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FORMULATION AND EVALUATION OF EXTENDED RELEASE MUCOADHESIVE MICROSPHERES OF ATORVASTATIN

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Abstract:

The objective of the present study was to prepare and evaluate the mucoadhesive microspheres of Atorvastatin. Atorvastatin microspheres were prepared by orifice- ionotropic gelation method using polymers such as HPMC (K 100 M), Carbopol 940P, Sodium CMC, Guar gum, Sodium Alginate, Ethyl Cellulose, Methyl Cellulose and Xanthan gum. Totally 15 different formulations of Atorvastatin were prepared by using the above polymers. The microspheres were characterized for drug content, entrapment efficiency, mucoadhesive property by in vitro wash-off test and in-vitro drug release. The formulation F10 was selected as an ideal formulation based on the in vitro release profile which shows an extended drug release of 96.11% upto 8 hours in phosphate buffer of pH 7.0. Surface morphology (SEM analysis) and drug-polymer interaction studies (FT-IR analysis) were performed only for the ideal formulation (F10). The microspheres were smooth and elegant in appearance showed no visible cracks as confirmed by SEM and FT-IR studies indicated the lack of drug-polymer interactions in the ideal formulation (F10). The in vitro release data of all microsphere formulations were plotted in various kinetic equations to understand the mechanisms and kinetics of drug release. The ideal formulation (F10) followed Higuchi kinetics and value of "n," is calculated to be 0.86 indicated that the drug release shows non-fickian diffusion."

***Key Words**: SEM, FT-IR, Carbopol 940,HPMC (K 100 M),orifice- ionotropic gelation method, Atorvastatin, Sodium Alginate , Sodium CMC.*

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INTRODUCTION

Mucoadhesive formulations orally would achieve a substantial increase in the length of stay of the drug in GI tract stability problem in the intestinal fluid can be improved. Mucoadhesive microsphere [1] carrier systems are made from the biodegradable polymers in sustained drug delivery. Recently, dosage forms that can precisely control the release rates and target drugs to a specific body site have made an enormous impact in the formulation and development of novel drug delivery systems. Microspheres form an important part of such novel drug delivery system. They have varied applications and are prepared using assorted polymers. It would, therefore be advantageous to have means for providing an intimate contact of the drug delivery system with the absorbing membrane [2]. This can be achieved by coupling bioadhesion characteristics to microspheres and developing bioadhesive microspheres. Bioadhesive [3] microspheres have advantages such as efficient absorption and enhanced bioavailability of drugs owing to high surface to volume ratio, a much more intimate contact with the mucus layer and specific targeting of drugs to the absorption site [4].

To overcome the relativity short GI time and improve localization for oral controlled or sustained release drug delivery systems [5]. The polymers which adhere to the mucin epithelial surface are effective and lead to significant improvement in oral drug delivery based on these three broad categories [6].

Atorvastatin [7] is anti hyperlipidemic used to control elevated cholesterol, or hypercholesterolemia. Atorvastatin is a member of the statin class of pharmaceuticals; it is structural analog of HMG-CoA (3-hydroxy-3-methylglutaryl-coenzyme). Like other assents, it inhibits the enzyme hydroxyl methylglutaryl-CoA (HMG-CoA) reductase. It has an extremely high affinity for this enzyme and was considered the most potent agent of the HMG-CoA class. Atorvastatin is inactive lactone prodrug and hydrolyzed in the gastrointestinal tract to the active ß - hydroxy derivative. It decreases total cholesterol, LDL cholesterol, triglycerides, and apolipoprotein B, while increasing HDL.

In the present study, an attempt was made to develop mucoadhesive Atorvastatin microspheres by orifice-ionotropic gelation technique using polymers such as sodium alginate, HPMC (K 100 M), carbopol 940P, sodium CMC, guar gum, ethyl Cellulose, methyl cellulose and xanthan gum. The prepared microspheres were evaluated for drug content, entrapment efficiency, mucoadhesive property, surface morphology, drug polymer interaction and *in vitro* drug release studies.

MATERIALS AND METHODS

Materials

Atorvastatin was obtained as a gift sample from Pharma train (Hyderabad, India). HPMC (K 100 M), Carbopol 940P, Sodium CMC, Guar gum, Sodium Alginate, Ethyl Cellulose, Methyl Cellulose, Xanthan gum, Calcium chloride were supplied by SD Fine Chemicals Ltd., Mumbai. All solvents used were of analytical grades and were used as obtained.

Preparation of Atorvastatin Microspheres:

Atorvastatin and all other polymers were individually passed through sieve no ≠ 60. The required quantities of Sodium alginate and the mucoadhesive polymer were dissolved in purified water to form a homogenous polymer solution. The Drug, Atorvastatin was added to the polymer solution and mixed thoroughly with a stirrer to form a viscous dispersion. The resulting dispersion was then added manually drop wise into calcium chloride (10 % w/v) solution through a syringe with a needle of size no. 18. The added droplets were retained in the calcium chloride solution for 15 minutes to complete the curing reaction and to produce the spherical rigid microspheres. The microspheres were collected by decantation, and the product thus separated was washed repeatedly with water and dried at 45°C for12 hours.

Drug Content:

Powder equivalent to 10 mg of Atorvastatin was dissolved in 20 ml methanol and volume made up to 100 ml with p^H 7.0 phosphate buffer with 0.5%SLS. The Solution was filtered through Whatmann filter paper no. 41 to obtain the stock Solution A. The Stock Solution A (1 ml) was

Diluted to10ml to obtain the stock Solution B .The Absorbance of the resulting solution was measured at wavelength maximum of 239nm using double beam UV-Visible Spectrophotometer with 1cm pathlength sample cells.

Entrapment Efficiency:

Entrapment efficiency was calculated using the following formula:

$$\text{Entrapment Efficiency} = \frac{\text{Estimated percentage drug content}}{\text{Theoretical percentage drug content}} \text{X } 100$$

In *Vitro* Wash-off Test [7] :

The mucoadhesive properties of the microspheres were evaluated by the *In vitro* wash-off test.

A 4-cm by 4-cm piece of goat intestine mucosa was tied onto a glass slide using thread. Microspheres were spread (∽100) onto the wet, rinsed, tissue specimen and the prepared slide was hung on to one of the groves of a USP tablet disintegrating test apparatus. The disintegrating test apparatus was

operated such that the tissue specimen wasgiven regular up and down movements in the beakers containing the simulated gastric fluid USP (pH 1.2), and the pH 7.0 Phosphate buffer. At the end of 30 minutes, 1 hour, and at hourly intervals up to 8 hours, the number of microspheres still adhering onto the tissue was counted. The results of the in Vitro wash-off test of batches F1 to F15 are shown in Table No: 11-12

$$\text{Mucoadhesion Property} = \frac{\text{No.ofmicrospheresadhered}}{\text{No.ofmicrospheresapplied}} \text{ X } 100$$

In *Vitro* Dissolution Studies of Microspheres:

900ml of pH 7.0 phosphate buffer was placed in the dissolution vessel and the USP dissolution apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temperature of 37°C± 0.5°C. Microspheres were placed in the dissolution vessel and the vessel was covered, the apparatus was operated for 8hrs at 50 rpm. At definite time intervals the 5 ml of the dissolution fluid was withdrawn, filtered and again 5ml blank sample was replaced. Suitable dilutions were done with the dissolution fluid and the samples were analyzed spectrophotometrically at λmax 239 nm using a UV-spectrophotometer (Lab India).The results are given in Table No: 2-6.

Release Kinetics

The analysis of the drug release mechanism from a pharmaceutical dosage form is an important but complicated process and is practically evident in the case of mucoadhesive controlled release systems. As a model-dependent approach, the dissolution data was fitted to four popular release models such as zero-order, first-order, diffusion and Korsemeyer - Peppas equations, which have been described in the literature. The order of drug release from mucoadhesive controlled release systems was described by using zero order kinetics or first orders kinetics(Martindale *et al* 2005). The mechanism of drug release from the mucoadhesive controlled systems was studied by using the Higuchi equation and the Korsemeyer - Peppas equation. The results are given in Table No – 8.

Zero Order Release Kinetics

It defines a linear relationship between the fractions of drug released versus time.

$$Q = k_o t$$

Where, Q is the fraction of drug released at time t and $k_o$is the zero order release rate constant.

A plot of the fraction of drug released against time will be linear if the release obeys zero order release kinetics.

First Order Release Kinetics:

Wagner assuming that the exposed surface area of a tablet decreased exponentially with time during dissolution process suggested that drug release from most of the slow release tablets could be described adequately by apparent first-order kinetics(Kalyanakar T.M *et al* 2010).The equation that describes first order kinetics is

$$\text{In } (1\text{-}Q) = - K_1 t$$

Where, Q is the fraction of drug released at time t and k_1 is the first order release rate constant.

Thus, a plot of the logarithm of the fraction of drug undissolved against the time will be linear if the release obeys the first order release kinetics.

Higuchi Equation:

It defines a linear dependence of the active fraction released per unit of surface (Q) and the square root of time.

$$Q=K_2 t^{½}$$

Where, K2 is the release rate constant.

A plot of the fraction of drug released against square root of time will be linear if the release obeys Higuchi equation. This equation describes drug release as a diffusion process based on the Fick's law, square root time dependant.

Power Law:

In order to define a model, which would represent a better fit for the formulation, dissolution data was further analyzed by Peppa's and Korsemeyer equation (Power Law).

$$M_t/M_\alpha = K.t^n$$

thedrug release, The value of n can be used as abstracted in Table No – 8 . A plot between logs of M_t/M_α against log of time will be linear if the release obeys Peppa's and Korsemeyer equation and the slope of this plot represents "n" value.

Drug-Polymer Interaction Study

The FTIR spectra of the drug (alone), polymer (alone) and the drug-polymer mixture were recorded by the potassium bromide pellet method.

Morphology Study:

The External surface morphology was evaluated by using the SEM (Horizon 230, CIPRA Labs, Hyderabad) .The microspheres were mounted directly on the SEM sample stub using the double sided sticking tape and coated with gold film (thickness 200nm) under the reduced pressure (0.001 mm of Hg). The voltage was used is 5KV.

RESULTS AND DISCUSSION

FT IR Studies:

From the infrared spectra it is clearly evident that there were no interactions of the drug. IR Spectrum of the pure drug shows the characteristic peaks at 3550cm^{-1}, 1043 and 1011cm^{-1}. The IR Spectrum of Drug and polymer exhibited peaks at 3429.27$cm^{-1}$and 1055cm^{-1}.This confirms the undisturbed structure of

the drug in the formulation (This proves the fact that there is no potential incompatibility of the drug with the polymers used in the formulation. Hence, the formula for preparing Atorvastatin mucoadhesive microspheres can be reproduced in the industrial scale without any apprehension of possible drug-polymer interactions.

SEM Studies

It was observed that the optimized formulation (F10) of the mucoadhesive microspheres were spherical and completely covered with the coat polymer (fig no.09). At higher magnification, pores were observed. The pores can influence the rate of release of the drug from the microspheres.

Discussion

Microspheres of Atorvastatin with a coat consisting of sodium alginate and different mucoadhesive polymers - Sodium CMC, Methylcellulose, Carbopol 940P, HPMC K100M, Ethyl cellulose, in 1:1, with HPMC K100M, Carbopol 940P, Guar gum, Xanthan gum, Methyl cellulose in 1:2, with Guar gum ,and Xanthan gum 1:3 could be prepared by the orifice-ionic gelation process. The Microspheres were found to be discrete, spherical, free-flowing, and of the mono- lithic matrix type. The prepared batches of microsphere were evaluated for Micromeritic study such as tapped density, bulk density, Carr's index, Hausner ratio and angle of repose(Table No: 10).Microspheres with a coat consisting of sodium alginate and a mucoadhesive polymer exhibited good mucoadhesive properties in the in vitro wash-off test. (Table No: 11-12). The microencapsulation efficiency was in the range of 57% to 96% being highest for F4 and lowest for F5.Result of *in vitro* wash-off test studies indicate that the formulation F10, F13, F14, and F15 having considerable mucoadhesive property.

Atorvastatin release from the microspheres was studied in phosphate buffer (pH 7.0) for 8 hours. Drug release from the microspheres was slow and depended on the composition of the coat. Drug Release followed zero-order kinetics (R^2 = 0.953). From the all batches F10 (Drug: Sod. Alginate : Methyl cellulose = 1:2:1) batch is considered to be the most promising formulation batch because among all the batches it shows better extent of drug release 96.11% (8hrs) , good entrapment efficiency (78%), and *in vitro* wash-off test shows good mucoadhesive property. Atorvastatin release from alginate – Methyl cellulose (F10) wasslow and extended over a period of 8hrs and these microspheres were found suitable for the oral controlled release formulation.

Higuchi plot showed a "R^2" value of 0.980 in the optimized formulation (F10) suggesting that the diffusion plays an important role in the controlled release formulations. The data was fitted to Korsemeyer -Peppas equation and the value of diffusional exponent 'n' (0.86) indicated that the drug release shows non-fickian diffusion. Observation of all formulation for physical characterization had shown that, all of them comply with the specification of official pharmacopoeias and/or standard references. The FTIR studies indicated the lack of drug – polymer interactions in the Optimized formulation (F10). (Table no: 13, Figure No: 05 - 08).The SEM results indicated that the shape of Mucoadhesive microspheres were spherical and completely covered with the coat polymer (fig no.09).

CONCLUSION

The microspheres exhibited good mucoadhesive properties for optimized formulation (F10) in the in vitro wash off test. Atorvastatin release from these muco-adhesive microspheres was slow and extended over up to 8 hrs and depended on the composition of the coat. Drug release was diffusion controlled and followed Higuchi kinetics. These mucoadhesive microspheres are thus suitable for oral controlled release of Atorvastatin. The FTIR studies ruled out the drug-polymer interaction in the optimized formulation (F10). The SEM results have shown the Size and Surface Morphology of the Atorvastatin Mucoadhesive Microspheres.

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Table 1: Composition of Different Formulations of Atorvastatin Microspheres

Batch code	Coat Composition	Ratio
F1	Drug: Sod. Alginate	1:1
F2	Drug: Sod. Alginate : Carbopol**(**940**)**	1:0.9:0.1
F3	Drug: Sod. Alginate : HPMC (K100M**)**	1:0.9:0.1
F4	Drug: Sod. Alginate : Sod.CMC	1:0.9:0.1
F5	Drug: Sod. Alginate : Ethyl cellulose	1:0.9:0.1
F6	Drug: Sod. Alginate	1:2
F7	Drug: Sod. Alginate : Carbopol**(**940**)**	1:2:1
F8	Drug: Sod. Alginate : HPMC **(**K100M**)**	1:2:1
F9	Drug: Sod. Alginate : Guar gum	1:2:1
F10	Drug: Sod. Alginate : Methyl cellulose	1:2:1
F11	Drug: Sod. Alginate : Xanthan gum	1:2:1
F12	Drug: Sod. Alginate : Guar gum	1:3:1
F13	Drug: Sod. Alginate : Xanthan gum	1:3:1
F14	Drug: Sod. Alginate : Xanthan gum	1:3:0.5
F15	Drug: Sod. Alginate : Xanthangum : Guar gum	1:3:1:1

Table 2: Dissolution Data of Mucoadhesive Microspheres of Atorvastatin

Time (hrs)	Cumulative Percent Drug Release (n = 3±SD)		
	F1	**F2**	**F3**
0.5	12.6 ± 2.0	21.42 ±1.00	10.46 ±2.48
1	34.42 ±3.2	35.68 ±1.25	21.27±1.2
2	50.55 ±1.21	64.73 ±1.34	36.3±7.34
3	80.04 ±1.65	75.91 ±1.9	69.26 ±8.7
4	87.68 ±3.47	92.67 ±1.30	102.8 ±2.8
6	107.4 ±2.02	101.18 ±0.93	---

Table No. 3: Dissolution Data of Mucoadhesive Microspheres of Atorvastatin

Time (hrs)	Cumulative Percent Drug Release*		
	F4	**F5**	**F6**
0.5	12±1.8	13.7±2.2	22.5±0.9
1	22.86±5.52	16.87±0.67	49.28±5.8
2	55.6±5.3	26.37±7.17	82.86±3.06
3	73.46±1.22	42.22±7.65	89.74±1.92
4	97.89±1.48	48.39±4.19	107.82±1.35
6	105.67±1.88	56.78±4.84	----
8	----	59.21±3.84	----

***(Mean of three values ±SD)**

Table 4: Dissolution Data of Mucoadhesive Microspheres of Atorvastatin

Time (hrs)	Cumulative Percent Drug Release (n = 3±SD)		
	F7	F8	F9
0.5	13.65±4.56	32.79±2.51	12.45±1.58
1	40.27±3.03	42.42±1.59	31.69±4.34
2	53.16±3.67	65.94±1.73	56.89±2.52
3	63.54±5.75	94.39±0.99	73.41±1.87
4	85.24±4.2	102.59±1.56	88.58±5.8
6	105.75±6.76	----	108±1.73

Table 5: Dissolution Data of Mucoadhesive Microspheres of Atorvastatin

Time (hrs)	Cumulative Percent Drug Release (n = 3±SD)		
	F10	F11	F12
0.5	**8.05**±0.18	11.49±2.52	14.4±0.61
1	**15.26**±0.63	19.54±4.51	29.34±0.62
2	**23.11**±1.25	30.46±7.02	36.26±2.22
3	**27.95**±0.15	35.66±7.59	54.9±3.83
4	**33.5**±4.13	39.39±7.81	54.9±0.67
6	**56.07**±3.16	53.93±1.89	73.65±3.21
8	**96.11**±2.98	65.52±3.44	---

Table 6: Dissolution Data of Mucoadhesive Microspheres of Atorvastatin

Time (hrs)	Cumulative Percent Drug Release (n = 3±SD)		
	F13	F14	F15
0.5	12.17±3.1	4.15±0.83	12.3±1.08
1	28.29±5.19	7.00±1.76	17.9±0.609
2	34.69±3.75	15.43±1.31	22.96±0.254
3	39.68±1.34	23.83±3.88	29.84±2.26
4	43.51±1.97	29.31±3.67	38.56±1.82
6	53.79±2.99	43.97±4.57	48.22±0.95
8	63.29±7.87	61.5±4.68	61.18±3.2

Table 7: Quality Control Parameters of Mucoadhesive Microspheres of Atorvastatin

S.No	Batch code	Drug Content		Encapsulation efficiency
		Theoretical (percentage)	Practical (Percentage)	
1	F1	50	39.70	79.40±0.025
2	F2	50	42.02	84.05±0.027
3	F3	50	39.03	78.07±0.027
4	F4	50	48.33	96.67±0.02
5	F5	50	28.73	57.47±0.012
6	F6	33.33	26.24	78.73±0.013
7	F7	25	19.14	76.57±0.032
8	F8	25	17.47	69.91±0.013
9	F9	25	18.60	74.40±0.017
10	**F10**	**25**	**19.37**	**77.51±0.025**
11	F11	25	18.10	69.64±0.019
12	F12	20	14	70.0±0.014
13	F13	20	13.62	65.75±0.017
14	F14	22.22	16.49	71.46±0.015
15	F15	16.66	10.59	61.18±0.012

Table 8: Release Kinetics of Atorvastatin Mucoadhesive Microspheres

(Coefficient Of Correlation (R^2) values of different batches of Atorvastatin Mucoadhesive microspheres)

Formulation	Zero Order	First Order	Higuchi's	Peppa's
F1	0.939	0.943	0.984	0.961
F2	0.904	0.964	0.978	0.940
F3	0.980	0.820	0.927	0.969
F4	0.936	0.822	0.976	0.944
F5	0.872	0.929	0.957	0.945
F5	0.872	0.929	0.957	0.945
F6	0.926	0.965	0.967	0.957
F7	0.937	0.933	0.976	0.977
F8	0.951	0.918	0.985	0.992
F9	0.950	0.976	0.996	0.985
F10	**0.953**	**0.913**	**0.980**	**0.826**
F11	0.944	0.986	0.989	0.987
F12	0.987	0.946	0.954	0.961
F13	0.878	0.968	0.967	O.969
F14	0.998	0.996	0.966	0.996
F15	0.965	0.994	0.981	0.980

Table 9: Dissolution Parameters of Atorvastatin Mucoadhesive Microspheres

Formulation	Dissolution Parameters					
	N	K_0(mg/L/hr)	K_1(hr^{-1})	T_{50}(hrs)	T_{75}(hrs)	T_{90}(hrs)
F1	0.629	8.64	0.557	2	2.7	4.3
F2	0.591	5	0.610	1.5	3	4
F3	1.141	15.71	0.400	2.5	3.2	3.5
F4	0.882	4.16	0.950	1.8	3.3	4
F5	0.610	2.93	0.090	4.5	--	--
F6	0.558	4.68	0.835	1	1.8	3
F7	0.538	12.06	0.414	1.5	3.5	4.7
F8	0.668	11.2	0.780	1.3	2.4	3
F9	0.684	9.56	0.550	1.3	3.2	4.3
***F10**	**0.861**	**10.86**	**0.13**	**5.3**	**6.8**	**7.5**
F11	0.553	4.14	0.117	5	--	--
F12	0.730	8.92	0.310	2.7	4.2	4.8
F13	0.380	4.85	0.105	5.2	--	--
F14	0.38	7.46	0.09	6.6	--	--
F15	0.593	4.83	0.101	6	--	--

***Optimized Formulation.**

Table 10: Flow Properties of Different Formulations

Formulation	Angle of Repose	Bulk density(g/ml)	Tapped density(g/ml)	Hausner ratio	Compressibility index
F1	13	0.816	0.816	1	0
F2	14	0.672	0.617	1.06	6.2
F3	12	0.546	0.602	1.18	6.6
F4	14	0.692	0.721	1.04	4.02
F5	15	0.297	0.361	1.24	9.2
F6	13	0.656	0.772	1.27	7.8
F7	17	0.454	0.552	1.21	16.75
F8	19	0.762	0.721	1.06	5.96
F9	14	0.659	0.621	1.09	8.59
***F10**	**18**	**0.601**	**0.689**	**1.08**	**10.04**
F11	17	0.721	0.867	1.10	17.03
F12	16	0.426	0.618	1.16	15.02
F13	17	0.618	0.723	1.17	14.28
F14	15	0.536	0.590	1.10	9.1
F15	19	0.917	0.871	1.06	5.4

Table 11: Percent Mucoadhesive Property of the Microspheres of Atorvastatin in p^H 1.2 HCl buffer.

Time (hr)	Percent Mucoadhesive property														
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
0.5	33	41	22	40	54	40	41	50	78	76	54	61	66	84	74
1	**21**	**35**	8	**35**	46	28	32	38	69	68	40	46	58	**71**	66
2	---	**21**	---	**24**	**34**	10	24	**21**	43	52	21	37	42	62	**51**
3	---	**12**	---	**13**	**26**	---	**16**	---	36	43	**10**	28	30	46	**36**
4	---	---	---	---	**14**	---	**4**	---	24	**37**	---	22	26	26	**28**
5	---	---	---	---	---	---	---	---	12	**28**	---	12	18	11	**13**
6	---	---	---	---	---	---	---	---	**5**	**14**	---	----	9	7	**6**
7	---	---	---	---	---	---	---	---	---	---	---	--	---	---	---
8	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---

Table 12: Percent Mucoadhesive Property of the Microspheres of Atorvastatin in pH 7.0 Phosphate buffer.

Time (hr)	Percent Mucoadhesive property														
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
0.5	44	51	48	30	57	52	28	54	70	78	56	64	60	80	70
1	20	36	31	**29**	**37**	44	17	42	54	69	42	54	51	70	**61**
2	---	14	27	---	**29**	**13**	---	34	40	60	32	38	47	62	**53**
3	---	---	---	---	**13**	---	---	**12**	28	**55**	25	37	38	51	**49**
4	---	---	---	---	---	---	---	---	18	**43**	**15**	24	29	43	**40**
5	---	---	---	---	---	---	---	---	10	**39**	**8**	---	20	33	**34**
6	---	---	---	---	---	---	---	---	---	**26**	---	----	11	28	**21**
7	---	---	---	---	---	---	---	---	---	**8**	---	---	7	11	**9**
8	---	---	---	---	---	---	---	---	---	--	---	---	---	---	---

Table 13 : Data for IR Spectra of Atorvastatin

Functional Group	Frequency (cm^{-1})
C-OH Aromatic (stretching)	3550
C=O (stretching) Acid Ester	1011
C-O-C (stretching)	1043

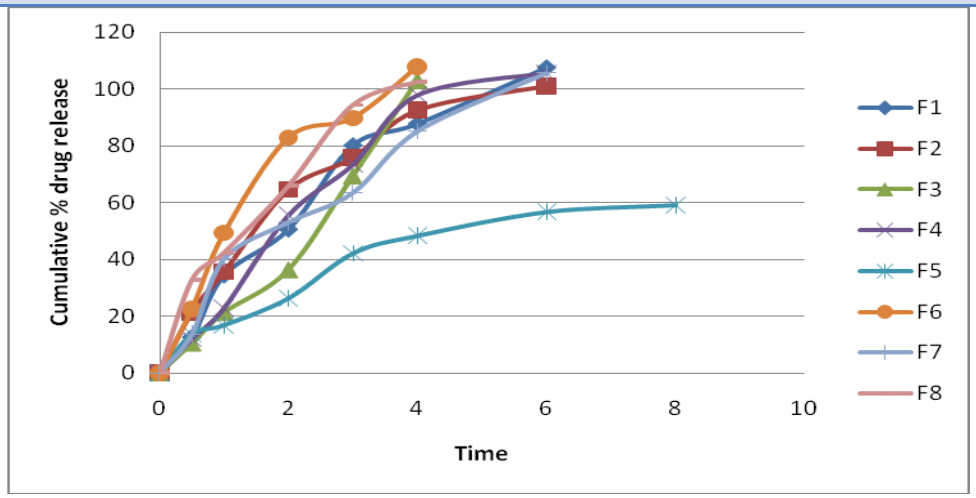

Fig 1: Dissolution Profile of Mucoadhesive Microspheres of Atorvastatin (F1 – F8) Formulations.

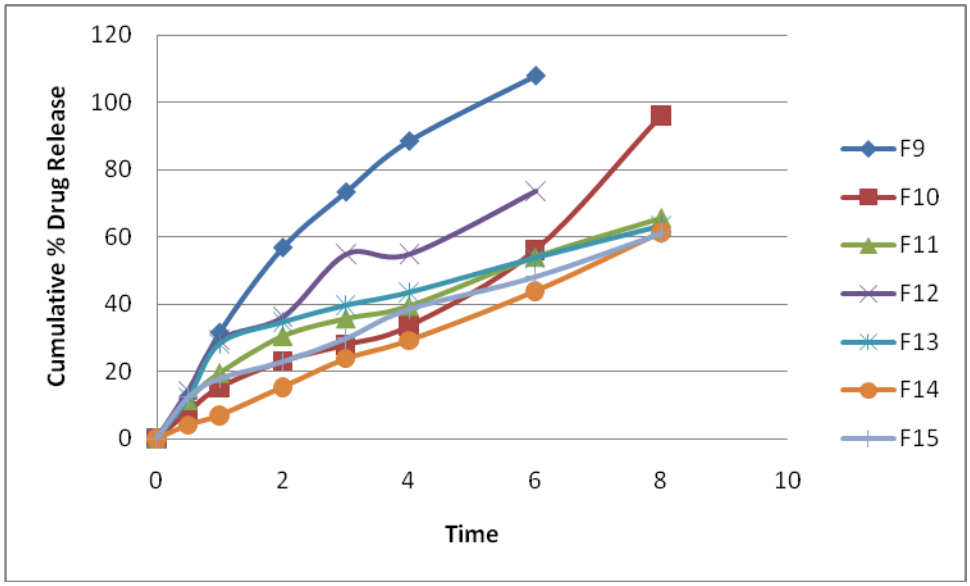

Fig 2: Dissolution Profile of Mucoadhesive Microspheres of Atorvastatin (F9 – F15) Formulations.

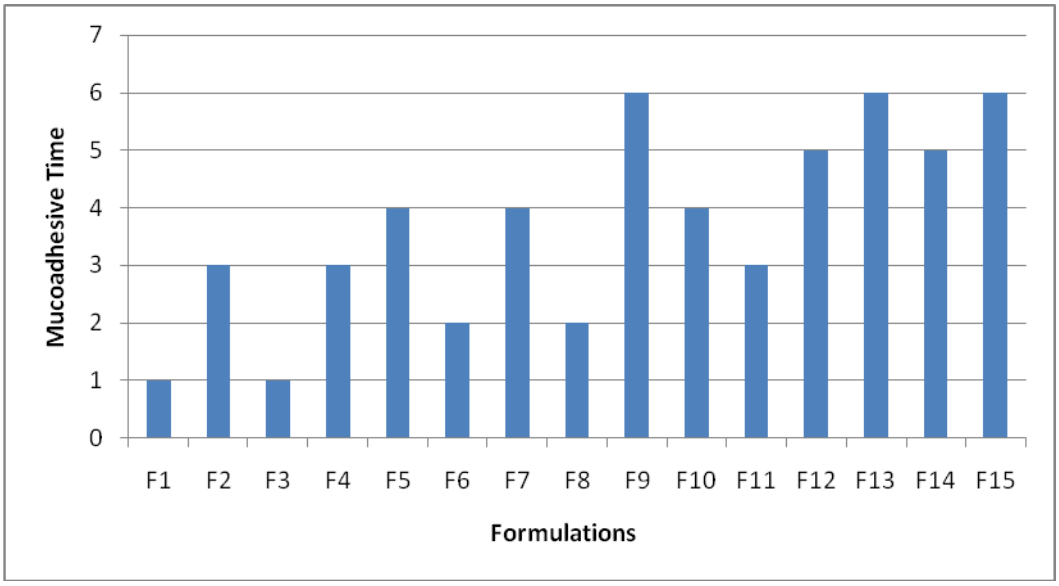

Fig 3: Mucoadhesive Property of Different Formulations in p^{H} 1.2 HCl buffer.

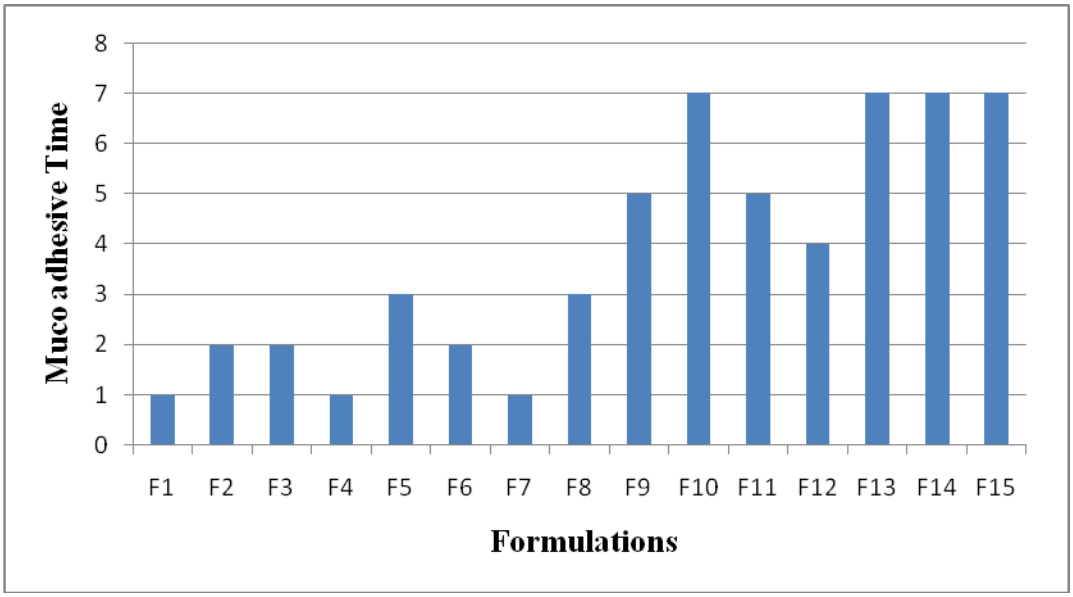

Fig 4: Mucoadhesive Property of different formulations in pH 7.0 Phosphate buffer.

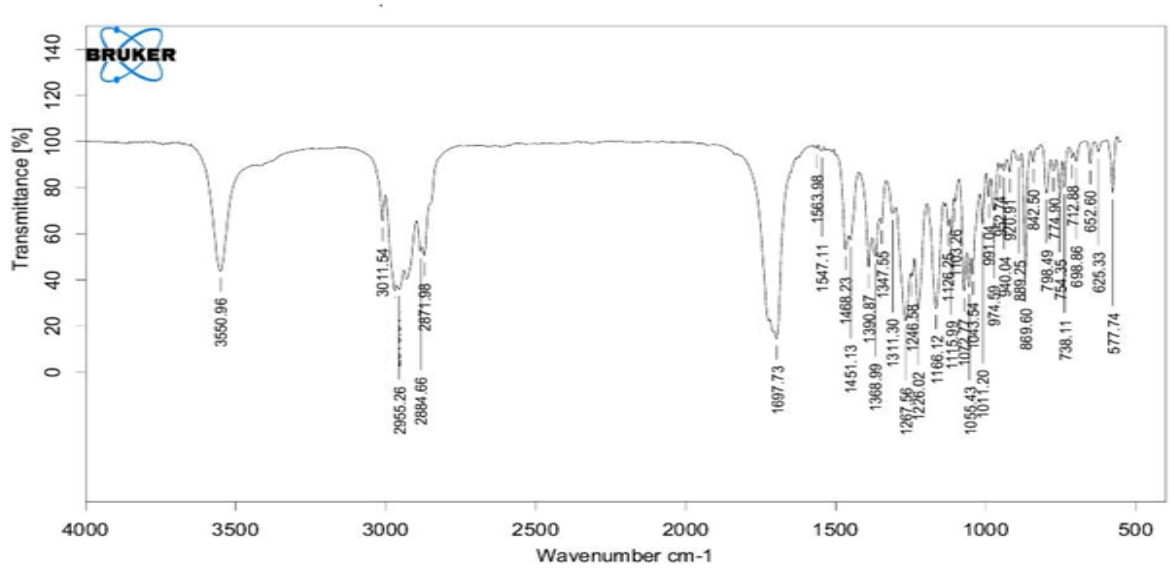

Fig No 5: FTIR Spectrum of Atorvastatin

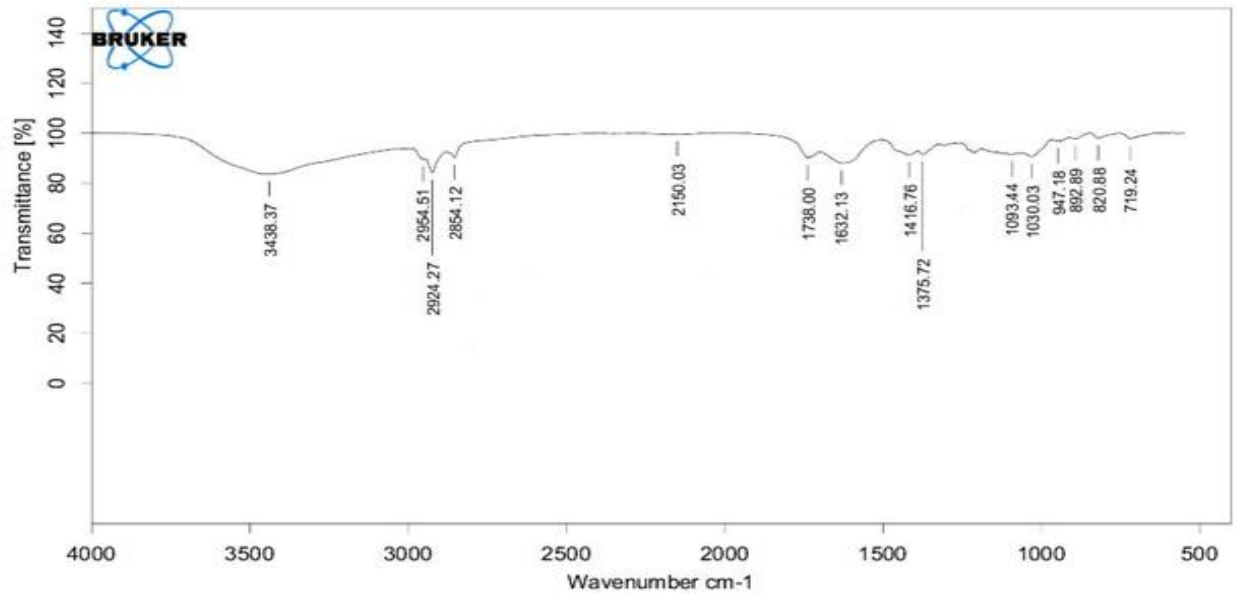

Fig 6: FTIR Spectrum of Sodium Alginate

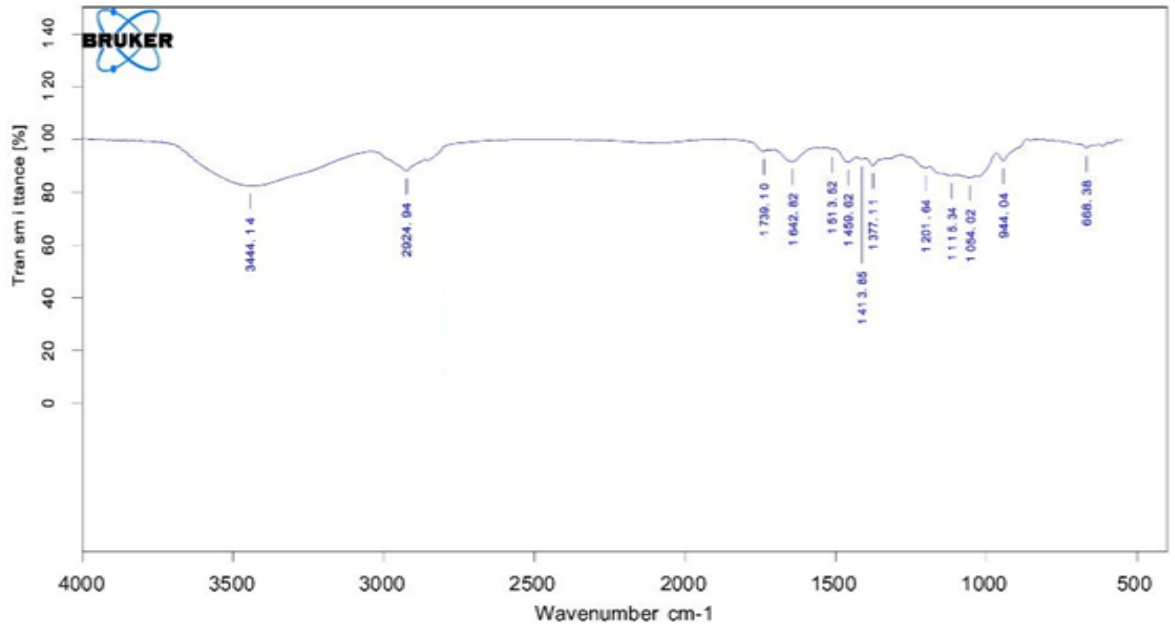

Fig 7: FTIR Spectrum of Methyl Cellulose

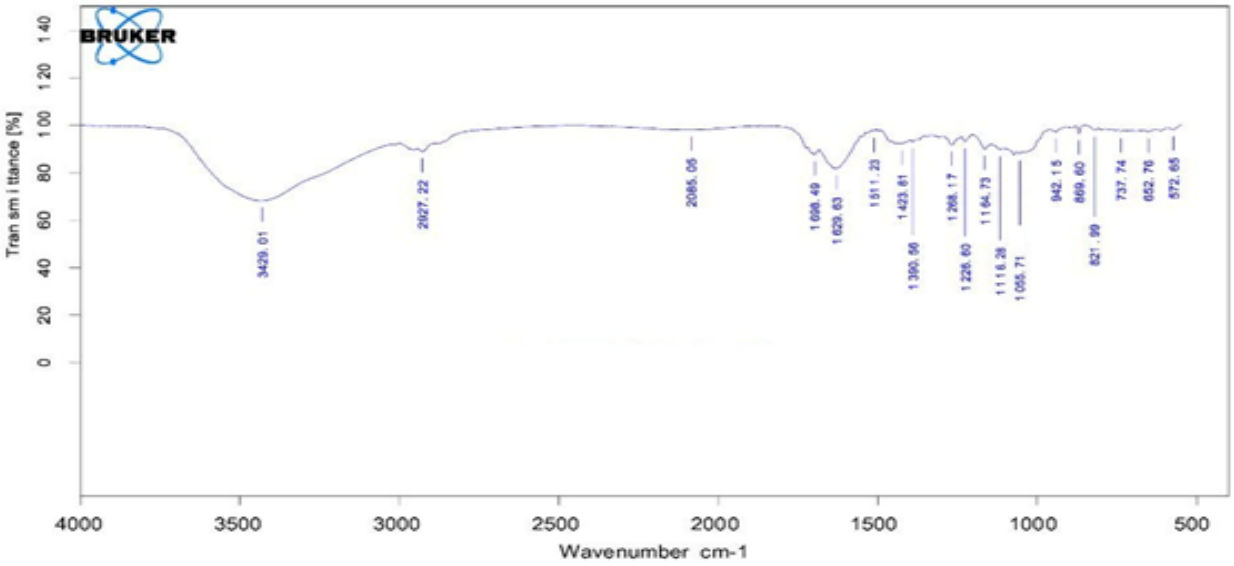

Fig 8: FTIR Spectrum of Optimized Formulation

Fig 9: SEM images of Optimized Formulation (F10)