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Original Research Article

FORMULATION AND EVALUATION OF SIMVASTATIN FAST DISSOLVING TABLETS

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ABSTRACT

Fast dissolving tablets are the fast growing and highly accepted drug delivery system in now a day mainly to improve patient compliance. Fast dissolving tablets have number of advantages over conventional dosage forms, because of those fast dissolving tablets have emerged as an alternative to conventional dosage forms. Fast dissolving tablets of Simvastatin were prepared using superdisintegrants viz; crospovidone, croscarmellose sodium and sodium starch glycolate using direct compression technique. The tablets prepared were evaluated for thickness, uniformity of weight, hardness, friability, wetting time, in vitro disintegration time and in vitro dissolution time. The different formulations showed disintegration time between 60 to 130 s. Drug release was between the time ranges of 30 to 60 min. Among all the formulations, F9 (containing 6% of Sodium starch glycolate) showed 99% drug release within 30 min and it showed least disintegration time (60s). Thus, F9 was considered best among the formulations and compared with tablet prepared with different technique (granulation) and marketed formulation and F9 was best among all the formulations.

Key Words: Fast dissolving tablet, Simvastatin, Sodium starch glycolate, Croscarmellose sodium, Crospovidone.

INTRODUCTION

Recent developments in technology have presented viable dosage alternatives for pediatric, geriatric, bedridden, nauseous or non compliant patients. Traditional tablets and capsules administered with 250 ml of water may be inconvenient or impractical. For such patients hence commonly disintegrating rapidly in the saliva without the aid of water is convenient. Also this dosage form offers an advantage of convenience of administration while traveling where they may not be accesses to water [1]. Fast dissolving tablets (FDDT) are solid single unit dosage forms that are placed in the mouth, allowed to dissolve in the saliva and then swallowed without need of water [2]. The proper choice of disintegrants is critical importance to the formulation of such tablets. In more recent time, increasing attention has been paid to formulating not only fast dissolving tablets that are intended to dissolve and /or disintegrate rapidly in the mouth and produce quick on set of action[3]. Most commonly used methods to prepare these tablets are; Freeze drying/Lyopilization, Tablet moulding, and direct compression methods. In the present study an attempt was made to develop fast dissolving tablets of Simvastatin using superdisintegrants to improve its bioavailability [4].

Simvastatin belongs to a group of drugs called HMG CoA reductase inhibitor and used to lower cholesterol and tryglicerides in the blood and used to lower the risk of stroke, heart attack, and other heart complications in the people with diabetes, coronary heart disease or other risk factors[5].

MATERIALS AND METHODS

Materials:

Simvastatin was a gift sample from Natco labs Ltd, Andhra Pradesh, India. Croscarmellose sodium, CrosPovidone, Sodium starch glycolate, Magnesium sterate and Talc were purchased from S.D. Fine Chemicals, Mumbai, India. All other chemicals, solvents and reagents used were of either pharmacopoeial or analytical grade.

Methods:

Preparation of fast dissolving Tablets

All the ingredients were passed through sieve No.60.Blended and Superdisintegra nts were incorporated in the powder mixture and finally magnesium sterate and talc were added as lubricant. The powder mix was weighed individually and compressed with 6mm biconcave surface punches using hydraulic press single tablet punching machine [6][Table 1].

Evaluation of the prepared tablet: [7-9] [Table 2, 3]

1. Pre-compression parameters:

a) Compatibilities study

The compatibility of drug and polymers under experimental condition was conducted using FTIR studies. In the present study, the potassium bromide disc (pellet) method was employed.

b) Flow properties

The powdered blend was evaluated for flow properties viz., Angle of repose, loose bulk density (LBD), tapped bulk density (TBD), Carr's compressibility index, and

Hausner's ratio.

2. Post Compression Parameters

a) *Thickness test*

Thickness was determined using screw gauge (Mitutoyo, New Delhi, India). 5 tablets from each batch were used and the average values were calculated.

b) Hardness test

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in Kg/cm^2. Three tablets were randomly picked and analyzed for hardness. The mean and standard deviation values were also calculated.

c) Friability test

The friability of tablets was determined using Roche Friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The % friability was then calculated by eq.1.

$F = W_{initial} - W_{final} / W_{initial} \times 100$ ..... (1)

Where F= Friability (%), $W_{initial}$ = initial weight, W_{final} = Final weight

d) Weight variation test

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (Denver APX-100, Arvada, Colorado) and the test was performed according to the official method.

e) Drug content uniformity

Tablet containing 20 mg of drug is dissolved in 100ml of 7.4 pH phosphate buffer taken in volumetric flask. The drug is allowed to dissolve in the solvent. The solution was filtered, 1ml of filtrate was taken in 50ml of volumetric flask and diluted up to mark with 7.4 pH phosphate buffer and analyzed spectrophotometrically at 240 nm. The concentration of Simvastatin in mg/ml was obtained by using standard calibration curve of the drug. Drug content studies were carried out in triplicate for each formulation batch.

f) Wetting time

The tablet was placed in a petridish of 6.5 cm in diameter, containing 10 ml of water at room temperature, and the time for complete wetting was recorded. To check for reproducibility, the measurements were carried out six times and the mean value calculated.

g) Water absorption ratio

A piece of tissue paper folded twice was placed in a small petridish containing 6ml of distilled water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using eq.2

$$R = 10 \times \frac{(Wa - Wb)}{Wb} \quad \text{..... (2)}$$

Where,

Wb = weight of the tablet before water absorption

Wa = weight of the tablet after water absorption

Three tablets from each formulation were analysed performed and standard deviation was also determined.

h) In vitro dispersion time

Tablet was placed in 10 ml phosphate buffer solution, pH 7.4. Time required for complete dispersion of a tablet was

measured.

i) In-vitro disintegration time

The process of breakdown of a tablet into smaller particles is called as disintegration. The *in-vitro* disintegration time of a tablet was determined using disintegration test apparatus as per I.P. specifications. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 7.4 maintained at 37±2^{0}C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 7.4 maintained at 37±2^{0}C. The time taken up by the tablet for complete disintegration with no palpable mass remaining in the apparatus was measured and recorded.

j) In-vitro dissolution studies

In vitro release studies were carried out using tablet dissolution test apparatus USP XXIII. The following procedure was employed throughout the study to determine the *in-vitro* dissolution rate for all the formulations [Table 4].

RESULTS AND DISCUSSION

The FTIR spectrum of formulated blend showed characteristic peaks of drug which indicated that the compatibility of the drug with the excipients used. The spectrum was shown in [Fig 1, 2, 3]. The results obtained for angle of repose of the powdered blends was less than 23^0, the loose bulk density was ranged from 0.422±0.10 to 0.542±0.06 g/cm^3, the tapped bulk density was ranged from 0.487±0.12 to 0.643±0.08 g/cm^3, and the percent compressibility was ranged from 11.22 to 17.24 %. All these values were represented in [Table 1]. The mean thickness values were found in the range from 3.95±0.15 to 4.25±0.08 mm, the hardness of formulated tablets was found to be 3.94±0.26 to 4.25±0.13 kg/cm^3. The loss in friability was ranged from 0.21±0.06 to 0.56±0.09 %. The Wetting Time was ranged from 92 ± 1.51 to 99 ± 1.47 sec, the disintegration Time was ranged from 60±1.36 to 130±2.23 sec. These values were represented in [Table 2]. The *in-vitro* dissolution profile of formulated tablets was shown in [Fig 4, 5, 6, and 7]. The dissolution parameters were shown in [Table 4].

All the formulations showed angle of repose within 23^0 which indicates good flow. The values of loose bulk density and tapped bulk density help in calculating the % compressibility of the powder. All formulations show good compressibility. The formulated tablets were elegant and almost uniform thickness. All the formulations were almost uniform in specific method and possess good mechanical strength with sufficient hardness. The weight loss after friability test was found well within the approved range (<1%) in all the formulation, indicates the tablets possess good mechanical strength. All the tablets passed weight variation test as per the pharmacopoeial limits. All formulations showed quick wetting, this may be due to ability of swelling and also capacity of absorption of water. All superdisintegrants have high water absorption capacity and cause swelling. All formulations showed disintegration time less than 130 seconds, indicates

the swelling of disintegration substance suggested mechanism of disintegration. By observing the above results use of Sodium starch glycolate, cross cormilose sodium and cross Povidone, in direct compression method results in hydrophilicity and swelling which in turn causes rapid disintegration. Thus these disintegrants are suitable in preparing the rapidly disintegrating tablets. This rapid dissolution might be due to fast breakdown of particles of superdisintegrants. In all formulations the drug release was nearer to 100% within 60 minutes. Formulation F9 showed release (100%) in 30 minutes hence F9 was optimized and compared to marketed formulation Simvotin 20 and was shown in [Fig 8].

CONCLUSSION:

The present work revealed that sodium starch glycolate showed better disintegration and dissolution property than Croscarmellose sodium and Crospovidone in the formulation of fast dissolving tablets. The effect of diluents and the concentration of the diluents on disintegration and dissolution of Simvastatin were also considered and hence Simvastatin fast dissolving tablet was successfully prepared.

ACKNOWLEDGEMENT:

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Table.1. Composition of Simvastatin Fast dissolving tablets

Ingredients	Quantity for tablet (mg)									
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
Simvastatin	20	20	20	20	20	20	20	20	20	20
Dicalcium phosphate	158	-	-	-	-	-	-	-	-	-
Micro crystalline cellulose	-	158	-	-	-	-	-	-	-	-
Spray dried lactose	-	-	158	183	208	208	208	204	200	-
Sodium starch glycolate	8	8	8	8	8	-	-	12	16	16
Croscarmellose	-	-	-	-	-	8	-	-	-	-
Crospovidone	-	-	-		-	-	8	-	-	-
Sucrose	10	10	10	10	10	10	10	10	10	10
Lactose	-	-	-	-	-	-	-	-	-	200
Talc	2	2	2	2	2	2	2	2	2	2
Magnesium sterate	2	2	2	2	2	2	2	2	2	2
Iso propyl Alcohol	-	-	-	-	-	-	-	-	-	5ml
Total weight	200	200	200	225	250	250	250	250	250	250

***F10- granulation**

Table.2. Physical Characteristics of Simvastatin Fast dissolving tablets

Formulation code	Bulk density (gm/cm³)	Tapped density (gm/cm³)	Carr's index (%)	Hausner's ratio	Angle of repose (°)
F1	0.542±0.06	0.643±0.08	15.70±0.06	1.18±0.06	22.47±0.12
F2	0.521±0.521	0.592±0.08	11.99±0.05	1.13±0.05	19.64±0.12
F3	0.483±0.483	0.561±0.06	13.90±0.09	1.16±0.09	20.13±0.11
F4	0.445±0.445	0.502±0.07	11.34±0.09	1.12±0.08	18.52±0.14
F5	0.422±0.422	0.487±0.12	13.35±0.08	1.15±0.04	19.84±0.16
F6	0.432±0.432	0.522±0.10	17.24±0.13	1.20±0.05	18.89±0.15
F7	0.510±0.510	0.609±0.11	16.25±0.12	1.19±0.07	21.25±0.13
F8	0.489±0.489	0.580±0.12	15.68±0.11	1.18±0.09	19.65±0.12
F9	0.468±0.468	0.559±0.13	16.27±0.15	1.19±0.10	22.10±0.10
F10	0.501±0.501	0.610±0.09	17.8±0.13	1.19±0.08	20.25±1.12

Table.3. Evaluation of Physical Parameters of Simvastatin Fast dissolving tablets

F*CODE	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Wetting Time (sec)	Dispersion time(Sec)	DT* (sec)	Drug content %
F1	4.25±0.08	4.38±0.13	0.35±0.11	95±0.51	110±0.10	120±0.12	99.21±0.23
F2	4.02±0.05	4.10±0.17	0.56±0.09	92±1.51	105±0.12	110±0.12	98.12±0.32
F3	3.95±0.15	3.95±0.19	0.29±0.09	95±5.21	95±0.14	105±0.13	99.25±0.56
F4	4.06±0.01	3.95±0.51	0.26±0.08	99±1.47	90±0.17	100±0.15	100.21±0.45
F5	4.11±0.02	3.94±0.26	0.54±0.05	98±1.58	85±0.16	95±0.16	100.36±0.25
F6	4.04±0.04	4.20±0.24	0.21±0.06	97±1.56	115±0.11	130±0.12	99.36±0.35
F7	4.10±0.03	4.29±0.21	0.24±0.05	94±1.23	105±0.10	125±0.12	99.65±0.52
F8	4.05±0.02	4.10±0.12	0.23±0.24	92±1.45	60±0.09	80±0.16	99.56±0.24
F9	4.12±0.05	4.32±0.11	0.25±0.34	94±1.25	45±0.08	60±0.12	99.45±0.56

F*CODE-Formulation Code **DT-** Disintegration Time

Table.4. Release Parameters of Simvastatin Fast dissolving tablets

Formulation	Time(min)						
	0	10	20	30	40	50	60
F1	0	35.60±0.55	54.20±0.89	66.76±0.63	77.53±0.45	85.50±0.45	91.69±0.36
F2	0	38.65±0.45	55.45±0.45	66.15±0.56	78.76±0.56	88.65±0.58	93.23±0.56
F3	0	41.23±0.23	58.56±0.56	76.50±0.65	82.46±0.68	94.32±0.69	-
F4	0	42.56±0.15	59.38±0.12	72.78±0.45	84.65±0.32	97.23±0.56	-
F5	0	51.05±0.5	70.32±0.45	88.65±0.52	98.15±0.25	-	-
F6	0	45.14±0.45	60.65±0.56	72.45±0.23	87.34±0.39	96.61±0.42	-
F7	0	40.68±0.23	58.15±0.53	69.76±0.25	81.78±0.25	95.25±0.26	-
F8	0	49.67±0.52	68.61±0.35	82.89±0.45	97.84±0.52	-	
F9	0	60.61±0.51	81.23±0.38	99.07±0.26	-	-	-

Table.5. Fist order Release exponent (n) and Correlation coefficient of Simvastatin Fast dissolving tablets

Formulation Code	Correlation coefficient (r^2)		First order Release exponent (n)	t 50% (min)	t 90% (min)
	Zero order	First order			
F1	0.9096	0.9924	0.645	19	60
F2	0.9075	0.9846	0.542	19	58
F3	0.9209	0.9461	0.412	16	47
F4	0.9233	0.9345	0.527	15	45
F5	0.9044	0.9346	0.569	10	32
F6	0.9267	0.9350	0.496	16	43
F7	0.9273	0.9395	0.601	15	45
F8	0.9134	0.9233	0.562	10	37
F9	0.9056	0.9366	0.523	7	27

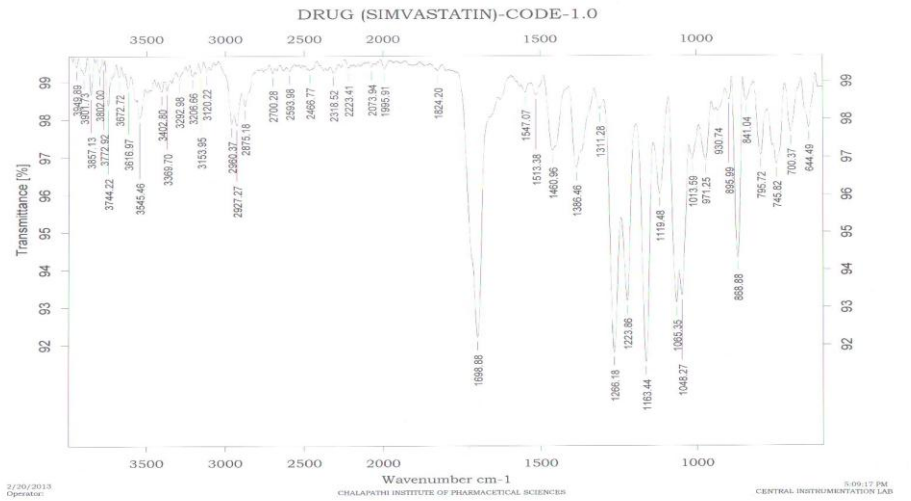

Fig.1. I.R Spectrum of Simvastatin Pure drug

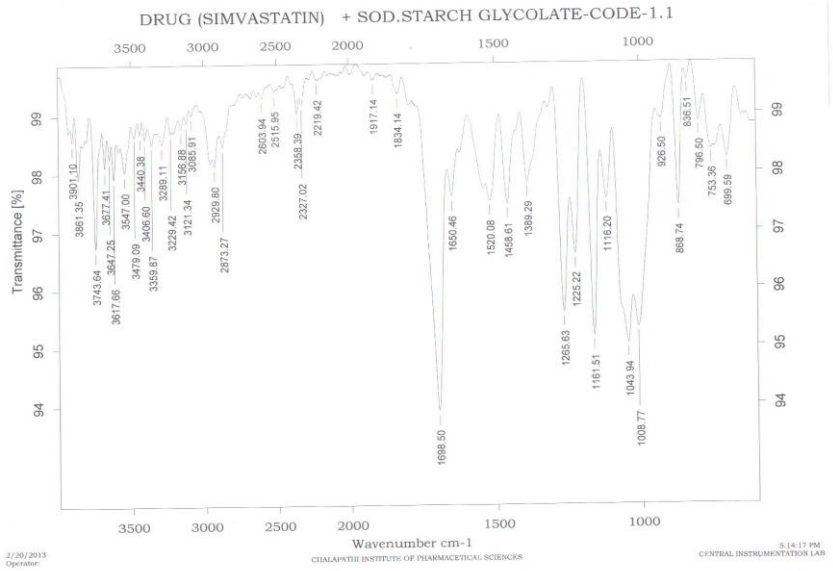

Fig.2. I.R Spectrum of Simvastatin with Sodium starch glycolate

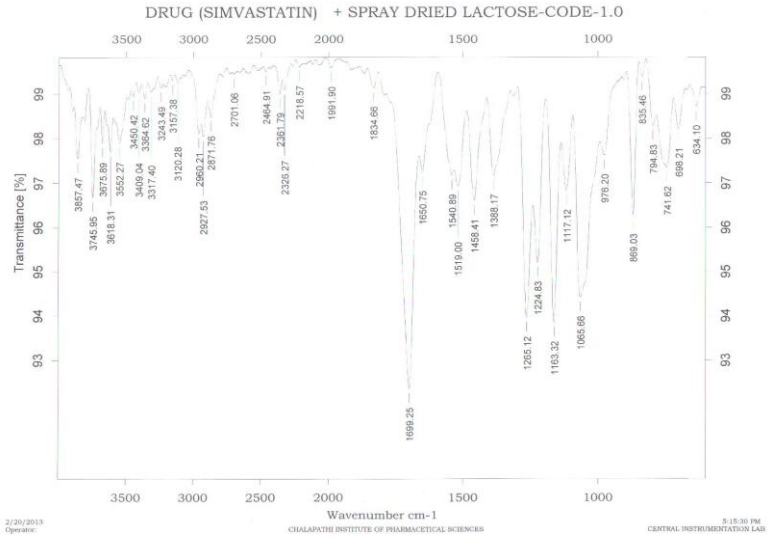

Fig.3. I.R Spectrum of Simvastatin with Spray dried lactose

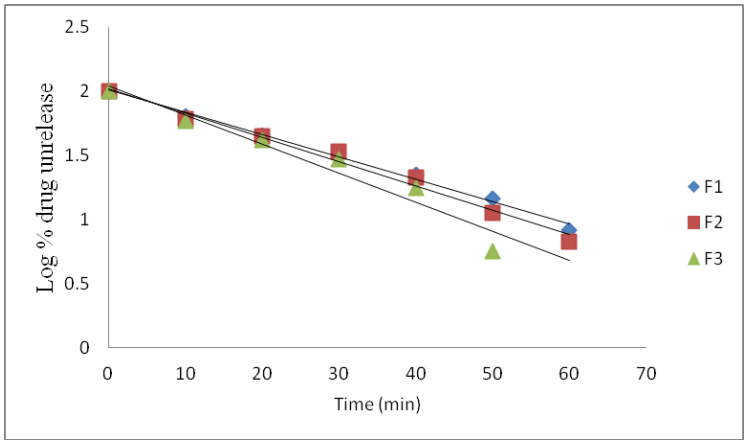

Fig.4. First order Release profile of Simvastatin Fast dissolving tablets using different Diluents

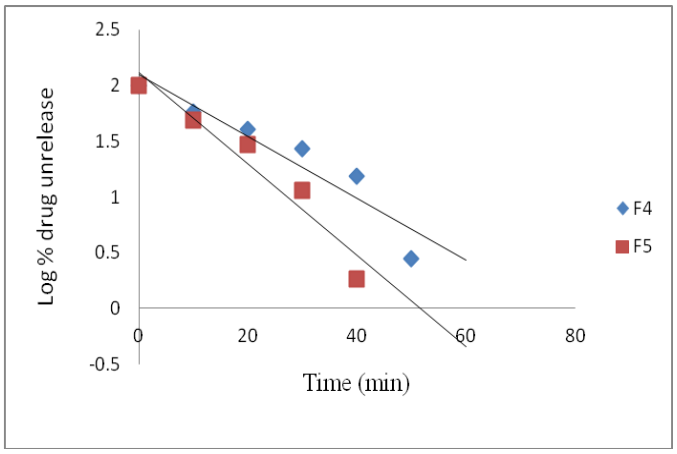

Fig.5. First order Release profile of Simvastatin Fast dissolving tablets using different Concentration of diluents

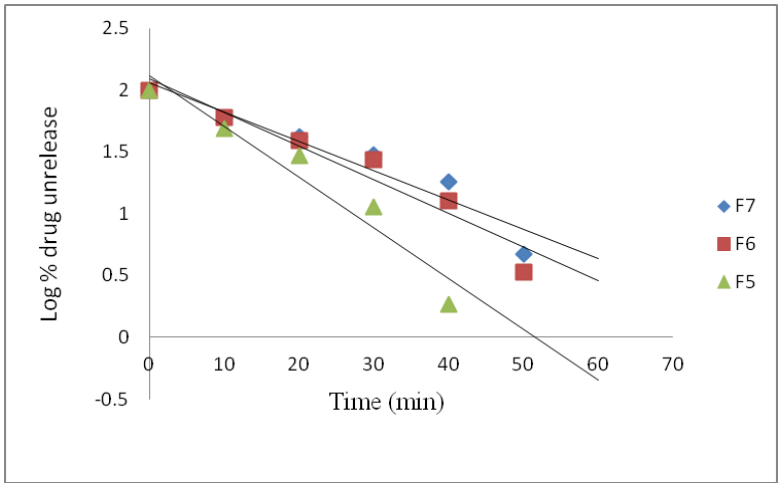

Fig.6. First order Release profile of Simvastatin Fast dissolving tablets using different Superdisintegrants

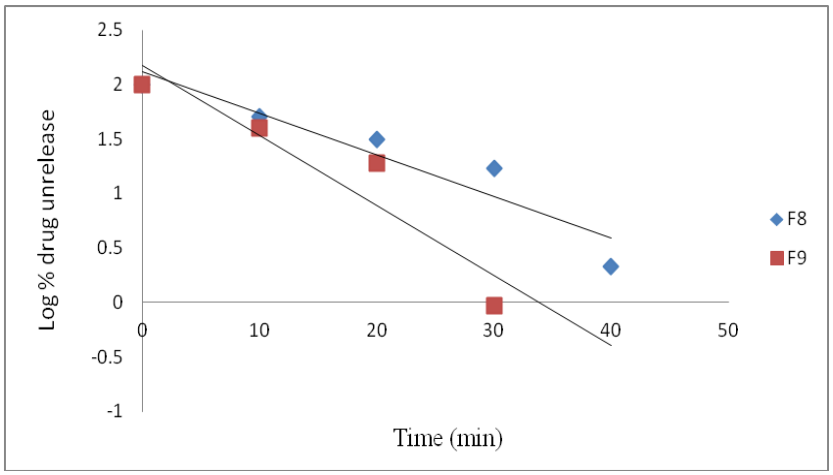

Fig.7.First order Release profile of Simvastatin Fast dissolving tablets using different Compression technique

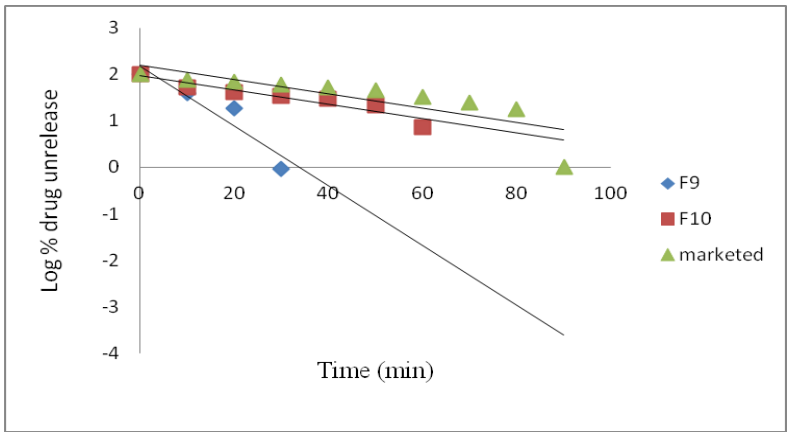

Fig.8. Fist order Release profile of Simvastatin Fast dissolving tablets of optimized and marketed tablet