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FORMULATION AND EVALUATION OF ROSUVASTATIN ORAL DISPERSIBLE TABLET

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ABSTRACT

The objective of the study was to develop the oral dispersible tablets of various concentrations of polymers on in-vitro release rate from the prepared rosuvastatin tablets. The effect of drug to polymer ratio on the in vitro drug release behavior was significant. Formulation F5 showed better in vitro drug release and this indicates the ideal drug, polymer and excipients combination. Formulations In vitro dissolution results showed that maximum cumulative % drug release was more in formulation F5 when compared to formulation F1 to F9.Stability studies were conducted formulations F5 stored at 250C/60% RH and 400C/75% RH for 30 days. Various parameters like hardness, friability, drug content uniformity, in vitro disintegration, wetting time were analyzed at a time of interval of 10 days till a period of 30 days. Not much variation or change was observed in any parameters throughout the study period. Best –selected formulations F5 found to be stable. Hence it is concluded that the prepared tablets disintegrate in seconds without need of water and enhance the absorption, this leads to increased bioavailability of Rosuvastatin.

The results of stability study on Formulation F5 after a period of one month indicates that the formulation was stable. Based on result it is concluded that formulated oral dispersible tablet of Rosuvastatin may have wide acceptance as compared to conventional dosage form.

Key Words: Rosuvastatin, Oral dispersible, Crospovidone, Direct Compression Method.

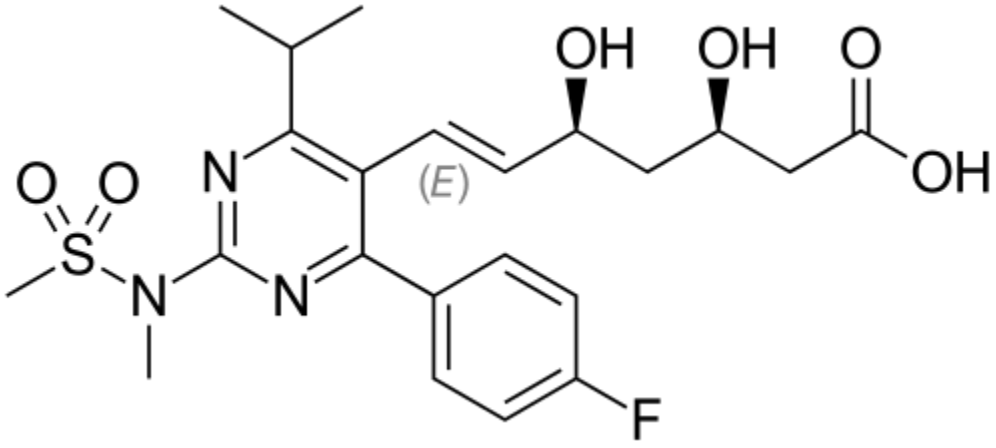
Introduction

Solid medicaments may be administered orally as powders, pills, cachets, capsules or tablets. These dosage forms contain a quantity of drug which is given as a single unit and they are known collectively as solid unit dosage forms, even in the case of sustained action preparations which, technically, contain the equivalent of several normal doses of drug**.**

The treatment of acute or chronic illness has been achieved by delivery of drug to the patients for many years. These drug delivery systems include capsules, tablets, injectables, creams, liquids, aerosol, suspensions and ointments. The term drug delivery can be defined as technique that is used to get therapeutic agent inside the human body. [2,3]

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via different dosage forms. Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules.

Fig 01 Rosuvastatin Structure



Materials and Methods:

Gift samples of standards Rosuvastatin were provided Wokhardt Pharmaceutical at, Aurangabad. Crospovidone, Croscarmellose sodium, Sodium starch glycolate, Lactose, Microcrystalline cellulose, Magnesium Stearate, were provided Lupin Pharmaceutical at, Aurangabad.

Formulation of Orally Disintegrating Tablets

Weigh all the ingredients accurately according. Mix all the ingredients geometrically except Talc and Magnesium Stearate. Then lubricate the blend with Talc, Magnesium Stearate and passed through sieve no 40 .The blend was compressed using rotary tablet machine-10 station with 6mm flat punch. Each tablet contains 10mg and other pharmaceutical ingredients as in Table no 1.

Table 1 Composition of fast dissolving tablets of Rosuvastatin

Ingredients (mg)	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drug	10	10	10	10	10	10	10	10	10
Crospovidone	15	_	_	20	_	_	25	_	_
Crosscarmellose sodium	_	15	_	_	20	_	_	25	_
SSG	_	_	15	_	_	20	_	_	25
Lactose	20	20	20	20	20	20	20	20	20
MCC	51	51	51	46	46	46	41	41	41
Mg.sterate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Total weight	100	100	100	100	100	100	100	100	100

Results and Discussion:

A. Preformulation Studies:-

1. Melting point determination:

The melting point of Rosuvastatin was found to be in the range of 151^0C to value as reported in literature, thus indicating purity of the drug sample. Any impurity, if present, will cause variation in the melting point of a given drug substance.

2. Identification of pure drug:

The IR spectrum of pure drug (Figure no 2) was found to be similar to the standard spectrum of Rosuvastatin. The spectrum of the Rosuvastatin shows the following functional groups at their frequencies.

Cm-1	Group
3364	O−H Stretching
3320	RCO-OH Stretching
1338	S=O Asymmetric
1963	C=N/ C=O
1380	C−N Stretching
2935	AR-CH

3. Solubility study:

Sparingly soluble in water, soluble in organic solvents like methanol and slightly soluble in ethanol.

4. Compatibility studies:

From the spectra of pure drug Rosuvastatin and the combination of drug with polymers, it was observed that all the characteristic peaks of Rosuvastatin were present in the combination spectrum, thus indicating compatibility of the drug and polymer. IR spectra of the pure drug and in combination with the polymers are shown in Figure no 2 to5.

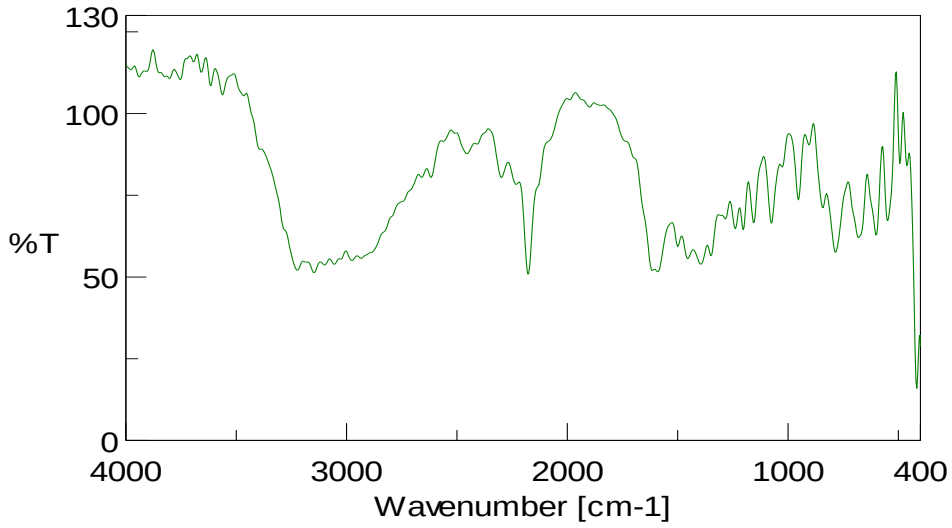


Fig 2: FT-IR Spectra of Rosuvastatin

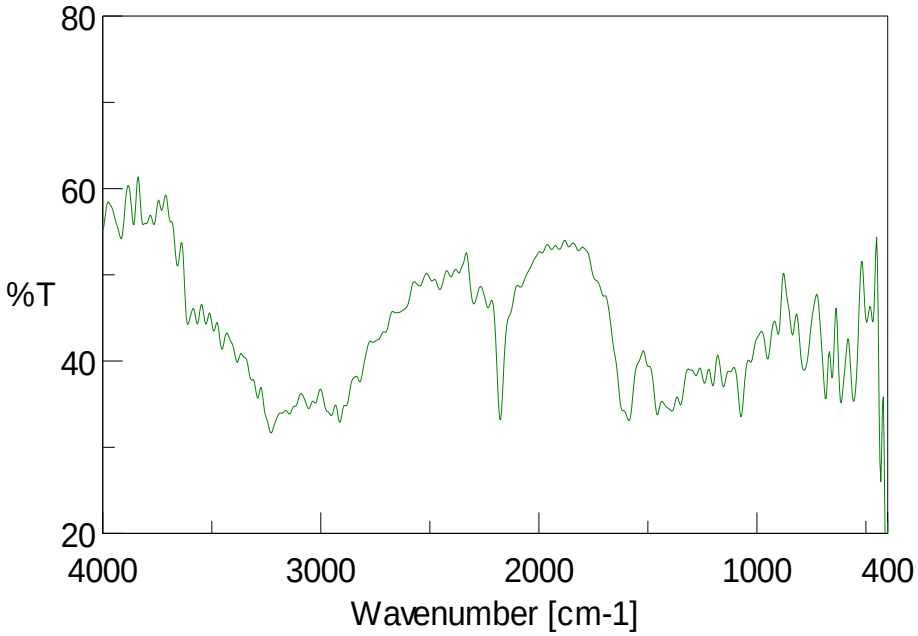


Fig 3: FT-IR Spectra of Rosuvastatin & CPVP

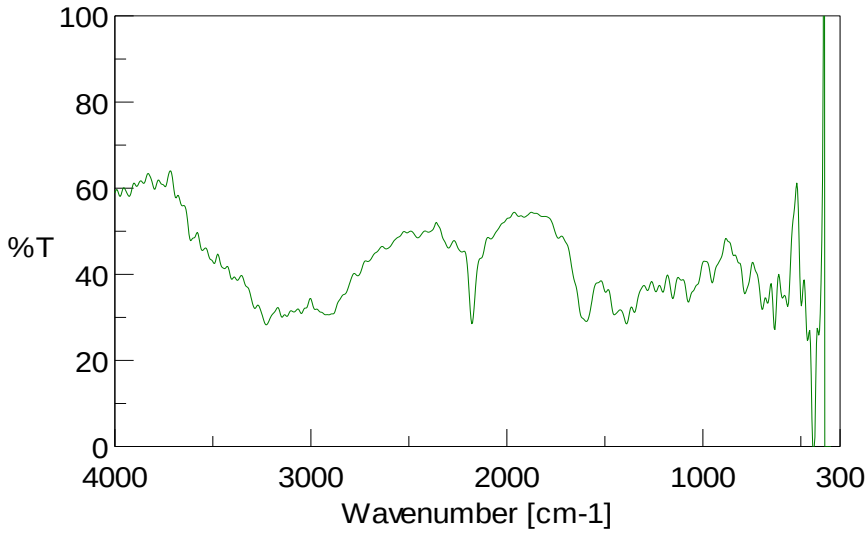


Fig 4: FT-IR Spectra of Rosuvastatin & CCS

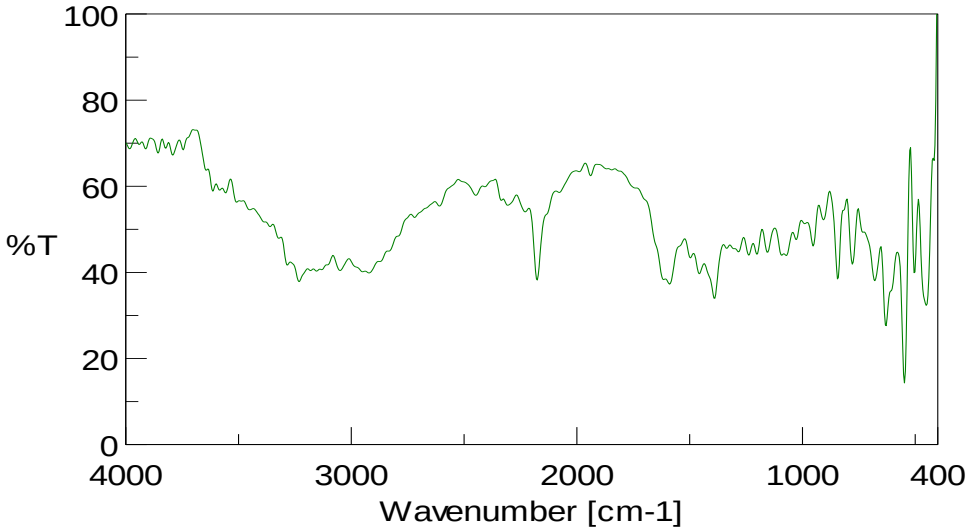


Fig 5: FT-IR Spectra of Rosuvastatin & SSG

5. Differential scanning calorimetery (DSC):-

The DSC themogram Rosuvastatin featured a single sharp melting endotherm, having peak temperature of 155^{o}C. It indicates that drug is in pure and amorphas state. DSC thermogram show in fig no 6.

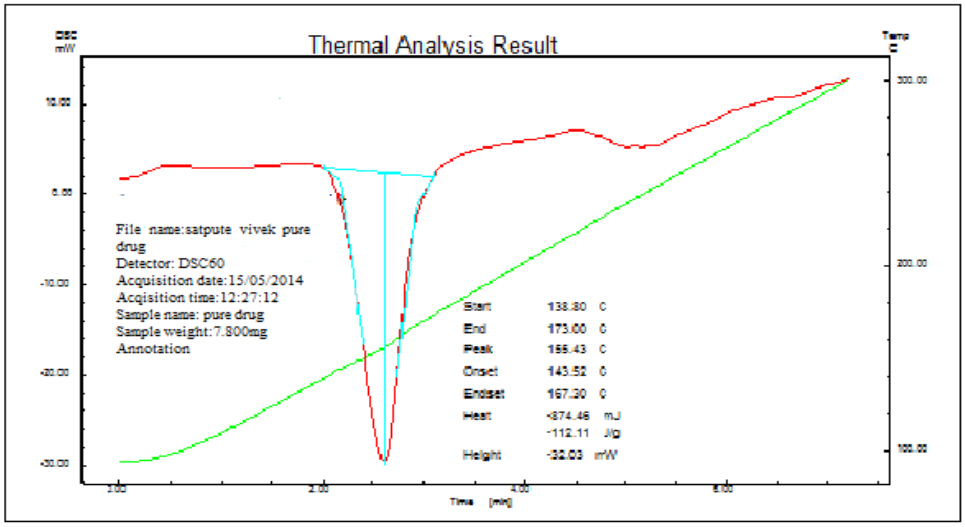


Fig No.6: DSC of Rosuvastatin Pure Drug

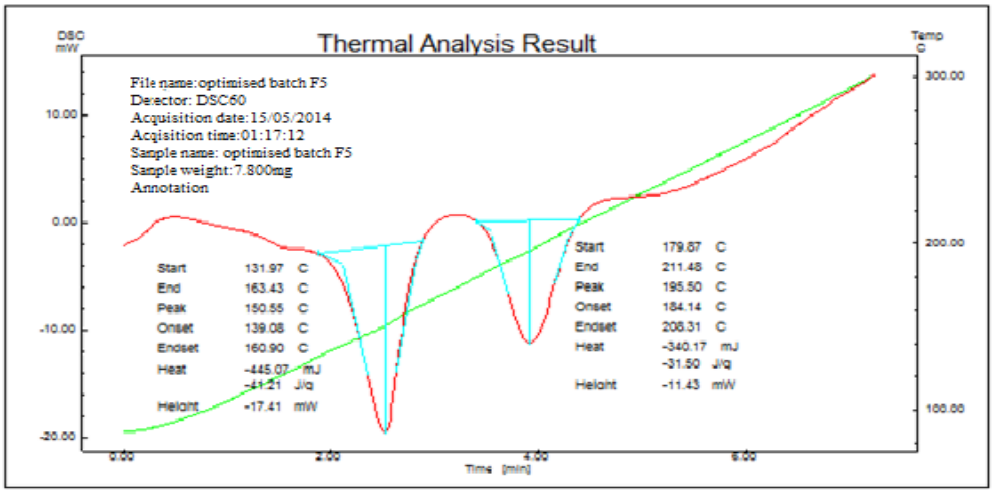


Fig No.7: DSC of Optimized Batch F5

B. Standard Calibration Curve:

1. Scanning of drug:

The pure drug Rosuvastatin was scanned over a range 200-400 nm to determine its λmax. The peak was observed at the 246 nm for Rosuvastatin. The obtained results conforms the identification of Rosuvastatin in Phosphate buffer PH(6.8).

2. Preparation of standard calibration curve of Rosuvastatin in PH6.8 buffer:

The standard calibration curve of Rosuvastatin was obtained by plotting Absorbance V/s. Concentration. Table 8 shows the absorbance values of Rosuvastatin. The standard curve is shown in Figure no8. The standard calibration curve shows the slope of 0.0355 and correlation coefficient of 0.992. The curve was found to be linear in the concentration range of 2-26 πg/ml (Beer's range) at 246 nm.

Table No.2 Calibration curve Phosphate buffer PH(6.8).

Sr. No	Concentration(µg/ml)	Absorbance
0	00	00
1	10	0.144
2	20	0.426
3	30	0.680
4	40	0.906
5	50	1.186

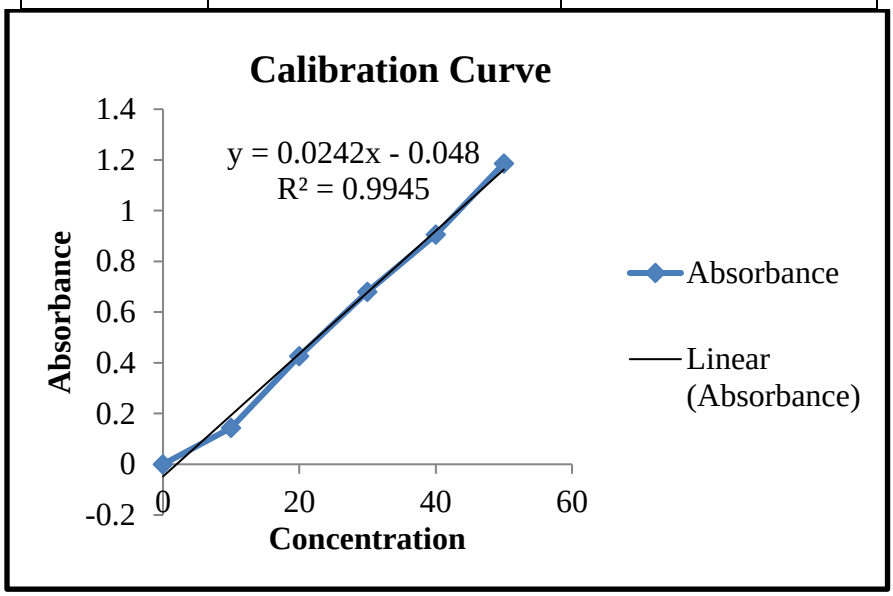


Fig No.8: Calibration curve in Phosphate buffer PH(6.8).

C. Determination of Flow Properties:-

Table 3: Angle of repose, Loose bulk density, Tapped bulk density, Carr's Compressibility Index

Formulation Code	Angle of Repose (θ)	Loose Bulk Density (gm/cm^3)	Tapped Bulk Density (gm/cm^3)	% Compressibility
F1	25.13	0.65	0.70	7.14
F2	28.32	0.61	0.71	14.08
F3	29.53	0.59	0.68	13.23
F4	30.13	0.64	0.69	7.24
F5	25.01	0.56	0.75	25.33
F6	29.63	0.61	0.72	15.27
F7	29.21	0.68	0.74	8.108
F8	29.17	0.63	0.73	13.69
F9	27.12	0.60	0.68	11.76

D. Formulation of Oral Disintegrating Tablets.

Fast dissolving tablets of Rosuvastatin were prepared by direct compression method using rotary tablet machine-10 station with 6mm flat punch. Each tablet contains 10mg atorvastatin and other pharmaceutical ingredients.

E. Evaluation of Formulated Tablets.

Table 4 Evaluation of tablet parameters

Formulation Code	Uniformityof Thickness (mm)	Hardness (kg/cm2)	Friability %	Uniformity of Weight (mg)	Drug Content (%)
F1	2.68±0.04	2.12±0.02	0.4291	95±10	95
F2	2.72±0.06	2.25±0.15	0.3261	97±10	96
F3	2.76±0.02	3.41±0.11	0.3451	96±10	97
F4	2.80±0.07	3.40±0.01	0.3647	102±10	98
F5	2.60±0.05	2.10±0.05	0.2291	100±10	100
F6	2.66±0.03	3.20±0.14	0.3860	98±10	95
F7	2.70±0.08	2.30±0.11	0.5792	99±10	94
F8	2.77±0.07	3.51±0.20	0.3474	100±10	93
F9	2.68±0.03	2.50±0.15	0.3493	97±10	96

F. Wetting Time, Water Absorption Ratio

Table 5: Wetting Time, Water Absorption Ratio

Formulation Code	Wetting Time (sec)	Water Absorption Ratio (%)
F1	56	65.66 ± 0.70
F2	70	60.44 ± 0.66
F3	65	58.28 ± 1.25
F4	72	61.63 ± 0.76
F5	40	80.01 ± 0.33
F6	66	65.26 ± 1.71
F7	50	78.31 ± 1.12
F8	55	70.04 ± 1.23
F9	58	58.30 ± 1.12

***7.* In vitro disintegration time:**

Internal structure of the tablets that is pore size distribution, water penetration into tablets and swelling of disintegration substance are suggested to be the mechanism of disintegration. The results are shown in Table 7.

8. In vitro dispersion time:

In vitro dispersion time gives direct information regarding the nature of superdisintegrating agent used in the formulations. In vitro dispersion time is measured by observing the time taken by the tablets to undergo uniform dispersion in pH 6.8 buffer. Rapid dispersion of the tablets was observed in all the formulations. This indicate that the efficiency of superdisintegrants was in the order crospovidone > crosscarmellose > sodium starch glycolate & the values obtained are recorded in Table no 7.

Table 7: In Vitro Disintegration time, In Vitro Dispersion time

Formulation Code	In vitro Disintegration Time (Sec)	In vitro Dispersion Time (sec.)
F1	30 ± 2.53	40.94 ± 0.76
F2	40 ± 2.15	58.23 ± 1.28
F3	38± 0.75	55.63 ± 1.36
F4	36 ± 1.69	30.01 ± 0.38
F5	28 ± 1.69	25.41 ± 0.35
F6	37± 1.14	76.34 ± 1.59
F7	45 ± 2.18	45.21 ± 1.43
F8	45± 0.65	30.53 ± 1.55
F9	30 ± 1.42	65.74 ± 1.57

11. In vitro dissolution studies:

In vitro release studies were carried out using tablet dissolution test apparatus USP XXIII with paddle speed 75rpm using 900ml phosphate buffer PH(6.8) as a dissolution medium

Formulations F1, F2, F4, F5, F6, F8, F9 showed, more than 90% of drug release within 25 mins. This result exhibit a direct relationship between concentration of superdisintegrants and drug release. Amongst various formulations, tablets of batch **F5** prepared with 20% superdisintegrants i.e, croscarmellose sodium showed better (99%) release of Atorvastatin within 15 mins as shown in Table no 8.

Table 8. In Vitro Dissolution Profile And% of Drug Release of the All Formulations

Time (min)	Percentage (%) Of Drug Release								
	Formulation Code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	28	15	25	30	45	25	30	15	35
10	35	25	45	45	70	45	55	28	40
15	45	35	68	70	99	69	68	56	58
20	68	65	77	88		80	89	76	76
25	80	85	90	99		96	97	92	90

In comparative study of the best formulations of F1, F2 and F3 of showed 80%, 85%, 90% drug release respectively at the end of 25 minutes, graphical representation is shown in Figure 9.

In comparative study of the best formulations of F4, F5 and F6 of showed 99%, 99% and 96% drug release respectively at the end of 25 minutes, graphical representation is shown in Figure 10.In comparative study of the best formulations of F7, F8 and F9 of showed 97%, 92% and 90% drug release respectively at the end of 25 minutes, graphical representation is shown in Figure

Figure 9: Comparative In vitro release profile of Rosuvastatin oral dispersible tablet formulation F1, F2, F3.

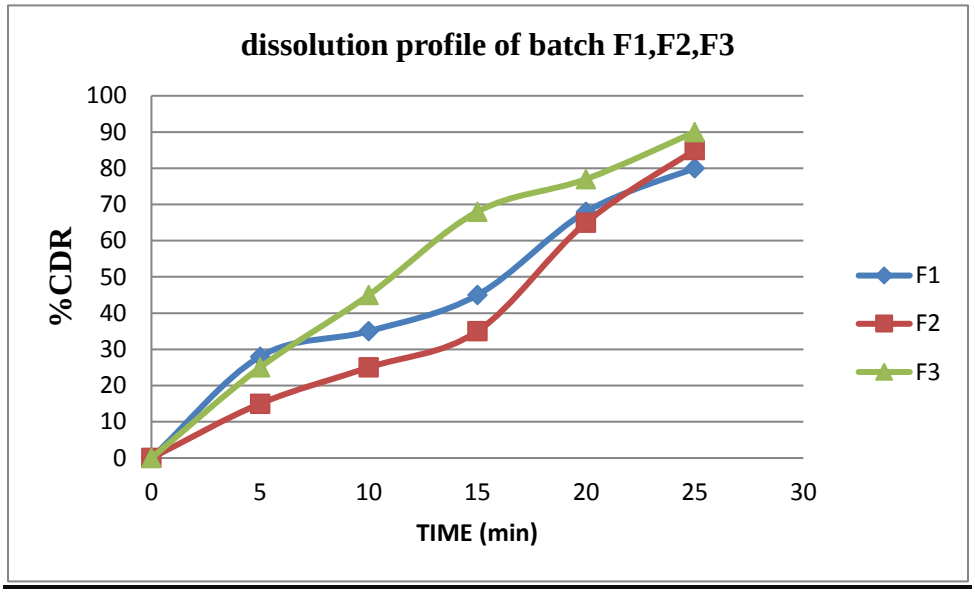


Figure 10: Comparative In vitro release profile of Rosuvastatin calcium oral dispersible tablet formulation F4, F5, F6.

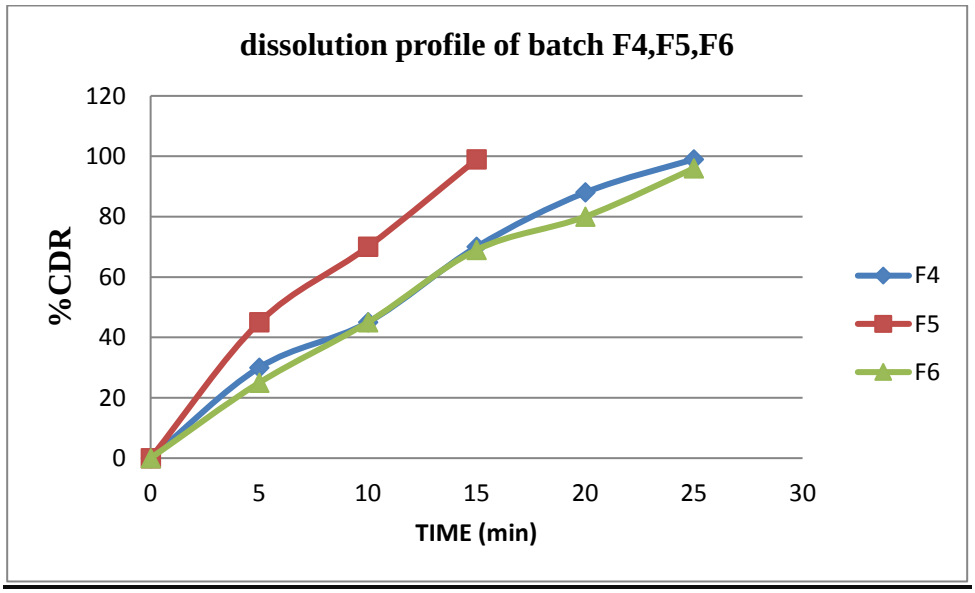
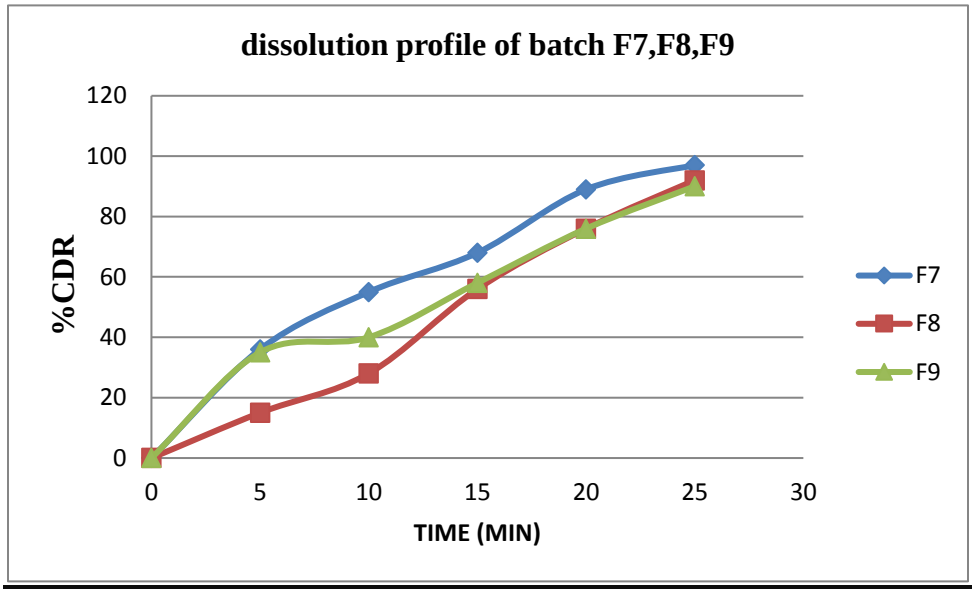


Figure 11: Comparative In vitro release profile of Rosuvastatin oral dispersible tablet formulation F7, F8, F9.



12. Stability Studies

The formulations F5 were selected for stability studies on the basis of their high cumulative % drug release and also results of *in vitro* disintegration time, wetting time, and *in vitro* dispersion studies. The stability studies were carried out at 25$_0$C/60% RH and 40$_0$C/75% RH for all the selected formulations up to 30 days.. The results obtained are tabulated in Table 9 & 10. From these results it was concluded that, formulations F5 are stable and retained their original properties.

Table no.9 Selected formulations for stability studies F5 stored at 25^{0}C/60% RH

Batch code	Tested after time (in days)	Hardness (kg/cm$_2$)	Disintegration time (sec)	Wetting time (sec)	Drug content (n=5)	Friability %
F5	10	2.9± 0.10	25± 1.10	40	96	0.2291
	20	2.9± 0.15	24± 0.1	42	95	0.3542
	30	2.9± 0.05	23	39	94	0.4568

Table no.10 Selected formulations for stability studies F5 stored at 40^0C/75% RH

Batch code	Tested after time (in days)	Hardness (kg/cm2)	Disintegration time (sec)	Wetting time (sec)	Drug content (n=5)	Friability %
F5	10	2.8	26	40	96	0.2896
	20	2.7	25	38	95	0.3658
	30	2.8	23	39	94	0.4685

Conclusion

Rosuvastatin calcium is one of the most widely used antilipidemic agent. Designing a orodispersible formulation for the drug rosuvastatin calcium may enhance the patient compliance, rapid onset of action, increase bioavailability, good stability. Hence, an attempt was made to formulate a orodispersible tablet of Rosuvastatin .it is a hydroxymethylglutaryl- CoA (HMG-CoA) reductase inhibitor (statin) is an antilipidemic agent.

Oral dispersible or fast dissolving tablets are gaining prominence as new drug delivery systems. The novel dosage forms dissolve or disintegrate in the oral cavity within a minute without the need of water or chewing. As the tablets disintegrate in the oral cavity, this could enhance clinical efficacy of drug through pre-gastric absorption from the mouth, pharynx and esophagus, which leads to an increase in bioavailability by avoiding first pass metabolism. In the present work.

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References

1. Vishwkarma DK, Tripathi AK, Yogesh P, Maddheshiya B. Review Article on Mouth Dissolving Film. Journal of Global Pharma Technology. 2011; 3(1): 1-8.
2. Mayuri R Patil, Nayan A Gujarathi, Bhushan R Rane. Formulation And Evaluation Of Mouth Dissolving Tablet: Review Article, Pharma Science Monitor 5(2), Apr-Jun 2014:7-20.
3. M.D. Nehal Siddiqui, Garima Garg and Pramod Kumar Sharma. A Short Review on "A Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents", Advances in Biological Research ,2011,5 (6): 291-303.
4. Waheeda Nasreen, Zahid Sadek Chowdhury, Yeakuty Marzan Jhanker, Mohammad Fahim Kadir. Mouth dissolving tablets- A unique dosage form curtailed for special purpose: a review**,** Journal of Pharmacy and Biological Sciences, Volume 6, Issue 5 *(*May. – Jun. 2013*)*, PP 53-61.
5. Prajapati BG, Ratnakar N. A Review on recent patents on fast dissolving drug delivery system. Int J Pharmtech Res 2009; 1(3): 790-798.
6. A Review On Fast Dissolving Tablets. Available at URL: www.webmedcentral.com
7. Ghosh T, Ghosh A, Devi Prasad. A Review on New Generation Orodispersible Tablets and Its Future Prospective. International Journal of Pharmacy and Pharmaceutical Sciences 2011; 3(1): 1-7.
8. Shukla D, Chakraborty S, Singh S, Mishra B. Mouth Dissolving Tablets I: An Overview of Formulation Technology. Sci Pharm. 2009; 77: 309–26.
9. Velmurugan S and Sundar Vinushitha. Oral Disintegrating Tablets: An Overview.International Journal of Chemical and Pharmaceutical Sciences 2010, Dec., Vol.1 (2):1-10.
10. Giri T, Tripathi D, Majumdar R, Formulation Aspects In The Development Of Orodispersible Tablets: An Overview. International Journal of Pharmacy and Pharmaceutical Sciences 2010; 2: 1-5.
11. Kaur T, Gill B, Kumar S, Gupta G. Mouth Dissolving Tablets: A Novel Approach TomDrug Delivery: International Journal of Current Pharmaceutical Research 2011; 3(1):1-7.

12. Gunjan J. Patel, Rutvij J. Patel, Palak K. Patel, Dr. P.D.Bharadia, V.M Pandya, D. A. Modi.An Overview on Future Trends in Oral Formulation Technologies: Orally Disintegrating Tablet, IJPI's Journal of Pharmaceutics and Cosmetology, Vol 1: 4 (2011):43-55.
13. Karambir Singh, Kamal Saroha, Ruchika Mohan, Amit kumar, Chetna pandit. Orodispersible Tablets: Development, Technologies AndEvaluation: An Overview, A journal of pharmacy research, Volume 8, Issue1. Page 128-147.
14. Manivannan R. Oral Disintegrating Tablets: A Future Compaction. International Journal Of Pharmaceutical Research And Development. 2009; 1(10).
15. Amit gupta,vandan sehgal,sidharth mehan. Hyperlipidemia : an updated review,international journal of biopharmaceutical & toxicological research,volume-1,issue-1,may-2011:81-89.
16. K.Harikumar, S. Abdul Althaf, B. Kishore kumar, M. Ramunaik, CH. Suvarna. A Review on Hyperlipidemic,International Journal Of Novel Trends In Pharmaceutical Sciences,vol-3:59-71.
17. Amit Kumar Nayak and Kaushik Manna. Current developments in orally disintegrating tablet technology. J Pharm Educ Res Vol. 2, Issue No. 1, June 2011:21-34.
18. Rakesh Kumar Bhasin, Nirika Bhasin, Pradip Kumar Ghosh. Advances in Formulation of Orally Disintegrating Dosage Forms: A Review Article, Indo Global Journal of Pharmaceutical Sciences, 2011; 1(4): 328-353.
19. Jaysukh J Hirani, Dhaval A Rathod, Kantilal R Vadalia. Orally Disintegrating Tablets: A Review, Tropical Journal of Pharmaceutical Research, April 2009; 8 (2): 161-172.
20. Manoj ashok wagh *et al*.techniques used in orally disintegrating drug delivery systeme,international journal of drug delivery 2(2010):98-107.