate. This indicates that at higher amounts of use of sodium alginate higher encapsulation efficiency was obtained due to retardation of drug migration and loss to the external aqueous phases. Similar results were observed with floating cimetidine microspheres prepared by using hydroxypropylmethyl cellulose and Sodium alginate as polymers. However, further reduction in sodium alginate produced significantly lower percent yield and encapsulation efficiency. Such an

effect may be explained by the fact that at lower sodium alginate ratios, the drug particles were not encapsulated completely due to less available active calcium-binding sites in the polymeric chains and, consequently, a lower degree of cross-linking with gelling agent and formation of lower strength matrix structure.

It is observed that increasing $CaCl_2$ concentration increased the drug percentage yield and encapsulation efficiency This may be due to better cross-linking reaction of sodium alginate present in the bead structure with the more abundant presence of calcium ions, thus a better barrier entrapping the drug inside the polymeric matrix structure of the beads is provided. Similar results were observed with calcium.

In-vitro drug release studies of Nevirapine was studied by USP 1 dissolution apparatus. Drug release was found to be highest F1, F13, F 14, F16. Drug release impeded in the following formulations F 25, F26, F27.Cumulative release of Nevirapine was decreased with increase in sodium alginate concentration and also calcium chloride concentration. The most retardant drug release effect observed indicates that the release rate is controlled by wall thickness: an increase in polymer ratio will increase the coat thickness surrounding the drug particles, thereby increasing the distance travelled by the drug through the coat causing a greater impedance to drug release. The release was found to be steady and extended upto16 hrs.

To ascertain the drug release mechanism and release rate, data of the above formulations were model fitted. The models selected were Zero order, First order, Higuchi Matrix, Korsemayer Peppas, Interpretation of data was based on the value of the resulting regression coefficients. The in vitro drug release showed the highest regression coefficient value for zero order models indicates diffusion to be the predominant mechanism of drug release. All the formulations follows zero order, except F11, F23, F25, F26, F27 Follows First order. In floating alginate bead formulation, Most of the formulations shown n value > 0.5 it indicates drug release is by non ficknian mechanism. These data were shown in table 6, 7.Among all formulation F13, F14, F1 was found to be the best formulation as it release Nevirapine in a sustained manner with constant fashion over extended period of time (16hr).The evaluation parameters of floating alginate beads, are compared with floating gel of Nevirapine for the following parameters Floating lag time, Duration of floating, in-vitro drug release. Among floating gel formulations G6 is the best formulation. The evaluation parameters of floating beads formulations F13, F14, F1 are compared with G4. Gel formulation G4 Shown increased floating lag time 15 min and decreased duration of floating 12 hrs , Drug release is 93.72% extended upto 14 hrs and it follows zero order and n value is < 5 so it follows Ficknian mechanism. These parameters are shown in

table 8,9 whereas floating beads shown decreased floating lag time and increased duration of floatation, drug release is extended upto 16 hrs with cumulative percentage of 95.66% .The comparative release data was shown in figure 4.

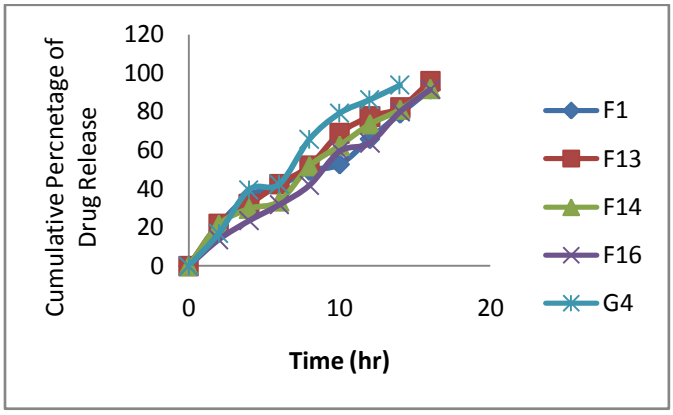

Figure 4: Comparative Evaluation of In-vitro Drug Release of Optimized Formulations of Floating Alginate Beads and Floating Gel.

Table 5:Invitro Drug Release studies

FC	*2hr*	*4hr*	*6hr*	*8hr*	*10hr*	*12hr*	*14hr*	*16hr*
F1	18.01±0.17	39.02±0.11	43.19±0.67	51.26±0.05	63.19±0.034	79.36±0.07	87.17±0.57	94.18±0.78
F2	12.17±0.23	23.68±0.08	31.72±0.13	47.36±0.27	57.31±0.05	63.81±0.25	78.61±0.09	88.78±0.27
F3	16.81±0.56	37.31±0.12	39.81±0.81	48.72±0.34	64.14±0.12	73.17±0.21	81.27±0.16	84.67±0.63
F4	21.17±0.78	36.28±0.34	41.69±0.61	49.26±0.45	52.63±0.96	65.72±0.34	78.91±0.17	91.36±0.41
F5	12.71±0.15	29.63±0.47	39.15±0.24	47.06±0.56	58.39±0.72	79.63±0.67	81.51±0.89	89.61±0.58
F6	7.19 ±0.09	19.21±0.41	28.31±0.35	36.72±0.78	46.36±0.37	53.29±0.19	69.72±0.63	75.18±0.59
F7	14.28±0.34	25.16±0.72	31.67±0.81	44.86±0.91	57.39±0.18	68.19±0.98	79.21±0.29	90.06±0.34
F8	8.33 ±0.26	24.84±0.34	29.64±0.96	38.71±0.32	52.28±0.65	61.82±0.71	73.79±0.78	83.14±0.76
F9	5.71 ±0.31	16.28±0.57	27.86±0.25	31.64±0.45	46.61±0.58	57.14±0.94	69.72±0.56	73.81±0.89
F10	16.29±0.56	21.72±0.81	26.34±0.56	37.67±0.67	41.68±0.95	56.33±0.54	71.81±0.67	83.38±0.91
F11	13.71±0.81	27.66±0.35	31.67±0.78	43.67±0.71	69.28±0.23	73.19±0.67	75.32±0.81	81.06±0.85
F12	8.67 ±0.56	15.78±0.23	29.81±0.34	33.41±0.16	45.67±0.34	51.78±0.61	69.37±0.87	78.39±0.67
F13	21.67±0.19	31.89±0.78	42.48±0.56	51.89±0.23	68.71±0.58	77.28±0.93	81.99±0.54	95.66±0.67
F14	21.35±0.45	29.61±0.91	33.48±0.71	51.69±0.76	62.36±0.21	73.41±0.45	80.96±0.91	91.66±0.54
F15	7.81 ±0.65	19.89±0.24	21.27±0.45	31.78±0.37	43.39±0.38	51.67±0.54	71.89±0.67	80.36±0.43
F16	13.67±0.67	23.39±0.56	31.67±0.86	41.78±0.63	59.39±0.6	63.71±0.67	79.89±0.8	91.36±0.29
F17	11.78±0.13	28.19±0.93	31.67±0.71	48.39±0.91	51.67±0.96	61.26±0.32	73.26±0.45	86.37±0.76
F18	8.96 ±0.87	21.67±0.57	32.67±0.45	46.37±0.29	54.67±0.83	64.71±0.91	71.25±0.34	79.36±0.37
F19	12.71±0.65	26.79±0.81	31.36±0.63	43.27±0.68	58.69±0.45	65.72±0.45	73.26±0.12	80.01±0.51
F20	11.36±0.13	19.26±0.23	29.39±0.56	31.37±0.54	42.31±0.46	51.67±0.67	63.57±0.63	78.92±0.81
F21	8.311±0.13	16.37±0.45	21.99±0.23	32.67±0.34	41.76±0.45	56.78±0.51	61.37±0.86	72.36±0.36
F22	13.31±0.21	19.26±0.65	23.66±0.42	31.07±012	42.31±0.18	51.67±0.41	63.41±0.73	74.21±0.19
F23	12.36±0.46	21.97±0.19	31.72±0.37	49.36±0.83	56.78±0.37	61.89±0.54	66.36±0.19	71.61±0.26
F24	8.67 ±0.71	13.96±0.13	26.97±0.45	36.37±0.45	41.19±0.98	56.79±0.91	67.38±0.57	70.32±0.72
F25	15.61±0.34	21.36±0.45	37.19±0.67	46.71±0.71	56.79±0.18	61.79±0.21	-	-
F26	13.21±0.31	16.71±0.76	23.16±0.12	31.16±0.34	43.91±0.14	51.71±0.35	-	-
F27	14.16±0.91	19.26±0.34	29.19±0.45	30.57±0.54	42.91±0.13	-	-	-

Table 6: Release kinetics

S.NO	Zero order		First order		Higuchi		Peppas	
	R^2	K_0 % hr^-	R^2	K_1	R^2	K_H	R^2	N
F1	0.9906	24.193	-0.9537	0.14	0.986	35.61	0.988	0.51
F2	0.9971	13.253	-0.9548	0.070	0.9886	44.92	0.998	0.84
F3	0.9856	23.605	-0.9746	0.141	0.9891	80.01	0.986	0.80
F4	0.9868	17.399	0.9738	0.105	0.9692	58.98	0.9847	0.43
F5	0.9891	19.483	0.9789	0.107	0.9878	66.045	0.9936	0.67
F6	0.9967	13.841	-0.9744	0.061	0.9874	46.918	0.9959	0.46
F7	0.9983	12.528	-0.9531	0.067	0.9841	42.46	0.9956	0.28
F8	0.9965	19.011	-0.9693	0.097	0.7504	64.44	0.9905	0.43
F9	0.9957	12.171	0.9816	0.0598	0.9851	41.20	0.9662	0.38
F10	0.9812	6.252	0.9291	0.033	0.9492	21.19	0.9856	0.68
F11	0.9700	16.062	0.9759	0.0875	0.9776	54.45	0.9856	0.85
F12	0.9921	8.187	0.9590	0.0409	0.9760	27.753	0.9949	0.82
F13	0.9953	11.762	0.9241	0.0609	0.9896	39.89	0.9947	0.51
F14	0.9931	9.511	0.8277	0.0551	0.9807	32.23	0.9807	0.71
F15	0.9852	13.921	0.9421	0.0725	0.9606	47.15	0.9606	0.49
F16	0.9952	11.192	-0.9335	0.0598	0.9791	37.94	0.9791	0.26
F17	0.9921	18.896	-0.9481	0.1024	0.9812	64.05	0.9812	0.63
F18	0.9946	14.635	0.9932	0.0759	0.9981	49.61	0.9983	0.57
F19	0.9930	16.213	0.9893	0.0875	0.9913	54.95	0.9913	0.43
F20	0.9871	9.096	0.9378	0.0461	0.9623	30.83	0.9623	0.27
F21	0.9952	9.279	-0.9778	0.04606	0.9788	31.45	0.9788	0.73
F22	0.9891	6.850	0.9541	0.0345	0.9618	23.22	0.9618	0.49
F23	0.9775	9.61	-0.9936	0.0575	0.9902	37.511	0.9902	0.30
F24	0.9927	6.091	-0.9827	0.0298	0.9823	20.648	0.9826	0.25
F25	0.9936	10.11	0.9132	0.0319	0.9173	21.36	0.9981	0.56
F26	0.9871	9.66	0.9038	0.0534	0.9031	24.57	0.9631	0.48
F27	0.9832	7.13	0.9176	0.0219	0.9457	23.61	0.9571	0.57

Table 7: Evaluation Parameters of Floating Gel

Formulation code	Drug content (%)	Floating lag time (min)	Duration of buoyancy(hr)
G1	79.67	15	14
G2	88.62	20	16
G3	93.12	27	16
G4	75.74	30	12
G5	78.91	35	12
G6	73.62	32	12

Table 9 : Drug Release Kinetics of Floating Gel

S.NO	Zero order		First order		Higuchi		Peppas	
	r^2	K_0	r^2	K_1	r^2	K_H	r^2	N
G1	0.966	30.754	-0.9961	0.2187	0.9878	86.46	0.9838	0.32
G2	0.9768	22.32	-0.9964	0.127	0.9946	75.68	0.9881	0.34
G3	0.992	13.004	0.9841	0.069	0.9806	44.069	0.9911	0.42
G4	0.9819	25.97	0.9793	0.1583	0.9887	88.06	0.9867	0.21

G5	0.9671	9.16	0.9876	0.0483	0.9768	31.07	0.9741	0.35
G6	0.9833	20.26	0.9931	0.1139	0.9913	68.69	0.9904	0.77

CONCLUSION

Floating alginate gel beads of Nevirapine showed excellent floating ability, good buoyancy and prolonged drug release. Erosion and Diffusion was found to be the main release mechanism. In context to the intense worldwide research to combat AIDS, it can be envisaged that future workers would indulge in optimization of the selected formulations F1, F13, F14, to promote its commercial scale up leading to floating alginate gel beads of Nevirapine for effective management of AIDS. These beads were capable of reducing the frequency of administration and dose dependent side effects associated with the repeated administration of conventional Nevirapine Tablets. From the compatibility studies, it was concluded that, HPMC K100M, Sodium alginate, Guar gum Nevirapine were compatible and thus suitable for the formulation of Nevirapine floating beads and floating gel. In vitro buoyancy studies were performed for all the formulations, FT1 to FT27 by using 0.1N HCl solutions .All the formulations were floated. The formulation containing Sodium bicarbonate showed more floating time (24h). In vitro dissolution studies were also performed for all formulations. The formulations showed the sustained release for 16 has compared to floating gel. Thus all formulations of floating beads were identified as ideal batch based on its results. Finally, it was concluded that Floating alginate beads shown extended drug release by 24 hours floating than floating gel. The developed floating beads of Nevirapine may be used in clinic for prolonged drug release for at least 16 h, thereby improving the bioavailability and patient compliance.

REFERENCES

1. Jain NK. In Controlled and Novel Drug Delivery. 1st edition, CBS Publishers & Distributors: 1998; 1-3.
2. Sinha VR, RachanaKumria. Preparation and evaluation of ketoprofen floating oral delivery system. Int J Pharm. 2001; 67: 24-226.
3. Gastroretentive drugs: A review., Express Pharma Pulse, 2003.
4. Dr.Jose Gutierrez-Rocca., HosseinOmidian and Khalid Shah., Progress in Gastroretentive Drug Delivery Systems, Pharmatech, 2003, 152- 160.
5. Timmermans J, Andre JM. Factors controlling the buoyancy and gastric retention capabilities of floating matrix capsules: new data for reconsidering the controversy. J Pharm Sci. 1994;83:18-24.

6. Vyas SP and Khar RK. Gastro Retentive System in Controlled Drug Delivery: Concepts and Advances. First edn, CBS Publication, New Delhi. 2002: 196-217.
7. Shaufeng Li, Senshang Lin, Bruke P, DaggyHaresh, L Mirchandani, Yie W Chien. Effect of HPMC and carbopol on the release and floating properties of gastric floating drug delivery system using factorial design. Int J Pharm. 2003; 253: 13-22.
8. Kiran Kumar M, Manish H Shah, AnantKetkar, Mahadik KR, ParadkarAnant. Effect of drug solubility and different excipients on floating behaviour and release from glyceryl mono-oleate matrices. Int J Pharm. 2004; 272: 151-160.
9. Yasunori Sato, Yoshiaki Kawashima, Hirofumi Takeuchi, Hiromitsu Yamamoto. *In* vitro and *in vivo* evaluation of riboflavin containing microballoons for a floating controlled drug delivery system in healthy humans. Int J Pharm. 2004; 275: 97-107.
10. Nicole Kavanagh, Owen I Corrigan. Swelling and erosion properties of HPMC matrices – influence of agitation rate and dissolution medium composition. Int J Pharm. 2004; 279: 141-152, 112
11. Anand Kumar Shrivastava, Devendra NR, Saurabh Wadhwa. Floating microspheres of cimetidine: Formulation characterization and *in-vitro* evaluation. Acta Pharm. 2005; 55: 277-285.