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FORMULATION AND EVALUATION OF SUSTAINED RELEASE FLOATING TABLET OF ORLISTAT

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ABSTRACT

Objective: The objective of present work is to formulate the gastro retentive floating tablets containing Orlistat. **Experimental work:** The floating tablets of orlistat were prepared by direct compression methodusing Polyox WSR 303 sustained release polymer and Sodium bicarbonate as a floating effervescent agent. Optimization was done with 3^2 factorial design by taking concentration of polyox WSR 303 and sodium bicarbonate as independent variables and floating lag time and % CDR as dependent factors. The optimized batch of floating tablet was subjected for the short term stability study at 40±2°c with RH of 75% for a period of one month. The prepared formulations were evaluated for hardness, friability, weight variation, swelling index, floating lag time, floating time and % drug release. **Result and discussions:** All the physiochemical properties of prepared floating tablets were found to be in acceptable range. The optimum concentration of polyox WSR 303 and Sodium bicarbonate were required to formulate floating tablet to increase gastric retention time. From the formulated factorial batches S3, batch containing 22.5% polyox WSR 303 and 7.5% sodium bicarbonate showed lowest lag time of 25.22±0.41 sec and highest % drug release at 12 hours of 98.53%. **Conclusion:** From the result obtained it was concluded that optimized formulation containing polyox WSR 303 and Sodium bicarbonate shows better swelling properties with desired drug release properties and floating behaviour. Hence polyox WSR 303 is a potential polymer candidate for formulation of sustained release floating effervescent tablet.

KEYWORDS: Floating drug delivery system, obesity, polyox WSR 303.

INTRODUCTION

Floating drug delivery systems (FDDS) or hydrodynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.[1-2] Different types of floating drug delivery system based on the mechanism of buoyancy are effervescent system and non- effervescent system. Orlistat is a drug designed to treat obesity. Its primary function is preventing the absorption of fats from the human diet, thereby reducing caloric intake. Orlistat works by inhibiting pancreatic lipase, an enzyme that breaks down triglycerides in the intestine.[3]

MATERIALS AND METHOD

Orlistat was obtained as a gift sample from Bills Biotech Ltd Vadodara. Polyox WSR 303 was obtained from Otto Kemi, Mumbai. All other excipients were used of analytical grade.

- **Solubility studies**

Solubility of drug in three different solvents (0.1N Hcl, 0.1 N NaOH and distilled water) was carried out by preparing saturated solutions of drug in respective solvents. Saturated solutions were prepared by adding excess of drug to vehicles and shaking them on shaker for 24 hrs under constant vibration. After this, the solutions were filtered and analyzed spectophotometricallyat ƛmax 210nm.[4]

- **Acid Stability of Orlistat**

In order to evaluate the stability of orlistat in 0.1N HCl solution, 100mg drug was weighed accurately and transferred to 100 ml volumetric flask. Dissolved and volume was made upto mark with 0.1 N HCl solution containing 0.02% Tween 80. Solution was kept aside for further analysis without any disturbance. 1ml was pipetted out at each time point upto 12 hrs and diluted in 10 ml volumetric flask with 0.1 N HCl solution to prepare 10µg/ml. The absorbance of the solution was measured by UV at ƛmax210nm to verify the stability of the drug in 0.1 HCl.[5]

- **Formulation of Floating tablet**:

All the ingredients were accurately weighed and passed through mesh 60#.In order to mix the ingredients thoroughly drug and polymer were blended for 15 minutes and other excipients were mixed one by one. After thoroughly mixing the ingredients, the blended powder waspassed through 44# sieve and compressed on rotary tablet punching machine.

Table 1: Formulation composition of floating tablets.

Ingredients (mg)	S1	S2	S3	S4	S5	S6	S7	S8	S9
Orlistat	309	309	309	309	309	309	309	309	309
Polyox WSR 303 (%)	22.5	22.5	22.5	25	25	25	27.5	27.5	27.5
Sodium bicarbonate (%)	2.5	5	7.5	2.5	5	7.5	2.5	5	7.5
PVP K30 (%)	5	5	5	5	5	5	5	5	5
MCC(mg)	67	53	39	53	39	25	39	25	11
Magnesium stearate (%)	1	1	1	1	1	1	1	1	1
Talc (%)	1	1	11	1	1	1	1	1	1
Total (mg)	**550**	**550**	**550**	**550**	**550**	**550**	**550**	**550**	**550**

Evaluation of floating tablets

Weight variation

Twenty tablets were taken at randomly from each formulation and average weight was determined. Then the individual tablet weight was compared with the average weight.[6]

Hardness

Three tablets were taken at randomly from each formulation and hardness was checked using Monsanto hardness tester.[7]

Friability

Pre-weighed sample of tablets was placed in the Roche Friabilator tester, which was then operated for 100 revolutions. Tablets were dedusted and reweighed.[8]

% Friability was calculated by using the formula

% Friability = $(W_O-W_f/ W_O) X 100$

Where W_O = initial weight, W_f = final weight

Floating lag time

The three tablets were placed in a 100 ml beaker containing 0.1 N HCl. The average time required for a tablet to rise to the surface for floating was determined as the lag time.[9]

Floating time

The tablets were placed in a 100 ml glass beaker containing 0.1 N HCl. The total time for which the tablet remained floating on the surface of medium was determined as floating time.[10]

Swelling index

The swelling index of tablets was determined by 0.1 N HCl at room temperature. The swollen weight of the tablets was determined at predefined time intervals. The swelling index was calculated by the following equation.[11]

Swelling index (S.I) = {(Wt-Wo)/Wo} x 100

Where, Wt = Weight of tablet at time t and Wo = Weight of tablet before immersion.

Drug content

10 tablets were weighed and powdered in a mortar. Accurately weighed tablet powder samples equivalent to 10 mg of orlistat tablets was transferred to a 10ml volumetric flask, and the drug was extracted into 10ml methanol. This solution was filtered through a Whattman No. filter paper and collected in to a 10ml volumetric flask. The solution was suitably diluted and the absorbance was measured.[12]

In-vitro drug release studies

Invitro drug release of tablets was studied using USP type I apparatus at 37±0.5° C in 900ml 0.1N HCl solution with a speed of 100 rpm. At appropriate time intervals 5ml of sample was withdrawn upto 12 hrs and analysed by UV at ƛmax210nm.[13]

RESULTS AND DISCUSSIONS

Table 2: Pre compression parameters of formulation S1-S9.

Batches	Bulk density (gm/cm^3) n=3±SD	Tapped density (g/cm^3) n=3 ±SD	Carr's Index (%) n=3 ±SD	Hausner's ratio (n=3 ±SD)	Angle of response (θ) n=3 ±SD
S1	0.435±0.036	0.519±0.039	16.18±0.017	1.21±0.023	27.12±1.18
S2	0.423±0.059	0.540±0.012	21.66±0.039	1.39±0.049	30.67±1.09
S3	0.469±0.052	0.537±0.045	12.66±0.039	1.19±0.061	24.99±0.49
S4	0.479±0.012	0.583±0.061	17.83±0.024	1.26±0.042	28.35±1.26
S5	0.458±0.027	0.529±0.09	13.42±0.054	1.33±0.031	31.17±0.96
S6	0.408±0.01	0.527±0.029	22.58±0.079	1.22±0.082	26.43±0.28
S7	0.486±0.026	0.619±0.081	21.48±0.022	1.30±0.053	29.72±0.78
S8	0.472±0.043	0.544±0.032	13.22±0.046	1.28±0.021	28.36±1.21
S9	0.467±0.022	0.572±0.072	18.35±0.082	1.36±0.073	26.76±0.79

Table 3: Post-compression parameter of formulation S1-S9.

Batch	Wt. Variation (mg) n=20 (±SD)	% Friability	Hardness n=3 (±SD)	Drug content n=10 (±SD)	Floating lag Time (Sec), n=3 (SD)	Total Floating time (hr)
S1	551.30±1.08	0.43	5.45±0.23	97.41±0.74	31.08±0.72	>12
S2	548.48±0.91	0.37	4.83±0.13	97.25±0.39	29.23±1.09	>12

S3	550.58±0.79	0.48	5.36±0.11	99.82±0.47	25.22±0.41	>12
S4	549.03±0.74	0.61	6.11±0.74	98.85±1.14	48.51±0.91	>12
S5	552.05±1.01	0.56	4.53±0.21	99.14±1.32	43.15±0.79	>12
S6	548.85±1.26	0.42	5.14±0.56	98.65±0.95	38.13±1.06	>12
S7	550.24±0.29	0.58	5.61±0.32	97.09±0.87	59.18±1.14	>12
S8	551.19±1.42	0.38	4.89±0.84	99.47±1.19	52.30±0.91	>12
S9	549.69±1.32	0.53	5.50±0.31	99.47±1.19	42.15±0.80	>12

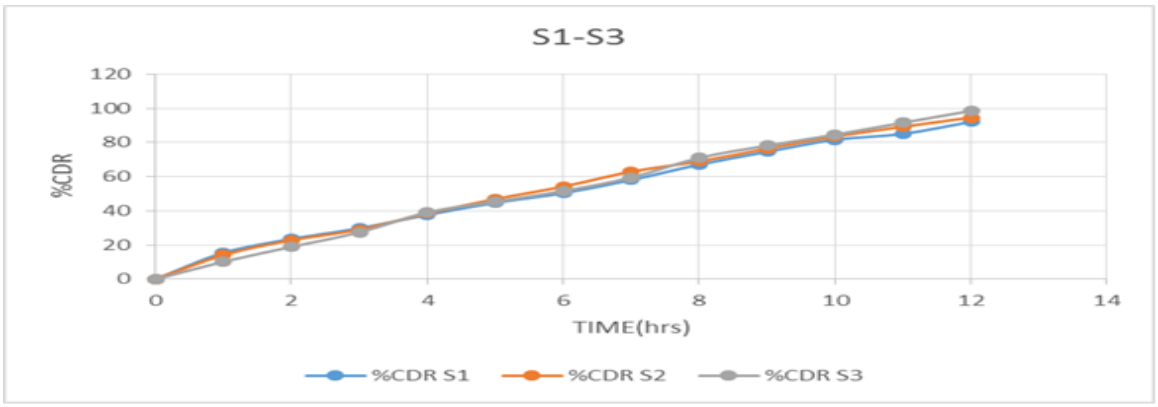

Fig. 1: In- vitro drug release of formulation S1-S3.

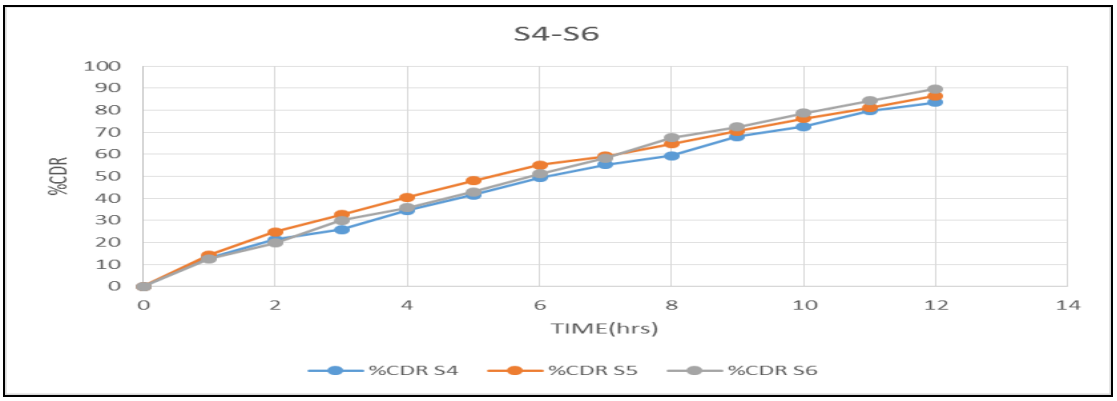

Fig. 2: In- vitro drug release of formulation S4-S6.

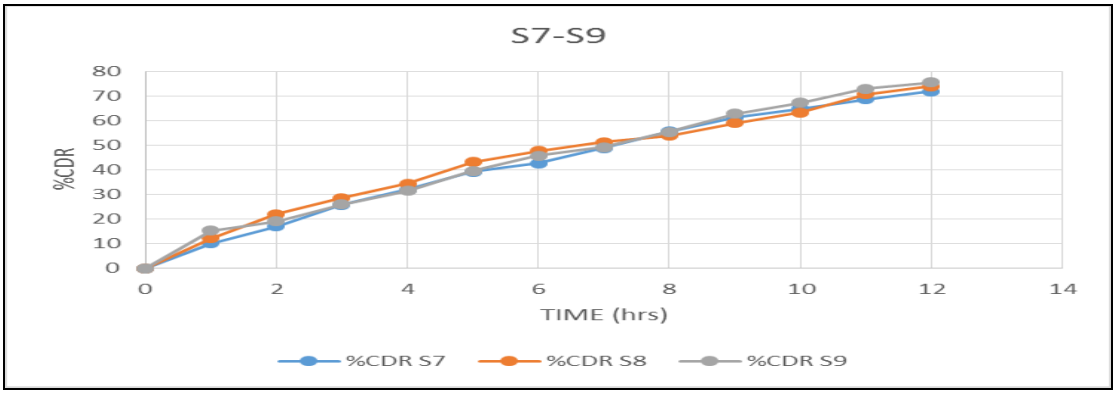

Fig. 3: In- vitro drug release of formulation S7-S9.

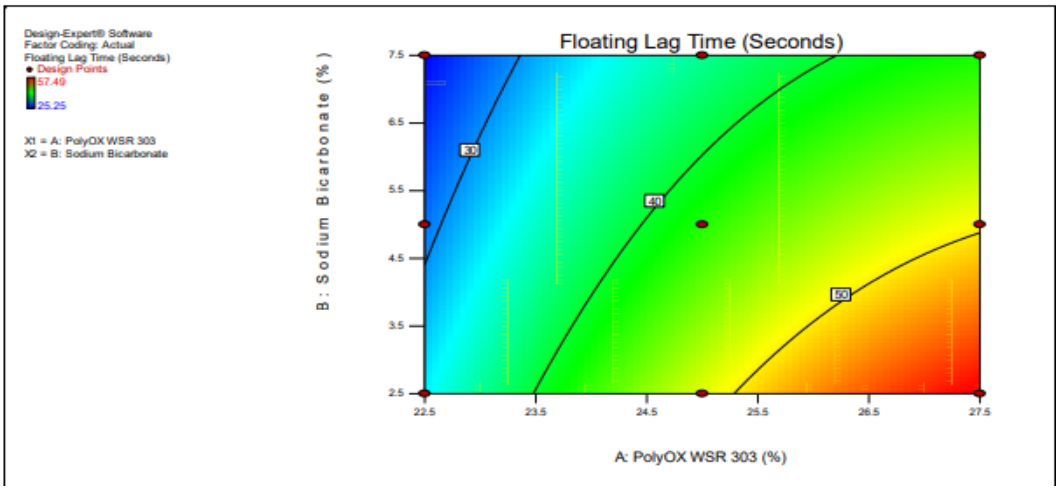

Fig. 4: Contour plot showing the effect of Polyox WSR 303 (%) (X1) and Sodiumbicarbonate (%) (X2) on response Y1 (Floating lag time) F.

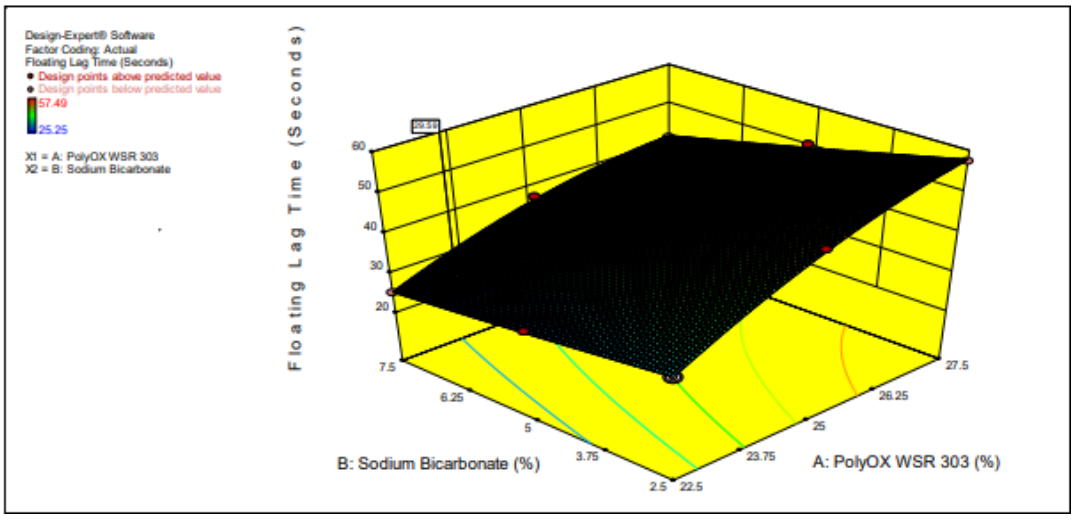

Fig. 5: Response surface plot of Floating lag time (sec).

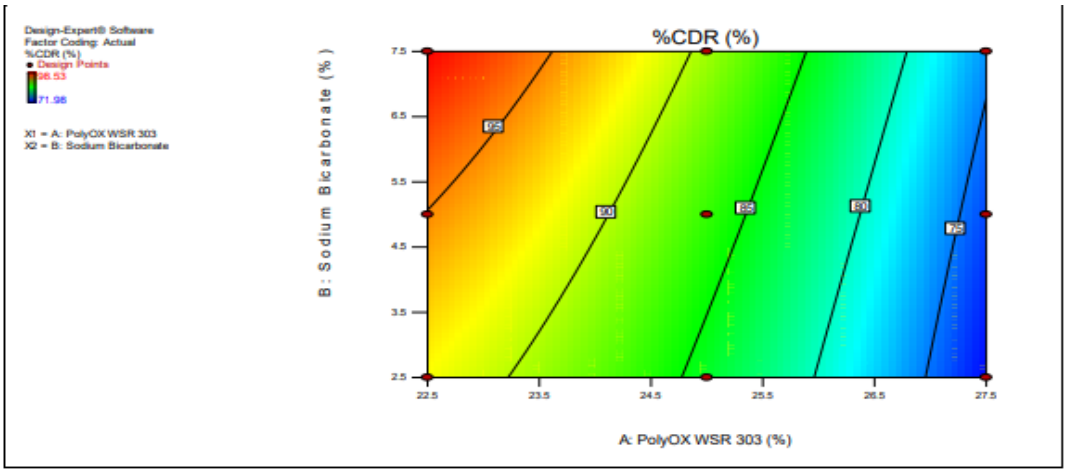

Figure 6: Contour plot showing the effect of Polyox WSR 303 (%) (X1) and Sodium bicarbonate (%) (X2) on response Y2 (Drug release).

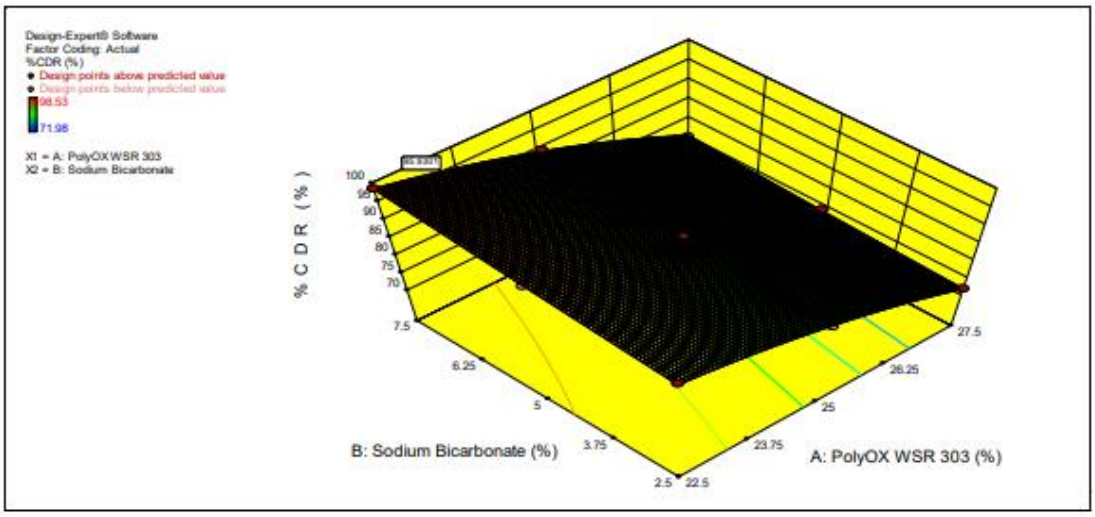

Figure 7: Response surface plot of % CDR.

Stability Study

Stability study was conducted for optimized batch S3 as at 40 ± 2°C with RH of 75% for a period of 30 days in stability chamber. Formulation was evaluated after one month period forin-vitro drug release.

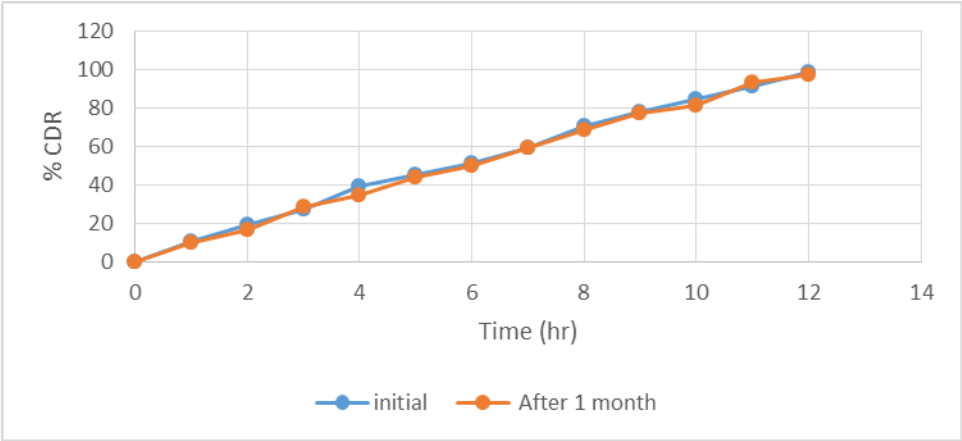

Fig. 8: In vitro drug release of S3 after stability study.

Summary and Conclusion

The tablets were formed by taking various concentration of polymers as a release retarding agent and sodium bicarbonate as an effervescent. Acid stability was performed for drug and results revealed that the drug is stable in acidic environment. The powders were evaluated for angle of repose, bulk density, tapped density, Carr's index & Hausner's ratio. The tablets were evaluated for hardness, friability, weight variation, drug content, floating lag time and in vitro drug release. Among all the formulation S3was found best in polymer and its

concentration. The precompression and post compression parameters are in within limits. From the stability studies, it was observed that formulation was stable.

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