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Research Article

STUDIES ON COMPRESSION AND DRUG RELEASE CHARACTERISTICS OF XANTHIUM GUM PELLETS OF DIFFERENT COMPOSITIONS

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ABSTRACT

The filler used in preparation of pellets affects physical properties, compression and drug release rates. The present investigation was aimed to develop a sustained drug delivery system for a short half life drug, Simvastatin with a view to prolong the release with a sustained release mechanism. Simvastatin is an antilipidaemic agent. Characterization of drug was done by performing the determination of solubility, melting point and FTIR spectroscopy. The prepared batches of pellets were evaluated for micromeritic study such as particle size determination, true density, bulk density, degree of compression, specific surface area and angle of repose. All the batches of pellets were compressed into tablets and evaluated for general appearance, weight variation, hardness, content uniformity, and dissolution study. From the results of all these studies, batch F6 was found to show the best results containing Xanthan gum (16%) and Lactose monohydrates (8%) and selected as an optimized batch. The optimized batch was subjected for further studies such as Scanning Electron Microscopy (SEM) to demonstrate pellets morphology and FTIR to determine the drug-polymer interaction. Optimized formulation was subjected to accelerated stability study for a period of 30 days at 40 ± 2^0C and 75 ± 5 % RH. Formulation was subjected for thickness, hardness, drug content and *in-vitro* drug release studies at interval of 15 and 30 days.

Keywords: Simvastatin, Xanthan gum, Lactose monohydrates, Scanning Electron Microscopy (SEM)

INTRODUCTION

This research aims at the study of the effects of fillers on the release characteristics of model drug and production of tablets for the sustained delivery of the Simvastatin because of the certain limitation of immediate-release Simvastatin such as short half-life period of 2-3 hrs, multiple daily dosing requires to maintain adequate effective concentration throughout 24 hr.

Mechanism of Pellet Formation and Growth [1]

One of the most significant properties of pellet is their ability to withstand the mechanical forces that act on them during processing or subsequent handling and coating.
Processing conditions do ply a very significant role in the development of good quality pellets, but it is the physical [bonding] forces which first bond the primary particles and initiate the pelletization process. These forces coupled with the elementary growth mechanisms ultimately determine strength and performance of the pellets.
Atherosclerosis[2,3] is an essentially metabolic disorder characterized by faulty transport, distribution and deposition of lipids. In familial hypercholesterolaemia the LDL receptor is defective and subsequent formation of athromatous plaques in intimal wall of arteries is mostly accepted. In order to inhibit and control the atherogenic process, the hypolipidaemic agents have been used prophylactically and therapeutically in man.

MATERIALS AND METHODS

Chemical used

Simvastatin supplied by Dr. Reddy's Lab. Ltd. Hyderabad, Xanthan Gum and ß-Cyclodextrin by Institute of Chemical Technology, Mumbai, Tribasic calcium phosphate and Magnesium Stearate by Loba chemicals, Mumbai. Lactose monohydrate Merck Chemical, Mumbai.

Equipment used

Hardness tester Dolphin Mumbai, Tablet Machine Cad mach Machinery Co. Pvt Ahmadabad, Single pan digital balance Afcoset Mumbai, Dissolution test apparatus (six stages) Electro lab, UV-visible Spectrophotometer Shimazdu 1700, pH Meter Hanna Instruments. Vernier Calliper Mututoyo Japan, Stability Chamber Skylab, Mumbai. IR Shimadzu FTIR84005.

Preparation of Pellets[4, 5]

In all cases following general procedure for the preparation of pellet were followed

1. All the formulation was based in MCC PH 101, simvastatin as a model drug, xanthan gum as a controlled release agent, povidone as a secondary binder and filler excipients were sifted through sieve no. 100 and accurately weighed.
2. Povidone was dissolved in ethanol / distilled water 50 %(v/v) and was added to powder blend in gradual manner and after each addition it was dispersed thoroughly in order to get optimum wet mass.
3. The damp mass was put into sieve no 14 to obtain extrudate.
4. Extrudates so obtained were spheronized by rotating in round box in circular motion to give the Pellets.
5. The pellets produced were dried at 45-50 °C.

Preparation of tablets[6]

Unlubricated pellets were compressed using a Cadmach single punch press was equipped with flat–faced punches of 8mm diameter. The punches and die were lubricated before every compaction with magnesium stearate suspension (1%w/w in ethanol) 200mg sample of pellets containing 20 mg of simvastatin of size fraction 1000-1400µm were accurately weighed and manually fill in to the die. The prepared tablets were stored in desecrator at room temperature for at least 48 hr before being subjected to any characterization to remove any residual humidity. Formulation Chart of Simvastatin tablets shown in Table 1.

Evaluation of Prepared Pellets [5,7, 8, 9,18]

Bulk density

Blend was weighed and transferred to a measuring cylinder. Then bulk volume was noted. Bulk density was calculated by using formula.

$$D_f = M / Vp$$

Where, D_f = Loose bulk density, M = Weight of samples in grams, Vp = Final volumes of granules in cm^3

Angle of repose

A funnel was fixed at a height approximately of 2-4 cm over the platform. The loose powder was slowly passed along the wall of funnel, till the cone of the powder formed. Determine the angle of repose by measuring the height of the cone of powder and radius of the heap of powder

$$\theta = \tan^{-1} h / r$$

True density

The True density of the pellet was determined by solvent displacement method

$$D_t = M / Vp$$

Where, D_t = True density density, M = Weight of samples in grams, Vp = Final volumes of liquid in cm^3

Degree of compression

The degree of compression of the pellets was calculated by applying

$$C\% = (Ho-Hp / Ho) \times 100$$

Where, Ho is the estimated height of pellet bed in-die before compression, Hp is the height of the compact.

Specific surface area

Specific surface area of pellet was determined by mathematical calculation method

$$SA = 6 / {}^{p}dvs$$

Where, SA = Specific Surface Area, dvs = mean volume surface diameter, ^{p} = true density

***In- vitro* drug release studies of formulated pellets [10, 11]**

In-Vitro drug release studies of simvastatin were carried out using USP type II Dissolution Testing Apparatus (6 vessel assembly, Paddle type) at 50 rpm**.** The dissolution medium consisted of 900 ml of PH 7**.**0 buffer solution containing 0**.**5% SLS in 0**.**01M sodium phosphate**.** Temperature maintained at 37±0**.**5^{0}C**.** Aliquots of 5ml was withdrawn at predetermined time intervals & an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced**.** Aliquots were filtered through whatman filter paper, suitably diluted using phosphate buffer pH 7**.**0 and analyzed spectrophotometrically at 238 nm**.**

Evaluation of Prepared Tablets

Hardness[12]

Hardness of tablet was measured using Monsanto hardness tester. It is the pressure required to fracture diametrically placed tablets by applying the force. The hardness of 6 tablets, from each batch was determined and means hardness was taken into account, which was expressed in kg/cm^2.

Weight variation test[12]

Weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weight to the average USP weight variation test.

Friability[12]

Roche friabilator was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Pre-weighed sample of tablets was placed in the friabilator, which was then operated for 100 revolutions. Tablets were re-weighed. The percentage friability was measured using the formula,

% Friability = Initial weight-Final weight / Final weight × 100

Content uniformity [12]

For this at least 30 tablets were randomly selected. Out of 30 tablets, 10 tablets were crushed into fine powder and assayed individually; the tablet should be within 85% to 115% of the labeled claim.

Thickness [12]

The thickness of the tablet was measured using Vernier caliper. Thickness of five tablets from each batch was measured and mean was calculated.

***In- vitro* drug release studies of formulated tablets [13,14]**

In-Vitro drug release studies of simvastatin were carried out using USP type II Dissolution Testing Apparatus (6 vessel assembly, paddle type) at 50 rpm**.** The dissolution medium consisted of 900 ml of pH 7**.**0 buffer solution containing 0**.5%**SLS in 0**.**01M sodium phosphate**.** Temperature was maintained at 37±0**.**5^{0}C**.** Aliquot of 5ml was withdrawn at predetermined time intervals & an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced**.** Aliquots were filtered through whatman filter paper, suitably diluted using phosphate buffer pH 7**.**0 and analyzed spectrophotometrically at 238 nm**.**

Model fitting[15, 16]

The model fitting for % cumulative release was done using Microsoft excel 2003 to find the best fits kinetic equation for the dissolution profile.

Kinetics of drug release

In order to understand the mechanism and kinetics of drug release, the results of the *in-vitro* dissolution study of the optimized batch of microspheres (batch) was fitted with various kinetic equations like

i. Zero order (% release =K t),
ii. First order (log Unreleased =Kt),
iii. Higuchi's model (%Release =$Kt^{0.5}$) and
iv. Pappas Korsmeyer Equation (% Release=Kt^n)

(Or) empirical equation (Power law expression) of

$$M_t / M_\infty = K\, t^n$$

Where, M_t = amount of drug release at time t, M_∞ = amount of drug release at infinite time, K = constant characteristics, and n = Diffusional exponent

If n = 0.5 indicates Fickian diffusion mechanism (Higuchi matrix)

n = 0.5 to 1indicates Anomalous Transport or Non Fickian transport.

n = 1 indicates Case II Transport (Zero order release)

n > 1indicates Super case –II transport

Coefficient of correlation (R^2) values were calculated for the linear curves obtained by regression analysis of the above plots

Stability studies of simvastatin tablets [17]

In the present study, stability studies were carried out on selected formulation**.** The tablets were stored at temp 40^0C & RH 75 % for duration of one month**.** After an interval of fifteen and thirty days each sample was withdrawn and tested for drug release**.**

Table 1: Formulation Chart of Simvastatin Tablets

Ingredients (%) / batch	Drug	Xanthan gum	ß-cd	Lactose monohydrate	Tribasic calcium phosphate	Povidone	Total Wt. (%)
F1	10	16	04	--	--	08	100
F2	10	16	08	--	--	08	100
F3	10	16	12	--	--	08	100
F4	10	16	16	--	--	08	100
F5	10	16	--	04	--	08	100
F6	10	16	--	08	--	08	100
F7	10	16	--	12	--	08	100
F8	10	16	--	16	--	08	100
F9	10	16	--	--	04	08	100
F10	10	16	--	--	08	08	100
F11	10	16	--	--	12	08	100
F12	10	16	--	--	16	08	100

Table 2: Micromeritics Studies of Pellets

Batches	Parameters					
	Average particle size (mm) ±s.d.	Bulk Density (g/cm^3) ±s.d	True density (g/cm^3) ±s.d	Degree of Compressibility (%) ±s.d	Specific surface area (mm^2/g) ±s.d	Angle of repose (θ) ±s.d
F1	1.36±0.01	0.53±0.02	0.43±0.022	70.60±0.02	10.259±0.023	30°27′±0.03
F2	1.28±0.03	0.56±0.01	0.4316±0.017	73.65±0.04	10.861±0.014	30°29′±0.05
F3	1.19±0.05	0.59±0.03	0.44±0.031	76.32±0.03	11.549±0.029	29°63′±0.04
F4	1.44±0.01	0.63±0.02	0.4613±0.017	76.76±0.01	9.057±0.024	28°39′±0.04
F5	1.11±0.02	0.71±0.02	0.41±0.013	70.02±0.03	13.183±0.013	33°64′±0.02
F6	1.32±0.04	0.73±0.04	0.43±0.016	71.06±0.02	10.632±0.008	32°21′±0.02
F7	1.33±0.05	0.76±0.03	0.45±0.019	72.05±0.01	10.092±0.017	29°13′±0.05
F8	1.21±0.02	0.79±0.04	0.48±0.021	73.72±0.03	10.330±0.022	30°23′±0.02
F9	1.22±0.03	0.73±0.03	0.28±0.027	70.79±0.04	17.564±0.011	30°29′±0.06
F10	1.38±0.03	0.87±0.01	0.37±0.023	72.44±0.03	11.750±0.019	30°11′±0.04
F11	1.32±0.04	0.92±0.02	0.42±0.019	75.37±0.05	10.822±0.026	29°24′±0.03
F12	1.11±0.01	1.21±0.05	0.59±0.013	70.18±0.03	9.161±0.018	31°84′±0.02

Table 3: Standard Physical Tests for Simvastatin Tablets

Parameters	Thickness (mm) ±s.d	Hardness (kg/cm^2) ±s.d	Friability (%) ±s.d	Drug content (%)	Weight variation
F1	2.86±0.06	6.0±0.37	0.62±0.02	105.19	Passes
F2	2.55±0.04	6.2±0.54	0.84±0.04	105.0	Passes
F3	2.30±0.07	6.2±0.43	0.59±0.01	101.47	Passes
F4	2.28±0.03	6.5±0.32	0.77±0.03	100.05	Passes
F5	2.70±0.01	6.1±0.18	0.51±0.04	97.36	Passes
F6	2.62±0.05	6.2±0.35	0.63±0.02	96.69	Passes
F7	2.87±0.03	6.2±0.24	0.48±0.03	101.13	Passes
F8	2.42±0.02	6.2±0.28	0.69±0.04	98.36	Passes
F9	2.83±0.04	6.0±0.12	0.63±0.02	102.83	Passes
F10	2.88±0.05	6.2±0.65	0.71±0.01	104.37	passes
F11	2.31±0.02	6.1±0.31	0.83±0.03	99.47	passes
F12	2.15±0.03	5.7±0.33	0.69±0.02	103.52	passes

Table 4: Percentage Cumulative Release of the Formulation F1, F2, F3 and F4

Time (hours)	Percentage Cumulative Release			
	f1 ±s.d.	f2 ±s.d.	f3 ±s.d.	f4 ±s.d.
0	0	0	0	0
1	17.76±0.231	21.83±0.145	24.81±0.235	28.02±0.243
2	24.58±0.289	28.69±0.365	35.36±0.147	44.89±0.344
3	36.29±0.342	43.82±0.258	50.49±0.364	54.81±0.482
4	42.63±0.621	52.39±0.439	58.63±0.347	62.73±0.619
5	55.72±0.183	61.53±0.647	67.4±0.439	75.88±0.490
6	63.79±0.267	73.57±0.243	79.23±0.160	83.62±0.451
7	71.42±0.374	78.39±0.375	84.36±0.299	89.53±0.388
8	79.84±0.422	83.71±0.143	87.64±0.231	91.02±0.417
9	82.47±0.238	85.92±0.249	90.3±0.378	91.02±0.417
10	86.82±0.376	88.38±0.342	90.3±0.378	91.02±0.417
11	86.82±0.376	88.38±0.342	90.3±0.378	91.02±0.417
12	86.82±0.376	88.38±0.342	90.3±0.378	91.02±0.417
13	86.82±0.376	88.38±0.342	90.3±0.378	91.02±0.417
14	86.82±0.376	88.38±0.342	90.3±0.378	91.02±0.417

Table 5: Percentage Cumulative Release of the Formulation F5, F6, F7 & F8

Time (hours)	Percentage cumulative release			
	f5 ±s.d.	f6 ±s.d.	f7 ±s.d.	f8 ±s.d.
0	0	0	0	0
1	18.13±0.125	16.28±0.562	12.73±0.246	10.81±0.430
2	32.29±0.378	29.67±0.243	27.86±0.334	23.84±0.183
3	45.85±0.241	37.82±0.254	34.59±0.313	28.36±0.249
4	54.63±0.433	45.63±0.447	43.65±0.484	36.39±0.618
5	66.17±0.359	53.71±0.272	51.82±0.218	44.57±0.427
6	71.19±0.723	59.76±0.412	57.38±0.313	51.42±0.382
7	78.81±0.611	66.83±0.309	62.84±0.220	58.67±0.176
8	81.23±0.424	71.36±0.222	66.39±0.586	61.34±0.477
9	83.37±0.538	76.21±0.327	71.32±0.551	64.56±0.541
10	85.15±0.394	81.18±0.368	73.16±0.458	67.59±0.362
11	85.15±0.394	83.27±0.436	78.2±0.328	73.62±0.401
12	85.15±0.394	85.84±0.460	81.93±0.432	75.91±0.267
13	85.15±0.394	89.59±0.402	84.72±0.354	76.83±0.173
14	85.15±0.394	91.87±0.156	87.54±0.236	78.38±0.188

Table 6: Percentage Cumulative Release of the Formulation F9, F10, F11 And F12

Time (hours)	Percentage cumulative release			
	f9 ±s.d.	f10 ±s.d.	f11 ±s.d.	f12 ±s.d.
0	0	0	0	0
1	20.62±0.391	36.27±0.614	37.29±0.416	49.22±0.210
2	28.83±0.428	43.86±0.283	53.82±0.335	58.36±0.44
3	39.32±0.372	53.28±0.522	62.38±0.447	67.15±0.300
4	45.87±0.294	66.87±0.450	76.42±0.528	79.87±0.289
5	56.58±0.582	72.34±0.501	81.28±0.415	84.32±0.445
6	69.13±0.376	76.41±0.514	86.92±0.291	87.23±0.512
7	76.55±0.473	83.26±0.620	86.92±0.291	87.23±0.512
8	79.27±0.532	87.42±0.623	86.92±0.291	87.23±0.512
9	81.13±0.495	87.42±0.623	86.92±0.291	87.23±0.512
10	84.53±0.390	87.42±0.623	86.92±0.291	87.23±0.512
11	84.53±0.390	87.42±0.623	86.92±0.291	87.23±0.512
12	84.53±0.390	87.42±0.623	86.92±0.291	87.23±0.512
13	84.53±0.390	87.42±0.623	86.92±0.291	87.23±0.512
14	84.53±0.390	87.42±0.623	86.92±0.291	87.23±0.512

Table 7: Percentage Cumulative Release of Batch F6 Pellets

Time (min)	Percentage cumulative release ±s.d.
0	0
10	71.59±0.428
20	95.83±0.352
30	95.83±0.352

Table 8: Drug Entrapment of Optimized Formulations after S.S.

Parameters	Before stability study ±S.D.	Stability study (After 15 days) ±S.D.	Stability study (After 30 days) ±S.D.
Thickness	2.62±0.02	2.63±0.04	2.63±0.02
Hardness	6.2. ±0.03	6.1. ±.0.04	6.1±0.02
Drug content	96.69%	95.83%	95.46%

Table 9: Dissolution Study of Optimized Formulations after Stability Study

Time (hours)	Percentage cumulative release		
	before s.s. ±s.d.	(after 15 days) ±s.d.	(after30 days)±s.d.
0	0	0	0
1	16.28±0.562	16.62±0.428	17.92±0.302
2	29.67±0.243	27.64±0.501	28.53±0.347
3	37.82±0.254	38.65±0.218	38.13±0.417
4	45.63±0.447	45.71±0.256	44.03±0.557
5	53.71±0.272	54.94±0.244	53.29±0.393
6	59.76±0.412	60.76±0.143	60.35±0.330
7	66.83±0.309	65.83±0.292	66.64±0.259
8	71.36±0.222	68.57±0.246	69.74±0.122
9	76.21±0.327	76.27±0.201	75.84±0.201
10	81.18±0.368	81.76±0.482	80.72±0.312
11	83.27±0.436	83.45±0.316	82.87±0.255
12	85.84±0.460	85.39±0.205	85.23±0.314
13	89.59±0.402	88.93±0.538	88.16±0.350
14	91.87±0.156	90.26±0.352	90.24±0.306

Table 10: Estimated Values of N and K By Regression of Log (M_t/ M_∞) On Log (T)

Batches	Best fit model	r	n	k
F1	Korsmeyer-peppas	0.9849	0.5881	16.5328
F2	Matrix	0.9823	0.5519	22.4969
F3	Korsmeyer-peppas	0.8750	0.5755	28.5675
F4	Korsmeyer-peppas	0.8912	0.5682	33.0485
F5	Korsmeyer-peppas	0.9823	0.7381	16.1811
F6	Korsmeyer-peppas	0.9918	0.7528	12.6274
F7	Korsmeyer-peppas	0.9847	0.7953	11.3917
F8	Matrix	0.9935	0.8514	9.8653
F9	Matrix	0.9936	0.5488	22.0687
F10	Korsmeyer-peppas	0.9960	O.5327	32.1901
F11	Korsmeyer-peppas	0.9940	0.5432	32.7854
F12	Korsmeyer-peppas	0.8918	0.5139	37.9094

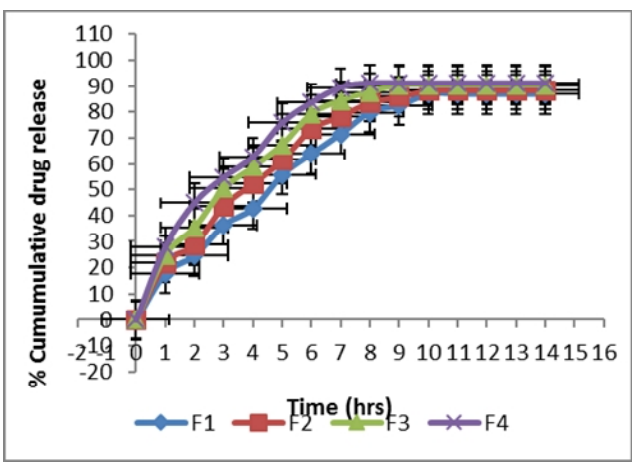


Figure 1: Drug release pattern of formulations batches f1, f2, f3 and f4

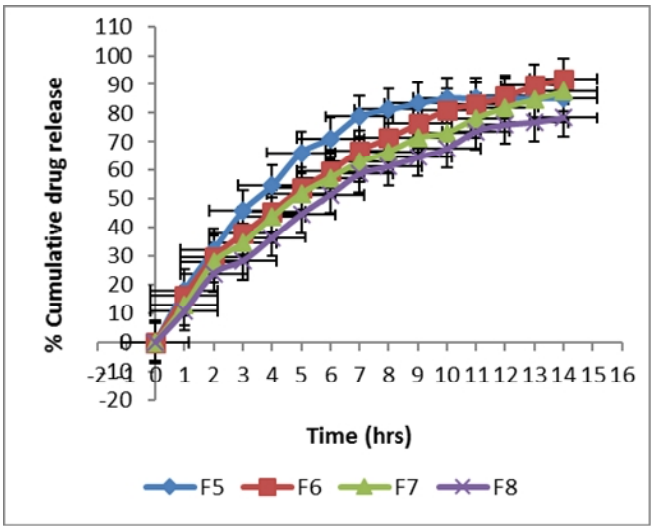


Figure 2: Drug release pattern of formulations batches F5, F6, F7 and F8

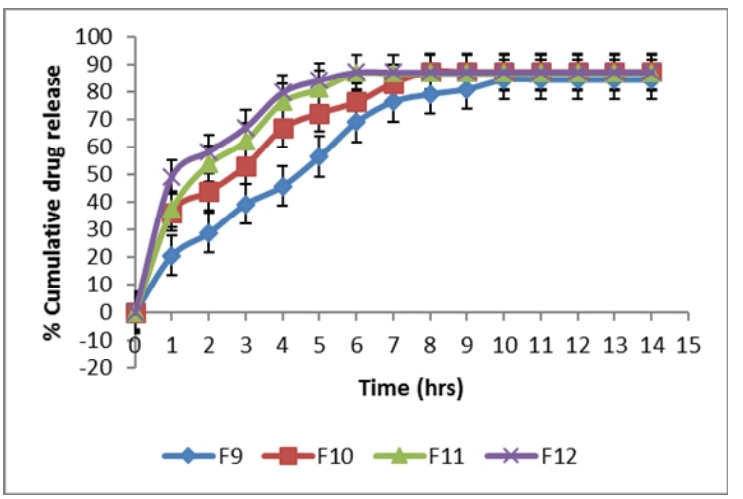
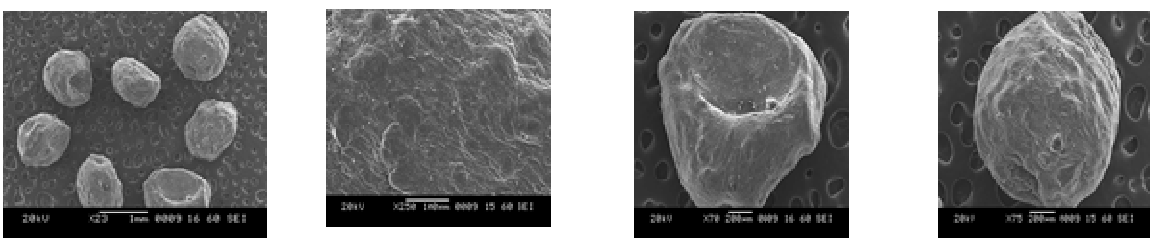


Figure3: Drug release pattern of formulations batches F9, F10, F11 and F12



SEM 1 SEM 2 SEM 3 SEM4

Figure 4: Morphological results with scanning electron microscopy

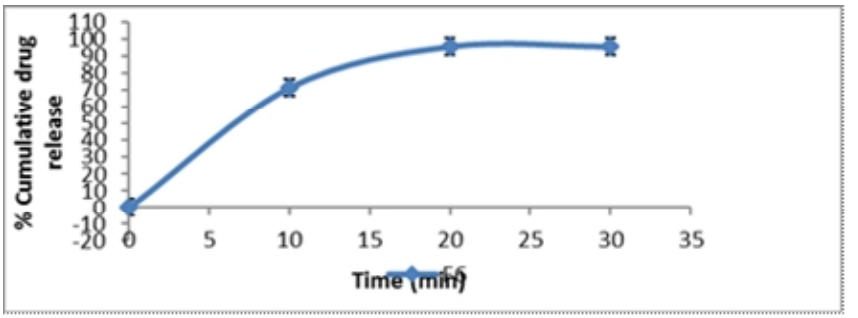


Figure 5: Drug release pattern of f6 batch of pellets

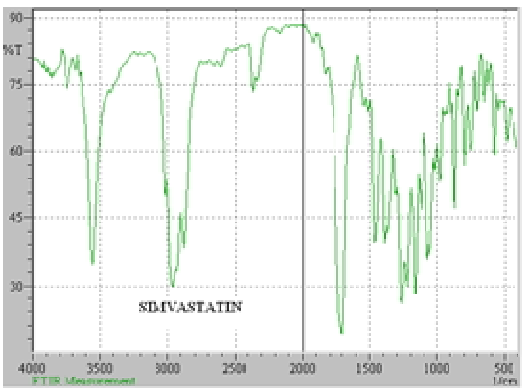


Figure 6: IR of simvastatin drug

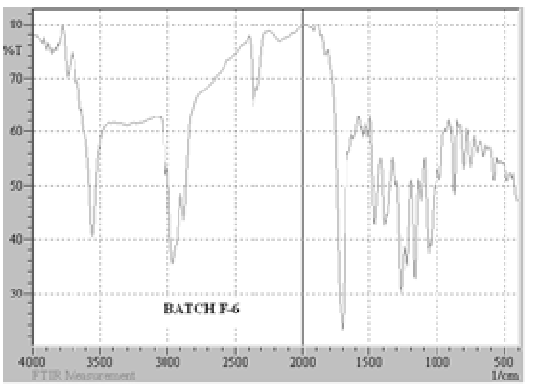


Figure7: IR of simvastatin tablet

RESULTS AND DISCUSSION

To study the effects of fillers on the release characteristics of model drug and production of tablets for the sustained delivery of the Simvastatin, a set of twelve formulations were prepared shown in table 1, The pellets of Simvastatin was prepared by using manual extrusion and spheronisation technique by varying the filler concentration, and keeping the other variables such as concentration of drug, xanthan gum and povidone was kept constant. Evaluation of pellets was done by Bulk density, True density, angle of repose, degree of compressibility and specific surface area. Various batches have the average particle size in the range of 1.11±0.002mm to 1.44±0.01mm. The bulk density value ranged from 0.53±0.02 to 1.21±0.05 g/cm^3, true density in between 0.28±0.027 to 0.59±0.013 g/cm^3, degree of compressibility in between 70.18±0.03 to 76.76±0.01%, from the analysis of results the matrix pellets of higher degree of compression have higher hardness and specific surface area within9.057±0.024 to 17.564±0.011mm^2/g for all filler pellets. Angle of repose was found within the range of 28°39′±0.04 to 33°64′±0.02which is an appreciable limit for pellets. Results were shown in Table 2 formulated tablet were subjected to various quality control test. Examination of tablets from each batch showed flat circular shape with no cracks having white color. The thickness of tablets ranged from 2.15±0.03 to 2.88±0.05mm. All the formulations showed uniform thickness. In weight variation test the Pharmacopoeial limit for percent of deviation for tablets of 200 mg is 7.5%. The average percent deviation of all tablets was found to be within limit and hence all formulations pass the weight variation test. The drug content was found to be uniform among all formulations and ranged from 96.69 % to 105.19%. The hardness of tablets of all formulations was ranged from 5.7±0.3 kg/cm^2 to 6.5±0.2kg/cm^2. The friability of all tablets ranged from 0.48±0.to 0.84±0.04%. Results were shown in table 3, Dissolution was carried out in pH 7.0 buffer solution containing 0.5% of SLS in 0.01Msodium phosphate as drug is soluble in the media and also it mimics the alkaline environment of small intestine. Dissolution of optimized batch of pellets was carried out in pH 7.0 buffer solution containing0.5% of SLS in 0.01Msodium phosphate as drug is soluble in the media and also it mimics the alkaline environment of small intestine.

The *in-vitro* dissolution was carried out on all the batches in pH 7.0 buffer solution, The release of drug from tablets of batches F1 to F4 was containing Simvastatin as model drug and xanthan gum as rate controlling polymer with ß-cyclodextrin as a filler was studied. As the concentration of ß-cyclodextrin increased the solubility of drug was found to increase and the released rate to increases. The released profiles of these batches are shown in Table 4 and Figure 1, The release of drug from batches F5 to F8 was containing Simvastatinas model drug and xanthan gum as a sustained released rate controlling polymer with lactose monohydrate as a filler was studied. In these batches release was linear with time. It could have concluded that batch F6 (91.87%) released approximately 100% drug over a period of 14 hours. Since it met the all requirement, that's why it was chosen as the optimized formulation.

The released profiles of these batches are shown in Table 5 and Figure 2, The release of drug from batches F9 to F12 containing Simvastatin as model drug and xanthan gum as a sustained released rate controlling polymer with tribasic calcium phosphate as a filler was studied. In the early incubation stage of batch F9, F10, F11 and F12 the dissolution rate of simvastatin was slightly faster especially during the first few hours. This was due to the porous nature of the tablets and the rapid penetration of aqueous solution into the tablets, which is also called burst effect. The released profiles of these batches are shown in Table 6 and Figure 3. Morphology of pellets was

examined by scanning electron microscopy. The outer surface of the pellets was smooth and dense, while the internal surface was porous. The shell of the pellets also showed some porous structure as Shown in Figure 4 Percentage cumulative release of the formulation F6**.** Shown in table 7 and Drug release pattern of formulations batches F6 shown in figure 5, The stability studies were carried out on optimized formulation F6. The formulations were stored at 40 ± 2^0C and 75 ± 5 % RH for a period of 30 days. After interval at 15th and 30th days samples were withdrawn and retested for thickness, hardness, drug content and drug release studies. Show in table 8 and Drug entrapment of optimized formulations after stability studies were shown in table 9, Dissolution study of optimized formulations after Stability Study**.** From the above studies it was concluded that product may be stable up to fifteen months. The in vitro release data of all the formulation were fitted in Korsmeyer-peppas and Matrix model and the rate constant and correlation coefficient were compared to get trend in the release pattern of the drug from the formulation. Regression values r^2 were found 0.875 to 0.994 from different formulation. The mean diffusional exponent values (n) was found to be ranged from 0.513 to 0.851 indicated all the formulation follows case II transport i.e. swelling and erosion simultaneously occur during the release. Since both swelling and erosion occurs simultaneously, zero order release is achieved from these matrices. This behaviour is responsible for maintaining zero order release in which the increase in diffusion path length due to swelling is balanced with the decrease in diffusion path length due to matrix erosion. Overall a constant diffusion path length is maintained. Thus it was found that drug release from simvastatin matrix tablet follows zero order model. Were shown in Table 10**.** IR interpretations for drug polymer interaction in formulation, Shown in Figure 6 and 7. The result shown that there was no incompatibility between drug Simvastatin and polymer used, as there was no significant change in the pattern of peaks of pure drug and formulation.

REFERENCES

1. Issac Ghebre-Sellassie in; Pharmaceutical Pelletization Technology, Marcel Dekker series 1989: 37: 123-140.
2. Kokate C. K.,Purohit A. P., Gokhale S. B., Pharmacognosy, , 18th ed .Nirali Prakashan 2002. P.157.
3. Trapathi K.D., Essentials of Medical Pharmacology, 6th ed, Jaypee Bros. Medical Publishers, 2009. p. 612-623.
4. Drug information online, www.drug.com, Pg. no. 1-36.
5. Berggrn J., Alderborn G., Effect of drying on porosity and tabletting behaviour of cellulose pellets, Int. J. Pharma.2001 :227: 81-96.
6. Santos H., Veiga F., Pina M. E., Souna J. J., Compaction, compression and drug release characteristics of xanthan gum pellets of different compositions; Euro. J. Pharma Sci., P. 271-281.
7. Raymond C.R., Paul J.S. Handbook of Pharmacetical Excipients. 4th ed, Pharmaceutical press, P.323 – 332.
8. Martin A., Swarbrick J., in Physical pharmacy, 3rd ed K.M.Verghese Company, Mumbai, 1999, p. 423-476.
9. Agrawal S.P., khanna R., Physical pharmacy, 2nd ed., CBS publishers and distributors new delhi. Bangalore, 2006. p.17-46.
10. Mazzo David J**.** Obetz C**.**L**.**, Shuster J**. '**Simvastatin**'**; In**:** Klaus Florey**'**s, Analytical Profiles of Drug Substances and Excipients, Volume 23, p**.** 359-372**.**
11. Mehta A.M., Issac Ghebre-Sellassie eds., Pharmaceutical Pelletization Technology, 1989, 37. Marcel Dekker inc, 241-264.
12. Lachman Leon, Liberman H. A. and Kanig J.L., The Theory and Practices of industrial pharmacy. 3 rd ed, Varghese publishing House, P. 430-456.
13. USP 24 NF 19, C, Asian ed 1991, P.1521-1526.
14. Wang L.,Asgharnejad M., Second-derivative U V spectrometric determination of Simvastatin in its tablet dosage form, J. of Pharma. and biomedical Analysis 2000:21: P. 1243-1248.
15. Newton J.M., Blanque D., Sternagel H., Podczeck F., Some factors influencing the formation and in vitro drug release from matrix pellets prepared by extrusion/spheronization, Int. J. of Pharma. 1995: 119 :P.203-211.
16. Korsmeyer.R.W, Gurny.R, Doelker.E, Bur.P and Peppas .N.A, Int**.** J**.** of Pharmacy, 1983:15:p. 25-35.
17. Ritger PL, Peppas NA; Journal of controlled release, 1987: 5: P. 23-36.
18. Raghavendra Kumar Gunda, J.N. Suresh Kumar, V. Satyanarayana, K.V. Ramanjaneyulu, B. Satya Prasad. Formulation development and evaluation of carvedilol phosphate gastro retentive floating tablets. Int. Res. J. Pharm. 2016;7(1):44-51 http://dx.doi.org/ 10.7897/2230-8407.0718

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