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R E S E A R C H A R T I C L E

Formulation and *In-vitro* Evaluation of Fluvastatin Sustained Release Tablets

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A B S T R A C T

The aim of the present study was to develop sustained release formulation of Fluvastatin to maintain constant therapeutic levels of the drug for over 12 hrs. Various natural polymers such as Guar gum Sodium CMC and Chitosan were employed as polymers. Fluvastatin dose was fixed as 20 mg. Total weight of the tablet was considered as 150 mg. Polymers were used in the concentration of 25, 50 and 100 mg concentration. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F6) showed better and desired drug release pattern i.e.,96.10 % in 12 hours. It followed zero order release kinetics mechanism.

Keywords: Fluvastatin, Guar gum, Chitosan, Sodium CMC and sustained release tablets.

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

Sustained Release: This term is constantly used to describe a pharmaceutical dosage form formulated to retard the release of the therapeutic agent such that its appearance in the systemic circulation is delayed and prolonged and its plasma profile is sustained in duration. The onset of its pharmacological action is often delayed, and the duration of its therapeutic effect is sustained. In orally administered dosage forms, this duration is in hours and critically depends on the residence time of the dosage form in GI tract, where as in the case of injectables this period may vary from days to months. Fluvastatin sodium is a novel compound that works against hyper lipoprotienemics. It exists as an amorphous and appears as a yellowish powder with melting point 194°C. Fluvastatin sodium has a relatively high aqueous solubility at neutral pH. It dissolves rapidly in intestinal fluid and reaches its maximum blood concentration with in 30 min. However; this compound has a variable elimination half life time about 1 hr to 6hrs in

humans, requiring a dosing frequency 20 to 40 mg twice a day5, 6, 7. In the view of these characteristics, many attempts have been made to develop SR preparation with extended clinical effects and reduce dosing frequency.

2. Materials and Methods

Materials and Methods: Fluvastatin, Guargum, Chitosan, Sodium CMC, MCC pH 102 , Magnesium stearate , Talc chemicals were Laboratory grade made of SD Fine chemicals Pvt Ltd

Formulation development of Tablets:

All the formulations were prepared by direct compression. The compositions of different formulations are given in Table 1.The tablets were prepared as per the procedure given below and aim is to prolong the release of Fluvastatin. Total weight of the tablet was considered as 150mg.

Procedure:

- Fluvastatin and all other ingredients were individually passed through sieve no ≠ 60.
- All the ingredients were mixed thoroughly by triturating up to 15 min.
- The powder mixture was lubricated with talc.
- The tablets were prepared by using direct compression method.

3. Results and Discussion

7.1. Analytical Method: Graphs of Fluvastatin was taken in Simulated Gastric fluid (pH 1.2) and in p H 6.8 phosphate buffer at 298 nm and 294 nm respectively.

Table 2: Observations for graph of Fluvastatin in 0.1N HCl (298nm)

Conc [µg/l]	Abs
4	0.104
8	0.205
12	0.302
16	0.411
20	0.503
24	0.608
28	0.710
32	0.808

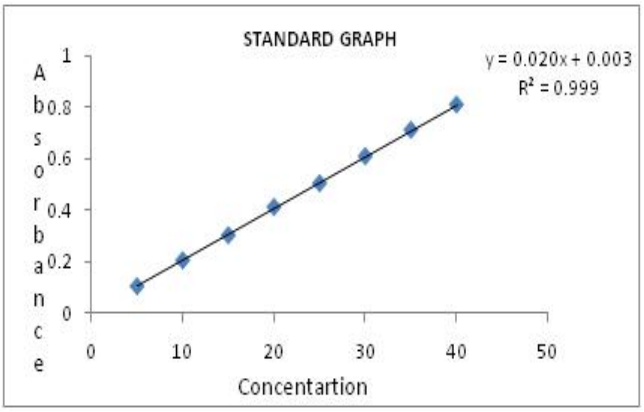

Figure 1: Standard graph of Fluvastatin in 0.1N HCl

Table 3: Observations for graph of Fluvastatin in p H 6.8 phosphate buffer (294nm)

Conc [µg/l]	Abs
4	0.098
8	0.195
12	0.298
16	0.392
20	0.490
24	0.595
28	0.690
32	0.776

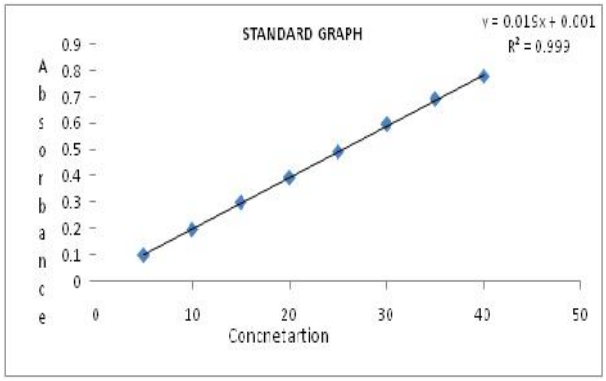

Figure 2: Standard graph of Fluvastatin p H 6.8 phosphate buffer (294nm)

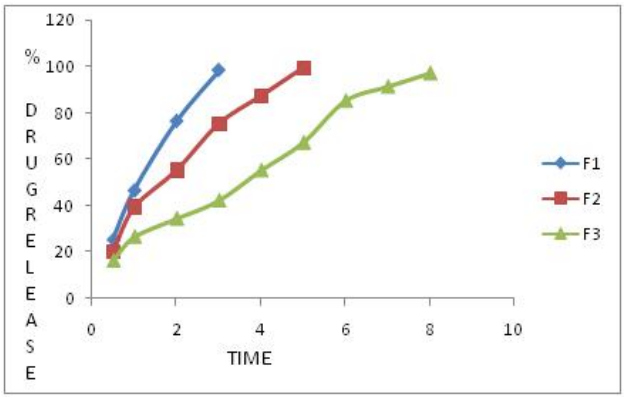

Figure 3: Dissolution profile of Fluvastatin (F1, F2, F3 formulations).

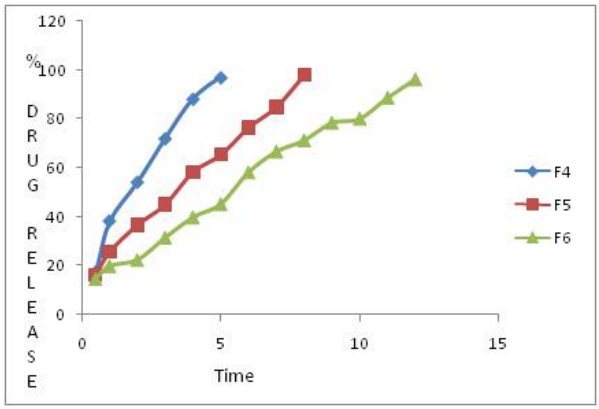

Figure 4: Dissolution profile of Fluvastatin (F4, F5, F6 formulations)

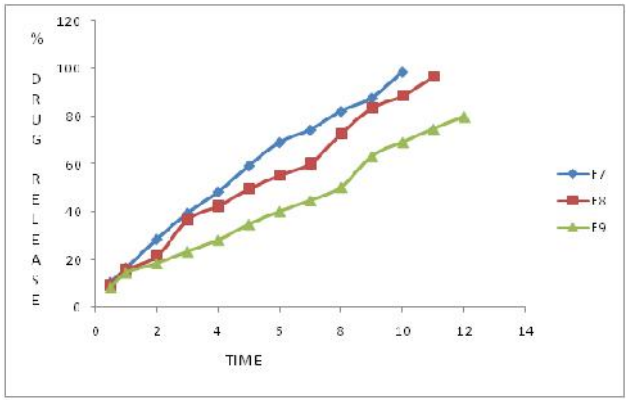

Figure 5: Dissolution profile of Fluvastatin (F7, F8, F9 formulations)

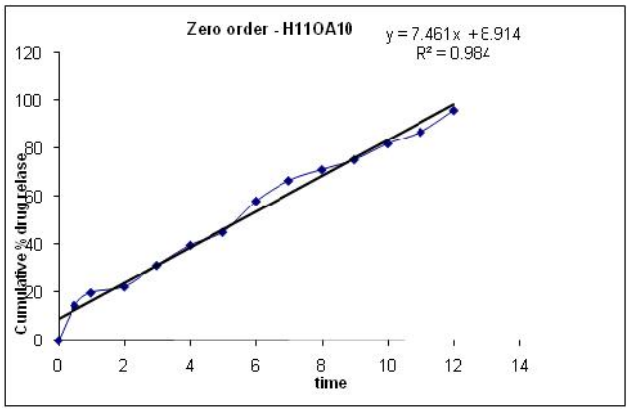

Figure 6: Zero order release kinetics

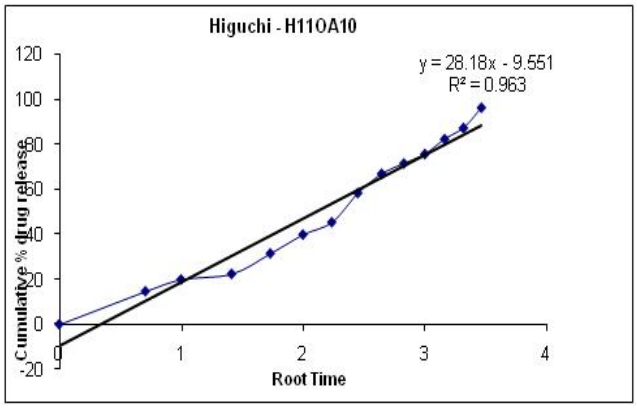

Figure 7: Higuchi release kinetics

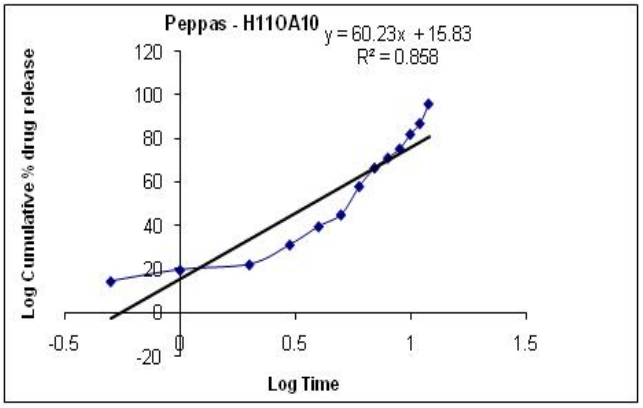

Figure 8: Kars mayer peppas

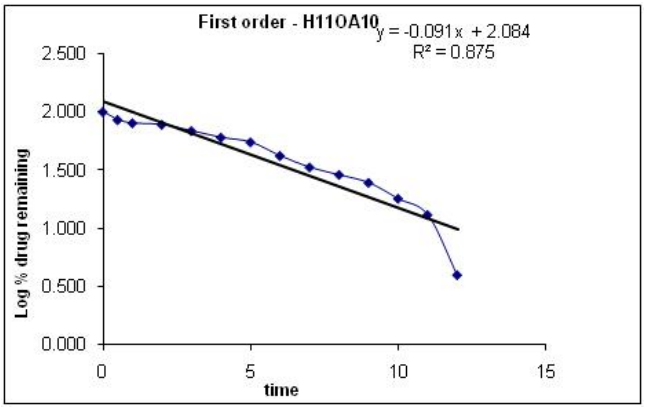

Figure 9: First order release kinetics

4. Conclusion

The aim of the present study was to develop sustained release formulation of Fluvastatin to maintain constant therapeutic levels of the drug for over 12 hrs. Various natural polymers such as Guar gum Sodium CMC and Chitosan were employed as polymers. Fluvastatin dose was fixed as 20 mg. Total weight of the tablet was considered as 150 mg. Polymers were used in the concentration of 25, 50 and 100 mg concentration. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F6) showed better and desired drug release pattern i.e.,96.10 % in 12 hours. It followed zero order release kinetics mechanism.

Table 1: Formulation composition for tablets

Formulation No.	Fluvastatin	Sodium CMC	Guar Gum	Chitosan	Mag. Stearate	Talc	MCC pH 102
F1	20	25			4	4	QS
F2	20	50			4	4	QS
F3	20	100			4	4	QS
F4	20		25		4	4	QS
F5	20		50		4	4	QS
F6	20		100		4	4	QS
F7	20			25	4	4	QS
F8	20			50	4	4	QS
F9	20			100	4	4	QS

All the quantities were in mg

Table 4: Pre-formulation parameters of blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	25.11	0.49±0.04	0.54±0.04	16.21±0.06	0.86±0.06
F2	25.67	0.52±0.09	0.52±0.04	16.87±0.05	0.98±0.05
F3	25.54	0.50±0.05	0.58±0.05	17.11±0.01	0.64±0.03
F4	25.43	0.51±0.06	0.54±0.07	17.67±0.08	1.12±0.04
F5	25.34	0.52±0.03	0.57±0.03	16.92±0.04	1.2±0.08
F6	24.22	0.53±0.04	0.56±0.06	17.65±0.09	1.06±0.09
F7	25.18	0.54±0.06	0.59±0.04	16.43±0.05	0.76±0.03
F8	24.22	0.58±0.04	0.67±0.02	17.97±0.02	1.15±0.09
F9	25.05	0.55±0.08	0.5 2±0.03	17.54±0.09	1.17±0.02

Table 5: In-vitro quality control parameters for tablets

Formulation codes	Weight variation(mg)	Hardness(kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content(%)
F1	152.5	4.5	0.50	6.8	99.76
F2	145.4	4.5	0.51	6.9	99.45
F3	148.6	4.4	0.51	4.9	99.34
F4	150.6	4.5	0.55	6.9	99.87
F5	149.4	4.4	0.56	6.7	99.14
F6	150.7	4.5	0.45	6.5	98.56
F7	152.3	4.1	0.51	6.4	98.42
F8	151.2	4.3	0.49	6.7	99.65
F9	148.3	4.5	0.55	6.6	99.12

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

Table 6: Dissolution Data of Fluvastatin Tablets Prepared With Sodium CMC

Time (hr)	Cumulative Percent Drug Dissolved		
	F1	**F2**	**F3**
0.5	25.5	20.1	16.4
1	46.7	39.4	26.7
2	76.5	55.3	34.6
3	98.4	75.3	42.4
4		87.3	55.4
5		99.4	67.4
6			85.4
7			91.5
8			97.3

Table 7: Dissolution Data of Fluvastatin tablets Prepared with Guar gum

Time (hr)	Cumulative Percent Drug Dissolved		
	F4	**F5**	**F6**
0.5	17.25	16.42	14.62
1	38.26	25.73	19.86
2	54.16	36.63	22.35
3	72.01	45.04	31.45
4	88.26	58.25	39.80
5	97.10	65.33	45.25
6		76.41	58.24
7		84.84	66.73
8		97.80	71.34
9			75.52
10			82.17
11			87.10
12			96.10

Table 8: Dissolution Data of Fluvastatin Tablets Prepared With Chitosan

Time **(hr)**	**Cumulative percent drug dissolved**		
	F7	F8	F9
0.5	10.4	9.4	8.5
1	16.5	15.6	14.5
2	28.6	21.4	18.4
3	39.5	36.7	23.4
4	48.5	42.4	28.2
5	59.4	49.6	34.8
6	69.2	55.3	40.2
7	74.5	60.3	44.8
8	82.3	72.8	50.4
9	87.78	83.52	63.34
10	98.78	88.65	69.27
11		96.56	74.86
12			79.97

Table 9: Release kinetics data for optimized formulation

Cumulative (%) Release Q	**Time (T)**	**LOG (%) Release**	**LOG (%) Remain**	**Release Rate (Cumulative % Release / t)**	**1/CUM % Release**	**PEPPAS log Q/100**	**% Drug Remaining**
0	0		2.000				100
14.62	0.5	1.165	1.931	29.240	0.0684	-0.835	85.38
19.86	1	1.298	1.904	19.860	0.0504	-0.702	80.14
22.35	2	1.349	1.890	11.175	0.0447	-0.651	77.65
31.45	3	1.498	1.836	10.483	0.0318	-0.502	68.55
39.8	4	1.600	1.780	9.950	0.0251	-0.400	60.2
45.25	5	1.656	1.738	9.050	0.0221	-0.344	54.75
58.24	6	1.765	1.621	9.707	0.0172	-0.235	41.76
66.73	7	1.824	1.522	9.533	0.0150	-0.176	33.27
71.34	8	1.853	1.457	8.918	0.0140	-0.147	28.66
75.52	9	1.878	1.389	8.391	0.0132	-0.122	24.48
82.17	10	1.915	1.251	8.217	0.0122	-0.085	17.83
87.1	11	1.940	1.111	7.918	0.0115	-0.060	12.9
96.1	12	1.983	0.591	8.008	0.0104	-0.017	3.9

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